AGGRESSIVE RECURRENCE OF PRIMARY HEPATIC EPITHELIOID HAEMANGIOENDOTHELIOMA (HEHE) AFTER LIVER TRANSPLANTATION

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ABSTRACTS

24th Annual Conference of APASL, March 12–15, 2015, Istanbul, Turkey

Oral Presentations

Topic 1: Acute on Chronic Liver Failure

No: 2076

AKI persistence at 48 h predicts mortality in patients with acute on chronic liver failure provided the peak creatinine is above 1.14 mg dl

Rakhi Maiwall[1], Guresh Kumar[2], Ajeet S. Bhadoria[3], Shiv K. Sarin[1]

Ilbs Hepatology New Delhi-India[1], Ilbs Biostatistics New Delhi-India[2], Ilbs Epidemiology New Delhi-India[3]

Background and aim: Diagnosis and management of renal dysfunction in cirrhotics has changed with advent of AKI criteria. We evaluated the impact of AKI persistence at 48 h on in-hospital mortality in a cohort of ACLF patients (APASL definition).
Methods: Consecutive patients of ACLF (n = 374) were included.
Results: AKI at admission was present in 167 (44.8 %) patients. At 48 h, 77.2 % patients had persistent AKI, 22.8 % had transient AKI and 9 % developed new onset AKI. High MELD (p, OR, 95 % CI) (≥33) (<0.01, 8.3, 3.5–19.4), SIRS (0.03, 2.65, 1.1–6.3) and age (≥42 years) (0.03, 2.4, 1.06–5.69) were significant predictors of AKI persistence. Persistent AKI was associated with higher in-hospital mortality ($P = 0.04$, HR 1.8, 95 % CI 1.4–2.4) as compared to conventional criteria using cut-off serum creatinine ≥1.5 mg/dl (0.04, HR 1.3, 95 % CI 1.01–1.8). A lower cut-off for serum creatinine of 1.14 mg/dl at 48 h had a sensitivity of 100 % and specificity of 75.6 % against the conventional 1.5 mg/dl cut-off. The new cut-off predicted mortality with higher odds (OR 2.4, 95 % CI 1.3–4.8) as compared to the conventional cutoff (OR 2.1, 95 % CI 1.1–4.1). Further, a smaller fold change of 26 % from baseline at 48 h was associated with increased mortality ($P = 0.02$, OR 3.3, 95 % CI 1.1–9.7) in these patients.
Conclusion: AKI persistence at 48 h predicts mortality better than serum creatinine of 1.5 mg/dl in patients with ACLF. Lower threshold as well as smaller increases in serum creatinine should therefore be considered for risk stratifying patients of ACLF for additional pharmacotherapy.

Topic 1: Acute on Chronic Liver Failure

No: 1683

Title does the different etiological profiles affect the outcome of acute on chronic liver failure in pediatric population

Seema Alam[1], Bikrant Bihari Lal[1], Rajeev Khanna[1], Vikrant Sood[1], Dinesh Rawat[1]

Institute of Liver and Biliary Sciences Pediatric Hepatology New Delhi-India[1]

Aim: To compare the prevalence and outcome of acute-on-chronic liver failure (ACLF) in children with chronic liver disease (CLD) due to various etiologies.
Methods: All children between the ages of 3 months to 18 years presenting with chronic liver disease from Dec'2010 to Sept'2014 were included. ACLF was defined as per Survival was observed within 12 weeks of development of ACLF.
Results: Out of the total 403 cases of childhood CLD, 27 (6.7 %) were diagnosed as ACLF with the median age of 9 years (1.5–17 years). Median bilirubin and INR were 17.5 mg/dl and 3.3 respectively. Commonest underlying etiology of CLD were Wilson's disease 14 (52 %), autoimmune hepatitis (AIH) 8 (29.7 %), and cryptogenic 3 (11.1 %). None of the cases with metabolic liver disease (n = 92) or chronic hepatitis B (n = 100) had ACLF. The common acute events were viral insult 6 (22.2 %), drugs 4 (14.8 %). Flare of the underlying condition was seen in 8 Wilson's disease and 6 AIH patients. Median PELD/MELD, CLIF-SOFA and APACHE-II scores were 27 (12–54), 9 (8–18) and 9 (0–30). of the 27 children, 10 (37 %) expired within 12 weeks and 2 were transplanted. Mortality was 57 % among Wilson's disease and 12.5 % in AIH (P = NS).
Conclusion: ACLF is common in children with Wilson's disease and AIH and the mortality is higher in those with Wilson's disease.

Topic 1: Acute on Chronic Liver Failure

No: 1008

Establishment and validation of alph Q score to predict mortality risk in patients with acute on chronic hepatitis B liver failure

Ming-hua Zheng[1], Sheng-jie Wu[2], Hua-dong Yan[3], Zai-xing Zheng[2], Ke-qing Shi[1], Fa-ling Wu[1], Yao-yao Xie[4], Yu-chen Fan[5], Bo-zhi Ye[2], Wei-jian Huang[2], Yong-ping Chen[1]

The First Affiliated Hospital of Wenzhou Medical University Department of Infection and Liver Diseases, Liver Research Center Wenzhou-China[1], The First Affiliated Hospital of Wenzhou Medical University Department of Cardiovascular Medicine, The Heart Center Wenzhou-China[2], Ningbo No. 2 Hospital Department of Infectious Diseases Ningbo-China[3], The First Affiliated Hospital of Wenzhou Medical University Department of Clinical Laboratory Wenzhou-China[4], Qilu Hospital of Shandong University Department of Hepatology Jinan-China[5]

Aim: There are no strong and powerful models in predicting the outcome of acute-on-chronic hepatitis B liver failure (ACHBLF). Here, we aimed to establish and validate a new prognostic score, named ALPH-Q that integrated electrocardiography parameters, to predict short-term mortality of patients with ACHBLF.
Method: 214 patients were included in this study. APLH-Q score was constructed by cox's proportional hazards regression analysis and was validated in an independent cohort. The area under the receiver operating characteristic curve was used to compare the performance of different models, including APLH-Q, Child-Pugh score (CPS), model of end-stage liver disease (MELD) and a previously reported logistic regression model (LRM).
Result: APLH-Q score was constructed with five independent risk factors, including age (HR = 1.034, 95 % CI 1.007–1.061), liver cirrhosis (HR = 2.753, 95 % CI 1.366–5.548), prothrombin time (HR = 1.031, 95 % CI 1.002–1.062), hepatic encephalopathy (HR = 2.703, 95 % CI 1.630–4.480) and QTc (HR = 1.008, 95 % CI 1.001–1.016). The performance of ALPH-Q score was significantly better than that of MELD and CPS in both training (0.896 vs. 0.712, 0.896 vs. 0.738, respectively, both $P < 0.05$) and validation cohorts (0.837 vs. 0.689, 0.837 vs. 0.585, respectively, both $P < 0.05$). Compared with LRM, APLH-Q also showed a better performance (0.896 vs. 0.825, 0.837 vs. 0.818, respectively).
Conclusion: We have developed a novel APLH-Q score with greater performance than CPS, MELD and LRM for predicting short-term mortality of patients with ACHBLF.

Topic 1: Acute on Chronic Liver Failure

No: 1252

Acute hepatitis A or E can trigger the development of acute on chronic liver failure (AOCLF) in sapporo Japan

J-h. Kang[1], T. Matsui[1], A. Tomonari[1], K. Nagai[1], K. Tanaka[1], K. Tsuji[1], Y. Kodama[1], Y. Sakurai[1], H. Maguchi[1], K. Takahashi[2], M. Arai[2], S. Mishiro[2]

Teine Keijinkai Hospital Center For Gastroenterology Sapporo-Japan[1], Toshiba General Hospital Department of Medical Sciences Tokyo-Japan[2]

Background and aims: Even in non-endemic areas including Japan, autochthonous infection of hepatitis A virus (AHV) or E (HEV) causes sporadic disease, however, their clinical impact for AoCLF is obscure. The aim of this study is to clarify whether acute HAV or HEV could trigger for AoCLF in industrialized countries.
Methods: The patients with acute hepatitis (AH) A, B or E diagnosed from 1998 until 2013 in single institute in Sapporo were enrolled. The incidences of acute liver failure (ALF), AoCLF and underlying liver disease were evaluated. Definition of ALF was prothrombin time (PT) INR $\geqq$1.5, and that of alcoholic liver disease (ALD) was ethanol intake $\geqq$80 g/day over 5 years. The APASL criteria for AoCLF were adopted.
Results: A total of 126 patients, 27 with AHA (16 male, median age 44 years), 54 with AHB (37 male, 33 years) and 45 with AHE (35 male, 51 years) were assigned. They were older in the order of HEV, HAV and HBV (< 0.03). Underlying liver diseases including ALD, fatty liver, HBV carrier etc. existed in 10 (37.0 %) patients in AHA, 5 (9.3 %) in AHB and 16 (35.6 %) in AHE, respectively. Ten patients in AHA, 21 in AHB and 20 in AHE developed ALF, and, among them, 5 AHA (18.5 %), no AHB, 7 AHE (15.6 %) patients presented AoCLF, respectively (HAV or HEV vs. HBV, $P < 0.003$). Body weight in AHA and alcohol intake in AHE was related with AcCLF ($P = 0.0904$, 0.0009), respectively. Four AHB and 2 AHE patients were deceased or underwent liver transplantation.
Conclusions: Acute HAV or HEV.

Topic 1: Acute on Chronic Liver Failure

No: 1414

An analysis of risk factors of secondary infection of patients with HBV related acute on chronic liver failure and its impact on prognosis

Ke Ma[1], Pei Li[2], Meifang Han[2], Tao Chen[2], Daofeng Yang[2], Jiaquan Huang[2], Yuancheng Huang[2], Xiping Zhao[2], Jianxin Song[2], Junying Qi[2], Qin Ning[2]

Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institute of Infectious Disease Wuhan-China[1], Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institution of Infectious Diseases Wuhan-China[2]

Aims: The aim of this study is to evaluate its impact on clinical outcome and identify the potential risk factors for its development in these patients.
Methods: In this retrospective and case controlled analysis, ninety eight patients with HBV-ACLF were enrolled and divided into two groups (infected 48 and non-infected n = 50). Clinical features and biochemical markers of these patients were collected. Univariate analysis was performed by Chi square test using SPSS19.0 software.
Results: Sites infections were occurred: abdominal infections (including spontaneous bacterial peritonitis) 13 cases (27.08 %), respiratory infections 10 cases (20.83 %), blood-borne infection 3 cases (6.25 %), biliary tract infection 2 cases (4.17 %), urinary tract infection 1 case (2.08 %), skin infections 1 case (2.08 %), location unknown 8 cases (16.67 %), more than two and two parts of the infection 10 cases (20.8 %). Patients survival in infected group were 25 %, significantly lower than that in non-infected group (96 %, $P < 0.001$). Univariate analyses indicated that risk factors for secondary infection include age > 45 years ($P = 0.046$), ascites ($P = 0.003$), hepatic encephalopathy ($P < 0.001$), hepatorenal syndrome ($P < 0.001$), serum total bilirubin > 400 μmol/L ($P = 0.029$), serum alanine aminotransferase > 410 U/L ($P = 0.029$), serum total protein < 62 ($P = 0.027$), serum globulin < 25 g/L ($P = 0.01$), platelet count < 100 × 109/L ($P = 0.026$).

Conclusion: Secondary infection including SBP and pneumonia frequently occurred in patients with HBV-ACLF and significantly increased mortality. Early identification and intervention of the risk factors may improve the survival.

Topic 1: Acute on Chronic Liver Failure

No: 1732

Predictors of outcomes in patients of acute on chronic liver failure presenting with secondary hemophagocytic lymphohistiocytosis undergoing plasmapheresis

Cyriac Abby Philips[1], Shiv Kumar Sarin[1], Meenu Bajpai[2], Guresh Kumar[3], Kapil Dev Jamwal[4]

Institute of Liver and Biliary Sciences Hepatology New Delhi-India[1], Institute of Liver and Biliary Sciences Transfusion Medicine New Delhi-India[2], Institute of Liver and Biliary Sciences Research New Delhi-India[3], Institute of Liver and Biliary Sciences Professor New Delhi-India[4]

Aim: Acute on chronic liver failure (ACLF) can present with secondary hemophagocytosis (HLH) with very high mortality. No guidelines exist for management of this entity. Predictors of mortality on plasmapheresis (PF) in ACLF-HLH are unknown.
Methods: From Feb 2012 to Nov 2014, 38 patients [M-25, F-13;median age 53.5 years (19 to 72)] of ACLF-HLH underwent total of 403 (daily, average 10.6) sessions of PF (Autopheresis-CTM, Fenwal, Germany). End point of study was survival at 6 wks.
Results: 16 patients died (42.1 %,M-10/25, F-6/13). Commonest acute insult (AI) was complementary and alternative drugs (DILI, n = 10/38) and reactivation of hepatitis B (HBVR, n = 10/38); chronic disease (CI) was HBV (n = 14) and NAFLD (n = 11). AI and CI significantly predicted mortality at 6 wks [DILI50 %, p value 0.027; HBV 52.6 %, p value 0.037]. Baseline variables were adjusted for post therapy using ANCOVA. Age [> 60, p value 0.023], baseline grade 4 HE [75 %, n = 12/16; p value < 0.001], absence of HE improvement predicted mortality [TABLE 1]. Post therapy hypoalbuminemia [mean;survived vs dead (2.7 vs 2.1 g/dL), p value < 0.001], ferritin [2074.55 vs 9225.81 ng/dL, p value < 0.001], total bilirubin [mean; 13.2 vs 26 mg/dL, p value 0.004], PT (not INR) [22.4 vs 28.8 s, p value 0.002], hypernatremia, hypophosphatemia, hypocalcemia [135.3 vs 150.7 mmol/L; p value < 0.001, 3.0 vs 2.4 mg/dL; p value 0.016; 7.9 vs 6.9 mg/dL; p value < 0.001] predicted mortality. CTP, MELD, SOFA score after PF [11 vs 13; p value < 0.001, 24 vs 35; p value < 0.001,12 vs 17; p value 0.005] predicted mortality. Higher BMI led to better survival [35.6 vs 26.3; p value < 0.001]. Post mortem, bilirubinostasis on liver biopsy significantly correlated with mortality (p value < 0.001) but presence of emperipolesis (bone marrow study) did not affect outcomes.
Conclusion: PF for ACLF-HLH even though promising, is affected by multiple factors that predict failure of treatment. Higher BMI, lower age and level of sodium, high normal calcium, phosphorous and significant reduction in HE and bilirubin predict better outcomes. Larger studies need to be done to implement on treatment failure scores for cost effectiveness and early prognostication.

Topic 1: Acute on Chronic Liver Failure

No: 1501

Hepatocyte death associated biomarkers promising prognostic indicators for hepatitis B virus related acute on chronic liver failure

Zhujun Cao[1], Fengdi Li[1], Yuhan Liu[1], Kehui Liu[1], Weiliang Tang[1], Lanyi Lin[1], Hong Yu[1], Qing Xie[1], Hui Wang[1]

Ruijin Hospital, Shanghai Jiaotong University School of Medicine Department of Infectious Diseases Shanghai-China[1]

Aim: Currently,survival data from Asia on Acute-on-chronic liver failure (ACLF) patients induced by reactivation of hepatitis B virus (HBV-ACLF) are urgently needed. This study aims to identify potential cell death biomarkers that could be of prognostic value in HBV-ACLF.
Method: 54 hospitalized patients with HBV-ACLF diagnosed as per Asia Pacific Association for study of Liver (APASL) guidelines were prospectively enrolled between February 2013 and August 2014. 40 chronic hepatitis B (CHB) patients and 40 healthy volunteers (HC) were studied as controls. All HBV-ACLF patients were followed up 3 months to identify the prognoses and subsequently divided into two groups, survivors (SR) and non-survivors (NSR). Three novel cell death biomarkers, M30-antigen (hepatocyte apoptosis marker), M65-antigen (hepatocyte total death marker) and HMGB1 (total cell death marker) were investigated.
Results: Demographic and clinical characteristics of study subjects were listed in Table 1. In our 54 HBV-ACLF cohort,sera levels of three cell death biomarkers all markedly elevated relative to controls ($P < 0.001$ for all). Median admission M30 and M65-antigen levels in NSR were significantly higher than SR[M30-antigen: 1,175.18 (756.57–3,224.94) U/L vs 491.39 (264.23–657.17)U/L, $P < 0.001$; M65-antigen,11,373.29 (4,681.56–15,000.00) U/L vs 2,744.84 (1,835.21–4,861.98) U/L, $P < 0.001$]. However,no significant difference were found in admission sera HMGB1 levels between SR and NSR ($P = 0.69$). By the analyses of receiver operating characteristic (ROC) curve, we compared M30-antigen and M65-antigen with the currently used prognosis scoring systems, MELD, MELD-NA or CTP. Better prognostic values of M30-antigen (area under the curve,AUC,0.86) and M65-antigen (AUC,0.83) in HBV-ACLF than MELD (AUC,0.81), MELD-NA (AUC,0.78) and CTP(AUC,0.74) were demonstrated.More importantly, the advantages of M30 and M65-antigen extended into the non-cirrhotic subgroup of HBV-ACLF, (AUC,M30-antigen: 0.92; M65-antigen: 0.90; MELD: 0.77; MELD-NA: 0.72; CTP: 0.74). In addition, we identified an optimal cut-off value of M30-antigen at ≥750.47U/L best predicted poor outcomes of HBV-ACLF patients with the highest Youden index of 0.65($P < 0.0001$).
Conclusion: Out of the three biomarkers,we identify M30 and M65-antigen as promising prognostic biomarkers for HBV-ACLF, especially in non-cirrhotic HBV-ACLF. Underlying mechanisms of hepatocyte death in the pathogenesis of HBV-ACLF are still under investigation.

Topic 1: Acute on Chronic Liver Failure

No: 1086

Safety and efficacy of telbivudine in patients with hepatitis B related acute on chronic liver failure initial experience from a tertiary centre in Bangladesh

Mamun Al Mahtab[1], Sheikh Mohammad Fazle Akbar[2], Salimur Rahman[1]

Bangabandhu Sheikh Mujib Medical University Hepatology Dhaka-Bangladesh[1], Toshiba General Hospital Medical Sciences Tokyo-Japan[2]

Aim: Although telbivudine is an effective and renal-friendly antiviral little is known about it's role in ACLF-B. The aim of this study

was to assess the safety and efficacy of telbivudine in treatment naive ACLF-B.
Methods: 12 ACLF-B patients, 20–62 years, 3 females, 9 males recruited. 4 had CHB and 8 HBV-cirrhosis. HBV flair was acute insult in all. Presented first time with ACLF. None had HCC. HBV DNA between 3.2 × 104 and 1.1 × 107copies/ml. 9 HBeAg(-ve) and 3 HBeAg(+ve). 7 ascites only, 4 ascites plus encephalopathy and 1 encephalopathy only. Bilirubin 6–35 mg/dl, ALT 460-5630U/L, albumin 1.8–3.0gm/L and INR > 1.9. All received telbivudine 600 mg orally daily. Bilirubin,albumin,creatinine,INR and blood counts monitored weekly for 2 weeks, at 1 month and monthly for 2 months. HBV DNA monitored at 2 week. At 3 month, HBV DNA and HBeAg rechecked. Treatment started immediately at presentation pending HBV DNA, aiming to discontinue if HBV DNA undetectable.
Results: At end of 3 months, 10 patients were alive. 1 had complete normalization of LFT, improvement in 5 and steady in 4. HBV DNA undetectable in 3 after 2 weeks and in 5 after 3 months. None had HBeAg sero-conversion.
Conclusion: The study demonstrates safety of telbivudine in ACLF-B and better survival. It's anti-viral efficacy is also evident. Further study with large pool of patients is recommended.

Topic 1: Acute on Chronic Liver Failure

No: 1419

Hsa MIR 181c was significantly down regulated in PBMC of acute on chronic liver failure patients caused by hepatitis B virus

Dong Xi[1], Faxi Wang[2], Ming Wang[2], Wen Ding[2], Wenwen Ma[2], Qin Ning[2]

Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institute of Infectious Disease Wuhan-China[1], Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institution of Infectious Diseases Wuhan-China[2]

Aim: A lot of research shows hepatocyte apoptosis induced by TNF-α/TNFR1 or Fas/FasL and high expression of IFN-γ are important pathway for the incidence of fulminant viral hepatitis. Accumulating evidence suggests that a limited number of microRNAs (miRNAs) are involved in severe exacerbation of hepatitis B. The relationship between circulating miRNAs and acute on chronic liver failure (ACLF) need to be further investigated.
Methods: miRNA expression profile by miRNA microarray analysis was performed on pooled Peripheral Blood Mononuclear Cell (PBMC) obtained from identified groups of patients with chronic hepatitis B (CHB) and HBV associated ACLF, respectively. Selected unnormal expressed miRNAs were verified in more clinical samples by quantitative real-time PCR (qRT-PCR). Targets were then subjected to a prediction by many bioinformatics target prediction software.
Results: Our results showed 7 kinds of miRNAs were down-regulated and 9 kinds of miRNAs were up-regulated in the PBMC of ACLF patients by the microarray. Expression of Hsa-miRNA-181c was significantly down-regulated in these patients by qRT-PCR and severe hepatitis B related TNF-α, FasL and IFN-γ were its potential targets.
Conclusion: Hsa-miRNA-181c might be a new diagnostic marker for ACLF patients. Acknowledgements This work was supported by the National High Technology Program (2012AA020801), National Twelfth 5 Years Project in Science and Technology (2013ZX10002-003) and the Ministry of Education Innovative Team Development Plan (IRT1131).

Topic 1: Acute on Chronic Liver Failure

No: 2025

The usefulness of simplified CLIF SOFA and hyponatremia for predicting mortality in patients with acute decompensation and chronic liver disease

Young Kul Jung[1], Tae Yeob Kim[2], Do Seon Song[3], Dong Joon Kim[4], Hee Yeon Kim[5], Dong Hyun Sinn[6], Eileen L Yoon[7], Joo Hyun Sohn[2], Chang Wook Kim[8], Ki Tae Suk[4], Jin Mo Yang[8], Heon Ju Lee[9]

Korea University Ansan Hospital Internal Medicine Ansan-Republic of Korea[1], Hanyang University Guri Hospital Internal Medicine Guri-Republic of Korea[2], The Catholic University College of Korea Internal Medicine Seoul-Republic of Korea[3], Hallym University, Chunchon Sacred Heart Hospital Internal Medicine Gangwon-do-Republic of Korea[4], College of Medicine, The Catholic University College of Korea Internal Medicine Seoul-Republic of Korea[5], Samsung Medical Center Internal Medicine Seoul-Republic of Korea[6], Inje University Sanggye Paik Hospital Internal Medicine Seoul-Republic of Korea[7], The Catholic University College of Korea Internal Medicine Seoul-Republic of Korea[8], Yeungnam University College of Medicine Internal Medicine Daegu-Republic of Korea[9]

Background: Recently Chronic Liver Failure-Sequential Organ Failure Assessment (CLIF-SOFA) scoring system showed the ability to better predict short-term survival in decompensated cirrhosis than the MELD score. Also, serum sodium concentrations (sNa) have been suggested as a useful predictor of mortality in patient with chronic liver failure. So, we want to evaluate whether sNa affects the prognosis of acute on chronic liver failure (ACLF) patients.
Methods: 1459 hospitalized patients with chronic liver disease (CLD) and acute decompensation (AD) were enrolled from January 2013 to December 2013 from 21 academic hospitals in Korea. The Kaplan–Meier method with log-rank test was used to calculate short-term mortality (28-day and 90-day).
Result: The 28-day and 90-day mortality rates were 35.6 % and 58.9 % in the patients with ACLF and 1.3 % and 3.7 % in the patients without ACLF, respectively ($P < 0.001$). The AUROCs of CLIF-SOFA score in the patients were 0.863 and 0.851 in predicting 28-day and 90-day mortality. Considering statistically discriminatory power, the cumulative survival rate has significantly difference by CLIF-SOFA score 7. [90.3 % vs 58.2 %: <7 vs. ≥7, ($P < 0.001$),respectively]. In the low and high CLIF-SOFA score, the presence of hyponatremia (Na < 130 mEq/L) showed poor prognosis than the absence of hyponatremia. [8.8 % vs 18.5 % at <7, 37.4 % vs. 51.8 % at ≥7, ($P < 0.001$),respectively]. In other hands, the presence of ascites influence the prognosis of low CLIF-SOFA score group. [5.2 % vs 12.7 % at <7 ($P < 0.001$),35.9 % vs. 44.5 % at ≥ 7, ($P = 0.155$)].
Conclusion: CLIF-SOFA score is good predictor of short-term mortality in ACLF patients. and also, hyponatremia could give more accurate information adding to CLIF-SOFA score than ascites.

Topic 1: Acute on Chronic Liver Failure

No: 1948

Defining a 'golden window' period and relevance of systemic inflammatory response syndrome (SIRS) in acute on chronic liver failure (ACLF) a tool for intervention and improved survival

Ashok Choudhury[1], Shiv Kumar Sarin[1], K. N. Chndan Kumar [2], C. Vashishtha[1], Z. Abbas[3], D. Amarpurkar[4], A. S. Butt[5], A. Chan[6], Y. K. Chawla[7], A. K. Dokmeci[8], H. Garg[9], H. Ghazinyan[10], S. S. Hamid[11], Ji-dong Jia[12], M. Kumar[1], Gh Lee[13], La Lesmana[14], M. Mahtab[15], Rakhi Maiwal[1], R. Moreau[16], Q. Ning[17], V. Pamecha[18], Da Payawal[19], S. Rahman[15], D. Samuel[20], S. Shah[21], G. Shiha[22], Bc Sharma[23], S. S. Tan[24], Mf Yuen[25], O. Yokosuka[26], H. C. Devarbhabi[27], C. E. Eapen[28], Apasl Aclf Working Party[29]

Institute of Liver and Biliary Sciences Hepatology New Delhi-India[1], Narayana Health City Gastroenterogy Banglore-India[2], Sindh Institute of Urology and Transplantation Hepatogastroenterology Karachi-Pakistan[3], Bombay Hospital and Medical Research Gastroenterology and Hepatology Mumbai-India[4], Aga Khan University Hospital Department of Medicine Karachi-Pakistan[5], The University of Hong Kong Hepatobiliary and Pancreatic Surgery, and Liver Transplantation Hong Kong-China[6], Post Graduate Institute of Medical Education and Research Hepatology Chandigarh-India[7], Ankara University School of Medicine Gastroenetrology Ankara-Turkey[8], Apollo Hospital Gastroneterology,hepatology New Delhi-India[9], Nork Clinical Hospital of Infectious Diseases Hepatology Yerevan-Armenia[10], Aga Khan University Hospital Medicine Karachi-Pakistan[11], Beijing Friendship Hospital, Capital Medical University Liver Research Center Beijing-China[12], National University Health System Department of Gastroenterology and Hepatology Singapore-Singapore[13], University of Indonesia Division of Hepatology Jakarta-Indonesia[14], Bangabandhu Sheikh Mujib Medical University Department of Hepatology Dhaka-Bangladesh[15], Labex Inflamex, Université Paris Diderot Paris 7 Inserm, U1149, Centre De Recherche Sur L Paris-France[16], Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department of Infectious Disease Wuhan-China[17], Institute of Liver and Biliary Sciences Department Hepatobiliary Surgery and Liver Transplant New Delhi-India[18], Cardinal Santos Medical Center Department of Hepatology Manila-Philippines[19], Hôpital Paul Brousse, Inserm Centre Hépatobiliarie Villejuif-France[20], Global Hospitals Department of Gastroenterology and Hepatology Mumbai-India[21], Egyptian Liver Research Institute and Hospital Department of Internal Medicine Cairo-Egypt[22], Gb Pant Hospital Gastroenterology New Delhi-India[23], Selayang Hospital Department of Hepatology Kepong-Malaysia[24], The University of Hong Kong Hepatobiliary and Pancreatic Surgery, and Liver Transplantation, Department of Surgery and Department of Medicine Hong Kong-China[25], Graduate School of Medicine, Chiba University Department of Gastroenterology and Nephrology Chiba-Japan[26], St Johns Medical College Gastroenterology Banglore-India[27], Christian Medical College Gastroenterology and Hepatology Vellore-India[28], Institute of Liver and Biliary Sciences Aarc New Delhi-India[29]

Background and aims: Systemic Inflammatory Response Syndrome (SIRS) is an early marker of sepsis and ongoing inflammation. Sepsis is the most common cause of mortality. The aim is to study the natural course of SIRS and sepsis in a hospitalized ACLF cohort without SIRS, sepsis at baseline and to define a window period for possible intervention.
Methods: Consecutive hospitalized patient of ACLF were prospectively evaluated for the development of SIRS/sepsis and associated complications till 90 days follow up, liver transplant or death. All patients received standard medical care, sepsis screening was done for initial 15 days, followed by 'on suspicion' screening.
Results: 201 patients with median age 46 yr (IQR = 38–45), male (91 %) and majority of ethanol (47 %) etiology. New onset SIRS, sepsis and septic shock at the end of first week were (77.6, 10 and 1 %) respectively. The time to development of SIRS, sepsis were 6.18 ± 1.7 and 7 days (IQR 4–7) respectively. Rate of development or resolution of SIRS 11–12 % per day. Development of SIRS associated with procalcitonin positivity ($P = 0.05$). Increasing no of organ failure (0, 3, 4) associated with higher incidence of SIRS (24, 87.5 and 100 % respectively, $P < 0.05$). SIRS at D7 leads to a median survival (12 vs. 29 weeks), first week mortality (23 % vs. none, $P < 0.005$) and 90 days mortality of (51.9 % vs. 37.8 %, $P = 0.12$).
Conclusion: SIRS and its dynamicity is an important predictor of early sepsis, organ failure and survival in ACLF. Prompt use of prophylactic antibiotics with onset SIRS and rigorous septic screen during in the Golden window could improve outcome.

Topic 2: Alcoholic Liver Disease

No: 1606

Effect of new lonal medicine in patient with alcoholic fatty liver disease

Sarnai Tsagaankuu[1], Badamsuren Dorjgotow[2], Badamjaw Sewjid[1], Ariunaa Zundui[3]

Mongolian National University of Medical Science, Professor's Department of Hepatology, Faculty of Internal Medicine, School of Medical Science Ulaanbaatar-Mongolia[1], 3th State Hospital Named By Shastin.p.n Department of Gastroenterology, Ulaanbaatar-Mongolia[2], Traditional Medical Science Technology and Production Corporation Traditional Medical Science Technology and Production Corporation Ulaanbaatar-Mongolia[3]

Introduction: According to the studies of World Health Organization and other researchers it is set that 12.8–51.6 percent of Mongolia's population overuse alcohol; 90–100 percent of alcohol over users suffers from fatty liver disease and 15–25 percent cases turn into liver cirrhosis in next 10 years. A brand new medicine called Lonal which was extracted from widely used in traditional medicine fruit Lonicera Altaica Pall with its liver protection effect (hepatoprotective effect) studied by chemical, general pharmacology and special pharmacology.
Aim: To study the effect of new lonal medicine patient with alcoholic fatty liver disease.
Objectives:

1. To define a favorable condition of the new Lonal medicine
2. To study effect of Lonal medicine on hepatic cytolysis
3. To study the effect of Lonal medicine on cholest http://www.dekonabstract.com/files/images/ico/forwd_16.pngasis
4. To study the effect of Lonal medicine on lipid metabolism exchange

Methodology: The research was conducted in accordance with WHO's Good Clinical Practice, international papers and issued by the Ministry of Mongolia "Guidelines for clinical trial". Based on permission given by Biomedical Ethical Community of the Ministry of Health 10 healthy people were involved in stage I and 40 people with approved diagnosis patient with alcoholic fatty liver disease in the stage II respectively. An open method was chosen for the research.
Conclusion:

1. It is not observed that any side effect and inconvenience in participants of stage I, II.
2. Lonal medicine decreases hepatic cytolysis due to content of large amount of flavonoids.
3. Lonal medicine showed an ability to conjugate bile acid.
4. Taking Lonal medicine during 21 days influences on the

Topic 2: Alcoholic Liver Disease

No: 1440

T regulatory cells prevent alcohol induced hepatic steatosis and proinflammatory response in mice

Hongwu Wang[1], Ting Wu[2], Yaqi Wang[2], Lan Li[2], Junying Qi[2], Xiaojing Wang[2], Weiming Yan[2], Xiaoping Luo[2], Qin Ning[2]

Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institute of Infectious Disease Wuhan-China[1], Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institution of Infectious Diseases Wuhan-China[2]

Background: Alcoholic fatty liver (AFL) is the most common and earliest response to chronic ethanol consumption,which renders the liver more susceptible to the development of advanced alcoholic liver diseases (ALD). However, whether Tregs play a role in the pathogenesis of AFL has not been studied.
Methods: The Leiber-DeCarli diet containing alcohol were fed to C57BL/6 mice for 6 weeks and the alcohol-feeding mice were injected with CD4 + CD25 + T cells or control CD4 + CD25- T cells intravenously from the fourth week, twice at 1-week intervals. Functional effects of Tregs on lipid metabolism, oxidative stress, and macrophage activation were examined.
Results: Chronic alcoholic feeding induced liver steatosis and increased serum alanine aminotransferase accompanied with the depletion of hepatic Tregs, but these liver damages were blunted by Treg adaptive transfer. The enhanced expression of nuclear Sterol regulatory element-binding protein 1c (SREBP1c), and its downsteam genes, were induced in alcohol-fed mice but not in Treg-transferred mice,in which hepatic oxidative stresses were also ameliorated.Moreover, Tregs increased the level of phosphorylatied adenosine monophosphate-activated protein kinase (AMPK), peroxisome proliferator-activated receptor (PPAR) α in nucleus, and its downstream genes for fatty acid metabolism, which were inhibited by alcohol-feeding. Furthermore,Tregs inhibited MCP-1 and TNF-α overproduction and macrophage activation in the liver. In vitro, Treg supress the expression of MCP-1, TNFα and CD14 on monocytes/macrophages undergone LPS and alcohol co-treatment.These suppression was markedly abrogated by neutralizing anti-IL-10 mAbs.
Conclusions: Our results indicate that Tregs suppress the development of (AFL), in part through modulating lipid metabolism, oxidative stress and macrophage pro-inflammatory response.

Topic 2: Alcoholic Liver Disease

No: 1761

Regular coffee intake improves liver enzyme levels and liver histology in patients with chronic alcohol consumption fatty liver and nash. Report of 259 cases

Ayşegül Gizem Söylemez[1], Ezgi Gurtay[1], Ugur Bozkurt[1], Berkan Colakoglu[1], Can Berk Alpayadin[1], Yusuf Yilmaz[2], Bulent Degertekin[1], Eser Vardareli[1], Onder Ergonul[3], Nurdan Tozun[1]

Gastroenterology and Hepatology University of Acibadem Istanbul-Turkey[1], Gastroenterolgy and Hepatology University of Marmara Istanbul-Turkey[2], Infection Diseases University of Koc Istanbul-Turkey[3]

Aim: Coffee has been associated with decreased liver inflammation, reduced steatosis and lower incidence of hepatocellular carcinoma. The purpose of this study was to determine the effect of chronic coffee consumption (>5 years) and type of coffee (granulated, decaffeinated and Turkish coffee) on liver histology and liver function tests (LFT's) in patients with nonalcoholic steatohepatitis (NASH), fatty liver and patients who has regular alcohol intake.
Method: n = 158 healthy individuals and n = 101 patients with histologically proven NASH were enrolled. Daily amount of coffee intake, amount of alcohol use, type of coffee, and HOMA-IR score were calculated for all patients. The degree of steatosis and fibrosis was analyzed by both liver ultrasound and fibroscan in all patients and additionally by liver biopsy in patients with NASH.
Conclusion: Patients who had regular coffee intake (n = 132) had lower liver enzyme levels compared to those who did not drink any coffee (n = 127) [ALT: 37.3 U/Lvs. 56.4 U/L($P = 0.010$), AST: 28.9 U/L vs. 37.6 U/L ($P = 0.032$)]. This difference was more significant for patients who had excessive amount of coffee intake (daily and > 5 years) [ALT: 31.1U/L vs. 56.4U/L ($P = 0.004$), AST: 24.3U/L vs. 37.6U/L ($P = 0.030$). Multiple regression analysis revealed that the positive protective effect of coffee on liver enzyme levels and liver histology was strongest in patients who had daily alcohol intake [ALT, OR = 0.74;95 % CI, (0.46-0.88), $P = 0.040$], [steatosis, OR = 0.80;95 % CI (0.53-0.98), $P = 0.042$], and [fibrosis, OR = 0.62;95 % CI, (0.38-0.96),$P = 0.030$]. Coffee seems to have a positive protective effect on liver histology and liver enzyme levels, and this effect is more significant in patients who have daily alcohol consumption. Coffee may play a protective role for alcoholic liver diseases.

Topic 3: Autoimmune Liver Diseases

No: 1005

Prednisolone combined with ursodeoxycholic acid and azathioprine in pure primary biliary cirrhosis with high levels of immunoglobulin G and transaminases efficacy and safety analysis

Yu-qing Fang[1], Wei Jia[1], Gui-qiang Wang[1]

Peking University First Hospital, Peking University The Center For Liver Diseases and Department of Infectious Diseases Beijing-China[1]

Aims: Some studies have revealed that glucocorticoids added to ursodeoxycholic acid (UDCA) might be superior in the treatment of primary biliary cirrhosis (PBC). The latest EASL guidelines of 2009 declare that further studies regarding glucocorticoid therapy in this disease should be a priority. This is the first study addressing the use of glucocorticoids in a comparatively special population—the pure PBC patients with high IgG and transaminase levels and without PBC-AIH overlap syndrome. We aimed to assess whether combination of prednisone, UDCA and azathioprine was superior to UDCA alone in these PBC patients.
Methods: Sixty patients were enrolled in this 3-year longitudinal retrospective study. Thirty-one underwent UDCA monotherapy, and twenty-nine were treated with prednisone, UDCA and azathioprine. We reviewed biochemistries, immune markers, liver synthetic function, non-invasive assessment of liver fibrosis, efficacy and adverse effects at baseline and at 1, 3, 6, 12, 24, 36 months.
Conclusions: ALP, GGT, ALT, AST levels and APRI and S-index improved dramatically in both groups, and IgG levels decreased in the combination group (all $P < 0.05$). ALB levels decreased in the UDCA group but increased with the combination treatment at 36 months. Significant differences between two groups were observed

at 36 months in the percentage of ALP ($P = 0.005$), IgG ($P = 0.002$), ALB ($P = 0.002$), APRI ($P = 0.015$) and S-index ($P = 0.020$). Prednisolone combined with UDCA and azathioprine showed higher efficacy. No cases with obvious steroid side effects were observed. Combination of prednisolone, UDCA and azathioprine is superior to UDCA alone in pure PBC patients with high levels of IgG and transaminases.

Topic 3: Autoimmune Liver Diseases

No: 1794

Paradoxical expression of MiR 139 5P between serum and liver in patients with primary biliary cirrhosis

Tomohiro Katsuni[1], Masashi Ninomiya[2], Kyoko Tomita[1], Kei Mizuno[1], Chikako Sato[1], Yuko Nishise[1], Kazuno Okumoto[3], Hisayoshi Watanabe[1], Takafumi Saito[1], Yoshiyuki Ueno[1]

Yamagata University Gastroenterology Yamagata-Japan[1], Tohoku University Gastroenterology Sendai-Japan[2], Yamagata University Gastrotenterology Yamagata-Japan[3]

Background: PBC is considered to be an autoimmune disease, although its pathogenesis remains unclear. Previously, we found that patients with PBC had serum miRNA profiles distinct from those in patients with other liver diseases. Accordingly, we evaluated these miRNAs in both serum and liver tissue using the laser capture microdissection (LCM) and digital PCR.
Methods: Patients with each of the three PBC subtypes, and healthy subjects as a control group, were enrolled (n = 5, respectively). Circulating miRNAs were detected using an Illumina Genome Analyzer IIx. Differences in the levels of miRNA expression were also examined by LCM using paraffin-embedded liver tissues of PBC. Areas containing hepatocytes and infiltrating lymphocytes were selectively dissected respectively, and the cell-derived miRNAs were quantified using a digital PCR.
Results: Among 1514 miRNAs obtained, the expression levels of 97 miRNAs were found to differ significantly among the four groups ($P < 0.05$). qRT-PCR using serum samples also confirmed these data from deep sequencing. Digital PCR using hepatic samples obtained by LCM demonstrated that the levels of expression of lymphocyte-derived miR-139-5p were higher than those from hepatocytes, which was also confirmed by ISH.
Conclusion: miR-139-5p was characteristically down-regulated in serum samples from two distinct clinical subtypes. Results obtained from liver samples suggested that infiltrating lymphocytes were the source of miR-139-5p, although the levels of expression did not reflect those in serum samples. Our present findings suggest the involvement of miR-139-5p in the pathogenesis of PBC, and especially in progressive clinical subtypes.

Topic 3: Autoimmune Liver Diseases

No: 2238

Expression of TGF β1 in patients with autoimmune liver diseases

Liudmila Palgova[1], K.L. Raikhelson[1], V.E. Karev[1], N.V. Marchenko[1], E.V. Pazenko[1], A.G. Kharitonov[1], N.V. Semenov[1], S.P. Trotsyuk[1]

"North-western State Medical University Named After I. I. Mechnikov" Under The Ministry of Public Health of The Russian Federation State Budget Institution of Higher Education Saint-Petersburg-Russia[1]

Introduction: Transforming growth factor-beta1 (TGFβ1) is key event in pathogenesis of hepatic fibrosis. High levels of TGF-β1 have been described in different acute and chronic liver diseases. However, its role in pathogenesis of autoimmune liver diseases (AiLD) and hepatitis C virus (HCV) remains unclear.
Objective: To evaluate expression of mononuclear phagocytes (CD68) and TGF-β1 in hepatic tissue of patients with AiLD, HCV.
Materials and methods: We processed liver biopsies for immunohistochemical cell characterization from 49 patients (15—primary biliary cirrhosis (PBC), 12—autoimmune hepatitis (AIH), 12—primary sclerosing cholangitis (PSC), 10—HCV). Expression of TGF-β1 was quantified as percent of positive cells rather CD68 as a whole. Patients with cirrhosis (6—AIH, 5—PBC) were also included in study with separate into account the results in cirrhosis and fibrosis stages. Activity scores were similar in all groups (METAVIR A2-A3).
Results: TGF-β1 expression in CD68 + nonparenchymal liver cells was significantly higher in patients with PSC compared with other AiLD (PBC $p > 0.05$, AIG $P = 0.0002$) and HCV ($P = 0.0001$). TGF-β1 expression in patients with HCV was significantly higher compared with PBC ($P = 0.016$). TGF-β1 expression in CD68 + was higher in patients with HCV and cirrhosis compared with non-cirrhotic patients ($P = 0.04$). Increased absolute count of CD68 + cells was higher in patients with HCV compared with AiLD (AIG $P = 0.002$; PBC $P = 0.007$; PSC $P = 0.003$, respectively).
Conclusions: Increased expression of TGFβ1 in AIH and PBC patients with cirrhosis confirms it's role in fibrogenesis in AiLD. Increased TGF-β1 in PSC patients suggesting the predominance of fibrotic process in the pathogenesis of PSC.

Topic 4: Basic Science of Hepatology

No: 1342

Leveraging a 'trans omics' strategy for prioritizing personalized candidate mut driver genes in hepatocellular carcinoma

Keyue Ding[1], Songfeng Wu[2], Wantao Ying[2], Qi Pan[1], Xiaoyuan Li[3], Dachun Zhao[4], Xiaohong Qian[2], Hong Ren[1]

The Second Affiliated Hospital of Chongqing Medical University, Institute of Viral Hepatitis, Key Laboratory of Molecular Biology for Infectious Diseases, Ministry of Education of China Chongqing-China[1], Beijing Proteome Research Center, Beijing Institute of Radiation Medicine, State Key Laboratory of Proteomics Beijing-China[2], Chinese Academy of Medical Sciences and Peking Union Medical College, Department of Medical Oncology, Peking Union Medical College Hospital Beijing-China[3], Chinese Academy of Medical Sciences and Peking Union Medical College, Department of Pathology, Peking Union Medical College Hospital Beijing-China[4]

Although a large of efforts has been made in identifying common cancer driver genes, there still remains the challenge to predict personalized drivers and assess patient-specific mutations. We aimed to undertake an integrated analysis of multi-omics data in prioritizing personalized mutation-driver genes. A patient of hepatitis B virus associated hepatocellular carcinoma was present at the Peking Union Medical College Hospital, who showed an extremely elevated prevalence of somatic mutations due to a nonsense mutation in MSH2. Using this patient as a model, we performed whole-exome

sequencing, transcriptome sequencing, and proteome profiling for the liver cancer tissues and its matched cirrhotic tissues. An integrated analysis of multi-omics data was employed to investigate the expression of somatic mutations at the mRNA and protein levels. We then explored the feasibility for identifying personalized mutation-driver genes by integrating the patterns of expression of somatic mutations, the known candidate drivers and pathway analyses. of 4,998 non-silent somatic mutations identify by whole exome sequencing, we found that mutant-type allele of 2,061 (41.6 %) and 177 (3.55 %) of somatic mutations were identified at the mRNA and protein levels, respectively. Clustering analysis showed distinct patterns of expression of somatic mutations at different levels. We identified at least five potential personalized mutation-driver genes (HNF1A, FAH, IDH1, GNMT, and SPTBN1) that may lead to hepatocarcinogenesis in the patient. These results suggested that potential mechanisms might account for the eliminating of a large proportion of mutations at the expression stages. As a proof-of-concept, leveraging a trans-omics' strategy may enable prioritizing personalized causal mutations.

Topic 4: Basic Science of Hepatology

No: 1416

KCTD9 contributes to NK cell activation may through KCTD9 SHb pathway

Aichao Shi[1], Xiaoping Zhang[2], Li Zhou[2], Lin Zhu[2], Tao Chen[2], Qin Ning[2]

Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institute of Infectious Disease Wuhan-China[1], Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institution of Infectious Diseases Wuhan-China[2]

Background and objective: Our previous study revealed that hepatic NK cells played an important role in virus-induced liver failure. KCTD9 was significantly up-regulated in hepatic and peripheral NK cells of HBV-ACLF patients. The elevated KCTD9 expressing NK92 cell shows enhanced activation and function in vitro. Bioinformatics analysis of human KCTD9 protein suggests it may interact with SHB molecule (Src homology 2 domain containing adapter protein B), which is known as an adapter protein in IL-2 receptor signaling. The aim of this study is to validate the interaction and function between KCTD9 and SHB.
Materials and methods: pHA-KCTD9 and pFLAG-SHB eukaryotic expression plasmid were constructed and then transfected into HEK 293T cell line. Anti-HA-label mouse monoclonal antibodies, anti-FLAG-label mouse monoclonal antibodies, Horseradish Peroxidase-conjugated AffiniPure Goat Anti-Mouse IgG Light Chain Specific were used in co-immunoprecipitation assay. Furthermore, stable expressing KCTD9 NK92 cell line (KCTD9-NK92) was established, and the expression of Fas, granzyme, perforin, NKG2A, NKG2D, NKG2C, NKP30, NKP44, NKP46 and cytotoxicity function was assayed.
Results: The interaction between KCTD9 and SHB was found by co-immunoprecipitation. The KCTD9-NK92 cell showed significantly elevated expression of activation receptor NKG2D, Fas and cytotoxicity to target cell. But, the expression of inhibitory receptor NKG2A was down-regulated.
Conclusion: The preliminary data showed that there was an interaction between KCTD9 and SHB, which may further contribute to the activation and cytotoxicity of NK cell.

Topic 4: Basic Science of Hepatology

No: 1661

The correlation between activated hepatic stellate cells and neoplastic hepatocytes in the liver of Balb C mice after injection with carcinogen

Wahyuni Atmodjo[1], Darti Wibisono[2], Graciella Wahjoepramono[2], George Mathew[3]

Medical Faculty, Universitas Pelita Harapan Anatomy Lippo Karawaci-Indonesia[1], Medical Faculty, Universitas Pelita Harapan Anatomical Pathologi Lippo Karawaci-Indonesia[2], Medical Faculty, Universitas Pelita Harapan Surgery Lippo Karawaci-Indonesia[3]

Aim: To analyze the correlation between activated hepatic stellate cells and neoplastic hepatocytes in the liver parenchymal of Balb/C mice after injection with diethylnitrosamine.
Methods: Ten of 5 weeks old male Balb/C mice were divided randomly into 2 groups as control and treated groups. Control group was injected with sterile saline and fed with basal diet and treated groups were injected intra peritoneal with DEN 75 mg/kg BW for 3 weeks, continued with 100 mg/kg BW for 3 continuous weeks, fed with basal diet. They were sacrificed at 20 weeks after the first injection of DEN. The liver sections were stained with H&E, Mason's Trichrome and anti α-smooth muscle Actin antibody. The number of α-SMA positive cells and neoplastic hepatocytes in the parenchymal area surrounding central vein were counted randomly in high-powered fields (×400). The correlation were analyzed statistically with considered significant at the 0.05 level.
Result: Liver sections of the mice after injection showed disruption of hepatic architecture with degeneration and necrotic of hepatocytes. Abundant neoplastic hepatocytes with variable size, large and hyperchromatic nuclei, and prominent nucleoli were scattered within parenchyma. Strong expression of α-SMA antibody were shown in the cytoplasm of neoplastic hepatocytes resided surrounding hepatic veins, parenchymal and perisinusoidal areas. Collagen fibers were seen along the bridging septa. The correlation between activated hepatic stellate cells and neoplastic hepatocytes is significant with $r = 0.460$ and regression linear, $y = 0.38 + 0.714x$.
Conclusion: Morphologically, we suggested that activated hepatic stellate cells have a role to the transformation of hepatocytes in liver carcinogenesis of Balb/C mice after injection with dietylnitrosamine.

Topic 4: Basic Science of Hepatology

No: 1429

Primary human hepatocytes have a sustained expression of microRNA122 as shown by an in vitro culture system

Ameer Memon[1], Kanwal Baloch[1], Bikha Ram Devrajani[1]

Liaquat University of Medical and Health Sciences Medical Research Centre Jamshoro-Pakistan[1]

Aims: Primary human hepatocytes based culture system is a natural model to study hepatocyte function in vitro. Using this system to study HCV replication cycle can be useful as hepatocytes are the primary site of viral replication and may provide important insights into virus-host relationship. Liver specific microRNA(miRNA)122 has been shown to support hepatitis C virus replication. Therefore loss of this miRNA in culture conditions may be responsible for loss of liver specific function and may explain the inability of primary

cultures to support HCV replication. Therefore, we aimed to assess miRNA122 expression by primary human hepatocytes and observe changes in its level over a period of time.
Methods: Hepatocytes were isolated from biopsy tissue of patients undergoing liver resection by a modified two-step collagenase perfusion method. Hepatocytes were grown in a collagen-matrigel sandwich and used for RNA extraction followed by Northern blot analysis. miRNA122 levels were determined by measuring band intensities using phosphor imager screen.
Results: Hepatocytes in the collagen sandwich configuration continued to proliferate, maintained typical hepatocytes specific features and grew in the form of three dimensional spheroids throughout their five days of culture.Northern blot analysis showed miRNA122 expression at all time points in primary human hepatocyte culture.
Conclusion: Our data suggests that expression of miRNA122 is sustained in primary human hepatocytes culture and does not diminish over a 5 days period of culture. Therefore, loss of miRNA122 is unlikely to be the underlying mechanism of failure to replicate HCV in primary hepatocyte cultures.

Topic 4: Basic Science of Hepatology

No: 1937

Imaging of reactive oxygen species by an in vivo electron spin resonance imaging system

Hitoshi Togashi[1], Masaaki Aoyama[2], Kazuo Oikawa[3]

Yamagata University Health Administration Center Yamagata-Japan[1], Yamagata Public Corporation For Development of Industry Institute For Life Supporting Technology Yamagata-Japan[2], Yamagata Research Institute of Technology Yamagata-Japan[3]

Purpose: We sought to image the biodistribution of reactive oxygen species (ROS) within the living body using an in vivo electron spin resonance (ESR) imaging system using a spin probe, 1-acetoxy-3-carbamoyl-2,2,5,5-tetramethylpyrroline (ACP) that produces ESR-detectable nitroxide upon reaction with ROS.
Methods: Acute hepatic injury was induced in mice by priming with heat-killed Corynebacterium parvum followed by injection of a low dose of lipopolysaccharide. ACP was administered intravenously and an in vivo ESR imaging system was used to visualize hepatic oxidative stress.
Results: In this immune-mediated hepatic injury model, significant oxidative stress was evident at 3 h after lipopolysaccharide administration before the onset of massive hepatic injury. ACP was administered intravenously at 3 h after lipopolysaccharide injection when significant hepatic oxidative stress had been observed, and the ESR imaging system detected a high signal for 3-carbamoyl-2,2,5,5-tetramethylpyrrolidine (carbamoyl-PROXYL), which had originated from the ACP-derived hydroxylamine and produced large amount of ROS within the living body. Using the ESR imaging system with ACP, we were able to visualize ROS in the abdomen before onset of hepatic injury.
Conclusion: We have succeeded in visualizing ROS within the body before onset of organ damage, representing a significant development in imaging for toxic molecules.

Topic 4: Basic Science of Hepatology

No: 1800

A novel TIS1 regulated epithelial mesenchymal transition of tumor cells contributes to local invasion and metastasis in human hepatoma

Sen-yung Hsieh[1], Ray-ming Peng[1], Chih-yung Chiou[1]

Chang Gung Memorial Hospital Liver Research Unit Taoyuan-Taiwan[1]

Human hepatocellular carcinoma (HCC) is characterized by frequent local invasion and recurrence, which are strongly associated with poor overall survival of HCC patients. Epithelial-mesenchymal transition (EMT) is an initiating event driving tumour invasion and metastasis. However, the molecular mechanisms of EMT in HCC remains largely unknown. We have performed a human kinome/phosphatome RNAi screen to identify novel genes that are involved in invasion and metastasis of HCC cells using Hep3B, a low motile HCC cell line, and identified TIS1 (Tumor Invasion Suppressor 1) as a potential cell motility suppressor. Mechanistic studies revealed that TIS1 was a novel actin binding protein that sequestrated globular actins and prevented actin filament (F-actin) formation, thereby suppressing the formation of filopodia, lamillepodia and invadopodia. Silencing of TIS1 enhanced EMT and tumor cell migration and invasion. Notably, F-actin polymerization induced by TIS1 silencing led to activation of the NOTCH signaling via induction of HIF1A, which in turn further supports EMT for sustaining tumor invasion and metastasis. Clinically, TIS1 was frequently downregulated in many human cancers including HCC and associated with tumor recurrence, local invasion, and poor prognosis. In conclusion, a novel TIS1-HIF/NOTCH signaling forms a positive feedback loop sustainingly driving mesenchymal transition of cancer cells for invasion and metastasis. This TIS1-mediated tumor invasion and metastasis signaling may serve as therapeutic targets for prevention and treatment of HCC invasion and metastasis.

Topic 4: Basic Science of Hepatology

No: 1139

In vitro generation of bipotent liver stem progenitor like cells from adult rat hepatocytes using small molecule inhibitors

Takeshi Katsuda[1], Masaki Kawamata[1], Keitaro Hagiwara[1], Takahiro Ochiya[1]

National Cancer Center Research Institute Division of Molecular and Cellular Medicine Tokyo-Japan[1]

Liver stem/progenitor cells (LSCs), which are believed to reside in canals of Hering, are one of the promising candidates for cell sources in liver regenerative medicine. However, these cells are difficult to isolate efficiently and expand stably in vitro. Our group recently reported that small molecule signaling inhibitors enable stable establishment of both embryonic and tissue stem cells (Kawamata and Ochiya, PNAS 2010; Kawamata et al., submitted). Here, we identified a combination of three small molecules, XYZ, which endowed rat adult primary hepatocytes with high proliferative capacity. The proliferating cells morphologically resembled LSCs in that they were small in size and had a high nuclei-to-cytoplasm ratio. of note, time-lapse imaging analysis revealed that these cells were derived from mature hepatocytes. Furthermore, by qRT-PCR and immunocytochemistry, we found that these cells expressed LSC markers. Thus, we term these cells as mature hepatocyte-derived LSCs (MH-LSCs). Then, we investigated in vitro whether we can direct MH-LSCs to both hepatocytes and cholangiocytes. Following the stimuli by oncostatin M, dexamethasone and matrigel, MH-LSCs re-differentiated to functional hepatocytes: they showed gene expression profiles similar to primary hepatocytes, and revealed a series of hepatic functions, including albumin secretion, CYP activity, and glycogen storage. On the other hand, when cultured in mTeSR medium on MEF

feeder cells, MH-LSCs formed ductal and cystic structures. Notably, these structures enlarged their lumen size upon secretin stimulation, and were able to excrete and store bile-mimicking fluorescent substrate into their luminal space.

Topic 4: Basic Science of Hepatology

No: 2203

Therapeutic hypothermia a treatment choice for cerebral oedema in acute liver failure report of two cases

Aslihan Yalcin[1], Sait Karakurt[1], Semiha Emel Eryuksel[1], Ender Dulundu[2], Feyza Gunduz[3], Osman Cavit Ozdogan[3]

Marmara University Medical Intensive Care Unit Istanbul-Turkey[1], Marmara University General Surgery, Transplantation Istanbul-Turkey[2], Marmara University Gastroenterology Istanbul-Turkey[3]

Background: Therapeutic hypothermia; is a recently described approach for severe cerebral oedema with acute liver failure (ALF). Hereby, we present two ALF cases, managed with hypothermia in our intensive care unit (ICU).
Case1: A 32-year-old female with acute Viral B Hepatitis was transferred to our ICU together with deterioration mental status. Intubation and emergency call for transplantation were carried out. Cranial CT showed severe cerebral oedema. Suitable donor could not be found. Therapeutic hypothermia was initiated for a period of 24 h followed by rewarming without any complication. Improvement in GCS was shown on day 10, patient regained consciousness on day 14, extubated on day 18. She is on her normal daily life, with no neurological sequel at the end of 6th month.
Case 2: Previously healthy, 18-year-old male was transferred to our ICU with worsening ALF. Initial evaluation confirmed fulminant hepatic failure of unknown aetiology. Mental status worsened rapidly and intubation was necessary. Emergency call for liver transplantation was carried out. Signs of intracranial pressure worsened despite medical therapy, cranial CT showed severe cerebral oedema. Therapeutic hypothermia was initiated, but had to be stopped at the 16th hour of hypothermia because of bradycardia and refractory hypotension. On day 4 signs of septic shock became evident. On day 5 patient died from refractory septic shock.
Conclusion: Therapodic hypothermia is a new treatment procedure in cases of acute liver failure with severe cerebral oedema. However, there is no established criteria for indications and possible complications to be considered.

Topic 4: Basic Science of Hepatology

No: 1054

Promotion of autophagy using amiodarone increased the survival and alleviates liver injury following 90 % massive hepatectomy

Chih-wen Lin[1], Yaw-sen Chen[2], Chia-chang Hsu[3], Gin-ho Lo[3], Chia-yen Dai[4], Wan-long Chuang[4], Ming-lung Yu[4]

E-da Hospital, I-shou University; Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University Medicine Kaohsiung-Taiwan[1], E-da Hospital, I-shou University Surgery Kaohsiung-Taiwan[2], E-da Hospital, I-shou University Medicine Kaohsiung-Taiwan[3], Kaohsiung Medical University Hospital, Kaohsiung Medical University Medicine Kaohsiung-Taiwan[4]

Background and aims: The use of pharmacological interventions offers the potential for improved hepatocyte proliferation and liver regeneration following partial hepatectomy (PHx). Autophagy, a process that results in cellular degradation, has been found to be involved in the human liver disease. This study aims to investigate the role of autophagy in the regulation of liver regeneration and hepatocyte proliferation after PHx. Furthermore, pharmacological modulation of autophagy could be an effective approach to promote liver regeneration and the survival after 90 % massive PHx.
Methods: We administrated autophagy enhancers to C57BL/6 mice intraperitoneally: amiodarone and chloroquine. This was followed by a 90 % PHx or sham-operation. The survival rate was collected. Furthermore, activation of autophagy, level of hepatocyte proliferation, and blood levels of liver enzyme were also measured.
Results: Enhancement of autophagy using amiodarone following 90 % massive PHx significantly promoted the survival rate. Moreover, amiodarone significant increase of autophagy and hepatocyte proliferation associated with alleviated liver injury.
We also found that pretreatment with chloroquine aggravated the liver injury associated with reduced the survival and hepatocyte proliferation. Moreover, amiodarone was associated with a significant increase of PCNA and cyclin D1 protein levels but also reduced termination of liver regeneration by decreasing TGF-β1 protein levels.
Conclusion: Pharmacological interventions by amiodarone that modulate autophagy may be effective to promote the survival, and liver regeneration and alleviate liver injury following 90 % massive PHx.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 1577

Risk factors for development of biliary complications following surgery for solitary liver hydatid cyst

Ali Surmelioglu[1], Ilter Ozer[2], Tahsin Dalgiç[2], Enver Reyhan[3], Yılmaz Ozdemir[2], Murat Ulaş[2], Erdal Birol Bostancı[2], Musa Akoglu[2]

Haydarpaşa Numune Training and Research Hospital Gastrointestinal Surgery Istanbul-Turkey[1], Turkiye Yuksek Ihtisas Education and Research Hospital Gastrointestinal Surgery Ankara-Turkey[2], Adana Numune Training and Research Hospital Gastrointestinal Surgery Adana-Turkey[3]

Background: Biliary leakage (BL) is the most common cause of post-operative morbidity following conservative liver hydatid cyst (LHC) surgery. The objective of this study was to determine incidence of BL and related risk factors in patients with solitary LHC who underwent conservative surgery.
Methods: Between January 2008 and May 2013, 186 patients who were operated on for solitary LHC were included in the study. Patients with more than one cyst, patients who received a radical surgical treatment (pericystectomy or hepatectomy) and patients who had a pre-operative endoscopic retrograde cholangiopancreatography (ERCP) were not included.

The risk factors identified for BL were age, gender, recurrent cyst, cyst diameter, perihilar (near hilum) or peripheral (far from hilum) location of the cyst, WHO Informal Working Group on Echinococcosis (WHO-IWGE) classification, surgical procedure performed for cavity control (omentoplasty, introflexion and external drainage), cyst content (bilious and/or purulent and clear), and alkaline phosphatase (ALP) level obtained in biochemical analyses. These factors were evaluated with univariate and multivariate analyses.

Results: 104 patients were female and 82 were male. The mean age was 43.5 ± 14.7 years. Post-operative BL was detected in 36 (19.4 %) patients. Cyst diameter ($P = 0{,}019$), cyst localization ($P = 0{,}007$), WHO-IWGE classification ($P = 0{,}017$) and ALP level ($P = 0{,}001$) were the most significant risk factors for BL.
Conclusions: Independent risk factors for BL were perihilar localization, large cyst diameter, high ALP level and advanced age according to WHO-IWGE classification.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 1580

Risk factors for biliary complications after surgery for multiple liver hydatid cysts

Yılmaz Ozdemir[1], Ilter Ozer[1], Ali Surmelioglu[2], Tahsin Dalgıç[1], Erol Aksoy[1], Mehmet Ali Çaparlar[1], Murat Ulaş[1], Yusuf Bayram Ozogul[1], Erdal Birol Bostancı[1], Musa Akoglu[1]

Turkiye Yuksek Ihtisas Education and Research Hospital Gastrointestinal Surgery Ankara-Turkey[1], Haydarpasa Numune Training and Research Hospital Gastrointestinal Surgery Istanbul-Turkey[2]

Background: Biliary leakage (BL) is the most common cause of post-operative morbidity following liver hydatid cyst (LHC) surgery. The objective of this study was to determine the incidence of post-operative BL and related risk factors in patients with multiple LHC.
Methods: Between 2007 and 2013, 130 patients who were operated on for multiple LHC were included. Patients with only one cyst were excluded. Age, gender, cyst number, recurrent cyst, cyst diameter, perihilar or peripheral location, WHO Informal Working Group on Echinococcosis (WHO-IWGE) classification, presence of symptoms, laboratory tests (ALP, AST, ALT, GGT, bilirubin levels, eosinophila), cyst content (bilious and/or purulent and clear) were identified as risk factors and were evaluated with univariate and multivariate analyses.
Results: 80 patients were female and 50 were male. The mean age was 43.45 ± 15.7 years. Post-operative BL was detected in 19.2 % of the patients. Postoperative morbidity and mortality rates were 33.1 and 1.5 %, respectively. Preoperative jaundice, fever, leucocytosis, eosinophilia, elevated ALP, AST, ALT, GGT, bilirubin levels, perihilar localization of the largest cyst, diameter of the largest cyst, dilatation of the bile ducts in preoperative imaging, purulent and/or biliary cyst content were associated with increased BL rate according to univariate analysis. However, multivariate analysis revealed that eosinophilia and dilatation of the bile ducts in preoperative imaging were the independent significant risk factors.
Conclusions: Eosinophilia and dilatation of the bile ducts in preoperative imaging were the strongest risk factors after surgery for multiple hydatic cysts.

Topic 6: Drugs Herbals and Liver

No: 1130

Study of hepatoprotective effect of *tragopogon Graminifolius L. hydroethanolic* leaf extract in male rat induced with carbon tetrachloride (CCL4)

Naser Mirazi[1], Leyla Sadat Nedaii[1]

Islamic Azaduniversity Hamedan Branch Islamic Azaduniversity Hamedan Branch Hamedan-Iran[1]

Introduction: The liver is the central organ of metabolism and detoxification. The hepatocyte cells could be inflammated and necrotic in toxic disorders when they induced with chemical and microbial toxins. Medicinal plants have hepatoprotectivity effects and can inhibit the toxicity progress in liver. In this study the hepatoprotectivity effect of *Tragopogon graminifolius* hydroethanolic extract (THE) in male rat were investigated which induced with carbon tetrachlorid.
Method and materials: 42 male rats with 250–300 gr body weight were divided randomly in 6 groups (n = 7): control (taking normal saline, 0.5 ml/daily, single dose, IP), sham (taking olive oil, 0.5 ml, single dose, IP), carbon tetrachloride (1:1 with olive oil, 0.5 ml single dose, IP), treated 1, 2 & 3 groups (carbon tetrachloride1: 1 with olive oil, 0.5 ml and 200, 400 and 800 mg/kg THE/daily, single dose for 96 h, IP). After the examination the blood samples were collected from heart directly and AST,ALT and ALP enzymes were analyzed and the liver tissue samples were isolated and then fixed with formaline for the preparation of histological sections were performed stained with H & E. Data were analyzed using one-way of statistics ANOVA and significant differences was considered between their standard of $P < 0.05$.
Results: Our results showed that the carbon tetrachloride has hepatotoxicity effect in liver. It can cause inflammation and necrosis in liver tissue ($P < 0.001$). The THE can inhibit the hepatotoxicity progressing in rats which induced with carbon tetrachloride ($P < 0.001$). The enzymes serum.

Topic 6: Drugs Herbals and Liver

No: 1746

Spheroid reservoir bioartificial liver treatment inhibits alpha amanitin induced fulminant hepatic failure in rhesus monkey model

Ji Bao[1], Yi Li[1], Yujia Wang[1], Qiong Wu[1], Xiujuan Wu[2], Yujun Shi[1], Bruce Amiot[3], Scott Nyberg[4], Hong Bu[1]

West China Hospital, Sichuan University Laboratory of Pathology Chengdu-China[1], Luzhou Medical College Department of Clinical Medicine Luzhou-China[2], Mayo Clinic Laboratory of Artificial Liver Rochester-United States[3], Mayo Clinic Division of Transplantation Surgery Rochester-United States[4]

High mortality rate in amanita phalloides intoxications is principally a result of the fulminant hepatic failure (FHF) following massive death of liver cells due to hepatocellular uptake of α-amanitin (α-AMA), the major amatoxin, with limited therapeutic options. Recovery would be more frequent if a supportive therapy were available to correct the toxic milieu of FHF to prevent its extrahepatic manifestations and to assist in liver regeneration. Therefore, a novel supportive therapy, the Spheroid Reservoir Bioartificial Liver (SRBAL) composed of over 100 gram porcine primary hepatocyte aggregates ("spheroids"), was developed. The spheroids were engineered by a novel rocked high-density suspension culture technique. Once formed, spheroids are placed in a continuous perfusion bioreactor, which provides functionality to the device.

Rhesus primates were induced to FHF via α-AMA and LPS intraperitoneal injection. Animals were randomized into three treatment groups: no therapy (n = 3), no cell device therapy (n = 3), and SRBAL therapy (n = 3). SRBAL treatment was 6 h in duration after toxin administration 12 h. There was no difference in the level of liver failure between groups prior to the initiation of treatment.

All treatment procedures were completed successfully without any adverse reaction.All samples presented negative PERV DNA and RT activity.The levels of antibodies were similar before and after

treatment. A significant survival benefit was observed with SRBAL compared to the two control groups (100 % vs. 0 % vs. 0 % at 60 h after toxin administration, $P < 0.001$). Animals treated with the SRBAL maintained stable plasma ammonia levels during treatment compared to control animals. Relatively low plasma concentrations.

Topic 6: Drugs Herbals and Liver

No: 1639

Impact of medicinal herbs against fat induced inflammatory iron burdens in adult *rattus norvegicus*

Afshan Syed Abbas[1], Nadeem Sheikh[1]

University of The Punjab Department of Zoology Lahore-Pakistan[1]

Iron stores of body are linked with fat induced inflammation in non alcoholic fatty liver disease (NAFLD). The current study was carried out to find out the impact of two medicinal herbs *N. sativa* seeds and *P. ovata* husk supplementation on iron stores of *Rattus norvegicus* under fat induced inflammation. Four groups of rat (n = 10) were designated as 0, I, II and III. Group 0 and I served as negative and positive controls and consumed rat chow or fat rich diet (FRD) respectively. The group II and III were provided with FRD supplemented with *Nigella sativa* seeds or *Plantago ovata* husks likewise. After sixteen weeks the serum samples were analyzed biochemically for iron stores of the body. The results revealed significant elevation of serum iron, hepcidin and ferritin in group I while a decline in group II and III was found in comparison with the control group 0. The intergroup comparison revealed significantly higher serum iron level in group I and lower in group III when compared with group II. However, there was a significantly lower serum total iron binding capacity (TIBC) of group I, when compared with group 0 and II, while it was significantly elevated in group III than group I and 0. Taking together these findings it can be inferred that P. ovata husk is effective to lower the fat induced inflammatory iron over burdens of body.

Topic 6: Drugs Herbals and Liver

No: 2240

Beneficial effects of coffee consumption on chronic liver diseases

Tarek Korah[1]

Faculty of Medicine, Menoufiya University, Egypt Int. Medicine Menoufiya-Egypt[1]

Coffee consumption is a part of daily life in most areas of the world. Recent studies demonstrated a significant inverse association between coffee consumption and reduced risk for NAFLD. Also, other studies suggest that regular coffee may modulate the risk for fibrosis in chronic liver disease.

Mechanisms by which coffee exerts its beneficial effects have not been clearly defined. Apparently, these effects extend across the spectrum of liver disease, ranging from hepatic steatosis to fibrosis, cirrhosis, and HCC.

Currently, coffee is considered the largest source of dietary antioxidants. Also, caffeine has been shown to exert direct hepatoprotective effects. Coffee has been also shown to decrease liver fat and collagen content and reduce the hepatic concentrations of proinflammatory TNF-α and interferon-γ as well as increase anti-inflammatory interleukin-4 and interleukin-10 in an animal model of steatohepatitis. Furthermore, there is evidence suggesting that coffee can attenuate the progression of liver fibrosis by inhibiting hepatic stellate cells.

Moreover, the risk of HCC was reduced with coffee consumption. This is likely the result of reduced cirrhosis evident in coffee drinkers, as well as improvement in the metabolic syndrome, because diabetes is known risk factor for HCC.

Topic 6: Drugs Herbals and Liver

No: 2167

Temozolomide induced liver injury

Firdevs Topal[1], Zeynep Zehra Gümüş[1], Elif Saritaş Yüksel[1], Belkis Ünsal[1], Ayşegül Sari[2], Sezgin Vatansever[1]

Gastro Gastro Izmir-Turkey, [2]Patoloji Patoloji Izmir-Turkey[1]

Temozolomide is used for malign melanoma and glioblastoma multiforme). The most common gastrointestinal side effects of TMZ are nausea, constipation and vomiting. Temozolomid- induced liver injury (TILI) is rare developed. However TMZ is used frequently, hence even rare side effects might be observed more than expected. Here we report the patient who was diagnosed with glioblastoma multiforme. 62-year-old female patient was consulted to gastroenterology clinic with elevated liver transaminases. There was no past alcohol consumption or immunoallergic features and no family history of liver disease. She denied the use of paracetamol or any other helping medicine. She had jaundice and on her physical examination, scleral icterus was observed. She underwent craniotomy for glioblastoma 5 months ago. Later, radiotherapy was commenced with temozolomide 135 mg/daily. On the 4th week of the radiotherapy and temozolomide, the weekly biochemical tests showed AST; 1342 U/L ALT; 475 U/L ALP: 330 U/L, GGT: 523 U/L serum albumin: 3,7 g/dL, INR: 1,11, serum glucose: serum total bilirubin: 5,76 mg/dl and serum direct bilirubin: 3,5 mg/dL. Complete blood count showed that platelet: 201.000 K/μL, hemoglobin: 12,8 g/dL and white blood cells: 6.630 K/μL.Ultrasound of the liver showed no significant biliary or liver abnormality. She hospitalized with the diagnosis of acute hepatitis and temozolomide was discontinued.

Viral hepatitis markers were negative for HBV. HCV RNA was 10^5IU/mL and anti HCV was positive. ANA, ASMA, AMA and anti-liver/kidney microsomal antibodies were also negative. On the eye examination, Kayser-Fleischer ring was.

Topic 6: Drugs Herbals and Liver

No: 1338

Investigations of plants used in traditional Mongolian medicine for the treatment of liver diseases

Tsend-ayush Damba[1], Badamsuren Dorjgotov[2], Tserentsoo Byambaa[1], Tserendagva Dalkh[3]

Institute of Traditional Medicine, Mongolian National University of Medical Sciences Theory of Traditional Medicine Ulaanbaatar-Mongolia[1], Shastin Clinical Hospital Internal Medicine Ulaanbaatar-Mongolia[2], Institute of Traditional Medicine, Mongolian National University Omedical Sciences Internal Medicine Ulaanbaatar-Mongolia[3]

Mongolian materia medica consists of plants, minerals, and animal parts or products, however, the plants have always made up the main part of the prescriptions. The traditional medicinal treatises include various proven prescriptions for liver diseases.

CCL4-induced experimental hepatitis was used for the study of Carthamus tinctorius L. (CT), and plasma biochemistry, coagulation test, histomorphology were performed and analyzed. Additionally, the in vitro cytotoxicity of some plant extracts that are used in Mongolian traditional medicine for their hepatoprotective activities was assessed. A cynaropicrin, a sesquiterpene lactone from *Saussurea amara* (SA) was tested in the human liver and breast cancer cell lines. Ethanol extract (70 %) from aerial part of *Scutellaria baicalensis* Georgi (SB) and Skullcap-preparation from the root of SB were used for study. Primary Cancer and MDCK cells were cultured and used for this assay. Proliferation, Migration, Cell adhesion and DNA ladder assayes; Reverse Transcriptase-PCR Analysis of Gene Expression in hematopoietic Stem Cells was performed for the screening of SB.

Carthamus tinctorius, cultivated in our country, exhibited a hepatoprotective effect, and reduced hepatocelullar decomposition. A sesquiterpene lactone from Saussurea amara L. exhibited a pronounced cytotoxic effect on the breast cancer cell line; original water extract exhibit moderate effect on hepatocellulocarcinoma cell line. The plant extract of *Scutellaria baicalensis* and Skullcap preparation did not show any destructive and decomposition effects on DNA of the cell genome. The ethanol extraction of this plant does not induce apoptosis, but transmembrane proteins can block cancer cell division by inhibiting their gene expression.

Topic 6: Drugs Herbals and Liver

No: 1866

Protective effects of apricot on acetaminophene induced liver damage in rats

Ismet Yilmaz[1], Aslı Çetin[2], Feride Karahan[2]

Inonu University Faculty of Pharmacy Pharmacology Malatya-Turkey[1], Inonu University Faculty of Medicine Histology - Embryology Malatya-Turkey[2], Inonu University Pharmacy Faculty, Department of Pharmacology, 44280, Malatya, Turkey. Inonu University Medical Faculty, Department of Histology and Embryology, 44280, Malatya, Turkey

Aim: This study was planned to observe the protective effects of apricot (10 % apricot) consumption on acetaminophen (APAP) induced liver damage.
Materials and methods: In this study, twenty-four Sprauge-Dawley rats were randomly divided into four equal groups.
Groups:

1. Group (n = 6): Control (Standard diet)
2. Group (n = 6): Acetaminophene (APAP) group (835 mg/kg single dose by orally)
3. Group (n = 6): APAP + 10 % Apricot (10 % rate sun dried organic apricot supplemented diet)
4. Group (n = 6): 10 % Apricot (10 % rate sun dried organic apricot supplemented diet)

At the end of the study, rats were sacrified under ketamine/xylazine anesthesia. For light microscopic evaluation, liver samples were fixed in 10 % formalin. The liver samples were processed by routine tissue techniques and were embedded in paraffin. Paraffin-embedded specimens were cut into 5 mm thick sections, mounted on slides and stained with Hematoxylen- Eosin (H-E). Sections examined under a Leica DFC280 light microscope by Leica Q Win and Image Analysis System (Leica Micros Imaging Solutions Ltd.; Cambridge, U.K).
Results: In control and 10 % apricot groups, liver showed normal histological appearance. In histological evaluation, hepatocytes and the portal area appeared to be normal. Some histological changes were observed in APAP group. These changes are disruption of radial arrangement of hepatocytes from central vein, vascular congestion, necrosis, mononuclear cell infiltration, haemorrhage and eosinophilic stained.

Topic 6: Drugs Herbals and Liver

No: 2169

Temozolomide induced liver injury

Firdesv Topal[1], Zeynep Zehra Gümüş[1], Elif Saritaş Yüksel[1], Belkis Ünsal[1], Sezgin Vatansever[1], Ayşegül Sari[1]

Gastro Gastro Izmir-Turkey[1]

Temozolomide is used for malign melanoma and glioblastoma multiforme). The most common gastrointestinal side effects of TMZ are nausea, constipation and vomiting. Temozolomid- induced liver injury (TILI) is rare developed. However TMZ is used frequently, hence even rare side effects might be observed more than expected. Here we report the patient who was diagnosed with glioblastoma multiforme. 62-year-old female patient was consulted to gastroenterology clinic with elevated liver transaminases. There was no past alcohol consumption or immunoallergic features and no family history of liver disease. She denied the use of paracetamol or any other helping medicine. She had jaundice and on her physical examination, scleral icterus was observed. She underwent craniotomy for glioblastoma 5 months ago. Later, radiotherapy was commenced with temozolomide 135 mg/daily. On the 4th week of the radiotherapy and temozolomide, the weekly biochemical tests showed AST; 1342 U/L ALT; 475 U/L ALP: 330 U/L, GGT: 523 U/L serum albumin: 3,7 g/dL, INR: 1,11, serum glucose: serum total bilirubin: 5,76 mg/dl and serum direct bilirubin: 3,5 mg/dL. Complete blood count showed that platelet: 201.000 K/μL, hemoglobin: 12,8 g/dL and white blood cells: 6.630 K/μL.Ultrasound of the liver showed no significant biliary or liver abnormality. She hospitalized with the diagnosis of acute hepatitis and temozolomide was discontinued.

Topic 6: Drugs Herbals and Liver

No: 1415

Protective effect of TH22 cells and intrahepatic il 22 in drug induced hepatocellular injury

Rongtao Lai[1], Xiaogang Xiang[1], Ruidong Mo[1], Rebecca Bao[2], Peng Wang[1], Simin Guo[1], Gangde Zhao[1], Honglian Gui[1], Shisan Bao[2], Qing Xie[1]

Ruijin Hospital, Shanghai Jiaotong University School of Medicine Department of Infectious Diseases Shanghai-China[1], Bosch Institute and School of Medical Sciences, University of Sydney Discipline of Pathology New South Wales-Australia[2]

Background & aims: Th22 cells play a pivotal role in regulating host immunity against pathogenic invasion. Th22 cells demonstrate protection against chronic hepatitis B; however the relationship between drug induced liver injury (DILI) and Th22/Th17 cells is still unclear.

We aimed to investigate the role of Th22 cells in the development of DILI.
Methods: The frequencies of peripheral Th22, Th17 and Th1 cells from DILI, non-DILI liver diseases, and healthy control were examined. Intrahepatic IL-22/IL-17 production was determined from DILI, non-DILI liver diseases and HC. The kinetics of plasma IL-22/IL-17 and the related cytokines were determined in DILI patients at weeks 0 (Defined as the occurrence of liver injury within 7 days), 4 and 24.
Results: The frequencies of Th22/Th17 cells were significantly higher from DILI onset patients than HC. Intrahepatic IL-22 production and plasma Th22-related cytokines were significantly higher in DILI patients with ALT $\geq$ fivefold (5 $\times$ ULN) than ALT levels $< 5 \times$ ULN. Significant increase of Th22 cells and the related cytokines levels were observed in DILI with hepatocellular injury type. There was a positive correlation between intrahepatic IL-22 level and hepatocyte-mediated liver regeneration. Plasma IL-22 level was higher in DILI patients with improved liver function than unimproved. High level of plasma IL-22 at 4 weeks was an independent predictor for the recovery patients.
Conclusion: Increased peripheral and intrahepatic IL-22-secreting cells are detected in DILI. Plasma IL-22 might be a reliable indicator to evaluate the prognosis of DILI. Th22 and its related cytokines might be hepato-protective, which might provide new perspective for understanding the immunopathogenesis of DILI.

Topic 7: ERCP and Interventional Hepatology

No: 1637

Is periampullary diverticulum a nightmare in endoscopic retrograde cholangiopancreatography

Canan Alkim[1], Salih Boga[2], Meltem Ergun[1], Ali Riza Koksal[1], Mehmet Bayram[1], Pinar Sayin[3], Huseyin Alkim[1]

Sisli Hamidiye Etfal Education and Research Hospital Department of Gastroenterology Istanbul-Turkey[1], Yale University School of Medicine, Yale New Haven Hospital Department of Digestive Diseases, Department of Liver Transplantation New Haven-United States[2], Sisli Hamidiye Etfal Education and Research Hospital Department of Anesthesiology and Reanimation Istanbul-Turkey[3]

Introduction: Although periampullary diverticulum (PAD) is usually asymptomatic and discovered incidentally during endoscopic retrograde cholangiopancreatography (ERCP), it may lead to unsuccessful cannulations and peri-ERCP morbidities. We aimed to evaluate ERCP results in patients with and without periampullary diverticulum in terms of complication and success rates of the procedure.
Methods: Clinical, laboratory, and ERCP data of 948 patients referred to Şişli Hamidiye Etfal Education and Research Hospital Gastroenterology Endoscopy Unit between 2011-2014 were analyzed retrospectively.
Results: PAD was identified in 112 of 948 patients (11.8 %). The total number of ERCP procedures were 1162. While 112 PAD patients had 136 ERCP procedures, 836 patients without diverticulum had a total of 1026 ERCP procedures. There was no significant difference in terms of procedure number per patient. Cannulation of common bile duct was failed in 7 of 112 PAD patients and 51 of 836 patients without diverticulum (6 % vs. 6 %). Twenty-one of 112 (19 %) PAD patients had multiple diverticulum. The mean age and female/male ratio of PAD patients were significantly higher than the patients without diverticulum (72.7 ± 12.2 vs. 56.8 ± 16.4, $P < 0.001$ and 72.2% vs. 54.6%, $P = 0.042$ respectively) While investigated in terms of bleeding, pancreatitis and perforation rates there were no significant differences between two groups.
Conclusion: Although there are studies reporting technical and cannulation difficulties and increased complication rates in PAD patients, we didn't find such a relationship. Our data suggests that PAD patients would not experience any additional risk if ERCP procedures are performed by skilled endoscopists working with high care.

Topic 8: Gall Bladder and Biliary Tract

No: 1646

Early postoperative complications after single port versus 4 port laparoscopic cholecystectomy in patients using oral anticoagulant

Musa Akoglu[1], Erdal Birol Bostanci[1], Erol Aksoy[1], Umit Koc[1], Fatih Sumer[1], Ilter Ozer[1]

Turkiye Yuksek Ihtisas Education and Research Hospital Gastrointestinal Surgery Ankara-Turkey[1]

Background: The aim of this study was to compare early postoperative complications after single port and 4-port laparoscopic cholecystectomy (LC) in patients who use oral anticoagulant.
Patient and method: Sixteen patients who underwent 4-port LC between 2009 and 2010 and 13 patients who underwent single port LC between 2012 and 2013 at Department of Gastrointestinal Surgery, Turkiye Yuksek Ihtisas Education and Research Hospital were enrolled to the study. All of the patients were using oral anticoagulant. The patients' data (age, gender, body mass index (BMI), cause of oral anticoagulant use, operation time, postoperative complications, length of hospital stay and re-operation) were compared. Oral anticoagulant was stopped a week before the operation and low molecular weight heparin was started. All of the operations were performed if INR was $\leq$ 1,5.
Results: Demographics, BMI and oral anticoagulant use were similar between single port and 4-port groups. Operation time was longer in single port group ($93,07 \pm 26,96$ min) compared to 4-port group ($51,25 \pm 16,07$) (p: 0,02). While there was no postoperative complication in single port group, 5 complications [hematoma at the port site ($n = 2$) and haemorrhage from the port site ($n = 3$)] were seen in 4-port group (p: 0,02). There was no need to reoperate the patients and length of hospital stay were similar between the groups.
Conclusion: Single port laparoscopic cholecystectomy increased operation time. Also there was no postoperative complication in single port group.

Topic 8: Gall Bladder and Biliary Tract

No: 1321

Three port two are located on the pfannenstiel line laparoscopic cholecystectomy comparison with traditional laparoscopic cholecystectomy a case matched study

Musa Akoğlu[1], Erdal Birol Bostancı[1], Muhammet Kadri Çolakoğlu[1], Erol Aksoy[1]

Türkiye Yüksek Ihtisas Training and Research Hospital Gastrointestinal Surgery Ankara-Turkey[1]

Laparoscopic cholecystectomy (LC) is seen as a gateway to minimally invasive surgery since the first operation was performed. Various modifications of LC have been developed year by year,

including three-port, two-port and single port LC. In this study, we defined a new three-port technique with different port sites and compared the postoperative results with traditional four-port LC procedure in a case-match study. In contrast to the other three-port approaches two 5-mm trocars placed from right and left inguinal region, 1 cm lateral to the plica umblicalis, to form isosceles triangles with 11-mm trocar that placed before and we performed the incisions under the bikini line.

Between June 2012 and May 2013, 104 consecutive patients underwent three-port LC.2963 consecutive patients underwent four-port LC in the same center and of these patients, a matched group of 104 patients was selected. The matching variables were age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score and previous abdominal operation of the patient.

The compared datas between two groups were patient age, gender, body mass index, ASA score, history of abdominal operations, intra-operative data about operating time and conversion to open surgery, and postoperative data about length of hospital stay and postoperative complications.

We concluded that our new three-port technique with different port sites is as feasible and safe as traditional four-port technique.

Topic 8: Gall Bladder and Biliary Tract

No: 2202

Deficiency of MAP3K4 induces epithelial mesenchymal transition via P38 NF κB snail pathway in intrahepatic cholangiocarcinoma

Qiang Gao[1], Liu-xiao Yang[1], Jian Zhou[1], Jia Fan[1]

Liver Cancer Institute, Zhongshan Hospital, Fudan University Depart. of Liver Surgery Shangahai-China[1]

Background & aims: Pathogenesis of intrahepatic cholangiocarcinoma, the second-most common liver cancer, is poorly understood and its incidence continues to increase worldwide. Desregulation of MAP3K4 has been linked to trophoblast hyperinvasion of human placenta, yet its role in human cancer, especially in intrahepatic cholangiocarcinoma (ICC), remains unknown.
Methods: The mRNA and protein expression (n = 71), as well as coding mutations (n = 124), of MAP3K4 were determined in ICC and matched nontumor liver tissues. Clinical relevance and prognostic significance of MAP3K4 was also investigated (n = 322). The functional effects and underlying mechanisms of MAP3K4 were determined by shRNA mediated knockdown and TALE mediated re-expression in cholangiocarcinoma cell lines.
Results: Our previous whole-exome sequencing of ICC tumors and matched normal tissues have found that MAP3K4 had recurrent somatic mutations, suggesting that MAP3K4 is a putative driver gene in ICC. Herein, we showed that levels of MAP3K4 mRNA and protein were significantly reduced in ICC than paired nontumor tissues. Tumors with deficiency of MAP3K4 were more likely to have aggressive characteristics, such as larger size, vascular invasion and intrahepatic metastases than those with high expression. Importantly, low MAP3K4 expression independently correlated with dismal survival and increased tumor recurrence after curative surgery. Knockdown of MAP3K4 in cholangiocarcinoma cells markedly enhanced cell proliferation and invasiveness in vitro and tumor progression in vivo, accompanied by a typical epithelial-mesenchymal transition (EMT) process, including down-regulation of E-cadherin, up regulation of N-cadherin, vimentin, and snail, and a morphological transformation from epithelium to mesenchyma. In contrast, overexpression of MAP3K4 in cholangiocarcinoma cells obviously reversed EMT and inhibited cell invasion. Likewise, immunohistochemical images of ICC tissues revealed a negative correlation between expression of MAP3K4 and mesenchymal markers. By using a dominant negative of p38 mutant vector and a p38 inhibitor (SB203580), we showed that p38 persistently activated by MAP3K4 functions as a negative regulator of EMT in ICC cells by antagonizing the activity of the NF-κB/snail pathway. Consistently, immunohistochemical results in 322 ICC patients showed a significantly negative correlation of nuclear expression of p-p65 with expression of MAP3K4 and p-p38. In addition, about 10 % ICC patients contain somatic mutations in MAP3K4 that predicted to be detrimental to the kinase activity.
Conclusions: Deficiency of MAP3K4 promoted aggressive behavior of ICC cells, and MAP3K4 as a negative regulator that controlled multiple facets essential for ICC invasiveness, especially the EMT processes.

Topic 8: Gall Bladder and Biliary Tract

No: 1103

Comparison on gallstone dissolution efficacy between CNU and UDCA according to stone density on CT scan

Jong Jin Hyun[1], Sang Jun Suh[1], Seung Young Kim[1], Sung Woo Jung[1], Young Kul Jung[1], Ja Seol Koo[1], Hyung Joon Yim[1], Hong Sik Lee[1], Sang Woo Lee[1]

Korea Univsersity Ansan Hospital Internal Medicine Ansan-Korea, South[1]

Aim: Gallstone dissolution is normally performed for radiolucent gallstones in functioning gallbladder. However, absence of visible gallstone on plain abdominal X-ray does not always preclude calcification. This study aims to compare the response and dissolution rate between ursodeoxycholic acid (UDCA) and CNU®(combination of UDCA and chenodoxycholic acid) according to stone density on CT scan.
Method: A total of 84 patients (CNU grou$P$ = 46, UDCA grou$P$ = 38) completed dissolution therapy which was started from December 2010 to March 2014. Partial dissolution of gallbladder stone was defined as reduction in stone volume of >50 %. Response was defined as complete dissolution or partial dissolution. Dissolution efficacy was defined as % decrease in the stone volume. Stone density on abdominal CT scan was divided into 4 categories: hypodense, isodense, hyperdense, and calcified. RESULTS: The baseline age (48.83 ± 14.68 years vs. 53.74 ± 17.72 years), treatment duration (183.17 ± 15.33 days vs. 181.37 ± 14.64 days), and pre-treatment stone size (8.81 ± 4.35 mm vs. 9.72 ± 4.76 mm) were not different between the two groups. Response to therapy was observed in 41.3 % (19/46) and 57.9 % (22/38) of patients after CNU and UDCA treatment, respectively (P = 0.133). Dissolution efficacy of CNU group and UDCA group was 37.55 ± 44.63 % and 54.98 ± 47.27 %, respectively (P = 0.087). When only isodense stones were analyzed, response to therapy rose to 80.0 % and 83.3 % with CNU and UDCA treatment, respectively (P = 0.577). Dissolution efficacy also increased to 77.34 % and 80.64 % with CNU and UDCA treatment, respectively.
Conclusion: Patients with gallbladder stones that were isodense showed much better response to dissolution therapy with CNU and UDCA showing comparable efficacy. Therefore, CT scan should be performed prior to medication therapy if stone dissolution is intended.

Topic 9: Hepatic Surgery

No: 1515

Clinical impact of preoperative virtual hepatectomy on surgical management for hepatocellular carcinoma

Junichi Shindoh[1], Yoshihiro Mise[2], Shoichi Sato[2], Yasuji Seyama[3], Masaji Hashimoto[1], Nobutaka Umekita[3], Goro Watanabe[1], Norihiro Kokudo[2]

Toranomon Hospital Department of Digestive Surgery Tokyo-Japan[1], University of Tokyo Hepatobiliary-pancreatic Surgery Division Tokyo-Japan[3], Tokyo Metropolitan Bokutoh Hospital Department of Surgery Tokyo-Japan[2]

Background: Recent developments in computer simulation technique have enabled preoperative simulations of various liver resections and contributed to adequate decision making during selection of surgical procedures. However, actual clinical impact of virtual hepatectomy through the computer simulation technique remains to be determined.
Methods: 746 patients who underwent liver resection for hepatocellular carcinoma (HCC) in three Japanese high-volume hepatobiliary centers were reviewed, and the clinical impact of preoperative liver simulation was assessed.
Results: Anatomic liver resection was more frequently adopted in patients who underwent preoperative liver simulation (182/256, 71 %) compared with those without preoperative simulation (206/490, 42 %) ($P < 0.001$). This tendency was evident especially in patients with decreased hepatic functional reserve [71 % vs. 48 % among patients with indocyanine green retention rate (ICG-R15) of 11-20 % ($P < 0.001$) and 49 % vs. 16 % among those with ICG-R15 > 20 % ($P < 0.001$)]. Recurrence-free survival rate in patients with oligonodular HCC (<= 3 nodules, <= 3 cm) with decreased hepatic functional reserve (ICG-R15 > 10 %) was significantly higher in patients who underwent preoperative liver simulation than those without preoperative simulation ($P = 0.04$).
Conclusions: With introduction of the computer-based liver simulation technique, more curative surgical options could be selected based on the objective measures for liver volume which is obtained through the virtual hepatectomy. Preoperative surgical planning through the virtual hepatectomy may contribute to improve the long-term outcomes of patients undergoing hepatectomies for HCC.

Topic 9: Hepatic Surgery

No: 1600

Utility of selective hepatic vascular exclusion for hepatectomy for tumor locating at hepatic vein trunk

Akira Maki[1], Yuta Kogure[1], Testuya Mitsui[1], Riki Ninomiya[1], Masahiko Komagome[1], Syoichi Sato[1], Fumihiko Ozawa[1], Masanori Mastuda[2], Hideki Fujii[2], Yoshifumi Beck[1]

Saitama Medical University Saitama Medical Center Surgery Kawagoe-Japan[2], University of Yamanashi Surgery Kofu-Japan[1]

Aim: Hepatectomy for tumor at the hepatic vein trunk still remain challenging procedure because of risk of profound hepatic venous bleeding. Selective hepatic vascular exclusion (SHVE) is a technique to reduce bleeding during hepatectomy by clamping hepatic venous flow selectively in addition to Pringle's maneuver. The aim of this study is to evaluate the utility of SHVE in the hepatectomy for the tumor at major hepatic vein trunk.
Patient and methods: 126 patients, who underwent hepatectomy in University of Yamanashi hospital since January 2010 to November 2012, were retrospectively reviewed. Selective encirclement of hepatic vein trunk was performed in 26 patients. Hepatic vein clamping was carried out in 14 out of those 26 patients; identified as SHVE. Only Pringle's maneuver was carried out in the other 12 patients; identified as Control. Operative time, Duration of blood flow control, estimated blood loss and morbidity during hospital stay were compared between the two groups.
Result: No mortality was recognized in both groups. The mean operative time were 515 min in SHVE and 475 min in Control. The duration of blood flow control were 67 min in SHVE and 52 min in Control. The mean estimated blood loss were 967 ml in SHVE and 621 ml in Control, significantly larger in SHVE. No difference in morbidity was found between two groups.
Conclusion: SHVE may not be inferior to the conventional Pringle's maneuver even though SHVE was tended to apply to the tougher case.

Topic 9: Hepatic Surgery

No: 1165

Anterior hepatic transection for caudate lobectomy to treat hepatic tumors situated in or involving the paracaval portion of the caudate lobe

Zhen-guang Wang[1], Wei-ping Zhou[1]

Eastern Hepatobiliary Surgery Hospital 3rd Department of Liver Surgery Shanghai-China[1]

Background: Caudate lobectomy using the anterior split liver approach is a proper but technically demanding operation for tumors situated in or involving the paracaval portion of the caudate lobe. This study was designed to share our experience in this operation
Method: From August 2004 to May 2014, 72 patients received caudate lobectomy using the anterior split liver approach in our department. The clinicopathologic and perioperative data, complications and survival were analyzed.
Results: The operations were successfully carried out and there was no 30-day or 90-day perioperative mortality. Seventeen patients (23.6 %) received isolated caudate lobectomy, 13 patients (18.1 %) took caudate lobectomy plus segmentectomy IV, V, VIII and 42 patients (58.3 %) received caudate lobectomy plus segmentations IV. The median tumor size was 8 cm (range, 2.4-30 cm), the operating time was 210 min (range, 120-445 min) and the blood loss was 800 ml (range, 200-5000 ml). The postoperative complication rate was 34.7 %. Patients in the isolated caudate lobectomy group (n = 17) had more liver cirrhosis ($P < 0.001$), smaller tumor size ($P < 0.001$), less platelet ($P < 0.001$), more operating time ($P = 0.046$) and were older ($P = 0.018$) than those in the associated resection group (n = 55), but had no significant difference in intraoperative blood loss, postoperative liver function and complications.
Conclusion: Caudate lobectomy using the anterior split liver approach was technically feasible and safe for patients with the tumor situated in or involving the paracaval portion of the caudate lobe. An associated resection with partial or whole mesohepatectomy was preferred in patients with no or mild liver cirrhosis.

Topic 9: Hepatic Surgery

No: 1420

Impact of sarcopenia on short and long term outcomes in patients undergoing hepatectomy for hepatocellular carcinoma

Yuhei Hamaguchi[1], Toshimi Kaido[1], Shinya Okumura[1], Yasuhiro Fujimoto[1], Kohei Ogawa[1], Akira Mori[1], Etsuro Hatano[1], Shinji Uemoto[1]

Kyoto University Department of Surgery Kyoto-Japan[1]

Background: Skeletal muscle depletion, referred to as sarcopenia, has been shown to be an independent predictor of lower disease-free and overall survival in various kinds of diseases. The quality of skeletal muscle has recently attracted much attention as a new parameter of sarcopenia, but the impact on outcomes in patients undergoing.
Patients and methods: We performed a retrospective analysis of 477 patients undergoing hepatectomy for HCC in our institution between April 2005 and August 2014. The quality of skeletal muscle was evaluated by intramuscular adipose tissue content (IMAC) using preoperative CT imaging at the umbilical level. The impact of IMAC on postoperative morbidity and mortality was analyzed.
Results: The overall and recurrence-free survival rates were significantly lower in patients with high IMAC than in patients with normal IMAC ($P < 0.001$, $P = 0.001$, respectively). Multivariate analysis showed that preoperative high IMAC was the significant risk factor for death (Odds ratio [OR] = 5.306; $P < 0.001$) and for HCC recurrence (OR = 1.754; $P = 0.005$). In addition, preoperative high IMAC was identified as an independent risk factor for increased severe (Clavien grade IIIa or higher) postoperative complications (OR = 1.634; $P = 0.039$) and infectious postoperative complications (OR = 1.949; $P = 0.023$).
Conclusion: Preoperative sarcopenia evaluated by measuring IMAC was closely involved with short- and long-term outcomes in patients undergoing hepatectomy for HCC.

Topic 10: Hepatitis B

No: 1863

Safety and efficacy of tenofovir disoproxil fumarate in patients with chronic hepatitis B related decompensated cirrhosis

Myeong Jun Song[1], Byung Seok Lee[2], Tae Hee Lee[3], Suk Bae Kim[4], Hee Bok Chae[5], Il Soon Jeong[1], Soon Young Ko[6]

The Catholic University of Korea Internal Medicine Daejeon-Korea, South[1], Chung Nam University Internal Medicine Daejeon-Korea, South[2], Konyang University Internal Medicine Daejeon-Korea, South[3], Dankook University Internal Medicine Chenan-Korea, South[4], Chung Buk University Internal Medicine Chengju-Korea, South[5], Konkuk University Internal Medicine Chungju-Korea, South[6]

Background: Data are limited on the safety and effectiveness of tenofovir disoproxil fumarate (TDF) other than lamivudine and adefovir dipivoxil for treatment of chronic hepatitis B (CHB) in patients with decompensated liver cirrhosis. We evaluated TDF as first line therapy in decompensated liver disease.
Methods: We enrolled 42 HBV-infected patients with decompensated cirrhosis primarily treated with 300 mg/day TDF in Korean six multicenter, and evaluated the clinical outcomes. We also compared the virological responses of 37 patients treated for 12 months (decompensated group) with those of 103 compensated cirrhosis patients (compensated group).
Results: Tenofovir treatment for 12 months resulted in improved Child and model for end-stage liver disease (MELD) scores. Seventy percent (26/37) of patients achieved CTP class A and 45.9 % (17/37) showed improvement in the CTP score of 2 points after 12 months of ETV. The 1-year cumulative rates of HBV DNA negativity and HBeAg loss were 89.1 % (33/37) and 11.1 % (2/18), respectively. The rates of HBV DNA negativity, HBeAg seroconversion/loss and ALT normalization at month 12 were similar for the decompensated and compensated groups.
Conclusion: TDF therapy for 12 months was similarly effective in both compensated and decompensated liver cirrhosis patients. In addition, it improved underlying liver function and maintained stable renal function in decompensated patients.

Topic 10: Hepatitis B

No: 1864

Long terms outcomes of entecavir and tenofovir combination therapy for chronic hepatitis B in patients with previous nucleos(t)ide treatment failure

Muzzaffar Gill[1], Sidra Gill[2], Ammara Nawaz[3], Misbah Malik[3], Faiza Irfan[3], Hafsa Aziz[4]

Maroof International Hospital Gastroenterologist/hepatologist Islamabad-Pakistan[1], Maroof International Hospital Gastroenterologist Islamabad-Pakistan[2], Maroof International Hospital Gastroenterologist Islamabad-Pakistan[3], Maroof International Hospital Gastroenterologist Islamabad-Pakistan[4]

Combination therapy with entecavir (ETV) and tenofovir disoproxil fumarate (TDF), two potent agents with non-overlapping resistance profiles, may provide a single regimen suitable for all patients who failed on other NUC regimens. we are presenting two year results of our ongoing study assessing ETV + TDF for patients with prior failure on NUC therapy.

Topic 10: Hepatitis B

No: 2113

A clinical study on anti HBV dc inducing therapy in the nonactive HBsAg carriers

Bang-fu Wu[1], Jiang-ying Yang[1], Yong Liu[2], Xuan-qin Wang[2], Xiang-hua Huang[2], Zheng-sheng Xiao[2], Xue-song Li[2], Ming Yang[2], Tuo-pu Wu[1]

Guangzhou Pubang Bio-immunological Tech Research Institute Tech Department Guangzhou-China[1], Southern Medical University Renkang Hospital Gastroenterology and Hepatology Center Dongguan-China[2]

Aims: To observe the clinical efficacy of the anti-HBV-dendritic cells (DC) inducing therapy in the nonactive HBsAg carriers.
Methods: 14 male and 16 female nonactive HBsAg carriers were recruited in the study. Patient's median age was 30 years (from 21 to 56 years). All patient's ALT was normal and HBVDNA was negative. The anti-HBV-DC inducing agent which been an admixture of hepatitis B vaccine containing 20 μg HBsAg, rhGM-CSF 50 μg and BCG polysaccharide nucleic acid 2 ml was injected hypodermically

to the patient once every two weeks for 18 practices applications totally. Quantitative HBVM (TRFIA) and HBVDNA were evaluated at week 0, 12, 24 and 36.

Results: The HBsAb positive conversion rate were 36.67 %(11/30), 83.33 %(25/30) and 96.67 %(29/30) at week 12, 24 and 36. The HBsAg negative conversion and the HBsAg seroconversion were observed in three patients (10.00 %, 3/30) at week 24 and in seven patients (23.33 %, 7/30) at week 36. The low levels positive HBVDNA was observed in three patients at week 12 and in one patient at week 24.

The rate of adverse effect was 36.85 %. The adverse effect include fever, headache, ache all over, bellyache, urticaria and hives, dyspnea, and tumefaction ache in the injection site after injected the anti-HBV-DC inducing agent.

Conclusions: The anti-HBV-DC inducing agent can induce the subcutaneous immature DC become to mature DC, and restart the immune responses against HBV. The anti-HBV-DC inducing therapy can be considered as an efficient approach for nonactive HBsAg carriers, which may effectively improve the HBsAb positive conversion and the HBsAg seroconversion.

Topic 10: Hepatitis B

No: 2152

Deep bradycardia and acute hepatitis caused by acute reactivation of chronic hepatitis B three case report

Hasan Karsen[1], A. Sezin Şeyhanoğlu[1]

Harran University Infectious Diseases Şanlıurfa-Turkey[1]

Chronic hepatitis B reactivation may be resulted in complications from a mild ALT elevation to fulminant hepatitis culminating lately in death. The cause of reactivation may generally be an immunosuppression, malignity, chemotherapy, coinfections with HIV, and physical and emotional stresses. In this article, we discussed the acute reactivation of chronic hepatitis B in three patients who were priorly in healthy HBV carrier state due to physical stress. In the result of reactivation developed HBeAg reversion, Anti-HBc IgM positivity, elevation of total bilirubin to 25 mg/dL and ALT elevation to 2000 U/L. All three patients presented with acute hepatitis and deep bradycardia. Recovery was available with medical treatment and insertion of a cardiac pacemaker into chests of two patients, while in the third patient was achieved with only medical treatment as teophylline. Because a deep bradycardia secondary to hepatitis B has not been reported until now as far as we know, this article was found to be worthy to be presented.

Topic 10: Hepatitis B

No: 1957

Performance evaluation and clinical application of a newly developed ultra sensitive hepatitis B virus surface antigen quantitative assay

Ruifeng Yang[1], Lai Wei[1]

Peking University People's Hospital Peking University Hepatology Institute Beijing-China[1]

Objective: We aimed to evaluate the performance of a new ultrasensitive HBsAg quantitative assay, the Fujirebio Lumipulse HBsAg assay, and analyze the correlation among serum HBsAg, HBV DNA and HBeAg in treatment naïve chronic hepatitis B (CHB) patients.

Methods: An HBsAg reference panel (03/262) was used to assess the sensitivity and accuracy of the Lumipulse assay. Serum HBsAg from 112 HBeAg positive treatment naïve CHB patients was quantified using the Lumipulse and Abbott Architect assays. HBsAg results yielded by the Lumipulse assay through different on-board dilutions (1: 1000, 1: 200 and 1: 100) were also compared. Serum HBV DNA was quantified using the Abbott Realtime assay. HBeAg was quantified using the Roche Elecsys assay. HBV was genotyped via S region direct sequencing. Moreover, 32 samples with coexistence of HBsAg and anti-HBs antibody were tested using the Architect and Lumipulse assays.

Results: The Lumipulse assay had a sensitivity of 0.0048 IU/ml HBsAg (95 % CI: 0.0032-0.0055 IU/ml). HBsAg results from both assays displayed an excellent linear correlation in either genotype B or C samples ($R2 = 0.98$, $P < 0.01$, Figure A). There was no difference among the results through different Lumipusle on-board dilutions ($P = 0.95$). Although the Lumipulse assay had a pre-treatment process when the antigen–antibody could be dissociated, no significantly higher HBsAg results were found using the Lumipulse than using the Architect assay in sera with concurrent HBsAg and anti-HBs antibody. Serum HBsAg level was strongly correlated with HBV DNA ($R = 0.74$, $P < 0.01$) and moderately correlated with HBeAg ($R = 0.49$, $P < 0.01$, Figure B&C).

Conclusions: The Lumipulse assay is sensitive and accurate for infection screening and CHB monitoring.

Topic 10: Hepatitis B

No: 1379

Total hepatitis B core antigen antibody a quantitative non invasive marker of hepatitis B virus induced liver disease

Quan Yuan[1], Liu-wei Song[1], Daniela Cavallone[2], Francesco Moriconi[2], Beatrice Cherubini[2], Piero Colombatto[2], Filippo Oliveri[2], Barbara Coco[2], Gabriele Ricco[2], Ferruccio Bonino[3], James Wai Kuo Shih[1], Ning-shao Xia[1]

National Institute of Diagnostics and Vaccine Development In Infectious Diseases, School of Public Health, Xiamen University State Key Laboratory of Molecular Vaccinology and Molecular Diagnostics Xiamen-China[1], University Hospital of Pisa Laboratory of Molecular Genetics and Pathology of Hepatitis Viruses, Hepatology Unit Pisa-Italy[2], University Hospital of Pisa General Medicine 2 Liver and Digestive Disease Pisa-Italy[3]

Background and aim: Non invasive immunologic markers of virus-induced-liver-disease are unmet needs. We tested the clinical significance of quantitative total and IgM-anti-HBc in well-characterized chronic-HBsAg-carriers.

Methods: Sera (212) were obtained from 111 HBsAg-carriers followed-up for 40 months (18-216 months) during different phases of chronic-HBV-genotype-D-infection; 10 HBeAg-positive, 25 inactive-carriers (HBV-DNA $\leq$ 2000 IU/ml, ALT $<$ 30 U/L), 66 HBeAg-negative/anti-HBe-positive-CHB-patients and 10 with HDV-superinfection. In 35 patients treated with Peg-IFN (180 μg/w for 12 m) sera were obtained at baseline, end-of-therapy and week-24 off-therapy and in 22 treated with nucleos(t)ide-analogues (for 60 months mean, 42-134 months range) at baseline and end-of-follow-up. IgM- and total-anti.HBc were measured by Architect (Abbott, USA) and double-antigen-sandwich-immune (Wantai, China) assays respectively.

Results: Total-anti-HBc was positive in all sera with lower levels ($P < 0.0001$) in HBsAg-carriers without CHB (immune-tolerant, inactive and HDV-superinfected, mean 3.26, range 2.26-4.49 Log10 IU/ml) versus untreated-CHB (mean 4.68, range 2.76-5.54 Log10 IU/ml). Thirty of 212 (14.2 %) sera were IgM-anti-HBc-

positive using acute-hepatitis-cut-off (1-S/CO value) and 102 (48.1 %) with chronic-hepatitis-cut-off" (0.130-S/CO.Total-anti-HBc declined in CHB-patients with SVR ($P < 0.0001$) treated with antivirals [Figure 1, groups a) inactive-carriers, b) baseline-untreated-HBeAg-negative-CHB, c) EOF-HBeAg-negative-CHB with SVR after Peg-IFN, d) EOF in NUC-treated-patients]; the lowest levels were found in SVR who cleared HBsAg subsequently. During spontaneous and therapy-induced CHB remissions and reactivations both total- and IgM-anti-HBc correlated with ALT ($P < 0.001$, $r = 0.351$ and $P = 0.008$, $r = 0.185$ respectively).
Conclusions: Total-anti-HBc qualifies as a useful marker of HBV-induced-liver-disease that might help to discriminate major phases of chronic HBV infection and to predict sustained response to antivirals.

Topic 10: Hepatitis B

No: 1540

Reactivation of hepatitis B virus and clinical outcome in Korean patients with hematologic malignancy

Ji Won Han[1], Hee Chul Nam[1], Hae Lim Lee[1], Si Hyun Bae[1], Jong Young Choi[1], Seok Goo Cho[1], Chang Ki Min[1], Hee Je Kim[1], Dong Wook Kim[1], Seung Kew Yoon[1]

The Catholic University of Korea Internal Medicine Seoul-Korea, South[1]

Backgrounds: To investigate the frequency, risk factors and outcome of HBV reactivation in Korean patients with hematologic malignancy.
Materials and methods: We retrospectively collected the clinical data of 4355 patients with hematologic malignancy, who visited hematology clinic between June, 2008 to May, 2014 at Seoul St. Mary's hospital, Korea.
Results: 112 of 4355 (2.6 %) patients were HBsAg-positive and 4243 patients were HBsAg-negative. In the latter group, anti-HBc test was performed only in 702 patients before chemotherapy or hematopoietic stem cell transplantation (HSCT) and 372 patients were anti-HBc-positive. HBV reactivation occurred in 18 of 372 (4.8 %) patients within a median of 23.5 months (range 3–76) after HSCT or chemotherapy. At the time of HBV reactivation, the median level of serum alanine aminotransferase (ALT) was 42 U/mL (range 19–1915), and the median level of serum HBV DNA was 7.67 log10 IU/mL (range 3.28–9.34). 13 of 18 patients with HBV reactivation were treated with tenofovir or entecavir. 5 of 13 patients achieved HBsAg seroclearance within a median of 4 months (2–28). 4 patients achieved a partial virologic response. 3 patients died due to the underlying disease before the response evaluation and 1 patient died due to the hepatic failure induced by HBV reactivation.
Conclusion: Clinical manifestation of HBV reactivation can vary asymptomatic to fatal hepatic failure. Periodic check of HBV DNA and serologic markers after initiation of chemotherapy and hematopoietic stem cell transplantation is needed, especially in HBsAg-negative, anti-HBc-positive patients.

Topic 10: Hepatitis B

No: 1410

Virologic characterization and association with disease progression in children with chronic hepatitis B virus BCP PC mutants

Yanwei Zhong[1], Hongfei Zhang[1], Shishu Zhu[10], Yi Dong[1], Zhiqiang Xu[1], Dawei Chen[1], Limin Wang[1], Yu Gan[1], Fuchuan Wang[1], Xiuchang Zhang[2]

Beijing 302 Hospital Pediatric Liver Disease Therapy and Research Center, Institute of Infectious Diseases, Beijing-China[1], He Bei North University Zhangjiakou-China[2]

Background/aims: To investigate virologic characterization and association with disease progression in children with chronic hepatitis B virus BCP/PC mutants
Methods: A total of 307 patients with a CHB infection, including 88 with hepatitis B related liver cirrhosis and 219 with chronic hepatitis B were enrolled. The HBV genotypes and the presence of mutations in the BCP/PC regions were determined by direct sequencing. Biochemical and serological parameters as well as HBV DNA level were routinely performed. Mutations at 11 interested sites of the BCP/PC region were compared among the two groups of patients.
Results: 46/307 (14.98 %) were infected with genotype B and 261/307 (85.02 %) with genotype C. LC and CHB patients both had a significantly higher ratio of genotype C to B (81.9 %-18.1 % vs. 70.1 %–29.9 %). The prevalence of BCP/PC wild-type virus was 54.3 % in CHB patients in contrast to 4.8 % in LC patients. In genotype C patients, the C1653T T1753C, A1762T, G1764A, G1896A mutations were significantly higher prevalent in LC patients. Genotype B virus had higher 1752 mutation frequency. Genotype C virus had higher prevalence of T1753C, T1758C, A1762T, G1764A, G1896A mutation frequency compared to genotype B virus. CHB patients with BCP/PC mutant virus had higher viral load, whereas LC patients with BCP/PC mutant virus had higher viral load and elevated alanine aminotransferase in comparison with those with the wild-type virus.
Conclusions: Children patients with genotype C virus, BCP/PC C1653T, A1762T, G1764A, G1896A mutant virus were more susceptible to develop LC, whereas high prevalence of the BCP/PC mutations was associated with CHB development.

Topic 10: Hepatitis B

No: 1893

Association between chronic hepatitis B virus infection and HLA gene RS3128917 and RS9380343 polymorphisms

Ersin Akgöllü[1], Hikmet Akkız[1], Ramazan Bilgin[2], Yakup Ülger[1], Oğuz Üsküdar[1], Aynur Bekar[1], Berrin Yalınbaş Kaya[1]

University of Çukurova Department of Gastroenterology Adana-Turkey[1], University of Çukurova Department of Chemistry Adana-Turkey[2]

Aim: Hepatitis B virus (HBV) affects approximately 350 million people worldwide. 10–15 % of chronic carriers develop liver cirrhosis (LC), liver failure and hepatocellular carcinoma (HCC), and the remaining individuals achieve nonreplicative state. Persistent HBV infection or HBV clearance is influenced by both viral and host factors. GWAS identified the human leukocyte antigen (HLA) gene polymorphisms rs3128917 and rs9380343 to be associated with chronic hepatitis B. HLA genes have been linked to immune response to infectious agents, but genetic variants that influence HLA mRNA expression might also affect antigen presentation. Therefore, antigen presentation can not be done adequately. We aim to evaluate the association between HLA gene polymorphisms and the risk for developing of chronic HBV infection.
Methods: HLA gene polymorphisms were investigated in a case–control study of 215 persistent HBV carriers and 214 persons with HBV natural clearance by using a polymerase chain reaction–restriction fragment length polymorphism (PCR–RFLP) assay.

Results: There is no association between the allele or genotype of HLA polymorphisms and the risk of chronic HBV infection in the Turkish subjects examined ($p > 0.05$). Additionally, no significant association was found between neither global test nor individual haplotypes, but the GT haplotype was increased the risk of chronic HBV infection (OR = 3.17; 95 % 1.00–10.0, $P = 0.05$).
Conclusions: Our results demonstrate for the first time that GT haplotype of HLA polymorphisms is a genetic susceptibility factor for chronic HBV infection in Turkish population. Further studies are needed to validate our findings in a larger series, as well as in patients of different ethnic origins.

Topic 10: Hepatitis B

No: 1425

Association between polymorphisms of sodium taurocholate cotransporting polypeptide gene (SLC10A1) and different phonotype of chronic HBV infection

Dengming He[1], Shiqi Tao[1], Xianghua Zeng[1], Maoshi Li[1], Shimin Guo[1], Yuming Wang[2]

Southwest Hospital, Third Military Medical University Institute of Infectious Disease Chongqing-China[1], Southwest Hospital, Third Military Medical University Institute For Infectious Diseases Chongqing-China[2]

Background and aim: Genetic background is an important factor of disease. Sodium taurocholate cotransporting polypeptide (NTCP, encoded by SLC10A1), a multiple transmembrane transporter predominantly expressed in the liver, was found as a functional receptor for HBV. We aimed to observer the association between SLC10A1 polymorphisms and the multiple clinical phenotypes of chronic HBV infection.
Methods: 1454 cases was divided into six groups, including HBV clearance (group A, 273 cases), chronic HBV infection (group B, 1181 cases), immune tolerance (group C, 101 cases), HBeAg-positive chronic hepatitis B (CHB) (group D, 365 cases), HBeAg-negative CHB (group E, 231 cases), and inactive HBsAg carrier (group F, 410 cases). Two SNPs for SLC10A1, rs12882299 and rs4646287, were selected for genotyping.
Results: For rs12882299, there was no significant difference between group A and group B ($P = 0.47$), group C and group D ($P = 0.39$), group E and group F ($P = 0.53$), group A and group F ($P = 0.54$). For rs4646287, there was no significant difference between group A and group B ($P = 0.45$), group C and group D ($P = 0.38$), group D and group E ($P = 0.51$), group E and group F ($P = 0.98$), group A and group F ($P = 0.32$). The significant difference was only seen in rs12882299 ($P = 0.02$, OR = 1.64 [1.07-2.49]) between group D and group E. The susceptibility of HBeAg-negative CHB for genotype T/T–T/C is significant higher than for genotype C/C compared with HBeAg-positive CHB.
Conclusions: Although polymorphisms of SLC10A1 are associated with the susceptibility of HBeAg-negative CHB compared with HBeAg-positive CHB, it seems no special value for the mechanism of different phenotypes of chronic HBV infection.

Topic 10: Hepatitis B

No: 1821

Viral hepatitis control in China a systematic identification of the barriers to clinical treatment

Jack Wallace[1], Marian Pitts[1], Chaojie (george) Liu[2], Vivien Lin[3], Lai Wei[4], Behzad Hajarizadeh[5], Jacqui Richmond[1]

La Trobe University Australian Research Centre In Sex, Health and Society Melbourne-Australia[1], La Trobe University China Health Program Melbourne-Australia[2], La Trobe University School of Public Health and Human Biosciences Melbourne-Australia[3], Peking People's University Hospital Beijing-China[4], La Trobe University/university of NSW Australian Research Centre In Sex, Health and Society/kirby Centre Sydney-Australia[5]

Background: China has the largest absolute number of people in the world infected with chronic viral hepatitis. Prevention interventions have successfully reduced new infections but there is an increasing burden of chronic viral hepatitis. This project aimed to reduce the burden of chronic viral hepatitis on people infected with hepatitis B and/or hepatitis C by documenting the personal impact of the infection, including barriers to clinical management.
Methods: The qualitative study used semi-structured interviews with people with chronic viral hepatitis in four Chinese cities during April 2014. The interview data was systematically reviewed to identify key issues, concepts and themes.
Results: While clinical services were accessible, essential barriers to these services include inadequate reimbursement of pharmaceutical treatments; poor understanding of the impact of the infection; the social impact of the infection including stigma and discrimination; inconsistent screening and diagnostic processes that are conducted by non-health related services, and the lack of understanding about viral hepatitis within the broader community. While most participants monitored their infection, treatment choices were determined by economic access. The lack of public funding for pharmaceutical treatments has a substantial individual, social and economic impact, particularly when several family members are affected by viral hepatitis.
Conclusion: Improving access to clinical services in China is imperative if the continued burden of the infection is to be reduced. There are clear barriers to this access that need to be addressed. Policy responses in China need to reduce barriers to treatment, raise public awareness and reduce stigma.

Topic 10: Hepatitis B

No: 1408

Correlates of disease specific knowledge among patients with chronic hepatitis B or hepatitis C infection in India

Aracely Tamayo[1], Samir R. Shah[2], Shiv K. Sarin[3], Abhijit Chowdhury[4], Padaki Nagaraja Rao[5], Phillip Dinh[6], Steven J. Knox[6], Bittoo Kanwar[6], Anuj Gaggar[6], G. Mani Subramanian[6], John G. Mchutchison[6], Virukalpatti Gopalratnam Mohan[7], Ajit Sood[8], Rajiv Mehta[9], Shobna Bhatia[10]

University of California Berkeley School of Public Health Epidemiology Berkeley-United States[1], Jaslok Hospital and Research Centre and Breach Candy Hospital Mumbai-India[2], Institute of Liver and Biliary Sciences New Delhi-India[3], Institute of Post Graduate Medical Education and Research Kolkata-India[4], Asian Institute of Gastroenterology Hyderabad-India[5], Gilead Sciences, Inc. Foster City-United States[6], Vgm Hospital Tamil Nadu-India[7], Dayanand Medical College & Hospital Ludhiana-India[8], Liver Clinic Surat-India[9], Seth Gs Medical College and Kem Hospital Mumbai-India[10]

Methods: Untreated patients chronically infected with HBV (n = 500) or HCV (n = 500) were enrolled at 19 centers across India. An India Hepatitis Knowledge Index (IHKI), adapted from the

National Health and Nutrition Analysis Survey questionnaire, was administered at a single visit to assess HBV/HCV knowledge, community disease awareness, treatment quality, and health care barriers. A higher IHKI score (range 0–10) indicated increased hepatitis knowledge. Multivariate regression models evaluated demographic and disease factors.
Results: The overall mean IHKI score was 5.6 out of 10, with higher scores among patients with HBV (5.9) than HCV (5.3); $P < 0.001$. Among HBV patients, higher IHKI was associated with duration of disease ($P = .014$) and residing in western India ($P = .04$). Among HCV patients, higher IHKI was associated with lower age ($P = .024$), longer duration of disease ($P = .033$), attending private health care clinics ($P = .001$), and residing in eastern India ($P = 0.009$). Among HBV patients, IHKI was independently associated with disease severity as assessed by MELD score (Figure), albumin, and APRI. This association was strongest for HBV patients with elevated ALT and HBV DNA > 2000 IU/mL. Among HCV patients, IHKI results had no associations with disease severity.
Conclusion: The association of IHKI with disease underscores the need to understand connections between hepatitis knowledge and disease progression and may guide efforts to address patient education and awareness of chronic viral hepatitis.

Topic 10: Hepatitis B

No: 1776

HIV HBV coinfected patient with high HBV DNA level responding to pegylated interferon treatment a case report

Alper Gunduz[1], Ahsen Bas Oncul[2], Dilek Yildiz Sevgi[2], Aziz Ahmad Hamidi[2], Ahmet Sanli Konuklar[2], Nuray Uzun[3], Ilyas Dokmetas[2]

Sisli Etfal Training and Research Hospital Infectious Diseases Istanbul-Turkey[1], Sisli Etfal Training and Research Hospital Infectious Diseases Istanbul-Turkey[2], Sisli Etfal Training and Research Hospital Infectious Diseases Istanbul-Turkey[3]

Background: Coinfection with HBV and HIV is accompanied by an increased risk for liver related morbidity and mortality compared with monoinfection if left untreated. Most of the guidelines advocate starting highly active antiretroviral therapy (HAART) including nucleos(t)ide as part of it if the patients meet the criteria for CHB treatment even in cases with high CD4 count. Pegylated interferon alfa treatment is favored in patients with CHB infection genotype A, low HBV DNA and high ALT levels.
Case report: We report the case of a 25-year-old homosexual man presenting with positive HIV-1 serology at first observation in March 2011. The laboratory tests showed HIV RNA 88.000 copy/ml, CD4 count 770/mm3, elevated transaminases. He was positive for HBsAg, HBeAg, anti-HBc and negative for anti-HBe, anti-HBs, anti-HDV. HBV DNA was 500.000.000 IU/ml. The patient was followed for 96 weeks and didn't receive any HAART. The transaminases fluctuated between 1.5-twofolds of the upper normal limit. Liver biopsy was performed and it revealed Ishak fibrosis score: 2 with histology activity index: 7. HIV RNA level was 76.000 copy/ml and CD4 count 730/mm3. Pegylated interferon alfa 2a 180 mcg weekly was initiated for 48 weeks. At week 48 HBV DNA level was below the detectable level 20 IU/ml with HBsAg loss without any seroconversion. Nine months after stopping treatment the patient still had undetectable HBV DNA, negative HBsAg, HBeAg and normal transaminases.
Result: To our opinion pegylated interferons might be a good choice especially in HIV/HBV coinfected very slow progressors and elite controllers.

Topic 10: Hepatitis B

No: 2200

Regional seroprevalence and burden of HIV HBV coinfection a global systematic review

Lucy Platt[1], Philippa Easterbrook[2], Erin Gower[3], Homie Razavi[3], Peter Vickerman[4]

London School of Hygiene Epidemiology London-United Kingdom[1], Who Hiv Geneva-Switzerland[2], Cda Cda Boulder-United States[3], University of Bristol Epidemiology Bristol-United Kingdom[4]

Background: There is a paucity of country level data on the prevalence of HIV-hepatitis B (HBV) co-infection, especially from resource-limited settings. Reliable estimates are needed to inform the development of regional and national strategies for hepatitis screening and management.
Methods: We undertook a global systematic review and meta-analysis of the prevalence of HIV-HBsAg coinfection through a comprehensive search of 12 bibliographic databases. Eligible studies had examined HBsAg prevalence among HIV-infected adults at country level between 2002 and 2013, and where available, stratified by population or risk group (Gen population (Genpop), PWID, MSMs, Heterosexuals (Hetero), and pregnant women (Preg)). Study quality was rated based on study design, sample size, potential for selection bias, and assay quality. Regional burden of co-infection was derived by applying HBsAg prevalence in HIV-infected gen pop/risk groups to 2014 UNAIDS country/regional estimates of no. HIV infected.
Results: The search identified 25,236 articles, of which 10,874 remained after de-duplication and 1,606 met inclusion criteria after screening of abstracts. There were 483 country-level HBsAg prevalence estimates from 75/193 (39 %) countries. Based on 170 estimates of HBsAg prevalence among HIV-infected persons in 5 populations from 11 geographic regions, median prevalence ranged 1-11 % (Genpop), 7-27 % (PWID), 4-22 % (MSM), 3-17 % (Hetero), 0.5-9 % (Preg). The estimated IQ range of global burden of HIV-HBsAg co-infection is 1.5 to 5.5 million.
Conclusion: Sub-Saharan Africa has the highest regional burden of HIV-HBsAg co-infection, followed by South-east Asia and eastern Europe. There are several key methodological and analytic challenges in generating reliable estimates of country and regional prevalence of HIV- HBsAg co-infection.

Topic 10: Hepatitis B

No: 2034

The predictor for virologic response in multi drug resistant chronic hepatitis B treated by tenofovir mono rescue therapy

Sangheun Lee[1], Jun Yong Park[2], Do Young Kim[2], Beom Kyung Kim[2], Seung Up Kim[2], Kijun Song[3], Hye Jin Ku[2], Kwang-hyub Han[2], Sang Hoon Ahn[2]

Catholic Kwandong University College of Medicine Internal Medicine Incheon Metropolitan City-Korea, South[1], Yonsei University College of Medicine Internal Medicine Seoul-Korea, South[2], Yonsei University College of Medicine Biostatistics Seoul-Korea

Background: Tenofovir disoproxil fumarate (TDF) has demonstrated high antiviral efficacy of lamivudine-resistant (LAM-R) chronic

hepatitis B (CHB) virus infection. However, TDF mono-rescue therapy for the multiple drug resistance (MD-R) including LAM-R + adefovir–resistant (ADV-R) and LAM-R + entecavir-resistant (ETV-R) have been studied rarely. We investigated whether TDF mono-rescue therapy can effectively control in CHB patients with MD-R.
Methods: Three hundred eighty-seven patients with LAM-R (n = 267), LAM + ADV-R (n = 34) and LAM + ETV-R (n = 86) were reviewed retrospectively. During TDF mono-rescue therapy, we categorized them into three groups including patients with LAM-R, LAM-R + ADV-R, and LAM-R + ETV-R. We monitored virologic response rate defined as HBV DNA level with less than 20 IU/mL.
Results: There were no significant differences between three groups in demographic characteristics. In the median treatment of 15 months (range, 3–24 months), the cumulative virologic response rates were 227 (85.0 %), 28 (82.4 %), and 70 (81.4 %) in patients with LAM-R, LAM-R + ADV-R and LAM-R + ETV-R, respectively ($P = 0.016$ analyzed by univariate cox-regression analysis). However, in multivariate analysis to predict the virologic response, MD-R did not influence on the achievement of virologic response. The baseline HBV DNA level showed the significant influence on achieving the virologic response during the TDF mono-rescue therapy.
Conclusion: The most important factor to induce virologic response in CHB patients with MD-R is the baseline HBV DNA. The further follow up study were required for the evaluation of efficacy and safety of TDF mono-rescue therapy for CHB patients with MD-R.

Topic 10: Hepatitis B

No: 2199

New who guidelines for care and treatment of persons with chronic hepatitis B (CHB) infection in resource limited settings (RLS)

Philippa Easterbrook[1], Brian Mcmahon[2], Fumi Lesi[3], Geoff Dusheiko[4], Stefan Wiktor[1]

Who Hiv Geneva-Switzerland[1], Cdc Alaska Hepatology Anchorage-United States[2], University of Lagos Hepatology Lagos-Nigeria[3], Royal Free Hepatology London-United Kingdom[4]

Background: CHB is a major public health problem, particularly in resource limited settings (RLS). Although, several international guidelines for management of CHB exist, our objective was to develop WHO guidance relevant to care in RLS, where access to certain tests such as HBV DNA viral load or liver biopsy is limited.
Methods: 10 Systematic reviews were commissioned on key topics across the continuum of CHB care (staging of liver disease; who to treat; first and second line antiviral regimens; duration of therapy; monitoring for disease progression including HCC, treatment response and toxicity). Recommendations were formulated by a regionally representative Guideline Development Group in June 2014, based on the GRADE approach (grading of recommendations, assessment, development and evaluation) that includes assessment of quality of evidence, consideration of overall balance of benefits and harms (at individual and population level), patient/health worker values and preferences, resource use, cost-effectiveness, and feasibility. The strength of recommendation was rated as strong or conditional.
Results: Of the 17 recommendations, 11 (65 %) were rated as strong (based on moderate (7) or low (4) quality of evidence). Key recommendations included: - use of APRI as the preferred non-invasive test for presence of cirrhosis; prioritization of antiviral treatment for those with cirrhosis (or APRI score > 2); use of the antivirals- tenofovir and entecavir, with a high barrier to drug resistance for first and second-line treatment; lifelong therapy in those with cirrhosis; and 6-12 monthly monitoring for disease progression and HCC, treatment response and toxicity with ALT, HBeAg, HBV DNA (if available), and ultrasound/AFP.
Conclusion: These inaugural WHO guidelines on management of CHB provide a major opportunity to save lives and improve clinical outcomes in persons with CHB in RLS. Implementation at country level will require consideration of HBV epidemiology, health systems capacity, and laboratory services and supply systems for drugs and diagnostics.

Topic 10: Hepatitis B

No: 1444

Highly expression of tumor necrosis factor related apoptosis inducing ligand (TRAIL) and its receptors DR4 and DR5 correlating with the severity of disease in chronic hbv infection

Meifang Han[1], Yuanya Zhang[2], Weiming Yan[2], Tao Chen[2], Xiaoping Luo[3], Qin Ning[2]

Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology[1], Department and Institute of Infectious Disease Wuhan-China Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institution of Infectious Diseases Wuhan-China[2], Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department of Paediatrics Wuhan-China[3]

Aims: High expression and activation of tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) on natural killer (NK) cells could mediate hepatocyte apoptosis in patients with chronic hepatitis B (CHB). The aim of this study is to understand whether and however the NK cell induced and TRAIL mediated immune responses correlate with the disease severity in chronic HBV infection.
Methods: Liver tissues were obtained either from samples of organ transplant or biopsy. Liver NK cells and hepatocytes were isolated from 12 patients with HBV acute on chronic liver failure (HBV-ACLF), 18 with mild CHB and 7 healthy controls by the Magnetic beads. Real-time Quantification RT-PCR, Western blot and Immunohistochemistry assays were performed to investigate the expression of TRAIL and its receptors DR4 and DR5 in the hepatic NK cells and hepatocytes respectively.
Results: Increased expression of TRAIL in NK cells and DR4 and DR5 in hepatocytes were observed in patients with HBV ACLF compared with mild CHB ($P < 0.05$). The expression levels of DR4 and DR5 of hepatocyte, TRAIL expression in hepatic NK cells correlated positively with the hepatocyte apoptosis as well as the alanine aminotransferase levels in these patients.
Conclusions: These data suggested a high expression of TRAIL in NK cells and their receptor DR4, DR5 in hepatocytes in HBV ACLF may mediate a strong immune response which accounts for massive hepatocyte apoptosis.

Topic 10: Hepatitis B

No: 2097

Influence of antiviral therapy with liver stiffness evaluation in chronic hepatitis HBV patients in a real world setting preliminary data in a multicentric study

Luca Rinaldi[1], Vincenzo Messina[2], Giovanna Valente[1], Valerio Rosato[3], Rosa Zampino[4], Vincenzo Sangovanni[5], Luca Fontanella[6], Aldo Marrone[4], Antonio Ascione[6], Guido Piai[1]

Ospedale S. Anna E S. Sebastiano Uosd Satte Caserta-Italy[1], Ospedale S. Anna E S. Sebastiano Malattie Infettive Caserta-Italy[2], Ospedale Di Marcianise U.o.c. Medicina Interna Marcianise-Italy[3], S.u.n. Medicina Interna Napoli-Italy[4], Ospedale Cotugno Iii Divisione Epatologia Napoli-Italy[5], Ospedale Buon Consiglio Fatebenefratelli Centro Malattie Fegato Napoli-Italy[6]

Aim: The antiviral therapy with nucleos(t)ide analogues have changed the course of chronic hepatitis HBV-correlates; the long-term effects on fibrosis are subject to evaluation. Liver biopsy(LB) is the gold standard for staging liver fibrosis although in recent years tend to use non-invasive methods. Transient elastography (TE) may play a non-invasive alternative method. The aim of our study is to evaluate in a real world setting, the effects of antiviral therapy on liver stiffness measurement (LSM).
Methods: 149 HBV patients were enrolled from four centers in the Southern Italy; median age was 46,3 (M 98, F 51); 141patients underwent LB and TE; LB was not performed in eight patients (inactive carriers patients). Metavir liver fibrosis stage were assessed by three pathologists. The fibrosis Metavir stage was: F0 in 5(3,4 %), F1 in 43(28,9 %), F2 in 35(23,5 %), F3 in 34(28,8 %), F4 in 24(16,1 %) patients. The area under receiver-operating characteristic curves were: 0,79 (0,95 % confidence intervals, 0,67-0,91) for $F \geq 2$ and 0,83 (0,69-0,97) for $F = 4$. Optimal LSM cut-off values were 7,2 and 11,0 kPa for $F \geq 2$ and F4. 103 patients were treated with nucleos(t)ide analogues and 46 untreated. All patients were reassessed with TE after at least 12 months of therapy: TE value decreased significantly after antiviral treatment compared on baseline ($P < 0{,}001$).
Conclusions: LSM appears to be reliable for detection of significant fibrosis or cirrhosis in HBV. Long-term therapy induced a significant reduction on the LSM; this result, according to the literature, may be related to the reduction of fibrosis.

Topic 10: Hepatitis B

No: 1628

Long term clinical outcome after hepatitis B surface antigen seroclearance in the endemic area of hepatitis B virus infection

Hyun Yang[1], Hee Chul Nam[1], Hae Lim Lee[1], Jeong Won Jang[1], Si Hyun Bae[1], Jong Young Choi[1], Seung Kew Yoon[1]

Catholic Liver Research Center, The Catholic University of Korea Internal Medicine Seoul-Korea, South[1]

Aim: Seroclearance of hepatitis B surface antigen (HBsAg) is an important factor for clinical outcome of chronic hepatitis B (CHB), including progression to hepatocellular carcinoma (HCC). However, long-term clinical outcome after HBsAg seroclearance was not clear. The aim of this study was to establish long-term clinical outcome after HBsAg seroclearance in the endemic area of hepatitis B virus (HBV) infection.
Method: From 1991 to 2014, 88 patients (2.2 %) with HBsAg seroclearance out of 4055 patients with CHB were retrospectively analyzed. The virological data, biochemical data and the progression to HCC was collected since the time of HBsAg seroclearance. The median follow-up period after HBsAg seroclearnace was 28.1 months (1.1–289.4).
Result: Patients were sorted by the initial presentation of liver disease at the time of HBsAg seroclearance; patients with CHB (76.1 %), LC (17.0 %) and HCC (6.8 %). The median age was 55.5 years (26–74). The hepatitis B envelope antigen was negative for all of the patients. The serum HBV DNA titer at the time of HBsAg seroclearance was undetectable in 94.1 % of patients, and the titer was low in patients with detected HBV DNA titer (61–236 copies/mL). 80.7 % of patients showed spontaneous seroclearance, while seroclearance was achieved by treatment in 19.3 %. During the follow-up, there was no HBsAg reappearance. Only two progressions to HCC was observed.
Conclusion: In our study, patients with CHB after HBsAg seroclearance had favorable outcome, including progression to HCC. However, rarely, HCC can occur after HBsAg seroclearance. Therefore, these patients require regular follow-up for HCC surveillance.

Topic 10: Hepatitis B

No: 1138

Dichotomy of antiviral effect at end of treatment and during off treatment period in patients with chornic hepatitis B treated by therapeutic vaccine versus pegylated interferon

Sheikh Mohammad Fazle Akbar[1], Mamun Al-mahtab[2], Julio Aguilar[3], Yoichi Hiasa[4], Shunji Mishiro[1]

Toshiba General Hospital Department of Medical Sciences Tokyo-Japan[1], Bangabandhu Sheikh Mujib Medical University Department of Hepatology Dhaka-Bangladesh[2], Center For Genetic Engineering and Biotechnology Vaccine Division Havana-Cuba[3], Ehime University Graduate School of Medicine Department of Gastroenetrology and Metabology Toon-Japan[4]

Background and aims: Persistent antiviral effect is warranted in patients with chronic hepatitis B (CHB) treating with commercially-available antiviral drugs (pegylated interferon or nucleoside analogs). However, this usually remains unobtainable at treatment-free period after end of treatment (EOT). The antiviral effect of a therapeutic vaccine containing HBsAg and HBcAg (HBsAg/HBcAg) were assessed in a phase III clinical trial in a head to head comparison with pegylated interferon in CHB patients.
Methods: Seventy-five patients with biochemical, virological and histological evidences of CHB patients received HBsAg/HBcAg vaccine (Center for Genetic Engineering and Biotechnology, Havana, Cuba), once in every two weeks for 10 times (5 vaccinations by nasal route and followed by 5 vaccinations via both nasal and subcutaneous route). Seventy-six patients with CHB received Pegylated-IFN (180 microgram, once weekly, subcutaneously) for 48 consecutive weeks.
Results: HBV DNA negativity (HBV DNA < 250 copies/ml) was almost similar (60 %) for vaccinated group and (59 %) for Pegylated-IFN group at EOT. However, 24 weeks after EOT, 57 % patients receiving HBsAg/HBcAg-based therapeutic vaccine and 37 % of patients receiving Pegylated-IFN remained HBV DNA negative ($P < 0.05$). The levels of HBV DNA were also significantly lower at 48 weeks after EOT in HBsAg/HBcAg-treated patients compared to pegylated-IFN-treated patients ($P < 0.05$). HBeAg negativity and anti-HBe seroconversion were significantly higher in HBsAg/HBcAg vaccinated CHB patients compared to pegylated-IFN treated patients ($P < 0.05$).
Conclusions: Albeit of prolonged follow up, it can be proposed that treatment-free HBV control may be attainable in more patients of CHB by therapeutic vaccine compared to pegylated IFN.

Topic 10: Hepatitis B

No: 1312

Addition of peginterferon ALFA 2B during long term nucleos(t)ide analogue therapy increases HBEAG seroconversion and hbsag decline—week 48 results from a multicenter randomized controlled trial (pegon study)

Qing Xie[1], Heng Chi[2], Ning Ping Zhang[3], Xun Qi[4], Liang Chen[4], Simin Guo[1], Qing Guo[1], Pauline Arends[2], Ji-yao Wang[3], Elke Verhey[2], Robert J. De Knegt[2], Bettina E. Hansen[2], Harry L.A. Janssen[2]

Ruijin Hospital, Jiaotong University Department of Infectious Diseases Shanghai-China[1], Erasmus Mc University Medical Center Rotterdam Department of Gastroenterology and Hepatology Rotterdam-Netherlands Antilles[2], Zhongshan Hospital, Fudan University Department of Gastroenterology and Hepatology Shanghai-China[3], Shanghai Public Health Clinical Center, Fudan University Department of Hepatitis Disease Shanghai-China[4]

Background: Addition of peginterferon (PEG-IFN) may increase serological responses during long-term nucleos(t)ide analogues (NA) therapy in HBeAg-positive chronic hepatitis B (CHB).
Methods: In this randomized controlled trial, 82 HBeAg-positive patients were treated for at least 12 months with Entecavir or Tenofovir with HBV-DNA $< 2{,}000$ IU/mL at randomization. Patients were randomized to 48 weeks PEG-IFN addition, or 48 weeks NA monotherapy continuation. At week 48, response (HBeAg seroconversion with HBV-DNA < 200 IU/mL) was assessed with subsequent follow-up until week 96. Week 48 results are presented here.
Results: 76 patients were eligible for intention-to-treat analysis, of which 74 have reached week 48 by the time of this analysis: 36 PEG-IFN add-on and 38 NA monotherapy. Ninety-six percent were of Asian ethnicity with an average age of 33 years. Baseline characteristics were comparable between treatment groups. Response was achieved in 17 % of patients who received PEG-IFN add-on compared to 5 % of patients who continued NA monotherapy ($P = 0.15$). HBeAg loss was achieved in 33 % of patients who received PEG-IFN add-on compared to 18 % in the NA monotherapy group ($P = 0.14$). PEG-IFN add-on resulted in more HBsAg decline at week 48 (0.59 vs. 0.29 log IU/mL, $P = 0.021$). HBsAg decline > 1 log IU/mL was achieved in 19 % of the PEG-IFN add-on group compared to 0 % in the NA monotherapy group ($P = 0.005$). Treatment was generally well tolerated.
Conclusion: A 48 week addition of PEG-IFN during long-term NA therapy increases HBeAg seroconversion and HBsAg decline and may therefore improve the possibility of finite treatment in HBeAg-positive CHB patients.

Topic 10: Hepatitis B

No: 1082

Predictors of response to 2 years telbivudine therapy among chronic hepatitis B patients in Bangladesh a 'real life' experience of 471 cases

M. Golam Azam[1], Mobin Khan[2]

Birdem General Hospital Gastroenterology and Hepatology Dhaka-Bangladesh[1], The Liver Centre Hepatology Dhaka-[2]

Introduction: Rapid and prolonged suppression of serum HBV-DNA is associated with clinical improvement. This study was designed to look for the predictors of better response with telbivudine (LdT) in real-life clinical setting in CHB patients. Methods: It was an open-label, observational study carried out at the Liver Centre, Dhaka, Bangladesh. All patients received LdT 600 mg/day continuously for 2 years. Serum levels of ALT, HBeAg status and HBV-DNA were evaluated with 6 months interval.
Results: A total of 471 CHB patients, male 394 (83.6 %), age 34.7 ± 12.2 yrs (mean $\pm$ SD), ALT 135.1 ± 10.2 (mean $\pm$ SEM), HBeAg-positive 190 (40.3 %) and HBV DNA 6.3 ± 2.1log copies/ml (mean $\pm$ SD) were enrolled. Serum ALT normalized in 80.6, 87.7 and 85.3 %; the cumulative rates of HBeAg negative were 12.6, 16.8 and 24.3 %; undetectable serum HBV-DNA level was achieved in 60.6, 72.7 and 80.3 % cases at months 6, 12, and 24 months of treatment respectively. The viral breakthrough rates at 1 year of telbivudine treatment were 12.7 and 9.3 % for HBeAg-positive and HBeAg-negative patients respectively. Age, sex, baseline HBeAg status had similar outcomes thus no predictive role; but baseline high serum ALT level and low HBV DNA levels had significant predictive role in the assessment of efficacy of telbivudine therapy.
Conclusions: The efficacy of telbivudine treatment for CHB patients was satisfactory in the 'real-life' clinical settings. Baseline high serum ALT levels, low HBV DNA levels and early viral suppression at 6 months of treatment is the most important factor associated with treatment responses and virological breakthrough during long-term telbivudine therapy.

Topic 10: Hepatitis B

No: 2177

Prolactin kinetics in patients with chronic hepatitis B

Iulianna Lupasco[1], Vlada-tatiana Dumbrava[2], Inna Venger[1], Natalia Taran[1]

State University of Medicine and Pharmacy "n.testemitanu" Scientific Laboratory of Gastroenterology Chisinau-Moldova[1], State University of Medicine and Pharmacy "n.testemitanu" Clinics of Gastroenterology, Department of Internal Medicine Chisinau-Moldova[2]

Introduction: Liver participates in hormonal metabolism, including sex hormones.
Aim: To study the prolactin levels in chronic hepatitis (CH) HBV patients.
Materials and methods: We have been studied 138 patients with CH HBV: group I - HBeAg +, group II - antiHBe + of minimal activity of liver process (ALP, group III - antiHBe +, of moderate-severe ALP. Prolactin level has been studied in all patients, traditionally and in the dynamics of original authors' stimulation test with euphyllin and glucose (TEG) in 1 and 2 h after the test. The control group consisted of 30 healthy people.

In HBeAg + group hyperprolactinemia was found at all points of TEG ($P < 0{,}01$, $P < 0{,}01$, $P < 0{,}01$) compared to control data. Patients gender influenced on prolactin levels: been higher in women (TEG fasting and 2) ($P < 0{,}01$, $P < 0{,}01$) compared to men.

In II group elevated prolactin levels were noted (TEG 1, 2) versus similar parameters of control group ($P < 0{,}01$, $P < 0{,}01$) more expressed in women (TEG 1, 2, $P < 0{,}05$, $P < 0{,}05$).

Analysis of the results in patients of III group with moderate ALP found markedly increased prolactin values in all intervals (TEG 1,2,3) ($P < 0{,}01$, $P < 0{,}01$, $P < 0{,}05$) versus control data. Elevated prolactin concentrations were more expressed in older patients (TEG 2,3), ($P < 0{,}01$, $P < 0{,}01$).
Conclusion: In chronic HBV hepatitis were found veridical changes of prolactin concentrations, more significant in active liver process.

Specific stimulation test in patients with CH HBV allows early diagnosis of hormonal profile disorders.

Topic 10: Hepatitis B

No: 1698

Impact on twenty five years after universal hepatitis B vaccination into newborn as part of Thailand EPI program

Yong Poovorawan[1], Nawarat Posuwan[1], Rujipat Wasitthankasem[1], Preeyaporn Vichaiwattana[1], Apiradee Theamboonlers[1], Montana Foonoi[2], Jamorn Makaroon[3], Klaita Srisingh[4], Duangporn Asawarachun[5], Somchai Owatanapanich[6], Viboonsuk Vuthitanachot[7], Norra Wutthiratkowit[8], Kraisorn Tohtubtiang[9], Pattaratida Sa-nguanmoo[1]

Center of Excellence In Clinical Virology, Faculty of Medicine, Chulalongkorn University Pediatrics Bangkok-Thailand[1], Uttaradit Hospital - Uttaradit-Thailand[2], Lablae Hospital - Uttaradit-Thailand[3], Naresuan University Hospital - Phitsanulok-Thailand[4], Pranakron Sri Ayuthaya Hospital - Ayuthaya-Thailand[5], King Narai Hospital - Lopburi-Thailand[6], Chumpair Hospital - Khon Kaen-Thailand[7], Naradhiwas Rajanagarindra Hospital - Naradhiwas -Thailand[8], Trang Hospital - Trang-Thailand[9]

Hepatitis B vaccination in newborns had been introduced as part of Thai EPI since 1988 in 2 provinces and extended to 12 provinces in 1990. Universal vaccination into newborn for the whole country has implemented in 1992. This year (2014), we did the national hepatitis B serosurveys among 5581 subjects in the different parts of the country. The long-term immunogenicity and impact of universal hepatitis B vaccination into newborn as part of EPI program for 25 years were evaluated by HBsAg, antiHBc and antiHBs. HBV carriers were markedly reduced. HBV infection by mean of detectable HBsAg, antiHBc and long term antibody response (antiHBs) was shown in the table. Base on the total Thai population with the government data recorded; we estimated that the total number of HBV carriers amounted to 2.06 million cases or 3.02 percent of the total populations. Most of them were in adult age group. HB vaccine represents the first vaccine shown to be effective in preventing the occurrence of HCC as shown by a drastic decline in Taiwanese children with HCC after the large scale HB vaccination program. It is believed that HB vaccine will facilitate the implementation of universal vaccination campaigns and thus contribute to the control and possible to the eventual eradication of this disease.

Topic 10: Hepatitis B

No: 1886

Efficacy of combination therapy with nucleotide analogues and interferon in children with genotype C HBV chronic hepatitis B

Hitoshi Tajiri[1], Tomoko Takano[1]

Osaka General Medical Center Pediatrics Osaka-Japan[1]

Introduction and aims: Sustained suppression of HBsAg production after interferon treatment was not reported for children with chronic hepatitis B (CHB), especially with genotype C HBV infection that is prevalent in Asia. In this study we investigated the efficacy of combination therapy with nucleotide analogues and interferon.
Subjects and methods: Seven children (four boys and three girls) with HBeAg-positive CBC and infected with genotype C HBV underwent the therapy with 3-month of nucleotide analogue and interferon followed by 3-month of interferon. Combination of lamivudine and conventional interferon was introduced in the first three patients while entecavir and peginterferon was adopted in the latest four. The median age of the patients was 8 (4–13) years. The effect on HBsAg production was assessed as well as levels of HBeAg, ALT and HBVDNA.
Results: Baseline ALT and HBVDNA levels were 272 (83-1090) U/l and 8.0 (7.0-9.0) log copies/ml, respectively. All the patients showed a favorable response to the therapy. The first three were followed more than five years and showed reduction in HBsAg in two and loss of HBsAg in one. In the latest four HBsAg titers (log IU/ml) were decreased from 4.0 $\pm$ 0.2 to 3.1 $\pm$ 0.7 as well as the titers of HBeAg and HBVDNA between 3 month and 9 month of the therapy.
Conclusion: Our preliminary results suggest that the combination therapy may be effective in suppression of HBsAg production as well as the titers of HBeAg and HBVDNA for children with genotype C HBV CHB.

Topic 10: Hepatitis B

No: 1534

Liver histology in immune tolerance phase patients with chronic hepatitis B virus infection according to different alanine transaminase level

Dengming He[1], Qinghua Shang[1], Yuqi Zhang[1], Yong An[1], Qingqiang Yi[1], Wei Zhang[1], Mingquan Ding[1]

The 88th Hospital Institute of Infectious Disease Tai'an-China[1]

Background and aim: A normal alanine transaminase (ALT) levels does not mean normal liver inflammation. We aimed to observe the difference of liver inflammation in immune tolerance phase chronic HBV infection according to two upper limits of normal ALT standards (30 U/L for males and 19 U/L for females vs. 40 U/L).
Methods: 202 patients were divided into low ALT group ($\leq$ 30 U/L for males and $\leq$ 19 U/L for females) and high ALT group (31-40 U/L for males and 20-40 U/L for females). Ishak and Metavir system were used to evaluate liver inflammation and fibrosis.
Results: Significant difference of Ishak inflammation score and fibrosis score were seen between low ALT group and high ALT group. Positive correlation was seen between ALT levels and Ishak inflammation score or fibrosis staging score. The proportion of mild inflammation was 97.9 % in low ALT group and 65.7 % in high ALT group. Metavir fibrosis staging in all cases of low ALT group is F0 and F1. In high ALT group, the proportion of F0, F1, F2, F3, and F4 was 51.4, 39.0, 7.6, and 1.9 %, respectively. Different distribution of Metavir mild, moderate, and severe or fibrosis staging was seen in age and sex, but not in HBV DNA levels.
Conclusions: For immune tolerance phase patients, the lower ALT ULN is better than the current one in evaluating liver histology. Sex and age are associated with the degree of liver histology for ALT levels $>$ 30 in males or $>$ 19 in females.

Topic 10: Hepatitis B

No: 1865

Long terms outcomes tenofovir df (tdf) treatment for chronic hepatitis B patients

Muzzaffar Gill[1], Sidra Gill[2], Ammara Nawaz[3], Misbah Malik[3], Faiza Irfan[3], Hafsa Aziz[4]

Maroof International Hospital Gastroenterologist/hepatologist Islamabad-Pakistan[1], Maroof International Hospital Gastroenterologist Islamabad-Pakistan[2], Maroof International Hospital Gastroenterologist Islamabad-Pakistan[3], Maroof International Hospital Gastroenterologist Islamabad-Pakistan[4]

Tenofovir DF (TDF) represents in clinical studies a very effective and tolerable treatment for CHB and is a recommended first-line therapy. Data on long-term efficacy/safety in daily practice are limited.

Topic 10: Hepatitis B

No: 1460

Improved function of natural killer cells correlates with seroconversion of hepatitis B envelope antigen via natural killer group 2 member d and interleukin 15 in patients with chronic hepatitis B

Tao Chen[1], Ling Ding[2], Lin Zhu[2], Wei Guo[2], Shuai Wang[2], Zeguang Wu[2], Li Xu[2], Weiming Yan[2], Xiaojing Wang[2], Xiaoping Luo[2], Hong Ma[2], Yuhong Dong[2], Jidong Jia[2], Qin Ning[2]

Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institute of Infectious Disease Wuhan-China[1], Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institution of Infectious Diseases Wuhan-China[2]

Aims: Natural killer (NK) cells play pivotal roles in the control and clearance of hepatitis B virus (HBV) in chronically infected patients. This study aimed to investigate the dynamic changes of NK cells post antiviral treatment and its correlation with treatment efficacy.
Methods: This study involved 54 hepatitis B envelope antigen (HBeAg)-positive chronic hepatitis B (CHB) patients who received telbivudine (LdT) for 52 weeks. Blood samples were collected at baseline and at weeks 12, 24, 36 and 48 of treatment, and tested for HBV DNA, HBsAg, HBeAg, ALT, AST, and additional immunological markers.
Results: Compared with baseline, the percentages of peripheral CD3-CD56 + NK cells were significantly higher at Weeks 36 and 48. The expression of activating receptors natural killer group 2, member D (NKG2D) and NKP46 was enhanced, while that of the inhibitory receptor NK group 2, member A decreased. NKG2D expression was significantly enhanced on peripheral NK cells in patients with HBeAg seroconversion. NK cells also secreted increased amounts of interferon-γ and CD107a. Purified peripheral NK cells from CHB patients cultured with telbivudine showed significantly enhanced expression of NKG2D and interleukin-15 (IL-15).
Conclusion: This study demonstrated that improved function of NK cells correlates with HBeAg seroconversion via NKG2D in CHB patients treated with telbivudine. It further suggested that activation of NKG2D may be mediated by the production of IL-15 by the NK cells.

Topic 10: Hepatitis B

No: 2075

Genome wide micro RNA signature of CD4 + t cells can discriminate different stages of liver disease due to HBV infection

Avishek Kumar Singh[1], Robert Geffers[2], Sheetalnath Babasaheb Rooge[1], Aditi Varshney[1], Nirupama Trehanpati[1], Madavan Vasudevan[3], Manoj Kumar Sharma[4], Ankit Bhardwaj[1], Shiv Kumar Sarin[1]

Department of Research, Institute of Liver & Biliary Sciences, New Delhi Research New Delhi-India[1], Array Facility, Helmholtz Centre For Infection Research, Braunschweig Array Facility Braunschweig-Germany[2], Bionivid Technology Pvt Ltd, Kasturi Nagar, Bangalore Research Bangalore-India[3], Department of Hepatology, Institute of Liver & Biliary Sciences New Delhi Hepatology New Delhi-India[4]

Background: CD4 + T cell immune responses play an important role in pathogenesis during various stages of hepatitis B virus infection. There is a paucity of knowledge about the underlying molecular mechanisms and specific micro RNAs affected during host response against HBV. We aimed to identify changes in miRNA expression of the CD4 + T cell at different stages of liver disease due to HBV infection.
Patients and methods: 3 group of patients [(Acute Viral Hepatitis, AVH-B, n = 4, Mean age 45 yr,M/F = 2); Chronic HBV with raised ALT (n = 9, HBeAg + = 5, Meanage 38 yr, M = 6) and Chronic HBV with persistently normal ALT (n = 12, HBeAg + = 3, Mean age 34 yr, M = 7)] and matched controls (n = 11, Mean age 33 yr, M = 6) were studied. Microarray based whole miRNA expression analysis of CD4 + T cell was performed using Agilent Platform. Differentially expressed miRNAs between groups, key pathways and biological processes regulated were identified by various statistical methods
Results: Micro RNA profiles can differentiate acute and chronic infection stage, and chronic infection with and without hepatic injury in CD4 + T cells.Fig-1a shows the number of differentially expressed miRNAs among the different patients groups and Fig-1b shows disease stage specific miRNAs. Major biological events and gene families targeted by differentially expressed miRNAs include Apoptosis, Calcium Signalling, Key Cellular processes (Adhesion, Cell cycle, Differentiation, Migration, Proliferation), Cell surface, Chemokines, & Cytokines, Immune response, MAPK signaling, NFKB signalling and TGF beta signalling pathway.
Conclusion: Micro RNA profiles in CD4 + T cells can differentiate acute and chronic infection stage, and chronic infection with and without hepatic injury.

Topic 10: Hepatitis B

No: 1647

Increase risk of progression to liver cirrhosis and hepatocellular carcinoma in chinese chronic hepatitis B patients with nonalcoholic fatty liver disease

Dong Ji[1], Guo-feng Chen[1], Qing Shao[1], Fan Li[1], Bing Li[1], Zhong-bin Li[1], Song-hai Chen[1], Chun-yan Wang[1], Xiao-xia Niu[1], Shi-ying Ding[1], Tao Yan[2], Vanessa Wu[3], April Wong[3], Athena Chau[3], Yu-dong Wang[3], George Kk Lau[3]

Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[1], 302 Hospital International Liver Diagnosis and Treatment Centre Beijing-China[2], Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[3]

Background & aims: In China, where hepatitis B infection is endemic, there is an increase incidence of nonalcoholic fatty liver disease (NAFLD) recently. We examine the natural history of NAFLD and the clinical outcomes of the CHB patients with or without NAFLD in Chinese.

Methods: We reviewed the medical records of 850 CHB and/or NAFLD cases with liver histopathology databases. The demographic data, baseline and last-follow-up laboratory data, and clinical outcomes (liver and non-liver-related) were noted. Kaplan–Meier survival analysis was used to describe the cumulative rate of development to hepatocellular carcinoma (HCC), overall survival, and liver disease related mortality.
Results: The mean follow-up of 11.2 ± 5.0 years were recruited and the difference of overall survival among the CHB group, CHB plus NAFLD group, and NAFLD group was not significant ($P > 0.05$). The percentage of the patients with progression to hepatic cirrhosis in CHB plus NAFLD group is significantly higher than that in CHB group ($P < 0.05$) and than that in NAFLD group ($P < 0.05$). The patients with CHB plus NAFLD had significantly higher cumulative hazard of progression to HCC than those in CHB group and those in NAFLD group ($P = 0.001$). Prevalence of hypertension, obesity, diabetes mellitus, and hyperlipidaemia in CHB plus NAFLD group were significantly higher when compared with those in CHB group ($P < 0.01$).
Conclusion: NAFLD in Chinese patients is a benign condition with little risk of disease progression. CHB Patients with NAFLD have higher risk of progression to liver cirrhosis and HCC.

Topic 10: Hepatitis B

No: 1474

Baseline quantitative HBsAg level is predictive of virologic response in entecavir treated patients

Ju-yeon Cho[1], Joon Hyeok Lee[1], Won Sohn[1], Dong Hyun Sinn[1], Geum-youn Gwak[1], Yong-han Paik[1], Moon Seok Choi[1], Kwang Cheol Koh[1], Seung Woon Paik[1], Byung Chul Yoo[1]

Samsung Medical Center Internal Medicine Seoul-Korea, South[1]

Background: Entecavir is a potent nucleoside analogue with high efficacy and a high barrier for resistance. Lower HBV-DNA levels and HBeAg-negative status are known predictors of virologic response. In this study, we sought to evaluate the role of quantitative hepatitis B surface antigen (qHBsAg) for virologic response in entecavir treated patients.
Methods: Between 2007 and 2012, treatment-naïve CHB patients treated with entecavir with baseline qHBsAg were included. Retrospective analysis for the cumulative rates of virologic response (HBV DNA < 60 IU/ml) and analysis of factors associated with virologic response was done.
Results: 126 HBeAg-negative and 145 HBeAg-positive patients had baseline qHBsAg levels prior to entecavir treatment. Compared to patients with qHBsAg < 5,000 IU/mL, the patients with greater qHBsAg levels had a significantly lower cumulative virologic response ($p \leq 0.001$). In HBeAg-positive patients, significantly greater HBeAg seroclearance was achieved in patients with qHBsAg < 5,000 IU/mL ($P = 0.002$). In the low viral load(HBV DNA ≤ 6log10 IU/mL) group, there was no significant difference in virologic response based on qHBsAg levels ($P = 0.378$). However, there was a significant difference in virologic response rate in the high viral load(HBV DNA > 6log10 IU/mL) group based on low (≤ 5,000 IU/mL) and high (> 5,000 IU/mL) qHBsAg levels ($P < 0.001$). The virologic response of the high viral load group at 6, 12, and 24 months was 46.7, 89.3, and 98.7 % in patients with qHBsAg ≤ 5,000 IU/mL and 20.7, 62.2, and 84.6 % in patients with qHBsAg > 5,000 IU/mL.
Conclusions: Baseline HBV DNA, qHBsAg levels and HBeAg status were predictors for virologic response during entecavir treatment. Furthermore, in patients with high viral load, qHBsAg is an effective tool in predicting virologic response.

Topic 10: Hepatitis B

No: 1874

The profile of hepatitis B virus genotypic resistance and the efficacy of rescue therapy in clinical practice

Ling-bo Liang[1], Hong Tang[1], En-qiang Chen[1], Lan-lan Chen[1], Lang Bai[1]

West China Hospital of Sichuan University Center of Infectious Diseases Chengdu-China[1]

Background: Until recently the profile of HBV drug-resistant mutations and the efficacy of rescue therapy in patients with treatment failure were most from clinical trials. This study aims to explore the correlation between different types of virological response and drug-resistant mutations as well as the efficacy of rescue therapy in clinical practice.
Methods: Prevalence and patterns of drug-resistant mutations were analyzed by sequencing. After genotypic resistance test, all patients received 24 weeks of follow-up with rescue therapy.
Results: A total of 168 patients failed their antiviral therapy were included. Among them there were 89 experienced virological breakthrough and 79 partial/null responders. Genotypic resistance was detected in 102 patients. The prevalence of genotypic resistance was significantly higher in patients experiencing virological breakthrough than in partial/null responders (80.9 %, 72/89 vs. 38.0 %, 30/79; $P < 0.001$). There were 118 (70.2 %) patients achieved undetectable serum HBV DNA with rescue therapy. The rate of virological response in patients harboring wild-type HBV was significantly higher than patients with drug-resistant HBV (81.8 %, 54/66 vs. 62.7 %, 64/102; $P = 0.008$). Rescue therapy with ETV + ADV and no evidence of genotypic resistance correlated independently with a higher rate of virological response (OR 4.01, 95 % CI 1.68-9.57, $P = 0.002$; OR 5.55, 95 % CI 2.08-14.80, $P = 0.001$). Previous sequential therapy correlated independently with a lower rate of virological response (OR 0.329, 95 % CI 0.131-0.828, $P = 0.018$).
Conclusions: Drug resistance is the main cause of treatment failure in patients experiencing virological breakthrough. Patients failing treatment but without signs of genotypic resistance may still have a good chance of gaining therapeutic success with an upgrade subsequent therapy.

Topic 10: Hepatitis B

No: 1466

Sequential therapy of chronic hepatitis B with peginterferon alpha 2a for 24 weeks followed by tenofovir in a developing country

Mohammad Golam Azam[1], Mobin Khan[2]

Birdem Dept of Ghpd Dhaka-Bangladesh[1], The Liver Centre Hepatology Dhaka-[2]

Background: Chronic hepatitis B (CHB) is a global problem which is not uncommon in Bangladesh. Considering the deadly consequences of long term infection and its correlation with persistent high viral load, clearance of cccDNA is the ultimate goal. Interferons have

immunomodulatory and antiviral effect but side effects are common and costly for a developing country like Bangladesh.
Aims and objectives: Sequential therapy with peginterferon alpha 2a for a shorter duration of 24 weeks irrespective of HBeAg status followed by tenofovir therapy may minimize the cost and side effects with better efficacy.
Materials and methods: A total of 33 patients (male 25, HBeAg positive 13 cases), age mean ± SD was 37 ± 9 years, baseline ALT mean ± SD was 108 ± 34 IU/L and baseline log HBVDNA mean ± SD was 7.1 ± 1.7 copies/ml. Peginterferon alpha 2a was given for 24 weeks 180 microgram s/c weekly followed by tenofovir for 18 months at 300 mg orally daily. Efficacy was assessed 6 monthly with serum ALT and HBV DNA load.
Results: HBVDNA viral load reduced, mean ± SD was 3.1 ± 1.5 copies/ml but did not come to undetectable level by PCR method at 6 month of peginterferon therapy. Further treatment with tenofovir significantly reduced HBV DNA load and maintained below the detection limit. Serum ALT level was also reduced and sustained in the similar manner.
Conclusion: Sequential therapy with peginterferon alpha 2a for a shorter duration of 24 weeks followed by tonofovir therapy showed better efficacy in this pilot study.

Topic 10: Hepatitis B

No: 1061

Impact of tenofovir disoproxil fumarate on the fasting lipid profile of chronic hepatitis B patients

Fehmi Tabak[1], Henry L.y. Chan[2], Sang Hoon Ahn[3], Seng Gee Lim[4], Calvin Pan[5], Ramazan Idilman[6], Lanjia Lin[7], Phillip Dinh[7], Eduardo B. Martins[7], Prista Charuworn[7], Tak Yin Tsang[8], Scott Fung[9], Wan-long Chuang[10], Arun Sanyal[11], Samuel Lee[12], Mehta Rajiv[13], Wendy Cheng[14], Patrick Marcellin[15]

University of Istanbul Cerrahpasa Medical Faculty Istanbul-Turkey[1], Prince of Wales Hospital, The Chinese University of Hong Kong Department of Medicine and Therapeutics and Institute of Digestive Disease Hong Kong-Hong Kong[2], Yonsei University College of Medicine Division of Gastroenterology Seoul-Korea, South[3], Yong Loo Lin School of Medicine, National University of Singapore Singapore-Singapore[4], Nyu Langone Medical Center, Nyu School of Medicine New York-United States[5], Ankara University School of Medicine Department of Gastroenterology Ankara-Turkey[6], Gilead Sciences Foster City-United States[7], Princess Margaret Hospital Hong Kong-Hong Kong[8], Toronto General Hospital Toronto-Canada[9], Kaohsiung Medical University Hospital, Kaohsiung Medical University Kaohsiung-Taiwan[10] Virginia Commonwealth University School of Medicine Richmond-United States[11] University of Calgary Calgary-Canada[12] Liver Clinic Surat-India[13] Royal Perth Hospital Perth-Australia[14] Hôpital Beaujon, University of Paris Paris-France[15]

Aim: The impact of tenofovir disoproxil fumarate (TDF) on lipid profile in chronic hepatitis B (CHB) patients is unknown. Data from GS-US-174-0149, a clinical trial evaluating pegylated interferon alfa-2a (PEG) ± TDF combination therapy in non-cirrhotic CHB patients, were analyzed for impact of antiviral treatment on fasting lipid profile.
Methods: 570 subjects with fasting baseline and week 24 total cholesterol, LDL, HDL, and triglyceride were included. Regression analyses of on-treatment changes in lipid profile were examined, adjusted for baseline lipid values, age, sex, race, and BMI.
Results: Comparing baseline and week 24 results, TDF monotherapy was significantly associated with reductions in total cholesterol, LDL, and HDL (−25.6 mg/dL, −16.4 mg/dL, and, −9.6 mg/dL, respectively, $P < 0.05$) with no significant change in triglyceride or total cholesterol/HDL ratio (p-values ≥ 0.05). Moreover, TDF + PEG × 48 weeks combination therapy was significantly associated with an even greater reductions in total cholesterol, LDL, and HDL, and a moderate triglyceride increase (−42.5 mg/dL, −29.0 mg/dL, and −18.1 mg/dL, +18.8 mg/dL, respectively, p-values < 0.05) compared to baseline. The changes were also significant relative to either monotherapy. In patients, who were on (TDF + PEG) × 16 weeks then continuing on TDF, the lipid impact of PEG lessened after its discontinuation. Only minor cardiovascular events, mostly palpitations, occurred up to Week 72.
Conclusion: TDF monotherapy was associated with significant improvements in total cholesterol and LDL in CHB patients. PEG + TDF × 48 weeks was associated with greater changes in lipid profile than either monotherapy.

Topic 10: Hepatitis B

No: 1545

Hepatitis B virus DNA and clinical characteristics of patients who developed hepatocellular carcinoma while receiving tenofovir disoproxil fumarate (TDF) following 8 years of therapy

W. Ray Kim[1], Rohit Loomba[2], Thomas Berg[3], Raul Aguilar Schall[4], Leland J. Yee[4], Phillip Dinh[4], John F. Flaherty[4], Eduardo B. Martins[4], Terry Therneau[5], Ira Jacobson[6], Scott Fung[7], Selim Gurel[8], Maria Buti[9], Patrick Marcellin[10]

Stanford University School of Medicine Division of Gastroenterology and Hepatology Palo Alto, Ca-United States[1], University of California At San Diego Division of Gastroenterology and Epidemiology La Jolla, Ca-United States[2], Universitätsklinikum Leipzig Department of Internal Medicine, Division of Gastroenterology and Rheumatology, Section of Hepatology Leipzig-Germany[3], Gilead Sciences Inc., Foster City, Ca-United States[4], Mayo Clinic Department Biostatistics Rochester, Mn-United States[5], Weill Cornell Medical College Division of Gastroenterology and Hepatology New York-United States[6], University of Toronto Department of Gastroenterology Toronto, Ontario-Canada[7], University of Uludag, Department of Gastroenterology Bursa-Turkey[8], Ciberehd Del Instituto Carlos Iii Liver Unit, Hospital General Universitari Vall D'hebron Barcelona-Spain[9], Univ Paris-Diderot and Inserm Cri/umr 1149, Viral Hepatitis Research Centre, Hoptial Beaujon Clichy-France[10]

Background: We have previously shown a decreased incidence of HCC among patients treated with tenofovir disoproxil fumarate (TDF) compared to predicted incidence using a validated risk model. Additional information is needed on the characteristics of those who do develop HCC while on therapy including understanding of potential patterns in HBV-DNA decline.
Methods: We studied the clinical and demographic characteristics of HCC cases during the initial 8 years of pivotal studies GS-US-174-0102 and GS-US-174-0103 including HBV-DNA patterns through 8 years.
Results: Following 8 years of TDF therapy, there were 14 cases of HCC in studies 102/103. Four cases occurred during the first calendar year. 9/14 cases were HBeAg-negative and 3 of these were cirrhotic. 5/14 cases were HBeAg-positive at baseline and 3 of these were cirrhotic. 12/14 cases were male. 3 patients had regression of histological fibrosis on repeat liver biopsies. Among the 14 HCC cases, 5 were genotype (gt)-D, 4 gt-C, 2 gt-B, 1 gt-E, 1 gt-F and 1 unable to genotype. HBV-DNA levels among HCC cases are provided in Figure 1. 11/14 cases achieved HBV-DNA undetectability within the first 48 weeks of treatment, with 2 others achieving undetectability at days

398 and 1084 of therapy. Only 1 patient never reached DNA undetectability.
Conclusions: During 8 years of TDF therapy, there were only 14 cases of HCC. Despite the small number of cases, HCC surveillance needs to be conducted in patients on long-time oral antivirals.

Topic 10: Hepatitis B

No: 1013

Original scientific paper antibody to hepatitis core antigen levels in the natural history of chronic hepatitis B

Wei Jia[1], Yu-qing Fang[1], Gui-qiang Wang[1]

Peking University First Hospital, Peking University Center For Liver Diseases and Department of Infectious Diseases Beijing-China[1]

Aim: Previous studies have revealed anti-HBc levels as predictors of treatment response in HBeAg positive chronic hepatitis B (CHB) patients in both interferon-α and nucleos(t)ide analogue therapy cohorts. However, there is limited information about anti-HBc levels in the natural history of CHB. This study aimed to define anti-HBc levels of different phases in the natural history of CHB.
Methods: 211 treatment naive CHB patients were included in the study. They were classified into four phases: immune tolerance phase (IT, n = 39), immune clearance phase (IC, n = 48), non/low-replicative phase (LR, n = 55) and HBeAg negative hepatitis (ENH, n = 69). 50 patients who were HBsAg negative and anti-HBc positive were also recruited as past HBV infection (PBI) control group. Anti-HBc levels were measured by a new-developed double-sandwich immunoassay. Correlation of anti-HBc levels with ALT and other HBV-related markers within each phase was performed.
Conclusions: Serum anti-HBc levels were statistically significant between patients in different phases of CHB ($P < 0.001$). The median anti-HBc levels were: IT (3.28 log10 IU/ml), IC (4.35 log10 IU/ml), LR (3.29 log10 IU/ml), ENH (4.12 log10 IU/ml) and PBI (0.61 log10 IU/ml). There existed a strong correlation in IC ($r = 0.519, P < 0.001$) and a poor correlation in ENH ($r = 0.275, P = 0.042$). Anti-HBc levels with HBeAg serostatus could be used to distinguish different phases of CHB. Anti-HBc levels show significant differences during the natural course of CHB. These results may provide some potentially useful insights into hepatitis B pathogenesis and immune status.

Topic 10: Hepatitis B

No: 2083

The investigation and follow up of HBsAg positive pregnant women and their babies

Gule Aydin[1]

Afyonkarahisar Zubeyde Hanim Gyneacology&obstetrics and Pediatric Hospital Clinical Microbiology and Infectious Diseases Department Afyonkarahisar-Turkey[1]

Background: The most important risk factor for acquisition of HBV infection in children is perinatal exposure to HBsAg positive mother. The aim of this study is to point out the importance of determining HBsAg carrier pregnant women and immunizing their newborns.
Material & method: We investigated the records of the data of 100 HBsAg positive pregnant women (all were carriers,all delivered in our hospital) and their babies between 2011-2014 retrospectively. These records include gender, date of birth, type of delivery, birth weight and 1 year follow ups after birth. Serum levels of HBsAg, anti-HBs were measured, upper than 10 mIU/ml anti-HBs levels were accepted as positive.The infants were given 20 mcg hepatitis B vaccine and 100 IU (0.5 ml) hepatitis B hyperimmunglobuline after birth and vaccination schedule was completed.
Results: There weren't any still births. All babies were found anti-HBs positive. 20 newborns began to show anti-HBs positivity at the end of the first month. 42 % of the babies were girls. There weren't any statistically significant relationship between antiHbs seropositivity and gender. Anti-HBs levels were determined as positive in the 97,2 % of the spontaneously born babies and in the 94,2 % of the babies,born by caesarean, the difference was statistically significant.The average birth weight of the anti-HBs negative results were more low and the difference was statistically significant. At the end of the first year anti-HBs positivity had continued.
Conclusion: All pregnant women should be examined about HbsAg during pregnancy and all babies, born from HBsAg carier mothers should be immunizated as soon as possible.

Topic 10: Hepatitis B

No: 1219

Reduction of HBsAg by 48 weeks of peg interferon therapy given sequentially after long term nucleot(s)ide analogue therapy

Masayuki Kurosaki[1], Nobuharu Tamaki[6], Takanori Hosokawa[6], Hiroyuki Nakanishi[6], Jun Itakura[6], Namiki Izumi[6]

Musashino Red Cross Hospital Department of Gastroenterology and Hepatology Tokyo-Japan[1]

Background: Seroclearance of HBsAg is the ideal endpoint of antiviral therapy for chronic hepatitis B, but it is rarely achieved by nucleot(s)ide analogues (NUC).
Aim: To elucidate the effect of peg-interferon on HBsAg reduction when given sequentially after long term NUC therapy.
Methods: A total of 52 patients were sequentially treated by 48 weeks of peg-interferon alpha-2a (180 microgram weekly) after long-term NUC therapy with an overlap of 4 weeks. NUC therapy was withdrawn thereafter. The average duration of preceding NUC therapy was 4.1 years. HBeAg was negative in 69 % of patients at the start of peg-interferon. Serial changes in the titer of HBsAg were measured by quantitative assay.
Results: HBV DNA remained undetected in 80 % of patients after start of peg-interferon and withdrawal of NUC. During At the end of peg-interferon, HBeAg became negative in 38 %. Titer of HBsAg was 3200 (1.98-36500) IU/mL at the start of peg-interferon which became 2655 (<0.05-22500) IU/mL at the end of therapy. Average HBsAg reduction was 0.76 Log/mL. The incidence of >2.0/1.0-1.9/0-0.9 Log IU/mL reduction was 13 %/16 %/61 %. HBs seroclearance was obtained in 7 % and extremely low titer of <1.0 IU/mL was obtained in 17 % of patients.
Conclusions: Peg-interferon given sequentially after long term NUC therapy could achieve profound reduction of HBsAg and even seroclearance.

Topic 10: Hepatitis B

No: 2239

Perceived social support and quality of life in patients with hepatitis B

Omer Ozturk[1], Seyfettın Koklu[2], Semra Ulusoy Kaymak[3], Osman Yuksel[1], Omer Basar[1], Tugrul Purnak[1], Cemil Kamilli[1]

Hacettepe University School of Medicine Gastroenterology Ankara-Turkey[1], Hacettepe University School of Medicine Psychiatry Ankara-Turkey[2], Ankara Atatürk Education and Research Hospital Gastroenterology Ankara-Turkey[3]

Background: Chronic Hepatitis B is a common chronic liver disease in Turkey with a prevalence of 2-8 %1. Nearly 3 million people were infected with Hepatitis B virus in our country. We hypothesised that the contamination risk may affect patients psychologically and their relationship more than other chronic liver disease. Although there are some studies evaluating of quality of life in patients with Hepatitis B, there is not enough data about the social support in these patients.
Aim: We aimed to compare perceived social support and quality of life between two chronic hepatic conditions; Hepatitis B and Hepatosteatosis and healthy controls
Method: A sample of 100 patients with Hepatitis B and 100 patients with hepatosteatosis and 100 healthy control subjects were included in this study. Multidimensional scale of perceived support (MSPS) and WHO Quality of Life Brief version (WHOQOL-BREF) and Hospital Anxiety and Depression Scale (HADS) were used. We used one way ANOVA and scheffe tests for the statistical multiple comparisons.
Results: The mean scores of MSPS of Hepatitis B, hepatosteatosis and control groups are 55.78 ± 22.32, 58.20 ± 18.65 and 59.42 ± 17.2 respectively. Hepatitis B patients but not hepatosteatosis patients had higher scores than healthy controls in the posthoc multiple comparison test (p: 0.017). Physical health (p: 0.045), psychological health (p: 0.046), environment scores (p: 0.015) of the WHOQOL-BREF separated between Hepatitis B (22.91 ± 3.38, 21.66 ± 3.10, 10.35 ± 2.25, 30.23 ± 4.43), hepatosteatosis (21.77 ± 3.14, 20.35 ± 3.11, 10.17 ± 2.51, 29.76 ± 4.58) and healthy control groups groups.
Conclusion: As we hypothesized Hepatitis B patients perceive socially unsupported when compared uninfected hepatic disease. Their quality of life, particularly physical and psychological manner, are lower in patients with Hepatitis B1. European Centre for Disease Prevention and Control (ECDC). Hepatitis B and C in the EU neighbourhood: prevalence, burden of disease and screening policies. September 2010.

Topic 10: Hepatitis B

No: 1314

Association between hbeag seroconversion and risk of hepatocellular carcinoma during treatment with lamivudine or entecavir for chronic hepatitis B

Young-suk Lim[1], Jihyun An[1], Hwa Jung Kim[2]

Asan Medical Center, University of Ulsan College of Medicine Gastroenterology Seoul-Korea, South[1], Asan Medical Center, University of Ulsan College of Medicine Clinical Epidemiology and Biostatistics Seoul-Korea, South[2]

Background/aims: HBeAg seroconversion has been identified to be associated with the reduced risk of hepatocellular carcinoma (HCC) during the natural course of patients with chronic hepatitis B (CHB). However, it is not clear whether HBeAg seroconversion achieved after antiviral treatment is associated with lowered risk of HCC.
Methods: In this historical cohort study, data from 5374 consecutive adult patients with CHB who started treatment with lamivudine (LAM, n = 3374) or entecavir (ETV, n = 2000) between 1999 and 2011 were analyzed.
Results: HBeAg was positive in 3587 (66.7 %) patients at baseline; 2419 (71.8 %) in the LAM group and 1168 (58.4 %) in the ETV group. During the study period, 525 (9.8 %) developed HCC. Multivariable analyses showed that baseline HBeAg-positivity was not an independent risk factor for HCC in the entire cohort (hazard ratio [HR], 0.96; 95 % confidence interval [CI], 0.79-1.16). Among HBeAg-positive patients at baseline, 1263 (35.2 %) achieved HBeAg seroconversion during treatment. In the LAM group, HBeAg seroconversion was significantly associated with a reduced risk of HCC by multivariable analysis (HR, 0.54; 95 % CI, 0.40-0.72; Table), but not in the ETV group (HR, 1.10; 95 % CI, 0.64-1.88).
Conclusions: In a large cohort of CHB patients, the achievement of HBeAg seroconversion was associated with a reduced risk of HCC during treatment with a low potency antiviral agent, LAM, but not during treatment with a high potency antiviral agent, ETV.

Topic 10: Hepatitis B

No: 1292

144 weeks tenofovir disoproxil fumarate monotherapy or switching from adefovir dipivoxil after 48 weeks results in potent viral suppression and a favorable safety profile in chinese patients with chronic hepatitis B

Jinlin Hou[1], Zhiliang Gao[2], Qing Xie[3], Jinming Zhang[4], Jifang Sheng[5], Jun Cheng[6], Chengwei Chen[7], Qing Mao[8], Wei Zhao[9], Hong Ren[10], Deming Tan[11], Junqi Niu[12], Shijun Chen[13], Chen Pan[14], Hong Tang[15], Hao Wang[16], Yimin Mao[17], Jidong Jia[18], Qin Ning[19], Min Xu[20], Shanming Wu[21], Jun Li[22], Xinxin Zhang[3], Jie Dong[23], Jie Li[23]

Nanfang Hospital Infectious Disease Guangzhou-China[1], 3rd Affiliated Hospital of Sun Yat-sen University Infectious Disease Guangzhou-China[2], Ruijin Hospital Affiliated To Jiaotong University Infectious Disease Shanghai-China[3], Huashan Hospital Affiliated To Fudan University Infectious Disease Shanghai-China[4], 1st Affiliated Hospital of Zhejiang University Infectious Disease Shanghai-China[5], Beijing Ditan Hospital Infectious Disease Beijing-China[6], Shanghai The 85th Hospital Affiliated To Nanjing Military Infectious Disease Shanghai-China[7], Southwest Hospital, Third Military Medical University Infectious Disease Chongqing-China[8], 2nd Hospital of Nanjing Infectious Disease Nanjing-China[9], 2nd Affiliated Hospital Chongqing Medical University Infectious Disease Chongqing-China[10], Xiangya Hospital Central-south University Infectious Disease Changsha-China[11], 1st Affiliated Hospital of Jilin University Infectious Disease Changchun-China[12], Jinan Hospital For Infectious Disease Infectious Disease Jinan-China[13], Fuzhou Infectious Disease Hospital Infectious Disease Fuzhou-China[14], West China Hospital, Sichuan University Infectious Disease Chengdu-China[15], Peking University People's Hospital Infectious Disease Beijing-China[16], Renji Hospital Affiliated To Shanghai Jiaotong University Infectious Disease Shanghai-China[17], Beijing Friendship Hospital Affiliated To Capital University Infectious Disease Beijing-China[18], Tongji Hospital of Tongji Medical College Infectious Disease Wuhan-China[19], Guangzhou Eighth Municipal People's Hospital Infectious Disease Guangzhou-China[20] Shanghai Public Health Clinical Center

Infectious Disease Shanghai-China[21], The First Affiliated Hospital With Nanjing Medical University Infectious Disease Nanjing-China[22], Glaxosmithkline R&d China China Medicine Development Shanghai-China[23]

Aims: Tenofovir disoproxil fumarate (TDF) has demonstrated long-term efficacy and a high resistance barrier in chronic hepatitis B (CHB) populations outside of China. This Phase III study provides long-term data on TDF treatment in Chinese CHB patients.
Methods: This was the open-label study period, involving single-treatment with TDF following a 48-week double-blind and randomized treatment involving TDF 300 mg QD versus Adefovir Dipivoxil (ADV) 10 mg QD. HBeAg-positive and negative subjects with HBV DNA $\geq$ 105 copies/mL were eligible for initial randomization. Totally 497/512 (97 %) subjects (198 HBeAg positive and 299 HBeAg negative) entered the open-label extension phase; 252 subjects originally randomized to TDF (TDF-TDF) and 245 subjects randomized to ADV (ADV-TDF). The majority of subjects (95.5 %) were treatment naïve. Virologic, serologic, biochemical, safety and resistance were monitored throughout the study.
Results: At Week 144, virologic suppression (HBV DNA $<$ 400 copies/mL) was achieved in the majority of treated subjects (TDF-TDF Vs. ADV-TDF) in HBeAg positive (94.2 % vs. 96.0 %, $p > 0.05$) and HBeAg negative (93.5 % vs. 94.8 %, $p > 0.05$). A higher proportion of subjects in the TDF-TDF group experienced HBeAg loss (35.9 % vs. 24.2 %, $p > 0.05$) and HBeAg seroconversion (32.0 % vs. 20.2 %, $p > 0.05$); these differences were not statistically significant. No subject experienced durable HBsAg loss/seroconversion. No TDF resistance mutations were identified. TDF treatment continued to be well tolerated.
Conclusions: TDF demonstrated high potency, no development of resistance, and a favorable safety profile in Chinese CHB subjects receiving 144-week TDF monotherapy or switching from an initial 48-week ADV treatment.

Topic 10: Hepatitis B

No: 1880

Long term treatment with tenofovir disoproxil fumarate for chronic hepatitis B infection is safe and well tolerated and associated with durable virologic response with no detectable resistance 8 year results from two phase 3 trials

Selim Gurel[1], Hakan Senturk[2], Ulus Salih Akarca[3], Patrick Marcellin[4], Robert Flisiak[5], Jorg Petersen[6], Naoky Tsai[7], John F Flaherty[8], Raul Aguilar Schall[8], Kathryn Kitrinos[8], G Mani Subramanian[8], John G Mchutchison[8], Harry Janssen[9], Maria Buti[10], Edward Gane[11]

Uludag Universitesi Tip Fakultesi Gorunkle-Turkey[1], Bezmi Alem University Istanbul-Turkey[2], Ege Universitesi Ismur-Turkey[3], Hospital Beaujon Clichy-France[4], University of Bialystok Bialystok-Poland[5], University of Hamburg Hamburg-Germany[6], University of Hawaii Honolulu-United States[7], Gilead Sciences Foster City-United States[8], University of Toronto Toronto-Canada[9], Universitari Vall D'hebron and Ciberehd Barcelona-Spain[10] Auckland City Hospital Auckland-New Zealand[11]

Aim: Through 5 years of treatment with tenofovir disoproxil fumarate (TDF), we reported sustained viral suppression with regression of fibrosis, and reversal of cirrhosis in 74 % of patients; no resistance to TDF was detected. Here we present Year 8 results from two Phase 3 studies in HBeAg- and HBeAg + chronic hepatitis B patients.
Methods: After 48 weeks of double-blind comparison (TDF vs. adefovir), all patients were eligible to continue open-label TDF. Patients were assessed every 3 months; resistance surveillance was performed annually, and annual bone mineral density (BMD) assessments were included from Years 4-8.
Results: 641 patients were randomized and treated; 585 (91 %) entered the open-label phase, and 412 (64 %) remained on study at Year 8. Durable viral suppression was maintained (75 % and 58 % of HBeAg- and HBeAg + patients had HBV DNA $<$ 69 IU/mL [ITT; missing = failure]; 99.6 % and 98 % had HBV DNA $<$ 69 IU/mL [Observed; missing = excluded]). At Year 8, 47 % and 31 % of HBeAg + patients had HBeAg loss and seroconversion (Observed; missing = excluded). By KM % 13 % and 1.1 % of HBeAg + and HBeAg- patients experienced HBsAg loss (10 %/0.7 % had anti-HBs seroconversion). No resistance to TDF was detected through Year 8. A confirmed renal event (>/= 0.5 mg/dL increase in serum creatinine from baseline, or serum phosphorus $<$ 2 mg/dL, or creatinine clearance $<$ 50 mL/min) was observed in 2.2 % of patients through 8 years, and BMD (hip and spine) results were stable over Years 4-8.
Conclusions: Long term results from these studies show TDF to be safe and effective with no evidence of resistance through 8 years.

Topic 10: Hepatitis B

No: 1317

Serum adipocytokine levels correlate with hbv viremia serum HBsAg levels and liver fibrosis stages in hbeag negative chronic hepatitis B patients

Ching-sheng Hsu[1], Wei-liang Liu[2], Ding-shinn Chen[3], Jia-horng Kao[2]

Taipei Tzu Chi Hospital Buddhist Tzu Chi Medical Foundation Internal Medicine New Taipei-Taiwan[1], National Taiwan University College of Medicine Graduate Institute of Clinical Medicine Taipei-Taiwan[2], Academia Sinica Genomics Research Center Taipei-Taiwan[3]

Background: Adipocytokines play an important role in lipid metabolism and liver disease progression. However, the interactions between hepatitis B virus (HBV) infection and adipocytokines remain largely unknown. AIMS: To investigate the association of HBV infection with adipocytokines in HBV-infected and non-infected subjects. The impact of adipocytokines on serum HBV DNA, HBsAg levels and the severity of liver fibrosis was also examined. METHODS: We conducted a case–control study including 187 HBeAg-negative patients (HBV group), and 184 age, gender and body mass index-matched non-HBV healthy controls (Control group). Fasting blood glucose, lipid profiles, serum adiponectin, leptin and visfatin levels were compared between the two groups. APRI and FIB-4 were calculated to estimate the severity of liver fibrosis.
Results: Among the enrolled 371 subjects, 228 (57.7 %) had lower ALT level (ALT $<$ ULN) and 381(96.5 %) had milder hepatic fibrosis[APRI $<$ 0.7]. HBV patients had serum higher adiponectin levels[HBV vs. control (mean $\pm$ SD): 13.5 $\pm$ 5.8 ng/dL vs. 12.3 $\pm$ 6.3 ng/dL], lower leptin levels(8.3 $\pm$ 5.5 ng/dL vs. 9.1 $\pm$ 1.1 ng/dL), and higher visfatin levels (47.6 $\pm$ 35.5 ng/dL vs. 29.9 $\pm$ 27.7 mg/dL) than controls, and these differences remained significant after adjustment for age, sex, BMI, ALT levels, and FIB-4 ($P < 0.05$). Serum adiponectin, leptin and visfatin levels were significantly associated with serum HBsAg and HBV DNA levels ($P < 0.05$). Although higher serum adiponectin ($P = 0.002$), but lower leptin levels ($P = 0.005$) were associated with advanced liver fibrosis

stage, only higher serum adiponectin level was associated with advanced liver fibrosis in elder male HBeAg-negative patients, but not in controls.
Conclusions: HBeAg-negative HBV patients have significantly higher serum adiponectin, visfatin but lower leptin levels than healthy controls. Serum adipocytokine levels independently correlate with HBV viremia, HBsAg levels and liver fibrosis stages.

Topic 10: Hepatitis B

No: 1493

Mother to child transmission of HBV and HCV in Mongolia

Bayarmaa Otgonbayar[1], Bekhbold Dashtseren[2], Naranjargal Dashdorj[3], Dahgwahdorj Yagaanbuyant[2]

"ach" Medical College Gastroenterology Ulaanbaatar-Mongolia[1], Mongolian National University of Medical Sciences; Onom Foundation Infectious Diseases Ulaanbaatar-Mongolia[2], Onom Foundation Ulaanbaatar-Mongolia[3]

Introduction: Mongolia has one of the highest prevalence of hepatitis B, C and D. Consequently, leading mortality rates of liver cirrhosis and hepatocellular carcinoma (HCC) in the world. It is widely accepted that vertical transmission is one of the main routes of transmission. However, currently there are no systemic intervention is given to prevent vertical transmission, except HBV vaccination. In addition, vertical transmission rate has never been studied in Mongolia.
Aim of study: To study mother-to-child transmission rate of HBV and HCV in Mongolia.
Method of study: This study included 34 subjects, who where born to hepatitis B surface antigen (HBsAg) positive mothers and 18 subjects born to anti-HCV positive mothers. All children and mothers were tested once for the presence of HBsAg and anti-HCV within 2-24 months of delivery.
Results: While two and twenty four months old 2 infants (5.9 %) were tested positive for HBsAg, 2-4 months old 8 infants (44.4 %) were tested positive for anti-HCV. Only 4 infants were older than 6 months and all of them tested negative for anti-HCV.
Conclusion: This study results indicate that the vertical transmission rate of HBV is relatively high in Mongolia. Therefore, it indicates the need of combination strategy of both passive and active immunoprophylaxis. Further follow-up is needed to determine the vertical transmission rate of HCV infection. It is planned that the subjects who were anti-HCV positive will be tested in every 6 months for 2 years.

Topic 10: Hepatitis B

No: 1101

Comparison of the efficacies of entecavir 0.5 and 1.0 mg combined with adefovir in patients with chronic hepatitis B who had failed on prior nucleos(t)ide analogue treatments

Yuri Cho[1], Jeong-hoon Lee[1], Su Jong Yu[1], Jung-hwan Yoon[1], Yoon Jun Kim[1]

Seoul National University College of Medicine Department of Internal Medicine and Liver Research Institute Seoul-Korea, South[1]

Entecavir (ETV) plus adefovir (ADV) combination therapy is one of the useful treatment option for the patients with chronic hepatitis B (CHB) who had failed on prior nucleos(t)ide analogue (NA) treatments. This study compared the efficacies of the combinations of ETV 0.5 mg plus ADV and ETV 1.0 mg plus ADV in patients who had failed on prior multiple NA treatments. This retrospective analysis included 148 consecutive patients with CHB infection in Korea ($n = 37$ with ETV 0.5 mg plus ADV and $n = 111$ with ETV 1.0 mg plus ADV). The virological and biochemical responses were compared between the two groups. The probability of viral suppression of ETV 0.5 mg plus ADV was not inferior to that of ETV 1.0 mg plus ADV (hazard ratio [HR], 0.64; 95 % confidence interval [CI], 0.38–1.08; $P = 0.094$). The changes in serum HBV DNA level in the ETV 0.5 mg plus ADV group were not different between the two groups over 12 months. Moreover, no significant difference was observed in acquiring ETV-resistant variants between the two groups during the treatment (HR, 0.95; $P = 0.953$). This study suggests the proof-of-concept that the lower dose of NA in combination with other NA might be the theoretical option for rescue combination therapy in patients with CHB who had failed on prior multiple NA treatments in order to reduce systemic exposure and possible side effects of NA.

Topic 10: Hepatitis B

No: 2196

Does tenofovir treatment in chronic HBV infection inhibit occurrence of liver cirrhosis and hepatocellular carcinoma

N. Ormeci[1], R. Güner[2], E. Oztaş[3], H. Ozkan[1], M. Ibis[4], S. Koklu[5], O. Ersoy[6], S. Coban[7], E. Ozarslan[8], M. Kucukazman[9], A.k. Dökmeci[1], I. Balık[10], I. Tosun[11]

Ankara University Medical School Department of Gastroenterology Ankara-Turkey[1], Yıldırım Beyazıt University Atatürk Education and Research Hospital Department of Infectious Diseases Ankara-Turkey[2], Türkiye Yüksek Ihtisas Hospital Department of Gastroenterology Ankara-Turkey[3], Gazi University Medical School. Department of Gastroenterology Ankara-Turkey[4], Hacettepe University Medical School Department of Gastroenterology Ankara-Turkey[5], Yıldırım Beyazıt University Atatürk Education and Research Hospital Department of Gastroenterology Ankara-Turkey[6], Dışkapı Education and Research Hospital Department of Gastroenterology Ankara-Turkey[7], Numune Education and Research Hospital Department of Gastroenterology Ankara-Turkey[8], Kecioren Education and Research Hospital Department of Gastroenterology Ankara-Turkey[9], Ankara University Medical School Department of Infectious Diseases Ankara-Turkey[10] Turgut Ozal University Medical School Department of Gastroenterology Ankara-[11]

Hepatitis B virus (HBV) infection is one of the most common infection in the world and 400 million people are chronically infected. It may cause liver cirrhosis in 20-40 % of chronically infected patients. Hepatocellular carcinoma (HCC) occurs in 3-5 % of patients with liver cirrhosis annually. It is controversial whether antiviral treatment can prevent to occur liver cirrhosis and HCC.
Aim: Aim of this three years retrospective and two years prospective cohort study is to search whether tenofovir treatment, 245 mg/per day, inhibits occurrence of liver cirrhosis and HCC or not.
Patients and methods: Two hundred and ninety nine patients who were diagnosed with chronic hepatitis B infection and taking tenofovir treatment, 245 mg/day, for at least three years were included into the study. Patients who had liver cirrhosis or co-infection at the time of diagnosis were excluded.
Results: Mean age was 47.8 (19-70). Male/Female ratio was 207/92. Mean follow-up time after enrollment into the study was 38, 27 (1-288) months. Seven patients (2.3 %) developed cirrhosis and five of

these patients (1.7 %) had HCC. All of five patients with HCC were male. For the 5 HCC cases, 3 patients have been taking TDF from 2009, 1 from 2010 and 1 from 2011. HBV DNA levels are higher than 400 copy/ml at the diagnosis of HCC. Anti HBe positivity was 60.5 % at enrollment. HBV DNA levels decreased to under 400 copy/ml in 90 % of patients at 12th months and 95 % at 36th months. ALT levels also became normal levels in 90 % of patients both at 12th and 36th months.

Conclusion: Tenofovir treatment is very effective in patients with chronic hepatitis B virus infection. Treatment with tenofovir results in decreasing of liver cirrhosis and HCC as compared to historical control.

Topic 10: Hepatitis B

No: 1750

Comparison of serum hepatitis B virus DNA and HBsAg levels between HBeAg negative and HBeAg positive chronic hepatitis B patients

Maryam Keshvari[1], Seyed Moayed Alavian[2], Heidar Sharafi[3]

High Institute For Research and Education In Transfusion Medicine Blood Transfusion Research Center Tehran-Iran[1], Middle East Liver Disease (meld) Center Department of Clinical Hepatology Tehran-Iran[2], Middle East Liver Disease (meld) Center Department of Molecular Hepatology Tehran-Iran[3]

Background: Chronic hepatitis B consists of different clinical phases. Laboratory and histological assessments can help to differentiate the clinical phases and find the better management. This study was conducted to determine laboratory and histological characteristics of HBeAg-negative and HBeAg-positive chronic hepatitis B patients.
Patients and methods: In this study, we evaluated 151 treatment naive chronic hepatitis B patients and divided them according to their HBeAg status. Liver function tests, serum HBV DNA and HBsAg levels, and liver biopsy were performed for the study population.
Results: There was a significant difference in age, HBV DNA and HBsAg levels between HBeAg-negative and HBeAg-positive groups but there was no statistically significant difference in sex, liver function tests, grading and staging on liver biopsy between the groups. HBV DNA and HBsAg levels correlated in both HBeAg-negative and HBeAg-positive chronic hepatitis B patients.
Conclusions: We concluded that the chronic hepatitis B patients had different HBV DNA and HBsAg levels regarding the HBeAg status.

Topic 10: Hepatitis B

No: 1438

Application of gene chip technique in the detection of HBV surface antigen "A" determinant gene mutations

Yanwei Zhong[1], Shengqi Wang[2], Qiqi Liu[2], Hongfei Zhang[1], Shishu Zhu[1], Yi Dong[1], Zhiqiang Xu[1], Dawei Chen[1], Limin Wang[1], Yu Gan[1], Fuchuan Wang[1]

302hospital Pediatric Liver Disease Therapy and Research Center, Institute of Infectious Diseases Beijing-China[1], Academy of Military Medical Sciences Beijing-China[2]

Aims: To establish and evaluate the application value of gene chip technology in the detection of Hepatitis B virus (HBV) surface antigen "a" determinant gene mutations.

Methods: Probes and primers were designed with bio-informatics software based on the sequence of HBV genome to detect HBV surface antigen "a" determinant gene mutation and establish oligonucleotide microarrays. Amplified by PCR, fluorescently labeled fragments were hybridized with oligonucleotide microarrays and then washed, scanned, and analyzed. A method of detecting HBV surface antigen "a" determinant gene mutation was established through specificity, sensitivity, repeatability tests.40 HBV DNA positive samples(suspected with "a" determinant gene mutation) were detected by gene chip technique, 35 HBV DNA-negative controls samples were assayed using the gene chip. The results were compared with HBV DNA sequencing.
Results: In 40 cases HBV DNA positive samples(suspected with "a" determinant gene mutation), 3 cases were wild type, 1 case were T118 K + G145A mutations, 2 cases were T118 K + G145R mutations, 2 cases were P120Q + T126I + G145R mutations, 2 cases were T126I + G145R mutations, 24 cases were T126I mutation, 2 cases were M133T mutations, 1 case M133L mutation, 1 case were G145A mutation, 1 case G145R mutations. The agreements between the microarray and sequencing data are 100 %.
Conclusions: Gene chip technique for the detection of HBV surface antigen "a" determinant gene mutations is reliable and effective method, it can give more information in one test and could be used to detect mutant HBV "a" determinant gene in clinical serum samples.

Topic 10: Hepatitis B

No: 2003

Serum gamma glutamyltransferase is useful for monitoring natural course and predicting treatment outcome of chronic hepatitis B virus infection

C. Wu[1], R. Huang[2], Y. Liu[3], R. Su[4], G.Y. Wang[1], X.M. Yan[1], Y.L. Xiong[1], Z.H. Sun[4], J. Xia[1]

Nanjing Drum Tower Hospital, Nanjing University Medical School Department of Infectious Diseases Nanjing-China[1], Nanjing Drum Tower Hospital Clinical College of Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine Department of Infectious Diseases Nanjing-China[2], Nanjing Drum Tower Hospital, Nanjing University Medical School Department of Laboratory Medicine Nanjing-China[3], Nanjing Drum Tower Hospital, Nanjing Medical University Department of Infectious Diseases Nanjing-China[4]

Aim: To compare serum gamma-glutamyltransferase (GGT) during the natural course of chronic hepatitis B (CHB) and investigate the relationship between GGT and HBeAg seroconversion during nucleos(t)ide analogues (NAs) treatment.
Methods: Two hundred and fifteen CHB patients were retrospectively included and classified according to the definitions of natural phases of CHB, including immune tolerance (IT), HBeAg-positive hepatitis (EPH), HBeAg-negative hepatitis (ENH) and inactive carrier (IC). Thirty-three EPH patients who received NAs treatment including lamivudine plus adefovir combination therapy ($n = 20$) or entecavir monotherapy ($n = 13$) were followed for 48 weeks.
Results: Serum GGT was significantly higher in patients with EPH and ENH as compared with IT, IC and healthy control (HC) groups (all $P < 0.01$). Seven (21.2 %) EPH patients achieved complete response (CR) (serum HBV DNA level < 500 copies/ml and undergone HBeAg seroconversion) after NAs therapy for 48 weeks. Baseline GGT levels were significantly higher in CR group than non-complete response (NCR) group (1.83 ± 0.39 vs. 0.93 ± 0.10 upper limit of normal (ULN), $P = 0.011$). The decline of GGT levels was

significantly more rapidly in CR group after 24 and 48 weeks of treatment compared with NCR group ($P = 0.012$ and $P = 0.008$, respectively). Based on the receiver operating characteristic curve, a cut-off of 0.89 × ULN of the baseline GGT had a sensitivity of 85.71 % and a specificity of 61.54 % to predict a CR .
Conclusions: Serum GGT elevated significantly in EPH and ENH patients. GGT may be a biomarker for prediction of subsequent HBeAg seroconversion in HBeAg-positive CHB with NAs treatment.

Topic 10: Hepatitis B

No: 1295

Assessment of initial nucleos(t)ide analogues for chronic hepatitis B treatment among second tier city hospitals in China a baseline report of the evolve study

Jidong Jia[1], Hong Tang[2], Qin Ning[3], Jiaji Jiang[4], Xiaoguang Dou[5], Jifang Sheng[6], Mingxiang Zhang[7], Shuqin Zhang[8], Jia Shang[9], Jie Liu[10], Wenzhong Tan[10], Hong Li[11]

Beijing Friendship Hospital, Capital Medical University Liver Research Center Beijing-China[1], West China Hospital of Sichuan University Department of Infections Diseases Chengdu-China[2], Tongji Hospital Tongji Medical College Huazhong University of Science and Technology Department of Tongji Hospital Infectious Disease Wuhan-China[3], The First Affiliated Hospital of Fujian Medical University Center of Liver Disease Fuzhou-China[4], Sheng Jing Hospital of China Medical University Infectious Disease Department Shenyang-China[5], The First Affiliated Hospital of Zhejiang University School of Medicine Infectious Disease Department Hangzhou-China[6], The Six Peopol Infectious Disease Department Shenyang-China[7], Hepatology Hospital of Jilin Province Internal Medicine Department Changchun-China[8], Henan Provincial People's Hospital Department of Infectious Disease Zhengzhou-China[9], Bristol-myers Squibb Medical Affairs Department Shanghai-China[10] Bristol-myers Squibb R&d-gheor Wallingford-United States[11]

Purpose: Nucleos(t)ide analogues (NA) treatments for naïve chronic hepatitis B (CHB) patients are heterogeneous in real life practice in China. Studies investigating characteristics of these patients and the effectiveness of various NA treatments in real life practice would improve CHB management.
Methods: A prospective observational study was planned to compare effectiveness of different NAs prescribed per local practice in China. Baseline data of the cohort were analyzed to show characteristics of naïve CHB patients and choices of initial NA treatments.
Results: A total of 3434 patients from 63 hospitals across China were enrolled from 2012 to 2014, with average age 39.5-year-old, 73.8 % males, 61.1 % HBeAg positive, 21.4 % compensated cirrhosis, 32.8 % attributable to maternal-neonatal transmission, 22.7 % having siblings with CHB, and 10.7 % with family history of hepatocellular carcinoma. Initial NA choices were mainly entecavir (53.0 %), lamivudine based (18.3 %), telbivudine (23.3 %), adefovir (4.6 %). Forty-two percent patients had a high viral load (HBV DNA $\geq$ 8log copies/mL); among them, initial treatments using entecavir, lamivudine based, telbivudine and adefovir were 51.0, 17.9, 28.5 and 1.7 % respectively.
Discussions: Nearly 60 % patients were between 30-50-year-old, suggesting a heavy disease burden among the productive population in China. Although most guidelines recommend potent NAs with high genetic barrier to resistance as the first line therapy for naïve patients, nearly a half of them, including those who had high viral load, started treatments using NAs of low barrier to resistance. Thus, this may create increasing concerns over NA-induced resistance among CHB patients in real life practice in China.

Topic 10: Hepatitis B

No: 1883

Clinical features of chronic hepatitis B patients after stopping nucleos(t)ide analogues

Ping Shi[1], Jun Li[1], Yao Liu[1], Longfeng Jaing[1], Yaping Han[1]

The First Affiliated Hospital With Nanjing Medical University Department of Infectious Diseases Nanjing-China[1]

Objective: This study aims to investigate the clinical features of chronic hepatitis B patients after stopping nucleos(t)ide analogues and related factors for hepatitis B relapse.
Methods: We investigated 73 chronic hepatitis B patients who withdrew nucleos(t)ide analogues and analyzed the reasons for withdrawal and related factors for hepatitis B relapse.
Results: Among 73 patients, 10(13.7 %) of them withdrew nucleos(t)ide analogues for economic reason, 15(20.5 %) for poor outcome, 11(15.1 %) for poor compliance and 17(23.3 %) for stable condition. Among patients with total treatment duration more than 24 months, those who stopped entecavir had longer relapse time compared with combination therapy ($P = 0.048$), and lower HBV DNA level while relapsed compared with lamivudine ($P = 0.039$). Among patients who didn't achieve cessation criteria, the correlation coefficient between total treatment duration and relapse time was -0.571($P < 0.001$), and the correlation coefficient between treatment duration after virological response and relapse time was -0.514($P < 0.001$). The COX proportional hazards model analysis showed that total treatment duration was the risk factor for hepatitis B relapse after stopping nucleos(t)ide analogues with patients who didn't achieve cessation criteria.
Conclusion: Most patients stopped nucleos(t)ide analogues without achieving cessation criteria. There was a still high relapse rate among patients in spite of they had achieved cessation criteria. The longer antiviral treatment duration was associated with a short time recurrence with those who didn't achieve cessation criteria.

Topic 10: Hepatitis B

No: 1858

The distribution and dynamic changes of serum 25(oh)d3 in chinese chronic hepatitis B patients with nucleoside analogue treatment results from a real life setting study

En-qiang Chen[1], Hong Tang[1], Lang Bai[1], Tao-you Zhou[1], Juan Wang[1]

West China Hospital, Sichuan University Center of Infectious Diseases Chengdu-China[1]

Aim: The role of vitamin D in chronic liver diseases is widely concerned, but the data in chronic hepatitis B (CHB) is limited. This study aimed to investigate the association of serum 25(OH)D3 levels with clinical parameters and long-term antiviral responses of CHB.
Methods: A total of 93 naïve patients (61 with positive HBeAg, 32 with negative-HBeAg) with nucleos(t)ide analogues treatment for more than 6 years were enrolled. The serum levels of HBV-DNA, HBsAg, and 25(OH)D3 were all quantified at baseline and 6-year of antiviral treatment.

Results: Of those 93 patients, 15 (16.1 %), 54(58.1 %), and 24 (25.8 %) had vitamin D deficiency (25(OH)D3 $<$ 10 ng/mL), vitamin D insufficiency (25(OH)D3 $\geq$ 10 and $<$ 20 ng/mL), or adequate vitamin D levels (25(OH)D3 $\geq$ 20 ng/mL), respectively. and the level of 25(OH)D3 in HBeAg-positive patients were significantly lower than that in HBeAg-negative patients (15.39 $\pm$ 5.53 vs. 18.96 $\pm$ 8.56 ng/mL, $P = 0.017$). Before antiviral therapy, the serum 25(OH)D3 was not correlated with the HBsAg and HBV-DNA titers; and its level was also not correlated with HBeAg seroconversion at 6-year of treatment. Interesting, after 6-year antiviral treatment, the serum levels of 25(OH)D3 were significantly increased [19.71 $\pm$ 7.42 vs.16.62 $\pm$ 6.89 ng/mL, $P = 0.000$]; and there were 2 (2.2 %), 57(61.3 %), and 34 (36.6 %) had vitamin D deficiency, vitamin D insufficiency, or adequate vitamin D levels, respectively.
Conclusions: Serum 25(OH)D3 lacking is very common in naïve CHB patients, and this lacking could be improved significantly after long-term effective antiviral therapy.

Topic 10: Hepatitis B

No: 1526

Liver histology in immune tolerance phase patients with chronic hepatitis B virus infection according to different alanine transaminase level

Dengming He[1], Qinghua Shang[1], Yuqi Znang[1], Yong An[1], Qingqiang Yi[1], Wei Zhang[2], Mingquan Ding[1]

The 88th Hospital Institute of Infectious Disease Tai'an-China[1], The 88th Hospital Institute O Infectious Diseases Tai'an-China[2]

Background and aim: A normal alanine transaminase (ALT) levels does not mean normal liver inflammation. We aimed to observe the difference of liver inflammation in immune tolerance phase chronic HBV infection according to two upper limits of normal ALT standards (30 U/L for males and 19 U/L for females vs. 40 U/L).
Methods: 202 patients were divided into low ALT group ($\leq$ 30 U/L for males and $\leq$ 19 U/L for females) and high ALT group (31-40 U/L for males and 20-40 U/L for females). Ishak and Metavir system were used to evaluate liver inflammation and fibrosis.
Results: Significant difference of Ishak inflammation score and fibrosis score were seen between low ALT group and high ALT group. Positive correlation was seen between ALT levels and Ishak inflammation score or fibrosis staging score. The proportion of mild inflammation was 97.9 % in low ALT group and 65.7 % in high ALT group. Metavir fibrosis staging in all cases of low ALT group is F0 and F1. In high ALT group, the proportion of F0, F1, F2, F3, and F4 was 51.4, 39.0, 7.6, and 1.9 %, respectively. Different distribution of Metavir mild, moderate, and severe or fibrosis staging was seen in age and sex, but not in HBV DNA levels.
Conclusions: For immune tolerance phase patients, the lower ALT ULN is better than the current one in evaluating liver histology. Sex and age are associated with the degree of liver histology for ALT levels $>$ 30 in males or $>$ 19 in females.

Topic 10: Hepatitis B

No: 1348

Telbivudine versus tenofovir treatment in hbeag negative chronic hepatitis B patients treatment intensification based on roadmap concept

Zahari Krastev[1], Iskren Kotzev[2], Mustafa K. Celen[3], David Mcneeley[4], Kamal Hamed[5]

University Hospital "sv. Ivan Rilski" Clinic of Gastroenterology Sofia-Bulgaria[1], University Hospital "sv. Marina" Clinic of Gastroenterology Varna-Bulgaria[2], Dicle University School of Medicine Department of Infectious Diseases Diyarbakir-Turkey[3], Novartis Pharmaceuticals Corporation Established Medicines Dev Franchise East Hanover, Nj-United States[4], Novartis Pharmaceuticals Corporation Global Medical Affairs East Hanover, Nj-United States[5]

Aim: To evaluate the efficacy and safety of telbivudine (LdT) versus tenofovir disoproxil fumarate (TDF) in HBeAg-negative chronic hepatitis B (CHB) patients following the Roadmap concept.
Methods: In this prospective, open-label study, patients were randomized (1: 1) to receive LdT 600 mg q.d. or TDF 300 mg q.d. After LdT/TDF monotherapy for 24 weeks, patients with HBV DNA $\geq$ 300 copies/mL received TDF/LdT add-on therapy until week 104, while those with $<$ 300 copies/mL continued monotherapy. The modified intent-to-treat (mITT) population comprised patients who did not discontinue before and not received add-on therapy at week 24.
Results: Of the 241 randomized patients (LdT, 121; TDF, 120), 232 (LdT, 115; TDF, 117) were included in the mITT population. The primary efficacy endpoint for non-inferiority (margin -10 %) was met, with 92.1 % and 95.0 % of patients on LdT and TDF achieving HBV DNA levels $<$ 300 copies/mL at week 52 [difference in percentages (95 % CI): -2.9 % (-9.1, 3.4)]. The change in eGFR from baseline was significantly greater in LdT monotherapy compared with TDF monotherapy at week 52 (4.21 versus -3.44; $P = 0.0053$) and at week 104 (6.14 versus -3.00; $P < 0.0001$). Compared with TDF monotherapy, twice as many patients on LdT monotherapy (60.5 % LdT versus 27.5 % TDF) with abnormal estimated glomerular filtration rate (eGFR) at baseline reverted to normal at week 104. Serious adverse events deemed unrelated to study treatment were reported in 17 patients (LdT, 8; TDF, 9).
Conclusion: LdT is non-inferior to TDF for treating HBeAg-negative CHB and is associated with improvement in eGFR compared with TDF.

Topic 10: Hepatitis B

No: 1896

Association of genetic variation in il28b rs12979860 with the development of hepatitis B related hepatocellular carcinoma

Abu Saleh Md. Sadequl Islam[1], Salimur Rahman[2], Mamun Al Mahtab[2], Humayun Sattar[3], Sheikh Mohammad Fazle Akbar[4], Ayub Al Mamun[2], Md. Rafiqul Islam[5]

Shaheed Ziaur Rahman Medical College Hospital Medicime Bogra-Bangladesh[1], Bangabandhu Sheikh Mujib Medical University Hepatology Dhaka-Bangladesh[2], Bangabandhu Sgeikh Mujib Medical University Immunology Dhaka-Bangladesh[3], Toshiba General Hospital Medical Sciences Tokyo-Japan[4], Shaheed Ziaur Rahman Medical College Medicine Bogra-Bangladesh[5]

Background: Hepatocellular carcinoma (HCC) is associated with hepatitis B virus (HBV) as an etiological agent in 80 % of cases and is the major cause of death among HBV carriers. Associations between environmental factors, viral factors and the development of HCC in chronic HBV infection have been identified, but the role of host genetic remains illusion. Bangladesh is a densely populated country, where HBsAg positivity in the healthy adult population is 7.2 %–7.5 %.

Objectives: To evaluate the role of host IL28B single nucleotide polymorphism (SNP) in predicting HBV-related HCC susceptibility.
Patients and methods: Single SNP in the IL28B gene (rs12979860C/T) were examined in 116 subjects (including 44 HBV-related HCC patients, 42 non-HCC patients with chronic hepatitis B and 30 healthy controls). This study was done in Department of Hepatology and Department of Immunology, BSMMU, Dhaka from January 2012 to December 2013.
Results: The frequency of CC homozygosity was 70 % in healthy controls and 45.5 % in HCC, the difference being statistically significant ($\chi^2 = 4.35$, $P = 0.037$). The statistically difference was seen between non-HCC patients with chronic hepatitis B (CHB) (69 %) and HCC (45.5 %) ($\chi^2 = 4.35$, $P = 0.037$). However, this significant finding was not seen between non-HCC patients with chronic hepatitis B (CHB) and healthy controls. Carriers of the minor T allele in rs12979860 had a higher risk of HCC compared with non-carriers ($\chi^2 = 12.78$, $P = 0.02$).
Conclusions: The T allele and non-CC genotypes have strong predictive effect of increasing susceptibility HCC. Further studies are needed to investigate other IL28B genes polymorphisms in HBV and HCC patients.

Topic 10: Hepatitis B

No: 1705

Quantitative fibrosis estimation by image analysis predicts development of decompensation and composite events in chronic hepatitis B

Chhagan Bihari[1], Archana Rastogi[1], Ajeet Singh Bhadoria[2], Shiv K. Sarin[3]

Ilbs Pathology Delhi-India[1], Ilbs Clinical Research Delhi-India[2], Ilbs Hepatology Delhi-India[3]

Aim: Study was designed to explore the role of amount of fibrosis in baseline liver biopsies to predict clinical outcomes in chronic hepatitis B (CHB) patients.
Patients and method: Liver biopsy and clinical parameters of CHB cases were analyzed. Fibrosis quantification was done on Masson's Trichrome stained section of adequately sized biopsy by image analysis. Follow-up information related to clinical outcome was collected for each case.
Result: 964 cases of CHB were analyzed, with Mean age of 38.6 ± 14.6 years. Median quantitative fibrosis (QF) was 3.7 % (IQR: 1.6–9.7 %) with substantial variation in various stages. Median QF was: F0, 1 % (0.7 %–1.65 %); F1, 3.03 % (2.07–4.0 %); F2, 7.1 % (5.6–8.7 %); F3, 12.7 % (10.15–16.7 %); F4, 26.9 % (20.3–36.4 %). QF positively correlated with METAVIR staging, FibroScan, and HVPG ($P < 0.001$) and negatively with serum albumin ($P < 0.001$). Upon multivariate logistic regression analysis and adjusting for METAVIR staging- QF, albumin and aspartate aminotransferase for composite events; QF and albumin for decompensation and only QF for Hepatocellular carcinoma, were found to be significant predictors for clinical outcomes. QF values were categorized into five stages: QF1, 0 – ≤5 %; QF2, ≥5 ≤10 %; QF3, >10 ≤15 %; QF4, > 15– ≤ 20 %; QF5, >20 %. Probability of event free survival was found to be decreased in advanced stages of QF.
Conclusion: Estimation of quantitative fibrosis in baseline liver biopsy predicts occurrence of cirrhosis, progression of disease, and disease outcome in CHB patients. QF defines the probability of event free survival in CHB cases.

Topic 10: Hepatitis B

No: 1853

Outcomes of chronic hepatitis B patients who discontinued nucleos(t)ide analogue therapy

Muzzaffar Gill[1], Sidra Gill[2], Ammara Nawaz[2], Misbah Malik[2]

Maroof International Hospital Gastroenterologist/hepatologist Islamabad-Pakistan[1], Maroof International Hospital Gastroenterologist Islamabad-Pakistan[2]

Discontinuation of nucleos(t)ide analogue (NA) treatment for chronic hepatitis B (CHB) is associated with risk of viral relapse and hepatitis flare prompting many experts to recommend lifelong treatment. We wanted to determine the frequency and outcome of NA discontinuation in CHB patients (pts) in our practice.

Topic 10: Hepatitis B

No: 1382

Association between polymorphisms of sodium taurocholate cotransporting polypeptide gene (SLC10A1) and different phonotype of chronic HBV infection

Dengming He[1], Shiqi Tao[1], Xianghua Zeng[1], Maoshi Li[1], Shimin Guo[1], Yuming Wang[2]

Southwest Hospital, Third Military Medical University Institute of Infectious Disease Chongqing-China[1], Southwest Hospital, Third Military Medical University Institute For Infectious Diseases Chongqing-China[2]

Background and aim: Genetic background is an important factor of disease. Sodium taurocholate cotransporting polypeptide (NTCP, encoded by SLC10A1), a multiple transmembrane transporter predominantly expressed in the liver, was found as a functional receptor for HBV. We aimed to observer the association between SLC10A1 polymorphisms and the multiple clinical phenotypes of chronic HBV infection.
Methods: 1454 cases was divided into six groups, including HBV clearance (group A, 273 cases), chronic HBV infection (group B, 1181 cases), immune tolerance (group C, 101 cases), HBeAg-positive chronic hepatitis B (CHB) (group D, 365 cases), HBeAg-negative CHB (group E, 231 cases), and inactive HBsAg carrier (group F, 410 cases). Two SNPs for SLC10A1, rs12882299 and rs4646287, were selected for genotyping.
Results: For rs12882299, there was no significant difference between group A and group B ($P = 0.47$), group C and group D ($P = 0.39$), group E and group F ($P = 0.53$), group A and group F ($P = 0.54$). For rs4646287, there was no significant difference between group A and group B ($P = 0.45$), group C and group D ($P = 0.38$), group D and group E ($P = 0.51$), group E and group F ($P = 0.98$), group A and group F ($P = 0.32$). The significant difference was only seen in rs12882299 ($P = 0.02$, OR = 1.64 [1.07-2.49]) between group D and group E. The susceptibility of HBeAg-negative CHB for genotype T/T-T/C is significant higher than for genotype C/C compared with HBeAg-positive CHB.
Conclusions: Although polymorphisms of SLC10A1 are associated with the susceptibility of HBeAg-negative CHB compared with HBeAg-positive CHB, it seems no special value for the mechanism of different phenotypes of chronic HBV infection.

Topic 10: Hepatitis B

No: 1711

A cross sectional study on intrahepatic cholestasis indicators of viral hepatitis patients

Jun Cheng[1], Jiangbin Wang[2], Wenhong Zhang[3], Yang Cao[4], Xingxiang Yang[5]

Beijing Ditan Hospital Capital Medical University Institute of Infectious Diseases Beijing-China[1], China-Japan Union Hospital of Jilin University Changchun-China[2], Huashan Hospital Affiliated To Fudan University Shanghai-China[3], Guangzhou Eighth People's Hospital Guangzhou-China[4], Sichuan Provincial People's Hospital Chengdu-China[5]

Aim: Intrahepatic cholestasis (IHC) is common in viral hepatitis patients. Although the patients are clinically asymptomatic, the IHC indicators, alkaline phosphatase (ALP) or gamma glutamyltransferase (GGT), remain abnormal. This study is to investigate the IHC indicators for in-patients with viral hepatitis when they are being discharged, and to explore the correlation between IHC indicators and liver fibrosis.
Materials & methods: It is a multi-center, cross-sectional study. A total of 1000 hospitalized patients with viral hepatitis were recruited from five big hospitals. Demographic characteristics, clinical and laboratory data including IHC indicators and liver fibrosis indicators (hyaluronic acid and type IV collagen) were collected. Chi square and multivariate logistic regression were performed to determine the correlation between abnormal IHC indicators and liver fibrosis.
Results: 998 of 1000 patients were included in the analysis (Table 1). 560 patients (56.17 %) had abnormal IHC indicators at discharge. Comparing to patients with normal IHC indicators, patients with abnormal IHC indicators had significantly more abnormal liver fibrosis indicators (hyaluronic acid and type IV collagen; severer Child-Pugh Classification. both $P < 0.001$). Multivariate analysis showed that patients with abnormal IHC indicators had significantly higher risk to have abnormal liver fibrosis indicators ($P = 0.0236$, OR = 1.542), and higher trend to have higher Child-Pugh Classification ($p > 0.05$, OR = 1.238).
Conclusions: More than half of the patients with viral hepatitis had abnormal IHC indicators at discharge, which are correlated with liver fibrosis in clinical practice. Therefore, monitoring and following up on IHC indicators after discharge are recommended for viral hepatitis patients.

Topic 10: Hepatitis B

No: 1869

The impacts of baseline clinical characteristics and hepatitis B virus mutations on curative effects of chronic hepatitis B treated with novaferon

D. M. Tan[1], D. X. Wu[1]

Xiangya Hospitalo of Central South University Department of Infectious Diseases Changsh-China[1]

Aim: To assess the impacts of baseline clinical characteristics of patients with chronic hepatitis B (CHB) and baseline hepatitis B virus (HBV) gene mutations on curative effects of CHB treated with Novaferon. [B]Methods[/B] Enrolled patients accepted Novaferon monotherapy for 24 weeks and follow up for 12 weeks. All mutations of four open reading frames(ORF) were determined prior to Novaferon treatment and all of clinical characteristics were determined at the beginning of treatment and 12 weeks after treatment.
Results: In total of 126 CHB patients who finished the treatment and follow-up, 38.9 % obtained virological response and 32.5, 25.4, 44.4, 23.8 % obtained HBeAg clearance, HBeAg seroconversion, biochemical response and combined response respectively. The baseline DNA level of virological response group was significantly lower than no-virological response group; the baseline ALT level were significantly higher in HBeAg clearance group and HBeAg seroconversion group; female and lower BMI level was prone to acquired biochemical response. Stepwise logistic regression analysis showed that PC-P159T(ntC2288A), BCP-N118T(ntA1726C), BCP-L134L (ntA1775C/G/T) were independent influence factors for virological response. The frequencies of PC-G182C (ntG2357T) was significantly higher in groups with HBeAg clearance group and PC-S64A/T(ntT2003G/A), PC-W28STOP (ntG1896A) was significantly higher in HBeAg seroconversion groups, combined response respectively.
Conclusions: Novaferon was an effective therapeutic drug for CHB patients, different response type was influenced by different clinical characteristics and mutations. Baseline mutations screening could predict curative effect of Novaferon efficiently and offered the optimal drugs for CHB patients.

Topic 10: Hepatitis B

No: 1418

Innate and adaptive immune responses correlate with peginterferon alfa treatment efficacy in chronic hepatitis B patients (the osst immunology study)

Weiming Yan[1], Di Wu[2], Xiaojing Wang[2], Tao Chen[2], Qintao Lai[2], Qi Zheng[2], Jiaji Jiang[2], Jinlin Hou[2], Meifang Han[2], Qin Ning[2]

Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institute of Infectious Disease Wuhan-China[1], Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institution of Infectious Diseases Wuhan-China[2]

Background and aims: The aim of this study was to characterize the immunological features responsible for improved treatment responses in 77 patients with chronic hepatitis B (CHB) treated with peginterferon (Peg IFN) alfa-2a after switching them from entecavir (ETV) therapy.
Methods: Peripheral natural killer (NK) cells, Toll-like receptors (TLRs), T cells, regulatory T cells (Tregs) and programmed death 1 (PD-1) were evaluated dynamically by flow cytometry. Response was defined as hepatitis B e antigen (HBeAg) seroconversion, hepatitis B surface antigen (HBsAg) loss, and HBsAg seroconversion (either as singular events or in combination at week 48).
Results: From week 12 to week 24, compared with ETV responders or Peg IFN alfa non-responders, Peg IFN alfa responders exhibited a significant decline in Treg proportions as well as a diminished negative regulation of CD8 + T cells by Tregs. Those HBeAg-negative patients at baseline treated with Peg IFN alfa also showed significantly decreased Treg proportions and a higher rate of HBsAg seroconversion. Moreover, Peg IFN alfa responders showed a significantly higher increase in the NKG2C + NK cell proportions from baseline to week 12 and of TLR2 + monocytes at week 12 than Peg IFN alfa non-responders.
Conclusions: Successful response to Peg IFN alfa correlates with an early significant restoration of impaired immune responses. Although antiviral treatment response can be achieved by both IFN and ETV,

the underlying immunological features vary which may explain the generally observed difference in off-treatment durability of response between the two treatments, as well as effects on HBsAg. (supported by 2013ZX10002003,NSFC81030007, NSFC81171558)

Topic 10: Hepatitis B

No: 1316

The viral characteristics of hbv reactivation from occult carrier status triggered by chemotherapy or immunosuppressive therapy

Tadashi Inuzuka[1], Yoshihide Ueda[1], Tsutomu Chiba[1], Hiroyuki Marusawa[1]

Kyoto University Gastroenterology and Hepatology Kyoto-Japan[1]

Aims: We investigated viral genetics in patients with reactivation from occult HBV infection triggered by chemotherapy or immunosuppressive therapy.
Methods: Using ultra-deep sequencing analysis of the entire HBV genome in serum, the viral characteristics of 14 individuals originally HBsAg-negative but anti-HBc-positive that experienced HBV reactivation were compared to those of 6 individuals that were originally HBsAg-positive with normal liver functions and experienced HBV reactivation. To investigate the viral genomic status in the livers of HBsAg-negative but anti-HBc-positive individuals, prevalence of the G1896A variant in latently infected livers was determined among 44 healthy individuals that were HBsAg-negative but anti-HBc-positive.
Results: Ultra-deep sequencing revealed that the genetic heterogeneity of reactivated HBV was significantly lower in patients with reactivation from occult HBV carrier status compared with that in patients from HBsAg carrier status. The reactivated viruses from occult HBV infection in each case were almost exclusively the wild-type G1896 or G1896A variant, and the G1896A variant was detected in 42.9 % (6/14), including two cases with fatal liver failure.
The viral population in the livers of healthy individuals that were HBsAg-negative but anti-HBc-positive was also characterized by low viral heterogeneity, and the prevalence of the G1896A variant infection was determined to be 11.4 % (5/44) of individuals with occult HBV infection.
Conclusions: Reactivation from occult HBV infection is characterized by low genetic heterogeneity, with the wild-type G1896 or G1896A variant prevalent. Occult HBV infection status is also characterized by low genetic heterogeneity, and the G1896A variant is predominant in about 10 % of the occult HBV carriers.

Topic 10: Hepatitis B

No: 1307

Tenofovir—best hope for chronic hepatitis B infection

Necati Ormeci[1], Burak Özbaş[1], Rahmet Guner[2], Hasan Özkan[1], Aysun Yalçr[3], Şahin Çoban[4], Abdulkadir Dökmeci[1], Çağdaş Kalkan[1], Osman Yüksel[5], Ömer Başar[5], Ismail Balık[3]

Ankara University Medical School Gastroenterology Ankara-Turkey[1], Atatürk Education and Research Hospital Infectious Diseases Ankara-Turkey[2], Ankara University Medical School Infectious Diseases Ankara-Turkey[3], Dışkapı Yıldırım Beyazıt Education and Research Hospital Gastroenterology Ankara-[4], Hacettepe University Medical School Gastroenterology Ankara-[5]

Aim: To evaluate the effectiveness of tenofovir in terms of HBV DNA supression, HBe Ag and HBs Ag seroconversion, ALT normalization in patients with chronic hepatitis B infection in a real life setting.
Methods: We performed a retrospective analysis of data from 164 patients with chronic hepatitis B who were treated with Tenofovir. Eighty-six patients (52.4 %) were naïve. Seventy eight (47. 6 %) patients were previously treated with anti-viral drugs with standard interferon ($n = 4$), PEG interferon ($n = 14$), standard interferon together with lamivudine ($n = 13$), lamivudine alone ($n = 41$), adefovir ($n = 2$), lamivudine together with adefovir ($n = 1$), entecavir ($n = 2$). Six patients (3.7 %) had liver cirrhosis before treatment of tenofovir.
Results: The patients who have HBV DNA > 104 copy/ml with chronic hepatitis B infection were included in the treatment of Tenofovir. Average follow up time was 30.31 ± 14.33 months. HBV DNA negativity and ALT normalization were 86. 5% and 71. 3% respectively at the last visit. HBe Ag seroconversion occured in 11(19.6 %) out of 164 patients. During the follow up period, 4 (2. 4 %) patients developed liver cirrhosis and in 5 (3 %) patients HCC occured out of 164 patients. HBs Ag seroconversion occured in one patient (0.6 %).
Conclusion: Tenofovir can be used safely and successfully in those patients that were naive, experienced with immune modulators and/or antivirals, HBe Ag positive and HBe Ag negative patients.

Topic 10: Hepatitis B

No: 2198

Natural course of patients with carrier of hepatitis B virus infection. Long term outcome

N. Ormeci[1], C. Savas[2], I. Koksal[3], H. Ozkan[1], M. Demir[4], E. Kayaçetin[5], O. Yuksel[6], R. Guner[7], E. Altıparmak[8], S. Coban[9]

Ankara University Medical School Department of Gastroenterology Ankara-Turkey[1], Gaziantep University Medical School Department of Gastroenterology Gaziantep-[2], Trabzon Technique University Medical Schoo Department of Infectious Diseases Trabzon-Turkey[3], Mustafa Kemal University Medical School Department of Gastroenterology Hatay-Turkey[4], Türkiye Yüksek Ihtisas Hospital Department of Gastroenterology Ankara-Turkey[5], Hacettepe University Medical School Department of Gastroenterology Ankara-Turkey[6], Department of Infectious Diseases Department of Gastroenterology Ankara-Turkey[7], Ankara Numune Education and Research Hospita Department of Gastroenterology Ankara-Turkey[8], Dışkapı Education and Research Hospital Department of Gastroenterology Ankara-Turkey[9]

Aim: Hepatitis B virus infection (HBV) is a dynamic process and it may spontaneously change according to several factors including viral load (HBV-DNA), hepatitis B e antigen (HBe Ag), hepatitis B e antibody (Anti HBe), hepatitis B surface antigen (HBs Ag) status, co-infection, immune system of the host, obesity, using of immunosuppressive drugs or alcohol.

We would like to search the changes of long term outcomes of HBV in terms of HBV-DNA, HBe Ag, Anti HBe, HBs Ag, Anti HBs, immune activation and occurrence of hepatocellular carcinoma.
Patients and methods: This is a retrospective cohort study from seven centers in Ankara, one center in Gaziantep, one center in Hatay. Eight hundred twenty five patients had positive HBs Ag and serum HBV-DNA < 104 copy/ml. Mean age was 45.67 ± 13 (12-89) year and there were 496 male (60.1 %) and 329 female (39.9 %). They

were followed up in terms of HBs Ag, HBe Ag, Anti HBe, Anti HBs, HBV-DNA, ALT, AST, immune activation, need for the treatment, developing of hepatocellular carcinoma (HCC) in every six months.
Results: The patients were followed-up for mean 52.18 months (Minimum 11, maximum 216). Forty six of 825 (5.57 %) patients had HBe Ag positive at the beginning. Thirteen of 46 patients (28.26 %) became HBe Ag negative at the follow up. HBV-DNA and AST levels ($P = 0.97$ and $P = 0.95$) were comparable at the beginning and at the end of follow up period. Serum ALT levels dropped from 42.13 ± 62.02 IU/ml to 25.90 ± 19.34 IU/ml ($P = 0.001$). Twenty two of 825 patients (2.66 %) became HBs Ag negative and 19 (2.30 %) of those developed Anti HBs. Fourteen of 825 patients (1.69 %) had viral activation and they were initiated antiviral therapy. None of the patients developed hepatocellular carcinoma during follow up.
Conclusion: Different from the pertinent literature, frequency of viral reactivation and development of HCC is so rare in Turkish chronic HBV carriers.

Topic 10: Hepatitis B

No: 1149

Characterization of HBsAg decline in the Tenofovir disoproxil fumarate (TDF) and peginterferon alfa 2A (PEG) combination study for chronic hepatitis B (CHB)

Henry L.y. Chan[1], Abdurrahman Kadayifci[2], George Papatheodoridis[3], Man-fung Yuen[4], Rong-nan Chien[5], W.c. Peter Kwan[6], Lanjia Lin[7], Phillip Dinh[7], Eduardo B. Martins[7], Prista Charuworn[7], G. Mani Subramanian[7], John G. Mchutchison[7], Joerg Petersen[8], Mitchell Shiffman[9], Hendrik W. Reesink[10], Seng Gee Lim[11], Young-suk Lim[12], Patrick Marcellin[13]

Prince of Wales Hospital, The Chinese University of Hong Kong Department of Medicine and Therapeutics and Institute of Digestive Disease Shatin-Hong Kong[1], University of Gaziantep Gaziantep-Turkey[2], Athens University Medical School, "laiko" General Hospital of Athens Athens-Greece[3], Queen Mary Hospital, University of Hong Kong-Hong Kong[4], Chang Gung Memorial Hospital, Chang Gung University College of Medicine Keelung-Taiwan[5], University of British Columbia Vancouver-Canada[6], Gilead Sciences, Inc. Foster City-United States[7], University of Hamburg Ifi Institute For Interdisciplinary Medicine At The Asklepios Klinik St. George Hamburg-Germany[8], Bon Secours Health System Liver Institute of Virginia Richmond and Newport News-United States[9], Academic Medical Center Amsterdam-The Netherlands[10], Yong Loo Lin School of Medicine, National University of Singapore Singapore - Singapore[11], Asan Medical Center, University of Ulsan College of Medicine Seoul-Korea, South[12], Hôpital Beaujon, University of Paris Paris-France[13]

Aim: In study GS-US-174-0149, finite treatment for CHB with (TDF + PEG) × 48 weeks increases rates of HBsAg loss at week 48 compared to TDF or PEG monotherapy (Kaplan–Meier estimate: 7.5, 0, and 2.4 %, respectively). Quantitative HBsAg data were analyzed to understand on-treatment HBsAg decline by treatment arm.
Methods: 740 patients with non-cirrhotic CHB were randomized 1: 1: 1: 1 to (TDF + PEG) × 48 weeks (Arm A); (TDF + PEG) × 16 weeks followed by TDF × 32 weeks (Arm B); continuous TDF (Arm C); PEG × 48 weeks (Arm D). Quantitative HBsAg levels at baseline and on-treatment were analyzed and compared using Fisher's or Wilcoxon tests.
Results: At baseline, for Arms A-D, respectively, 0.5 %, 1.6 %, 0 %, 1.1 % had HBsAg levels < 10 IU/ml ($p > 0.05$). By week 24, 11.1, 4.0, 0.6 and 5.8 % had HBsAg levels < 10 IU/ml for Arms A-D, respectively ($P < 0.05$). At Week 48, 15.8, 3.1, 1.2 and 11.3 % achieved HBsAg levels < 10 IU/ml for Arms A-D, respectively ($P < 0.05$); though there was no difference between Arms A vs. D ($P = 0.26$). Significant on-treatment reductions from baseline in HBsAg were seen at Week 48 in Arms A versus D (mean HBsAg change from baseline, −1.1 log10 IU/ml and −0.8 log10 IU/ml, respectively, $P < 0.05$).
Conclusion: PEG monotherapy and (TDF + PEG) × 48 weeks resulted in significant on-treatment HBsAg reductions. Despite achieving similar percentages of on-treatment HBsAg < 10 IU/mL, patients on TDF + PEG combination therapy for 48 weeks achieved higher rates of HBsAg loss and more profound drop in HBsAg titers than PEG monotherapy at week 48.

Topic 10: Hepatitis B

No: 1790

The relationship between hepatitis B virus pre s gene mutation and progression of liver disease in children with hepatitis B virus infection

Yanwei Zhong[1], Hongfei Zhang[1], Liming Liu[1], Fenglin Di[1], Chang Liu[1], Shishu Zhu[1], Yi Dong[1], Zhiqiang Xu[1], Hui Dong[1], Dawei Chen[1]

302hospital Pediatric Liver Disease Therapy and Research Center, Institute of Infectious Diseases Beijing-China[1]

Background/aim: To study the relationship between HBV preS gene variation and progression of liver disease in children with hepatitis B virus(HBV) infection.
Methods: 176 HBV infected patients (17 asymptomatic carriers (ASC), 73 with chronic hepatitis B (CHB), and 86 with HBV related liver cirrhosis (LC)) were analyzed, which aged from 1 to 18 years old. HBV preS genes were amplified by a nested polymerase chain reaction(PCR). and determined by derect DNA sequencing. Variations at 10 interested sites of the preS region were compared among the three groups of patients.
Results: 139/176 (78.97 %) were infected with genotype C and 37/176 (21.03 %) with genotype B. Mutations rate in preS regions of genotype C to genotype B in patients with LC, CHB and ASC were 43.37 % −10.84 % vs 38.71 % – 9.68 % vs 17.64 % – 1.49 %, respectively. The preS gene mutation rates were higher in LC and CHB group than ASC group. The frequencies of preS deletion mutations in the LC and in CHB or asymptomatic carrier (ASC) groups were 6.46 %, 6.45 % and 0, respectively. The detection rate of preS2 start coden mutation was significantly higher in LC group (13.25 %) than CHB(0) and ASC groups(0). With the disease progression, T53C mutations were more commonly found in the LC group with genotype C virus than CHB or asymptomatic carrier (ASC) groups, with the frequencies of 18.8 % in the LC group, 8.11 % in the CHB group, and 0 in the ASC group, respectively.
Conclusions: Children with HBV genotype C virus, preS2 start coden and T53C mutation might associated with disease development.

Topic 10: Hepatitis B

No: 1993

Hbsag loss with tenofovir disoproxil fumarate (TDF) plus peginterferon alfa 2A (PEG) combination therapy in chronic hepatitis B (CHB)

Patrick Marcellin[1], Sang Hoon Ahn[2], Xiaoli Ma[3], Florin Caruntu[4], Won Young Tak[5], Magdy Elkashab[6], Wan-long Chuang[7], Fehmi Tabak[8], Rajiv Mehta[9], Joerg Petersen[10], Eduardo Martins[11], Phillip Dinh[11], Lanjia Lin[11], Amoreena Corsa[11], Prista Charuworn[11], G. Mani Subramanian[11], John Mchutchison[11], Lillian Lou[12], Maria Buti[13], Giovanni Gaeta[14], George Papatheodoridis[15], Robert Flisiak[16], Henry Chan[17]

Hôpital Beaujon, University Paris-Diderot Service Hépatologie Paris-France[1], Yonsei University College of Medicine Division of Gastroenterology Seoul-Korea, South[2], Drexel University College of Medicine Philadelphia-United States[3], National Institute For Infectious Diseases "Matei Bals" Bucharest-Romania[4], Kyungpook National University Hospital Daegu-Korea, South[5], Toronto Liver Center Toronto-Canada[6], Kaohsiung Medical University, Chung-ho Memorial Hospital Hospital Kaohsiung City-Taiwan[7], University of Istanbul Cerrahpasa Medical Faculty Istanbul-Turkey[8], Liver Clinic Surat-India[9], University of Hamburg Hamburg-Germany[10], Gilead Sciences, Inc Foster City-United States[11], Nexus Development Palo Alto-United States[12], Hospital Universitari Vall D'hebron Barcelona-Spain[13], Second University of Naples Naples-Italy[14], Athens University Medical School, "laiko" General Hospital of Athens Athens-Greece[15], Medical University of Bialystok Bialystok-Poland[16], The Chinese University of Hong Kong Hong Kong-Hong Kong[17]

Background: Although desirable, rates of HBsAg loss in CHB patients treated with nucleos(t)ide analogues or PEG therapy are relatively low. We present the Week 72 analysis of an ongoing trial evaluating TDF + PEG combination therapy.
Methods: 740 patients with non-cirrhotic CHB were randomized 1: 1: 1: 1 to receive TDF + PEG × 48 weeks (Arm A); TDF + PEG × 16 weeks followed by TDF × 32 weeks (Arm B); continuous TDF (Arm C); PEG × 48 weeks (Arm D). The analysis at Week 72 (primary endpoint) was pre-specified.
Results: Of the 740 patients, 58.4 % were HBeAg(+), mean age 37 years, 74.9 % Asians and HBV genotype distribution (A, B, C, D, E–H) was 8.2, 27.3, 42.3, 20.8 and 1.1 %, respectively. At week 72, patients receiving PEG + TDF for 48 weeks had significantly higher rates of HBsAg loss than either TDF or PEG alone (Kaplan–Meier estimate: 9.0, 0, and 2.8 %, respectively). Arm A had higher rates of HBs seroconversion (8.0 %) than Arms B (0.6 %), C (0 %) or D (2.9 %). Across all arms, of patients with HBsAg loss at week 72, 65 % (11/17) were HBeAg(+) at baseline and had the following genotype distribution: 23.5 % A, 29.4 % B, 29.4 % C, and 17.6 % D. Rates of HBeAg loss were also higher in arms receiving PEG + TDF (Arm A 29.6 %, Arm B 24.8 %, Arm C 14.7 %, Arm D 25.5 %). No unexpected AEs were observed in the combination arms.
Conclusion: CHB patients treated with TDF and PEG combination therapy for 48 weeks achieved significantly higher rates of HBsAg loss than either therapy given alone at Week 72.

Topic 10: Hepatitis B

No: 1532

Liver histology in immune tolerance phase patients with chronic hepatitis B virus infection according to different alanine transaminase level

Dengming He[1], Qinghua Shang[1], Yuqi Znang[2], Yong An[1], Qingqiang Yi[1], Wei Zhang[1], Mingquan Ding[1]

The 88th Hospital Institute of Infectious Disease Tai'an-China[1], Southwest Hospital, Third Military Medical University Institute of Infectious Disease Tai'an-China[2]

Background and aim: A normal alanine transaminase (ALT) levels does not mean normal liver inflammation. We aimed to observe the difference of liver inflammation in immune tolerance phase chronic HBV infection according to two upper limits of normal ALT standards (30 U/L for males and 19 U/L for females vs. 40 U/L).
Methods: 202 patients were divided into low ALT group ($\leq$ 30 U/L for males and $\leq$ 19 U/L for females) and high ALT group (31-40 U/L for males and 20-40 U/L for females). Ishak and Metavir system were used to evaluate liver inflammation and fibrosis.
Results: Significant difference of Ishak inflammation score and fibrosis score were seen between low ALT group and high ALT group. Positive correlation was seen between ALT levels and Ishak inflammation score or fibrosis staging score. The proportion of mild inflammation was 97.9 % in low ALT group and 65.7 % in high ALT group. Metavir fibrosis staging in all cases of low ALT group is F0 and F1. In high ALT group, the proportion of F0, F1, F2, F3, and F4 was 51.4, 39.0, 7.6, and 1.9 %, respectively. Different distribution of Metavir mild, moderate, and severe or fibrosis staging was seen in age and sex, but not in HBV DNA levels.
Conclusions: For immune tolerance phase patients, the lower ALT ULN is better than the current one in evaluating liver histology. Sex and age are associated with the degree of liver histology for ALT levels >30 in males or >19 in females.

Topic 10: Hepatitis B

No: 1855

Elevated serum levels of alt are associated with metabolic syndrome independent of fatty liver diagnosed by ultrasound

Muzzaffar Gill[1], Sidra Gill[2], Ammara Nawaz[2], Misbah Malik[2], Faiza Irfan[2]

Maroof International Hospital Gastroenterologist/hepatologist Islamabad-Pakistan[1], Maroof International Hospital Gastroenterologist Islamabad-Pakistan[2]

Elevated levels of alanine aminotransferase (ALT), a surrogate marker of liver injury, are mainly due to fatty liver (FL) and are considered an indicator of metabolic syndrome (MS). However, limited information is available on the influence of FL on this association between elevated ALT and MS.

Topic 10: Hepatitis B

No: 2101

Screening of epigenetic compound library using primary hepatocyte persistently infecting hepatitis B virus

Shingo Nakamoto[1], Tatsuo Kanda[1], Shuang Wu[1], Xia Jiang[1], Yuki Haga[1], Reina Sasaki[1], Masato Nakamura[1], Hiroshi Shirasawa[1], Osamu Yokosuka[1]

Chiba University Graduate School of Medicine Chiba-Japan[1]

The liver cancer cell lines producing hepatitis B virus (HBV) do not exactly recapitulate the lifecycle of HBV. We used the HBV infected primary hepatocytes from mouse with humanized liver for drug screening targeted HBV using epigenetic compound library
Methods: Primary hepatocyte (Phoenix Bio, Hiroshima, Japan) was infected with HBV and treated with a collection of 51 epigenetics compounds (Selleck Chemicals, TX, USA) with or without entecavir. HBV production in the culture medium was analyzed at 7 and 14 days after infection. The concentration of the compound was determined based on the half maximal inhibitory concentration. Cell viability was analyzed using cell proliferation assay.
Results: At day 7 and 14 after infection, HBV DNA in the medium reached around 6 log copies/ml in the control and showed 10-100 fold decrease by entecavir. HBV DNA was decreased by 6 of 23 HDAC inhibitors tested. of the 6 HDAC inhibitors, 5 have HDAC1 inhibitory activity while 4 HDAC inhibitors targeting HDAC3, 6, or 8 selectively did not affect HBV production. Quisinostat showed fivefold decreases in HBV DNA level with less than 100nM of concentration without apparent cytotoxicity at day 7. The effect of the compounds was sustained after off-treatment until week 8. Quisinostat did not affect the efficacy of entecavir on HBV DNA level.
Conclusions: HDAC inhibitors may affect the HBV production in primary hepatocytes through epigenetic mechanism. The primary cell culture model may be useful for drug screening targeting HBV as well as analyzing the long term effect of the drug.

Topic 10: Hepatitis B

No: 1407

Association of IL28b cc status with high replicative state and lower alt levels (immune tolerant state) in patients with chronic hepatitis B infection in India

Nirupma Trehanpati[1], Abhijit Chowdhury[2], Samir R Shah[3], Padaki Nagaraja Rao[4], Xin Guo[5], Dongliang Ge[5], Steven J. Knox[5], Anuj Gaggar[5], G. Mani Subramanian[5], John G. Mchutchison[5], Shyam Kottilil[6], Shiv K. Sarin[7]

Institute of Liver and Biliary Sciences Clinical & Cellular Transplant Immunology and Research New Delhi-India[1], Institute of Post Graduate Medical Education and Research Kolkata-India[2], Global Hospitals Mumbai-India[3], Asian Institute of Gastroenterology Hyderabad-India[4], Gilead Sciences, Inc. Foster City-United States[5], Niaid Bethesda-United States[6], Institute of Liver and Biliary Sciences New Delhi-India[7]

Background: Up to 40 million people in India are chronically infected with the hepatitis B virus (HBV). We attempted to characterize regional differences in viral and host factors associated with chronic HBV infection.
Methods: 500 HBV patients not receiving antiviral therapy were enrolled at 19 centers across India. Blood samples to assess HBV genotype, HBV DNA, hepatitis B e antigen status, and hepatitis B surface antigen levels were collected at a single clinic visit. Genotype was determined using TaqMan® SNP Genotyping Assays (ABI) in immune response genes including IL28B (rs12979860), TLR7 (rs3853839), NOD2 (rs2067085), IFNL4 (rs74597329), RIG-I (rs11795404), and PNPLA3 (rs738409).
Results: HBV infection with a low replicative state (HBV DNA < 2000 IU/mL) represented 57 % of patients. Genotype D HBV was most prevalent (63 %). Overall, 65 % of patients had the IL28B-CC genotype; 72 % of patients with HBV DNA ≥ 2000 IU/mL and 59 % of patients with HBV DNA < 2000 IU/mL ($P = 0.004$, Fisher's exact test). This association of IL28B-CC with active viral replication can be largely explained by the association among the patient subgroup with lower ALT levels ($P < 0.001$). In CHB patients with active viral replication, the IL28B-CC genotype was associated with lower ALT levels ($P = 0.022$, Figure). No differences in the frequency of other SNPs were observed.
Conclusions: Across India, most patients with CHB had HBV infection with low replicative state. The association of the IL28B CC genotype with low ALT levels is a novel finding, consistent with a previous observation of higher HCV RNA levels with the IL28B CC genotype.

Topic 10: Hepatitis B

No: 1779

Efficacy of entecavir tenofovir combination therapy for chronic hepatitis B patients with multidrug resistant strains

Yun Bin Lee[1], Jeong-hoon Lee[2], Dong Hyeon Lee[2], Hyeki Cho[2], Hongkeun Ahn[2], Won-mook Choi[2], Young Youn Cho[2], Minjong Lee[2], Jeong-ju Yoo[2], Yuri Cho[2], Eun Ju Cho[2], Su Jong Yu[2], Yoon Jun Kim[2], Jung-hwan Yoon[2], Chung Yong Kim[2], Hyo-suk Lee[2]

Cha Bundang Medical Center, Cha University Department of Internal Medicine Seongnam-Korea, South[1], Seoul National University College of Medicine Department of Internal Medicine and Liver Research Institute Seoul-Korea, South[2]

Background/aim: The emergence of multidrug-resistant (MDR) strains of hepatitis B virus (HBV) is a major concern. This study aimed to investigate the efficacy and safety of combination therapy with entecavir (ETV) plus tenofovir disoproxil fumarate (TDF) against MDR HBV.
Methods: To adjust for differences in baseline characteristics, inverse probability weighting (IPW) using propensity scores for the entire cohort and weighted Cox proportional hazards models were applied.
Results: Ninety-three consecutive patients who were treated with ETV-TDF combination therapy for >6 months were included; at baseline, 45 were infected with HBV strains with genotypic resistance to lamivudine (LAM) and ETV (the LAM/ETV-R group), 28 with strains resistant to LAM and adefovir (ADV) (the LAM/ADV-R group), and 20 with strains resistant to LAM, ETV, and ADV (the LAM/ETV/ADV-R group). The median duration of rescue therapy was 13.0 (range, 6.7 to 31.7) months. Seventy-four of 93 patients (79.6 %) achieved complete virologic suppression. The cumulative probability of complete virologic suppression at month 6 was 63.6 % (55.7, 75.0, and 65.0 % in the LAM/ETV-R, LAM/ADV-R, and LAM/ETV/ADV-R groups, respectively). During the treatment period, these probabilities were not significantly different across the resistance profiles before and after IPW ($P = 0.072$ and $P = 0.510$, respectively). In multivariate analysis, a lower baseline HBV DNA level, but not resistance profiles, was an independent predictor of complete virologic suppression. Renal dysfunction was not observed during the treatment period.
Conclusions: Rescue therapy with ETV-TDF combination is efficient and safe in patients infected with MDR HBV strains regardless of the antiviral drug resistance profiles.

Topic 10: Hepatitis B

No: 1854

Out comes of therapeutic response to tenofovir dipivoxil fumarate (TDF) in chronic hepatitis B pregnant patients

Muzzaffar Gill[1], Sidra Gill[2], Misbah Irfan[2], Ammara Nawaz[2], Faiza Irfan[2]

Maroof International Hospital Gastroenterologist/Hepatologist Islamabad-Pakistan[1], Maroof International Hospital Gastroenterologist Islamabad-Pakistan[2]

Antiviral therapy may be required during pregnancy to control maternal disease and to prevent vertical transmission at third trimester. We prospectively studied the efficacy and safety of TDF in managing these patients.

Topic 10: Hepatitis B

No: 1222

Expression pattern of chemokines ip 10 and rantes in patients suffering from hepatitis B

Arttrika Ranjan[1], Manjita Srivastava[1], Sundeep Goyal[1], V.K. Dixit[1], S.K. Shukla[1], A.K. Jain[1]

Institute of Medical Sciences Gastroenterology Varanasi-India[1]

Chemokines represent a large group of small 8-12 Kd proteins which have the ability to recruit various cell types into sites of inflammation. Regulated upon Activation Normal T cell Expressed and secreted (RANTES) and interferon gamma inducible protein (IP-10), both chemokines are chemotactic for immunocompetent cells and play role in cell mediated antiviral defense. The role of these chemokines has been recently emphasized. In this study the expression pattern of RANTES and IP-10 genes in peripheral blood of hepatitis B patients has been assessed.

96 chronic hepatitis B (CHB) and 80 Acute Viral Hepatitis-B samples were collected. Freshly isolated blood sample were subjected to RNA isolation. Expression study of IP-10 and RANTES was done via RealTime-PCR using specific primers and the fold change was calculated.

Among CHB and AVH both IP-10 and RANTES showed up regulated expression. Expression of both the chemokines was highest in AVH. However among CHB group, in case of e-antigen positive subjects both IP-10 and RANTES showed up regulation of 0.7 fold and 4.2 fold respectively. Whereas e-antigen negative subjects showed a down regulation of about 0.2 folds in case of IP-10.

Expression of chemokines IP-10 and RANTES was elevated in both e antigen positive CHB and AVH. Thus in conclusion, both these chemokines play important role in trafficking inflammatory cells to the site of inflammation in response to viral infection and thus help in mounting a strong immune response. Low expression levels in case of e antigen negative cases can be correlated with attenuated immune response.

Topic 10: Hepatitis B

No: 1352

Lack of hepatitis B surface antigen clearance with prolonged tenofovir disoproxil fumarate or entecavir for Chinese patients with HBEAG negative chronic hepatitis B infection

Bing Li[1], Guo-feng Chen[1], Qing Shao[1], Fan Li[1], Zhong-bin Li[1], Song-hai Chen[1], Chun-yan Wang[1], Dong Ji[1], Xiao-xia Niu[1], Shi-ying Ding[1], Tao Yan[2], Vanessa Wu[3], April Wong[3], Athena Chau[3], Yu-dong Wang[3], Fu-sheng Wang[4], George Kk Lau[3]

Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[1], 302 Hospital International Liver Diagnosis and Treatment Centre Beijing-China[2], Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[3], 302 Hospital The Institute of Translational Hepatology Beijing-China[4]

Background and aims: Clinical and serological data related with prolonged nucleos(t)ide analogues (NUCs) therapy with high resistant barrier, tenofovir disoproxil fumarate (TDF) or entecavir (ETV), for HBeAg negative Chinese patients, is lacking.
Methods: 346 nucleos(t)ide-naïve HBeAg negative Chinese patients treated with either TDF (n = 158) or ETV (n = 188) for over six years, were studied. At baseline, the median age was 48 yrs (range: 29-83 yrs), 57 % were male, ALT was 77 ± 64 IU/L, serum HBV DNA was 6.11 × 104 (range: 1.24 × 104 – 2.44 × 106) IU/mL, HBV genotype B/C (215/131), quantitative HBsAg (qHBsAg) was 3.44 ± 0.42 log10 IU/ml, and liver stiffness measurement (LSM) was 8.6 (range: 3-45) KPa. All patients were followed up at 3-6 monthly intervals. Multivariable regression analysis was performed to identify the independent predictors of HBsAg loss.
Results: Nine (2.6 %) patients had serological clearance of HBsAg (TDF/ETV-4/5, P = NS). They were all taken off from NUCs and two relapsed (both treated with TDF). One patient suffered from fulminant hepatic failure, with good response to re-initiation of TDF. Amino acid substitutions in HBV DNA polymerase associated with resistance to TDF or ETV, were not detected in any patients. HBsAg decline of $\geq$ 1 log10 IU/ml at wk 48 (HR = 12.7, 95 % CI 6.6–38.7; $P < 0.001$) predicted loss of HBsAg. LSM value significantly decreased after TDF/ETV therapy with a median change of LSM value/year −0.78. Five patients developed HCC (TDF/ETV-3/2, P = NS).
Conclusion: Serological clearance of HBsAg is low in treatment-naïve chronic HBeAg negative Chinese patients with prolonged therapy (>6 yrs) with either TDF or ETV.

Topic 10: Hepatitis B

No: 1411

Genomic changes in genotype c hepatitis B virus associated with the development of hepatocellular carcinoma a cohort observational study

Danbi Lee[1], Heather Lyu[2], Young-hwa Chung[1], Jeong A. Kim[1], Priya Mathews[2], Elizabeth Jaffee[2], Lei Zheng[2], Eunsil Yu[3], Young Joo Lee[4]

University of Ulsan, Asan Medical Center Gastroenterology & Hepatology Seoul-Korea, South[1], Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine Internal Medicine Baltimore-United States[2], University of Ulsan, Asan Medical Center Pathology Seoul-Korea, South[3], University of Ulsan, Asan Medical Center Hepatobiliary Surgery Seoul-Korea, South[4]

Background and aims: Genomic changes in hepatitis B virus (HBV) have been suggested to play significant roles in the development of hepatocellular carcinoma (HCC). We aimed to determine the genomic changes in HBV and evaluate their role in the development of HCC in patients chronically infected with HBV of genotype C.
Methods: A total of 240 chronic hepatitis B (CHB) patients were subjected and followed for a median of 105 months. HCC was diagnosed in accordance with the guidelines of the American Association for the Study of Liver Diseases. The entire X, S, basal core

promoter (BCP), and precore regions of HBV were sequenced using the direct sequencing method.
Results: All the subjects were infected with HBV genotype C. of the 240 patients analyzed, 25 (12 %) and 33 (15 %) had the C1653T and T1753 V mutations in X region, respectively; 157 (65 %) had the A1762T/G1764A mutation in BCP region; 50 (24 %) had the G1896A mutation in the precore region; and 67 (28 %) had the pre-S deletion. HCC occurred in 6 patients (3 %). The prevalence of the T1753 V mutation was significantly higher in patients who developed HCC than in those without HCC. The cumulative occurrence rates of HCC were 5 % and 19 % at 10 and 15 years, respectively, in patients with the T1753 V mutation, which were significantly higher than 1 % and 1 % in those with wild-type HBV ($P < 0.001$).
Conclusion: The presence of T1753 V mutation in HBV X-gene significantly increases the risk of HCC development in patients chronically infected with HBV of genotype C.

Topic 10: Hepatitis B

No: 1395

Prevalence and impact of coexistence of hbsag and anti HBS positivity in patients with chronic hepatitis B infection

Ayse Batirel[1], Fatma Bozkurt Kaya[2], Sabahat Cagan Aktas[1], Serdar Ozer[1]

Kartal Dr.lutfi Kirdar Training and Research Hospital Infectious Diseases and Clinical Microbiology Istanbul-Turkey[1], Kartal Dr.lutfi Kirdar Training and Research Hospital Clinical Microbiology Istanbul-Turkey[2]

Aim: To determine the prevalence of "co-detection/co-existence of HBsAg and anti-HBs" (CHAP) and to compare the rate of hepatocellular carcinoma (HCC) development in HBV infected subjects.
METHODS: Data of two groups of patients (Group 1: patients with CHAP, Group 2: HBsAg-positive/anti-HBs-negative patients matched for age, gender, HBeAg status, HBV-DNA level with anti-HBs-positive patients), who had HBsAg positivity for more than six months, were compared.
Results: A total of 1221 consecutive HBsAg positive cases were screened for CHAP. The prevalence of CHAP was 5.2 % [36(56 %) males]. Mean age was 50.5 ± 16.7 (range: 18-90)years. Sixty-four patients with CHAP (Group 1) were matched with 70 HBsAg-positive/anti-HBs-negative patients (Group 2). None of the patients had received HBV vaccination or HBIG. Mean duration of follow-up was 6.28 ± 4.2 years. In Group 1: Serum anti-HBs levels were more than 10 mIU/mL in all patients. Mean anti-HBs level was 72.8 ± 123(range: 10.5-729.6). Only two (3 %) patients were HBeAg-positive, two(3 %) patients had HBV-HDV co-infection. Two patients experienced acute exacerbation of CHB. Mean ALT and AST were 100.2 ± 313 (range: 7-2130) and 58.5 ± 131 (range: 10-762), respectively. Mean HBV-DNA was 11.5 × 106 ± 30.2 × 106 IU/mL. Mean alpha-fetoprotein (AFP) was 3.5 ± 2.2. Only one (1.5 %) patient in Group 1 developed HCC but none (0 %) in Group 2. Concurrence of HBsAg-and-anti-HBs was persistant for a minimum of 6 months in 47 patients who were periodically tested. No significant difference with regard to mean transaminase and AFP levels, and liver imaging findings (except for one patient with HCC) was detected between Group 1 and 2 patients.
Conclusion: Patients with CHB, who have CHAP, particularly in advanced age, should be closely monitored for disease progression and development of HCC.

Topic 10: Hepatitis B

No: 1085

Prevalence and risk factors of hepatitis B infection in pregnant women at the prenatal clinic of the University of the Philippines Philippine General Hospital

Aq Taguba[1], Ga Carpio[2], Lq Tan[3], Jp Ong[1], Mo Daez[1]

University of The Philippines- Philippine General Hospital Section of Gastroenterology, Department of Medicine Manila-Philippines[1], University of The Philippines-Philippine General Hospital Department of Medicine Manila-Philippines[2], University of The Philippines- Philippine General Hospital Department of Obstetrics and Gynecology Manila-Philippines[3]

Background: Perinatal transmission remains to be the leading cause of spread of hepatitis B virus (HBV) in the Philippines. This study aimed to determine the prevalence of HBsAg and hepatitis B e antigen (HBeAg) and associated risk factors for HBV in subjects seeking prenatal care at the Philippine General Hospital (PGH).
Methods: Outpatient charts of consecutive pregnant patients at the prenatal clinic of PGH from January to July 2014 were reviewed. Information on age, marital status, educational attainment, residence, employment status, gravidity, number of sexual partners, history of abortion or stillbirth, surgery, sexually transmitted infection, and results of screening test for syphilis were recorded. Univariate analysis and simple logistic regression were used to determine independent predictors of HBsAg positivity. A p value of < 0.05 was considered as statistically significant.
Results: A total of 768 outpatient charts were reviewed. The prevalence of HBsAg seropositivity was 9.6 %. Among these, 11 were HBeAg positive (15.9 %). HBsAg positive subjects compared with HBsAg negative subjects, tend to be older ($P = 0.016$), married ($P = 0.0032$), have multiple pregnancies ($P = 0.0157$), and have history of spontaneous abortion ($P = 0.0458$). The odds of having HBV infection increased by 5 % for every 1 year increase in age. It was 2.22 times higher among married compared to single subjects; 1.83 times higher among those with history of abortion compared with those without; and 2.00 times higher among those with multiple (< 3) pregnancies than those with fewer pregnancies.
Conclusions: Prevalence of HBsAg seropositivity in pregnant women in PGH remains to be high despite screening guidelines and nationwide HBV vaccination.

Topic 10: Hepatitis B

No: 1599

Long term outcome of sequential therapy with lamivudine followed by interferon in nucleoside naïve hbeag positive patients with chronic hepatitis B virus genotype c infection

Masaru Enomoto[1], Shuhei Nishiguchi[2], Akihiro Tamori[1], Sawako Uchida-kobayashi[1], Shuji Iwai[1], Hiroyasu Morikawa[1], Yoshiki Murakami[1], Hisato Jomura[3], Susumu Shiomi[4], Norifumi Kawada[1]

Osaka City University Department of Hepatology Osaka-Japan[1], Hyogo College of Medicine Department of Internal Medicine Nishinomiya-Japan[2], Wakakoukai Clinic Department of Internal Medicine Osaka-Japan[3], Osaka City University Department of Nuclear Medicine Osaka-Japan[4]

Whether combination with a nucleos(t)ide analogue and interferon is superior to monotherapy for treating chronic hepatitis B is still unclear. Here, we report the long-term outcome of sequential therapy with lamivudine followed by interferon. This study included 24 hepatitis B e-antigen (HBeAg)-positive patients with chronic hepatitis B virus (HBV) genotype C infection who were treated with lamivudine alone for 16–32 weeks, then with interferon and lamivudine for 4 weeks, and lastly with interferon alone for 20 weeks. All patients were followed for 7.1 ± 2.8 post-treatment. The rate of response, defined as ALT normalization, HBeAg loss and HBV DNA < 10[SUP]4[/SUP] copies/ml, was 5/24 (21 %) at 24 weeks post-treatment. The patients with the short-term response were younger than those with no response ($P = 0.039$). The proportion of patients with detectable HBV DNA at the start of interferon was lower among the short-term responders than among non-responders ($P = 0.0059$). Subsequently, 4/5 short-term responders remained drug-free for 4.2 ± 3.5 years post-treatment; the proportion of drug-free patients was higher among the short-term responders than among non-responders ($P = 0.035$). At the last visit, decrease in HBsAg from baseline was larger in patients subsequently given interferon than in patients given nucleos(t)ide analogues only ($P = 0.10$), as was decrease in hepatitis B core-related antigen (HBcrAg) ($P = 0.12$). The rate of response to sequential therapy was limited in HBeAg-positive patients with chronic HBV genotype C infection at 24 weeks post-treatment. In a majority of the short-term responders, the response was sustainable in the long-term. In the non-responders, repeated use of interferon may be beneficial for suppressing HBsAg and HBcrAg levels subsequently.

Topic 10: Hepatitis B

No: 1791

The characterization of hepatitis B virus cccdna in renal tissues from patients with chronic hepatitis B

Yanwei Zhong[1], Jingmin Zhao[1], Hongfei Zhang[1]

302hospital Pediatric Liver Disease Therapy and Research Center, Institute of Infectious Diseases Beijing-China[1]

Background/aim: HBV infection can cause multiple organ damage had been reported. However, it remains unclear whether HBV cccDNA replicates in extrahepatic tissues, particularly in renal tissues, which may serve as a reservoir for the maintenance of infection. The study is to explore the characterization of HBV cccDNA in renal tissues.
Methods: The renal tissues were obtained from 10 patients with chronic hepatitis B. The samples were fixed by 10 % formaldehyde, paraffin imbedded and treated with 0.05 % poly-L-Lysine. The tissue sections were firstly treated by plasmid safe ATP dependent DNase (PSAD) so as to digest relaxed circular DNA(rcDNA) prior to RCA. Four pairs of primers were designed for mediating RCA for the first round amplification of HBV cccDNA. HBV cccDNA was further amplified by a pair of selective primers and digoxigenin labeled probes that targets the gap region between the two direct repeat regions (DR1 and DR2) of the virus after RCA. HBV DNA, HBV surface antigen (HBsAg) and HBV core antigen (HBcAg) were routinely performed.
Results: Of the 10 patients with chronic hepatitis B, HBV DNA, HBsAg and HBcAg were detected in the renal tissues of 2(20 %), 2(20 %) and 2(20 %), respectively. However, none of the detected HBV cccDNA in the renal tissues.
Conclusions: HBV can infect renal tissues but do not replicate in it. Renal tissues may not support viral replication. Further large sample studies are needed to verify our findings.

Topic 11: Hepatitis C

No: 1218

Liver cirrhosis risk calculator for patients infected with hepatitis C virus

Mei-hsuan Lee[1], Hwai-i Yang[2], Sheng-nan Lu[3], Chin-lan Jen[2], Li-yu Wang[4], Yong Yuan[5], Gilbert L.[5], Chien-jen Chen[2]

Institute of Clinical Medicine National Yang-ming University Taipei-Taiwan[1], Academia Sinica Genomics Research Center Taipei-Taiwan[2], Kaohsiung Chang-gung Memorial Hospital Department of Gastroenterology Kaohsiung-Taiwan[3], Medical College Taipei-Taiwan[4], Bristol-myers Squibb Global Health Economics and Outcome Research Nj-United States[5]

Background and aims: We aimed to develop easy-to-use models incorporating non-invasive clinical parameters for predicting risk of liver cirrhosis (LC) among patients infected hepatitis C virus (HCV).
Methods: The cohort consisted of 975 anti-HCV-seropositives who were seronegative for HBsAg. The participants were enrolled in 1991-1992, and followed for their newly-developed LC by abdominal ultrasonography every 6-12 months and computerized data linkage with the National Health Insurance Profile till 2011. The Cox's proportional hazards models were utilized to estimate the regression coefficients of each LC risk predictor. Two risk models were developed: model 1 included age, alanine aminotransferase (ALT), the ratio of aspartate aminotransferase (AST) to ALT; model 2 included the predictors in model 1 and serum HCV RNA additionally. The area under receiver operating curve (AUROC) was used to evaluate the performance of the LC risk models.
Results: Two models for predicting 5-, 10-, and 15-year risk of LC were developed with varied total risk scores. Based on the total risk score for each participant, the study cohort was categorized into three groups with low-, medium-, and high-risk for LC in two prediction models, respectively. The 19-year cumulative LC risk for these three risk groups was 11.3 %, 25.4 %, 38.6 %, respectively, for model 1($P < 0.001$); and 10.3 %, 31.1 %, 41.6 %, respectively, for model 2 ($P < 0.001$). The AUROCs for these two models ranged from 0.69 to 0.72.
Conclusions: LC risk scoring systems were developed for patients infected with HCV, which may be used to triage patients with high risk scores for more intensive care.

Topic 11: Hepatitis C

No: 2218

Shortening overall treatment to 12 weeks of simeprevir plus pegylated interferon ribavirin according to early virologic response in treatment naïve patients with chronic HCV genotype 4 infection and mild to moderate fibrosis

Tarik Asselah[1], Christophe Moreno[2], Michael Gschwantler[3], Antonio Craxi[4], Faisal Sanai[5], Robert Ryan[6], Oliver Lenz[7], Gino Van Dooren[7], Isabelle Lonjon-domanec[8], Michael Schlag[9], Maria Buti[10]

Beaujon Hospital, University of Paris Department of Hepatology Paris-France[1], Cub Hôpital Erasme Hospital, Université Libre De Bruxelles Department of Gastroenterology Brussels-Belgium[2], Wilhelminenspital 4th Department of Internal Medicine Vienna-Austria[3], University of Palermo Department of Internal Medicine Palermo-Italy[4], Division of Gastroenterology, Department of Medicine, King Abdulaziz Medical City, Department of Hepatobilary Sciences and Liver Transplant Jeddah-Saudi Arabia[5], Janssen Research & Development Department of Infectious Diseases Titusville-United States[6], Janssen Infectious Diseases Bvba Department of Infectious Diseases Beerse-Belgium[7], Janssen Pharmaceuticals Department of Infectious Diseases Paris-France[8], Janssen-Cilag Department of Infectious Diseases Vienna-Austrlia[9], Hospital Valle Hebron and Ciberehd Del Institut Carlos Iii Department of Hepatology Barcelona-Spain[10]

Aims: HCV genotype 4 (GT4) is highly prevalent in the Middle East and Sub-Saharan Africa, and is expanding in Europe. To prevent disease progression, short and effective regimens are needed for these patients. This study aims to assess whether treatment with simeprevir + Peg-IFN/ribavirin can be shortened to 12 weeks, based on early viral kinetics, in patients with mild-to-moderate fibrosis.
Design: Phase-3, open-label study, including treatment-naïve patients in Europe and Saudi Arabia with HCV GT4. In patients with HCV-RNA < 25 IU/mL (detectable/undetectable in IL28B CC, undetectable in CT/TT [Roche COBAS[SUP]®[/SUP] Taqman®] at Week 2, and undetectable at Weeks 4 and 8, all treatments were stopped at Week 12. Otherwise, Peg-IFN/ribavirin was continued to Week 24.

On-treatment and SVR4 data from the European patients are presented.
Results: 50 patients were enrolled (male: 72 %, white: 83 %, GT4a/d/other: 36/40/24 %, METAVIR F0–F1/F2: 78/22 %, IL28B non-CC: 84 %). 46 patients completed simeprevir; three discontinued due to an AE; one met a virologic stopping rule. 24/50 were eligible for 12 weeks of treatment. 14/26 patients extending to 24 weeks are currently ongoing with Peg-IFN/ribavirin. Treatment with simeprevir + Peg-IFN/ribavirin was well tolerated: SAE (n = 1); grade 3/4 AE: 26 %/0 %.

Of the 24 patients eligible for 12 weeks (Table), none discontinued or relapsed to date. Among initial patients evaluable, SVR4 was 94 % (16/17; one patient missing SVR4 data).
Conclusions: 48 % of GT4 patients met the criteria for stopping treatment at Week 12. of these patients, preliminary SVR4 rates are promising in GT4a/d, with SVR12/24 data and SVR data in Saudi Arabian patients forthcoming.

Topic 11: Hepatitis C

No: 2233

Hepatitis C virus associated mixed cryoglobulinaemia

Ramin Farajpour[1], Ali Ghavidel[2], Shiva Farajpour[3], Mohammadhosein Soomi[2], Mehdi Farhoodi[4]

Student Research Committee of Tabriz Medical University Faculty of Medicine Tabriz-Iran[1], Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences Tabriz-Iran[2], Vice Chancellor For Research and Technology of Tabriz Medical University Nsrcc (neuroscience Research Center) Tabriz-Iran[3], Nsrcc (neuroscience Research Center) Nsrcc (neuroscience Research Center) Tabriz-Iran[4]

Abstract: Mixed cryoglobulinaemia (MC) is common in patients with chronic hepatitis C virus (HCV) infection. However, clinically significant vasculitis occurs only in a minority of these patients. The classical presentation of MC is a triad of cutaneus vasculitis, peripheral neuropathy and arthralgia. Anti-viral therapy is the standard treatment and good response depends on viral clearance. We hereby report a driver man with chronic HCV infection and MC presenting with polyarthralgia and skin purpura of the lower limbs. He later developed clinical remision and anti-viral therapy resulted in good clinical response.

Topic 11: Hepatitis C

No: 1635

Hepatitis C virus genotype analysis in people with spontaneous virus clearance using a novel serotyping assay

Ruifeng Yang[1], Lai Wei[1]

Peking University People's Hospital Peking Univesity Hepatology Institute Beijing-China[1]

Objective: We aimed to evaluate the accuracy of a new HCV serotyping assay and detect the genotypes in people with spontaneous HCV clearance.
Methods: Paired serum samples were drawn from 140 consecutive chronic hepatitis C (CHC) patients before pegylated interferon alpha treatment and after 24 weeks off-treatment. 114 patients achieved a sustained virological response. Genotype was determined using the serotyping assay and the NS5B or core sequencing method. Subsequently, 51 people with HCV spontaneous clearance were serotyped. These people had a positive anti-HCV antibody results by the Vitros anti-HCV assay. All patients provided informed consent.
Results: All the 140 baseline samples from CHC patients were successfully genotyped using the sequencing method. There were 67.1 % (94/140) genotypes 1, 27.9 % genotype 2 (39/140), and 5.0 % genotype 3 (7/140) samples. The serotyping assay failed to genotype 14.3 % (20/140) samples, but was highly consistent with the sequencing method with a consistency of 90.0 % (108/120). Furthermore, all paired samples at baseline and after therapy from the 108 patients yielded the same genotyping results by using the serotyping assay. In 51 samples from people with spontaneous HCV clearance, all remained high anti-HCV level (S/Co 7.97-16.50). 46 were successfully serotyped. 69.6 % (32/46), 26.1 % (12/46) and 4.3 % (2/46) were genotypes 1, 2 and 3, respectively. There was no significant difference of genotype distribution between the people with spontaneous clearance and CHC patients ($P = 0.75$).
Conclusions: The newly developed HCV serotyping assay is suitable to genotype samples with or without HCV RNA. Genotype distribution in those with spontaneous viral clearance is similar with that in CHC patients.

Topic 11: Hepatitis C

No: 1421

ACH 3422 a novel nucleotide prodrug inhibitor of HCV NS5b polymerase exhibits no selective impairment of mitochondrial biogenesis and function in vitro

Wengang Yang[1], Yongsen Zhao[1], Dharaben Patel[1], Guangwei Yang[1], Joanne Fabrycki[1], Steven Podos[1], Jason Wiles[2], Avinash Phadke[2], Mingjun Huang[1]

Achillion Pharmaceuticals Biology New Haven-United States[1], Achillion Pharmaceuticals Chemistry New Haven-United States[2]

Background & aims: ACH-3422 is a uridine nucleotide prodrug inhibitor of HCV NS5B RNA polymerase in phase 1 clinical studies. Here we assess its mitochondrial toxicity potential by evaluating the activity of its triphosphate derivative (ACH-3430) on nuclear and mitochondrial polymerases with enzymatic assays and the effect of ACH-3422 on mitochondrial function and biogenesis with cell based-assays.
Methods: ACH-3430 inhibition of the following human enzymes was measured using recombinant enzymes or nuclear extracts: DNA polymerases α and β (chromosomal DNA replication), RNA polymerase II (mRNA synthesis), DNA polymerase γ (mitochondrial DNA replication), and RNA polymerase POLRMT (mitochondrial RNA synthesis). Potential mitochondrial dysfunction was assessed by comparison of ACH-3422 cytotoxicity in glucose- and galactose-based media. Mitochondrial DNA (mtDNA), mtRNA, and mtDNA-encoded protein levels were examined relative to chromosomally encoded comparators following cellular ACH-3422 treatment.
Results: ACH-3430 showed no inhibition of DNA polymerases α, β and γ (IC50 > 1000 μM), and very weak inhibition of RNA polymerase II (IC50 ~ 316 μM). ACH-3430 did not inhibit POLRMT (IC50 > 1000 μM) and was incorporated into RNA by POLRMT at least 1000-fold less efficiently than native UTP. ACH-3422 conferred similar cytotoxity in glucose- and galactose-based media, indicating the absence of any mitochondria-dependent cytotoxicity that might be masked in glucose-based media by excess glycolysis. Finally, ACH-3422 treatment caused no selective inhibition of mtDNA, mtRNA, or mtDNA-encoded protein synthesis in hepatic and non-hepatic cells.
Conclusions: The data presented here from enzymatic and cell-based assays indicate a low potential for mitochondrial toxicity of ACH-3422 in vivo.

Topic 11: Hepatitis C

No: 1031

Simeprevir and sofosbuvir with modified doses of ribavirin (RBV) therapy on telaprevir experienced co infected (with HIV) cirrhotics with chronic hepatitis C (CHC) a randomized open label clinical pilot study stop C

Patrick Basu[1], Niraj James Shah[2], Mark Alousius[3], Robert Brown Jr[4]

King's County Hospital Medical Center, Ny Gastroenterology and Hepatology New York-United States[1], James J. Peters Va Medical Center, Icahn School of Medicine At Mount Sinai, Ny Internal Medicine New York-United States[2], King's County Hospital Medical Center, Ny Surgery New York-United States[3], Columbia University College of Physicians & Surgeons, New York Presbyterian Medicine New York-United States[4]

Objectives: Co-infected cirrhotics (HIV + CHC) are at a greater risk for rapid decompensation affecting QOL and have a higher transplant risk burden. Interferon based therapy entails a longer duration with an increased susceptibility of infections and marrow suppression warranting use of growth factors and even discontinuation of therapy/treatment failure. Telaprevir; a protease inhibitor (PI) based therapy have proved efficacious in co-infected patients. Newer generation PI coupled with polymerase inhibitors and adjusted doses of RBV have shown favorable outcomes.
Methods: Fifty (n = 50) co-infected (HIV + CHC, non AIDS) cirrhotics with mean MELD 16, HIV RNA undetectable, mean CD 4 count 439, Hb 10.7, HCV RNA 1.7 million copies, mean platelet count 104, albumin 2.9 and WBC 4600. 18 genotype 1a and 32 genotype 1b. 16 null responders, 12 relapsers while 12 discontinued treatment.

Group A: Simeprevir 150 mg + Sofosbuvir 400 mg + RBV for 24 weeks.
Group B: Simeprevir 150 mg + Sofosbuvir 400 mg + RBV 1000 mg for 16 weeks.

Results: Group A, n = 22, 24 weeks, Simeprevir 150 + Sofosbuvir 400 mg + RBV Group B, n = 28, 16 weeks, Simeprevir 150 mg + Sofosbuvir 400 mg + RBV 1000 mg.

Undetectable 48 h 2 4
Undetectable 1 week 3 7
Undetectable 2 weeks 16 19
Undetectable 8 weeks 17 22
Undetectable 12 weeks 17 23
Undetectable 16 weeks 17 23
Undetectable 24 weeks 18

Conclusion: The combination of Interferon free oral regimen in special population with prior experienced PI demonstrated no difference of SVR in 16th week over 24th weeks. This regimen was well.

Topic 11: Hepatitis C

No: 1202

Serial spirometric changes in patients on interferon therapy for hepatitis C virus treatment

Salman Shakeel[1], Asif Mehmood[1], Ghias Un Nabi Tayyab[2]

Postgraduate Medical Institute Medicine Lahore-Pakistan[1], Postgraduate Medical Institute Gastroenterology Lahore-Pakistan[2]

Introduction: IFNα is used to treat HCV along with oral ribavirin. Several patients on IFN therapy experience dyspnea and dry cough. However, no prospective study has explored the serial spirometric changes during this therapy.
OBJECTIVE: To study the serial effects of IFN therapy on Pulmonary Function Tests using Spirometry.
Materials and methods: It is single centred, prospective analysis of 308 patients who presented to Hepatology Outpatient Clinic from November 2013 for standard HCV therapy. The Spirometry of these patients was done at 0,1,2,3,4,5,6,9 months. Data was analyzed in SPSS 20 with repeated ANOVA measurements. The quantitative data like age, FEV1, FVC, FEV1/FVC ratio was presented as mean ± S.D.
Results: 167 (54.2 %) males with mean age 39.4 years and 141 (45.8 %) females with mean age 41.8 years. The male: female ratio was 1.2: 1 respectively. The changes seen in Spirometry were; mean maximum reduction (SD) in FEV1 was 8.4 % (13.1 %), in FVC was 6.8 % (8.6 %), and FEV1/FVC was 2.4 % (4.1 %). Maximum declines were observed in group taking conventional INFα2b, followed by Peg INFα2b and then peg INFα2a. Absolute declines ≥ 10 % from baseline occurred in 106 (41 %) for FEV1, 99 (38 %) for FVC and 11 (4 %) for FEV1/FVC. The presence of symmetric declines in FEV1 and FVC combined with a normal FEV1/FVC is indicative of mild pulmonary restriction.
Conclusions: Patients with HCV who develop severe dyspnea during IFN therapy should have their PFTs checked especially those having pre-existing chronic pulmonary disease. Patients with respiratory adverse Events and with clinically relevant reductions in pulmonary function should be referred for further pulmonary consultation.

Topic 11: Hepatitis C

No: 1383

Fixed dose oral combination therapy with daclatasvir asunaprevir beclabuvir ± ribavirin for patients with chronic HCV genotype 1 infection and compensated cirrhosis unity 2 phase 3 results

Andrew Muir[1], Fred Poordad[2], Jacob Lalezari[3], Gregory Everson[4], Gregory Dore[5], Paul Kwo[6], Christoph Hézode[7], Paul Pockros[8], Albert Tran[9], Alnoor Ramji[10], Rong Yang[11], Eric Hughes[11], E. Scott Swenson[12], Philip Yin[12]

Duke Clinical Research Institute, Duke University School of Medicine, Medicine - Gastroenterology Durham-United States[1], Texas Liver Institute, University of Texas Health Science Center, San Antonio-United States[2], Quest Clinical Research, San Francisco-United States[3], University of Colorado School of Medicine, Denver-United States[4], Kirby Institute, Unsw Australia, Sydney-Ashmore and Cartier[5], Indiana University School of Medicine, Indianapolis-United States[6], Hôpital Henri Mondor, Université Paris-est, Créteil-France[7], Scripps Clinic, La Jolla-United States[8], Centre Hospitalier Universitaire De Nice, Nice-France[9], University of British Columbia, Vancouver-Canada[10], Bristol-myers Squibb, Princeton, Princeton-United States[11], Bristol-Myers Squibb, Wallingford-United States[12]

Introduction: The all-oral combination of daclatasvir (DCV; pangenotypic NS5A inhibitor), asunaprevir (ASV; NS3 protease inhibitor), and beclabuvir (BCV; BMS-791325; non-nucleoside NS5B inhibitor)—DCV-TRIO regimen—was studied with and without ribavirin (RBV) in treatment-naive and treatment-experienced patients with HCV genotype (GT)1 infection and compensated cirrhosis in a phase 3, international clinical trial.
Methods: Patients were randomly assigned to receive a fixed-dose combination (FDC) of DCV 30 mg, ASV 200 mg, and BCV 75 mg, with blinded RBV or placebo, twice-daily for 12 weeks. SVR12 rates in the treatment-naive and experienced cohorts were evaluated separately as key efficacy outcomes.
Results: SVR12 results in treatment-naive and -experienced cirrhotic patients are in the table below. Virologic failure was observed in 13 (6 %) patients. Baseline characteristics were comparable between treatment-naive (N = 112) and treatment-experienced (N = 90) groups. Overall, patients were 66 % male and 27 % IL28B (rs1297860) CC genotype; 74 % of patients had GT1a infection and 26 % had GT1b. There were 3 serious adverse events (SAEs) considered treatment-related, 1 AE leading to DCV-TRIO discontinuation, and no deaths. The most frequent AEs (>10 % of patients) were fatigue, headache, nausea, diarrhea, insomnia and pruritus. Hemoglobin < 9 g/dL on treatment was observed in 5 % of patients in the RBV-containing cohorts but in no patients in the RBV-free cohorts.
Conclusions: Twelve weeks of all-oral treatment with DCV/ASV/BCV FDC, with or without ribavirin, achieved high rates of SVR12 in 202 cirrhotic patients with GT1 infection. These results demonstrate the potent antiviral activity, tolerability and safety of the DCV-TRIO regimen in patients with compensated cirrhosis.

Topic 11: Hepatitis C

No: 1490

Cost effectiveness of sofosbuvir based therapy for chronic HCV genotype 1b infection in China

Yu-dong Wang[1], Guo-feng Chen[2], Vanessa Wu[1], April Wong[1], Athena Chau[1], Qing Shao[2], Fan Li[2], Bing Li[2], Dong Ji[2], Zhong-bin Li[2], Song-hai Chen[2], Chun-yan Wang[2], Xiao-xia Niu[2], Shi-ying Ding[2], Tao Yan[3], George Kk Lau[1]

Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[1], 302 Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[2], 302 Hospital International Liver Diagnosis and Treatment Centre Beijing-China[3]

Background and aims: Worldwide, China carries the largest number of chronic hepatitis C infected patients. Recently, sofosbuvir (SOF), an oral NS5B nucleotide polymerase inhibitor, is indicated for the treatment of patients infected with hepatitis C virus (HCV). We evaluate the long-term health economic outcomes of 12-weeks SOF + pegylated interferon-α/ribavirin (NEUTRINO regimen) compared with standard 48-weeks pegylated interferon-α/ribavirin (PR48) in patients infected with HCV genotype 1b in China.
Methods: We developed a decision-analytic Markov model to estimate health outcomes, number needed to treat and short-term and long-term economic outcomes, including incremental cost-effectiveness ratios and cost per sustained virological response (SVR). It considered chronic G1b HCV Chinese- treatment-naıve and treatment-experienced, at the hepatitis C centre, Beijing 302 hospital, China.
Results: There is a reduction in the incidence of new cases of liver-disease complications with NEUTRINO regimen compared with PR48 (55-75 %). According to the International Monetary Fund (2013), the gross domestic product per capital of China is 15 % of the USA counterpart. With the high cost of SOF (USD 84,000 for 12-weeks), high IL-28 CC genotype (allele frequency Rs12979860 C/T- 0.92/0.08) which increases SVR with PR48 therapy, and low health-care cost in China, NEUTRINO regimen is not dominated as compared to PR48 in treatment-naïve chronic G1b patients.
Conclusion: 12-weeks sofosbuvir + pegIFN/RBV (NEUTRINO regimen) failed to yield favorable health and economic outcomes than current PR48 treatment regimens for patients with chronic G1b patients in China.

Topic 11: Hepatitis C

No: 1655

Significance of insulin resistance according to liver status in chronic hepatitis C patients after peginterferon based therapy

Hyemin Park[1], Woo Jin Chung[1], Jung Min Kim[1], Chang Jae Hur[1], Kyung Ho Yang[1], Jung Min Lee[1], Eun Sung Choi[1], Sang Min Lee[1], Byoung Kuk Jang[1], Jae Seok Hwang[1], Eun Soo Kim[1], Kyung Sik Park[1], Kwang Bum Cho[1]

Keimyung University Hospital Gastroenterology Daege-Korea, South[1]

Background/aim: Homeostasis model assessment-insulin resistance(HOMA-IR) is used for assessment of insulin resistance(IR) and is associated with chronic hepatitis C (CHC) virus infection. This study aimed to evaluate interactions between IR and disease status of CHC patients.
Methods: We reviewed medical records of CHC patients who receive peginterferon based therapy from September 2009 to March 2013 at Keimyung University Dongsan Hospital. We analyzed the changes of HOMA-IR score before and after treatment.
Results: 1. 212 patients were included (108 men; mean age, 56.12 ± 11.1 years) for this study. The prevalence of genotype 1a, 1b, 2a, 2b, and 3a were 1.4, 53.3, 43.3, 0.9, and 0.9 %. Disease status were divided as chronic hepatitis (n = 166), cirrhosis (n = 15), and

HCC (n = 31). 2. 130 Patients (61.3 %) received peginterferon with ribavirin and 120 patients (92 %) achieved SVR. SVR rates were 98.5 % in 1a, 95.4 % in 1b, 98.9 % in 2a, 100 % in 2b and 100 % in 3a. 3. Before treatment, HOMA-IR were 2.53 ± 3.28 in hepatitis, 7.27 ± 11.63 in LC, and 9.62 ± 18.36 in HCC group ($P = 0.00$). After treatment, HOMA-IR were changed to 1.62 ± 1.30 in hepatitis ($P = 0.018$), and 2.02 ± 1.11 in LC group ($P = 0.952$). 4. Among initially high(> 2.5) HOMA-IR groups, SVR rates were 96 % in hepatitis and 100 % in LC group. Among initially low (≤ 2.5) HOMA-IR groups, SVR rates were 94.8 % in hepatitis and 67 % in LC group.

Conclusion: Aggravated IR was observed in more progressed disease status of CHC patients and, peginterferon based therapy improved insulin resistance in CHC patients regardless of initial HOMA-IR status. So, more data about improvement of IR after treatment may be needed in DAA era.

Topic 11: Hepatitis C

No: 1678

Failure of revolade to improve sustained virologic response of interferon associated therapy in patients with chronic HCV infection and child pugh class b diseases

Bing Li[1], Guo-feng Chen[1], Qing Shao[1], Fan Li[1], Dong Ji[1], Zhong-bin Li[1], Song-hai Chen[1], Chun-yan Wang[1], Xiao-xia Niu[1], Shi-ying Ding[1], Tao Yan[2], Vanessa Wu[3], Athena Chau[3], April Wong[3], Yu-dong Wang[3], George Kk Lau[3]

Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[1], 302 Hospital International Liver Diagnosis and Treatment Centre Beijing-China[2], Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[3]

Background and aims: Thrombocytopenia is a common limiting factor for the initiation for interferon-based therapy for cirrhotic patients with hepatitis C virus (HCV) infection. Recently, eltrombopag (Revolade, GSK) was shown to "enable" more patients with HCV infection and thrombocytopenia (platelet count < 75,000/μL) to achieve sustained virological response rate with 48 weeks pegylated interferon and ribavirin (PR48) therapy. We study the efficacy of eltrombopag enhanced 12 weeks sofosbuvir, pegylated interferon and ribavirin ("NEUTRINO" therapy) in chronic HCV GT1b cirrhotic patients thrombocytopenia.

Methods: Twenty-five patients Chinese with CHC GT1b, Child–Pugh class B disease, with thrombocytopenia (platelet count < 75,000/μL) were studied. They received open-label eltrombopag (25-100 mg/day) for at least 8 weeks. Patients whose platelet counts reached the predefined minimal threshold as described previously (Afdhal et al. Gastro 2014) were treated with "NEUTRINO" therapy. All patients, initiated "NEUTRINO" therapy were maintained on eltrombopag. The primary end point was sustained virologic response (SVR) 12 weeks after completion of antiviral therapy.

Results: Only nine (36 %) patients who received eltrombopag, achieved the required platelet threshold for the initiation of "NEUTRINO" therapy. The median time to achieve required platelet threshold was 5 weeks. Despite being kept on eltrombopag, only four patients did not need dose reduction or withdrawal of pegylated interferon. SVR12 was achieved in only 1 (4 %) patients.

Conclusions: Eltrombopag-enable "NEUTRINO" therapy was ineffective for CHC GT1b patients with Child-Pugh Class B patients. Pan-oral interferon-free regimen should be further explored in these patients.

Topic 11: Hepatitis C

No: 1499

Efficacy and safety of neutrino therapy for chronic hepatitis C virus genotype 1b treatment experienced Chinese patients

Qing Shao[1], Fan Li[1], Bing Li[1], Dong Ji[1], Zhong-bin Li[1], Song-hai Chen[1], Chun-yan Wang[1], Xiao-xia Niu[1], Shi-ying Ding[1], Guo-feng Chen[1], Tao Yan[2], Vanessa Wu[3], Athena Chau[3], April Wong[3], Yu-dong Wang[3], George Kk Lau[3]

Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[1], 302 Hospital International Liver Diagnosis and Treatment Centre Beijing-China[2], Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[3]

Background and aims: Twelve weeks sofosbuvir with peginterferon–ribavirin (NEUTRINO regimen) has been approved for treatment of genotype 1 (G1) chronic hepatitis C (CHC) infection, based on the reported rate of sustained virologic response of 90 % in treatment-naïve patients (Lawitz et al. NEJM 2013). However, its efficacy and safety in treatment-experienced GT1 patients are not determined.

Methods: Ninety-six treatment-experienced Chinese with CHC GT1b infection were treated with NEUTRINO regimen (Group 1, n = 32) or standard 48 weeks of pegylated interferon-α2a 180 μg weekly plus ribavirin 1200 mg daily (Group 2, n = 64). The primary efficacy end point was a sustained virologic response 12 weeks after the end of treatment for group 1 and 24 weeks for group 2. At baseline, liver stiffness measurement (LSM) using transient elastography (FibroScan®) was used to assess liver fibrosis and the single nucleotide polymorphism of interferon-λ 3 (IL-28, rs12979860, C or T) and IFLN4 (ss469415590, TT or ΔG) was determined.

Results: Sustained virologic response rate was higher in Group 1 than Group 2 (50 % Vs 15 %, $P = 0.001$). Using multivariate analysis, null responder, liver stiffness measurement > 20 kPa (by FibroScan®) and IL28 non-CC were associated with treatment failure. There was a significantly higher incidence of adverse events in Group 2 as compared to Group 1.

Conclusion: Twelve weeks sofosbuvir with peginterferon–ribavirin is more effective than standard 48-weeks peginterferon-ribavirin therapy, for treatment-experienced CHC Chinese with GT1b.

Topic 11: Hepatitis C

No: 1681

Implication of type 2 diabetes susceptibility loci in hepatitis C virus infection

Wei Zhang[1], Huiying Rao[1], Lai Wei[1]

Peking University Hepatology Institute Beijing-China[1]

Background/aims: There is a significant association between hepatitis C virus (HCV) infection and the risk of type 2 diabetes (T2D). However, the implications of genetic susceptibility loci for T2D in populations with HCV infection are unclear. We therefore conducted a study to detect susceptibility loci for T2D in Chinese infected with HCV.

Patients & methods: A total of 100 representative single-nucleotide polymorphisms (SNPs) in susceptibility loci for T2D that were previously reported in GWAS in East Asians were genotyped in 762 Han

Chinese with HCV infection by using using illumina infinium iSelect HD Custom Genotyping BeadChips.
Results: 607 patients infected with HCV (persisters) and 155 spontaneous resolvers were enrolled in this study. Baseline characteristics of the patients are shown in Table 1. Table 2 summarizes the results of these SNPs. From the results, the higher frequencies (>80 %) of risk allele of 14 SNPs (rs2943641, rs7578326, rs7578597, rs7593730, rs11708067, rs13081389, rs17036101, rs1801282, rs10010131, rs1801214, rs12255372, rs7957197, rs730570, rs8042680) located at,or near susceptibility genes (IRS1,THADA,RBMS1, ADCY5,PPARG, SYN2, PPARG, WFS1, TCF7L2, HNF1A, C14orf70, and PRC1) were reported in HCV persistence and spontaneous resolvers. There were no significant differences between the two groups ($P < 0.05$). 15 genetic variants (rs340874, rs243021, rs6712932, rs780094, rs4689388, rs12518099, rs864745, rs3802177, rs896854, rs564398, rs649891, rs1111875, rs1552224, rs1359790, rs7119) were not identified.
Conclusions: This is the first study performed to examine the prevalence of risk allele in susceptibility loci for T2D in Chinese with HCV infection. Our results suggested that 14 SNPs having risk allele frequencies of 80–100 % should be explored.

Topic 11: Hepatitis C

No: 1699

Twelve weeks sofosbuvir ribavirin therapy for treatment experienced chronic HCV genotype 2 Chinese patients

Guo-feng Chen[1], Qing Shao[1], Dong Ji[1], Fan Li[1], Bing Li[1], Zhong-bin Li[1], Song-hai Chen[1], Chun-yan Wang[1], Xiao-xia Niu[1], Shi-ying Ding[1], Tao Yan[1], Vanessa Wu[2], April Wong[2], Athena Chau[2], Yu-dong Wang[2], George Kk Lau[2]

Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[1], Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[2]

Background and aims: Previously, for chronic HCV genotype (GT) 2 treatment-naïve patients, 12-weeks sofosbuvir–ribavirin was shown to be non-inferior to 24-weeks peginterferon–ribavirin (Fission study, Lawitz et al. NEJM 2013). However, the efficacy and safety of sofosbuvir–ribavirin in treatment-experienced GT2 cirrhotic patients, is unknown.
Methods: Thirty-eight treatment-experienced (null responder/relapse-22/16) Chinese with chronic HCV GT2 were studied. They all had documentation of cirrhosis by means of liver biopsy (Metavir score > 3 or Ishak score > 4) or FibroScan (≥14.6 kPa) and Child-pugh class A score of less than 7. They received 12-weeks sofosbuvir–weight-based ribavirin (Group 1, n = 13) or 24-weeks peginterferon–ribavirin (Group 2, n = 25). The primary efficacy end point was a sustained virologic response (SVR) with HCV RNA level of < 25 IU per milliliter (the lower limit of quantitation) 12 weeks after the end of study-drug administration. HCV RNA levels were measured with the use of the COBAS TaqMan real-time PCR assay (Roche version 2.0).
Results: There was a significantly higher rate of SVR in group 1 than group 2 (85 % Vs 24 %, $P = 0.001$). In group 1, SVR was not significantly different between the null responders and relapsers. However, in group 2, none of the null responders as compared to 6/11 relapsers had SVR ($P = 0.003$). There are less adverse events reported in group 1 than group 2.
Conclusion: 12-weeks sofosbuvir–ribavirin is more effective than 24-weeks peginterferon–ribavirin in treatment-experienced GT2 cirrhotic patients.

Topic 11: Hepatitis C

No: 1112

Shortening overall treatment to 12 weeks of simeprevir (SMV) plus peg ifn rbv in treatment naïve chronic hepatitis C (CHC) genotype 1 patients assessment of baseline and early (WEEK 2) on treatment predictors of high SVR

Tarik Asselah[1], Christoph Moreno[2], Christophe Sarrazin[3], Michael Gschwantler[4], Graham R Foster[5], Antionio Craxi[6], Peter Buggisch[7], R Ryan[8], Oliver Lenz[9], Guy Van Dooren[9], Isabelle Lonjon-domanec[10], Michael Schlag[11], Maria Buti[12]

Beaujon Hospital, University of Paris N/a Paris-France[1], Cub Hôpital Erasme Hospital, Université Libre De Bruxelles N/a Brussels-Belgium[2], Johann Wolfgang Goethe University Hospital N/a Frankfurt Am Main-Germany[3], Wilhe lminenspital N/a Vienna-Australia[4], Queen Mary Hospital, University of London, Barts Health N/a London-United Kingdom[5], University of Palermo N/a Palermo-Italy[6], Institute For Interdisciplinary Medicine N/a Hamburg-Germany[7], Janssen Research & Development N/a Titusville-United States[8], Janssen Infectious Diseases Bvba N/a Beerse-Belgium[9], Janssen Pharmaceuticals Paris-France[10] Janssen-cilag Vienna-Australia[11] Hospital Valle Hebron and Ciberehd Del Institut Carlos Iii Barcelona-Spain[12]

Purpose: Prospective study to assess whether Week-2 response with SMV + Peg-IFN/RBV can allow shortening to 12 weeks, irrespective of baseline factors.
Design: Phase 3, open-label study in treatment-naïve CHC genotype 1 patients with mild-to-moderate fibrosis (METAVIR F0-F2). In patients with HCV-RNA < 25 IU/mL (detectable/undetectable [Roche COBAS[SUP]®[/SUP] Taqman[SUP]®[/SUP] lower quantification limit: 25 IU/mL, detection: 15 IU/mL]) at Week 2 and < 25 IU/mL undetectable at Weeks 4 and 8, all treatments were stopped at Week 12. If these criteria were not met, Peg-IFN/RBV was continued to Week 24. Predictivity of the algorithm using Roche and Abbott RealTime assays was compared.
Results: Of 163 patients treated, 123 (76 %) fulfilled eligibility criteria for 12-week treatment (male: 53 %, white: 92 %, genotype 1a/b: 40/60 %, METAVIR F0/1: 76 %, IL28B CC/CT/TT: 26/59/15 %). One patient discontinued SMV and RBV (non-compliance). After SMV + Peg-IFN/RBV for 12 weeks, SVR12 was 65 % (n = 123). Responses varied by baseline parameters and on-treatment response (e.g.: CC genotype; Table 1a).
Treatment during the SMV + Peg-IFN/RBV phase was well tolerated (n = 163); 2.5 % (n = 4) experienced a serious AE (none SMV related), 1.8 % (n = 3) discontinued due to an AE (one possibly SMV-related). Most frequent AEs: influenza-like illness 35.6 %, pruritis 32 %, fatigue 27 %. The more sensitive Abbott assay showed higher predictivity for patients to receive shorter treatment (Table 1b).
Conclusions: Week-2 response alone did not predict outcomes as baseline factors influenced SVR rates. High SVR12 rates were in: IL28B CC genotype patients, patients with low baseline viral load, or those with mild fibrosis (METAVIR F0/1) and undetectable HCV RNA at Week 2.

Topic 11: Hepatitis C

No: 1851

The impact of ITPA polymorphisms on sustained virological response to treatment with pegylated interferon and ribavirin in Iranian patients with chronic hepatitis C infection

Mohammad Pouryasin[1], Maryam Keshvari[2]

College of Science, Tabriz Branch, Islamic Azad University Department of Biology Tabriz-Iran[1], High Institute For Research and Education In Transfusion Medicine Blood Transfusion Research Center Tehran-Iran[2]

Introduction: Recently some studies showed that treatment of hepatitis C virus (HCV) infection may be altered by ITPA polymorphisms (rs1127354 and rs7270101), whereas other studies showed no significant relationship between these two polymorphisms and achievement of SVR. This study aimed to assess the impact of ITPA polymorphisms on SVR in Iranian patients with HCV infection who were treated with Pegylated Interferon and Ribavirin combination therapy.
Materials and methods: In this study, 96 patients (mean ± SD of age: 42.6 ± 11.4, 94.8 % male) with chronic HCV infection (55.2 % HCV genotype 1 and 44.8 % HCV genotype 3) were genotyped for rs1127354 and rs7270101 polymorphisms by restriction fragment length polymorphism (RFLP).
Results: In this study, 86.5 % of patients achieved SVR. In univariate analysis, no association between age, sex, rs1127354 and HCV genotype with achievement of SVR was found ($P > 0.05$). However, HCV RNA level ($P = 0.03$), rapid virological response (RVR) ($P < 0.01$) and early virological response (EVR) ($P < 0.01$) were found to have dramatic impact on achieving SVR. rs7270101 ($P = 0.07$) and rs12979860 ($P = 0.12$) seemed to have borderline association with achievement of SVR. In multivariate analysis, HCV RNA level ($P = 0.02$, OR = 0.08, 95 % CI = 0.01-0.71) and rs12979860 ($P = 0.03$, OR = 5.92, 95 % CI = 1.15-30.30) were found to have significant association with achievement of SVR.
Conclusion: In this study, ITPA polymorphisms had no effect on the rate of SVR however HCV RNA level and rs12979860 were found to be strong pretreatment predictors of treatment response in patients with chronic HCV infection.

Topic 11: Hepatitis C

No: 1030

Interferon ineligible naive chronic hepatitis C genotype i subjects treated with simeprevir and sofosbuvir in special population (PSYCHIATRIC). An open label prospective clinical pilot study; inspire c study

Patrick Basu[1], Niraj James Shah[2], Mark Alousius[3], Robert Brown Jr[4]

King's County Hospital Medical Center, Ny Gastroenterology and Hepatology New York-United States[1], James J. Peters Va Medical Center, Icahn School of Medicine At Mount Sinai, Ny Internal Medicine New York-United States[2], King's County Hospital Medical Center, Ny Surgery New York-United States[3], Columbia University College of Physicians & Surgeons, New York Presbyterian Medicine New York-United States[4]

Objectives: Pegylated Interferon Alfa 2a with Ribavirin was the main stay of therapy. Interferon is contraindicated in psychiatric population (Schizophrenic. major depression, bipolar and schizoaffective disorder). These population have a majority of co morbidities, substance abuse and advanced fibrosis along with a poor QOL score.
Methods: sixty CHC subjects [n = 60, schizophrenia 20/60 (33.3 %), major depression 15/60 (25 %), bipolar disorder 20/60 (33.3 %) and prior suicidal attempts with depression 5/60 (8.3 %) with psychiatric disorder were recruited.

GROUP A; (n = 20); Simeprevir 150 mg + Sofosbuvir 400 mg + Ribavirin1000 mg daily, 12 weeks.
GROUP B; (n = 20); Placebo + Sofosbuvir 400 mg + Ribavirin1000 mg daily, 16 weeks.
GROUP C; (n = 20); Simeprevir 150 mg + Sofosbuvir 400 mg + Vitamin D 5000 mg daily, 16 weeks.

Laboratory analysis: HCV RNA viral load, CBC with ANC: Day 0 and 2 day, 1,4,8 and 12th week TFT, haptoglobin, coombs test, renal function, liver function test: 14 th 30 th 40 th 60 th 90 th day].
Q89 k polymorphism in 90 days.
Fibroscan and serum fibrosis markers: Base line and one year post therapy.
Results:

Group A	Group B	Group C
Undetectable 48 h	15	13 15
Undetectable 1 week	23	21 25
Undetectable 2 weeks	28	24 25
Undetectable 4 weeks	29	25 27
Undetectable 8 weeks	29	26 27
Undetectable 12 weeks	29	26 27
Retention	29/30, 96.7 %	29/30, 96.7 % 30/30, 100 %

Conclusion: Oral combination therapy for Interferon ineligible group shows similar SVR rates with better tolerability and safety profile. This special

Topic 11: Hepatitis C

No: 1724

Quick viral response in patients of chronic hepatitis virus infection predicts outcomes on antiviral therapy earlier than conventional monitoring

Cyriac Abby Philips[1], Amrish Sahney[1], Awinash Kumar[1], Manoj Kumar Sharma[1], Shiv Kumar Sarin[1]

Institute of Liver and Biliary Sciences Hepatology New Delhi-India[1]

Aims: Quick viral response (QVR, 2log reduction of HCV RNA at day 7) is shown to have positive correlation to IL28B CT/TT genotype in genotype 3 HCV. Aggressive approach to defining QVR at days 1, 4 and/or 7 and correlation with viral response is unknown.
Methods: 113 patients [68 males (60.2 %), 45 females (39.8 %); 82 (72.6 %) genotype 3, 31(27.4 %) genotype 1, median age 47.31] were treated with PEG-interferon-α 2b and Ribavarin as per standard guidelines. HCV RNA response was assessed at 1, 4 and 7 days, with RVR (4 weeks), EVR (12 weeks) and SVR (6 months post therapy). Mean duration for Genotype 1 was 46.1 ± 9.65 wks, Genotype 3 was 41 ± 17.2 wks. QVR at 1, 4, and/or 7 were assessed.
Results: 34 patients achieved RVR [n = 113, 30.09 %; 95 CI (21.8-39.4)], 80 EVR [n = 113, 70.8 %; 95 CI (64.5-78.97)], 89 SVR [n = 113, 78.8 %; 95 CI (70.1-85.9)]. Logistic regression analysis with QVR and its significance is shown in Table. Fibroscan, HAI, fibrosis stage, ALT at baseline didn't show significance with QVR at any point. IL28B polymorphism showed strong correlation with QVR at any point. CC/CC genotype had higher QVR achievement (p value 0.001) and that of CT/CC didn't (p value 0.002). CONCLUSION: QVR on day 1 predicted EVR in genotypes 1 and 3, on day 4 and/or 7 predicted RVR and EVR and day 7 predicted SVR. IL28b CC/CC genotype favored QVR as against CT/CC. Future studies can utilize this insight helping early monitoring or cost effective discontinuation of therapy in patients of HCV genotypes 1 and 3.

Topic 11: Hepatitis C

No: 1680

Efficacy of prolonged treatment with pegylated interferon (PEG IFN) and ribavirin in thalassemic patients with hepatitis C who relapsed after previous PEG ifn based therapy

Saleh Sandoughdaran[1], Seyed Moayed Alavian[1], Heidar Sharafi[1], Bita Behnava[1], Shima Salimi[1], Leila Mehrnoush[1], Maryam Keshvari[2]

Baqiyatallah University of Medical Sciences Baqiyatallah Research Center For Gastroenterology and Liver Disease Tehran-Iran[1], High Institute For Research and Education In Transfusion Medicine Blood Transfusion Research Center Tehran-Iran[2]

Background: Most thalassemic patients with chronic hepatitis C virus (HCV) infection do not respond to therapy with pegylated interferon (Peg-INF) plus ribavirin (RBV) due to hepatic siderosis and RBV dose reduction caused by RBV-induced anemia. In the present study, we recruited HCV genotype 1-infected thalassemic patients who had relapsed after 48-week treatment with Peg-INF plus RBV in order to evaluate the efficacy of a 72-week regimen of Peg-INF plus RBV.
Patients and methods: Twenty-one thalassemic patients with HCV genotype 1 infection who had prior relapse after treatment with Peg-IFN and RBV for 48 weeks were consecutively enrolled in this study for evaluation of the efficacy of 72-week treatment regimen with Peg-IFN-α-2b (Pegintron, Schering-plough) and RBV (Rebetol, Schering-plough).
Results: The mean age of the patients was 29.7 years; 81 % were men and 27.8 % had cirrhosis. At the end of the treatment, 9 (42.9 %) patients had undetectable level of HCV RNA in their sera. However, six months after treatment completion 4 of these patients relapsed and the sustained virological response (SVR) was found in 5 (23.8 %) patients. Undetectable HCV level at week 4 ($P = 0.02$), undetectable HCV level at week 12 ($P < 0.01$) and baseline ferritin level ($P = 0.04$) were found to be predictors of SVR. There was an average 47.9 % increase in blood transfusion during therapy and 13 (61.9 %) patients prematurely discontinued treatment.
Conclusion: The present study suggests that thalassemic patients with chronic HCV genotype 1 infection who did not achieve SVR after a course of therapy with Peg-IFN and RBV may benefit from being re-treated with 72-week regimen.

Topic 11: Hepatitis C

No: 1320

Spectrum of hepatitis C patients at a tertiary care centre in India

Varun Gupta[1], Ashish Kumar[1], Praveen Sharma[1], Vikas Singla[1], Anil Arora[1]

Sir Ganga Ram Hospital Gastroenterology and Hepatology New Delhi-India[1]

Background: In India the prevalence of HCV virus has increased exponentially in recent years. In this paper we have shown a complete spectrum of HCV presentation at a single tertiary care center in India.
Methods: In this retrospective study, all patients who tested positive for Anti- HCV from 2009-2014 and presented to department of Gastroenterology and Hepatology at our center were included and were assessed for status of liver disease, genotype and other comorbidities. Chronic hepatitis and early cirrhotic patients were offered treatment with antiviral therapy (PEG-IFN and ribavirin).
Results: A total of 777 patients were included in the study with median age of 49 (15-95) years. Males were predominant accounting for 69 % of the patients. Co-infection with HBV and HIV was seen in 13 (1.7 %) patients and 7 (0.9 %) respectively. Past history of blood transfusion 248 (32 %) and surgery 274 (34 %) were the most common risk factor in our population. At presentation 439 (56 %) patients had cirrhosis; including 51 (7 %) with HCC and 287 (37 %) had chronic hepatitis. Genotype 3 was the most common genotype 319/470 (68 %) followed by Genotype 1 121/470 (26 %). Antiviral therapy was offered to 342 eligible patients but therapy was started in only 189/342 (55.2 %) patients.
Conclusion: More than 50 % of patients have cirrhosis at the time of disease presentation. Genotype 3 is the predominant genotype in India. Only one fourth of the total HCV patients received antivirals. Decompensated disease, high cost of therapy followed by preference for alternative therapies were the major reason of not acquiring antivirals.

Topic 11: Hepatitis C

No: 1394

Characteristics and therapy of 21 patients infected hepatitis C virus genotype 6 in guangxi region of China

Ming-hua Su[1], Jian-ning Jiang[1], Zhi-hong Liu[1], Qi Wei[1], Zhi Wei[1], Wei Tang[1], Shuang-long Yan[1], Jin-yao Qin[1]

The First Affiliated Hospital of Guangxi Medical University Department of Infectious Diseases Nanning-China[1]

Objective: To investigate the characteristics and therapy of 21 patients infected Hepatitis C virus (HCV) genotype 6 in Guangxi region of China.
Methods: The NS5B region was amplified from 150 HCV-positive plasma samples from patients in Guangxi region of China and sequenced. The sequences obtained were compared with the sequences deposited in Genebank to construct a phylogenetic tree. We evaluated the viral responses of 10 HCV 6 patients who received interferon plus ribavirin for 48 weeks in the times of 4 weeks, 12 weeks and 48 weeks and 24 weeks after ending of treatment.
Results: A total of 21 samples (including 3 HIV/HCV individuals)were confirmed to be genotype 6 (20 genotype 6a, 1 genotype 6d) in Guangxi region, accourting for 14 %(21/150). Among the routes of infection of 21 patients,there were 7 cases infected through injection drug use (IDU), 4 cases by blood transfusion,3 cases by unexplained infections and 7 infected through other routes such as oral therapy, surgery, tattoos, piercings and sexual transmission. Phylogenetic tree showed that there was very near evolutionary distance between HCV 6 strains of Guangxi and Hongkong strains(Y12083, DQ480515) and Vietnam strain (EU246930). All of 10 HCV 6 patients achieved sustained virological response (SVR) after 48 weeks of antiviral therapy.
Conclusion: There was higher homology among HCV 6 strains of Guangxi and Hongkong strains and Vietnam strain. 6a subtype of Guangxi region was mainly found from 30 to 40 years patients who were IDUS.In addition,6d subtype was detected in Guangxi region,but its prevalence is unclear at present. HCV 6 patients treated with interferon plus ribavirin for 48 weeks can get favorable rate of SVR.

Topic 11: Hepatitis C

No: 1747

Interferon and ribavirin free regimen with ledipasvir and sofosbuvir improves fatigue and vitality during treatment and after achieving sustained virologic response

Zobair Younossi[1], Maria Stepanova[2], Fatema Nader[1], Linda Henry[2], Sharon Hunt[3]

Center For Liver Diseases, Inova Fairfax Hospital Medicine Falls Church-United States[1], Cldq Llc Washington-United States[2], Betty and Guy Beatty Center For Integrated Research, Inova Health System Falls Church-United States[3]

Background: Fatigue is an important extrahepatic manifestation of chronic hepatitis C (CH-C) which is exacerbated by Interferon (IFN) and ribavirin (RBV).
Aim: Assess fatigue in CH-C patients receiving IFN-free RBV-free vs. RBV ± IFN-containing regimens.
Methods: 1294 CH-C patients receiving PEG-IFN + RBV + sofosbuvir (SOF) (NEUTRINO trial) or RBV + SOF (FUSION) or ledipasvir (LDV) + SOF (ION-1, ION-2, ION-3) for 12 weeks completed CLDQ-HCV, FACIT-F, SF-36 questionnaires before, during and after treatment. Fatigue was assessed by FACIT-F, Activity domain of CLDQ-HCV and Vitality scale of SF-36. Subjects were blinded to virologic data.
Results: Baseline scores were similar between regimens ($p > 0.05$). By the end of treatment, significant decrements in vitality, fatigue and activity scores were noted for PEG-IFN + RBV + SOF (vitality -19.9 %, fatigue -19.5 %, activity -19.3 %, $P < 0.001$) while moderate declines were noted for SOF + RBV (-10.1 %, -9.9 %; and -8.5 %, $P < 0.001$). In contrast, patients receiving LDV/SOF experienced improvement in all scores during treatment (up to +1.5 %, all $P < 0.03$). By week 4 post-treatment, decrements in vitality remained in PEG-IFN + RBV + SOF (-3.2 %) and RBV + SOF (-6.5 %), while additional improvement was noted in LDV/SOF (up to +6.5 %) (all $P < 0.05$). Patients achieving SVR-12 experienced significant improvement in their scores regardless of the regimen (up to +9.8 %, all $P < 0.001$). In multivariate analysis, after adjustment for confounders, receiving IFN and RBV were associated with lower scores at the end of treatment (IFN: up to -18.9 %, RBV: up to -7.7 %). At SVR12, having received IFN remained associated with lower scores (up to −5.1 %) (all $P < 0.05$).
Conclusions: LDV/SOF leads to improvement fatigue-related scores during and post-treatment while IFN and RBV substantially worsen fatigue.

Topic 11: Hepatitis C

No: 1947

Sofosbuvir plus ribavirin for the treatment of Russian patients with chronic HCV genotype 1 or 3 infection

Konstantin Zhdanov[1], Vasily Isakov[2], Kathryn Kersey[3], Yanni Zhu[4], Evgenia Svarovskaia[5], Benedetta Massetto[3], Sergey Zhuravel[6], Svetlana Romanova[7], Elena Nurmukhametova[8], Viacheslav Morozov[9], Galina Kozhevnikova[10], Larisa Gogova[11], Natalia Geyvandova[12], Natalia Gankina[13], Evgenii Chesnokov[14], Eduard V. Burnevich[15], Elena Bessonova[16], Djamal Abdurakhmanov[17], Diana M. Brainard[3], John G. Mchutchison[3], Vladimir Chulanov[10], Igor G. Bakulin[18]

Military Medical Academy Infectious Diseases St Petersburg-Russia[1], Institute of Nutrition of Russian Academy of Medical Sciences Gastroenterology and Hepatology Moscow-Russia[2], Gilead Sciences, Inc. Clinical Research Foster City-United States[3], Gilead Sciences, Inc. Biostatistics Foster City-United States[4], Gilead Sciences, Inc. Clinical Virology Foster City-United States[5], Scientific Research Institute of Emergency Care N.a. N.v. Sclifosovskiy Gastroenterology and Hepatology Moscow-Russia[6], Center For Prevention and Control of Aids and Infectious Diseases Infectious Diseases St Petersburg-Russia[7], Infectious Clinical Hospital Number 1 Infectious Diseases Moscow-Russia[8], Medical Company Hepatolog, Llc Gastroenterology and Hepatology Samara-Russia[9], Central Research Institute of Epidemiology Gastroenterology and Hepatology Moscow-Russia[10], Central Clinical Hospital of The Russian Academy of Sciences Gastroenterology and Hepatology Moscow-Russia[11], Stavropol Regional Clinical Center of Special Medical Care Gastroenterology and Hepatology Stavropol-Russia[12], Krasnoyarsk Regional Center For Prevention and Control of Aids and Infectious Diseases Infectious Diseases Krasnoyarsk-Russia[13], Consultation and Diagnostic Centre Gastroenterology and Hepatology Tymen-Russia[14], City Clinical Hospital Number 24 Gastroenterology and Hepatology Moscow-Russia[15], Sverdlovsk Regional Clinical Hospital Number 1 Gastroenterology and Hepatology Ekaterinburg-Russia[16], I.m.sechenov First Moscow State Medical University Gastroenterology and Hepatology Moscow-Russia[17], Moscow Central Scientific Institute of Gastroenterology Gastroenterology and Hepatology Moscow-Russia[18]

Background and aims: This study was conducted in Russia to evaluate the efficacy and safety of an interferon-free regimen of sofosbuvir (SOF) plus ribavirin (RBV) in patients with chronic HCV infection.
Methods: Treatment-naïve patients from 16 sites in Russia with HCV genotype (GT) 1 or GT3 infection were randomized to receive SOF (400 mg daily) + RBV (1000-1200 mg daily) for 16 or 24 weeks; randomization was stratified by genotype and the presence or absence of compensated cirrhosis. The primary efficacy endpoint was sustained viral response 12 weeks post-treatment (SVR12).
Results: 127 treatment-naïve patients (65 GT1b, 1 GT1a and 61 GT3a) were enrolled and treated. 15 % and 18 % of GT1 and GT3 patients had compensated cirrhosis. SVR12 rates are shown in the table. All virologic failures were due to relapse. AEs reported by ≥ 5 % of patients who received SOF + RBV were headache, asthenia, viral respiratory tract infection, fatigue, alopecia, and insomnia. All treatment-related AEs were mild or moderate in severity and no AE resulted in discontinuation of treatment.
Conclusions: In treatment-naïve genotype 1 HCV-infected Russian patients, the SVR12 rate of 76 % with 24 weeks SOF + RBV was comparable to the rates observed with this regimen in other studies in GT1 patients. In treatment-naïve genotype 3 HCV-infected Russian patients, both 16 and 24 weeks of treatment resulted in high SVR12 rates of 87 % and 90 %, respectively. SOF + RBV was well tolerated with a safety profile consistent with the use of RBV.

Topic 11: Hepatitis C

No: 1707

Dual direct antiviral agents (DAAS) with sofosbuvir plus daclatasvir for chronic HCV treatment experienced genotype 1b: impact of viral kinetics on sustained virologic response

Dong Ji[1], Guo-feng Chen[1], Qing Shao[1], Fan Li[1], Bing Li[1], Zhong-bin Li[1], Song-hai Chen[1], Chun-yan Wang[1], Xiao-xia Niu[1], Shi-ying Ding[1], Tao Yan[2], Vanessa Wu[3], April Wong[3], Athena Chau[3], Yu-dong Wang[3], George Kk Lau[3]

Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[1], 302 Hospital International Liver Diagnosis and Treatment Centre Beijing-China[2], Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[3]

Background and aims: For chronic hepatitis C patients who are interferon-ineligible or intolerant, there is a need for pan-oral interferon-free regimen. We examine the efficacy and safety of sofosbuvir, an NS5B nucleotide polymerase inhibitor and daclatasvir, an NS5A replication complex inhibitor in Chinese treatment-experienced cirrhosis patients with chronic GT1b infection.
Methods: Twenty-five GT1b treatment-experienced and interferon-ineligible or intolerant cirrhotic Chinese were treated with 12-weeks sofosbuvir 400 mg daily plus daclatasvir 60 mg daily. Liver stiffness measurement using transient elastography (FibroScan®) was used to define liver cirrhosis (≥14.6). Single nucleotide polymorphism of IFLN3 (IL-28, rs12979860, C or T) and IFLN4 (ss469415590, TT or ΔG) were determined. Serial measurements of plasma HCV RNA levels were performed with COBAS TaqMan (Roche version 2.0), at baseline, Day 2, 4, 7, Week 2, 4, 8 and 12, post-treatment Week 12.
Results: Twenty-three (92 %) patients had SVR12 and there was no withdrawal from therapy due to adverse events. The cumulative rate of plasma HCV RNA undetectability, is 12, 36, 72, 88, 92 and 100 % by Day 2, 4, 7, Week 2, 4 and 8, respectively, and this is not affected by the SNPs variation of IL-28 and IFLN-4. These rates were superior to the historical control rate, with standard 48 weeks pegylated interferon-ribavirin therapy. The three most common adverse events were fatigue (n = 7, 30 %), headache (n = 6, 26 %), and nausea (n = 1, 4.3 %).
Conclusion: Interferon-free pan-oral therapy with 12-weeks sofosbuvir and daclatasvir are highly effective and safe in CHC GT1b treatment-experienced interferon-ineligible or intolerant Chinese patients with liver cirrhosis.

Topic 11: Hepatitis C

No: 1734

Interferon and ribavirin free regimen with ledipasvir and sofosbuvir improves fatigue and vitality and fatigue during treatment and after achieving sustained virologic response

Zobair Younossi[1], Maria Stepanova[2], Fatema Nader[1], Linda Henry[2], Sharon Hunt[3]

Center For Liver Diseases Inova Fairfax Hospital Medicine Falls Church-United States[1], Cldq Llc Washington-United States[2], Betty and Guy Beatty Inova Health System Inova Fairfax Health System Falls Church-United States[3]

Background: Fatigue is an important extrahepatic manifestation of chronic hepatitis C (CH-C) which is exacerbated by Interferon (IFN) and ribavirin (RBV).
Aim: Assess fatigue in CH-C patients receiving IFN-free RBV-free vs. RBV ± IFN-containing regimens.
Methods: 1294 CH-C patients receiving PEG-IFN + RBV + sofosbuvir (SOF) (NEUTRINO trial) or RBV + SOF (FUSION) or ledipasvir (LDV) + SOF (ION-1, ION-2, ION-3) for 12 weeks completed CLDQ-HCV, FACIT-F, SF-36 questionnaires before, during and after treatment. Fatigue was assessed by FACIT-F, Activity domain of CLDQ-HCV and Vitality scale of SF-36. Subjects were blinded to virologic data.
Results: Baseline scores were similar between regimens ($p > 0.05$). By the end of treatment, significant decrements in vitality, fatigue and activity scores were noted for PEG-IFN + RBV + SOF (vitality −19.9 %, fatigue −19.5 %, activity −19.3 %, $P < 0.001$) while moderate declines were noted for SOF + RBV (−10.1 %, −9.9 %; and −8.5 %, $P < 0.001$). In contrast, patients receiving LDV/SOF experienced improvement in all scores during treatment (up to +1.5 %, all $P < 0.03$). By week 4 post-treatment, decrements in vitality remained in PEG-IFN + RBV + SOF (−3.2 %) and RBV + SOF (−6.5 %), while additional improvement was noted in LDV/SOF (up to +6.5 %) (all $P < 0.05$). Patients achieving SVR-12 experienced significant improvement in their scores regardless of the regimen (up to +9.8 %, all $P < 0.001$). In multivariate analysis, after adjustment for confounders, receiving IFN and RBV were associated with lower scores at the end of treatment (IFN: up to -18.9 %, RBV: up to -7.7 %). At SVR12, having received IFN remained associated with lower scores (up to -5.1 %) (all $P < 0.05$).
Conclusions: LDV/SOF leads to improvement fatigue-related scores during and post-treatment while IFN and RBV substantially worsen fatigue.

Topic 11: Hepatitis C

No: 1704

Cost effectiveness of sofosbuvir based therapy for chronic HCV genotype 1b infection in China

Yu-dong Wang[1], Guo-feng Chen[2], Vanessa Wu[1], April Wong[1], Athena Chau[1], Qing Shao[2], Fan Li[2], Bing Li[2], Dong Ji[2], Zhong-bin Li[2], Song-hai Chen[2], Chun-yan Wang[2], Xiao-xia Niu[2], Shi-ying Ding[2], Tao Yan[3], George Kk Lau[1]

Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[1], 302 Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[2], 302 Hospital International Liver Diagnosis and Treatment Centre Beijing-China[3]

Background and aims: Worldwide, China carries the largest number of chronic hepatitis C (CHC) infected patients, with GT1b being the predominant genotype. Recently, sofosbuvir (SOF), an oral NS5B nucleotide polymerase inhibitor, has been made available for the treatment of CHC patients. We evaluate the long-term health economic outcomes of 12-weeks SOF + pegylated interferon-α/ribavirin (NEUTRINO regimen) compared with standard 48-weeks pegylated interferon-α/ribavirin (PR48) in patients infected with HCV GT1b in China.
Methods: We developed a decision-analytic Markov model to estimate health outcomes, number needed to treat and short-term and long-term economic outcomes, including incremental cost-effectiveness ratios and cost per sustained virological response (SVR). It considered chronic GT1b HCV Chinese- treatment-naive and treatment-experienced, at Hong Kong-Beijing 302 hepatitis C centre, China.
Results: There is a reduction in the incidence of new cases of liver-disease complications with NEUTRINO regimen compared with PR48 (55-75 %). According to the International Monetary Fund (2013), the gross domestic product per capital of China is 15 % of the USA counterpart. With the high cost of SOF (USD 84,000 for 12-weeks), high IL-28 CC genotype (allele frequency Rs12979860 C/T- 0.92/0.08) which increases SVR with PR48 therapy, and low health-care cost in China, NEUTRINO regimen is not dominated as compared to PR48 in treatment naïve chronic GT1b patients.
Conclusion: 12-weeks sofosbuvir + pegIFN/RBV (NEUTRINO regimen) failed to yield favorable health and economic outcomes than current PR48 treatment regimens for patients with chronic GT1b patients in China.

Topic 11: Hepatitis C

No: 1644

HCV genotype and IFNL3 and IFNL4 in China

Fan Li[1], Qing Shao[1], Bing Li[1], Dong Ji[1], Zhong-bin Li[1], Song-hai Chen[1], Chun-yan Wang[1], Xiao-xia Niu[1], Shi-ying Ding[1], Tao Yan[2], Vanessa Wu[3], April Wong[3], Athena Chau[3], Yu-dong Wang[3], Guo-feng Chen[1], George Kk Lau[3]

Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[1], 302 Hospital International Liver Diagnosis and Treatment Centre Beijing-China[2], Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[3]

Background and aims: Treatment of chronic hepatitis C (CHC) infection is governed by both host (genetics, diseases status) and viral factors (HCV genotype and viral load). We investigate the epidemiology of HCV infection and host single nucleotide analogues in IFNL3 and IFNL4 in Chinese with CHC infection and their effect on standard of care pegylated interferon-ribavirin therapy.
Methods: We studied all serum samples collected from 1365 treatment naïve CHC Chinese patients who had attended the Hong Kong Humanity and Health Medical Centre and special Hong Kong-Beijing Hepatitis C clinic in Beijing 302 hospital, from 2009-2014. HCV genotype and subtype were determined with NS5B or core clonal sequencing. The IL28B genotype and IFNL4 SNPs determined by PCR sequencing of the rs12979860 (C or T) and ss469415590 (TT or ΔG). The SNPs of both IL28 and IFNL4 were correlated to sustained virologic response to PR24-48 therapy for GT1 and non-GT1 CHC.
Results: The prevalence of GT1b, GT6a, GT3a, GT1a, GT2a were 56.7 %, 25.3 %, 6.9 %, 5.2 %, 3.5 % respectively. Fifty-three percent and fifty percent of GT1b was IL28B CC genotype and IFNL4 TT/TT genotype. There is no association between IL-28 and IFNL4 and viral load or disease severity. The response to PR therapy was significantly better with IL28B CC genotype with SVR of 68 % in GT1 and 90 % for GT2. No additional predictive value was added by including IFNL4.
Conclusions: For treatment naïve Chinese, the most common CHC genotype is GT1b and their response to PR therapy is good with a response rate of 68 %, especially if they have the IL28B-CC genotype.

Topic 11: Hepatitis C

No: 1602

Sofosbuvir plus ribavirin an interferon free regimen in the treatment of Egyptian patients with chronic genotype 4 HCV infection

Gamal Shihai[1], Gamal Esmat[2], Mohamad Hassany[3], Rabab Fouad[2], Waleed Samir[1], Radi Hammad[3], Marwa Khairy[2], Reham Soliman[1], Benedetta Masssetto[4], Steven J. Knox[4], Kathryn Kersey[4], Deyuan Jiang[5], Brian Doehle[6], Diana Brainard[4], John G. Mchutchison[4], Wahid Doss[3]

Egyptian Liver Research Institute and Hospital (elriah) Hepatology and Gastroenterology Mansoura-Egypt[1], Cairo University Hepatology and Gastroenterology Cairo-Egypt[2], National Hepatology and Tropical Medicine Research Institute Hepatology and Gastroenterology Cairo-Egypt[3], Gilead Sciences Clinical Research Foster City-United States[4], Gilead Sciences Biostatistics Foster City-United States[5], Gilead Sciences Virology Foster City-United States[6]

Introduction: Egypt has the highest prevalence of hepatitis C infection worldwide and over 90 % of those chronically infected have hepatitis C virus (HCV) genotype (GT) 4. Sofosbuvir (SOF) is a nucleotide HCV NS5B inhibitor approved for the treatment of chronic HCV infection. The current study was conducted in Egypt to assess the safety and efficacy of SOF plus RBV in patients with chronic GT4 HCV infection.
Methods: This was an open-label, randomized study. Treatment-naïve and treatment-experienced patients with GT4 HCV infection were randomized to 12 or 24 weeks of SOF (400 mg daily) + RBV (1000-1200 mg daily). Randomization was stratified by prior treatment experience and by the presence or absence of cirrhosis. The primary endpoint was SVR12.
Results: 103 patients were randomized. Most were male (67 %), mean age 47 years, 17 % had compensated cirrhosis, 52 % were treatment-experienced, 81 % had IL28B non-CC genotype, and 52 % had HCV RNA $\geq$ 800,000 IU/mL at baseline. SVR12 rates are shown in the table. Concordance between SVR12 and SVR24 was 100 %. The most common adverse events (> 10 % of patients) were fatigue, headache, insomnia, and dyspepsia. The overall adverse event profile was consistent with a RBV-containing regimen.
Conclusions: 24 weeks of SOF + RBV is a highly effective, simple, well-tolerated, interferon-free regimen for patients with GT4 HCV infection.

Topic 11: Hepatitis C

No: 1393

IL28B genotype may not be a factor predicting progression to cirrhosis in HCV infection*

Abdülkadir Dökmeci[1], Reşat Özaras[2], Mehmet Demir[3], Iftihar Köksal[4], Şebnem Gürsoy[5], Yusuf Önlen[6], Hakan Leblebicioğlu[7], Yaşar Nazlıgül[8], Şahin Çoban[9], Necati Örmeci[1], Fatih Özdener[10], Seda Erdoğan[10]

Ankara University School of Medicine Gastroenterology Ankara-Turkey[1], Istanbul University Cerrahpaşa School of Medicine Infectious Diseases Istanbul-Turkey[2], Mustafa Kemal University School of Medicine Gastroenterology Hatay-Turkey[3], Karadeniz Technical University School of Medicine Infectious Diseases Trabzon-Turkey[4], Erciyes University School of Medicine Gastroenterology Kayseri-Turkey[5], Mustafa Kemal University School of Medicine Infectious Diseases Hatay-Turkey[6], Ondokuz Mayıs University School of Medicine Infectious Diseases Samsun-Turkey[7], Keçiören Training and Research Hospital Gastroenterology Ankara-Turkey[8], Dışkapı Yıldırım Beyazıt Training and Research Hospital Infectious Diseases Ankara-Turkey[9], Clinical Trials Roche Pharmaceuticals Istanbul-Turkey[10]

Introductions and aim: Host IL28B genotype influences spontaneous clearance of acute HCV infection and response to interferon-based treatment in patients with chronic hepatitis C (CHC). Whether IL28B genotype influences progression of hepatic fibrosis is unclear. The large prospective international Gen-C study was designed to evaluate relationships between IL28B genotypes and fibrosis stage in patients with CHC. The present is a sub-analysis of patients included in Gen-C study in Turkey, aiming to determine whether IL28B polymorphism might predict progression to the cirrhosis.
Results: Seventeen centers participated in Gen-C throughout Turkey. A total of 302 treatment-naïve CHC patients were enrolled.; 85.9 % had genotype 1. 104 (34.6 %) had cirrhosis or transition to cirrhosis. 24.5 % had rs12979860-CC and 49 % rs8099917-TT.

In treatment-experienced group, there were 121 patients; 94 % had genotype 1. 25 (26.6 %) had cirrhosis or transition to cirrhosis. 14 % had rs12979860-CC and 39 % had rs8099917-TT.

A logistic regression analysis revealed that in treatment-naïve group; age (per 10 years increment), gender (being male), ALT ratio (per unit increment), and low platelets are the variables predicting cirrhosis or transition to cirrhosis. Similarly, in treatment-experienced group; AST ratio (per unit increment), and low platelets are the variables predicting cirrhosis or transition to cirrhosis.

No association with cirrhosis and IL28B genotypes was detected.
Conclusion: IL28B genotypes do not seem to predict progression to cirrhosis in CHC patients.

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Topic 11: Hepatitis C

No: 1728

Comparison of patient reported outcomes in a phase 3 study of all oral dual combination of daclatasvir plus asunaprevir (DCV + ASV) versus telaprevir plus peginterferon alfa ribavirin (TVR) in treatment naive japanese patients chronically infected with HCV genotype 1b

Ajay Behl[1], Hiromitsu Kumada[2], Joji Toyata[3], Kazuaki Chayama[4], Hiroki Ishikawa[5], Anupama Kalsekar[1]

Bristol-myers Squibb Wwheor Virology Princeton-United States[1], Toranomon Hospital Tokyo-Japan[2], Sapporo-Kosei General Hospital Sapporo-Japan[3], Hiroshima University-Japan[4], Bristol-myers K.k. Tokyo-Japan[5]

Background and aim: Health-related quality of life (HRQOL) is frequently of concern in patients infected with HCV due to side effects of interferon and ribavirin. The efficacy and safety were evaluated in patients participating in a Japanese phase 3 study (AI447-031) who received DCV + ASV all-oral regimens (n = 119) vs. TVR (n = 111). The objective of this analysis was to compare HRQOL for DCV + ASV combination with TVR therapy.
Methods: The HRQOL was measured using Short Form 36 (SF-36) and Fatigue Severity Scale (FSS) in pre and post treatment. Higher scores for SF-36 indicate better quality of life and a change of 2-3 points is considered clinically relevant. For FSS, with a scale from 1 to 7, higher scores indicate greater fatigue and a change of 1 point is considered clinically relevant.
Results: In the DCV + ASV cohort, the mean SF-36 summary scores, physical component summary (PCS) and mental component summary (MCS), remained stable (0.11 and 0.51 points respectively). For the TVR cohort, PCS and MCS statistically significantly decreased during the first 12 weeks of treatment (-7.15 and -9.06 points respectively). All scores returned to near baseline values at 12 weeks post-treatment. Similar trends were observed in FSS scores: the TVR cohort worsened but the DCV + ASV cohort remained stable.
Conclusion: DCV + ASV regimens are associated with maintenance of HRQOL while on treatment. In contrast, interferon based regimens show significant decrements in quality of life.

Topic 11: Hepatitis C

No: 2050

Identification of susceptibility loci for type 2 diabetes in hepatitis C virus infection

Wei Zhang[1], Huiying Rao[1], Lai Wei[1]

Peking University Peking University People's Hospital,hepatology Institute, Beijing Key Laboratory of Hepatitis C and Immunotherapy For Liver Diseases Beijing-China[1]

Background/aims: Type 2 diabetes (T2D) is a frequent extrahepatic manifestations of hepatitis C virus (HCV) infection. It is also known that T2D shows considerable heritability. However, the implications of genetic susceptibility loci for T2D in populations with HCV infection are unclear. The aim of this study was to assess the presence of these loci in an East Asian population with HCV infection.
Patients & methods: A total of 762 unrelated Chinese Han individuals, including 607 patients infected with HCV (persisters) and 155 spontaneous resolvers, were genotyped using the infinium iSelect HD BeadChips (Illumina). We tested r $\sim$ 50 susceptibility loci for T2D reported in Candidate gene and genome-wide association studies .
Results: Variants located at susceptibility loci (PROX1,RNA5SP94 - MIR4432,MRPS9 - GPR45,GCKR,WFS1,LOC101929495,JAZF1, SLC30A8,TP53INP1,CDKN2B-AS1,PTPRD,HHEX - EXOC6,AR-AP1,KCNJ11,LINC01080 - SPRY2,and HMG20A) were not identified in our study. In comparison with data from HapMap, the higher frequencies of risk allele of 21 single-nucleotide polymorphisms(SNPs) located at RBMS1, ZPLD1,ADAMTS9,CDKAL1,KLF14,SLC30A8,CDKN2A/B,TCERG1L,CDC123,CAMK1D,HHEX,KIF11,KCNQ1,KCNJ11,C14orf70,ZFAND6,C2CD4A, C2CD4B,FLJ16165, and HUNK loci were reported in HCV persistence and spontaneous resolvers. There were no significant differences between HCV persistence and spontaneous resolvers ($P < 0.05$). Among them, the risk allele frequency of rs1495377 mapped in TSPAN8 - LGR5 was three times higher than that in general population in China.
Conclusions: These results suggest that many loci associated with T2D have higher risk allele frequencies in Chinese populations with HCV infection. This is the first study to assess the prevalence of susceptibility loci for T2D in individuals with HCV infection.

Topic 11: Hepatitis C

No: 1177

Long term efficacy and safety of the interferon and ribavirin free regimen of abt 450 r and ombitasvir in HCV genotype 1b infected treatment experienced Japanese patients

Kazuaki Chayama[1], Kazuo Notsumata[2], Masayuki Kurosaki[3], Ken Sato[4], Lino Rodrigues, Jr[5], Carolyn Setze[6], Prajakta Badri[7], Tami Pilot-matias[8], Regis Vilchez[9], Hiromitsu Kumada[10]

Hiroshima University Department of Gastroenterology and Metabolism Hiroshima-Japan[1], Fukui-ken Saiseikai Hospital Department of Internal Medicine Fukui-Japan[2], Musashino Red Cross Hospital, Musashino-shi Department of Gastroenterology and Hepatology Tokyo-Japan[3], Gunma University Graduate School of Medicine Department of Medicine and Molecular Science Gunma-Japan[4], Abbvie Inc Clinical Development North Chicago-United States[5], Abbvie Inc Statistics North Chicago-United States[6], Abbvie Inc Clinical Pharmacokinetics North Chicago-United States[7], Abbvie Inc Discovery North Chicago-United States[8], Abbvie Inc Medical Affairs North Chicago-United States[9], Toranomon Hospital Department of Hepatology Tokyo-Japan[10]

Aim: Efficacy through post-treatment week 48 and safety of ABT-450 (identified by AbbVie and Enanta), dosed with ritonavir (ABT-450/r), and ombitasvir in HCV genotype 1b (GT1b)-infected patients enrolled in the Phase 2 study, M12-536, are described.

Methods: Partial or null responders to peginterferon (IFN)/ribavirin (RBV), non-cirrhotic, Japanese patients with HCV GT1b received 12 or 24 weeks of ABT-450/r (100/100 mg or 150/100 mg QD) and ombitasvir (25 mg QD). SVR rates (HCV RNA < 25 IU/ml, as measured using COBAS TaqMan RT-PCR) are reported. Treatment-emergent adverse events (TEAE) from first dose through 30 days after last dose were summarized for any patient who received at least one dose of study drugs.
Results: A total of 73 HCV GT1b-infected patients were enrolled in the study; 49 % (36/73) male, 96 % (70/73) IL28B non-CC GT. All achieved end of treatment response. SVR rates are shown in the table. Reasons for not achieving SVR24 were premature discontinuation (serious AE of fluid retention) and post-treatment relapse. No patient who achieved SVR24 relapsed through post-treatment week 48. SVR rates were not influenced by baseline NS3 or NS5A resistance-associated amino acid variants. No meaningful differences in the percentage of patients experiencing TEAEs were observed with treatment duration or ABT-450 dose. Four patients experienced serious TEAEs.
Conclusions: In this difficult to treat population of patients with prior pegIFN/RBV failures, high SVR24 rates were achieved, with no subsequent relapses through 48 weeks post-treatment with the IFN/RBV-free oral regimen of ABT-450/r and ombitasvir. Treatment duration or ABT-450 dose did not influence maintenance of response or safety.

Topic 11: Hepatitis C

No: 1482

All oral 12 week treatment with daclatasvir plus sofosbuvir in patients with chronic hepatitis C virus genotype 3 infection ally 3 phase 3 study

David Nelson[1], James Cooper[2], Jacob Lalezari[3], Eric J Lawitz[4], Paul Pockros[5], Bradley Freilich[6], Ziad Younes[7], William Harlan[8], Reem Ghalib[9], Godson Oguchi[10], Paul Thuluvath[11], Grisell Ortiz-lasanta[12], Mordechai Rabinovitz[13], David Bernstein[14], Michael Bennett[15], Trevor Hawkins[16], Natarajan Ravendhran[17], Aasim Sheikh[18], Peter Varunok[19], Kris Kowdley[20], Delphine Hennicken[21], Fiona Mcphee[21], Khurram Zafar Rana[21], Eric Hughes[21]

University of Florida, Division of Gastroenterology, Hepatology, and Nutrition, Gainesville-United States[1], Inova Fairfax Hospital, Falls Church-United States[2], Quest Clinical Research, San Francisco-United States[3], Texas Liver Institute, University of Texas Health Science Center, San Antonio-United States[4], Scripps Clinic, La Jolla-United States[5], Kansas City Research Institute, Kansas City-United States[6], Gastro One, Germantown-United States[7], Asheville Gastroenterology Associates, Asheville-United States[8], Texas Clinical Research Institute, Arlington-United States[9], Midland Florida Clinical Research Center, Deland-United States[10], Mercy Medical Center, Baltimore-United States[11], Fundación De Investigación De Diego, Santurce-puerto Rico[12], University of Pittsburgh, Pittsburgh-United States[13] Hofstra North Shore-long Island Jewish School of Medicine, Manhasset-United States[14], Medical Associates Research Group, San Diego-United States[15], Southwest Care Center, Santa Fe-United States[16], Digestive Disease Associates, Baltimore-United States[17], Gastrointestinal Specialists of Georgia, Marietta-United States[18], Premier Medical Group of Hudson Valley, Poughkeepsie-United States[19], Swedish Medical Center, Seattle-United States[20], Bristol-myers Squibb Research and Development, Princeton-United States[21]

Aim: Options for treating HCV genotype (GT) 3 infection are limited in treatment-naive and -experienced patients. The currently available all-oral regimen requires 24-week treatment that includes ribavirin (RBV); newer RBV-free regimens are being studied to shorten treatment duration. The combination of daclatasvir (DCV; potent, pangenotypic NS5A inhibitor) and sofosbuvir (SOF; NS5B polymerase inhibitor) for 12 weeks was evaluated in patients chronically infected with GT 3.
Methods: Two cohorts of treatment-naive or treatment-experienced patients received open-label DCV 60 mg + SOF 400 mg once daily for 12 weeks. Efficacy (sustained virologic response at posttreatment Week 12 [SVR12; primary endpoint]) and safety outcomes are reported.
Results: 152 patients were treated: 101 (66 %) treatment-naive and 51 (34 %) treatment-experienced; 21 % were cirrhotic, 61 % non-CC < I>IL28B </I > genotype, 71 % HCV RNA ≥ 800 K IU/mL. Baseline characteristics were comparable between cohorts except for a higher proportion of cirrhotic patients in the treatment-experienced cohort. Overall, 90 % and 86 % of treatment-naive and -experienced patients, respectively, achieved SVR12; response rates were higher in noncirrhotic versus cirrhotic patients (Table). One serious adverse event (AE) was reported on-treatment; there were no deaths or AEs leading to discontinuation. Few Grade 3/4 laboratory abnormalities were observed—only for platelets (n = 2), lymphocytes (n = 1), international normalized ratio (INR; n = 2), and lipase (n = 3); none led to treatment discontinuation.
Conclusion: The all-oral, 12-week combination of DCV + SOF in HCV GT 3 infection achieved SVR12 rates of 90 % and 86 % in treatment-naive and -experienced patients, respectively, with higher rates in those without cirrhosis. This combination was safe and well tolerated.

Topic 11: Hepatitis C

No: 2244

Real life characteristics of hepatitis C virus treatment Turkey's results of pegbase study

Resat Ozaras[1], Mehmet Demir[2], Yusuf Onlen[3], Gurdal Yilmaz[4], Ramazan Idilman[5], Sebnem Gursoy[6], Özgür Günal[7], Aysun Yalci[8], Sener Barut[9], Ozlem Altuntas Aydin[10], Fatih Ozdener[11], Seda Erdoğan[11], Abdulkadir Dokmeci[5]

Istanbul University Cerrahpasa School of Medicine Infectious Diseases Istanbul-Turkey[1], Mustafa Kemal University School of Medicine Gastroenterology Hatay-Turkey[2], Mustafa Kemal University School of Medicine Infectious Diseases Hatay-Turkey[3], Karadeniz Technical University School of Medicine Infectious Diseases Trabzon-Turkey[4], Ankara University School of Medicine Gastroenterology Ankara-Turkey[5], Erciyes University School of Medicine Gastroenterology Kayseri-Turkey[6], Tokak Gaziosmanpasa University School of Medicine Infectious Diseases Tokat-[7], Ankara University School of Medicine Infectious Diseases Ankara-Turkey[8], Tokat Gaziosmanpasa School of Medicine Infectious Diseases Tokat-Turkey[9], Haseki Training and Research Hospital Infectious Diseases Istanbul-Turkey[10] Roche Pharmaceuticals Clinical Research Istanbul-Turkey[11]

Introductions and aim: Real life data provide more comprehensive and reliable information than clinical studies, which by definition contain many inclusion and exclusion criteria. Turkey contributed the prospective international Peg-Base study which was designed to evaluate in routine clinical practice the efficacy of peginterferon alfa (Peg-IFN) plus ribavirin combination therapy and treatment regimens

containing direct-acting anti-virals (DAA) in patients with CHC receiving such therapies according to local label and to document the predictive value of baseline characteristics on treatment outcome The present is a sub-analysis of patients included in Peg-Base study in Turkey, aiming to determine the main characteristics of the patients with CHC.. Chronic hepatitis C (CHC) is a considerable health care concern in Turkey. Its prevalence is 0.5 to 1 %. Pegylated interferon (PEG-IFN) and ribavirin are reimbursed for every HCV-RNA-positive patient whereas direct-acting antivirals are reimbursed for relapsers and for those with advanced fibrosis.

Patients and methods: This multicenter study included treatment naïve and experienced patients HCV genotype 1 patients. Baseline characteristics, treatment options, the response to therapy, adherence, safety, and response outcomes of on-treatment, end of treatment response (EOT) and sustained virologic response at least 12 weeks post-treated (SVR12) were recorded.

Results: A total of 148 patients were included into this interim analysis.

Sixty-five naïve patients (26 male/39 female, mean age 52.6 years) received PEG-IFN plus ribavirin (PR) therapy.

Fifteen naïve patients with advanced fibrosis (4 male/11 female, mean age 59.2 years) were given PR plus telaprevir (PR + T).

Sixty-eight treatment-experienced patients (24 male/44 female, mean age 57.1 years) were given PR + T.

In patients given PR; EOT-R and SVR12 were 77 % and 52.3 % respectively.

In naïve patients given PR + T; EOT-R and SVR12 were 80 %, and 66.7 %, respectively.

In treatment experienced patients given PR + T; EOT-R and SVR12 were 85.3 % and 60.3 %, respectively.

Conclusion: In summary, treatment naïve G1 patients in Turkey with PR achieved SVR rates similar to international clinical trials, while the SVR was slightly lower in treatment naïve and experienced patients receiving PR + T.

Topic 11: Hepatitis C

No: 1075

How much do routine blood tests tell about liver fibrosis in chronic hepatitis C

Ragesh Babu Thandasssery[1], Anil John[1], Saad Al Kaabi[1]

Hamad Medical Corporation Gastroenterology Doha-Qatar[1]

Purpose: There are many simple noninvasive scores to predict liver fibrosis that can be calculated from routine blood parameters. We aim to compare these simple noninvasive scores for evaluation of liver fibrosis with liver biopsy in patients with chronic hepatitis C (HCV).

Methods: In 1602 HCV patients who underwent liver biopsy, we compared the liver biopsy (Scheuer classification) fibrosis scores with APRI (AST/Platelet ratio), Fibrosis-4 (FIB-4), Lok score, GUCI score, Fibro-alpha score, Forns' score, King score, AAR (AST/ALT ratio), Fibrosis index (FI), Pohl score, Fibro-Q score, FCI (Fibrosis cirrhosis index) and three new scores, mean platelet volume (MPV), RPR (Red cell distribution width/platelet count ratio) and globulin/platelet count index (GPI).

Results: Mean age of patients was 41.8 ± 9.6 years (1365 males), genotype 4 (65.6 %) was the commonest followed by genotype 1 (10.9 %). Liver biopsy showed stage-0 fibrosis (F0) in 1.9 %, stage-1(F1) in 32.9 %, stage-2(F2) in 39.5 %, stage-3(F3) in 19 % and stage-4(F4) in 6.6 % patients.

of the baseline parameters, AST (adjusted OR = 1.015, CI = 1.008-1.022, $P = 0.001$), albumin (adjusted OR = 0.842, CI = 0.742-0.915, $P = 0.001$) and platelet count (adjusted OR = 0.981, CI = 0.974-0.989, $P = 0.001$) were independent predictors of cirrhosis. We derived a study score [8.5-0.2(albumin, g/dl) + 0.01(AST, IU/l) - 0.02(platelet count, 109/l)], at a cut off of > 4.7, it had high predictive accuracy (AUROC = 0.868, CI 0.833-0.904) for cirrhosis.

All the scores except AAR and Pohl score showed high predictive accuracy for cirrhosis (Table 1). of the new scores, MPV and RPR had relatively low and GPI had high predictive accuracy for cirrhosis.

Topic 11: Hepatitis C

No: 2106

Efficacy safety and pharmacokinetics of 12 weeks of simeprevir in combination with tmc647055 ritonavir and JNJ 56914845 in genotype 1 hepatitis C virus infected patients

S. Bourgeois[1], F. Nevens[2], C. Moreno[3], H. Van Vlierberghe[4], K. Arastéh[5], Y. Horsmans[6], H. Orlent[7], J. Schattenberg[8], P. Buggisch[9], S. Francque[10], L. Vijgen[11], T.n Kakuda[12], E. Hoeben[13], T. Kirsila[11], B. Jacquemyn[11], P. Van Remoortere[12], R. Verloes[13]

Zna Antwerp Department of Gastroenterology & Hepatology Antwerp-Belgium[1], University Hospitals Leuven Department of Liver and Biliopancreatic Disorders Leuven-Belgium[2], Cub Hôpital Erasme, Université Libre De Bruxelles Brussels-Belgium[3], Universitair Ziekenhuis Gent Department of Hepatology and Gastroenterology Ghent-Belgium[4], Epimed/Vivantes-auguste-viktoria-klinikum Berlin-Germany[5], Cliniques Universitaires Saint-luc, Université Catholique De Louvain Hepato-gastroenterology Brussels-Belgium[6], Az Sint. Jan Av Department of Gastroenterology and Hepatology Bruges-Belgium[7], University Medical Center, Johannes Gutenberg University of Mainz Department of Medicine Mainz-Germany[8], Ifi, Liver Center Hamburg, Asklepiosklinik St. Georg Hamburg-Germany[9], Universitair Ziekenhuis Antwerpen Department of Gastroenterology and Hepatology Antwerp-Belgium[10], Janssen Infectious Diseases Bvba Beerse-Belgium[11], Janssen Pharmaceuticals Llc Titusville, Nj-United States[12], Janssen Research & Development Bvba Beerse-Belgium[13]

Aim: Simeprevir is an approved, once-daily (QD) hepatitis C virus (HCV) NS3/4 protease inhibitor. TMC647055 is a potent non-nucleoside polymerase inhibitor and JNJ-56914845 is a potent NS5a replication complex inhibitor. The Phase 2a, open-label TMC647055HPC2001 study assessed in Panel 4 simeprevir + TMC647055 + ritonavir (RTV) + JNJ-56914845 in chronic genotype (GT)1 HCV-infected treatment-naïve and prior relapse patients.

Methods: HCV GT1a or GT1b-infected patients were randomised 1: 1 to 12 weeks of simeprevir 75 mg QD + TMC647055 450 mg QD + RTV 30 mg QD + JNJ-56914845 30 mg QD (Arm 1) or 60 mg QD (Arm 2). Randomisation was stratified by HCV geno/subtype. The primary endpoint was SVR12 (Table). A population pharmacokinetic model was used to predict simeprevir exposure (area under the curve [AUC0]-24 h] and trough plasma concentration [C0 h]).

Results: Baseline demographic/disease characteristics are shown (Table). 10/14 (71 %) and 14/15 (93 %) GT1a patients in Arms 1 and 2 achieved SVR12 compared with 15/15 (100 %) GT1b patients in both Arms. In Arm 1, no patients had viral breakthrough, while 4 (29 %) GT1a patients experienced viral relapse. In Arm 2, 1 (7 %) GT1a patient had viral breakthrough at Week 10, while no patients

experienced relapse. No deaths, serious adverse events (AEs), Grade 4 AEs or AEs leading to treatment discontinuation occurred. Considering the variability, simeprevir exposure was comparable between Arms 1 and 2 (Table).
Conclusion: The combination of simeprevir + TMC647055 + RTV + JNJ-56914845 was well tolerated, with 71 % and 93 % of GT1a patients on JNJ-56914845 30 mg and 60 mg, respectively, achieving SVR12 vs 100 % of GT1b patients. There was no difference in simeprevir exposure between groups.
Funded by Janssen.

Topic 11: Hepatitis C

No: 2195

Diagnostic and prognostic role of serum il 6 in malign transformation of liver cirrhosis

M. Yakut[1], H. Özkan[1]

Ankara University, School Medicine The Department of Gastroenterology Ankara-Turkey[1]

Background and aim: AFP is still the most commonly used and the single most recommended marker in diagnosis of HCC. IL-6 is a circular cytokine and its role on carcinogenesis in various hematological and solid tumors is clearly documented. A combination of serum IL-6 and AFP may provide beneficial information regarding early diagnosis of HCC. In this study, the effect of plasma IL-6 level on the diagnosis of HCC was investigated. The efficiency of IL-6 in early stages of HCC and its correlation with survival in this disease was also evaluated.
Materials and methods: A total of 130 patients with liver cirrhosis, together with 30 control cases were enrolled in the trial. A diagnosis of HCC was present in 75 patients (57.6 %) in the liver cirrhosis group. Blood samples were obtained from the enrolled study and control cases. AFP was quantified by chemoluminescence method. Plasma IL-6 levels of samples obtained at −80 °C were quantified by Human IL-6 BMS213/2 BMS213/2TEN kit.
Results: The HCC patients were older than the patients in the cirrhosis group ($P = 0.016$). Upon comparison of the HCC patients with the control group; AFP ($P < 0.001$) and IL-6 ($P < 0.001$) were significantly higher among the HCC patients. Comparison of HCC patients with liver cirrhosis cases with no diagnosis of HCC, revealed significantly high AFP ($P < 0.001$) and IL-6 levels ($P < 0.001$) in HCC group. Cut-off value for IL-6 was calculated as 5.73 (pg/mL). No difference was detected in AFP ($P = 0.600$) and IL-6 (0.344) in all three subgroups. A total of 17 patients died during a mean follow-up period of 32.9 months. No correlation was found between mean AFP values and IL-6 values and survival rates.
Conclusion: Plasma IL-6 level was found to be significant in the diagnosis of HCC. AFP and IL-6 provided no advantage in terms of early diagnosis of HCC and no correlation was observed between these markers and survival.

Topic 11: Hepatitis C

No: 1975

Sofosbuvir plus ribavirin for 12 16 or 24 weeks results in sustained virologic response over 97 % in genotype 1 and 6 HCV infection in Hong Kong

Ching-lung Lai[1], Man-fung Yuen[1], Jenny C. Yang[2], Steven J. Knox[2], Hongmei Mo[2], Ling-ling Han[2], Diana M. Brainard[2], John G. Mchutchison[2], Vincent Wai Sun Wong[3], Henry Lik-yuen Chan[3]

The University Department of Medicine, Queen Mary Hospital Department of Medicine Hong Kong-China[1], Gilead Sciences, Inc. Foster City-United States[2], Department of Medicine and Therapeutics and Institute of Digestive Disease, The Chinese University of Hong Kong Hong Kong-China[3]

Background and aims: In Hong Kong, most patients with hepatitis C virus (HCV) have genotype (GT) 1b or 6a infection. We evaluated the efficacy and safety of sofosbuvir (SOF) 400 mg plus weight-based ribavirin (RBV) 1000-1200 mg in treatment-naïve, HCV genotype 1 or 6-infected patients in Hong Kong.
Methods: Patients in an open-label, Phase 3 study were randomized 1: 1: 1 to SOF + RBV for 12, 16, or 24 weeks. Randomization was stratified by HCV subtype and presence of cirrhosis. The primary endpoint was SVR12 (HCV RNA < lower limit of quantitation (LLOQ = 25 IU/mL; COBAS® TaqMan® HCV Test Version 2.0) 12 weeks after completion of treatment).
Results: 31 patients were enrolled. Baseline characteristics are tabulated below. Most patients had favorable predictors of response: 90 % age < 65 years, 71 % BMI < 25 kg/m2, 65 % GT1b, 87 % non-cirrhotic, and 87 % IL28B CC genotype. All patients had HCV RNA < LLOQ by Week 4 and maintained through end-of-treatment. Overall SVR12 was 97 % (30/31); 1 patient in the 24-week group relapsed. Frequent adverse events (AE) reported in ≥ 10 % were malaise, upper respiratory tract infection (URTI), and anemia. No Grade 3 or 4 adverse events (AE) or serious AEs were reported. One patient discontinued SOF + RBV early due to AE of URTI. Three (10 %) patients had treatment-emergent hemoglobin (Hgb) < 10 g/dL; no patients had Hgb < 8.5 g/dL.
Conclusions: The IFN-free SOF + RBV regimen for 12, 16 or 24 weeks was well-tolerated and highly effective in treatment-naïve, HCV GT1b and GT6-infected patients with favorable predictors of response.

Topic 11: Hepatitis C

No: 1588

Twelve weeks sofosbuvir ribavirin therapy for treatment experienced chronic HCV genotype 2 Chinese patients

Guo-feng Chen[1], Qing Shao[1], Dong Ji[1], Fan Li[1], Bing Li[1], Zhong-bin Li[1], Song-hai Chen[1], Chun-yan Wang[1], Xiao-xia Niu[1], Shi-ying Ding[1], Tao Yan[2], Vanessa Wu[3], April Wong[3], Athena Chau[3], Yu-dong Wang[3], George Kk Lau[3]

Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[1], 302 Hospital International Liver Diagnosis and Treatment Centre Beijing-China[2], Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[3]

Background and aims: Previously, for chronic HCV genotype (GT) 2 treatment-naïve patients, 12-weeks sofosbuvir–ribavirin was shown to be noninferior to 24-weeks peginterferon–ribavirin, with the rates of sustained virologic response of 67 % (Fission study, Lawitz et al. NEJM 2013). However, the efficacy and safety of sofosbuvir–ribavirin in treatment-experienced GT2 cirrhotic patients, is unknown.
Methods: Thirty-eight treatment-experienced (null responder/relapse-22/16) Chinese with chronic HCV GT2 were studied. They all had documentation of cirrhosis by means of liver biopsy (Metavir

score > 3 or Ishak score > 4) or FibroScan (≥ 14.6 kPa) and Child–Pugh class A score of less than 7. They received 12-weeks sofosbuvir–weight-based ribavirin (Group 1, n = 13) or 24-weeks peginterferon–ribavirin (Group 2, n = 25). The primary efficacy end point was a sustained virologic response (SVR) with HCV RNA level of < 25 IU per milliliter (the lower limit of quantitation) 12 weeks after the end of study-drug administration. HCV RNA levels were measured with the use of the COBAS TaqMan real-time PCR assay (Roche version 2.0).
Results: There is a significantly higher rate of SVR in group 1 than group 2 achieved SVR (85 % Vs 24 %, $P = 0.001$). In group 1, SVR is not significantly different between the null responders and relapsers. However, in group 2, none of the null responders as compared to 6/11 relapsers had SVR ($P = 0.003$). There are less adverse events reported in group 1 than group 2.
Conclusion: 12-weeks sofosbuvir–ribavirin is more effective than 24-weeks peginterferon–ribavirin in treatment-experienced GT2 cirrhotic patients.

Topic 11: Hepatitis C

No: 1686

HCV genotype and IFNL3 and IFN4 in China

Fan Li[1], Stephen Ho[2], Qing Shao[1], Bing Li[1], Dong Ji[1], Zhong-bin Li[1], Song-hai Li[1], Chun-yan Wang[1], Xiao-xia Niu[1], Shi-ying Ding[1], Tao Yan[3], Vanessa Wu[4], Athena Chau[4], April Wong[4], Yu-dong Wang[4], Guo-feng Chen[1], George Kk Lau[4]

Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[1], Chan & Hou Medical Laboratories Ltd. Medical Testing Hong Kong-China[2], 302 Hospital International Liver Diagnosis and Treatment Centre Beijing-China[3], Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[4]

Background and aims: Treatment of chronic hepatitis C (CHC) infection is governed by both host (genetics, diseases status) and viral factors (HCV genotype and viral load). We investigate the epidemiology of HCV infection and host single nucleotide analogues in IFNL3 and IFNL4 in Chinese with CHC infection and their effect on standard of care pegylated interferon-ribavirin (PR) therapy.
Methods: We studied 1,365 treatment naïve CHC Chinese patients who had attended the Hong Kong Humanity and Health Medical Centre or the special Hong Kong-Beijing Hepatitis C clinic in Beijing 302 hospital, from 2009-2014. HCV genotype and subtype were determined with NS5B or core clonal sequencing. The IL28B genotype and IFNL4 SNPs determined by PCR sequencing of the rs12979860 (C or T) and ss469415590 (TT or ΔG). The SNPs of both IL28 and IFNL4 were correlated to sustained virologic response to PR therapy.
Results: The prevalence of GT1b, GT6a, GT3a, GT1a, GT2a were 56.7, 25.3,6.9, 5.2, and 3.5 %, respectively. Fifty-three percent and fifty percent of GT1b was IL28B CC genotype and IFNL4 TT/TT genotype. There was no association between IL-28 and IFNL4 SNPs variation with viral load or disease severity. The response to PR therapy was significantly better with IL28B CC genotype with SVR of 68 % in GT1 and 90 % for GT2. No additional predictive value was added by including IFNL4.
Conclusions: For treatment-naïve Chinese CHC patients, the most common HCV genotype is GT1b and their response to PR therapy is good with a response rate of 68 % if they have the IL28B-CC genotype.

Topic 11: Hepatitis C

No: 2057

Ledipasvir sofosbuvir is effective as a single tablet regimen for treatment of patients with genotype 1 chronic hepatitis C virus including those with traditional negative predictors

Paul Y. Kwo[1], Saleh Alqahtani[2], Ira M. Jacobson[3], Kris V. Kowdley[4], Jenny C. Yang[5], Yanni Zhu[6], Rob Hyland[5], Philipp S. Pang[5], John G. Mchutchison[5], Mark Sulkowski[7]

Indiana University School of Medicine Division of Gastroenterology/hepatology Indianapolis-United States[1], Johns Hopkins University Clinical Liver Research Lutherville-United States[2], Weill Cornell Medical College The Division of Gastroenterology and Hepatology New York-United States[3], Virginia Mason Medical Center Liver Care Network and Organ Care Research Seattle-United States[4], Gilead Sciences, Inc Clinical Research Foster City-United States[5], Gilead Sciences, Inc Biostatistics Foster City-United States[6], Johns Hopkins University Infectious Disease Center For Viral Hepatitis Lutherville-United States[7]

Background: Simple, safe and effective treatment of genotype 1 (GT 1) chronic hepatitis C virus (HCV), without the use of pegylated-interferon (PegIFN) and ribavirin (RBV), remains an unmet medical need. The once-daily single-tablet-regimen of Ledipasvir (LDV), an NS5A inhibitor, and sofosbuvir, an NS5B nucleotide polymerase inhibitor, resulted in high rates of sustained virologic response (SVR) in phase 2 studies

Methods: Three open-label phase 3 clinical trials evaluated the safety and efficacy of LDV/SOF administered with or without (±) RBV for treatment of GT 1 chronic HCV. Treatment-naïve patients were randomized to 8, 12 and 24 weeks of LDV/SOF ± RBV in the ION-1 and ION-3 studies. HCV treatment-experienced patients were randomized to 12 and 24 weeks of LDV/SOF ± RBV in the ION-2 study.
Results: Of the 1952 patients 16 % were black, 12 % had compensated cirrhosis, 26 % had a BMI ≥ 30 kg/m2, 82 % had a high HCV viral load ≥ 800,000 IU/mL, and 23 % were treatment-experienced. of these 440 treatment-experienced subjects, 231 (53 %) were prior HCV protease-inhibitor (PI) + PegIFN + RBV treatment failures. Overall, 97 % of all patients achieved SVR12. The intent-to-treat SVR12 rates in all treatment arms are show in Figure 1. SVR12 rates for subgroups of patients with traditional predictors of poor response in comparison to patients without these characteristics will be presented.
Conclusion: LDV/SOF was highly effective in patients with genotype 1 HCV infection, including those with compensated cirrhosis and those who had previously failed PI + PegIFN + RBV. SVR12 rates were similar irrespective of baseline characteristics traditionally associated with a poor response to IFN-based regimens.

Topic 11: Hepatitis C

No: 2054

Safety of ledipasvir sofosbuvir with and without ribavirin for the treatment of patients with chronic HCV genotype 1 infection an analysis of the phase 3 ion trials

Saleh Alqahtani[1], Nezam H. Afdahl[2], Stefan Zeuzem[3], Stuart C. Gordon[4], Alessandra Mangia[5], Paul Y. Kwo[6], Jenny C. Yang[7], Xiao Ding[8], Phillip S. Pang[7], John G. Mchutchison[7], Patrick Marcellin[9], Kris V. Kowdley[10], Mark S. Sulkowski[11]

Johns Hopkins University Clinical Liver Research Lutherville-United States[1], Beth Israel Deaconess Medical Center Division of Gastroenterology Boston-United States[2], J.w. Goethe University Department of Internal Medicine Frankfurt-Germany[3], Henry Ford Hospital Department of Gastroenterology/transplant Detroit-United States[4], Ospedale Casa Sollievo Della Sofferenza Liver Unit San Giovanni-Italy[5], Indiana University School of Medicine Division of Gastroenterology/hepatology Indianapolis-United States[6], Gilead Sciences, Inc Clinical Research Foster City-United States[7], Gilead Sciences, Inc Biostatistics Foster City-United States[8], Hôpital Beaujon- Hôpitaux De Paris Department of Hepatology Clichy-France[9], Virginia Mason Medical Center Liver Care Network and Organ Care Research Seattle-United States[10] Johns Hopkins University Infectious Disease Center For Viral Hepatitis Lutherville-United States[11]

Background: The once-daily fixed-dose combination tablet of ledipasvir/sofosbuvir (LDV/SOF) was evaluated with and without ribavirin (RBV) for the treatment of HCV genotype 1 infection in three phase 3 studies. Overall, SVR rates were high (97 %) regardless of RBV use. The purpose of this analysis was to characterize the safety profile of RBV in an interferon-free regimen.
Methods: Treatment-naïve and -experienced patients with HCV genotype 1 infection, including those with compensated cirrhosis, were randomized to 8, 12, and 24 weeks of LDV/SOF ± RBV. Treatment-emergent adverse events (AEs) and laboratory abnormalities were assessed.
Results: 1952 patients (-RBV, n = 1080; +RBV, n = 872) were treated in the studies: 224 (11 %) had compensated cirrhosis, 501 (26 %) had a BMI ≥ 30 kg/m2, and 440 (23 %) were treatment-experienced. Overall, 97 % of all patients achieved SVR12. Treatment-related AEs occurred in 71 % and 45 % of patients treated with and without RBV. For both groups, treatment-related serious AEs (0.3 %) and treatment-discontinuations due to AEs (0.7 %) were uncommon. More patients taking RBV than LDV/SOF required dose modification or interruptions of study treatment due to AEs (13.5 %v0.6 %) and other medications during treatment (63 % v53 %) including topical corticosteroids (7 %v3 %), antihistamines (11 %v5 %), and sleeping aids (17 %v10 %). Anemia was observed in 7 % of patients taking RBV and < 0.01 % of patients taking LDV/SOF. Similar patterns of AEs were observed among cirrhotic patients.
Conclusions: The addition of RBV did not increase the rate of treatment discontinuation or treatment-related serious AEs, but was associated with greater incidence of AEs including fatigue, insomnia, irritability and rash/pruritus, and concomitant medication use.

Topic 11: Hepatitis C

No: 1563

All oral therapy with sofosbuvir plus ribavirin for the treatment of HCV genotypes 1 2 3 and 4 infection in patients co infected with HIV (photon 2)

Chloe Orkin[1], Jean-michel Molina[2], David M. Iser[3], Francisco X. Zamora[4], Mark Nelson[5], Christoph Stephan[6], Benedetta Massetto[7], Anuj Gaggar[7], Liyun Ni[7], Evgenia Svarovskaia[7], Diana Brainard[7], G. Mani Subramanian[7], John G. Mchutchison[7], Massimo Puoti[8], Juergen K. Rockstroh[9]

Barts Health Nhs Trust Infection & Immunity London-United Kingdom[1], University of Paris Diderot, Paris 7 and Department of Infectious Diseases, Saint-Louis Hospital Paris-France[2], Infectious Diseases Unit, Alfred Hospital Melbourne-Australia[3], Hiv Unit, Internal Medicine Service, Hospital Universitario La Paz, Idipaz Madrid-Spain[4], Chelsea and Westminster Hospital, St. Stephens Centre London-United Kingdom[5], Infectious Diseases Unit At Medical Department, Hospital of The Johann Wolfgang Goethe-university Frankfurt-Germany[6], Gilead Science, Inc. Foster City-United States[7], Division of Infectious Diseases, Ao Ospedale Niguarda Ca Milan-Italy[8], Department of General Internal Medicine I, University Hospital of Bonn Bonn-Germany[9]

Background and aims: HIV/HCV co-infected patients require effective interferon-free HCV therapy that is tolerable and simply administered in combination with antiretroviral therapy (ART). This study evaluated the safety and efficacy of the oral HCV NS5B inhibitor sofosbuvir (SOF) with ribavirin (RBV) in individuals coinfected with HIV and HCV genotypes (GT) 1-4.
Methods: 274 individuals infected with HIV and HCV GT1-4, were enrolled to receive SOF 400 mg QD and weight based RBV 1000-1200 mg/day; GT 1, 3, 4 treatment naïve and GT 2, 3 treatment experienced patients received 24 weeks of therapy and GT 2 treatment naive 12 weeks. This analysis evaluated the sustained virologic response 24 weeks after treatment (SVR24). Safety assessments included HIV RNA and CD4 cell levels.
Results: SVR24 rates ranged from 81 % to 91 % across GT1-4 (table). Across all groups the overall concordance between SVR12 and SVR24 was 98 %. of 4 patients who achieved SVR12 but not SVR24, 2 patients relapsed and 2 were re-infected based on phylogenetic sequence analysis. Treatment discontinuations from SOF due to adverse events (AEs) were observed in 5/274 (2 %) of patients and grade 3/4 AEs were reported in 15/274 (6 %). No change in CD4 % was observed. Four patients on ART had a transient HIV-RNA rebound that resolved spontaneously within Follow-Up 24.
Conclusions: HCV GT 1-4 treatment naive and experienced HIV coinfected patients achieved high rates of SVR24 with 12 or 24 weeks of an interferon-free, oral regimen of SOF + RBV. This treatment was well-tolerated and safely co-administered with multiple ART regimens.

Topic 11: Hepatitis C

No: 1368

Shortening overall treatment to 12 weeks of simeprevir (SMV) plus peg IFN RBV in treatment naïve chronic hepatitis C (CHC) genotype 1 patients assessment of baseline and week 2 on treatment predictors of SVR

Tarik Asselah[1], Christophe Moreno[2], Christoph Sarrazin[3], Michael Gschwantler[4], Graham R. Foster[5], Antonio Craxi[6], Peter Buggisch[7], Robert Ryan[8], Oliver Lenz[9], Gino Van Dooren[9], Isabelle Lonjon-domanec[10], Michael Schlag[11], Maria Buti[12]

Beaujon Hospital, University of Paris Hepatology Department Clichy-France[1], Cub Hôpital Erasme Hospital, Université Libre De Bruxelles Clinique D'hépatologie Brussels-Belgium[2], Johann Wolfgang Goethe University Hospital Medical Department 1 Frankfurt-Germany[3], Wilhelminenspital 4th Department of Internal Medicine Vienna-Austria[4], Queen Mary Hospital, University of London, Barts Health Hepatology Department London-United Kingdom[5], University of Palermo Dept. of Internal Medicine and Medical Specialities Palermo-Italy[6], Institute For Interdisciplinary Medicine Liver Center Hamburg Hamburg-Germany[7], Janssen Research & Development Medical Affairs, Infectious Disease Titusville-United States[8], Janssen Infectious Diseases Bvba Infectious Diseases Beerse-Belgium[9], Janssen Pharmaceuticals Virology Department Paris-France[10], Janssen-Cilag Virology Department Vienna-Australia[11], Hospital Valle Hebron and Ciberehd Del Institut Carlos Iii Internal Medicine Barcelona-Spain[12]

Purpose: To assess whether Week-2 response with SMV + Peg-IFN/RBV can allow shortening treatment to 12 weeks, irrespective of baseline and on-treatment factors.
Design: Phase-3, open-label study in treatment-naïve CHC genotype 1-patients with no-to-moderate fibrosis (METAVIR F0-F2). In patients with HCV-RNA < 25 IU/mL (detectable/undetectable [Roche COBAS[SUP]®[/SUP] Taqman[SUP]®[/SUP] LLOQ: 25 IU/mL, LLOD: 15 IU/mL]) at Week 2 and undetectable at Weeks 4 and 8, all treatments were stopped at Week 12. If these criteria were not met, Peg-IFN/RBV was continued to Week 24. Concordance of response between Roche and Abbott RealTime assays was also determined.
Results: Of 163 patients treated, 123 (76 %) fulfilled eligibility criteria for 12-week treatment (male: 53 %, white: 92 %, genotype 1a/b: 40/60 %, METAVIR F0/1: 76 %, IL28B CC/CT/TT: 26/59/15 %). After SMV + Peg-IFN/RBV for 12 weeks, SVR12 was 65 % (n = 123). Responses varied by baseline parameters and on-treatment response (Table 1).

One patient discontinued SMV and RBV (non-compliance). Treatment during the SMV + Peg-IFN/RBV phase was well tolerated (n = 163); 2.5 % (n = 4) experienced a serious AE (none SMV related), 1.8 % (n = 3) discontinued SMV + Peg-IFN/RBV due to an AE (1 possibly SMV-related [urinary incontinence]). Most frequent AEs were influenza-like illness 35.6 %, pruritis 32 %, fatigue 27 %.
Conclusions: Week-2 response alone did not predict outcomes as baseline factors influenced SVR rates. High (> 80 %) SVR12 rates were in: IL28B CC genotype patients, patients with low baseline viral load, or those with mild fibrosis (METAVIR F0/1) or GT1b and undetectable HCV RNA at Week 2.

Topic 11: Hepatitis C

No: 1539

Simeprevir plus peginterferon ribavirin in treatment naïve patients with chronic hepatitis C virus genotype 1 infection results from the phase III tiger study conducted in East Asian patients living in China and Korea

L. Wei[1], T. Han[2], D. Yang[3], J. Heo[4], J. Shang[5], J. Cheng[6], X. Chen[7], Q. Xie[8], J. Kim[9], R. Kalmeijer[10], S. Ouwerkerk-mahadevan[11], O. Lenz[12], R. Sinha[13], M. Li[14], J. Scott[15], M. Peeters[12], J. Witek[13]

Peking University People's Hospital and Peking University Hepatology Institute and Peking Key Laboratory For Hepatitis C and Immune Therapy Peking University People's Hospital and Peking University Hepatology Institute and Peking Key Laboratory For Hepatitis C and Immune Therapy Beijing-China[1], Tianjin Third Central Hospital Tianjin-China[2], Union Hospital of Tongji Medical College, Huazhong University of Science and Technology Wuhan-China[3], Pusan National University and Medical Research Institute Busan-Korea, South[4], Henan Provincial People's Hospital Zhengzhou-China[5], Beijing Ditan Hospital, Capical Medical University Beijing-China[6], Beijing You An Hospital, Capital Medical University Beijing-China[7], Ruijin Hospital, Shanghai Jiaotong University School of Medicine Shanghai-China[8], Gachon University Gil Medical Center Incheon-Korea, South[9], Janssen Global Services Llc Titusville-United States[10], Janssen Research & Development Bvba Beerse-Belgium[11], Janssen Infectious Diseases Bvba Beerse-Belgium[12], Janssen Research & Development Llc Titusville-United States[13], China R&d and Scientific Affairs, Xi'an Janssen Pharmaceutical Company Beijing-China[14], Janssen Global Services, Llc High Wycombe-United Kingdom[15]

Aim: The Phase III, randomised TIGER study (NCT01725529) evaluated simeprevir plus peginterferon/ribavirin (PR) in treatment-naïve East Asian patients.
Methods: Patients received simeprevir 150 mg plus PR, simeprevir 100 mg plus PR or placebo plus PR for 12 weeks. Patients in the simeprevir arms received PR alone for a further 12 or 36 weeks based on response-guided criteria (RGT). Patients in the placebo arm received 36 weeks of PR alone. Primary efficacy endpoint: sustained virologic response 12 weeks after planned end of treatment (SVR12). Safety, tolerability and patient-reported outcomes (PROs) were assessed.
Results: 457 patients were randomised 1: 1: 1 and treated (China/Korea 80.3/19.7 %, HCV genotype 1a/1b 1.1/98.9 %, METAVIR F3-F4/S3-S4 17.6 %, IL28B non-CC 20.4 %). Virologic response is summarised (Table). Overall SVR12 rates were superior for simeprevir 100 mg (88.9 %; $P = 0.003$) and 150 mg (90.8 %; $P < 0.001$) versus placebo (75.7 %). For simeprevir 100 mg and 150 mg, 143/153 (93.5 %) and 143/152 (94.1 %) of patients met RGT criteria, respectively. of these, 134/143 (93.7 %) patients in each simeprevir arm achieved SVR12. During the first 12 weeks, 28.8 % of patients in the simeprevir 100 mg arm reported grade 3-4 AEs versus 33.6 % for simeprevir 150 mg and 30.9 % for placebo. 7 (2.3 %) simeprevir patients and 1 (0.7 %) placebo patient discontinued simeprevir/placebo due to AEs. SAEs were infrequent (1.0 %) and not related to simeprevir. No deaths occurred. Simeprevir-treated patients reported improved quality of life on EQ-5D and reduced fatigue on FSS.
Conclusion: Simeprevir (100 mg and 150 mg QD) plus PR achieved superiority in SVR versus placebo in treatment-naïve HCV GT1-infected East Asian patients, and was generally well tolerated.
Funded by Janssen.

Topic 11: Hepatitis C

No: 1391

IL28B CC genotype associates higher HCV RNA levels*

Abdülkadir Dökmeci[1], Reşat Özaras[2], Mehmet Demir[3], Iftihar Köksal[4], Şebnem Gürsoy[5], Yusuf Önlen[6], Şener Barut[7], Gaye Usluer[8], Meral Akdoğan[9], Oğuz Karabay[10], Necati Örmeci[1], Fatih Özdener[11], Seda Erdoğan[11]

Ankara University School of Medicine Gastroenterology Ankara-Turkey[1], Istanbul University Cerrahpaşa School of Medicine Infectious Diseases Istanbul-Turkey[2], Mustafa Kemal University School of Medicine Gastroenterology Hatay-Turkey[3], Karadeniz Technical University School of Medicine Infectious Diseases Trabzon-Turkey[4], Erciyes University School of Medicine Gastroenterology Kayseri-Turkey[5], Mustafa Kemal University School of Medicine Infectious Diseases Hatay-Turkey[6], Gaziosmanpaşa University School of Medicine Infectious Diseases Tokat-Turkey[7], Osmangazi University School of Medicine Infectious Diseases Eskişehir-Turkey[8], Ankara Yüksek Ihtisas Training and Research Hospital Gastroenterology Ankara-Turkey[9], Sakarya Korucuk Training and Research Hospital Infectious Diseases Sakarya-Turkey[10], Roche Pharmaceuticals Clinical Trials Istanbul-Turkey[11]

Introductions and aim: Host IL28B genotype influences spontaneous clearance of acute HCV infection and response to interferon-based treatment in patients with chronic hepatitis C(CHC). Whether IL28B genotype influences progression of hepatic fibrosis is unclear. The large prospective international Gen-C study was designed to evaluate relationships between IL28B genotypes and fibrosis stage in

patients with CHC. The present is a sub-analysis of patients included in Gen-C study in Turkey, aiming to investigate the relationship of IL28B genotype and viral load.

Patients and methods: This multicenter study included treatment naïve and experienced patients. Demographic characteristics were recorded and viral studies (HCV-RNA, genotyping, subtyping, IL28B genotyping; rs12979860 [CC vs. TC vs. TT] and rs8099917 [TT vs. GT vs. GG]) were performed.

Results: Seventeen centers participated in Gen-C throughout Turkey. A total of 302 treatment naïve CHC patients were enrolled. The patients with rs8099917-TT had 6.07 Log10 IU/mL HCV-RNA; while TG and GG patients had lower levels (5.77 and 5.84 Log10 IU/mL, respectively ($P = 0.0018$). In rs12979860-CC patients, viral load was 6.33 Log10 IU/mL, higher than TC (5.96 Log10 IU/mL), and TT (6.05 Log10 IU/mL) ($P = 0.0353$).

Conclusion: Favorable IL28B genotypes (rs12979860-CC and rs8099917-TT) associate a higher viral load when compared to the unfavorable ones. Despite higher viral load, a higher sustained virological response remains to be explained.

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Topic 11: Hepatitis C

No: 1331

Geographic barriers and complex therapies for patients with hepatitis C can be overcome by innovative and effective strategy utilising telehealth

Saroj Nazareth[1], Nick Kontorinis[1], Sherman Picardo[1], Marion Mcinerney[1], Nadine Leembruggen[1], Wendy Cheng[1]

Royal Perth Hospital Gastroenterology and Hepatology Perth-Australia[1]

Background: The well-established Royal Perth Hospital Hepatitis C Telehealth (TH) Service has received increasing referrals for rural HCV patients with comorbidities requiring complex treatment.

Aims: To compare (1) patient profiles and treatment outcomes of TH with face to face (FTF) clinics (2) regional notification with treatment uptake.

Retrospective analysis of TH (2005-2014) and all patients treated FTF. Statistical analysis was performed using the Chi Square test.

Results: Baseline characteristics were similar for TH (n = 93) and FTF patients (n = 1094): mean age 45 years; weight 83.7kgs; 58.1 % male; 52.7 % genotype 1; 84.0 % treatment naïve; 53.8 % reported comorbidities (depression, hypertension, asthma) and 30 % cirrhosis. Although notification is highest in southern and eastern regions, more patients were treated in the northern and eastern regions.

There was no significant difference in sustained virological response (SVR) rate - 50.5 %(TH) versus 57.7 %(FTF) with no difference in discontinuation rates.

Dose reductions were more frequent in TH patients (22.6 %) than FTF(10.9 %) ($P < 0.001$). Hospitalisations (decompensation, depression) were significantly higher in the TH group (6.8 % versus 1.9 %) ($P < 0.005$). More TH patients received pegylated interferon alpha-2a (68.8 %) compared to FTF(44.9 %) ($P < 0.05$).

Conclusions: Patients with comorbidities and cirrhosis in remote WA can be managed safely by TH service with similar SVR. TH patients however had higher rates of dose reductions and hospitalisations.

Topic 11: Hepatitis C

No: 1806

Impact of ITPA polymorphisms on ribavirin induced hemoglobin decline in patients with chronic hepatitis C infection underwent treatment with pegylated interferon and ribavirin

Mohammad Pouryasin[1], Maryam Keshvari[2]

College of Science, Tabriz Branch, Islamic Azad University Department of Biology Tabriz-Iran[1], High Institute For Research and Education In Transfusion Medicine Blood Transfusion Research Center Tehran-Iran[2]

Introduction: Red blood cell ITPase deficiency, which is caused by rs1127354 and rs7270101 polymorphisms of ITPA gene, has great impact on prevention of ribavirin (RBV)-induced anemia among hepatitis C virus (HCV)-infected patients. This study aimed to assess the RBV-induced hemoglobin (Hb) decline and related parameters in Iranian patients with HCV infection who were treated with Pegylated Interferon (PegIFN) and RBV combination therapy.

Materials and methods: In this retrospective study, 100 patients (mean ± SD of age: 41.4 ± 11.3) with chronic HCV infection (55 % HCV genotype 1 and 45 % HCV genotype 3) were genotyped for rs1127354 and rs7270101 polymorphisms by restriction fragment length polymorphism (RFLP).

Results: The observed frequency for rs7270101 genotypes was 80 % AA (wild type) and 20 % AC (heterozygous). The prevalence of rs1127354 genotypes was 79 % CC (wild type), 20 % CA (heterozygous) and 1 % AA (homozygous). In Univariate analysis, no association between rs7270101, gender, age, HCV RNA level, BMI and rs12979860 with Hb decline was found ($P > 0.05$) however rs1127354 and dose of RBV were found to influence the Hb decline in the first month of hepatitis C combination therapy ($P < 0.05$). In multivariate analysis, rs1127354 wild type ($P < 0.001$, OR: 16.9, 95 % CI = 3.6-83.3) and higher RBV dose ($P < 0.001$, OR: 3.5, 95 % CI = 1.4-8.8) were found to have great role on Hb decline at week 4 of therapy.

Conclusion: rs1127354 ITPA gene variant has great role in Hb decline at week 4 of PegIFN/RBV therapy.

Topic 11: Hepatitis C

No: 1934

Sofosbuvir containing regimens could eradicate HCV gt1 and gt2 from Japanese patients

Tatsuo Kanda[1], Makoto Arai[1], Shin Yasui[1], Akinobu Tawada[1], Yuki Haga[1], Reina Sasaki[1], Masato Nakamura[1], Xia Jiang[1], Shingo Nakamoto[1], Fumio Imazeki[1], Osamu Yokosuka[1]

Chiba University Hospital Gastroenterology Chiba-Japan[1]

Background: Sofosbuvir (SOF) is a potent inhibitor of HCV NS5B polymerase. In the present study, we treated Japanese patients with HCV GT1 and GT2 using SOF-containing regimens and evaluated their efficacy.

Methods: Total 18 HCV-infected Japanese patients were included. Ten HCV GT1 (mean age 59 years, male/female: 2/8) consisted of 5 treatment-naïve, 2 peginterferon (P)/ribavirin (RBV)-null responders, 1 P/RBV/telaprevir-relapser, and 2 interferon-intolerant/interferon ineligible patients. Eight HCV GT2 patients (mean age 61 years, male/female: 4/4) included 3 treatment-naïve, 1 P-relapser, 3 P/RBV-

relapsers and 1 P/RBV-null responder. HCV GT1 and GT2 patients were treated with SOF 400 mg plus HCV NS5A inhibitor ledipasvir (LDV) 90 mg ± weight-based RBV daily for 12 weeks, and SOF 400 mg plus weight-based RBV daily for 12 weeks, respectively. HCV RNA was detected and quantified by TaqMan PCR v2.0. Sustained virological response (SVR) was defined as undetectable HCV RNA 12 weeks after end of treatment. Ultra-deep sequence analysis for the detection of HCV NS5A mutations at baseline was performed in HCV GT1 patients.

Results: All 10 HCV GT1 patients achieved < 25 IU/mL and undetectable HCV RNA at week 4 and 8, respectively. All 8 HCV GT2 patients achieved < 25 IU/mL and undetectable HCV RNA at week 4 and 5, respectively. However, all the patients achieved SVR, irrespective of IL28B genotype or HCV G1 NS5A mutations at baseline.

Conclusion: SOF-containing regimens represent important therapeutic options for Japanese patients with HCV GT1/GT2 infection who are treatment-naive and treatment-experienced including those who are interferon-intolerant and interferon-ineligible.

Topic 11: Hepatitis C

No: 2166

Association between itpa gene rs1127354 polymorphism and rbv induced anemia in Turkish patients with hepatitis C virus genotype 1

Hikmet Akkız[1], Ersin Akgöllü[1], Aynur Bekar[1], Macit Sandıkçı[1], Sedef Kuran[1], Oğuz Üsküdar[1], Ümit Karaoğullarından[1]

University of Çukurova Department of Gastroenterology Adana-Turkey[1]

Aim: Although the combination of pegylated interferon (IFN)-α and ribavirin (RBV) is the standard therapy for patients with chronic hepatitis C (HCV) infection, Ribavirin-induced anemia is a major causes of discontinuation and dose reduction of treatment during antiviral therapy. Host genetic factors, such as inosine triphosphate pyrophosphatase (ITPA) gene polymorphism, influence RBV-induced anemia. The aims of this study were to analyze the correlation between ITPA gene rs1127354 (C/A) polymorphism and RBV-induced anemia in the Turkish population.

Material and method: Genotypes of the ITPA gene rs1127354 (C/A) single nucleotide polymorphism (SNP) were determined in 333 patients with HCV infection by using a polymerase chain reaction-restriction fragment length polymorphism (PCR–RFLP) assay.

Results: The associations between ITPA gene rs1127354 (C/A) polymorphism and RBV-induced severe anemia, age, baseline hemoglobin were observed in comparisons by using multivariate analysis ($P < 0.05$).

Conclusions: In conclusion, the rs1127354 (C/A) polymorphism would be a useful biomarker for predictive RBV-induced anemia. However, determination of ITPA gene rs1127354 variants might be applied to establish tailored dosages in PegIFNα/RBV therapy. Consequently, we suggest determining ITPA gene rs1127354 polymorphism of patients with HCV genotype 1 before onset of treatment.

Topic 11: Hepatitis C

No: 2214

Economic burden of chronic hepatitis C and its complications in Turkey

Sait Bagci[1], Ismail Balik[2], Hurrem Bodur[3], Osman Ersoy[4], Rahmet Guner[5], Zeki Karasu[6], Simten Malhan[7], Necati Ormeci[8], Hasan Ozkan[8]

Gulhane Medical School Gastroenterology Ankara-Turkey[1], Ankara University Infectious Diseases Ankara-Turkey[2], Numune Training Hosp Infectious Diseases Ankara-Turkey[3], Yildirim Beyazit University Gastroenterology Ankara-Turkey[4], Yildirim Beyazit University Infectious Diseases Ankara-Turkey[5], Ege University Gastroenterology Izmir-Turkey[6], Baskent University Health Care Management Ankara-Turkey[7], Ankara University Gastroenterology Ankara-Turkey[8]

*The authors written in alphabetical order

Objective: Hepatitis C virus (HCV) infection is an important cause of death about 350.000 annually worldwide due to its serious complications. HCV infection is associated with significant economic burden. Chronic Hepatitis C (CHC) may lead to several sequelae including compensated cirrhosis, sensitive ascites, refractory ascites, variceal haemorrhage and hepatocellular carcinoma (HCC) and liver transplantation. The objective of the present study was to evaluate the economic burden of chronic HCV infection in Turkey. The cost of CHC infection and its sequelae were calculated based on health care perspective.

Method: In the present study, the impact of CHC and its complications on the national economy was examined by countrywide experts in the light of relevant literature. Study population included patients from national tertiary care infectious disease and gastroenterology units. Direct costs related to medical management of CHC patients were calculated using "cost-of-illness" methodology.

Results: An expert panel consisting of 9 prominent specialists convened to share their clinical experience and opinions about the issue to estimate the direct costs of care of patients with hepatitis C and its complications in Turkey. Cost data have been reported as mean annual cost per patient annually. Patients who received pegylated interferon (PegIFN)/interferon(IFN) plus ribavirin comprised 80 % of the whole population whereby PegIFN/IFN plus ribavirin plus boceprevir/telaprevir was the remaining 20 %. The cost of CHC without complications was estimated as $13,556.44; refractory ascites $16,116.32; sensitive ascites $1,032.65; hepatic encephalopathy $2,781.78; variceal haemorrhage $5,009.73; compensated cirrhosis $14,158.46; HCC $18,717.41 and liver transplantations $42,574.62 per person annually. While total number of viremic infections is approximately 514.000 in Turkey, annual number of treated patients is 4.220; number of compensated cirrhosis 51.000; HCC 2,230 and transplantation 154. Variceal haemorrhage occurs in 20 % of decompensated cirrhosis, hepatic encephalopathy in 20 %, sensitive ascites in 2/3, and refractory ascites in 1/3 as assessed by experts. Total annual economic burden inflicted by CHC and its complications is $166.970.270. This value is 0,027 % of the gross national product.

Conclusion: The national economic burden of CHC and advanced stage liver disease were projected to further increase. Cost reductions are possible with timely interventions aimed at minimizing the health burden of advanced liver disease.

Topic 11: Hepatitis C

No: 1665

Efficacy of 24 week pegylated interferon alpha and ribavirin combination therapy in highly selected patients with hepatitis C virus genotype 1 infection

Heidar Sharafi[1], Seyed Moayed Alavian[2], Maryam Keshvari[3]

Middle East Liver Disease (meld) Center Department of Molecular Hepatology Tehran-Iran[1], Middle East Liver Disease (meld) Center Department of Clinical Hepatology Tehran-Iran[2], High Institute For Research and Education In Transfusion Medicine Blood Transfusion Research Center Tehran-Iran[3]

Background: Previous studies using pegylated interferon (PegIFN) and ribavirin (RBV) combination therapy suggested that patients with HCV genotype 1 infection and low pretreatment HCV RNA level can be treated for 24 weeks without compromising sustained virological response (SVR) rate. This study aimed to investigate the efficacy of PegIFN alfa-2a plus RBV administered for 24 weeks in patients with chronic HCV genotype 1 infection and low baseline serum HCV RNA level.

Materials and methods: A total of 20 patients with HCV genotype 1 infection and favorable baseline characteristics and on-treatment response were treated with Pegaferon[SUP]®[/SUP] (PegIFN alpha-2a by Pooyesh Darou) and Ribabiovir[SUP]®[/SUP] (Ribavirin by Bakhtar Bioshimi) for 24 weeks. A group of 23 patients with same criteria who underwent 48-week treatment was selected as well.

Results: The majority of patients had no fibrosis on liver elastography. There was no statistically difference between age, sex, alanine transaminase (ALT), rs12979860 polymorphism and the level of fibrosis between two studied groups. All patients in 24-week treatment group achieved SVR and all the subjects who received 48-week treatment achieved SVR as well ($P > 0.99$).

Conclusion: This case–control study confirms that the efficacy of 24-week regimen of PegIFN alfa-2a plus RBV is similar to 48-week treatment in patients with HCV genotype 1 infection and low baseline HCV RNA level who achieved rapid virological response (RVR) by week 4 of therapy. Response guided therapy can be effective and cost benefit among selected HCV genotype 1-infected patients.

Topic 11: Hepatitis C

No: 2092

The effectiveness of therapy in patients with extrahepatic manifestations of chronic hepatitis C hepatitis C indolent lymphoma associated (IL + C)

Segey Lepkov[1], Irina Subortseva[2], Svetlana Kosura[1], Oleg Kolomeitsev[3], Uylia Ryabykhina[3]

Russian National Research Medical University Named After Ni Pirogov Therapy Moscow-Russia[1], National Haematology Research Center Haematology Haematology Moscow-Russia[2], Blokchins Cancer Research Center Haematology Oncology Moscow-Russia[3]

B-cell non-Hodgkin's lymphoma is typical manifestation of chronic extrahepatic hepatitis C. The incidence of HCV infection in patients with B-cell non-Hodgkin's lymphomas is approximately 15 %.

In our study included 93 patients with indolent lymphoma and hepatitis C markers (IL + C) and control group of 146 patients with indolent lymphomas without markers of hepatitis C (IL-C).

In 93 patients with IL + C 43 patients received antiviral therapy as the first treatment. 50 patients with IL + C received polychemotherapy therapy as first line of therapy.

Antiviral therapy(AVT) in patients with IL + C received complete remission(CR)-77 %, partial remission(PR) - 11 %, stabilization-4 %, 8 % progression.

On chemotherapy in patients with IL + C CR received in 64 %, PR-23 %, stabilization-9 %, 4 %-progression.

On chemotherapy in patients in control group with IL-C received CR in 53 %, PR-31 %, the stabilization-5 %, 11 %-progression.

The median relapse-free survival(RFS) in patients with IL + C on AVT was 36 months. The median RFS in patients with IL + C on chemotherapy was 19 months. The median RFS in patients with IL-C on chemotherapy was 33 months.

37 patients with relapse IL + C after chemotherapy was conducted AVT. CR was received in 81 % of patients, PR was achieved in 11 % and stabilization/progression + 8 % of patients. The median RFS in patients with IL + C recurrence after chemotherapy for AVT was 31 months.

The effectiveness of AVT was significantly higher than chemotherapy in patients with IL + C. Median disease-free for patients with IL + C significantly more on antiviral therapy. AVT should be the first line therapy in patients with the IL + C.

Topic 11: Hepatitis C

No: 1715

Increasing gap between high response and ineligible to IFN α in chronic hepatitis C patients

Huiying Rao[1], Hong Li[2], Hong Chen[3], Qing Xie[4], Jia Shang[5], Jun Li[6], Zhiliang Gao[7], Ruifeng Yang[1], Yinghui Gao[1], Lai Wei[1]

Peking University People's Hospital, Peking University Hepatology Institute Hepatology Beijing-China[1], Bristol-myers Squibb Gheor Wallingford-United States[2], The First Affiliated Hospital of Lanzhou University Hepatology Lanzhou-China[3], Shanghai Ruijin Hospital Hepatology Shanghai-China[4], Henan Provincial People's Hospital Hepatology Zhengzhou-China[5], Jiangsu Province Hospital Hepatology Nanjing-China[6], The Third Affiliated Hospital of Sun Yat-sen University Hepatology Guangzhou-China[7]

Aim: Given the high percentage of CC genotype among the Han ethnic population in China, IFN-based treatment should be ideal. However, many patients are ineligible for this standard of care therapy. Therefore, better understanding of this group of patients would be helpful to improve quality of care and efficiency in healthcare resource utilization.

Methods: Han ethnic Chinese HCV infection naïve subjects ($n = 997$) were enrolled from 28 hospitals in China (CCgenos study). The definition of this ineligibility includes seven criteria: older than 70 years old, cytopenia, cirrhosis, hypertension, diabetes, autoimmune diseases, and thyroid dysfunction. A total of 512 patients out of 997 patients were enrolled in follow-up cohort, including 264 patients were ineligible to IFN-α/RBV.

Results: In the CCgenos study, as high as 52.5 % (523/997) may be ineligible for IFN-α/RBV treatment, of which, 29 % of patients met one criterion and 23.5 % of patients met more than one criteria. The estimated ineligible population is significantly older, more female, and predominately carrying HCV virus genotype 1b. 5.4 % (54/997) decompensated cirrhotic patients were absolutely contraindicated to IFN-based treatments. Among 264 ineligible patients enrolled in the follow-up cohort, 138 (52.3 %) patients receiving antiviral treatment, and 84 patients (60.9 %) completed antiviral treatment. of which, 61 patients (72.6 %) got the sustained virologic response (SVR). Overall, SVR rate for these ineligible patients was 23.1 % (61/264) by IFN-α/RBV treatment.

Conclusions: Given the high proportion of patients ineligible to receive the current standard of care and low SVR rate by current treatment, there is certainly a need for more efficacious treatment options, such as DAA for HCV patients in China.

Topic 11: Hepatitis C

No: 1163

Epidemiological aspects of intrafamilial spread of HCV infection in Egyptian population a pilot study

Mahmoud El-bendary[1], Gamal Esmat[2], Mustafa Neamatallah[3], Emily Kamel[4], Tarek Besheer[1], Hatem Elalfy[1], Maged El-setouhy[5], Dalia Omran[2]

Mansoura Faculty of Medicine Tropical Medicine & Hepatology Mansoura-Egypt[1], Cairo Faculty of Medicine Tropical Medicine & Hepatology Cairo-Egypt[2], Mansoura Faculty of Medicine Medical Biochemistry Mansoura-Egypt[3], Mansoura Faculty of Medicine Public Health & Preventive Medicine Mansoura-Egypt[4], Ain Shams Faculty of Medicine Department of Community, Environmental and Occupational Medicine Cairo-Egypt[5]

Liver disease is a leading cause of morbidity and mortality among Egyptians infected with HCV, with about 140 000 newly reported cases annually. The objectives of this study were to determine the prevalence of anti-HCV antibodies among household contacts of HCV index cases and to identify the possible risk factors of transmission of HCV among Egyptian families.

Methods: The present external pilot study (double centre study) was performed on a convenient sample of 125 index cases and their 321 household family contacts where 2 questionnaires were used to collect data from the index & their related contacts. The all were exposed to clinical examinations & screening for the prevalence of Anti-HCV antibodies.

Results: The prevalence of anti-HCV seropositivity among household contacts of index cases was found to be 13.7 % which husbands of female index cases ranked first followed by wives of male index cases (36.36 % versus 17.86 % respectively, $P < 0.0001$) while sons & daughter followed later (6.84 % & 4.94 % respectively).

When the distribution of household contacts by risky behaviour towards index cases was investigated, it was found that significant prevalence of anti-HCV antibodies positivity was detected between household contacts reporting their index cases having haematemsis &/or bleeding wound ($P < 0.05$), and household contacts giving IV injection to their index cases ($P < 0.05$) &household contacts visiting the same dentist as the index cases ($P < 0.01$) when compared to household contacts not exposed to the same risk factors.

Conclusion: Transmission might occur during family contact and sexual behavior.

Topic 11: Hepatitis C

No: 1056

Safety tolerability efficacy and viral resistance of vaniprevir when concomitantly administered with peginterferon α 2b and ribavirin in Japanese patients with genotype 1 chronic hepatitis C infection who had failed previous interferon based treatment

Satoshi Mochida[1], Fumitaka Suzuki[2], Kazuaki Chayama[3], Yoshiyasu Karino[4], Keisuke Nakamura[5], Go Fujimoto[6], Anita Y.m. Howe[7], Steven W. Ludmerer[8], Niloufar Mobashery[9], Hiromitsu Kumada[2]

Saitama Medical University Department of Gastroenterology and Hepatology Saitama-Japan[1], Toranomon Hospital Department of Hepatology Tokyo-Japan[2], Hiroshima University Department of Gastroenterology and Metabolism Hiroshima-Japan[3], Sapporo-Kosei General Hospital Department of Gastroenterology Hokkaido-Japan[4], Msd K.k. Japan Development Clinical Research 1 Tokyo-Japan[5], Msd K.k. Japan Development Clinical Statistics Tokyo-Japan[6], Merck Sharp & Dohme Corp., Whitehouse Station Late Discovery Bacteriology Nj-United States[7], Merck Sharp & Dohme Corp., Whitehouse Station Biomarkers and Animal Models Nj-United States[8], Former Employee of Merck Sharp & Dohme Corp., Whitehouse Station Nj-United States[9]

Background: Vaniprevir (MK-7009) is a potent inhibitor of HCV NS3/4A protease. Two Phase 3 studies were conducted to evaluate the safety, tolerability, and efficacy of vaniprevir when administered concomitantly with peginterferon α-2b and ribavirin (PR) in Japanese patients with genotype 1 chronic hepatitis C (CHC) infection who had relapsed (Protocol [PN] 044) or were non-responders (PN045) to prior interferon (IFN)-based treatment.

Methods: In PN044, patients were randomized in a 1: 1 ratio to receive vaniprevir 300 mg twice daily for 12 weeks or 24 weeks, both with PR for 24 weeks. In PN045, patients received vaniprevir 300 mg twice daily with PR for 24 weeks. SVR24 was the primary efficacy endpoint. Safety was assessed using safety data up to 24 weeks after completion of all study therapy. Viral resistance was evaluated on baseline and post baseline samples.

Results: In PN044, SVR24 in the 12-week and 24-week arms were 92.0 % (23/25) and 96.2 % (25/26), respectively. In PN045, SVR24 among all prior non-responders was 61.9 % (26/42) and among just the prior null-responders was 55.2 % (16/29). Vaniprevir with PR was generally safe and well tolerated in these populations. The most common baseline RAVs were variants at Y56, Q80 and V170; however, these baseline variants did not appear to impact treatment outcome. Failure to study therapy was principally associated with the emergence of mutations at R155 or D168.

Conclusion: Vaniprevir demonstrated potent antiviral activity and was generally safe and well tolerated in Japanese patients with CHC genotype 1 who failed prior IFN-based treatment.

Topic 11: Hepatitis C

No: 2105

Efficacy safety and pharmacokinetics of 12 weeks of simeprevir in combination with tmc647055 and ritonavir with or without ribavirin in genotype 1 hepatitis C virus infected patients

S. Bourgeois[1], H. Van Vlierberghe[2], C. Moreno[3], H. Orlent[4], L. Vijgen[5], T.n Kakuda[6], E. Hoeben[7], T. Kirsilä[5], B. Jacquemyn[5], P. Van Remoortere[6], R. Verloes[7]

Zna Antwerp Department of Gastroenterology & Hepatology Antwerp-Belgium[1], Universitair Ziekenhuis Gent Department of Hepatology and Gastroenterology Ghent-Belgium[2], Cub Hôpital Erasme, Université Libre De Bruxelles Brussels-Belgium[3], Az Sint. Jan Av Department of Gastroenterology and Hepatology Bruges-Belgium[4], Janssen Infectious Diseases Bvba Beerse-Belgium[5], Janssen Pharmaceuticals Llc Titusville, Nj-United States[6], Janssen Research & Development Bvba Beerse-Belgium[7]

Aim: Simeprevir is an approved, once-daily (QD) hepatitis C virus (HCV) NS3/4 protease inhibitor. TMC647055 is a potent non-nucleoside HCV polymerase inhibitor. The Phase 2a, open-label TMC647055HPC2001 study assessed the combination of simeprevir + TMC647055 + ritonavir (RTV) ± ribavirin (RBV) in chronic genotype (GT)1 HCV-infected treatment-naïve and prior-relapse patients.

Methods: The study consists of 4 panels; results from Panels 1-3 are presented. Patients received 12 weeks of simeprevir 75 mg QD + TMC647055 450 mg QD + RTV 30 mg QD with (Panel 1 [n = 10; GT1a] and Panel 2-Arm 1 [n = 12; GT1b]) or without (Panel 2-Arm 2 [n = 9; GT1b]) RBV 1000–1200 mg/day. In Panel 3, patients received simeprevir 75 mg QD + TMC647055 600 mg QD + RTV 50 mg QD with (GT1a; n = 7) or without (GT1b; n = 8) RBV 1000–1200 mg/day. Patients with Week 4 HCV RNA matching the criterion for follow-up therapy initiation received 12/36 weeks of peginterferon-α + RBV and were considered failures in primary analysis. The primary endpoint was SVR12 (Table).
Results: The Table shows baseline demographic/disease characteristics. In Panels 1-2, 50 % of GT1a + RBV and GT1b + RBV patients achieved SVR12, vs 33 % of GT1b-RBV patients. In Panel 3, 86 % of GT1a + RBV and 50 % of GT1b-RBV patients achieved SVR12 (Table). No deaths, serious adverse events (AEs), Grade 4 AEs or AEs leading to treatment discontinuation occurred. Exposure to simeprevir, TMC647055 and RTV across groups is shown in the Table. A positive correlation between TMC647055 and simeprevir exposures was observed.
Conclusion: The simeprevir + TMC647055 + RTV ± RBV combination was well tolerated, with 50–86 % of GT1a/b-infected patients receiving RBV achieving SVR12.
Funded by Janssen.

Topic 11: Hepatitis C

No: 2220

Personalized therapy of chronic hepatitis C and B co infected patients with pegylated interferon plus ribavirin a randomized study

Ming-lun Yeh[1], Chung-feng Huang[1], Jee-fu Huang[1], Chia-yen Dai[1], Ming-lung Yu[1], Wan-long Chuang[1]

Kaohsiung Medical University Hospital Division of Hepatobiliary, Department of Internal Medicine Kaohsiung-Taiwan[1]

Background: The optimal treatment strategy for hepatitis B virus (HBV) and hepatitis C virus (HCV) dual-infections with active hepatitis C has not been fully elucidated. This randomized-controlled study was aimed at investigating the efficacy of a tailored regimen of PEGylated interferon (Peg-IFN) alpha plus ribavirin (RBV) according to rapid virological response and baseline viral loads in the treatment of patients with HBV and HCV dual-infections.
Materials and methods: This is an open label, randomized-controlled, comparative trial. HBV and HCV dual infected patients with negative hepatitis B e antigen (HBeAg) were included in this study. Eligible subjects were randomized into 2 groups, the fixed and tailored duration groups. The endpoint was HCV sustained virological response (SVR).
Results: Two hundred and three HBV/HCV dually infected patients, including 125 with genotype (GT) 1 HCV and 78 with GT 2/3 HCV infections, were enrolled. There was no significant difference of HCV SVR rates between the fixed and tailored duration groups in patients with GT 1 infections (69.4 % vs 63.5 %, $P = 0.571$) and GT 2/3 infections (90.0 % vs 81.6 %, $P = 0.342$). In patients infected with HCV GT 1, pretreatment low serum glucose levels (OR: 0.96, 95 % CI 0.943 – 0.986, $P = 0.002$) and rapid virological response (RVR) (OR: 5.15, 95 % CI 1.921–13.815, $P = 0.001$) were the independent factors associated with SVR. RVR was the only independent factor associated with SVR (OR: 12.27, 95 % CI 2.085–72.197, $P = 0.006$) in patients with HCV GT 2/3 infections.
Conclusion: A tailored regimen of Peg-IFN plus RBV according to baseline viral load and RVR is applicable in the treatment of HBeAg-negative HBV/HCV dual infections.

Topic 11: Hepatitis C

No: 1392

The main characteristics of chronic hepatitis C patients in Turkey*

Abdülkadir Dökmeci[1], Reşat Özaras[2], Mehmet Demir[3], Iftihar Köksal[4], Şebnem Gürsoy[5], Yusuf Önlen[6], Orhan Sezgin[7], Hatice Rahmet Güner[8], Hayat Kumbasar Karaosmanoğlu[9], Ulus Salih Akarca[10], Necati Örmeci[1], Fatih Özdener[11], Seda Erdoğan[11]

Ankara University School of Medicine Gastroenterology Ankara-Turkey[1], Istanbul University Cerrahpaşa School of Medicine Infectious Diseases Istanbul-Turkey[2], Mustafa Kemal University School of Medicine Gastroenterology Hatay-Turkey[3], Karadeniz Technical University School of Medicine Infectious Diseases Trabzon-Turkey[4], Erciyes University School of Medicine Gastroenterology Kayseri-Turkey[5], Mustafa Kemal University School of Medicine Infectious Diseases Hatay-Turkey[6], Mersin University School of Medicine Gastroenterology Mersin-Turkey[7], Yıldırım Beyazıt University Atatürk Training and Research Hospital Infectious Diseases Ankara-Turkey[8], Haseki Training and Research Hospital Indectios Diseases Istanbul-Turkey[9], Ege University School of Medicine Gastroenterology Izmir-Turkey[10], Roche Pharmaceuticals Clinical Trials Istanbul-Turkey[11]

Introductions and aim: Chronic Hepatitis C (CHC) is a global health problem. Several host and viral factors affect the natural course of the disease and predict the response to therapy. Turkey contributed a prospective international Gen-C study designed to evaluate relationships between IL28B genotypes and fibrosis stage in patients with CHC. The present is a sub-analysis of patients included in Gen-C in Turkey, aiming to determine the main characteristics of the patients with CHC.
Patients and methods: This study included treatment naïve and experienced patients. Co-infection with hepatitis B, decompensated cirrhotics, organ transplanted patients and those with renal failure were excluded.
Age, gender, HCV-RNA, viral genotype, ITPA genotype, IL28B genotype, liver histology were determined.
Results: Seventeen centers participated in Gen-C throughout Turkey. A total of 423 consecutive CHC patients were enrolled.
Conclusion: CHC patients in Turkey have unfavorable predictive factors for response as elderly, cirrhotic (nearly in 1/3), high viral load (more than a half), and non-CC IL28B genotype (more than ¾).
*This study was supported by F. Hoffmann-La Roche Ltd.

Topic 11: Hepatitis C

No: 1349

Gene silencing of host cell proteins as a potential anti viral system for the treatment of hepatitis C virus infection

Kanwal Baloch[1], Ameer Memon[1], Bikha Ram Devrajani[1]

Liaquat University of Medical and Health Sciences Medical Research Centre Jamshoro-Pakistan[1]

Aims: Hepatitis C virus (HCV) is responsible for chronic liver disease in approximately 3 % of world's population. A number of host cell proteins are shown to play a role in viral replication cycle and can be used as potential anti-HCV targets. Using well known gene silencing ability of small interfering RNAs (siRNAs), we aimed to assess role of these host cell proteins in modulating HCV replication.
Materials and methods: A GFP tagged JFH1 subgenomic replicon plasmid was used as a template for in vitro transcription of viral RNA. This viral RNA and siRNA against host genes VAPA, STAT3 and ACTN1 were co-transfected in Huh7.5 cell line by nucleofection. Levels of GFP (indicator of viral replication) were measured by flow cytometry. Western blot was done to validate host protein knock down.
Result: Gene specific siRNAs successfully reduced expression of cellular proteins. Median fluorescence intensity (MFI) was measured in the cells co-transfected with JFH1 and gene specific duplexes or the scrambled control. For VAPA and STAT3, there was significant reduction in the viral replication in the knock down group as compared to control (p value = 0.007 and 0.0004 respectively). No difference was seen in case of ACTN1 knock down (p value = 0.95).
Conclusion: Knocking down VAPA and STAT3 proteins individually lead to a significant reduction in viral replication, suggesting a positive role of these proteins in HCV replication cycle. These targets, when combined with current regimen, can be utilized as potential anti-HCV drug molecules to improve its therapeutic efficacy.

Topic 11: Hepatitis C

No: 1673

Prolonged thearpy of chronic hepatitic c genotype 3 decompensated cirrhosis with sofobuvir ribavirin therapy

Fan Li[1], Qing Shao[1], Bing Li[1], Dong Ji[1], Zhong-bin Li[1], Song-hai Chen[1], Chun-yan Wang[1], Xiao-xia Niu[1], Shi-ying Ding[1], Tao Yan[2], Vanessa Wu[3], Athena Chau[3], April Wong[3], Yu-dong Wang[3], Guo-feng Chen[1], George Kk Lau[3]

Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[1], 302 Hospital International Liver Diagnosis and Treatment Centre Beijing-China[2], Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[3]

Background and aims: Patients with chronic hepatitis C infection (CHC) with genotype 3 (GT3) and liver decompensation, represents the most-difficult-to-treat populations. Sofosbuvir, an NS5B nucleotide polymerase inhibitor was recently made available but the safety and efficacy of prolonged therapy in GT3 decompensated patients is unknown.
Methods: Five CHC GT3 Chinese treatment-experienced patients (M/F-5/0; mean age-44 ± 8 yrs old) and a plasma HCV RNA level of more than 10,000 IU per milliliter, were studied. Eligible patients had documentation of cirrhosis by means of ultrasound or FibroScan result (≥ 14.6 kPa within 6 months before screening or during screening), a Child–Pugh class B or C score at screening. All five GT3 patients were treated with sofosbuvir 400 mg daily plus ribavirin weight-based therapy for over 36 weeks.
Results: The cumulative rate of plasma HCV RNA rendered negative was 25 % by week 4, 50 % by week 8, 75 % by week 10 and 100 % by week 16. The loss of detectable HCV RNA was associated with improvement of liver function. There was no withdrawal from treatment due to adverse events.
Conclusions: Prolonged treatment (> 36 weeks) of sofosbuvir 400 mg daily with weight-based ribavirin therapy is effective in improving the liver function for CHC GT3 Child–Pugh class B or C cirrhosis, with no major adverse events.

Topic 11: Hepatitis C

No: 1594

Current status of IL28BSNP RS.8099917 distribution of HCV infected outpatients Japan

Tatsuo Kanda[1], Yuki Haga[1], Shingo Nakamoto[2], Reina Sasaki[1], Masato Nakamura[1], Xia Jiang[1], Shin Yasui[1], Makoto Arai[1], Fumio Imazeki[3], Osamu Yokosuka[1]

Chiba University, Graduate School of Medicine Department of Gastroenterology and Nephrology Chiba-Japan[1], Chiba University, Graduate School of Medicine Department of Molecular Virology Chiba-Japan[2], Chiba University Safety and Health Organization Chiba-Japan[3]

Background: IL28B genotype is a strong predictor of treatment-response in HCV-infected patients treated with interferon-including regimens. By the present approach, we examine the current status of IL28BSNP rs.8099917 distribution of outpatients infected with HCV.
Methods: Between February 2010 and April 2014, blood samples were obtained from 432 HCV-infected outpatients (mean age 59.9 years, male/female: 224/208, HCV genotypes 1/2/3/unknown: 314/102/1/15) in our hospital. IL28BSNP rs.8099917 was determined by TaqMan SNP genotyping assay using the ABI Step One real-time PCR system. Clinical backgrounds including the present status of HCV RNA positivity were also examined.
Results: In the total 432 patients, IL28BSNP rs.8099917 TT/TG/GG was 301/126/5, respectively, and 87.7 % were treated at least once with interferon-including regimen, resulting in 184/184/64 sustained virological response (SVR), non-SVR, and untreated/others, respectively. In 314 patients with HCV genotype 1, IL28BSNP rs.8099917 TT/TG/GG was 218/92/4, respectively, and 122/143/49 were SVR, non-SVR, and untreated/others, respectively. In 143 patients with HCV genotype 1 with non-SVR or untreated, TT/TG/GG was 85/56/2, respectively, and 15.4 % of these patients are now interferon-intolerant or ineligible. In 118 patients with HCV genotype non-1, IL28BSNP rs.8099917 TT/TG/GG was 83/34/1, respectively, and 62/41/14 were SVR, non-SVR, and untreated/others, respectively. In 41 patients with HCV genotype non-1 with non-SVR or untreated, TT/TG/GG was 27/13/1, respectively, and 24.4 % of these patients are now interferon-intolerant or ineligible.
Conclusion: In respect to the current status of IL28BSNP rs.8099917 distribution, we re-confirmed that it is important for the HCV-infected population in Japan to be treated with interferon-free regimens.

Topic 11: Hepatitis C

No: 1619

Cost effectiveness of one time screening for HCV in South Korea

Do Young Kim[1], Kwang-hyub Han[1], Byungyool Jun[2], Tae Hyun Kim[2], Sohee Park[2], Thomas Ward[3], Samantha Webster[3], Phil Mcewan[4]

Yonsei University College of Medicine Department of Internal Medicine Seoul-Republic of Korea[1], Yonsei University Graduate School of Public Health Seoul-Republic of Korea[2], Heor Ltd Wales-United Kingdom[3], Swansea University School of Human & Health Sciences Wales-United Kingdom[4]

Introduction: The hepatitis C virus (HCV) is one of the leading causes of liver disease and hepatocellular carcinoma (HCC) in South Korea. With an estimated population prevalence of 0.78 %, it represents a significant healthcare resource burden. The objective of this study was to investigate the cost-effectiveness of a one-time screening followed by treatment in South Korean population aged 40–70, compared to current practice (no national screening).
Methods: A published Markov model was used in conjunction with a screening and treatment decision tree. Three cohorts (stratified by age) were modelled: 40–49, 50–59 and 60–69 years. Based on a published seroepidemiology study, HCV prevalence in each cohort was estimated at 0.60, 0.80 and 1.53 %, respectively. It was estimated that 71.70 % of the population would be screened. After diagnosis, the treatment rate (with peginterferon-alfa + ribavirin) was assumed to be 42.8 % over 10 years. Treatment costs, disease state-specific transition rates and health utilities were obtained from published sources. Costs associated with screening were estimated based on national health insurance reimbursement cost and expert opinion.
Results: Compared to current practice, screening is estimated to be cost-effective in all cohorts, with ICERs of $5,239, $6,423 and $8,696, respectively. Incremental costs of $91,554,108, $85,380,418 and $94,410,245 associated with screening/treating identified patients were partially offset by reductions in complication (decompensated cirrhosis and HCC) costs: $68,869,483, $64,051,681 and $69,790,176, respectively.
Conclusion: This study indicates that one-time screening for HCV infection in South Korean population aged 40-70 is likely to be highly cost-effective compared to current practice.

Topic 11: Hepatitis C

No: 1517

Dual direct antiviral agents (DAAS) with sofosbuvir plus daclatasvir for chronic HCV treatment experienced genotype 1b—impact of viral kinetics on sustained virologic response

Dong Ji[1], Guo-feng Chen[1], Qing Shao[1], Fan Li[1], Bing Li[1], Zhong-bin Li[1], Song-hai Chen[1], Chun-yan Wang[1], Xiao-xia Niu[1], Shi-ying Ding[1], Tao Yan[2], Vanessa Wu[3], April Wong[3], Athena Chau[3], Yu-dong Wang[3], George Kk Lau[3]

Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[1], 302 Hospital International Liver Diagnosis and Treatment Centre Beijing-China[2], Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[3]

Background and aims: For those chronic hepatitis C patients, who are interferon-ineligible or intolerant, there is a burning need for the development of pan-oral interferon-free regimen. We examine the efficacy and safety of sofosbuvir, an NS5B nucleotide polymerase inhibitor and daclatasvir, an NS5A replication complex inhibitor in Chinese treatment-experienced cirrhosis patients with chronic GT1b infection.
Methods: Twenty-five GT1b treatment-experienced cirrhotic patients were treated with 12 weeks sofosbuvir 400 mg daily plus daclatasvir 60 mg daily. The primary efficacy end point was a sustained virologic response 12 weeks after the end of treatment (SVR12). At baseline, liver stiffness measurement (LSM) was used to assess liver fibrosis and the single nucleotide polymorphism of interferon-λ 3 (IL-28, rs12979860, C or T) and IFLN4 (ss469415590, TT or ΔG) were determined. Serial measurements of plasma HCV RNA levels were performed at baseline, Day 2,4 and 7, Week 2,4 and 12, Post-treatment week 12.
Results: Twenty-three (92 %) patients had SVR12 and there was no withdrawal from therapy due to adverse events. The cumulative rate of plasma HCV RNA undetectability, was 12, 36, 72, 88 and 92 % by Day2, Day4, Day7, Week2, Week4 and this was not affected by the SNPs variation of IL-28 and IFLN-4. These rates were superior to the historical control rate, with standard 48 weeks pegylated interferon-ribavirin therapy. The three most common adverse events were fatigue (n = 7, 30 %), headache (n = 6, 26 %), and nausea (n = 1, 4.3 %).
Conclusion: Interferon-free pan-oral therapy with twelve weeks sofosbuvir and daclatasvir are highly effective and safe in CHC GT1b treatment-experienced Chinese patients with liver cirrhosis.

Topic 11: Hepatitis C

No: 1059

Correlation between serum hyaluronic acid and fibrosis steatosis non alcoholic steatohepatitis and necroinflammation in chronic HCV infection

Hasan Ali[1], Ali Ghweil[1], Ghada Osman[2], Mohamed Helal[3], Hamdy Moustafa[4]

Lecturer Tropical Medicine and Gastroenterology Qena-Egypt[1], Lecturer Pathology Qena-Egypt[2], Ass. Lecturer Tropical Medicine and Gastroenterology Qena-Egypt[3], Professor Tropical Medicine and Gastroenterology Assiut-Egypt[4]

Background: Hyaluronic acid (HA) is an attractive alternative marker for noninvasive diagnosis of liver fibrosis instead of liver biopsy for both patients and physicians. We aimed to assess the role of HA not only for diagnosis of liver fibrosis but also for diagnosing the progression of steatosis, steatohepatitis (SH) and necroinflammation (NI) in Chronic HCV patients. Patients and methods: 90 patients with chronic HCV infection; 77 (85.6 %) males and 13 (14.4 %) females, were included. Blood samples were collected for routine laboratory investigations, liver function tests and serum HA measurement. Liver biopsy was taken for histopathological examination.
Results: Steatosis was found in 51 patients (56.7 %), fibrosis in 61 patients (67.8 %) and NI in 81 patients (90 %). Mean serum HA was 66.4 ± 48.2 ng/L. HA was significantly higher in patients with fibrosis (81.6 ± 52.1 vs 34.5 ± 3.5), SH (141.7 ± 52 vs 44.9 ± 12) and NI (70.4 ± 49.2 vs 30.7 ± 2.8) than those without (P value = 0.01, 0.001 and 0.01 respectively). HA was significantly higher in patients with advanced fibrosis, SH and NI than those with mild degrees (P value = 0.000, 0.001 and 0.001 respectively). Positive correlations were found between serum HA and the degree of fibrosis, SH and NI (P value = 0.000) and r = + 0.758, 0.774 and 0.811 respectively). Mean HA Cut off value for diagnosis of fibrosis, SH and NI was 50, 70 and 45 ng/L respectively with significant Sensitivity, Specificity, PPV, NPV and Accuracy.
Conclusion: Serum HA is a good noninvasive marker for the diagnosis of fibrosis, SH and NI in patients with chronic HCV infection.

Topic 11: Hepatitis C

No: 1204

All oral fixed dose combination therapy with daclatasvir asunaprevir beclabuvir for patients with chronic HCV genotype 1 infection without cirrhosis unity 1 phase 3 results

Frederick Poordad[1], William Sievert[2], Lindsay Mollison[3], Norbert Bräu[4], James Levin[5], Thomas Sepe[6], Samuel Lee[7], Nathalie Boyer[8], Jean-pierre Bronowicki[9], Ira Jacobson[10], Navdeep Boparai[11], Eric Hughes[11], Scott Swenson[12], Philip Yin[12]

University of Texas Health Science Center, Texas Liver Institute San Antonio-United States[1], Monash Health and Monash University, Melbourne-Australia[2], Fremantle Hospital, Hepatitis Services Fremantle-Australia[3], James J Peters Veterans Affairs Medical Center New York-United States[4], Dean Foundation, Madison-United States[5], University Gastroenterology, Providence-United States[6], University of Calgary, Calgary-United States[7], Hôpital Beaujon, Service D Cichy-France[8], Université De Lorraine, Centre Hospitalier Universitaire De Nancy Vandoeuvre Les Nancy-France[9], Weill Cornell Medical College, New York-United States[10] Bristol-myers Squibb, Princeton, Princeton-United States[11] Bristol-myers Squibb, Wallingford-United States[12]

Introduction: The all-oral combination of daclatasvir (DCV; pangenotypic NS5A inhibitor), asunaprevir (ASV; NS3 protease inhibitor), and beclabuvir (BCV; BMS-791325; non-nucleoside NS5B inhibitor)—DCV-TRIO regimen—was evaluated without ribavirin in HCV genotype (GT) 1-infected treatment-naive and -experienced patients without cirrhosis in a Phase 3, open-label, international clinical trial.
Methods: Patients received a fixed-dose combination (FDC) of DCV 30 mg, ASV 200 mg, and BCV 75 mg twice daily for 12 weeks. SVR12 rates in the treatment-naive and -experienced cohorts were evaluated separately as key efficacy outcomes.
Results: SVR12 was achieved by 92 % of treatment-naive patients (Table). Among treatment-experienced patients, 89 % achieved SVR12. Virologic failure occurred in 34 (8 %) patients overall. Baseline characteristics were comparable between the treatment-naive (N = 312) and treatment-experienced (N = 103) cohorts. Overall, patients were 58 % male and 26 % < I>IL28B </I > (rs1297860) CC genotype; 73 % were infected with GT 1a and 27 % with GT 1b. One death reported posttreatment was considered not related to study treatment. There were 7 serious adverse events, all considered unrelated to study treatment, and 3 (< 1 %) adverse events leading to treatment discontinuation. The most common adverse events (in > 10 % of patients) were headache, fatigue, diarrhea, and nausea.
Conclusions: In this Phase 3 study of 415 patients, 12 weeks of all-oral treatment with DCV/ASV/BCV FDC achieved high SVR12 rates in patients with chronic HCV GT 1 infection and was well tolerated. These findings demonstrate the potent antiviral activity, safety, and tolerability of the DCV-TRIO regimen in treatment-naive and treatment-experienced patients without cirrhosis.

Topic 11: Hepatitis C

No: 1405

SNPS in the PNPLA3 and IL28B genes are associated with elevated serum alt levels among HCV gt3 infected patients in India

Nirupma Trehanpati[1], Abhijit Chowdhury[2], Samir R. Shah[3], Padaki Nagaraja Rao[4], Xin Guo[5], Dongliang Ge[5], Steven J. Knox[5], Anuj Gaggar[5], G. Mani Subramanian[5], John G. Mchutchison[5], Shyam Kottilil[6], Shiv K. Sarin[7]

Institute of Liver and Biliary Sciences Clinical & Cellular Transplant Immunology and Research New Delhi-India[1], Institute of Post Graduate Medical Education and Research Kolkata-India[2], Global Hospitals Mumbai-India[3], Asian Institute of Gastroenterology Hyderabad-India[4], Gilead Sciences, Inc. Foster City-United States[5], Niaid Bethesda-United States[6], Institute of Liver and Biliary Sciences New Delhi-India[7]

Background: Infection with the hepatitis C virus (HCV) represents a significant public health burden in India. The objective of this observational study was to characterize viral and host genetic factors associated with disease characteristics.
Methods: Patients with chronic HCV infection (n = 500) not currently receiving antiviral therapy were enrolled across 20 sites representing all regions in India. During a single clinic visit, clinical examination was performed and blood was collected for hematology, chemistry, virology (HCV genotype, HCV RNA). Host genotyping was determined using TaqMan® SNP Genotyping Assays (ABI) for the following innate immune genes of clinical relevance: IL28B, IFNL4, TLR7, NOD2, RIG-I and PNPLA3.
Results: The most prevalent HCV genotype was GT3 (54.4 %), followed by GT1 (25 %) and GT4 (6 %). The overall frequency of the host IL28B-CC (IFN-responsive) genotype was 65.4 %, and of the PNPLA3-CG/GG (risk alleles for NAFLD) was 46.3 %; the frequencies of these SNPs were similar across patients with different HCV GTs. Among HCV GT-3 patients only (Figure), a greater proportion of patients with the PNPLA3-CG/GG allele had serum ALT > ULN than those with the CC-allele (79 % vs 61 %; $P = 0.002$). This association was strengthened in patients with IL28B-CC. This was not observed in other HCV genotypes. No other associations of SNPs with disease characteristics were observed.
Conclusions: The favorable IL28B-CC genotype was more common in Indian than in Caucasian or black patients. The association of the PNPLA3-CG/GG and IL28B-CC genotype in HCV GT-3 with higher ALT levels may constitute a novel finding warranting further biological exploration.

Topic 11: Hepatitis C

No: 2090

The effectiveness of therapy in patients with extrahepatic manifestations of chronic hepatitis C hepatitis C indolent lymphoma associated (Il + C)

Segey Lepkov[1], Irina Subortseva[2], Svetlana Kosura[1], Oleg Kolomeitsev[3], Uylia Ryabykhina[3]

Russian National Research Medical University Named After Ni Pirogov Therapy Moscow-Russia[1], National Haematology Research Center Haematology Haematology Moscow-Russia[2], Blokchins Cancer Research Center Haematology Oncology Moscow-Russia[3]

The effectiveness of therapy in patients with extrahepatic manifestations of chronic hepatitis C - Hepatitis C indolent lymphoma associated (IL + C).

Topic 11: Hepatitis C

No: 1506

Sofosbuvir in combination with ribavirin for 12 weeks achieves 97 % SVR12 in Japanese patients with chronic genotype 2 hepatitis C infection

Masao Omata[1], Shuhei Nishiguchi[2], Yoshiyuki Ueno[3], Hitoshi Mochizuki[1], Namiki Izumi[4], Fusao Ikeda[5], Hidenori Toyoda[6], Osamu Yokosuka[7], Kazushige Nirei[8], Takuya Genda[9], Takeji Umemura[10], Tetsuo Takehara[11], Naoya Sakamoto[12], Yoichi Nishigaki[13], Kunio Nakane[14], Nobuo Toda[15], Tatsuya Ide[16], Mikio Yanase[17], Keisuke Hino[18], Juan Betular[19], Bing Gao[20], Hongmei Mo[21], Akinobu Ishizaki[19], Masa Omote[22], Diana Brainard[22], Steven Knox[22], William Symonds[22], John Mchutchison[22], Hiroshi Yatsuhashi[23], Masashi Mizokami[24]

Yamanashi Prefectural Hospital Organization Department of Gastrointestinal Medicine Kofu-Japan[1], Hyogo College of Medicine Department of Liver, Gallbladder and Pancreas Internal Medicine Nishinomiya-Japan[2], Yamagata University Department of Gastroenterology Yamagata-Japan[3], Musashino Red Cross Hospital Department of Gastrointestinal Medicine Musashino-Japan[4], Okayama University Department of Molecular Hepatology Okayama-Japan[5], Ogaki Municipal Hospital Department of Gastroenterology Ogaki-Japan[6], Chiba University Department of Gastroenterology and Nephrology Chiba-Japan[7], Nihon University Department of Gastroenterology Tokyo-Japan[8], Juntendo University Department of Gastroenterology Izunokukni-Japan[9], Shinshu University Gastroenterology, Department of Medicine Matsumoto-Japan[10] Osaka University Department of Gastrointestinal Internal Medicine Suita-Japan[11] Hokkaido University Department of Gastroenterology and Hepatology Sapporo-Japan[12] Gifu Municipal Hospital Department of Gastroenterology Gifu-Japan[13] Akita City Hospital Department of Gastroenterology Akita-Japan[14] Mitsui Memorial Hospital Department of Gastroenterology Tokyo-Japan[15] Kurume University Department of Gastrointestinal Medicine Kurume-Japan[16] National Center For Global Health and Medicine Department of Gastroenterology Tokyo-Japan[17] Kawasaki Medical School Department of Hepatology and Pancreatology Kurashiki-Japan[18] Gilead Sciences Clinical Operations Foster City-United States[19] Gilead Sciences Biostatistics Foster City-United States[20] Gilead Sciences Clinical Virology Foster City-[21] Gilead Sciences Clinical Research Tokyo-Japan[22] National Hospital Organization Nagasaki Medical Center Department of Hepatology Omura-Japan[23] National Center For Global Health and Medicine The Research Center For Hepatitis and Immunology Ichikawa-Japan[24]

Aim: This open-label, single-arm Phase 3 study evaluated the efficacy and safety of sofosbuvir (SOF) 400 mg administered orally, once daily with weight-based ribavirin (RBV; 600-1000 mg/day) in Japanese patients with chronic genotype (GT) 2 hepatitis C virus (HCV) infection.

Methods: Treatment-naïve and treatment-experienced Japanese adults with chronic GT-2 HCV infection received SOF + RBV for 12 weeks. Up to 40 % could have had cirrhosis; platelet count $\geq$ 50,000/μL at entry. The primary efficacy endpoint was Sustained Virologic Response measured 12 weeks after the last dose of study drug (SVR12).

Results: 153 Japanese patients were enrolled (90 treatment-naïve and 63 treatment-experienced). Mean age was 57 years (range 25-74), 54 % (83/153) female, 79 % (121/153) IL28B-CC, 11.1 % (17/153) had cirrhosis. All patients achieved undetectable HCV RNA by Week 4 and completed the full 12 weeks of treatment. SVR12 was 96.7 % (148/153); there were no virologic breakthroughs but 5 patients relapsed. SVR12 was 98 % and 95 % in treatment-naïve and treatment-experienced patients, respectively.

Adverse events were generally mild, and laboratory abnormalities were infrequent and consistent with the safety profile of RBV. No AEs led to treatment discontinuation.

Conclusions: Treatment-naïve and treatment-experienced Japanese patients with chronic GT-2 HCV infection, including those with compensated cirrhosis, achieved high rates of SVR12 with 12 weeks of an IFN-free, all-oral regimen of SOF + RBV. The regimen was safe and well-tolerated with no treatment discontinuations and an AE profile consistent with that observed with RBV. The data suggest that SOF + RBV may offer an improved, IFN-free treatment for Japanese patients with chronic GT-2 HCV infection.

Topic 11: Hepatitis C

No: 1078

Prolonged expression of interferon stimulated genes is maintained by unphosphorylated interferon stimulated gene factor 3 during hepatitis C virus infection

Pil Soo Sung[1], Hyeonjoo Cheon[2], Do Youn Park[3], Seung Kew Yoon[4], George R. Stark[2], Eui-cheol Shin[1]

Kaist Graduate School of Medical Science and Engineering Daejeon-Korea, South[1], Cleveland Clinic Department of Molecular Genetics Cleveland-United States[2], Pusan National University Department of Pathology Busan-Korea, South[3], The Catholic University of Korea Department of Internal Medicine Seoul-Korea, South[4]

Background: Upregulation of interferon-stimulated genes (ISGs) is sustained in the liver during hepatitis C virus (HCV) infection, and is known to be associated with spontaneous clearance and treatment response in HCV infection. While ISGs induction is known to be mediated by ISGF3 composed of IRF-9, tyrosine-phosphorylated STAT1 (PY-STAT1) and PY-STAT2, it was recently demonstrated that the unphosphorylated ISGF3 (U-ISGF3) induces prolonged expression of ISGs after type I IFN stimulation. In the present study, we examined a significance of U-ISGF3 in ISGs induction during HCV infection.

Methods: Expression of IRF9, STAT1, PY-STAT1, STAT2, and ISGs was studied in non-viral liver tissues and chronically HCV-infected liver tissues. Primary human hepatocytes and Huh-7-TLR3 cells were infected by cell culture-produced HCV (JFH-1; genotype 2a). IRF9, STAT1, and STAT2 were overexpressed by lentiviral transduction, or their expression was silenced with siRNAs.

Results: In HCV-infected cells and liver tissues of HCV-infected patients, the expression of IRF9, STAT1, and STAT2 was elevated without tyrosine-phosphorylated STAT1, and U-ISGF3-downstream ISGs were upregulated. Moreover, the U-ISGF3 components were detected in the nucleus of HCV-infected cells. Induction of U-ISGF3 by forced expression of IRF9, STAT2, and phosphorylation-defective STAT1 was sufficient to upregulate ISGs. Finally, we found that U-ISGF3 induction depended on IFN-lambdas and -beta produced by HCV-infected cells.

Conclusions: In HCV-infected cells, endogenously produced IFNs induce ISGs expression via U-ISGF3 without STAT1 phosphorylation. Our data demonstrate that U-ISGF3 induced by endogenous IFNs drove prolonged expression of a set of ISGs, leading to chronic activation of innate responses in HCV infection.

Topic 11: Hepatitis C

No: 1325

Boceprevir or telaprevir plus peginterferon ribavirin in HCV chronic infection the real life experience of the Italian association of hospital hepatologists (CLEO)

Antonio Ascione[1], Cleo Group[2]

Centre For Liver Disease, Fatebenefratelli Hospital, Napoli-Italy[1], Club Epatologi Ospedalieri, Roma-Italy[2]

Aim: Boceprevir/Telaprevir (DAAs), approved for reimbursement in Italy in December 2012, were used from January 2013. Since then the group of the Association of Hospital Hepatologists (CLEO Group) has been deeply involved in using DAAs. In September 2013 the Association decided to collect the data coming from all Centres in order to check safety and efficacy of this type of treatment in the real-world setting. For this reason, this study can be qualified as retrospective/prospective.
Methods: A database was prepared and used by all Centres for the data collection and updated continuously. Last update: November 3rd, 2014. HCV RNA testing: COBAS TaqMan 2.0 (Roche) with LLQ 25 IU/mL. All patients consecutively treated were included.
Results: 37 Centres enrolled 670 patients: male 64 %; median age 58 (range 18-78), of whom 20 % over 65y; mean BMI 25.6 (range 16-37); Genotype 1b (79 %); diagnosis of cirrhosis (37 %), fibrosis F3/4 (70 %). DAAs used: Telaprevir (67 %); PEGIFN-2a (70 %); patients naïve (28 %), relapsers (32 %), non-responders (40 %). Therapy was stopped in 14 % because of side-effects (anaemia 37 % and rash 26 %) or for virological failure (16 %). RVR was achieved in 68 % of cases, while EOT in 64 %. There were no fatalities. Since the study is on-going, we have 403 patients with complete follow-up (SVR = 50 %).
Conclusion: DAAs, in the everyday practice, are safe but with moderate efficacy. These data confirms the limited effectiveness of DAAs in certain groups of patients such as those widely represented in our series: advanced fibrosis, non responder to PEGIFN/RIBA and over 65y.

Topic 11: Hepatitis C

No: 1511

Simeprevir exposure in Asian treatment naïve patients with chronic hepatitis C virus genotype 1 infection results from a population pharmacokinetic model in the phase III tiger study

E. Hoeben[1], A. Viberg[2], K. Petersson[2], M. Lee[3], I. Vanwelkenhuysen[3], J. Witek[3], M. Peeters[4], S. Ouwerkerk-mahadevan[3], A. Brochot[3]

Janssen Research & Development Llc Pharmacological Modeling, Model Based Drug Development Beerse-Belgium[1], Qpharmetra Llc Huddinge-Sweden[2], Janssen Research & Development Llc Titusville-United States[3], Janssen Infectious Diseases Bvba Beerse-Belgium[4]

Aim: TIGER (TMC435HPC3005) is a Phase III, randomised study evaluating simeprevir + peginterferon-α-2a/ribavirin (PR) in treatment-naïve genotype-1 hepatitis C virus (HCV) infected Chinese and Korean patients. Week-60 interim population pharmacokinetic (popPK) model-derived exposure data of simeprevir are reported.
Methods: Patients (n = 457) received simeprevir (150 mg [n = 152] or 100 mg [n = 153] QD), or placebo (n = 152) + PR for 12 weeks. Simeprevir patients received PR alone for an additional 12 or 36 weeks based on response-guided treatment criteria; patients receiving placebo had 36 additional weeks of PR. An integrated popPK model, including data from Japanese and Global patients and healthy volunteers had previously been developed to predict simeprevir plasma concentration time profiles. The model, in combination with plasma concentration data from the study, was used to predict exposure (area under the curve [AUC24 h] and trough plasma concentration [C0 h]) in each simeprevir-treated patient.
Results: Geometric mean exposure (AUC24 h) was 2.6-fold higher with simeprevir 150 mg than 100 mg (overall population). Drug exposure was similar with 100 mg and 2.4-fold higher with 150 mg versus that observed in non-Asians from global Phase III simeprevir 150 mg studies. Considering the variability in simeprevir exposures, drug exposures with both simeprevir doses seem to be similar in Chinese and Korean patients (Table). A post hoc exposure–response model projected ~ 2.5 % increase in rash incidence with simeprevir 150 mg vs 100 mg in this population.
Conclusion: This popPK model adequately predicted individual simeprevir exposure in Chinese and Korean patients. There appear to be no differences in exposure between patients from China and Korea.
Funded by Janssen.

Topic 11: Hepatitis C

No: 1271

All oral dual combination of daclatasvir plus asunaprevir compared with telaprevir plus peginterferon alfa ribavirin in treatment naive Japanese patients chronically infected with HCV genotype 1b results from a phase 3 study

Y. Karino[1], F. Suzuki[2], Y. Suzuki[2], J. Toyota[3], K Chayama[3], Y. Kawakami[4], S. Fujiyama[5], T. Ito[6], Y. Itoh[7], E. Tamura[8], T. Ueki[8], H. Ishikawa[8], M. Linaberry[9], E. Hughes[9], H. Kumada[2]

Sapporo-Kosei General Hospital Department of Gastroenterology and Metabolism Sapporo-Japan[1], Toranomon Hospital, Tokyo-Japan[2], Sapporo-Kosei General Hospital, Sapporo-Japan[3], Hiroshima University, Department of Gastroenterology and Metabolism Hiroshima-Japan[4], Kumamoto Shinto General Hospital, Kumamoto-Japan[5], Showa University Koto Toyosu Hospital, Tokyo-Japan[6], Kyoto Prefectural University of Medicine, Molecular Gastroenterology and Hepatology Kyoto-Japan[7], Bristol-myers Kk, Toyko-Japan[8], Bristol Myers Squibb Research and Development, Princeton-United States[9]

Aim: This Japanese, phase 3 study (AI447-031) was the first head-to-head comparison of the safety and efficacy of an all-oral regimen (daclatasvir + asunaprevir [DCV + ASV]) vs telaprevir plus peginterferon alfa-2b/ribavirin (TVR + P/R) for HCV genotype (GT-)1b infection.
Methods: Treatment-naive patients were randomized to receive DCV 60 mg QD plus ASV 100 mg BID (N = 119) for 24 weeks or TVR 750 mg TID plus P/R for 12 weeks then P/R for 12 weeks (N = 111). Prior relapsers on P/R treatment (N = 22) received 24 weeks of DCV + ASV. The primary endpoint was sustained virologic response at posttreatment Week 12 (SVR12).
Results: Treatment-naïve baseline characteristics were comparable between treatment arms (median age: ~ 57 yrs; IL28B-CC ~ 67 %; mean HCV RNA ~ 6.8 log10 IU/mL). Relapsers had mean HCV RNA 7.0 log10 IU/mL, median age 65 yrs and IL28B-CC 73 %. In treatment-naïve patients, the SVR12 primary endpoint was higher for

DCV + ASV than TVR + P/R (see Table; treatment difference 26 % [95 % CI: 16,36]). SVR12 in relapsers treated with DCV + ASV was high (21/22; 96 %). Serious on-treatment adverse events occurred in 4 % (DCV + ASV) and 5 % (TVR + P/R) of treatment-naive patients. Discontinuations for adverse events occurred in 5 % on DCV + ASV and 62 % (any drug; 20 % all drugs) on TVR + P/R. No deaths occurred. DCV + ASV was superior to TVR + P/R for anemia (0 % vs 48 %) and rash-related events (0 % vs 14 %). Grade 3/4 ALT increases were more frequent with DCV + ASV (13 %) than TVR + P/R (3 %). DCV + ASV safety in relapsers was comparable to treatment-naive patients.
Conclusion: DCV + ASV achieved a higher SVR12 rate than TVR + P/R in treatment-naïve GT-1b-infected Japanese patients. DCV + ASV was well tolerated.

Topic 11: Hepatitis C

No: 1487

Dapsang twelve weeks of treatment with ritonavir boosted danoprevir (HCV protease inhibitor) fixed dose combination plus peginterferon alfa 2a ribavirin produces 94 % svr12 in HCV genotype 1 infected non cirrhotic patients of Taiwanese origin

J-h. Kao[1], S-y. Tung[2], Y. Lee[3], S. Thongsawat[4], T. Tanwandee[5], I-s. Sheen[6], H. Li[7], J. Zhou[7], J. A. Thommes[8], G. Hill[9]

National Taiwan University Hospital, Hepatitis Research Center, Taipei-Taiwan[1], Chang Gung Memorial Hospital, Department of Gastroenterology, Chia Yi-Taiwan[2], Pusan Paik Hospital, Inje University, Pusan-Korea[3], Chiang Mai University, Faculty of Medicine, Chiang Mai-Thailand[4], Siriraj Hospital, Department of Medicine, Bangkok-Thailand[5], Chang Gung Memorial Hospital, Department of Hepato-gastroenterology, Linkou-Taiwan[6], Roche, Product Development, Shanghai-China[7], Genentech, South San Francisco-United States[8], Roche, Product Development Shanghai-China[9]

Aim: Evaluate the safety and antiviral activity of ritonavir-boosted danoprevir (DNVr) fixed-dose combination (FDC) plus PegIFN-2a/RBV in treatment-naive Asian CHC patients with HCV G1 infection.
Methods: Phase II open-label study in treatment-naive G1 patients in Taiwan, Thailand and South Korea with serum HCV RNA level ≥ 10[SUP]5[/SUP] IU/mL. Patients received DNVr/FDC 125/100 mg BID plus standard doses of PegIFN-2a/RBV for either 12 weeks in non-cirrhotic patients (Arm A) or 24 weeks in cirrhotic patients (Arm B). The primary endpoint was SVR12.
Results: No patients withdrew for safety reasons. Three cirrhotic patients (Arm B) experienced serious AEs, none of which was considered to be related to DNVr. No grade 3/4 ALT elevation was reported. Overall SVR12 rates were 88 % (30/34) and 89 % (24/27) in Arms A and B, respectively (Table). Among HCV G1b-infected patients with a CC genotype, the SVR12 rate was 95 % (n = 20/21) in both Arms A and B. Relapse occurred only in G1a-infected patients (4/7). 26/28 Taiwanese patients achieved SVR12 including 16/17 (94 %) non-cirrhotic patients.
Conclusion: DNVr plus PegIFN-2a/RBV is safe and effective in HCV G1 Asian patients with and without cirrhosis. There was no clinically significant increase in exposure to DNV in Asian as compared to historical Caucasian patients. The safety profile of DNVr plus PegIFN-2a/RBV was comparable to that observed with PegIFN-2a/RBV. Given the high SVR12 rate observed in non-cirrhotic Taiwanese patients (94 %) after 12 weeks' treatment, further study in mainland China is warranted, where the majority of HCV patients are G1b-infected and [I]IL28B[/I] CC predominates.

Funded by Roche.

Topic 11: Hepatitis C

No: 1977

Korean patients with genotype 1 and 2 HCV infection achieved over 97 % sustained virologic response following 12 weeks of ledipasvir sofosbuvir or sofosbuvir plus ribavirin

Sang Hoon Ahn[1], Sook-hyang Jeong[2], Seung-woon Paik[3], Jenny C. Yang[4], Hongmei Mo[4], Bing Gao[4], Steven J. Knox[4], Diana M. Brainard[4], Philip S. Pang[4], John G. Mchutchison[4], Young-suk Lim[5], Kwang-hyub Han[6]

Yonsei University College of Medicine Department of Internal Medicine Seoul-Korea, South[1], Seoul National University Bundang Hospital, Seoul National University College of Medicine Seongnam-Korea, South[2], Samsung Medical Center, Sungkyunkwan University School of Medicine Seoul-Korea, South[3], Gilead Sciences, Inc. Foster City-United States[4], Asan Medical Center, University of Ulsan College of Medicine Seoul-Korea, South[5], Yonsei University College of Medicine Seoul-Korea, South[6]

Background and aims: In Korea, chronic hepatitis C virus (HCV) infection is accounted for by genotype (GT) 1 and GT2 in similar proportions. A growing number of patients have failed interferon (IFN)-based therapy, or may be ineligible/intolerant of current treatment options. Highly effective, safe and well-tolerated IFN-free therapies are needed to address the burden of HCV-related liver disease in Korea.
Methods: Two Phase 3 studies enrolled treatment-naïve and –experienced patients with GT1- and GT2-infection in Korea. GT1 patients received ledipasvir/sofosbuvir (LDV/SOF) 90 mg/400 mg QD and GT2 patients received SOF 400 mg QD + ribavirin (RBV 1000 mg-1200 mg) for 12 weeks. There was no upper age limit, we included patients with cirrhosis, no entry restriction applied for neutrophils and the platelet requirement was ≥ 50,000/μL. The primary efficacy endpoint was SVR12.
Results: Table 1 presents summary results. Overall SVR12 was 99 % (92/93) in GT1 and 97 % (125/129) in GT2. Three patients were virologic failures and 2 were lost-to-follow-up. Treatment-emergent HCV NS5A or NS5B resistance was not observed in any patient; the 1 GT1 patient that relapsed had Y93H, NS5A resistance, detected at baseline and at relapse. Eight patients (4 %) experienced serious adverse events (AE) all unrelated to study drug. In SOF + RBV recipients, 17 (13 %) patients had post-baseline hemoglobin (Hgb) < 10 g/dL; 3 patients (2 %) had Hgb < 8.5 g/dL; 9 (7 %) patients required RBV dose interruption or modification due to anemia.
Conclusions: 12-weeks of LDV/SOF in GT1 and SOF + RBV in GT2-infected Korean patients was well tolerated and achieved SVR12 rates ≥ 97 %, including those who were elderly, treatment-experienced and with compensated cirrhosis.

Topic 11: Hepatitis C

No: 1807

High treatment success rate with pegylated interferon in Iranian patients with chronic hepatitis C and its relation to interferon lambda polymorphisms

Maryam Keshvari[1], Arghavan Haj-sheykholeslami[2], Khalil Hemmati[2], Fatemeh Mohammadzadehparjikolaei[2], Ali Pouryasin[3], Heidar Sharafi[4]

High Institute For Research and Education In Transfusion Medicine Blood Transfusion Research Center Tehran-Iran[1], Digestive Disease Research Institute, Tehran University of Medical Sciences Digestive Oncology Research Center Tehran-Iran[2], Islamic Azad University-arsanjan Branch Department of Genetics Arsanjan-Iran[3], Middle East Liver Disease (meld) Center Department of Molecular Hepatology Tehran-Iran[4]

Background: Interferon lambda (IFNL) polymorphisms may influence the treatment success with pegylated interferon in patients with chronic hepatitis C virus (HCV) infection. In this study we evaluated the rate of sustained virologic response (SVR) in Iranian patients and its relation to IFNL polymorphisms.
Methods: In 2011, all consenting adult treatment-naïve patients referred to Tehran Blood Transfusion Hepatitis Clinic were enrolled to the study. Patients were treated with Pegaferon[SUP]®[/SUP] (PegIFN alpha-2a by Pooyesh Darou) and Ribabiovir[SUP]® [/SUP](Ribavirin by Bakhtar Bioshimi) for 24 or 48 weeks depending on HCV genotype and weight.
Results: A hundred and fifty two patients (92.8 % male, mean age: 41.9 ± 10 Yrs., 61.2 % HCV genotype 1, 36.8 % HCV gentype 3, and 2 % mixed genotypes) underwent treatment. SVR was achieved in 85.5 % with no difference between the viral genotypes. Treatment success in rs12979860 CC subjects was 91.2 % compared to 82.1 % in non-CCs and 89.7 % in rs8099917 TT vs. 86.7 % in non-TT subjects. In regression analysis rs12979860 CC was the only variable with significant association with SVR achievement (odd's ratio: 6.23 & CI95 %: 1.2-31.9).
Conclusion: SVR achievement rate was high in our Iranian treatment naïve patients. Although rs12979860 CC showed a strong relationship with treatment success but 82.1 % of the non-CC ones also reached SVR.

Topic 11: Hepatitis C

No: 1742

High treatment success rate with pegylated interferon in Iranian patients with chronic hepatitis C and its relation to interferon lambda polymorphisms

Maryam Keshvari[1], Arghavan Haj-sheykholeslami[2], Khalil Hemmati[2], Fatemeh Mohammadzadehparjikolaei[2], Heidar Sharafi[3]

High Institute For Research and Education In Transfusion Medicine Blood Transfusion Research Center Tehran-Iran[1], Digestive Disease Research Institute, Tehran University of Medical Sciences Digestive Oncology Research Center Tehran-Iran[2], Middle East Liver Disease (meld) Center Department of Molecular Hepatology Tehran-Iran[3]

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Conclusion: SVR achievement rate was high in our Iranian treatment naïve patients. Although rs12979860 CC showed a strong relationship with treatment success but 82.1 % of the non-CC ones also reached SVR.

Topic 11: Hepatitis C

No: 1980

Over 98 % sustained virologic response in Taiwanese patients with genotype 1 and 2 infection treated with ledipasvir sofosbuvir or sofosbuvir plus ribavirin for 12 weeks

Wan-long Chuang[1], Rong-nan Chien[2], Ting-tsung Chang[3], Cheng-yuan Peng[4], Jenny C. Yang[5], Hongmei Mo[5], Steven J. Knox[5], Diana M. Brainard[5], Philip S. Pang[5], John G. Mchutchison[5], Chi-jen Chu[6], Jia-horng Kao[7]

Kaohsiung Medical University Hospital, Kaohsiung Medical University Department of Internal Medicine and Hepatobiliary Division Kaohsiung-Taiwan[1], Chang Gung Memorial Hospital and University Keelung-Taiwan[2], National Cheng Kung University Hospital and Medical School Tainan-Taiwan[3], China Medical University Hospital Taichung-Taiwan[4], Gilead Sciences, Inc. Foster City-United States[5], Taipei Veterans General Hospital and National Yang-ming University Taipei-Taiwan[6], National Taiwan University College of Medicine and National Taiwan University Hospital Taipei-Taiwan[7]

Background and aims: In Taiwan, the most prevalent hepatitis C virus (HCV) genotypes (GT) are GT1 and GT2. Patients are aging, are often treatment-experienced with progressive liver disease. Highly effective, safe and well-tolerated IFN-free regimens are needed to address the burden of HCV-related liver disease.
Methods: Two Phase 3 studies enrolled treatment-naïve and –experienced patients with GT1- and GT2-infection. Patients with GT1- and GT2-infection received ledipasvir/sofosbuvir (LDV/SOF) 90 mg/400 mg and SOF 400 mg + ribavirin (RBV 1000-1200 mg) for 12 weeks respectively. No upper age limit applied, up to 20 % of patients may have had cirrhosis, with no minimum neutrophil count and platelet count ≥ 50,000/μL. The primary efficacy endpoint was SVR12.
Results: Table 1 presents summary results. The SVR12 was 98 % (83/85) in GT1; 1 patient relapsed, 1 withdrew consent. In GT2 the SVR12 was 100 % (87/87). Treatment-emergent HCV NS5B resistance was not observed in any patient; 1 GT1 relapse patient had no NS5A resistance detected at baseline but had L31 V/Y93H at relapse. Overall, 3 patients (2 %) experienced serious adverse events, all unrelated to study drug. In SOF + RBV recipients, 6 (7 %) patients had treatment-emergent hemoglobin (Hgb) < 10 g/dL; no patients had Hgb < 8.5 g/dL; 4 (5 %) patients had RBV dose decreased or interrupted due to anemia.
Conclusions: 12-weeks of LDV/SOF in GT1 and SOF + RBV in GT2-infected treatment-naïve and -experienced Taiwanese patients including the elderly and those with cirrhosis achieved SVR12 rates ≥ 98 %. The regimens were safe and well tolerated. The data suggest these regimens may offer improved IFN-free therapeutic options to Taiwanese patients with chronic hepatitis C.

Topic 11: Hepatitis C

No: 1497

Treatment with the single tablet regimen ledipasvir sofosbuvir for 12 weeks results in 100 % svr12 in Japanese patients with chronic genotype 1 hepatitis C infection

Masashi Mizokami[1], Namiki Izumi[2], Osamu Yokosuka[3], Naoya Sakamoto[4], Masaaki Korenagai[1], Hitoshi Mochizuki[5], Kunio Nakane[6], Hirayuki Enomoto[7], Mikio Yanase[8], Hidenori Toyoda[9], Fusao Ikeda[10], Takuya Genda[11], Takeji Umemura[12], Hiroshi Yatsuhashi[13], Tatsuya Ide[14], Nobuo Toda[15], Kazushige Nirei[16], Yoshiyuki Ueno[17], Yoichi Nishigaki[18], Juan Betular[19], Bing Gao[20], Hadas Dvory-sobol[21], Akinobu Ishizaki[19], Masa Omote[22], Phillip Pang[22], Steven Knox[22], William Symonds[22], John Mchutchison[22], Tetsuo Takehara[23], Masao Omata[5]

National Center For Global Health and Medicine The Research Center For Hepatitis and Immunology Ichikawa-Japan[1], Musashino Red Cross Hospital Department of Gastrointestinal Medicine Musashino-Japan[2], Chiba University Department of Gastroenterology and Nephrology Chiba-Japan[3], Hokkaido University Department of Gastroenterology and Hepatology Sapporo-Japan[4], Yamanashi Prefectural Hospital Organization Department of Gastrointestinal Medicine Kofu-Japan[5], Akita City Hospital Department of Gastroenterology Akita-Japan[6], Hyogo College of Medicine Department of Liver, Gallbladder and Pancreas Internal Medicine Nishinomiya-Japan[7], National Center For Global Health and Medicine Department of Gastroenterology Tokyo-Japan[8], Ogaki Municipal Hospital Department of Gastroenterology Ogaki-Japan[9], Okayama University Department of Molecular Hepatology Okoyama-Japan[10] Juntendo University Department of Gastroenterology Izunokukni-Japan[11] Shinshu University Gastroenterology, Department of Medicine Matsumoto-Japan[12] National Hospital Organization Nagasaki Medical Center Department of Hepatology Omura-Japan[13] Kurume University Department of Gastrointestinal Medicine Kurume-Japan[14] Mitsui Memorial Hospital Department of Gastroenterology Tokyo-Japan[15] Nihon University Department of Gastroenterology Tokyo-Japan[16] Yamagata University Department of Gastroenterology Yamagata-Japan[17] Gifu Municipal Hospital Department of Gastroenterology Gifu-Japan[18] Gilead Sciences Clinical Operations Foster City-United States[19] Gilead Sciences Biostatistics Foster City-United States[20] Gilead Sciences Virology Foster City-United States[21] Gilead Sciences Clinical Research Tokyo-Japan[22] Osaka University Department of Gastrointestinal Internal Medicine Suita-Japan[23]

Aim: This open-label, Phase 3 study evaluated the efficacy and safety of ledipasvir 90 mg/sofosbuvir 400 mg Fixed-Dose Combination (LDV/SOF FDC) ± ribavirin (RBV) administered orally, once daily for 12 weeks in treatment-naïve and treatment-experienced Japanese subjects with chronic genotype 1 hepatitis C virus (HCV) infection.
Methods: Eligibility requirements included: age ≥ 20 years; HCV-RNA ≥ 105 IU/mL; platelets ≥ 50,000/μL. Primary endpoint was Sustained Virologic Response 12 weeks after treatment completion (SVR12).
Results: 341 Japanese patients were enrolled (166 treatment-naïve and 175 treatment-experienced). Mean age was 59 years; 42 % were male; 22 % had cirrhosis; mean baseline HCV-RNA was 6.6 log10 IU/mL. All patients in both arms had HCV RNA < LLOQ at Weeks 4-12 of treatment. SVR12 was achieved in 100 % (171/171) of patients in the LDV/SOF group and 98 % (167/170) of patients in the LDV/SOF + RBV group. In the LDV/SOF + RBV group, one subject relapsed, one discontinued RBV due to a RBV-related rash, and one died due to cardiac arrest. All treatment-experienced patients achieved SVR12 regardless of previous HCV regimen or previous treatment response.

Treatment-emergent adverse events (TEAEs) were reported by 65 % of patients in the LDV/SOF arm and 75 % in the LDV/SOF + RBV arm, with the most frequent being nasopharyngitis (29 % and 24 % respectively) and anemia (2 % and 14 % respectively). Most TEAEs were mild to moderate in severity.
Conclusions: LDV/SOF FDC ± RBV for 12 weeks achieved SVR12 in 99 % of patients. LDV/SOF for 12 weeks provides a highly effective, well-tolerated, interferon- and RBV-free treatment for Japanese patients with chronic HCV GT1 infection.

Topic 11: Hepatitis C

No: 2019

Association between il28b gene rs8099917 polymorphism and svr in Turkish patients with hepatitis C virus genotype 1

Hikmet Akkız[1], Ersin Akgöllü[1], Aynur Bekar[1], Selçuk Yıldırım[1], Macit Sandıkçı[1], Yakup Ülger[1], Berin Yalınbaş Kaya[1], Sedef Kuran[1], Oğuz Üsküdar[1]

University of Çukurova Department of Gastroenterology Adana-Turkey[1]

Aim: The hepatitis C virus (HCV) which infects 3 % of the world's population is a global challenge. Recently, Genome-Wide Association Studies (GWAS) have identified that the IL28B gene rs8099917 polymorphism was associated with the response to the pegylated-interferon alpha/ribavirin (PegIFNα/RBV) combination therapy in patients infected with HCV genotype 1. IL28B gene rs8099917 polymorphism should be determined before beginning treatment of HCV-infected patients to predict an individual's response. The aims of this study were to analyze the correlation between IL28B gene rs8099917 (T/G) polymorphism and PegIFNα/RBV therapy outcome in the Turkish population.
Material and method: Genotypes of the IL28B gene rs8099917 (T/G) single nucleotide polymorphism (SNP) were determined in 308 patients with HCV infection by using a polymerase chain reaction-restriction fragment length polymorphism (PCR–RFLP) assay. One group consisted of 148 patients with a sustained virological response (SVR), whereas the second group consisted of 160 nonresponders (non-SVR).
Results: Allele and genotype associations of IL28B gene rs8099917 polymorphism with a sustained virological response were observed in comparisons between the SVR and non-SVR groups ($P < 0.001$). In addition, the characteristics of the subjects did not differ between these two groups except for age and fibrosis stage ($P < 0.05$). Additionally, neither SVR nor rs80999917 genotypes were associated by HCV RNA levels.
Conclusions: In conclusion, the rs8099917 polymorphism was thus found strongly associated with a sustained virological response to therapy in Turkish patients infected with HCV genotype 1. Consequently, we suggest determining IL28B gene rs8099917 polymorphism of patients with HCV genotype 1 before onset of treatment.

Topic 11: Hepatitis C

No: 1424

All oral dual therapy with daclatasvir and asunaprevir in patients in Korea and Taiwan with HCV genotype 1b infection

Jia-horng Kao[1], Cheng-yuan Peng[2], Ting-tsung Chang[3], Jeong Heo[4], Chi-jen Chu[5], Youn-jae Lee[6], Chun-che Lin[7], Ki-tae Yoon[8], Sang-young Han[9], Jin-woo Lee[10], Jung-hwan Yoon[11], Young Seok Kim[12], Heon-ju Lee[13], Young Suk Lim[14], Seung Woon Paik[15], Won Young Tak[16], Jung Hyun Kwon[17], Misti Linaberry[18], Stephanie Noviello[18], Anne Torbeyns[19], Eric Hughes[18], Sang Hoon Ahn[20]

National Taiwan University Hospital Department of Internal Medicine, Graduate Institute of Clinical Medicine Taipei-Taiwan[1], China Medical University Hospital Department of Internal Medicine Taichung-Taiwan[2], National Cheng Kung University Department of Internal Medicine Tainan-Taiwan[3], Pusan National University Hospital Department of Internal Medicine Busan-Republic of Korea[4], Taipei Veterans General Hospital Division of Gastroenterology, Department of Medicine Taipei-Taiwan[5], Inje University Busan Paik Hospital Department of Internal Medicine Busan-Republic of Korea[6], Chung Shan Medical University Hospital Department of Internal Medicine Taichung-Taiwan[7], Pusan National University Yangsan Hospital Department of Internal Medicine Yangsan-Republic of Korea[8], Dong-a University Medical Center Department of Internal Medicine Busan-Republic of Korea[9], Inha University Hospital Department of Gastroenterology Incheon-Republic of Korea[10] Seoul National University Hospital Department of Internal Medicine Seoul-Republic of Korea[11] Soonchunhyang University Bucheon Hospital Department of Internal Medicine Bucheon-si-Republic of Korea[12] Yeungnam University Medical Center Department of Internal Medicine Daegu-Republic of Korea[13] Asan Medical Center Department of Gastroenterology Seoul-Republic of Korea[14] Samsung Medical Center Department of Internal Medicine Seoul-Republic of Korea[15] Kyungpook National University Hospital Department of Internal Medicine Daegu-Republic of Korea[16] The Catholic University of Korea, Incheon St. Mary's Hospital Department of Internal Medicine Incheon-Republic of Korea[17] Bristol-myers Squibb Research and Development Princeton, Nj-United States[18] Bristol-myers Squibb Global Biometric Sciences Research and Development -Belgium[19] Yonsei University Severance Hospital Department of Internal Medicine Seoul-Republic of Korea[20]

Aim: Daclatasvir (DCV; pangenotypic HCV NS5A inhibitor) plus asunaprevir (ASV; protease inhibitor) oral therapy demonstrated potent antiviral activity in HCV genotype 1b (GT1b) in a phase 3 study (AI447028). A sub-analysis of data from Korean and Taiwanese participants was performed due to high HCV GT1b prevalence in these countries.
Methods: Treatment-naive patients were randomly assigned (2: 1; double-blinded) to receive DCV 60 mg QD plus ASV 100 mg BID (Korea n = 21; Taiwan n = 25) or matching placebo (Korea n = 13; Taiwan n = 14) for 12 weeks. The DCV + ASV group continued treatment for 12 weeks; placebo recipients entered another DCV + ASV study. Non-responders to peginterferon/ribavirin (PEG/RBV) (null/partial; Korea n = 21; Taiwan n = 22) and those ineligible for, or previously intolerant of, PEG/RBV (ineligible/intolerant; Korea n = 23; Taiwan n = 24) received DCV + ASV for 24 weeks. The primary endpoint was sustained virologic response at posttreatment Week 12 (SVR[SUB]12[/SUB]).
Results: Among Korean and Taiwanese patients, 45 % were male, 31 % were IL28B non-CC and 34 % had cirrhosis. SVR[SUB]12[/SUB] rates for DCV + ASV-treated patients in naive, null/partial and ineligible/intolerant groups were 95, 86 and 70 % in Korean patients, and 88, 77 and 92 % in Taiwanese patients (Table). Serious adverse events occurred in 8 % of Korean and 8 % of Taiwanese patients with no deaths. Adverse events leading to discontinuation occurred in no Korean and 2 Taiwanese patients. Grade 3/4 laboratory abnormalities were uncommon with low incidences of ALT elevations (2 Taiwanese and 0 Korean patients).
Conclusions: DCV + ASV provides high SVR[SUB]12[/SUB] rates and is generally well tolerated in Korean and Taiwanese treatment-naive, null/partial responder and ineligible/intolerant HCV GT1b patients, including cirrhotics.

Topic 11: Hepatitis C

No: 1627

Boceprevir based therapy for treatment experienced chronic HCV Chinese patients

Qing Shao[1], Guo-feng Chen[1], Fan Li[1], Bing Li[1], Dong Ji[1], Zhong-bin Li[1], Song-hai Chen[1], Chun-yan Wang[1], Xiao-xia Niu[1], Shi-ying Ding[1], Tao Yan[2], Guo-qing Yin[3], Vanessa Wu[4], Athena Chau[4], April Wong[4], Yu-dong Wang[4], George Kk Lau[4]

Hospital Liver Fibrosis Diagnosis and Treatment Centre Beijing-China[1], 302 Hospital International Liver Diagnosis and Treatment Centre Beijing-China[2], Medical School of Southeast University Department of Infectious Diseases Nanjing-China[3], Humanity and Health Gi and Liver Centre Department of Gastroenterology and Hepatology Hong Kong-China[4]

Background and aims: Due to rapid development of direct anti-viral agents (DAAs) for the treatment of chronic hepatitis C (CHC) infection, first generation protease inhibitors such as boceprevir (BOC) was replaced by more potent DAAs, such as sofosbuvir (SOF), an NS5B nucleotide polymerase inhibitor and daclatasvir (DCV), an NS5A replication complex inhibitor. There is little clinical data of DAAs in CHC Chinese. We examine the effect BOC-based therapy in treatment-experienced CHC Chinese and the respond of BOC-failure to SOF-DCV combination therapy.
Method: Twenty-four treatment-experienced cirrhotic Chinese with CHC GT1b, were treated with BOC with peginterferon alfa and weight-based ribavirin for 28-48 weeks based on HCV RNA results (week 8 & 24). The primary efficacy end point was a sustained virologic response 24 weeks after the end of treatment (SVR24). At baseline, liver stiffness was measured using transient elastography (FibroScan®) and the single nucleotide polymorphism (SNPs) of IFLN3 (IL-28, rs12979860, C or T) and IFLN4 (ss469415590, TT or ΔG) were determined.
Results: Fourteen (59 %) patients had SVR24. Among them, 4 were null responders and 10 were relapsers ($P = 0.036$). There is no significant association between IFNL3/4 SNPs variation with SVR24. Four treatment failure patients were subsequently treated with sofosbuvir (SOF) 400 mg daily plus daclatasvir (DCV) 60 mg daily for twelve weeks and all achieved SVR12.
Conclusion: The sustained virologic response rate in treatment-experienced CHC GT1b is similar in Chinese, as compared to Caucasians and is not affected by SNPs variation of IFLN3/4. BOC-failure GT1b CHC respond well to 12-weeks SOF-DCV therapy.

Topic 11: Hepatitis C

No: 2183

Efficacy of pegylated interferon alpha and ribavirin treatment on the risk of hepatocellular carcinoma in patients with chronic hepatitis C a prospective study

Hikmet Akkız[1], Macit Sandıkçı[1], Ersin Akgöllü[1], Aynur Bekar[1], Sedef Kuran[1], Oğuz Üsküdar[1], Ümit Karaoğullarından[1]

University of Çukurova Department of Gastroenterology Adana-Turkey[1]

Aim: Chronic hepatitis C virus (HCV) infection is a leading cause of end-stage liver disease and hepatocellular carcinoma (HCC). The effects of pegylated interferon (PegIFN) and ribavirin (RBV) treatment of chronic HCV infection on the incidence of HCC have been poorly investigated. We have investigated the impact of treatment outcome on the development of HCC in chronic hepatitis C patients received PegIFN and RBV.
Material and method: Four hundred and twelve chronic hepatitis C patients with no history of HCC were prospectively recruited. Among 412 subjects, 314 were chronic hepatitis C patients and 126 were HCV-related cirrhotic patients. All patients received PegIFN alpha and RBV and the follow-up period started at the end of antiviral treatment (median follow-up period of 3.4 years). The cumulative incidence rate of HCC was estimated using the Kaplan–Meier method, according to treatment outcome.
Results: Sixteen patients (5.0 %) developed HCC during the follow-up period in the non-cirrhotic group, the 5-year cumulative incidence rates of HCC for sustained virological response (SVR) (1.8 %) and transient virological response (3.3 %) groups were significantly lower than those of non-virological response (NVR) group (7.9 %) ($P = 0.003$ and $P = 0.03$). In cirrhotic patients group, the 5-year cumulative incidence rates of HCC among patients who achieved SVR (20.0 %) and TVR groups (21.2 %) were also significantly lower than those of the NVR group (40 %) ($P = 0.03$).
Conclusions: In conclusion, SVR and TVR were associated with a lower HCC development risk when compared with NVR. Additionally, cirrhosis was found to be independent risk factor in development of HCC.

Topic 11: Hepatitis C

No: 1684

Cost effectiveness of one time screening for HCV in South Korea

Do Young Kim[1], Kwang-hyub Han[1], Byungyool Jun[2], Tae Hyun Kin[2], Sohee Park[2], Thomas Ward[3], Samantha Webster[3], Phil Mcewan[3]

Yonsei University College of Medicine Department of Internal Medicine Seoul-Korea, South[1], Yonsei University Graduate School of Public Health Seoul-Korea, South[2], Heor Ltd Cardiff-United Kingdom[3]

Introduction: The hepatitis C virus (HCV) is one of the leading causes of liver disease and hepatocellular carcinoma (HCC) in South Korea. With an estimated population prevalence of 0.78 %, it represents a significant healthcare resource burden. The objective of this study was to investigate the cost-effectiveness of a one-time screening followed by treatment in South Korean population aged 40–70, compared to current practice (no national screening).
Methods: A published Markov model was used in conjunction with a screening and treatment decision tree. Three cohorts (stratified by age) were modelled: 40–49, 50–59 and 60–69 years. Based on a published seroepidemiology study, HCV prevalence in each cohort was estimated at 0.60, 0.80 and 1.53 %, respectively. It was estimated that 71.70 % of the population would be screened. After diagnosis, the treatment rate (with peginterferon-alfa + ribavirin) was assumed to be 42.8 % over 10 years. Treatment costs, disease state-specific transition rates and health utilities were obtained from published sources. Costs associated with screening were estimated based on national health insurance reimbursement cost and expert opinion.
Results: Compared to current practice, screening is estimated to be cost-effective in all cohorts, with ICERs of $5,239, $6,423 and $8,696, respectively. Incremental costs of $91,554,108, $85,380,418 and $94,410,245 associated with screening/treating identified patients were partially offset by reductions in complication (decompensated cirrhosis and HCC) costs: $68,869,483, $64,051,681 and $69,790,176, respectively.
Conclusion: This study indicates that one-time screening for HCV infection in South Korean population aged 40-70 is likely to be highly cost-effective compared to current practice.

Topic 12: Hepatitis D

No: 1745

Seroepidemiology and clinical features of hepatitis delta among hbsag carriers a study from hepatitis clinic of Iranian blood transfusion organization

Maryam Keshvari[1], Seyed Moayed Alavian[2], Badro-al-sadat Aghaee[1], Bita Behnava[2], Heidar Sharafi[3]

High Institute For Research and Education In Transfusion Medicine Blood Transfusion Research Center Tehran-Iran[1], Middle East Liver Disease (meld) Center Department of Clinical Hepatology Tehran-Iran[2], Middle East Liver Disease (meld) Center Department of Molecular Hepatology Tehran-Iran[3]

Background: Hepatitis B is a significant health problem and more than 350 million individuals are infected with hepatitis B virus (HBV) globally. About 5 % of these individuals are coinfected with hepatitis D virus (HDV). HBV-HDV coinfection increases the rate of fulminant hepatitis, chronic hepatitis, and cirrhosis. The present study aimed to evaluate the epidemiology of HDV in individuals positive for HBsAg who referred to Tehran Blood Transfusion Hepatitis Clinic from 2011 to 2012.
Materials and methods: HBsAg-positive individuals attending this clinic were tested for anti-HDAb. All samples positive for anti-HDAb were also tested for detection of HDV RNA by RT-PCR. A questionnaire consisted of demographic characteristics and potential risk factors for acquisition of HDV was filled for each individual.
Results: Among 1038 individuals, HBsAg was detected in 660 (63.6 %) cases following blood donation and in 378 (36.4 %) cases following blood testing. In this study, 23 (2.2 %, 95 % CI = 1.3 %-3.2 %) patients were HDV-seropositive. In HDV-seropositive patients, 14 (60.9 %, 95 % CI = 39.1 %-78.3 %) were positive for HDV RNA. HDV-seropositive cases were more likely to have evidence of severe forms of hepatitis than the group of individuals without anti-HDAb ($P < 0.01$). Familial history of hepatitis D infection was more observed in HDV-seropositive patients than in individuals negative for anti-HDAb ($P < 0.01$).
Conclusion: The seroprevalence of HDV in HBsAg-positive individuals in this study was about 2 % which seems to be lower than the global prevalence of HDV.

Topic 12: Hepatitis D

No: 1098

Rare genetic variation in hepatitis delta virus (hdv) that influence genotype determination

Shadab Perveen[1], Abid Azhar[1], Obaid Yusuf Khan[2]

University of Karachi Kibge Karachi-Pakistan[1], University of Karachi Genetics Karachi-Pakistan[2]

Background: Hepatitis delta virus only infects the hepatic cells already infected with Hepatitis B virus. The delta virus infection leads to a severe clinical outcome than HBV infection alone varying with the delta virus genotype. During sampling a variant of Genotype I delta virus was encountered that was initially misdiagnosed as genotype II. Correct genotype determination of the new strains was carried out to analyze its origin and propagation in our population.
Methods: Blood samples were collected from patients with chronic hepatitis D infection. Viral RNA was extracted, reverse transcribed and used to amplify HDV R0 region by RT-Nested PCR. The PCR products were screened with RFLP using SmaI restriction enzymes for determining genotype. Nucleotide sequencing was carried out and used for phylogenetic analysis for clade determination. In silico recombination analysis was also performed to determine the origin of the delta virus isolates of interest.
Results: PCR–RFLP analysis using SmaI enzyme showed that three of our delta virus isolates belonged to genotype II. Upon nucleotide sequencing and subsequent phylogenetic analysis, the so-called genotype II clustered with genotype I sequences. A deeper nucleotide analysis exposed a selectively neutral mutation at the SmaI restriction site within the B-cell epitope, causing these strains to be falsely categorized as genotype II. Sequences analyzed in silico for recombination showed putative exchange of genetic material within and across genotype I and II.
Conclusions: Misdiagnosis proved the short-comings of SmaI PCR–RFLP based diagnosis of delta virus genotype. Recombination analyses suggested a possible reason for the high frequency of this mutation in our sampling.

Topic 12: Hepatitis D

No: 1469

Prevalence of hdv infection in Mongolia

Delgersaikhan Zulkhuu[1], Otgon Nasan[2], Bekhbold Dashtseren[3], Bayarmaa Otgonbayar[4], Naranjargal Dashdorj[5], Dahgwahdorj Yagaanbuyant[3], Naranbaatar Dashdorj[5]

State First Hospital of Mongolia Gastroenterology Ulaanbaatar-Mongolia[1], National Center of Communicable Disease of Mongolia Hepatology Ulaanbaatar-Mongolia[2], Mongolian National University of Medical Sciences; Onom Foundation Infectious Diseases Ulaanbaatar-Mongolia[3], "ach Medical College" Internal Medicine Ulaanbaatar-Mongolia[4], Onom Foundation Ulaanbaatar-Mongolia[5]

Introduction: Mongolia has one of the highest prevalence of hepatitis B and C. Consequently, leading mortality rates of liver cirrhosis and hepatocellular carcinoma (HCC) in the world. In clinical practice it is thought that HDV infection is on the rise. However, HDV infection was not formally studied in Mongolia.
Aim of study: To study the prevalence of HDV infection in Mongolia.
Method and subject: The study was approved by the Ethics Committee at the Health Sciences University of Mongolia and the Health Ethics Committee of the Ministry of Health of Mongolia. Study subjects were chosen based on three-stage cluster sampling method. Total of 1,158 subjects were enrolled in the study. All participants on-site tested for HBsAg using rapid tests (CTK Biotech, San-Diego, US). Also, 5-10 ml of blood was drawn from antecubital vein and sera were separated following a standard protocol. Rapid test positive tested subjects' serum specimens were tested for HBsAg, anti-HD-Ab and HD-Ag by enzyme-linked immunosorbent assay (Diasorin, Italy).
Results: In this study, total of 499 (43.1 %) men and 659 (56.9 %) female. The overall prevalence of HBsAg among study subjects were 10.6 % (123/1158). From 123 HBsAg positive subjects 83 were tested positive for HD-Ab (67 % of HBsAg positive population and 7.2 % of total population) and 8 subjects were tested positive for HD-Ag (6.5 % of HBsAg positive population).
Conclusion: Prevalence of HDV infection is alarmingly high in Mongolian population. It indicates that there is an urgent need for concerted action from all stakeholders within the Mongolian health-care system.

Topic 13: Hepatitis E

No: 1020

The HEV genotype 2 with base substitutions in the intergenic junction restores the crex 'stem loop' integrity through compensatory mutations crucial for rna replication

Mohammd Khalid Parvez[1]

King Saud University College of Pharmacy Dept. of Pharmacognosy Riyadh-Saudi Arabia[1]

Among the human hepatitis E virus(HEV) strains (genotypes-1,2,3 and 4), the Mexican genotype-2 has two 'double-base' substitutions (5′U5100G5101 → CU and 3'C5117U5118 → GG) flanking the conserved cis-reactive element(CRE, nts. 5105-5116) in the intergenic-junction. While the 'C5100U5101′ natural mutations in the upstream ORF1 coding-region replaces 'alanine' for the conserved valine', the 'G5117G5118' doublet resides in the downstream non-coding/promoter-region of ORF3. Though a stable 'stem-loop' structure containing CRE, critical for virus replication had been reported, the phenotypic effect of genotype-2 'CU/GG' variations were neither mentioned nor explored. In this study, the evolutionary significance of such tolerable mutations in the conserved regulatory-sequences was investigated, in silico as well ex vivo. Multiple sequence alignment (ClustalW 1.83) of intergenic-junction of HEV strains showed further base conservations flanking the CRE sequences. In silico analysis(RNAfold) of the conserved sequences (nts. 5099-5121) of the representative genotypes revealed a stable RNA 'stem-loop' structure (CREX). of the four genotype-specific CREX, the Mexican mutant bases 'CU/UG' very interestingly, compensated and complemented themselves (5′C5100: 3′G5118 and 5′U5101: 3′G5117) in the 'lower-stem'. Substitution of 'GG' mutations in the ORF3 promoter-region, did not affect its 'optimal-context' and therefore, negated its regulatory role at 'nucleotide' level. Virtual mutations introduced to break the two base-pairings in the CREX 'lower-stem', completely destabilized the secondary structure. Further molecular characterization of the CREX mutants in HEV-SAR55 replicon background showed a drastic down regulation (up to 75 %) of viral RNA replication in hepatoma S10-3 cells(FACS). In conclusion, the compensatory mutations in the intergenic-junction of Mexican HEV strictly conserved the 'stem-loop' integrity, and suggested a greater regulatory role of CREX at structural-level in viral RNA replication.

Topic 13: Hepatitis E

No: 1263

New immunoassays for total iga and igm antibodies against hepatitis E virus prevalence in Italian blood donors and patients with chronic liver or kidney disease

Gabriele Ricco[1], Barbara Coco[1], Ferruccio Bonino[2], Maria Lanza[3], Fabrizio Scatena[3], Carlo M. Alfieri[4], Piergiorgio Messa[4], Edoardo Marchisio[5], Giovanni Mascolo[5], Alessandro Zanetti[6], Luisa Romanò[6], Cristina Galli[6], Thian-cheng Li[7], Tatsuo Miyamura[7], Maurizia R. Brunetto[1]

Hepatology Unit University Hospital of Pisa Pisa-Italy[1], General Medicine 2 Unit University Hospital of Pisa Pisa-Italy[2], Blood Bank Unit University Hospital of Pisa Pisa-Italy[3], Nephrology, Dialysis and Kidney Transplantation Unit Foundation Irccs "cà Granda Ospedale Maggiore" Policlinic of Milan Milan-Italy[4], Dia.pro Diagnostic Bioprobes Srl Milan-Italy[5], Department of Biomedical Sciences For Health University of Milan Milan-[6], Department of Virology Ii National Institute of Infectious Diseases Tokyo-Japan[7]

Background: Hepatitis E virus (HEV) causes zoonosis and acute hepatitis E in humans by fecal-oral transmission and accounts for outbreaks in developing countries and sporadic infections in developed countries. The global spread of HEV remains underestimated because of the subclinical course of most infections and variable diagnostic performances of serological assays.
Aim: To study the seroprevalence of HEV antibodies (Ab) in chronic-liver-disease (CLD), chronic-renal-disease (CRD) and blood-donors, using newly developed assays for IgA, IgM and total anti-HEV.
Methods: 396 sera from 199 (50.3 %) blood-donors, 109 (27.5 %) CLD-patients and 88 (22.2 %) CRD-patients and three standard references panels were tested by a reference anti-HEV assay (Wantai, Beijing, China) and new IgA, IgM and total anti-HEV assays (Dia.-Pro, Milan, Italy) developed using purified HEV-like-virus-particles (V-LPs) produced by recombinant baculo-viruses N-terminal 111-amino acid (aa)-deleted DNA fragments of genotype-1, genotype-3 and genotype-4 HEV-ORF2.
Results: Overall, total anti-HEV were detected in 12.9 %; 7.0 % blood-donors, 9.2 % and 30.7 % CLD and CRD-patients, respectively. The same samples were tested in parallel with IgG Wantai assay and new total/IgA/IgM assays (table 1). We observed a higher anti-HEV prevalence in older subjects and in chronic-kidney-disease patients ($P < 0.001$) with an optimal and slightly better performance of the new versus the commercially available reference assay.
Conclusions: Newly developed anti-HEV assays using recombinant HEV-V-LPs showed optimal diagnostic performances and assessed that HEV infection is endemic in Italy with anti-HEV prevalence ranging from 12-30 % in blood-donors and immunocompromised hosts respectively.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 1857

Impact of gadoxetic acid enhanced magnetic resonance imaging on hepatic nodules management a prospective study

Jing-houng Wang[1], Tai-yi Chen[2], Hsin-you Ou[2], Chi-chi Wang[3], Yueh-wei Liu[3], Chao-hung Hung[1], Chien-hung Chen[1], Chung-huang Kuo[1], Tsung-hui Hu[1], Yu-fan Cheng[2], Sheng-nan Lu[1]

Kaohsiung Chang Gung Memorial Hospital Department of Internal Medicine Kaohsiung-Taiwan[1], Kaohsiung Chang Gung Memorial Hospital Department of Radiology Kaohsiung-Taiwan[2], Kaohsiung Chang Gung Memorial Hospital Department of Surgery Kaohsiung-Taiwan[3]

Objectives: To evaluate the impact of gadoxetic acid-enhanced magnetic resonance imaging (EOB-MRI) on management of hepatic nodule.
Methods: Consecutive patients with hepatic nodule with suspicion of hepatocellular carcinoma (HCC) in Barcelona Clinic Liver Cancer (BCLC) early stage by dynamic imaging, well liver function reserve and admitted for resection evaluation were enrolled prospectively. Additional EOB-MRI was performed. The management was based on consensus in a liver cancer conference. Impact of EOB-MRI on the diagnosis, BCLC staging and treatment decision were recorded. The diagnostic validity and effectiveness of EOB-MRI and dynamic study in HCC characterization was assessed.
Results: A total of 103 patients (male/female: 77/27, mean age: 60.3) were enrolled with diagnoses of 90 HCCs, 4 cholangiocarcinomas (CCC) and 9 benign nodules (tumor size: 2.5 ± 1.1 cm). For 68 and 35 patients with typical and atypical HCC features in dynamic imaging studies, EOB-MRI characterized 3 (4.4 %) benign and 33 (94.3 %) HCC patients, respectively. Additional EOB-MRI changed BCLC stage in 19 (20.2 %) patients with HCC and altered treatment plans in 18 (19.1 %) patients. There were 66 patients who underwent resections with 78 nodules including 65 HCCs, 4 CCCs and 9 benign nodules. EOB-MRI detected 77 (98.7 %) nodules which was more than 69 (88.5 %) by dynamic imaging studies ($P = 0.009$). The diagnostic sensitivity and accuracy in HCC diagnosis for EOB-MRI was 98.5 % and 85.7 %, which was superior to 60 % and 57.9 % for 69 (88.5 %) nodules for dynamic study ($P < 0.001$).
Conclusions: Additional EOB-MRI improved HCC diagnosis in sensitivity, accuracy but not specificity or effectiveness. It also changed BCLC staging and treatment decision in about 20 % of patients.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 1166

Demographic profile and treatment outcomes of Filipino patients with hepatocellular carcinoma in a liver tumor registry

Gian Carlo Carpio[1], Allyn Lomboy[2]

Philippine General Hospital Medicine Quezon City-Philippines[1], Philippine General Hospital Gastroenterology Manila-Philippines[2]

Background: Previous studies using older diagnostic criteria pointed to chronic Hepatitis B and alcohol as the most common etiologies of HCC in the Philippines. No recent studies using updated criteria for diagnosis have been published. This study used the diagnostic criteria from the latest APASL guidelines to describe the profile of patients with HCC.
Methods: This is a cross-sectional study of adult HCC cases from a liver tumor registry in the Philippine General Hospital from 2009-2012. Demographics, AFP levels, BCLC stage, Child Pugh Score, ECOG performance status, treatments received, and mortality were presented in percentages.
Results: The HCC prevalence rate was 7.8 %, mostly occurring between ages 40-64 years. It is more common in males (M: F = 4: 1). The most common risk factors are chronic Hepatitis B and alcohol use. Most of the HCC cases were diagnosed at early stages, with lesser severity of liver functional impairment compared to older studies. Most patients with serum AFP determination had values less than the cut-off for HCC diagnosis. Resection was the most common treatment undertaken (50 %), and overall mortality rate was 25 %.
Conclusions: The profile of HCC patients in this study is similar to previous studies. More cases were recognized at earlier stages with better liver function, implying better treatment outcomes with surgery, although selection bias is recognized. A bigger study using the latest guidelines on diagnosis of HCC needs to be done to determine associations among HCC stage, treatments, and mortality.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 2247

Clinical profile prognostic factors and survival of patients with hepatocellular carcinoma in two Philippine tertiary centers

Mara Panlilio[1]

University of The Philippines-Philippine General Hospital Section of Gastroenterology, Department of Medicine Manila-Philippines[1]

Hepatocellular carcinoma is the fourth leading cause of cancer-related death in the world. Most of the burden of disease is seen in developing countries, with highest incidence rates reported in regions where Hepatitis B (HBV) is endemic. In the Philippines, HCC is the third leading site of cancer for both sexes.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 1949

Value of alpha feto protein in hepatocellular carcinoma detection

Nikhil Patel[1], Sulabhsinh Solanki[2], Payal Patel[2], Pallavi Furkunde[2], Chetan Lakhani[3]

Jivandeep Hospital Gastroenterology Anand-India[1], An Patel Institute Mlt Anand-India[2], Darpan Laboratory Pathology Anand-India[3]

Background: Hepatocellular carcinoma (HCC) is increasing worldwide due to rise in liver disease. Screening for HCC in cirrhosis includes alfa-feto protein(AFP) and ultrasonography or CT scan. Recently, due to its low sensitivity, AFP is omitted from the screening protocol. This study was planned to evaluate usefulness of AFP in clinical practice.
Methods: This observational prospective study was carried out in a tertiary care centre over the 3 months period. Consecutive patients diagnosed to have chronic liver disease(CLD) were evaluated for AFP, sonography and etiology. Those who showed elevated AFP and/or lesion on sonography were subjected to CT scan to diagnose for HCC. Those with elevated AFP and no lesion on imaging were reevaluated at 3- and 6- month for AFP and sonography/CT scan.
Result: Out of total 65 patients[age = 52.6 ± 20.5 years, male = 45(69.23 %), cirrhosis = 41(63.07 %), chronic hepatitis = 13(20 %), HCC = 11(16.92 %)], etiologies were: NAFLD = 17(26.15 %), HBV = 17(26.15 %), HCV = 4(06.15 %), cryptogenic = 2(03.07 %), alcohol = 25(38.46 %). Table-1 shows results. Significant elevation was seen in 1 case of hepatitis B cirrhosis without HCC. 3 patients with HCC had mild elevation. 4 patients of chronic hepatitis (HBV related) had mild elevation. In 3 patients, elevated AFP with normal sonography led to CT scan which diagnosed HCC.
Conclusion: AFP is neither highly specific nor sensitive marker For HCC. But, nevertheless it picks up few HCC which had normal sonography. Until new sensitive/specific markers are available, AFP should be.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 1432

Absolute lymphocyte count as a predictive factor of prognosis in patients with hepatocellular carcinoma after hepatectomy

Keisuke Kohno[1], Kiyoshi Fukunaga[1], Shinji Hashimoto[1], Yukio Ohshiro[1], Soichiro Murata[1], Tatsuya Oda[1], Nobuhiro Ohkohchi[1]

University of Tsukuba Department of Gastroenterological and Hepato-biliary-pancreatic Surgery Tsukuba-Japan[1]

Background: Absolute lymphocyte count (ALC) is considered a surrogate marker for immunosuppressive and nutritional status of patients and a prognostic factor for survival and recurrence in several cancers. We hypothesized that a lower ALC may represent poor hepatocellular carcinoma (HCC) outcome after hepatectomy. The aim of this study was to investigate the prognostic value of ALC for the overall survival and disease-free survival after hepatectomy.
Methods: A total of 105 patients who underwent hepatectomy without preoperative therapy for HCC in our department between 2004 and 2012 were evaluated. Clinicopathological parameters, including ALC, were evaluated to identify predictive factors of overall and disease-free survival after hepatectomy. Univariate and multivariate analyses were performed using the Cox proportional-hazards regression model.
Results: When stratifying patients according to ALC ($< 1{,}000/\mu L$ vs. $\geq 1{,}000/\mu L$), univariate analyses showed that ALC was significantly associated with overall ($P = 0.01$) and disease-free ($P = 0.04$) survival. Multivariate analysis showed ALC remained an independent predictive factor for overall survival ($P = 0.004$). Furthermore, multivariate analysis showed that ALC ($< 1{,}000/\mu L$) was the only independent prognostic factor for disease-free survival in stage II/III patients ($P = 0.024$).
Conclusion: This is the first report that shows ALC as an independent predictive factor of survival after hepatectomy in patients with HCC. ALC is a useful surrogate marker for prediction of overall and disease-free survival in patients with HCC after hepatectomy.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 1216

Risk of late finding primary liver cancer in patients with pyogenic liver abscess a population base cohort study

Hsueh-chou Lai[1], Che-chen Lin[2], Cheng-yuan Peng[3], Po-heng Chuang[3], Jung- Ta Kao[3], Shih-wei Lai[4], Wen-lung Ma[5], Fung-chang Sung[6]

China Medical University Graduate Institute of Clinical Medical Science, and School of Medicine, Taichung-Taiwan[1], China Medical University Hospital Management office For Health Data Taichung-Taiwan[2], China Medical University Hospital Division of Hepatogastroenterology, Department of Internal Medicine Taichung-Taiwan[3], China Medical University Hospital Department of Family Medicine Taichung-Taiwan[4], China Medical University and Hospital Sex Hormone Research Center Taichung-Taiwan[5], China Medical University Department of Public Health, College of Public Health Taichung-Taiwan[6]

Background & aims: The relationship between pyogenic liver abscess (PLA) with late finding primary liver cancer is unclear. We defined late finding primary liver cancer in PLA patients was who had primary liver cancer after one year of diagnosing PLA. We investigate the association from a population based, retrospective, cohort study.
Methods: From the claims data of Taiwan National Health Insurance, a cohort of 22648 patients with pyogenic liver abscess were newly diagnosed from 2000-2008. The available sample included 17531 PLA patients. A control cohort of 70124 persons without PLA was selected from the same dataset frequency matched for age, sex and

index year. Both cohorts were follow-up until the end of 2011. The risk of primary liver cancer estimated for both cohorts.
Results: The primary liver cancer incidence was near twofold greater in PLA patients than in control cohort (2.93 vs. 1.62 per 1000 person-years). The hepatocellular carcinoma (HCC) incidence and intrahepatic cholangiocarcinoma (ICC) incidence were 1.5- fold greater (2.21 vs. 1.50 per 1000 person-years) 11-fold greater (6.73 vs. 0.62 per 1000 person-years) in PLA patients than control cohort, respectively. The PLA cohort also had a high risk of all primary liver cancer (adjust hazard ratio [aHR], 1.56; 95 % confidence interval [CI], 1.35-1.81), HCC (aHR, 1.34; 95 % CI, 1.15-1.57), and ICC (aHR, 6.94; 95 % CI, 4.23-11.57), respectively.
Conclusions: Patients with PLA increased the risk and incidences of late finding primary liver cancer including HCC and ICC in the present large cohort study. This study highlights the necessary close follow-up in patients with PLA.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 1611

The correlation between the contrast enhanced ultrasound and pathological differentiation in small hepatocellular carcinoma

Qin Si[1], Xiaoli Qian[1], Shengxi Huang[1], Lu Yang[1], Yuanyuan Liu[1]

81st Hospital of Pla Department of Ultrasound Nanjing-China[1]

Objective: To investigate the relationship between the contrast-enhanced ultrasound perfusion characteristics of small hepatocellular carcinoma (SHCC) and pathology and its clinical value.
Methods: Three hundred and sixty-nine cases liver focus lesions detected by conventional ultrasound were examined by contrast-enhanced ultrasound (CEUS). The CEUS imaging characteristics and pathological results of SHCC were analyzed and compared.
Results: (1) Compared with pathological results of 254 malignant lesions and 124 benign lesions, the sensitivity of CEUS in diagnosis of SHCC was 98.8 % (242/245), the specificity was 92.7 % (357/369), Jorden index was 0.92, the positive likelihood ratio was 13.7, negative likelihood ratio was 0.013. (2) The CEUS characteristics of SHCC were rapid enhancement in early artery period, rapid clearance in late artery period or early portal period, that was characterized by fast enhancement and clearance. The enhancement pattern of fast in and out was accounted for 87.2 %(219/251) in malignant tumor lesions compared with 1.7 %(2/118) in benign lesions. The difference has statistical significance ($P < 0.05$). (3) The difference of CEUS enhancement time and peak time in different pathological differentiation of SHCC were no statistically significant ($P > 0.05$), but the differentiation of SHCC was (102.4 ± 2.236) s (76.02 ± 3.88) s(49.40 ± 4.95) s, respectively. The clearance time in high differentiation of SHCC was significantly longer than that of the low differentiation degree of SHCC ($P < 0.05$).
Conclusion: CEUS has important clinical value in the diagnosis of SHCC and the evaluation of pathological differentiation degree.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 1941

Etiological roles of diabetes bmi and past hepatitis B infection in the development of non b non c non alcoholic hepatocellular carcinoma

Hyun Yang[1], Hae Lim Lee[1], Si Hyun Bae[1], Jong Young Choi[1], Seung Kew Yoon[1], Jung Suk Oh[2], Ho Jong Chun[2]

The Catholic University of Korea Internal Medicine Seoul-Korea, South[1], The Catholic University of Korea Radiology Seoul-Korea, South[2]

Introduction: Obesity and diabetes are risk factors for the development of HCC. Past hepatitis B virus infection has been considered as major
cause of NBNC and non-alcoholic(NA) HCC. The aim of this study is to investigate the etiologies and prevalence of NBNC-NA HCC.
Methods: Between 2002 and 2010, a total of 2545 consecutive patients with HCC were categorized into two groups: NBNC-NA HCC and HBV, HCV-alcohol related HCC group. Patients' records were reviewed for the presence of diabetes and IgG anti-HBc and for BMI at the time of diagnosis. NBNC-NA HCC was defined as absence of HBs Ag, anti-HCV antibody without history of significant alcohol consumption.
Results: 203 (7.98 %) of total 2545 patients with HCC were categorized as the NBNC-NA HCC group. Mean ages of the two groups (NBNC- NA HCC 66.5 ± 11.20 vs. HBV, HCV-alcohol related HCC 57.09 ± 10.86, $P < 0.001$) were significantly different. Among the risk factors of NBNC-NA HCC, the proportion of diabetes in NBNC-NA HCC group(OR: 2.002, CI: 1.47-2.73, $P < 0.001$) was significantly higher than HBV, HCV-alcohol related HCC group, and differences of body mass index(BMI) were insignificant. Presence of anti-HBc in NBNC-NA HCC group was higher in proportion (80.14 %) than the control group composed of NBNC patients admitted due to the other diseases without HCC (154 of 326 patients, 47.24 %). The proportion of NBNC-NA HCC increased in correlation with age, 0 % in 30 s, 3.34 % in 40 s, 3.80 % in 50 s, 9.01 % in 60 s, and 22.0 % in over 70 s, respectively.
Conclusion: Past infection of HBV should be still considered as important risk factor for HCC. and, diabetes contributes to the development of NBNC-NA HCC.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 1712

Easy detection of liver tumor using new technology virtual ultrasound sonography

Chikara Ogawa[1], Masatoshi Kudo[2], Soichi Arasawa[1], Masako Izuta[1], Mitsushige Shibatouge[1]

Takamatsu Red Cross Hospital Department of Gastroenterology and Hepatology Takamatsu-Japan[1], Kinki University of Medicine Department of Gastroenterology and Hepatology Osakasayama-Japan[2]

Purpose: To evaluate the usefulness of a virtual ultrasound (US) imaging device as a tool to assist novice sonographers.
Materials and methods: A prospective blinded pilot study was conducted involving patients with liver lesions. Two sonographers and 2 medical doctors with less than 5 years of experience performed US examinations. The time needed to detect liver lesions on US and the success rate for detecting liver lesions with and without using the virtual US imaging device SYNAPSE VINCENT® (Fujifilm Medical Co., Tokyo, Japan) before US examination were evaluated.
Results: Thirty-two patients with the following 42 liver lesions were included: liver cyst (n = 24), hemangioma (n = 8), hepatocellular carcinoma (n = 6), and liver metastasis (n = 4). The maximal diameter of these lesions ranged from 0.3 to 1.5 cm (mean ± SD, 0.8 ± 0.4). The average time for detecting liver lesions on US was

47.8 s (range, 7-113) with VINCENT and 112.9 s (range, 14–313) without VINCENT before US examination. There were significant differences in the duration of US examination with and without VINCENT ($P = 0.0002$, Student's t test). The rates for accurately detecting liver lesions were 100 and 76.2 % (16/21) in US beginners with and without VINCENT, respectively. Significantly higher detection rates were found in the US beginners who used VINCENT compared to those who did not use VINCENT ($P = 0.047$, Fisher's exact test).
Conclusion: Before US examination, a reference with VINCENT could contribute to the successful detection of liver lesions and could be time-saving for US beginners.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 1612

Contrast enhanced ultrasonography perfusion characteristics and its clinical value in metastasis hepatic carcinoma

Qin Si[1], Xiaoli Qian[1], Shengxi Huang[1], Xiaoping Lv[1], Yanli Huang[1]

81st Hospital of Pla Department of Ultrasound Nanjing-China[1]

Objective: To analyze the characteristics of contrast-enhanced ultrasound (CEUS) perfusion in metastasis hepatic carcinoma (MHC) and evaluate the clinical value of CEUS.
Methods: One hundred and twenty-seven MHC patients with 194 hepatic lesions confirmed by pathology were examined by CEUS. The characteristics of blood supply perfusion were analyzed and compared with contrast enhanced CT(CECT).
Results: (1) One hundred and seventy-three MHC lesions and 21 benign lesions in 194 hepatic lesions were diagnosed by pathology.MHC lesions detection rate by CEUS was significantly higher than that before contrast and superior to that of contrast-enhanced CT.The results were as follows: pre-contrast 124 leslons, post-contrast 171 lesions,contrast-enhanced CT 168 lesions(included 1 false positive lesion). (2) The detection rate was 95.7 % (45/47) by CEUS in smaller lesions (length-diameter < 1.0 cm). (3) The CEUS characteristic of MHC lesions showed: 89.6 % (155/173) with peripheral annularbulge-like or sparse-like fast filling, 9.2 % (16/173) with quick whole filling; 95.9 % (166/173) were rapid clearance in the arterial phase and 2.9 % (5/173) with slow clearance in the middle and late portal venous phase or parenchymalphase; 1.2 % (2/173) with no significant enhancement and clearance in all phases. (4) The sensitivity, specificity, accuracy of CEUS and CECT diagnosed MHC with regard to pathology were 98.8 %(171/173), 100 % (21/21), 98.9 % (192/194) and 96.5 % (167/173), 95.2 % (20/21), 96.4 % (187/194). Both diagnostic accuracies were good (Az $>$ 0.9,95 % CI: 0.985 $\sim$ 1.004 in CEUS and 0.904 $\sim$ 1.014 in CECT).
Conclusions: CEUS has an important clinical value for diagnosis and differential diagnosis of MHC.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 1909

A clinical and immunohistochemical journey in the combined hepatocellular cholangiocarcinoma

Tommaso Abbate[1], Amedeo Sciarra[1], Lorini Matteo[2], Destro Annarita[2], Raschioni Carlotta[2], Donadon Matteo[3], Torzilli Guido[3], Roncalli Massimo[4], Di Tommaso Luca[4]

Università Degli Studi Di Milano Pathology Rozzano-Italy[1], Humanitas Research Hospital Pathology Rozzano-Italy[2], Humanitas Research Hospital Chirurgia Epatobiliare Rozzano-Italy[3], Humanitas Research Hospital Anatomia Patologica Rozzano-Italy[4]

Combined hepatocellular-cholangiocarcinoma (cHCC-CC) is a rare primary liver cancer poorly understood due to its low incidence and elusive nature. Aim of this study is to correlate its heterogeneous morphological aspects to the expression of markers of hepatocellular (HSA, Arginase, CD10, pCEA), Cholangiocellular (CK7, CK19, EMA) and stem-cell (EpCAM, NCAM, SALL-4, c-KIT, YAP) differentiation as well as potential therapeutic targets (FGFRs, c-met). Classical hepatocellular (HCC) and Cholangiocellular (CC) carcinoma were used as controls.

Our series includes 23 cases of cHCC-CC classified (WHO 2010) as typical (11) or stem cell (12) subtypes. Among the latter, cases were further distinguished into classical (7), intermediate (1) and cholangiocellular (4). The majority of patients were male, diagnosed after 2008, with a prevalence of about 4 % of all primary liver cancers in our hospital. Among hepatocellular markers HSA (63 % positive cases, 21 % immunoreactive cells) and Arginase1 (54 %, 17 %) were the most sensitive for the typical subtype; CD10 (80 %, 20 %) and pCEA (83 %, 34 %) for the stem-cell subtypes. Among Cholangiocellular markers, CK7 and CK19 showed strong, diffuse immunoreactivity in almost all cases. Strikingly, EpCAM was highly expressed throughout the specimens (100 %, 70 %). FGFR2 and c-met showed faint but definite immunoreactivity in 27 % of cases. Survival data showed no difference among typical and stem cell subtypes; cholangiocellular variant (mostly G1 tumors) had a better but still not significant outcome.

Our results showed an ubiquitous expression of stem-cell markers and similar outcome in all subtypes of cHCC-CC questioning whether to differentiate a typical from a stem-cell variant.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 1917

Trends of hepatocellular carcinoma (HCC) in HIV infected patients over time 1995–2013

Caitlin Citti[1], Ayse Aytaman[2], Maaz B. Badshah[3], Heather Platt[4], Meritxell Ventura[5], Ting-yi Chen[6], Luciana Kikuchi[7], Beatriz Minguez[5], Sonja Marcus[8], Michael Yin[4], Judith Aberg[9], Douglas Dieterich[10], Myron Schwartz[11], Norbert Bräu[12]

Icahn School of Medicine At Mount Sinai Dept. of Medicine New York, NY-United States[1], Va New York Harbor Hcs & Suny Downstate Medical Center Brooklyn, NY-United States[2], Indiana University School of Medicine Indianapolis, In-United States[3], Columbia University Medical Center Division of Infectious Diseases New York, NY-United States[4], Hospital Universitario Vall D Barcelona-Spain[5], University of Texas Southwestern Medical Center Dallas, Tx-United States[6], Universidade De São Paulo São Paulo-sp-Brazi[7], James J Peters Va Medical Center Bronx, NY-United States[8], Icahn School of Medicine At Mount Sinai Division of Infectious Diseases New York, NY-United States[9], Icahn School of Medicine At Mount Sinai Division of Liver Diseases New York, NY-United States[10] Icahn School of Medicine At Mount Sinai Division of Hepatobiliary Surgery New York, NY-United States[11], James J Peters Va Medical Center & Icahn School of Medicine At Mount Sinai Divisions of Infectious Diseases & Liver Diseases Bronx, NY-United States[12]

Background: Cases of HCC in HIV-positive patients have become more common, but their frequency as well as trends over time are unknown.

Methods: Patients were retrospectively identified from 1995-2013 in 38 centers in 7 countries. Time of diagnosis was divided into earlier (1995-2007) and later years (2008-2013).
Results: Among 365 HIV-infected patients with HCC (HCV, 79 %; HBV, 20 %, non-viral, 1.4 %), the number of cases rose steadily between 1995 and 2009 and then started to decline. Compared to diagnosis pre-2008 (n = 169), patients with a diagnosis 2008 or later (n = 196) were older (mean, 55.2 vs. 51.3 years, $P < 0.001$), less commonly abused alcohol (19 % vs. 39 %, $P < 0.001$), had HCC screening more often (70 % vs. 54 %, $P = 0.002$), and tended to have a lower mean Child-Turcotte-Pugh score (6.6 vs. 7.0, $P = 0.073$). Patients diagnosed 2008 or later also had a smaller median tumor size (3.2 vs. 4.3 cm, $P = 0.015$) and tended to have a lower median alpha-fetoprotein level (69 vs. 198 ng/ml, $P = 0.051$). They also received effective HCC therapy more often (73 % vs. 54 %, $P < 0.001$) and had longer median survival (27.8 vs. 10.0 months, $P < 0.001$). In multi-variable Cox regression analysis, only HCC screening, effective HCC therapy, Child-Turcotte-Pugh score, log10 AFP level, and alcohol abuse were independently predictive of survival, but not year of diagnosis before or after 2008.
Conclusion: In HIV-infected patients with HCC, a diagnosis in 2008-13 was associated with better survival than in 1995-2007 due to more frequent screening and HCC therapy, as well as lower CTP scores and AFP levels and less alcohol abuse.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 1489

Real time image fusion technique for detection of small hepatocellular carcinoma with contrast enhanced ultrasonography using the new agent sonazoid

Chikara Ogawa[1], Masatoshi Kudo[2], Soichi Arasawa[1], Masako Izuta[1], Mitsushige Shibatouge[1]

Takamatsu Red Cross Hospital Gastroenterology and Hepatology Takamatsu-Japan[1], Kinki University of Medicine Gastroenterology and Hepatology Osakasayama-Japan[2]

Objective: Evaluation of usefulness of real-time image fusion techniques (Volume navigation system) for detection of small hepatocelluar carcinoma using new second agent Sonazoid.
Methods: A total of 16 patients with 18 HCC nodules within 2 cm who underwent surgical resection were evaluated in this study. All patients underwent CE-US using the new agent Sonazoid, CTHA, CTAP and Gd-EOB-DTPA MRI within one and a half months before operation. Additionally all tumors were evaluated using real-time image fusion techniques (Volume navigation system: Logiq E9, GE). The mean age was 66.4 years and the mean tumor size was 14.9 cm.
Results: 5 tumors were diagnosed as well-differentiated HCC, 9 tumors as moderately-differentiated, 3 tumor as poorly-differentiated, and 1 tumor was combined HCC and CCC. 17/18 nodules was able to be detected easily using Sonazoid and real-time image fusion techniques, but one nodule was not detected because of the size, location and depth from the surface of liver.
Conclusion: Real-time image fusion technique (Volume navigation) with the new agent Sonazoid is extremely useful for detection of small hepatocellular carcinoma.

Topic 14: Hepatocellular Carcinoma Diagnosis

No: 1955

Consecutive increment of serum alpha feto protein level is a useful surrogate marker in predicting hepatocellular carcinoma in liver cirrhosis patients

Hae Lim Lee[1], Hee Chul Nam[1], Hyun Yang[1], Si Hyun Bae[1], Jong Young Choi[1], Se Hyun Cho[1], Seung Kew Yoon[1], Joon Yeol Han[1], Jung Suk Oh[2], Ho Jong Chun[2]

The Catholic University of Korea Internal Medicine Seoul-Korea, South[1], The Catholic University of Korea Radiology Seoul-Korea, South[2]

Background: The role of AFP in the diagnosis of HCC is getting smaller due to the advances of imaging modalities. However, consecutive increment of AFP level in cirrhosis patients is associated with the higher risk of developing HCC.
Methods: From 2002 to 2012, 1931 patients were diagnosed with HCC in Seoul St. Mary's hospital. Among them, 133 patients were found to have a serial record of AFP for over one year. We assessed AFP levels at the diagnosis of HCC was made and compared them with that of patients at 3, 6 and 12 months prior to the diagnosis.
Results: Median AFP level was 45.53 ng/mL (1.4-32134), and the level of 12, 6 and 3 months before the diagnosis of HCC was 6.19 ng/mL (1.12-513), 7.53 ng/mL (0.96-1287.86), 11.94 ng/mL (0.91-1461), 45.53 ng/mL (1.4-23134), respectively. Consecutive increment of AFP level was statistically significant in time dependent manner ($P \leq 0.000$) with linear relationship ($P = 0.001$). In elevated AFP (> 45 ng/mL) group (n = 67), median AFP level of 12, 6 and 3 months before the diagnosis of HCC and at the time of the diagnosis of HCC was 11.76 ng/mL (1.3-513), 26.82 ng/mL (1.4-1287.86), 76.92 ng/mL (3-1461), 476 ng/mL (45.53-23134), respectively. In non-elevated AFP (< 45 ng/mL) group (n = 66), median AFP level was 5.37 ng/mL (1.12-74.78), 6.09 ng/mL (0.96-91), 5.51 ng/mL (0.91-30.01), 5.63 ng/mL (1.4-40.1), respectively.
Conclusions: Increase in serial AFP level as a strong surrogate marker can predict HCC and those with consecutive increments of AFP levels for more than 2 times should be candidates for active surveillances for HCC.

Topic 15: Hepatocellular Carcinoma Treatment

No: 1309

Cause of death in patients with hepatocellular carcinoma within milan criteria

Hyunwoo Lee[1], Dong Hyun Sinn[1]

Samsung Medical Cancer Hepatology Seoul-Korea, South[1]

Background: Hepatocellular carcinoma (HCC) is a unique condition where the cause of death may not only be due to progressive cancer, but also form liver failure. Milan criteria can be applied. We analyzed patterns of cancer progression, and assessed cause of death in HCC patients within Milan criteria.
Methods: We screened a prospectively enrolled HCC registry at Samsung Medical Center between Jan. 2008 and Dec. 2012. Among 1,240 HCC patients within the Milan criteria, mortality was identified in 215 patients. We excluded 59 patients who received liver transplantation (n = 13) or lost to follow-up (n = 37), and 156 cases of mortality was assessed.

Results: Among 156 patients, 65 patients (42 %) died in hospital and 91 patients (58 %) died out of hospital, but within 3 months from last hospital visit (median 0.8 months). At mortality or last follow-up, extrahepatic metastasis was seen in 74 patients (48 %), locally advanced state in 28 patients (17 %), mUICC stage I or II in 19 patients (11 %), and in complete remission in 35 patients (22 %). Among 54 patients with tumor that was mUICC stage I or II or at complete remission state, 28 cases was liver complication related mortality, 14 had other identifiable cause, and 12 cases had unidentifiable cause. Independent risk factor for cancer progression at mortality was PIVKA-II levels > 40 mIU/ml, while Child-Pugh Class were risk factor for liver-failure related mortality.
Conclusion: Cancer progression-related mortality was identified in 65 % of HCC patients within Milan criteria.

Topic 15: Hepatocellular Carcinoma Treatment

No: 1944

Percutaneous ultrasound guided radiofrequency ablation for extrahepatic neoplasms

Shinpei Sato[1], Toshihiro Kawai[1], Masatsugu Ishii[1], Takafumi Sugimoto[1], Yoko Yashima[1], Shuntaro Obi[1]

Gastroenterology Kyoundo Hospital Tokyo-Japan[1]

Objective: Radiofrequency ablation (RFA) is a minimally invasive treatment widely performed for the treatment of liver neoplasms. Recently, resulting of long prognosis has made by surgery, ablation and chemotherapy, extrahepatic neoplasms have found out in the clinical practice. The aim of this study was to describe our experience with percutaneous ulrtrasound-guided RFA of extrahepatic neoplasms.
Methods: From 2010 to 2014, 15 radiofrequency ablation (RFA) in 15 selected patients with extrahepatic neoplasms were performed. Extrahepatic neoplasms were adrenal grand metastases in 5 patients, abdominal seeding in 4 patients, splenic metastases in 2 patients, bone metastases in 3 patients renal metastases in 1 patients. The patients had contraindications to surgery. The average tumor size was 2.5 cm(2.0-9.5) in diameter with mean age of 68 years. RFA was performed based on percutaneously under ultrasound guidance with monopolar Cool-tip RFA needle. The procedure was performed under sedation using propofol or general anesthesia. The absence of contrast enhanced CT was considered to be a successful treatment.
Results: The average follow up was 12 months. In 15 tumors (95 %), total absence of contrast enhancement was obtained after initial RFA. All the patients were done with successful. There were no complications. Local recurrence was observed in 3 lesions (25 %) out of 15 lesions. Median survival time was 14.5 months after RFA. The cause of death was liver failure due to progression of hepatic neoplasms, not progression of extrahepatic neoplasms.
Conclusion: RFA of extrahepatic neoplasms is a promising alternative treatment which could be considered for patients who are not suitable for surgery.

Topic 15: Hepatocellular Carcinoma Treatment

No: 1281

Treatment of hepatocellular carcinoma in child pugh class C liver cirrhosis patients

Ju-yeon Cho[1], Dong Hyun Sinn[1], Won Sohn[1], Geum-youn Gwak[1], Yong-han Paik[1], Moon Seok Choi[1], Joon Hyeok Lee[1], Kwang Cheol Koh[1], Seung Woon Paik[1], Byung Chul Yoo[1]

Samsung Medical Center Internal Medicine Seoul-Korea, South[1]

Background: Child Pugh class C patients diagnosed with hepatocellular carcinoma are allocated to stage D of the Barcelona Clinic Liver Cancer (BCLC) staging system and best supportive care is the recommended treatment. However, in clinical practice prolonged survival is evident after treatment of HCC in Child Pugh C patients. This study aimed to clarify the survival benefit of treatments for advanced liver cirrhosis patients with HCC.
Methods: Between January 2005 and December 2010, Child Pugh C liver cirrhosis patients diagnosed with HCC were reviewed. After excluding patients with concurrent other malignancies, 88 patients(HBV: 84.1 %) were included in the study. Applied treatment, liver function changes after treatment, survival, and factors affecting survival were analyzed.
Results: Among the 88 patients included, 43 patients received best supportive care, 23 patients were treated with non-transplant modalities, and 22 patients underwent liver transplantation. The overall survival of the group that received non-transplant modalities compared to the patients that received best supportive care was significantly longer(27.4 months vs. 2.9 months, $P < 0.001$). For HBV-related HCC ($n = 53$), the survival of patients treated with non-transplant modalities was significantly longer than best supportive care (29.6 months vs. 2.6 months, $P < 0.001$). Excluding the liver transplanted patients, multivariate analysis revealed that treatment of HCC as an independent prognostic factor for overall survival (HR = 0.492, 95 % CI 0.248-0.974, $P = 0.042$). The 30 day mortality after non-transplant treatment was 8.6 % (2/23).
Conclusions: Child-Pugh class C liver cirrhosis patients diagnosed with HCC who were treated had significantly prolonged overall survival compared to patients that had best supportive care.

Topic 15: Hepatocellular Carcinoma Treatment

No: 2140

Real life experience with sorafenib used to treat hepatocellular carcinoma in Korea analysis of Gideon data

Do Young Kim[1], Hye Jin Kim[2], Kwang-hyub Han[3], Jeong Heo[4], Soon Ho Um[5], Yeul Hong Kim[5], Sang Young Han[6], Young Oh Kweon[7], Ho Yeong Lim[8], Byung Seok Lee[9], Han Chu Lee[10], Baek Yeol Ryoo[10], Seung Kew Yoon[11]

Yonsei University College of Medicine Internal Medicine Seoul-Korea, South[1], Bayer Healthcare Pharmaceuticals Medical Affairs Seoul-Korea, South[2], Yonsei University College of Medicine Internal Medicine Seoul-Korea, South[3], Pusan National University School of Medicine Internal Medicine Busan-Korea, South[4], Korea University College of Medicine Internal Medicine Seoul-Korea, South[5], Donga University College of Medicine Internal Medicine Busan-Korea, South[6], Kyungpook National University College of Medicine Internal Medicine Daegu-Korea, South[7], Sungkyunkwan University School of Medicine Internal Medicine Seoul-Korea, South[8], Chungnam National University College of Medicine Internal Medicine Daejeon-Korea, South[9], University of Ulsan College of Medicine Internal Medicine Seoul-Korea, South[10] The Catholic University of Korea Internal Medicine Seoul-Korea, South[11]

Objectives: We report clinical real-life experience of use of sorafenib to treat HCC in Korea, using a subset of data from GIDEON (Global

Investigation of therapeutic DEcisions in HCC and of its treatment with sorafeNib); a large, prospective, observational study.
Methods: Between January 2009 and April 2012 a total of 497 patients were enrolled from 13 regions of Korea. Of these, 482 were evaluable in terms of treatment safety. The safety and efficacy data were recorded for all patients.
Results: More patients of Child-Pugh class A received sorafenib for > 8 weeks than did patients of Child-Pugh class B (55.5 % vs. 34.3 %). Child-Pugh class did not seem to influence the commencement dose of sorafenib, and approximately 70 % of patients in both the Child-Pugh A and B classes received the recommended initial daily dose of 800 mg (69.0 % and 69.5 %). The median overall survival (OS) and time to progression (TTP) were 8.5 and 2.5 months, respectively, in the two classes of patients. In Child-Pugh class A patients, the median OS and TTP were 10.2 months and 2.5 months. The most frequent treatment-caused, drug-related adverse event (AE) was a hand-foot skin reaction (31.7 %), followed by diarrhea (18.0 %), rash/desquamation (9.3 %), and anorexia (8.1 %). The incidence of treatment-emergent AEs was similar in both Child-Pugh class A (85.4 %) and B (84.8 %) patients.
Conclusions: The efficacy of sorafenib in Korean patients was consistent with that exhibited in earlier pivotal Phase III trials. Sorafenib was well-tolerated by Korean HCC patients treated in clinical settings, and the safety profile did not seem to differ by Child-Pugh status.

Topic 15: Hepatocellular Carcinoma Treatment

No: 2061

Radiofrequency ablation in very elderly patients with liver tumors

Nobuhito Taniki[1], Ryo Shimizu[1], Ryo Kanazawa[1], Tomoyasu Ito[1], Hiroaki Saito[1], Jinkan Sai[1], Sumio Watanabe[1], Shuichiro Shiina[1]

Juntendo University School of Medicine Department of Gastroenterology Tokyo-Japan[1]

Aims: Choosing Radiofrequency Ablation (RFA) in very elderly patients with liver tumors must be decided by considering radicality and tolerability. We aimed to evaluate the safety and efficacy of RFA in very elderly patients (VEP: 85 years old or older) in this study.
Methods: Patients were 34 VEP who underwent RFA between December 2012 and November 2014 at our institute. We investigated the rate of cases which were beyond the general indication of RFA, 3 or fewer nodules, all 3 cm or less in diameter, the rate of complications, technical success (It was defined that complete ablation of the tumor was demonstrated by contrast-enhanced CT scan) rate, and 1-year survival.
Result: A total of 55 RFA treatments were performed in 34 VEP. In 30 HCC patients, 8 of 45 treatments (18 %) were beyond the general indication. Grade II complications occurred in 1 of 45 (intraperitoneal bleeding required blood transfusion). Technical success rate was 100 % and 1-year survival was 90 % (9 of 10 patients, 1 patient died of HCC). In 4 metastatic liver cancer patients, 3 of 8 treatments (38 %) were beyond the general indication. Complications did not occur. Technical success rate was 100 % and 1-year survival was 100 % (3 of 3).
Conclusions: RFA was performed safely in VEP. Short-term efficacy judged by technical success rates and 1-year survival was satisfactory, although there were many patients beyond the general indication of RFA. RFA may be a treatment of choice in VEP not only with HCC but also with metastatic liver tumors.

Topic 15: Hepatocellular Carcinoma Treatment

No: 1127

Survival advantage with the use of metformin in hepatocellular carcinoma patients receiving radiotherapy a propensity score matching analysis

Won Il Jang[1], Mi-sook Kim[1], Hyung Jun Yoo[1], Young Seok Seo[1], Jung Sub Lim[2], Chul Ju Han[3], Su Cheol Park[3], Chul Seung Kay[4], Myungsoo Kim[4], Hong Seok Jang[4], Dong Soo Lee[4], Ah Ram Chang[5], Kyubo Kim[6], Hae Jin Park[6]

Korea Institute of Radiological and Medical Sciences Radiation Oncology Seoul-Korea, South[1], Korea Institute of Radiological and Medical Sciences Pediatrics Seoul-Korea, South[2], Korea Institute of Radiological and Medical Sciences Internal Medicine Seoul-Korea, South[3], College of Medicine, The Catholic University of Korea Radiation Oncology Seoul-Korea, South[4], Soonchunhyang University Hospital Radiation Oncology Seoul-Korea, South[5], Seoul National University College of Medicine Radiation Oncology Seoul-Korea, South[6]

Introduction: Metformin use has been associated with a decreased risk of cancer and mortality. However, its effects on the survival of hepatocellular carcinoma (HCC) patients are not defined. We performed this study to evaluate effects on the clinical outcomes of HCC patients received radiotherapy.
Methods: The medical records of 217 HCC patients treated with stereotactic body or hypofractionated radiotherapy. of the enrolled patients, 48 had type 2 diabetes and 19 used metformin. Patients were divided into the metformin group (n = 19, 9 %) and the non-metformin group (n = 198, 91 %) including those with diabetes (n = 29, 13 %) or without (n = 169, 78 %). We matched 19 patients of the metformin group with 57 of the non-metformin group using propensity score and performed a retrospective cohort study comparing the two groups.
Results: In the propensity score–matched cohort (n = 76), the overall survival (OS) and progression-free survival (PFS) rates were higher in the metformin group than non-metformin group (2 years, 76 % vs. 37 %, $P = 0.022$; 46 % vs. 16 %, $P = 0.045$, respectively). The adjusted Cox proportional hazards model revealed that metformin usage was a significant factor for mortality.
Conclusions: The use of metformin in hepatocellular carcinoma patients receiving radiotherapy was associated with higher overall survival. Therefore, metformin might be useful in the combination treatment for inoperable HCC.

Topic 15: Hepatocellular Carcinoma Treatment

No: 1141

Case matched study of pure laparoscopic left lateral sectionectomy versus open approach for patients with HCC and cirrhosis

Tan To Cheung[1], Kenneth Sh Chok[1], Chung Mau Lo[1]

The University of Hong Kong Surgery Hong Kong-Hong Kong[1]

Introduction: The data on long term outcome of laparoscopic left lateral section resection in patients with HCC and cirrhosis is still limited. The aim of this study is to analyze the survival outcome of laparoscopic left lateral sectionectomy when compared to open approach in patients with HCCs.

Method: Between January 2004 and September 2014, 967 patients had HCC with liver resection done in our center. 25 patients had undergone pure laparoscopic left lateral sectionectomy for hepatocellular carcinoma (HCC). Thirty-five patients who had received open left lateral sectionectomy for HCC were included for comparison. These patients were comparable in terms of Comorbid illness, Child Pugh Grade, hepatitis B or C infection, and preoperative liver function evaluations.
Results: Comparing laparoscopic group to open resection group, the median operation time was 195 min vs 195 min ($P = 0.958$), the median blood loss was 100 ml vs 300 ml ($P = 0.001$). Hospital stay was 5 days in laparoscopic group vs 6 days in the open group ($P = 0.017$). There was no difference between the two groups in terms of complications. The median survival in laparoscopic group was $>$ 115 months vs $>$ 125 months in the open group ($P = 0.785$). 100 % of the patients in our center received pure laparoscopic liver left lateral sectionectomy in recent 2 years.
Conclusion: Laparoscopic left lateral sectionectomy for HCC is a safe and simple procedure associated with less blood loss. It is becoming a standard approach even for patients with liver cirrhosis.

Topic 15: Hepatocellular Carcinoma Treatment

No: 2110

Decreased frequency of NKG2D + CD56DIM NK cells correlates with early recurrence of hbv associated hepatocellular carcinoma

Jian Gao[1], Zhaojun Duan[1], Tao Shen[1], Fengmin Lu[1]

Peking University Health Science Center Department of Microbiology Beijing-China[1]

The clinical significance of dysfunctional natural killer (NK) cells in HCC patients was investigated. In a cohort of HBV related-HCC patients who underwent hepatectomy, we observed the reduced frequencies of peripheral CD56[SUP]dim[/SUP] NK cells in HCC patients, characterized with decreased NKG2D and increased NKG2A on CD56[SUP]dim[/SUP] NK cells. No differences of CD69, CD38, HLA-DR and NKG2C on NK cells were found. Moreover, lower frequencies of circulating NKG2D[SUP] + [/SUP]CD56[SUP]dim[/SUP] NK cells at one month post-surgery were positively associated with early recurrence and shorter overall survival. In contrast, recurrence-free patients always exhibited an enhanced NKG2D expression on CD56[SUP]dim[/SUP] NK cells after surgery, compared with their pre-operative levels. The underlying mechanisms were also explored in this study. Negative correlation between serum TGF-β/sMICA and the frequencies of circulating NKG2D[SUP] + [/SUP]CD56[SUP]dim[/SUP] NK cells was presented in HCC patients, which could be explained by the statistically increase of TGF-β and ADAM9 mRNA levels, as well as MICA in tumor tissues. Consistently, the concentrations of TGF-β and soluble MICA (sMICA) were statistically higher in tumor tissue homogenates than para-tumor and hepatic hemangiomas counterparts. In line with this, our data showed that both TGF-β and sMICA had the capacity to significantly inhibit the expression of NKG2D on CD56[SUP]dim[/SUP] NK cells in vitro. Our study indicated that higher concentrations of TGF-β and sMICA attributed to the down-regulation of NKG2D on CD56[SUP]dim[/SUP] NK cells, and the recovery of higher proportion of circulating NKG2D + CD56[SUP]dim[/SUP] NK cells at one month after resection surgery would predicate a good survival of HCC patients.

Topic 15: Hepatocellular Carcinoma Treatment

No: 1280

Predictive factors for early massive recurrence of hepatocellular carcinoma after radiofrequency ablation

Ju-yeon Cho[1], Moon Seok Choi[1], Won Sohn[1], Geum-youn Gwak[1], Yong-han Paik[1], Joon Hyeok Lee[1], Kwang Cheol Koh[1], Seung Woon Paik[1], Byung Chul Yoo[1]

Samsung Medical Center Internal Medicine Seoul-Korea, South[1]

Background: Radiofrequency ablation(RFA) for small hepatocellular carcinoma(HCC) has demonstrated high local control and good overall survival rate. However, early massive recurrence(recurrence of HCC beyond Milan criteria within 2 years) after RFA disastrously impacts the prognosis of patients with HCC. Therefore, we sought to determine the factors associated with early massive recurrence.
Methods: Between 2006 and 2009, among a total of 1,051 patients newly diagnosed with HCC within 3 cm in size and without vascular invasion or distant metastasis, 477 patients underwent RFA as the initial treatment modality. After excluding 17 patients with incomplete ablation, 438 patients were included. Retrospective analysis of the baseline patient age, sex, etiology of the liver disease, Child-Pugh class, ECOG status, AFP levels, tumor size, number, conspicuity, and proximity to the surface of the liver, colon, diaphragm and vessels was done.
Results: The majority of the patients were male (75.3 %) with a median age of 57 (30-82) years. During the median follow up period of 68.4 months, recurrent HCC was confirmed in 302 (68.9 %) patients. The median time to recurrence was 19.7 months. Early massive recurrence was noted in 27 patients. On univariable analysis to identify the factors associated with early massive recurrence, initial tumor size $\geq$ 20 mm ($P = 0.016$), tumor near the surface ($P = 0.022$) and tumor adjacent to the colon ($P < 0.001$) were statistically significant. Multivariable analysis identified initial tumor size $\geq$ 20 mm (OR = 2.300; 95 % CI 1.024-5.164; $P = 0.044$) and tumor adjacent to the colon (OR = 4.637;95 % CI 1.747-12.312; $P = 0.002$) as independent risk factors predictive of early massive recurrence.
Conclusions: Patients with HCC $\geq$ 20 mm in size or tumor located adjacent to the colon have a significantly higher probability of developing early massive recurrence even after achieving complete RFA.

Topic 15: Hepatocellular Carcinoma Treatment

No: 1370

Impact of hypovascular nodules combined with hypervascular hepatocellular carcinoma diagnosed by computed tomography during arterial portography and hepatic arteriography

Sadahisa Oasawara[1], Tenyu Motoyama[1], Tetsuhiro Chiba[1], Naoya Kanogawa[1], Tomoko Saito[1], Eiichiro Suzuki[1], Yoshihiko Ooka[1], Akinobu Tawada[1], Masaharu Yoshikawa[1], Osamu Yokosuka[1]

Department of Gastroenterology and Nephrology Chiba University, Graduate School of Medicine Chiba-Japan[1]

Aim: Hepatocellular carcinoma (HCC) is known to develop by multistep carcinogenesis from dysplastic nodules to early HCC and to overt hypervascular HCC. The multistep changes in the blood supply have been well studied by computed tomography during arterial

portography (CTAP) and hepatic arteriography (CTHA). However, it is controversial whether hypovascular nodules combined with hypervascular HCC is a prognostic factor and whether treating hypovascular nodules has a survival benefit.
Methods: A total of 170 patients with hypervascular HCC ($\leq$ 3 cm, $\leq$ 3 nodules) who underwent initial local ablation were analyzed retrospectively. All patients received CTAP and CTHA prior to treatment. The overall survival (OS) was compared among Group A (no hypovascular nodules), Group B (hypervascular HCC with hypovascular nodules that were not treated), and Group C (hypervascular HCC with hypovascular nodules treated simultaneously).
Result: OS of Group A (80.1 months; 95 % CI, 55.8–104.3) was significantly longer than that of group B (49.6 months; 95 % CI, 39.4–59.7) ($P < 0.001$). OS of Group C (63.8 months; 95 % CI, 48.8–78.9) was not significantly longer than that of Group B ($P = 0.142$). The Cox proportional-hazards model identified absence of hypovascular nodules as an independent prognostic factor. On the other hand, treating hypovascular nodules at the initial ablation was not an independent prognostic factor.
Conclusion: The prognosis for patients with hypovascular nodules detected during CTAP and CTHA is poor. However, simultaneously treating hypovascular nodules with hypervascular HCC may not influence the prognosis.

Topic 15: Hepatocellular Carcinoma Treatment

No: 2103

Impact of HBV DNA level and antiviral agent on the recurrence of patients after liver resection for hepatitis B virus–related hepatocellular carcinoma

Tae Yoo[1], Kyung-suk Suh[2], Kwang-woong Lee[2], Nam-joon Yi[2], Geun Hong[2], Youngrok Choi[2], Hyeyoung Kim[2], Haewon Lee[2], Min-soo Park[2], Sukwon Suh[2]

Hallym University College of Medicine Surgery Hwaseong-si-Korea, South[1], Seoul National University College of Medicine Surgery Seoul-Korea, South[2]

Aims: To investigate the significance of HBV DNA levels & antiviral agent for predicting recurrence in HCC patients who underwent curative liver resection.
Methods: From 2005 to 2010, 341 HBV-related HCC patients who underwent tumor resection in SNUH were enrolled. HBV DNA levels (pre-, postop. period) & antiviral treatment were analyzed for association with HCC recurrence, together with other clinical variables.
Results: Of the 294 patients, patients(n = 164) with low postop. HBV DNA (1X10[SUP][/SUP]3 IU) had better outcome than those(n = 130) with high load in recurrence (5 yr-Recurrence free survival(RFS) = 43.2 vs. 22.2 %, $P < 0.001$). In terms of Antiviral agents, untreatment group(n = 136) had worse outcome than treatment group(n = 158) in recurrence (5 yr-RFS = 28.3 vs 56.3 %, $P < 0.001$). In subgroup analysis, if the treatment group had high HBV viremia postoperatively, they had good RFS as group with low viremia (5 yr-RFS = 54.1 vs. 58.3 %). But, even if untreated patients had low viremia, they had poor outcomes as untreatment group with high viremia (5-yr RFS = 37.1 vs. 11.9 %). Moreover, whether it is advanced stage(3) or not, low postop. HBV load showed the better recurrence outcome but, antiviral treatment did not present difference in advanced stage. Finally, postop AFP levels as well as well as postop HBV DNA antiviral therapy, tumor size, microvascular invasion were independent risk factors for RFS in multivariated analysis.
Conclusions: Low HBV DNA load and antiviral therapy may be important factors after the curative treatment of HBV-related HCC in terms of tumour recurrence. Therefore, to maintain the low level of HBV viremia, antiviral therapy should be considered after curative treatment of HCC.

Topic 15: Hepatocellular Carcinoma Treatment

No: 2094

Sequential therapy (PEI RFA → PELIT → IVR) for large sized advanced hepatocellular carcinoma

Kazutaka Kurokohchi[1], Masaaki Masuhara[2], Shuko Ishida[2], Kazuo Mizumoto[1], Fuminori Takeda[2], Shingo Yamagata[1], Yutaka Ishibashi[1]

Shimane University Faculty of Medicine General Medicine Izumo-Japan[1], Ohda Municipal Hospital Gastroenterology Ohda-Japan[2]

According to algorithm for the treatment of liver cancer larger than 3 cm in diameter, TAE or resection is first choice of the treatment. However, some cases exist difficult to treat. We've been reporting the effectiveness of the combination therapy of ethanol injection and RFA (PEI-RFA) and ethanol-lipiodol injection therapy (PELIT). Thus, we performed combined sequential therapy PEI-RFA → PELIT → IVR for the treatment of large sized HCC.
Methods: PEI-RFA was performed by injecting the ethanol into the tumor prior to RFA. PELIT was performed by injecting the mixture of ethanol and lipiodol. (3) IVR was performed targeting on the injected lipiodol as a label and miriplatin hydrate and 5FU were injected.
Results: By the first PEI-RFA, large amounts of HCC could be ablated at one time and almost the entire area of mass reduction could be achieved. By adding PELIT and IVR treatment, it was possible to achieve CR in some cases with large sized HCC. Case presentation: A 70 years old woman lived in Shodoshima, Japan admitted with HCC 5 cm in diameter located in the right lobe of the liver seven years ago. Combined sequential therapy PEI-RFA → PELIT → IVR was performed for the treatment. Even now seven years after the treatment, she is healthy without causing recurrence of liver cancer.
Conclusions: Combined PEI-RFA → PELIT → IVR is effective for the treatment of large sized HCC larger than 3 cm in diameter.

Topic 15: Hepatocellular Carcinoma Treatment

No: 1950

Assessment of percutaneous radiofrequency ablation treatment with soloist and leveen needles for hepatocellular carcinoma patients

Hang Dao[1], Diep Luu[1], Long Dao[1]

Bach Mai Hospital Gastroenterology Department Hanoi-Vietnam[1]

Background: Hepatocellular carcinoma (HCC) is a common disease in the world as well as in Vietnam. Radiofrequency ablation (RFA) is a local therapy to destroy tumor tissue by heat.
Study subjects and method: An interventional longitudinal study on HCC patients having $\leq$ 3 tumors with each tumor size $\leq$ 3 cm or one tumor $\leq$ 5 cm; Child Pugh A or B (Barcelona stage A). The needles including Soloist and LeVeen, were chosen suitably to tumor sizes. The study was conducted in Gastroenterology Department of Bach Mai Hospital from November 2011 to June 2014.

Results: 106 patients was performed 320 times of RFA in which 64 were treated only by RFA, 42 patients treated RFA combined with TACE. The procedure was safe with complication rate being 1.24 % treated well by internal medicine. Fever and abdominal pain occurred in 16.5 % ablation times. After 1 month of the first RFA: 96 patients had positive response (90.6 %), after 10 months: 85 % had positive response according to mRECIST criteria. 39 patients (36.8 %) had better clinical response with gain weight and less fatigue. During following-up, 3 patients died due to liver failure(2.8 %), 15 patients had a new lesion (14.2 %), 3 patients had portal vein thrombosis (2.8 %), 1 patient had abdominal lympho node(0.94 %), 1 patient had needle seeding (0.94 %).
Conclusion: Percutaneous RFA with Soloist and Leveen needle chosen suitably for tumor size is a safe technique and effective to improve the quality of life of HCC patient.

Topic 15: Hepatocellular Carcinoma Treatment

No: 1147

Treatment of periductal hepatocellular carcinoma using percutaneous microwave ablation with intraductal cooling of the central bile duct

Ye-fa Yang[1]

Eastern Hepatobiliary Surgery Hospital Eastern Hepatobiliary Intervention Center Shanghai-China[1]

Backgrounds and aims: Periductal hepatocellular carcinoma is contraindicated for ablation therapies. The aim of this article is to report a new method of preventing biliary complication in percutaneous microwave ablation (PMWA) for periductal hepatocellular carcinoma (HCC) by intraductal cooling using percutaneous transhepatic cholangial drainage tube.
Methods: Two patients with HCCs close to main bile duct were treated with PMWA associated with intraductal cooling. The reasonable procedure was explored and the clinical outcome were reported and analysed.
Results: No significant complications were observed. The enhanced MR scan revealed that both patients gained a complete response according to EASL criteria.
Conclusion: A new microinvasive technique that spares the proximal biliary ducts from thermal damage was successfully performed.

Topic 16: Hepatology Research

No: 2151

Splenectomy correlates with increased risk of pyogenic liver abscess a nationwide cohort study in Taiwan

Kuan-fu Liao[1], Shih-wei Lai[2], Chung-yi Lin[3], Chin-ming Lin[3]

Taichung Tzu Chi General Hospital, China Medical University Gastroenterology and Hepatology,graduate Institute of Integrated Medicine Taichung-Taiwan[1], China Medical University Hospital Family Medicine Taichung-Taiwan[2], Taichung Tzu Chi General Hospital Gastroenterology and Hepatology Taichung-Taiwan[3]

Objectives: Little is known about the risk of pyogenic liver abscess in patients with splenectomy. We explore the relationship between splenectomy and pyogenic liver abscess in Taiwan.
Methods: We conducted a nationwide cohort analysis using the hospitalization dataset of the Taiwan National Health Insurance Program. There were 17779 subjects aged 20-84 years who were newly diagnosed with splenectomy in 1998 to 2010 as the splenectomy group and 70855 randomly selected subjects without splenectomy as the non-splenectomy group. Both groups were matched by sex, age, other comorbidities and hospitalization year of receiving splenectomy. The incidence of pyogenic liver abscess at the end of 2011 was measured. The multivariable Cox proportional hazards regression model was used to estimate the hazard ratio (HR) and 95 % confidence interval (CI) for pyogenic liver abscess associated with splenectomy and other comorbidities.
Results: The overall incidence rate was 3.75-fold higher in the splenectomy group than that in the non-splenectomy group (2.15 vs. 0.57 per 1000 person-years, 95 % CI 3.57, 3.94). After controlling for potential confounding factors, the adjusted HR of pyogenic liver abscess was 3.89 in subjects with splenectomy (95 % CI 3.20, 4.72), when compared with subjects without splenectomy. In further analysis, the HR markedly increased to 14.34 for those with splenectomy and comorbid with any one of comorbidities including alcoholism, biliary stone, chronic kidney disease, chronic liver diseases and diabetes mellitus (95 % CI = 10.61, 19.39).
Conclusions: Patients with splenectomy are at an increased hazard of developing pyogenic liver abscess, particularly comorbid with any comorbidity.

Topic 16: Hepatology Research

No: 1812

Use of non anesthesiologist administrated propofol sedation in major endoscopic procedures

Sana Tahir[1], Umar Muhammad[1], Hamama-tu-bushra Khar[1], Kazim Abbas Virk[1], Gul Nisar[1], Burhan-ud-din Rabbani[1]

Holy Family Hospital Center For Liver and Digestive Diseases Rawalpindi-Pakistan[1]

Aim: Sedation during complex endoscopic procedures is essential for efficient execution of procedures and safety and comfort of the patients. The aim of this study was to determine risks related to use of Non-Anesthesiologist-Administrated Propofol (NAAP) sedation during Endoscopic Retrograde Cholangiopancreatography (ERCP) and Endoscopic Ultrasound (EUS).
Meterials and methods: A total of 389 patients went through EUS and ERCP by using NAAP during the year 2014 for the preliminary study at Centre for Liver and Digestive Diseases Rawalpindi, Pakistan. All the patients were given NAAP sedation and sedation levels were kept at mild to moderate level. The primary outcome of the study was risk estimation for sedation related complications.
Results: The EUS procedure was performed on 158 patients, while the ERCP procedure was adopted for 231 patients. The common complication encountered in both procedures was hypoxemia 6.3 % and 3 % in EUS and ERCP, respectively. The rarest complication was cardiac arrhythmia 0.6 % and 0.4 % in EUS and ERCP, respectively. The sedation related complications were seen in 11.99 % in EUS group and 5.1 % in ERCP. The risk estimates were significantly less in low to medium dose group (OR: 0.04; LR: 59.0 $P < 0.01$ for EUS and OR: 0.1; LR: 11.3 $P = 0.001$for ERCP).
Conclusion: The risk of adverse effects was significantly less in low to medium dose of NAAP. Hence, it can be considered safe for major endoscopic procedures with improved comfort level.

Topic 16: Hepatology Research

No: 1777

Increased vitality of primary porcine hepatocyte isolated with n acetylcysteine and formulated collagenase combination

Ji Bao[1], Qiong Wu[1], Yujia Wang[1], Yi Li[1], Yujun Shi[1], Hong Bu[1]

West China Hospital, Sichuan University Laboratory of Pathology Chengdu-China[1]

Successful porcine hepatocyte isolation is crucial for bioartificial liver (BAL) development. Either Liberase or Collagenase NB8 is a formulated collagenase that has been shown to improve the viability of isolated porcine hepatocytes. N-acetylcysteine (NAC) has been shown to improve the viability of isolated human hepatocytes. The aim of this study was to determine the effect of both reagents in combination on the outcome of hepatocyte isolation from porcine liver.

Porcine hepatocytes were isolated by a novel three-step perfusion method from bama mini pig weight from 6.5 ± 0.8 kg. Animals were randomized into three groups: control (no NAC + collagenase IV, n = 5), Li (NAC + Liberase, n = 5), and NB8 (NAC + Collagenase NB8, n = 5). Viability and success were defined as hepatocyte spheroids formation after 24 h of rocked culture. Metabolic function was assessed by means of albumin and urea synthesis.

All procedures harvested hepatocytes successfully. Cells from Li and NB8 groups had almost 100 % viability, significantly higher than control with 85.6 ± 4.7 %. The NB8 group resulted in the higher median viable cell yield of 8.1 × 107 cells/g tissue compared to Li (5.3 × 107 cells/g tissue) or control (3.2 × 107 cells/g tissue). A significant spheroids formation rate benefit was also observed with NB8 compared to the Li or control group (66.7 % vs. 60.2 % vs. 33.3 %, $P < 0.05$). Albumin and urea synthesis were similar or superior in the NB8 and Li groups.

NAC and formulated collagenase improve the porcine hepatocyte isolation with a significantly higher yield of viable cells, especially the Collagenase NB8.

Topic 16: Hepatology Research

No: 1220

Aetiology and outcomes of acute viral hepatitis in type 2 diabetic patients in Dhaka Bangladesh

Riad Md. Moshaed Hossain[1], Mohammad Golam Azam[1], Tareq Mahmud Bhuiyan[1], Md. Mohsin Kabir[1], Md. Nazmul Hoque[1], Md. Abdullah Al Mamoon[1], Indrajit Kumar Datta[1], Md. Anisur Rahman[1]

Birdem General Hospital Department of Ghpd Dhaka-Bangladesh[1]

Background: Diabetes and its complications are major causes of morbidity and mortality throughout the world. It has been observed that several patients having prolonged or complicated course of acute viral hepatitis (AVH) have underlying diabetes and this may be due to impaired hepatocyte regenerating capacity.
Materials and methods: In this study a total of 60 patients with AVH admitted at gastrointestinal, hepatobiliary and pancreatic disorders (GHPD) department of BIRDEM General Hospital were included. of them, 30 patients were diabetic (group A) and 30 patients were non-diabetic (group B). We compared the outcomes of AVH considering clinical improvement and biochemical parameters among these two groups of patients.
Results: Aetiology of AVH of all cases was hepatitis E (80 %), hepatitis B (16 %) and hepatitis A (4 %). Among two groups (group A vs group B respectively); age in years (mean ± SD) was 47.8 ± 10.8 vs 30.7 ± 11.0, sex was (M/F) 18/12 vs 25/5; baseline serum bilirubin mg/dl (mean ± SEM) 15.6 ± 6.2 vs 9.8 ± 5.5 ($P = 0.001$), serum ALT mg/dl (mean ± SEM) 735.5 ± 92.2 vs 1491.3 ± 189.0 ($P = 0.01$) and serum AST mg/dl (mean ± SEM) 567.9 ± 66.9 vs 1024.8 ± 209.2 ($P = 0.036$) respectively. Mean duration of hospital course in days was 17.9 ± 8.2 vs 11.0 ± 5.1 ($P < 0.001$). Subacute hepatic failure developed among 5 (16.6 %) cases of group A and only 1 (3.3 %) case in group B. Interestingly, 3 (10.0 %) cases of group A developed acute pancreatitis who recovered with conservative treatment.
Conclusion: Complications of AVH in diabetic patients were more than non diabetics. Rational and appropriate management in diabetic patients may reduce the morbidity and mortality rate.

Topic 16: Hepatology Research

No: 1533

Detailed structural quantification of hepatic cirrhosis progression and regression

Hailin Liu[1], Xiaoli Huang[1], Chuwen Lin[1], Yan Wang[2]

Southern Medical University Department of Hepatobiliary Surgery, Zhujiang Hospital Guangzhou-China[1], Southern Medical University State Key Laboratory of Organ Failure Research, Guangdong Provincial Key Laboratory of Viral Hepatitis Research, Dept. Infectious Diseases, Nanfang Hos Guangzhou-China[2]

Aim: To identify details in change of fibrosis structure in the dynamic process of cirrhosis.
Method: We used a rat model with CCl4-induced cirrhosis. Liver specimens (n = 3 ~ 5) were collected at 0, 6, 8 and 12 wks with treatment, and 2, 4, 8 wks after treatment, respectively. Samples' procession, imaging and analysis were performed as reported before.
Result: During the pathogenesis process of cirrhosis (0 ~ 12 wk), speeds of changes (meanT1/meanT2/wk) in values of all structural parameters were illustrated in Fig. 1; the most dramatic change occurred to sinusoid, e.g. the highest ratio of change in FCF length reached to 845.88 ($P = 0.00$). At developmental stage (0 ~ 6 wk), the most significant changes happened to septal bridge; top 2 parameters with the highest ratio of change are crosslink number of septa collagen fiber (SCF) (67.44, $P = 0.01$) and long SCF number (65.04, $P = 0.03$). At progressing stage (6 ~ 12 wk), the most significant changes mainly located in sinusoidal space; top 2 are number of sinusoidal CF (FCF) (6.12, $P = 0.03$) and FCF crosslink (3.90, $P = 0.00$). During cirrhotic regression, at early 2 and 4 wks, the highest ratio of decrease happened to portal location; then it changed to septa at wk 8; changes happened fast at wk 2. Although at the same stage of Metavir F4, there was significant decrease in the values of almost all structural parameters of regressing cirrhosis versus progressing cirrhosis ($P < 0.05$).
Conclusion: The present model showed that cirrhosis had different velocities and patterns of changes during its stages of progression or regression.

Topic 16: Hepatology Research

No: 1803

Correlation between serum alanine amino transferase and liver stiffness measurement using transient elastography

Sana Tahir[1], Umar Muhammad[1], Bushra Khar[1], Kazim Abbas Virk[1], Noor-ul-ain Toor[1], Iqra Ashraf[1], Fatima Majid[1], Gul Nisar[1]

Holy Family Hospital Center For Liver and Digestive Diseases Rawalpindi-Pakistan[1]

Aim: The Transient Elastography (TE) is a non-invasive technique that measures the stiffness of the liver tissue by shear velocity (expressed in KPa) directly related to it. It has a good role in differentiation of mild to significant Liver fibrosis. There are various serum indices which correlate significantly with liver stiffness measurement (LSM) including the AST/ALT ratio. Based on its cost-effectiveness it can be beneficial to find a correlation between Serum Alanine amino Transferase levels and LSM which is the aim of the study.
Materials and methods: Total 275 patients of different etiologies were enrolled in the study. After informed consent their LSM measured with the help of transient elastography using a fibro scan machine, at the same time their serum ALT levels were assessed. The study was carried out in center for liver and digestive diseases, Holy Family Hospital, Rawalpindi.
Results: Out of 275 patients 55.6 % were males and 44.4 % were females. 68 % of the patients are of Hepatitis C etiology. The serum ALT levels and LSM were 70.4 ± 7.8 and 16.6 ± 2.1 respectively. The data was positively skewed hence the data transformation was dine to log 10. The Pearson coefficient was calculated to be $r = 0.53$, $P = 0.38$. Thus, no significant correlation was detected.
Conclusion: The Serum Alanine amino Transferase levels are not significantly correlated with Liver stiffness measurement.

Topic 16: Hepatology Research

No: 2006

Increases of resident hepatic macrophages and circulation derived monocytes in the livers of patients with chronic liver diseases

C. Wu[1], R. Huang[2], H.Y. Wu[3], R. Su[4], G.Y. Wang[1], Y. Liu[5], X.M. Yan[1], Y.L. Xiong[1], J. Xia[1]

Nanjing Drum Tower Hospital, Nanjing University Medical School Department of Infectious Diseases Nanjing-China[1], Nanjing Drum Tower Hospital Clinical College of Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine Department of Infectious Diseases Nanjing-China[2], Nanjing Drum Tower Hospital, Nanjing University Medical School Department of Pathology Nanjing-China[3], Nanjing Drum Tower Hospital, Nanjing Medical University Department of Infectious Diseases Nanjing-China[4], Nanjing Drum Tower Hospital, Nanjing University Medical School Department of Laboratory Medicine Nanjing-China[5]

Aim: To investigate the contribution of resident hepatic macrophages and circulation-derived monocytes to the liver inflammation and fibrosis in chronic liver diseases (CLD).
Methods: Ninety-three patients with different types of CLD including chronic hepatitis B virus infection (CHB), autoimmune hepatitis (AIH), alcoholic liver disease (ALD) and primary biliary cirrhosis (PBC) were included. Twenty-three normal liver tissues (HC) were included as controls. The degrees of hepatic inflammation and fibrosis of liver fibrosis in patients were graded using the modified histology activity index described by Scheuer. Resident hepatic macrophages (CD68 +) and circulation-derived monocytes (MAC387 +) were determined by immunohistochemistry in the paraffin-embedded liver tissues.
Results: Resident hepatic CD68 + macrophages and MAC387 + monocytes were significantly increased in the liver tissues of CLD patients compared to normal tissues ($P < 0.001$ and $P < 0.01$, respectively). In the different etiologies of CLD patients, the numbers of resident hepatic CD68 + macrophages and MAC387 + monocytes were all significantly increased (all $P < 0.01$). CLD patients with higher G scores had more CD68 + macrophages and MAC387 + monocytes in their livers than those with lower G scores ($P < 0.05$). Significantly more MAC387 + monocytes were found in the liver tissues of CLD patients with higher S scores than those with lower S scores ($P < 0.05$). CD68 + macrophage numbers were positively correlated with serum ALT ($r = 0.284$, $P = 0.007$), AST ($r = 0.350$, $P = 0.001$) and total bilirubin ($r = 0.254$, $P = 0.016$) levels. MAC387 + monocyte numbers were negatively correlated with serum albumin ($r = -0.258$, $P = 0.014$).
Conclusions: Resident hepatic CD68 + macrophages and circulation-derived MAC387 + monocytes may play a pathological role in exacerbating chronic liver inflammation and fibrosis in CLD.

Topic 16: Hepatology Research

No: 1137

Interaction of myeloid derived suppressor cells and dendritic cells in an animal model of chronic hepatitis B virus infection

Sheikh Mohammad Fazle Akbar[1], Shiyi Chen[2], Masanori Abe[3], Mamun Al-mahtab[4], Yoichi Hiasa[3]

Toshiba General Hospital Department of Medical Sciences Tokyo-Japan[1], The Second Affiliated Hospital of Department of Endocrinology and Metabology Guangdong-China[2], Ehime University Graduate School of Medicine Department of Gastroenterology and Metabology Toon-Japan[3], Bnagabandhu Sheikh Mujib Medical University Department of Hepatology Dhaka-Bangladesh[4]

Aim: Although cells of myeloid origin (classical macrophages and monocytes) stimulate immunity, a new subset of myeloid cells, myeloid-derived suppressor cells (MDSC) suppress immunity in tumor-bearing hosts. We explored mechanisms underlying immune suppression of MDSC in HBV transgenic mice (TM) by exploring MDSC/dendritic cells (DC) interactions.
Methods: HBV TM expressing HBV DNA, HBsAg, and HBeAg were used as an animal model of HBV carrier state along with age and sex-matched normal C57BL/6 mice as controls. Two types of myeloid cells, MDSC (co-expressing CD11b and GR1, CD11b + GR1 +) and immunogenic myeloid cells (expressing only CD11b, but not GR1, CD11b + GR1−) were also isolated from liver and spleen by dual-color flow cytometry and subjected to multiple functional analyses.
Results: The frequencies of MDSC in the liver of HBV TM were significantly higher than those of control C57BL/6 mice ($P < 0.05$). MDSC from HBV TM suppressed T cell proliferation in allogenic MLR and HBsAg-specific T cell proliferation ($P < 0.05$), whereas, non-MDSC myeloid cells had exacerbated immune modulatory capacity ($P < 0.05$). DC isolated from MDSC/DC co-culture showed impaired capacities to stimulate HBsAg-specific T lymphocytes ($P < 0.05$), induced decreased levels of proinflammatory cytokines ($P < 0.05$), and expressed significantly lower levels of immunogenic cell surface markers ($P < 0.05$).
Conclusions: This study has shown immune suppression by MDSC may be mediated by its interaction with DC in murine model of HBV carrier state. Both MDSC and DC may be target for immune therapy in chronic HBV infection.

Topic 16: Hepatology Research

No: 2181

Testosterone levels in different chronic diffuse liver diseases

Iulianna Lupasco[1], Vlada-tatiana Dumbrava[2], Inna Venger[1], Natalia Taran[1], Elena Chirvas[1]

State University of Medicine and Pharmacy "n.testemitanu" Scientific Laboratory of Gastroenterology Chisinau-Moldova[1], State University of Medicine and Pharmacy "n.testemitanu" Clinics of Gastroenterology, Department of Internal Medicine Chisinau-Moldova[2]

Introduction: Chronic diffuse liver diseases (CDDL), especially chronic hepatitis (CH) and liver cirrhosis (LC), is a major problem of contemporary hepatology.

The CDLD medical and social importance is high due to the spread of disease among the young population of working age, and in the case of disease progression can lead to disability. Timely diagnosing of sexual hormones metabolic disorders that occur in liver pathology is necessary due to their influence on the course of the disease and quality of life of patients.

Aim: To study the testosterone levels in different CDLD.

Materials and methods: We have been evaluated 595 patients, of whom with CH—26,72 %, hepatopathy—51,60 %, fatty liver—18,32 %, LC—3,36 %. The control group consisted of 133 healthy individuals.

Results: The lowest testosterone level was found in patients with liver steatosis (4,86 ± 0,23 nmol/l) ($P < 0,01$), in LC (5,79 ± 1,25 nmol/l) ($P < 0,05$) and to a lesser extent—in hepatopathies (6,55 ± 0,34 nmol/l) ($P < 0,01$) compared to patients with chronic hepatitis (8,70 ± 0,23 nmol/l) ($P < 0,01$) and control data (8, 34 ± 0,19 nmol/l) ($P < 0,01$).

In overweight patients with CH testosterone data where lower (6,45 ± 0,27 nmol/l) in comparison to patients with normal weight (10,02 ± 0,77 nmol/l) ($P < 0,01$).

Regardless of the CDLD form testosterone levels were higher in men than in women.

Conclusion: The presented data testifies that level of testosterone is influenced by liver disease form and body weight.

Topic 16: Hepatology Research

No: 2016

Intrahepatic neurons changes after liver transplantation and their associations with a variety of liver diseases

Kei Mizuno[1], Keigo Murakami[2], Kyoko Tomita[1], Tomohiro Katsumi[1], Chikako Sato[1], Yuko Nishise[1], Kazuo Okumoto[1], Hisayoshi Watanabe[1], Takafumi Saito[1], Naoki Kawagishi[3], Yoshiyuki Ueno[1]

Yamagata University Gastroenterology Yamagata-Japan[1], Tohoku University Hospital Pathology Sendai-Japan[2], Tohoku University Hospital Transplant Surgery Sendai-Japan[3]

Background and aim: It is known that liver metabolism is regulated by a 'metabolic highway' mediated by the autonomic nervous system. The aim of the present study was to examine the role of the autonomic nervous system in the liver, and to clarify the association between these nerves and a variety of liver diseases.

Methods: As neuron markers, we evaluated changes in S-100 or N-CAM immunostaining over time (n = 90). Specimens of normal liver were used as immunostaining controls (n = 5). Also, we evaluated a diverse group of liver diseases (NASH n = 18, chronic hepatitis B n = 10, chronic hepatitis C n = 10) to evaluate whether these diseases show differences in the ratio of positivity for neuron markers.

Results: In normal liver, the S-100 positivity ratio was 28.57, 50.91 and 85.19 % in small, medium and large portal areas, respectively. These ratios decreased with time after liver transplantation. Similarly, in the clinical samples from a variety of liver diseases, the corresponding S-100 positivity ratios were 23.44, 66.67 and 92.31 % in NASH, and 55.88, 80.65 and 100 % in viral hepatitis, respectively.

Summary and conclusion: In human liver, the presence of autonomic neurons depends on the size of the accompanying portal tract, and the numbers of these neurons decrease with time after liver transplantation. Also, inflammation induces an increase of neurons in the portal tracts. However, there were differences in the proportion of neurons according to the nature of the underlying liver diseases, especially in metabolic diseases such as NASH.

Topic 16: Hepatology Research

No: 1145

Research on R2*map of tracking bone mesenchymal stemcells labeled by super para magnetic iron oxide in rat liver

Xiao An[1]

Shanghai First People Neoplasms and Interventional Radiology Shanghai-China[1]

Objectives: To track rat bone mesenchymal stemcells (BMSCs) labeled by new super para-maganetic iron oxide(SPIO) which be injected into rat liver by MR R2*map technique.

Methods: Murine BMSCs were established from SD rat by flushing femurs and tibias. After osteogenesis, chondrogenesis and adipogenesis differentiation, BMSCs CD surface markers were identified by Flow Cytometry. New SPIO (Polyethyleneimine-Coated Magnetic Iron Oxide Nanoparticles, Fe3O4 − PEI NPs) were synthesized by a modified hydrothermal method. Incubated with medium containing Fe3O4 − PEI NPs for 4 h, the labeled stemcells were injected into rat mesenteric vein during surgery. GE 3.0T Signa TwinSpeed MR was used to scan the rats with multi-echo fast gradient echo sequence. Observation time were before administration to 12 h later and R2* value of regions of interest were measured.

Results: Signal intensity of rats liver decreased significantly on T2*-WI map after injection. With time passing during 12 h post-injection the enhancement of signal intensity was shown a curved line and little variant from different areas in the liver. While before and after Fe3O4 − PEI NPs administered R2* value which statistical significance level were high could provide more sensitive quantitative data. Liver autopsy displayed labeled BMSCs relatively concentrated at the periphery of liver.

Conclusion: R2* imaging were useful in detecting Fe3O4 − PEI NPs labeled BMSCs in rat liver, but perfer to delineate approximate scope rather than pinpoint small target area. Meanwhile successful MR scan is a good attempt to explore fractional factorial design of the project and suitable microenvironment for clinical applications of stemcell transplantation.

Topic 16: Hepatology Research

No: 1430

Differential hepatic expression of p62 between autoimmune hepatitis and nonalcoholic steatohepatitis

Kazuhisa Nakashima[1], Yasuji Komorizono[1], Katumi Sako[1], Toshihiko Shibatou[1]

Nanpuh Hepatology Kagoshima-Japan[1]

Background and aims: p62 has been identified as a major Mallory body component in nonalcoholic steatohepatitis (NASH). At present, the hepatic expression of p62 in patients with autoimmune hepatitis (AIH) is still unknown. This study aimed to clarify the difference in hepatic p62 expression between AIH and NASH.
Methods: We retrospectively identified and enrolled 53 biopsy-proven patients with AIH or NASH in the study. Patients with AIH met the simplified criteria for the diagnosis of AIH according to the International Autoimmune Hepatitis Group. The diagnosis of NASH was made by histological findings according to the Brunt grading and staging system. Patients with AIH were 4 men and 37 women; patients with NASH, 12 women. We compared the hepatic expression of p62 between the two groups by immunohistochemical analysis.
Results: Among patients with AIH, the histological fibrosis score was F0 in 24 patients, F1 in 15, F2 in 1, F3 in 1, and F4 in 0, and the activity score was A0 in 14 patients, A1 in 24, and A2 in 3. Among patients with NASH, 3 were classified as grade 1, 2 as grade 2, and 7 as grade 3, and 8 were classified as stage I and 4 as stage II, by Brunt's classification. Readily detectable staining of p62 was observed in 75 % (9/12) of NASH patients and 22 % (9/41) of AIH patients ($P = 0.001$).
Conclusion: The hepatic expression of p62 differed between AIH and NASH. p62 may play an important role in hepatocarcinogenesis in chronic liver diseases.

Topic 16: Hepatology Research

No: 2111

Correlation between hepatocyte progenitor cell (HPC) with haematopoietic stem cell (HSC) based on metavir degree of liver of patients with chronic hepatitis B

Okto Dewantoro[1], Ari Fahrial Syam[2], andry Sanityoso Sulaiman[3], Rino A. Gani[3], Irsan Hasan[3], C Rinaldi Lesmana[3], Juferdy Kurniawan[3], Suhendro Suwarto[4], Ening Krisnuhoni[5]

University of Indonesia Faculty of Medicine Internal Medicine Jakarta-Indonesia[1], University of Indonesia Faculty of Medicine Gastroenterology Jakarta-Indonesia[2], University of Indonesia Faculty of Medicine Hepatology Jakarta-Indonesia[3], University of Indonesia Faculty of Medicine Tropic and Infectious Disease Jakarta-Indonesia[4], University of Indonesia Faculty of Medicine Pathology of Anatomy Jakarta-Indonesia[5]

Background: Hepatocyte progenitor Cell (HPC) is a stem cell from the liver that will arise in the event of chronic liver damage such as chronic hepatitis B to cirrhosis of the liver. HPC as an active attempt to regenerate liver cells followed by migration of Haematopoietic Stem Cell (HSC) to liver cells with the goal of helping the regeneration of liver cells.
Aims: This study aims to determine the correlation between HPC and HSC as the basis for the conduct of stem cell therapy in liver cirrhosis by using the HPC and HSC.
Methods: Patients with chronic hepatitis B who meet the inclusion and exclusion criteria and had undergone liver biopsies examined paraffin blocks which divided by degrees of metavir as mild-moderate and severe. Then performed immunohistochemical staining for HPC with CK-19 and HSC with CD34 +. After calculation the amount of HPC and HSC, then analyzed the data.
Results: There were 17 patients with mild-moderate fibrosis and 13 with severe fibrosis, and 21 with mild-moderate nekroinflamasi and 9 with severe nekroinflamasi. In mild-moderate and severe fibrosis obtained mean significant HPC with $P = 0.003$ and mean significant HSC with $P = 0.001$. In nekroinflamasi obtained mean mild-moderate and severe HPC significant with $P = 0.014$ and the mean HSC significant with $P = 0.012$. There is a statistically significant correlation between HPC and HSC on mild-moderate fibrosis with $r = 0.673$ and $P = 0.003$.
Conclusions: There is a statistically significant correlation between HPC and HSC on mild-moderate fibrosis with $r = 0.672$ and $P = 0.003$.

Topic 16: Hepatology Research

No: 2234

Budd chiari syndrome in a young patient with systemic lupus erythematosus

Ramin Farajpour[1], Ali Ghavidel[2], Mohammadhosein Soomi[2], Shiva Farajpour[3], Mehdi Farhoodi[3]

Student Research Committee(src) Medical Faculty Tabriz-Iran[1], Vice Chancellor For Research and Technology Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences Tabriz-Iran[2], Nsrc(neurosciense Researche Center Nsrc(neurosciense Researche Center Tabriz-Iran[3]

Hepatic venous outflow block or Budd-Chiari syndrome is a severe liver disease with a three year survival rate of %50. Several conditions have been implicated as a cause of Budd- Chiari syndrome, including myeloproliferative disorders, paroxysmal nocturnal haemoglobinuria, the presence of lupus anticoagulant, oral contraceptives, pregnancy, and others. In a small number of cases Budd-Chiari syndrome is associated with the presence of lupus anticoagulant Anticardiolipin antibodies are similar to lupus anticoagulant antiphospholipid antibodies, which have been described in patients with recurrent arterial and venous thrombosis, thrombocytopenia, fetal loss or miscarriage.
Case report: The case of a 22 year old woman is reported with Budd-Chiari syndrome in whom lupus anticoagulant. and anticardiolipin antibodies were shown; 9 months after diagnosis of SLE treatment with stroids admitted with GI problems,abdominal pain and ascites and treated oral anticoagulants induced a considerable improvement. This treatment was continued after one year; but interruption was followed by redevelopment of ascites. Further treatment with anticoagulants was continued for five years with noticeable improvement. In conclusion patients with Budd-Chiari syndrome should be tested for lupus anticoagulants and anticardiolipin antibodies, Budd-Chiari syndrome resulting from this cause may have a good response to treatment with oral anticoagulants; this treatment should be maintained permanently, and pregnancy in such patients may initiate serious difficulties.the condition of the patient at follow-up was good.
Results: Patients with Budd-Chiari syndrome should be tested for lupus anticoagulants and anticardiolipin antibodies.

Topic 16: Hepatology Research

No: 1802

Predictibility of previous interferon therapy for outcome of hepatocellular carcinoma in hepatitis C related cirrhotic patients

Sana Tahir[1], Umar Muhammad[1], Kazim Abbas Virk[1], Bushra Khar[1], Saima Ambreen[1]

Holy Family Hospital Center For Liver and Digestive Diseases Islamabad-Pakistan[1]

Aim: Hepatocellular carcinoma is the fifth most common malignant disease and the third leading cause of cancer related death worldwide. In Pakistan patients with HCC are mostly having hepatitis C related cirrhosis. The interferon therapy alters the natural history of chronic hepatitis C. It is still unknown whether interferon therapy can predict or alter the outcome in hepatocellular carcinoma in Hepatitis C related cirrhotic patients.The objective of this study is to determine the predictability of previous interferon therapy for outcome of hepatocellular carcinoma.
Materials and methods: A prospective study was conducted at research clinic for hepatocellular carcinoma, center for liver and digestive diseases, Holy Family Hospital, Rawalpindi from June 2010 to December 2013. The data recorded of total of 325 patients as they were inquired about previous interferon therapy. They were followed for variable period of time for the outcome. The primary outcome was the survival of the patients.
Results: Out of 325 patients the 94 lost follow up at some point during the study. At the end of three year 61.5 % (n = 200) patients were dead and 9.5 % (n = 31) were alive. 15.9 % took interferon therapy out of which 4.6 % were non responders, 9.5 % were relapses and 0.6 % was non-compliant. The binary logistic regression showed that previous interferon therapy is not a strong predictor of outcome in Hepatitis C related hepatocellular carcinoma probably because of other co-variates. (CI 95 % $P = 0.42$ OR: 0.8).
Conclusion: The previous interferon therapy is not a predictor of outcome of hepatocellular carcinoma patients in Hepatitis C related cirrhotic patients.

Topic 16: Hepatology Research

No: 1842

Shearwave elastography assessment of liver fibrosis stage versus type of viral hepatitis body mass index and co morbidities

Binafsha Manzoor Syed[1], Bikha Ram Devrajani[2], Noshad A. Shaikh[3], Jawaid Naeem Qureshi[3], Sanam Maree[2], Zainab Memon[1]

Liaquat University of Medical & Health Sciences Medical Research Centre Jamshoro-Pakistan[1], Liaquat University of Medical & Health Sciences Medicine Jamshoro-Pakistan[2], Liaquat University of Medical & Health Sciences Surgery Jamshoro-Pakistan[3]

Introduction: Viral hepatitis is a major risk factor for development of liver fibrosis. There are also co-morbidities such as diabetes and high cholesterol may have some influence on the same. This study aims to assess association of the co-morbid conditions with the viral hepatitis type in terms of the liver fibrosis stage assessed on shearwave elastography.
Methods: All patient with a confirmed diagnosis of viral hepatitis came to the shearwave elastography unit during a period of six months (i.e. April—October 2014) were included. They were grouped into eight categories including HBV, HCV, HDV, HBV + HCV, HBV + HDV, HBV + HCV + HDV and HCV + HDV. All patients were non responders to conventional therapy. Their liver fibrosis was assessed by using Supersonic imagine Aixplorer, shearwave elastography system. The liver fibrosis stage was defined according to metavir scoring system. Body mass index was categorized into three classes normal, heavy weight and obese.
Results: A total of 374 patients had confirmed viral hepatitis, out of which 61.4 % (N = 227) had no co-morbid condition, 35.7 %had metabolic syndrome and 3 % had multiple problems other than metabolic syndrome. Among viral hepatitis groups, D virus was associated with high stage of fibrosis. Metabolic syndrome regardless of the type of viral hepatitis showed significant association with advance stage of liver fibrosis ($P = 0.01$). However body mass index does not produce any effect on the stage of liver fibrosis.
Conclusion: This study suggests that obesity does not not directly influence liver fibrosis stage however metabolic syndrome further worsen liver damage caused by the viral hepatitis

Topic 16: Hepatology Research

No: 2170

Frequency of B catenin mutations in patients with hepatocellular carcinoma associated with hepatitis C virus infection

Hikmet Akkız[1], Macit Sandıkçı[1], Aynur Bekar[1], Süleyman Bayram[2], Ilhan Tuncer[3], Sedef Kuran[1], Oğuz Üsküdar[1], Ümit Karaoğullarından[1]

University of Çukurova Department of Gastroenterology Adana-Turkey[1], Adıyaman University, School of Health Department of Nursing Adıyaman-Turkey[2], University of Çukurova Department of Pathology Adana-Turkey[3]

Aim: Hepatocellular carcinoma is one of the most common fatal cancers worldwide. Hepatitis B (HBV) and hepatitis C virus (HCV) infections have been identified as major risk factors. However, the molecular mechanisms underlying their development are still poorly understood. Recently β-catenin, one of the key components of Wnt signaling pathway, has been implicated in hepatocellular carcinogenesis.
Material and method: To determine the clinically significance of β-catenin in hepatocellular carcinoma we performed mutational analysis at exon 3 of the gene and analysed their clinicopathologic and prognostic significance in 35 patients with HCC.
Results: By single-strand conformation polymorphism (SSCP) followed by direct DNA sequencing, somatic mutations of β-catenin gene were detected in 14 (40 %) HCC patients with HCV infection. All mutations were single nucleotid substitutions occurring at different putative phosphorylation sites of serine/theronine of codon 32, 33, 37, 41 and codon 45. We also analyzed adjacent cirrhotic, non-tumorous liver. β-catenin mutations were not determined in the adjacent tissues. HCV RNA was tested by PCR and positive in all cases. All patients were negative for HBsAg.
Conclusions: In conclusion, these results suggest that activation of Wnt signaling pathway by β-catenin mutation contributes significantly to the hepatocellular carcinogenesis associated with HCV infection.

Topic 16: Hepatology Research

No: 1090

Hepatic impairment in scrub typhus in sub himalayan region of north India. Focus on outcome and differentiating from other causes

Dhiraj Kapoor[1], Vishnu Agarwal[2], Shivani Sandhu[2]

R.p.Govt Medical College Deptt. of Medicine Dharamshala-India[1], R.p.Govt Medical College Deptt of Medicine Dharamshala-India[2]

Background: Scrub typhus is a potentially fatal infectious disease but if recognized and treated early leads to dramatic recovery. There is little attention given to hepatic impairment in the adults with scrub typhus.
Methods: It was a cross sectional observational study.184 adult patients with scrub typhus were reviewed. The patients were divided into three groups, normal, mild, and moderate to severe groups based on the elevated serum ALT and/or total bilirubin levels.
Results: 174 patients (94.5 %) had abnormal liver function. AST more than ALT was seen in 82.6 % of patients. Among the patients with hepatic impairment 42 cases (22.8 %), 132 cases (71.7 %) had mild, moderate to severe hepatic damage respectively. The incidence of new onset of renal dysfunction during hospital stay with no evidence of renal disease prior to hospitalization was 19.04 % in the mild hepatic impairment group,and 25.75 % in the moderate to severe hepatic impairment group ($P = 0.00$). Additionally, the patients with moderate to severe hepatic impairment ($n = 132$) as compared to mild impairment ($n = 42$) had higher incidences of episodes of thrombocytopenia (42.42 % vs. 19.04 %, $P = 0.00$), hypoalbuminemia (84.8 % vs. 85.8 %, $P = 0.00$) and hyponatremia in (50 % vs 23.8 %, $P = 0.00$).
Conclusions: The degree of hepatic impairment induced by scrub typhus is associated with renal dysfunction.The differentiation is by higher levels of AST and presence of thrombocytopenia,hypoalbuminemia,and hyponatremia.

Topic 16: Hepatology Research

No: 1754

SRBAL treatment inhibits amatoxin and endotoxin induced fulminant hepatic failure in rhesus monkey model

Ji Bao[1], Yi Li[1], Yujia Wang[1], Qiong Wu[1], Xiujuan Wu[2], Yujun Shi[1], Bruce Amiot[3], Scott Nyberg[4], Hong Bu[1]

West China Hospital, Sichuan University Laboratory of Pathology Chengdu-China[1], Luzhou Medical College Department of Clinical Medicine Luzhou-China[2], Mayo Clinic Laboratory of Artificial Liver Rochester-United States[3], Mayo Clinic Division of Transplantation Surgery Rochester-United States[4]

High mortality rate of fulminant hepatic failure (FHF) is due to massive death of liver cells with limited therapeutic options. A novel supportive therapy, the Spheroid Reservoir Bioartificial Liver (SRBAL) containing 100 gram porcine primary hepatocyte aggregates (spheroids) was developed. The spheroids were engineered via rocked high-density suspension culture. Once formed, spheroids are placed in a continuous perfusion bioreactor, which provides functionality to the device.

The SRBAL was recently evaluated in an primate model of α-AMA and LPS induced FHF. Rhesus monkeys were randomized into three treatment groups: no therapy ($n = 3$), no cell device therapy ($n = 3$), and SRBAL therapy ($n = 3$). SRBAL treatment was 6 h in duration after toxin administration 12 h.

All treatment procedures were completed successfully without any adverse reaction.All samples presented negative PERV DNA and RT activity. A significant survival benefit was observed with SRBAL compared to the two control groups (100 % vs. 0 % vs. 0 % at 60 h after toxin administration, $P < 0.001$). Animals treated with the SRBAL maintained stable plasma ammonia levels during treatment compared to control animals. Relatively low plasma concentrations of S-100β protein, as a marker of astrocytic damage, from FHF monkeys during SRBAL therapy were noted. SRBAL therapy can prevent irreversible brain damage from hepatic encephalopathy via reduce the ICP peak. The clinical symptoms such as acratia,anorexia and abdominal distension were improved and recovered at 5 days after SRBAL treatment.

Results of this pivotal preclinical study demonstrate that the SRBAL improved survival in a xenogeneic model of amatoxin and endotoxin induced FHF.

Topic 17: Liver Cirrhosis and Complications

No: 1299

Electrolytes concentration in cirrhosis and chronic liver disease

Dr. Saira Baloch[1], Prof. Dr. Bikha Ram Devrajani[1], Dr. Mohsin Ali Baloch[2]

Medical Research Center, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan. Medical Research Center, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan. Jamshoro-Pakistan[1], Faculty of Pharmacy University of Sindh, Jamshoro, Pakistan Faculty of Pharmacy University of Sindh, Jamshoro, Pakistan Jamshoro-Pakistan[2]

Abstract: Serum electrolytes are severity independent predictors in patients with cirrhosis and chronic liver disease. The aim of this study was to evaluate the concentration of electrolytes in cirrhosis and chronic liver disease as compared with the healthy control subjects. This cross sectional study included 80 patients with cirrhosis and chronic liver disease admitted into the department of Medicine L.U.H, Hospital from April 2013 to April 2014, patients were enroll and full written consent, patients were included in the study on the basis of diagnosis of cirrhosis and chronic liver disease confirmed by clinical, biochemical, and ultrasonographic findings. Results showed a significance appearance of hyponatremia in cirrhotic patients when compared with the healthy group and a significance hyperkalemia in chronic liver patients when compared with healthy group. A strong correlation between the type of liver disease and the concentration of electrolytes indicates that cirrhosis liver lead to hyponatremia, and chronic liver leads to hyperkalemia. However, more studies are needed to elucidate the perception of causality correlation along with severity of liver diseases and electrolyte disorder.
Corresponding Author:
Dr. Saira Baloch saira.baloch@lumhs.edu.pk
Assistant Professor
Medical Research Center,
Liaquat University of Medical and Health Sciences,
Jamshoro, Pakistan.

Topic 17: Liver Cirrhosis and Complications

No: 1023

The effects of electro acupuncture on the muscle cramps of liver cirrhosis patients pilot study

Chang Hyeong Lee[1], Seung Mo Kim[2], Byung Seok Kim[1], Han Na Choi[1], Hyun Hee Kim[1], Min A Kwak[2], Jung Chul Seo[3], Ji Suk Kim[1]

Dept of Gastroenterology and Hepatology Catholic University of Daegu School of Medicine Daegu-Korea, South[1], Internal Medicine Daegu Hanny University Daegu-Korea, South[2], Cimi Daegu-Korea, South[3]

Background/aim: Muscle cramps mean involuntary painful muscle contractions intermittently occured in liver cirrhosis patients. The purpose of this clinical trial is to investigate the effects of electro-acupuncture on muscle cramps of liver cirrhosis patients.
Methods: 16 liver cirrhosis patients with muscle cramps more than once a week regardless of body portion were treated by electro-acupuncture at 16 acupuncture points three times a week for four weeks (12 times in total). The electrical stimulation was a frequency of 100 Hz. Frequency of the muscle cramps were measured by questionnaire of subjective symptoms. We analyzed the frequency of muscle cramps 4 times(screening and 2, 4, 8 weeks after starting electro-acupuncture).
Results: 14 patients have completed the clinical trial. Two patients have dropped due to personal considerations without any side effect of electro-acupuncture. The number of patients have occurred muscle cramps 'more than once a week' were reduced to 14, 8, 4, 2 at screening, 2, 4, 8 weeks after starting acupuncture(table 1, $P < 0.000$). We could not find any deterioration of liver function and complications of cirrhosis in all patients. We also could not find any adverse events related to electro-acupuncture during the entire clinical trial.
Conclusions: This study suggest that electro-acupuncture treatment will be beneficial for liver cirrhosis patients to improve muscle cramps. Electro-acupuncture is thought to be a safe and efficacious treatment for cirrhotic patients complained muscle cramps. To demonstrate the full therapeutic effects of this treatment, long-term clinical follow up and a randomized trial are needed in the future.

Topic 17: Liver Cirrhosis and Complications

No: 1584

Idiopathic noncirrhotic portal hypertension in a young filipino female a case report

Josephine Anne Lucero[1], Anton Jr. Faltado[1], Mara Teresa Panlilio[2], Gail Culla[3]

University of The Philippines Philippine General Hospital Medicine Manila-Philippines[1], University of The Philippines Philippine General Hospital Gastroenterology Manila-Philippines[2], University of The Philippines Philippine General Hospital Hematology Manila-Philippines[3]

Background and aim: Portal hypertension is a condition of increased portal pressures in the portal vein system. When left untreated, it carries high morbidity and mortality often due to bleeding varices. Common etiologies for portal hypertension include liver cirrhosis, schistosomiasis, and splenomegaly. Portal hypertension in the background of a noncirrhotic liver may result from a myriad of etiologies including thrombophilias, genetic disorders, and other anatomical abnormalities. This case report aims to present the approach to diagnosis of a young patient with noncirrhotic portal hypertension.
Summary of the case: This is a case of a 19-year-old Filipino female presenting with an eleven year history of recurrent abdominal pain, hematemesis and melena. Initially, supportive management was given with blood transfusions and octreotide. Physical exam revealed a normal appearing young female with no signs of liver disease. Esophagogastroduodenoscopy revealed four long columns of esophageal varices and the ultrasound revealed a normal liver and an enlarged spleen. Work-up over eleven years revealed a noncirrhotic liver, with no portal vein thrombosis, an essentially normal liver biopsy, no thrombophilias or other inherited illnesses. When admitted at the Philippine General Hospital, she underwent a splenectomy and splenorenal shunting, providing a long term solution to her medical problems. Since discharge, there has been no recurrence of bleeding.
Significance: A systematic approach to identifying the etiology of portal hypertension is important in order to provide the best management strategy for patients. Not all varices point to cirrhosis and noncirrhotic portal hypertension has an excellent long term prognosis.

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No: 1179

Impact of cannabis in developing esophageal varices in end stage liver disease secondary to chronic hepatitis C (CHC). A retrospective study

Patrick Basu[1], Niraj James Shah[2], Robert Brown Jr[3]

King's County Hospital Medical Center, NY Gastroenterology and Hepatology New York-United States[1], James J. Peters Va Medical Center, Icahn School of Medicine At Mount Sinai, NY Internal Medicine New York-United States[2], Columbia University College of Physicians & Surgeons, New York Presbyterian Medicine New York-United States[3]

Background: Marijuana is the most commonly used "illicit" drug in the United States, with about 12 % of population 12 years of age or older reporting use in the past year. According to the 2012 National Survey on Drug Use and Health, an estimated 2.7 million people 12 years of age and older met the DSM-IV criteria for dependence on marijuana. Clinical reviews have reported a positive association between daily cannabis use and the progression of liver fibrosis or steatosis in hepatitis C patients. This study identifies the effect of cannabis on portal hypertension in cirrhotics with CHC.
Methods: Inclusion criteria: Three centers, over a period of 10 years, CHC, either genotype, underwent interferon based therapy for 24-48 weeks, history of marijuana use (recent to the UGIE) > 6 years.
Exclusion criteria: Post-transplant,Hepatocellular carcinoma, daily alcohol use > 30 grams, Cocaine abuse, BMI > 28 %, HBV, HIV, Ferritin > 600, transferrin saturation > 35 %, autoimmune hepatitis, Schistosomiasis, HOMA > 2 NCPTN.
Three hundred (n = 300) patients with CHC (three centers, over a period of 10 years) who were retrospectively analyzed for regular use of marijuana. 214/300 (71.3 %) with compensated cirrhosis (CC) with mean MELD of 6 and 86/300 (28.7 %) with decompensated cirrhosis (DC) with mean MELD of 18. All underwent screening upper endoscopy for portal hypertension.
Conclusion: This retrospective case controlled matched population reveals that the concomitant daily use of cannabis has direct impact on variceal development in cirrhotics with CHC.

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No: 1843

Partial splenic artery embolization (PSAE) in cirrhosis is a safe and useful procedure

Hasnain Ali Shah[1], Fakhar Ali Qazi Arisar[1]

Aga Khan University Hospital Medicine (gastro) Karachi-Pakistan[1]

Background: Portal Hypertension is a common complication of cirrhosis. It leads to splenomegaly which manifests with features of hypersplenism. This results in leucopenia which increases the likelihood of sepsis and prevents treatment with interferon. Thrombocytopenia increases the risk of bleeding including variceal bleeds which make the anemia worse. Partial Splenic Artery Embolization (PSAE) is practiced in many medical centers worldwide as a treatment of severe hypersplenism, especially where splenectomy is not possible. Its efficacy and safety in cirrhosis is however not established.
Aims: To study the usefulness and safety of PSAE in cirrhosis.
Methods: We carried out a retrospective analysis of case records of patients presenting to our university hospital with cirrhosis and portal hypertension who underwent PSAE.
Results: From 2008 to 2014, 16 patients of cirrhosis having mean age of 44.06 ± 11.37 years underwent PSAE, of which 12 (75 %) were males. Indications were severe hypersplenism which precluded treatment with Interferon and Ribavirin (n = 7), recurrent Gastro-oesophageal variceal (GOV) bleeds due to advanced Child-Pugh grade and thrombocytopenia (n = 9). Mean child pugh score of enrolled patients was 6.94 ± 1.28. Hematological parameters improved significantly following PSAE and are presented in Table 1. Four patients successfully completed IFN + ribavirin treatment for HCV infection post PSAE, and GOV bleeds stopped in 5 patients. Complications included mild LUQ pain n = 7 (41 %), post-embolization syndrome n = 4 (23 %), and clinically insignificant pleural effusion n = 3 (18 %). 2 patients developed SBP which was appropriately managed. 1 patient needed re-emobilization after 6 months.
Conclusions: PSAE is a safe and efficacious procedure in the treatment of hypersplenism of cirrhosis.

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No: 1626

Clinical effects of entecavir alone vs lamivudine and adefovir combination on hbv related compensated liver cirrhosis one year preliminary data of a prospective multicenter and non intervention study

Xiaoning Wu[1], Guofeng Chen[2], Wen Xie[3], Huiguo Ding[4], Xiaojuan Ou[1], Xiaoyuan Xu[5], Hui Ma[6], Anlin Ma[7], Youqing Xu[8], Xiaoqing Liu[9], Jialing Zhou[1], Dongyang Sun[1], Yuanyuan Kong[10], Wei Wei[10], Hong Ma[1], Hong You[1], Jidong Jia[1]

Beijing Friendship Hospital Liver Research Center Beijing-China[1], Beijing 302 Hospital Liver Research Center Beijing-China[2], Beijing Ditan Hospital Liver Center Beijig-China[3], Beijing Youan Hospital Department of Digestive Disease Beijing-China[4], The First Hospital Affiliated To Beijing University Department of Infectious Disease Beijing-China[5], The People Liver Research Center Beijing-China[6], The China-Japan Friendship Hospital Department of Infectious Disease Beijing-China[7], Beijing Tiantan Hospital Department of Digestive Disease Beijing-China[8], Peking Union Medical College Hospital Department of Infectious Disease Beijing-China[9], Beijing Friendship Hospital Evidence Based Medicine Center Beijing-China[10]

Aims: To investigate clinical effects of two early anti-viral therapies entecavir alone vs Lamivudine and adefovir combination on HBV related compensated liver cirrhosis.
Patients and methods: Patients ages from 18 to 70 years old who clinically diagnosed as HBV-induced compensated cirrhosis or histologically confirmed of chronic HBV-induced cirrhosis were eligible for recruitment if they are HBeAg-positive with HBVDNA > 2×103 IU/ml or HBeAg-negative with HBVDNA > 2×102 IU/ml. Patents received either entecavir alone or Lamivudine and adefovir combination according to the willness of patients. Data are collected at baseline, and every three months for blood count, liver function test, renal function test and HBVDNA, every six months for AFP, prothrombin time, liver ultrasonography, and Fibroscan.
Results: Two hundred and forty of 382 enrolled patients were analysed. Two hundred patients were treated with entecavir alone, fourty patients were treated with combination of lamivudine and adefovir. HBVDNA decrease 3.08 ± 1.76 log10 IU/ml vs 3.20 ± 1.24 log10 IU/ml;3.81 ± 1.82 log10 IU/ml vs 3.72 ± 2.05 log10 IU/ml;3.79 ± 1.52 log10 IU/ml vs 1.81 ± 1.76 log10 IU/ml after 3, 6, and 9 months of therapy. HBVDNA undetectable rate of entecavir alone or lamivudine and adefovir combination was 60.8 % vs 87.5 % ($P = 0.093$), 73.0 % vs 100 % ($P = 0.074$), 75.0 % vs 60.0 % ($P = 0.536$) after 3, 6, and 9 months of therapy. Liver stiffness decrease in both group but did not reach statistical significance.
Conclusions: There were no significant differences in viral suppression in HBV related compensated liver cirrhosis patients treated with entecavir alone or lamivudine and adefovir combination therapy in one year.

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No: 1974

The model for critically ill cirrhotics (MCIC) a novel prognostic score for predicting mortality in critically ill cirrhotics admitted to ICU

Amrish Sahney[1], Ashok Choudhary[1], Awinash Sinha[1], Lovkesh Anand[1], Abby Philips[1], Shiv Kumar Sarin[1]

Ilbs Hepatology Delhi-India[1]

Background & aims: Cirrhoticpatients admitted to an Intensive Care Unit (ICU) generally have a poor outcome. The present study was to determine and assess the prognostic markers in critically ill cirrhotics.
Patients and methods: 380Consecutive cirrhotic patients admitted to LiverICU for various reasons were followed since admission till discharge or death. The first152 patients were evaluated and a logistic regression analysis was done to derive the predictors of mortality. The score was derived using these predictors and was validated in a subsequent set of 228 patients. The predictive accuracy of this score was evaluated using AUROC.
Results: Both the derivation and validation cohorts were comparable in demographic, clinical and lap profiles. The predictors of mortality in multivariate analysis in derivation set were baseline INR,serum Creatinine (CR) and time weighted average serum lactate over first 24 h (LacTW24). The MCIC score was derived in an equation form using forward logistic regression. The AUROC for the MCIC score was 0.87 and that for SOFA, MELD, APACHE II and CTP score were 0.80, 0.76, 0.84 and 0.67 respectively. In validation cohort, the AUROC for MCIC: was: 0.86, SOFA: 0.82 MELD: 0.73 and APACHE: 0.75. The dynamic lactate level as assessed by LacTW24 is an important predictor of mortality with AUROC of 0.75, it also enhances the predictive accuracy of other scores i.e. MELD-LacTW24: 0.78, SOFA- LacTW24: 0.86, and APACHE- LacTW24: 0.83.
Conclusions: The MCIC score is the first model considering dynamic lactate index in addition to liver specificINR and associated organ failure i.e. CR in predicting mortality among critically ill cirrhotic patients.

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No: 2197

Is etiologic profile of the liver cirrhosis different than worldwide in Turkey

N. Ormeci[1], Y. Tuna[2], C. Savas[3], E. Dolar[4], A. Bektas[5], M. Ibis[6], M. Kurt[7], H. Ozkan[1], M. Kucukazman[8], A. Altınbas[9], M. Yasa[10], A. Demir[11], K. Guven[12], S. Koklu[13], M. Arslan[14]

Ankara University Medical School Department of Gastroenterology Ankara-Turkey[1], Akdeniz University Medical School Department of Gastroenterology Antalya-Turkey[2], Gaziantep University Medical School Department of Gastroenterology Gaziantep-Turkey[3], Uludag University Medical School Department of Gastroenterology Bursa-Turkey[4], 19 Mayıs University Medical School Department of Gastroenterology Samsun-Turkey[5], Gazi University Medical School Department of Gastroenterology Ankara-Turkey[6], Abant Izzet Baysal University Medical School Department of Gastroenterology Bolu-Turkey[7], M. Keciören Education and Research Hospital Department of Gastroenterology Ankara-[8], Numune Education and Research Hospital Department of Gastroenterology Ankara-Turkey[9], Adnan Menderes University Medical School Department of Gastroenterology Aydın-Turkey[10], Selcuk University Medical School Department of Gastroenterology Konya-Turkey[11], K. Erciyes University Medical School Department of Gastroenterology Kayseri-Turkey[12], Hacettepe University Medical School Department of Gastroenterology Ankara-Turkey[13], Karadeniz Technical University Medical School Department of Gastroenterology Trabzon-Turkey[14]

Liver cirrhosis is characterised by degeneration, regeneration and fibrosis of liver parenchyma because of various inflammations such as viral, metabolic, autoimmune, biliary obstructions and NASH.
Aim: Aim of the study is to evaluate etiologic profile and characteristics of patients who were diagnosed liver cirrhosis in Turkey.
Patients and method: A thousand and thirty one patients, female 427 (41.40 %), male 604 (58.60 %), who were diagnosed liver cirrhosis were included into the study. All patients were evaluated in terms of etiology, smoking, alcohol consumption, occurrence of complications and hepatocellular carcinoma (HCC). Mean age of the patients was 57.35 ± 13.32 years (youngest 16, oldest 90) and mean follow-up time was 38.27 ± 36.60 (minimum1- maximum 288) months.
Results: The etiologic profile of the patients with liver cirrhosis is seen in table 1. Eighty four patients out of 1031 had HCC during the follow-up. Twenty six patients had HCC in compensated stage of liver cirrhosis while 58 out of 84 had in decompensated stage of liver cirrhosis. HCC occurred mainly in male ($P = 0.014$) and in patients with high AFP and ALT levels. The other complications are seen in table 2.
Conclusion: The most common reason of liver cirrhosis is HBV in Turkey. HCC occurs mainly in males in both compensated and decompensated cirrhosis. High AFP and ALT levels in males are predictive factors for HCC.

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No: 1022

The effects of electro acupuncture on the muscle cramps of liver cirrhosis patients pilot study

Chang Hyeong Lee[1], Seung Mo Kim[2], Byung Seok Kim[1], Han Na Choi[1], Hyun Hee Kim[1], Min A Kwak[2], Jung Chul Seo[3]

Dcumc Gastroenterology and Hepatology Daegu-Korea, South[1], Daegu Hanny University Internal Medicine Daegu-Korea, South[2], Cimi Comprehensive Medicine Daegu-Korea, South[3]

Background/aim: Muscle cramps mean involuntary painful muscle contractions intermittently occured in liver cirrhosis patients. The purpose of this clinical trial is to investigate the effects of electro-acupuncture on muscle cramps of liver cirrhosis patients.
Methods: 16 liver cirrhosis patients with muscle cramps more than once a week regardless of body portion were treated by electro-acupuncture at 16 acupuncture points three times a week for four weeks (12 times in total). The electrical stimulation was a frequency of 100 Hz. Frequency of the muscle cramps were measured by questionnaire of subjective symptoms. We analyzed the frequency of muscle cramps 4 times(screening and 2, 4, 8 weeks after starting electro-acupuncture).
Results: 14 patients have completed the clinical trial. Two patients have dropped due to personal considerations without any side effect of electro-acupuncture. The number of patients have occurred muscle cramps 'more than once a week' were reduced to 14, 8, 4, 2 at screening, 2, 4, 8 weeks after starting acupuncture(table 1, $P < 0.000$). We could not find any deterioration of liver function and complications of cirrhosis in all patients. We also could not find any adverse events related to electro-acupuncture during the entire clinical trial.
Conclusions: This study suggest that electro-acupuncture treatment will be beneficial for liver cirrhosis patients to improve muscle cramps. Electro-acupuncture is thought to be a safe and efficacious treatment for cirrhotic patients complained muscle cramps. To demonstrate the full therapeutic effects of this treatment, long-term clinical follow up and a randomized trial are needed in the future.

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No: 1454

Hepatic encephalopathy in Mongolian adults

Bayarmaa Ochirkhuree[1], Baatarkhuu Oidov[2], Bira Namdag[3]

First Central Hospital of Mongolia Gastroenterological Centre Ulaanbaatar-Mongolia[1], Mongolian National University of Medical Science Department of Infectious Diseases Ulaanbaatar-Mongolia[2], Mongolian National University of Medical Science Department of Gastroenterology Ulaanbaatar-Mongolia[3]

Aim: To investigate the duration of the first bout of HE,precipitating factors, clinical features and laboratorical changes, predictive or key factors and their correlation to the severity of chronic hepatic failure and encephalopathy.
Methods: A hospital based retrospective study was carried out on 120 patients in GI centre of First Central Hospital of Mongolia and Chingeltei-Uul district hospital from 2011-2013. Patients with cirrhosis were diagnosed on the basis of biochemical, ultrasonographic and endoscopic findings as well. Patients with hepatic failure were subdivided into 3 groups as following:

I-patients with clinical evidence of hepatic failure but no HE, II–patients with I-II grade of HE.

III–patients with III-IV grade of HE and clinically by Child-Pugh classification. For data collection, a questionnaire was developed. A detailed clinical history of the patient was taken regarding the present and past illness.
Conclusion: Hepatic virus infection is the most common cause (75 %) of patients with cirrhosis.

The occurrence of the first bout of hepatic encephalopathy within 5 years after diagnosing of cirrhosis was 77 % of all patients.

Among the precipitating factors there were infection-44.2 %, GI bleeding-40.6 % and other-15.2 %. Fatique and sleep disturbances (100 %) are the main clinical signs of hepatic encephalopathy. Bilirubin/r = 0.39/, albumin/r = (0.48)/and INR/r = 0.42/are the main predictive factors and have a mean correlation to severity of chronic hepatic failure. Hyperammonemia/r = 0.61/is the key factor of HE and has a mean correlation to severity of HE.

Based on these we have to improve early and effective infection control and varices bleeding management.

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No: 1786

Dynamic contrast enhanced MRI (DCE MRI) is a new non invasive modality for accurate prediction of liver cirrhosis

Pik-eu Chang[1], Choon-hua Thng[2], Thong-san Koh[2], Kiat-hon Lim[3], Chee-kiat Tan[1]

Singapore General Hospital Gastroenterology & Hepatology Singapore-Singapore[1], National Cancer Centre Oncologic Imaging Singapore-Singapore[2], Singapore General Hospital Pathology Singapore-Singapore[3]

Background/aims: Chronic liver injury leads to accumulation of fibrous tissue in Disse's space. We postulate that the fractional interstitial volume (FIV) measured using dynamic contrast-enhanced MRI (DCE-MRI) estimates the volume of Disse's space and can be used to predict severity of liver fibrosis/cirrhosis. This pilot study aims to evaluate the accuracy of DCE-MRI to predict severity of liver fibrosis in patients with chronic liver disease.
Methods: Chronic liver disease patients undergoing liver biopsy received DCE-MRI and liver stiffness measurement(LSM) via Fibroscan® within 1 month in a prospective study. AUROC of DCE-MRI was compared against Fibroscan® for diagnosis of significant fibrosis (METAVIR $\geq$ F2), advanced fibrosis (METAVIR $\geq$ F3) and cirrhosis (F4).
Results: Thirty patients with mean age 48.4 $\pm$ 11.4 years and 63.3 % males were recruited. Etiology of liver disease was HBV (47 %), HCV (20 %), NASH (17 %), AIH/PBC (16 %). Eight patients did not complete the study. The remaining 22 were divided into four groups based on liver histology: No/mild fibrosis, $<$ F2 (23 %), significant fibrosis, F2(30 %), advanced fibrosis, F3 (30 %) and cirrhosis, F4(17 %). Mean FIV on DCE-MRI was 8.5 $\pm$ 4.2, 9.7 $\pm$ 3.8, 10.4 $\pm$ 5.7, 19.8 $\pm$ 4.9 % and mean LSM was 12.7 $\pm$ 5.4, 11.3 $\pm$ 5.0, 14.9 $\pm$ 6.9, 15.7 $\pm$ 4.7 kPa respectively. AUROC for diagnosis of significant fibrosis, advanced fibrosis and cirrhosis by DCE-MRI was 0.65, 0.68 and 0.94 respectively vs. 0.52, 0.64 and 0.68 for Fibroscan®. An optimal FIV value $>$ 12.5 % was 94 % accurate in predicting cirrhosis with 100 % sensitivity and 89 % specificity.
Conclusions: Our results support the hypothesis that FIV measured by DCE-MRI correlates with liver fibrosis stage. DCE-MRI is particularly accurate for the non-invasive diagnosis of liver cirrhosis compared to Fibroscan® but is less discerning for lower stages of liver fibrosis.

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No: 2002

Spleen stiffness liver stiffness and apri alone or in combination are equally predictive for the presence of portal hypertension

Kerstina Boctor[1], Magdy Elkhashab[2], Marzena Magnes[1]

Toronto Liver Centre Hepatology Toronto-Canada[1], University of Toronto, Toronto Liver Centre Hepatology Toronto-Canada[2]

Background & aims: We examined the use of Spleen Stiffness Measurement (SSM) & LS/SS ratio individually as predictors of clinically significant portal hypertension(CSPH). We also assessed, whether Liver Stiffness Measurement (LSM) & APRI provided any additional benefit as predictors of CSPH.
Methods: 40 patients (11 cirrhotic, 29 non-cirrhotic) randomly underwent SSM in supine(S), and/or right lateral decubitus (RLD) positions. SSMs were initially conducted utilizing M-probe; if unsuccessful, XL-probe was then used. A SSM test was accepted based on A-mode verification & $\geq$ 8 successful readings current guidelines for LSM [1] were followed, & APRI [2] was calculated.
Results: 104 tests were conducted, with a 70.1 % success rate. Mean (and standard deviation) APRI score was 1.02 (0.68) & LSM was 18.1 (17.0). 27.5 % of patients were cirrhotic (81.8 % exhibited CSPH), with median LSM of 34.3 kPa, and 24.8 kPa with M and XL probe, respectively. CPSH was identified by: varices, ascites, or HVPG $>$9.
Best thresholds (Specificity, Sensitivity, and p-value from logistic regression) are:

Supine: APRI $>$ 0.8 (0.55, 1.00, 0.29), LS $>$ 23.3 kPa (0.91, 0.86, 0.03), SS $>$ 51.80 kPa (0.82, 0.83, 0.02), LS/SS $>$ 0.3 (0.73, 0.86, 0.10).

RLD: APRI $>$ 0.79 (0.88, 1.00, 0.05), LS $>$ 8.50 kPa (0.88, 1.000, 0.023), SS $>$ 19.45 kPa (0.88, 1.000, 0.03), LS/SS $>$ 0.75 (0.88, 0.63, 0.11).

Odds of CSPH if: SS $<$ 19.45 kPa were zero; SS $>$ 19.45 kPa were 8 to 1.
Conclusion: In RLD, SS, LS, and APRI are equally reliable in predicting the presence or absence of CSPH. Furthermore, combining LS, SS, & APRI did not provide additional benefit in the detection of CSPH. The LS/SS ratio showed a specificity of .88, & sensitivity of 0.63; this phenomenon will be further studied.

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No: 1049

The true efficacy of tolvaptan in patients with refractory ascites an experience of 60 cases compared to historical controls

Takamasa Ohki[1], Koki Sato[1], Tomoharu Yamada[1], Mari Yamagami[1], Daisaku Ito[1], Kentaro Kojima[1], Toshihiko Arizumi[1], Michiharu Seki[1], Nobuo Toda[1], Kazumi Tagawa[1]

Mitsui Memorial Hospital Gastroenterology Tokyo-Japan[1]

Aims: Tolvaptan (TLV) transiently improves refractory ascites. However, decompensated cirrhosis is a progressive disease which indicated that ascites will be uncontrollable sooner or later. Thus, we conducted this study to reveal the true out comes of TLV.
Patients and methods: We enrolled 60 refractory ascites patients treated with TLV and enrolled another 60 refractory ascites patients treated with large volume paracentesis as control group between January 1st 2009 and September 31 2012. We compared the patient's backgrounds between the two groups and also compared the cumulative incidence rates between the two groups, and elucidated factors which affected on incidence using multivariate analysis. Incidences were defined as an additional invasive procedure including paracentesis, or need for hospitalization for any reason.
Results: Serum sodium level was significantly lower in TLV group (133 mEq/l vs. 136 mEq/l, $P = 0.02$). However, there were no

significant differences about other parameters between the two groups. Cumulative incidence rate was significantly higher in the controls: median time for incidence was 30 days in TLV group and 20 days in the controls ($P = 0.01$). Cox hazard proportional multivariate analysis indicated that use of TLV (OR: 1.70 $P < 0.01$), lower total bilirubin level (OR: 0.91 per 1 mg/dl, $P = 0.02$), and higher sodium level (OR: 1.06 per 1 mEq/l, $P < 0.01$) as independent factors which contributed to incidence.
Conclusions: Administration of TLV achieved not only better control of refractory ascites but also better QOL avoiding additional invasive procedure including paracentesis or need for hospitalization compared to conventional ascites treatments.

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No: 1052

Spectrum and short term outcome of renal impairment in cirrhosis

Dr. Vinit Shah[1], Dr. Ashish Kumar[1], Dr. Praveen Sharma[1], Dr. Rinkesh Bansal[1], Dr. Pankaj Tyagi[1], Dr. Naresh Bansal[1], Dr. Vikas Singla[1], Dr. Mandhir Kumar[1], Dr. Piyush Ranjan[1], Dr. Munish Sachdeva[1], Dr. Anil Arora[1]

Sir Ganga Ram Hospital Gastroenterology and Hepatology New Delhi-India[1]

Background: Prospective, observational, cohort study to determine spectrum of acute kidney injury defined (AKI) as per (IAC/ADQI definition) in cirrhotics at admission or in hospital stay and classify AKI types and study outcome.
Methods: Cirrhotic patients diagnosed with AKI evaluated as per study protocol. Cause & type of AKI as per study definitions along with spectrum determined and patients followed up to see outcome both in hospital & at 1 and 3 months.
Results: 395 consecutive cirrhotics with renal impairment enrolled. In hospital mortality 154 (39 %). 226 (57.2 %) survived at 1 month and 173 (43.8 %) at 3 months. Median CTP 10 (5–14) & median MELD 25 (6–57). RRT required in 120 (30.4 %). VRAKI was commonest 198 (50.1 %).Among VNRAKI, HRS in 85 (21.5 %), ATN in 55 (13.9 %) and 9 (2.3 %) had AGN. Associated CKD in 48 (12.2 %). VRAKI had best outcome followed by AGN and associated CKD. ATN and HRS had poor outcomes. Outcome significantly poor in ACLF, terlipressin non responders and recurrent AKI. On multivariate analysis MELD score, Serum albumin, presence of SBP and hypotension with inotropes requirement significantly associated with HRS/ATN development. Presence of HE, low albumin and ATN/HRS significantly associated with death.
Conclusions: AKI in cirrhotics associated with significantly high in hospital mortality, higher need for RRT and progressively reduced 1 month, 3 month survival. VRAKI commonest with best outcome.HRS and ATN associated with dismal prognosis. ACLF, terlipressin non responders and recurrent AKI have poor outcome.Presence of HE, low albumin and ATN/HRS have significant mortality.

Topic 17: Liver Cirrhosis and Complications

No: 1463

Comparison of meld Na meso index and imeld for prediction of mortality in cirrhosis

Jatin Patel[1], Meghraj Ingle[1], Pathik Parikh[1], Prabha Sawant[1]

Lokmanya Tilak Municipal Medical College and General Hospital, Department of Gastroenterology, Mumbai,-India[1]

Background: To improve predictability of Model for End Stage Liver Disease (MELD) addition of serum sodium is suggested. We carried out the study to compare MELD-Na, MESO index and iMELD for prediction of mortality in cirrhosis.
Methods and materials: We included total 365 patients of cirrhosis. MELD, MELD-Na, MESO and iMELD were calculated on admission. Predictive accuracy of the scores was determined by the area under the receiver operating characteristic curve (AUC) of each score. Kaplan- Meier survival analysis curves were made using best cut-offs from the means of ROCs.
Results: At 3, 6 and 12 months non survivor group had higher mean scores (MELD, MELD-Na, MESO and iMELD) as compared to survivor group). At 3 months MELD-Na has highest AUC (0.859) followed by iMELD(0.844),MESO(0.835) and MELD(0.824). At 6 months and 12 months iMELD has highest AUC (0.895 and 0.906) followed by MELD-Na (0.894 and 0.894), MESO (0.880 and 0.870) and MELD (0.873 and 0.862). All the scores had good sensitivity (61.58 % to 82.81 %), specificity (72.76 % to 92.02 %) and negative predictive values (71.43 % to 95.3 %). Kaplan–Meier curves indicated that all the scores successfully discriminate between survivors and non survivors at 3, 6 and 12 months.
Conclusion: Incorporation of Na into MELD can enhance the predictive ability. The three new models (MELD-Na, MESO and iMELD) can predict the mortality in cirrhotic patients with good accuracy. iMELD and MELD-Na both have best predictive ability in our study and the predictive ability of iMELD and MELD-Na are comparable.

Topic 17: Liver Cirrhosis and Complications

No: 2146

Efficacy and long term safety of gastric variceal obliteration using n butyl 2 cyanoacrylate in patients with acute gastric variceal haemorrhage an experience from Turkey

Meltem Ergun[1], Ali Rıza Koksal[2], Salih Boga[2], Mehmet Bayram[2], Hüseyin Alkim[2], Canan Alkim[2]

Yeditepe University Gastroenterology Istanbul-Turkey[1], Sisli Etfal Education and Training Hospital Gastroenterology Istanbul-Turkey[2]

Background/aims: Unfortunately, optimal endoscopic treatment of gastric variceal bleeding in portal hypertensive patients is not standardized. N-butyl-2-cyanoacrylate (Histoacryl) is widely utilized for the management of bleeding gastric varices, in Eastern countries, but it is not FDA approved, and therefore it is not a routine treatment option in the West. We evaluate the long-term efficacy and safety of endoscopic injection of Histoacryl for treatment of bleeding gastric varices, in Turkish Patients.
Methods: We retrospectively analyzed the records of 12 patients with gastric variceal haemorrhage who were consecutively treated with histoacryl from September 2012 to September 2014. The patients' demographics, endoscopic findings, initial hemostasis, complications, rebleeding rates, and bleeding-related death rates were reviewed. The most common localization of varices is fundus posterior and degree F2-3. Endoscopic treatment with histoacryl and lipiodol solution was used in 1: 1. 4 out of 12 patients had esophageal variceal bant obliteration.
Results: Histoacryl treatment was used in 12 patient (mean age: 42 ± 5.4 years; range 18-66 years; -3 females) with gastric variceal

haemorrhage. Initial hemostasis was achieved all patients, little oozing were seen in two patients, but it was stopped spontaneously. Complications included fever (8 %), abdominal pain (16 %). In one patient splenic infarct areas was detected 48 h after the procedure. During long-term follow-up, 6 patients died, 5 as a consequence of the cirrhosis complications and 1 as a consequence of hepatocellular carcinoma.

Conclusions: This study indicated that histoacryl and lipiodol solution is effective for gastric variceal bleeding, and it may utilize with an acceptable complication rate.

Topic 17: Liver Cirrhosis and Complications

No: 1273

Malnutrition in cirrhosis increases morbidity and mortality

Sudhir Maharshi[1], Barjesh Chander Sharma[2], Siddharth Srivastava[3]

Senior Resident- G B Pant Hospital Gastroenterology New Delhi-India[1], Professor- G B Pant Hospital Gastroenterology New Delhi-India[2], Associate Professor- G B Pant Hospital Gastroenterology New Delhi-India[3]

Background and aims: Malnutrition is frequently seen in patients with cirrhosis and associated with increase risk of complications like ascites, hepatic encephalopathy, infections and death. Aims of this study were to determine the prevalence of malnutrition by various methods and its clinical importance in cirrhotic patients according to severity of disease.

Methods: Consecutive patients of cirrhosis were assessed. Nutritional assessment was done by anthropometric parameters [mid arm circumference (MAC), triceps skin fold thickness (TST)], hand grip (HG), serum albumin level, creatinine height index (CHI), total lymphocyte count and body composition analysis by measuring skeletal muscle mass and body fat mass.

Results: 290 patients (age 43.25 ± 10.52, 81 % male) were assessed. Etiology of cirrhosis was alcohol in 54 % patients. Child's class of cirrhosis was Child's B in 51 %, Child's C in 39 % and Child's A in 10 % of patients. Nutritional assessment revealed MAC 19.72 ± 3.51 cm, TST 10.15 ± 3.15 mm, HG 9.8 ± 3.8 kg, serum albumin 2.61 ± 0.48 g/dl, CHI 61.20 ± 11.10, total lymphocyte count 1042 ± 440/cmm, skeletal muscle mass 17.10 ± 5.82 kg and body fat mass 8.21 ± 1.72 kg. Prevalence of malnutrition were 71.4 % by HG and 66.5 % by body composition analysis. Malnutrition was more common in alcoholic vs nonalcoholic ($P = < 0.05$) and in Child's class C vs Child's class B and A($P = < 0.05$).Hepatic encephalopathy and spontaneous bacterial peritonitis and mortality were more in malnourished patients.

Conclusions: Malnutrition is more common in cirrhosis of alcohol etiology and with advance stage of cirrhosis. It is associated with high complications and mortality in cirrhosis.

Topic 17: Liver Cirrhosis and Complications

No: 1275

Presence of anemia predicts advanced grade at presentation in patients with hepatic encephalopathy

Nauman Arif Jadoon[1], Zeeshan Butt[2], Ahmed Shahzad[3], Kamran Mushtaq[3]

Ittefaq Hospital Medicine Lahore-Pakistan[1], Mayo Hospital Medicine Lahore-Pakistan[2], Nishtar Medical College Hospital Medicine Lahore-Pakistan[3]

Objective: The objective of our study was to assess the impact of anemia on HE grade at presentation.

Methods: Consecutive patients of HE admitted in the medical wards of Mayo Hospital, Lahore during March 2010 and May 2010 were enrolled in the study. HE grade at presentation was assessed by using West-Haven Criteria. Complete blood count, bleeding profile, liver function tests and ultrasound was done in emergency at presentation. Anemia was defined as hemoglobin level less than 12 g/dl. Univariate and multivariate logistic regression analysis was done to assess the impact of anemia on hepatic encephalopathy grade at presentation. P value < 0.05 was considered significant.

Results: 61 patients were included in the study. 20 % patients were in grade 1 HE; 20 % in grade 2; 39 % in grade 3; and 21 % in grade 4 HE. Advanced grade HE was defined as HE grade > 2. On univariate analysis prothrombin time > 15 s, diabetes, esophageal varices on endoscopy, and anemia were significant predictors of advanced grade HE (p values: 0.048, 0.048, 0.039, 0.037). Hypoalbuminemia was less common in advanced grade HE patients (p, 0.004). Child Pugh Score and MELD Score had no relation with HE grade at presentation. All the significant factors in univariate analysis were included in the multivariate logistic regression model. Only anemia was significant predictor of advanced grade HE in multivariate analysis (p, 0.018).

Conclusion: Sixty percent of HE patients present with advanced grade. Anemia is associated with advanced HE grade at presentation.

Topic 17: Liver Cirrhosis and Complications

No: 1552

Spectral electroencephalogram analysis in liver cirrhosis with minimal hepatic encephalopathy before and after lactulose therapy

B.c. Sharma[1], Vinod Puri[2], Siddharth Srivastava[1], Jatinder Pal Singh[1]

Gb Pant Hospital Gastroenterology New Delhi-India[1], Gb Pant Hospital Neurology New Delhi-India[2]

Background/aims: Minimal Hepatic Encephalopathy (MHE) represents the mildest form of Hepatic Encephalopathy (HE). Spectral EEG analysis (sEEG) improves the recognition of MHE by decreasing inter-operator variability and providing quantitative parameters of brain dysfunction. In this study we have compared sEEG in patients of cirrhosis with and without MHE and the effect of lactulose therapy on sEEG in patients with MHE.

Methods: 60 patients of cirrhosis (30 with MHE and 30 without MHE) enrolled. Assessment of MHE done by psychometric tests. sEEG performed at baseline in all patients. The spectral variables considered were the mean dominant frequency (MDF), i.e., the mean frequency weighted by the power of each frequency band and the relative power in the beta (13.5–25.5 Hz), alpha (8.5–13 Hz), theta (4–8 Hz) and delta (1–3.5 Hz) bands. Patients with MHE were given 3 months of lactulose therapy and psychometric tests and sEEG repeated in them. Statistical tests used as appropriate.

Results: MDF values found to be lower in cirrhotics with MHE (7.9 ± 1.1 Hz) as compared to cirrhotics without MHE (8.4 ± 1.2 Hz $P = 0.06$). Theta % was higher in patients with MHE than in patients without MHE (31.7 ± 12 % vs 24 ± 6.7 %, $P = 001$). However no significant difference was found in alpha, beta and delta bands. After

treatment with lactulose for 3 month, significant improvement seen in MDF and theta % in patients with MHE ($p \leq 0.05$).
Conclusions: Spectral EEG is useful measure for diagnosing MHE and monitoring treatment response.

Topic 17: Liver Cirrhosis and Complications

No: 1931

The automatic measurement system of cirrhotic status by second harmonic generation microscopy

Kai-wen Huang[1]

National Taiwan University Hospital Hepatitis Research Center Taipei-Taiwan[1]

Background & aims: Liver fibrosis is associated with an over-accumulation of collagen, and the histologic scoring by pathologists has been the standard assessment method. Second-harmonic generation (SHG) microscopy has emerged as a powerful modality for imaging collagenous area in liver and make automatic quantification of fibrotic tissue possible. In this study, we aimed to demonstrate the relevance of SHG microscopy with a morphology-based quantification algorithm for assessing collagen in fibrotic liver without staining.
Methods: The surgical specimens from 84 successive patients who underwent partial hepatectomy were examined with SHG microscopy. All of these patients are the victims of viral hepatitis. Comparing the measurements of the morphology-based algorithm, Fibro-C-Index, with liver fibrosis were explored by multiple linear regression analysis and the performances of Fibro-C-Index were evaluated with repeated measures analysis of variance and receiver operating characteristic curve
Results: The scoring method was applied to 84 biopsies from patients with chronic liver disease allowing a fast and accurate measurement of fibrosis correlated with the Fibro-C-Index ($rho = 0.80$, $P < 0.0001$), obtained by the median of 6 randomized sampling of 3x3 tiles region of interested. The technique also allowed discriminating of several levels of fibrosis within the same Metavir stage.
Conclusions: We showed the relationship between SHG signal and the extent of fibrosis in viral hepatitis patients, and confirmed the standard protocol to get Fibro-C-Index with high validation. We expect that this technology could easily be applicable in the study of liver fibrotic status for prevention and treatment of chronic liver disease.

Topic 17: Liver Cirrhosis and Complications

No: 1010

Acceptability reliability and applicability of liver biopsy and noninvasive methods for assessment of hepatic fibrosis and cirrhosis among hepatologists; a web based survey

Mohamed Alboraie[1], Marwa Khairy[2], Aisha Elsharkawy[2], Mohamed Elkassas[3], Noha Asem[4], Fathy Elghamry[1], Fuad Hassan[5], Gamal Esmat[2], Egyptian Liver Fibrosis Study Group[1]

Al-azhar University Department of Internal Medicine Cairo-Egypt[1], Cairo University Department of Endemic Medicine and Hepatology Unit Cairo-Egypt[2], Helwan University Department of Endemic Medicine and Hepatology Cairo-Egypt[3], Cairo University Department of Public Health and Community Medicine Cairo-Egypt[4], Kuwait University Department of Medicine, Faculty of Medicine Al-jabriya-kuwait[5]

Background and aims: Liver biopsy remains the standard reference for staging of hepatic fibrosis. Non-invasive methods for assessment of hepatic fibrosis and cirrhosis are becoming increasingly popular in the last decade. In this study we aimed at exploring the change in practice among hepatologists regarding the use of liver biopsy and non-invasive methods for staging hepatic fibrosis and cirrhosis.
Methods: A 56 questions survey was designed and hosted on an online survey's hosting website. Invitations were sent to practicing physicians interested in hepatology via e-mails and through major international hepatology societies' social media walls (Twitter, Facebook and LinkedIn).
Results: Liver biopsy is still considered the gold standard for assessment of hepatic fibrosis and cirrhosis by 85 % of participants. Liver biopsy was accepted by 76.33 % of their patients, 97.6 % of participants think that liver biopsy result is reliable while only 60.84 % admitted that liver biopsy was applicable for all patients. 94.23 % reported the needed of a more practical alternative to liver biopsy to assess disease progression or response to treatment. 91.89 % of participants know serum biomarkers, 93.36 % reported that they were acceptable by their patients, 85.26 % thought they are reliable and only 57.9 % applied them. 95.4 % were familiar with radiological methods of non-invasive assessment of hepatic fibrosis, 97.81 % reported that radiological methods were acceptable by their patients, 94.96 % think that they are reliable and 96.28 % reported they were applicable in clinical practice. 86.72 % think that combining non-invasive methods is better than using a single method and 39.41 % of physicians thought that radiological methods were cheaper than biomarkers (35.59 %), combination of both (24.55 %) or liver biopsy (0.45 %). 96.17 % of physicians agreed that we are in need of a guideline for using non-invasive methods for assessment of liver fibrosis.
Conclusions: Acceptability of non-invasive methods for assessment of hepatic fibrosis by patients was better than liver biopsy. Physicians trusted liver biopsy more than radiological methods or serum biomarkers and applied non-invasive radiological methods easier than liver biopsy or serum biomarkers.

Topic 17: Liver Cirrhosis and Complications

No: 1136

Liver fluke disease and the risk of cancer and cirrhosis

M.b. Rokni[1]

Tehran University of Medical Sciences Medical Parasitology Tehran-Iran[1]

Aim: Liver flukes including Clonorchis, Opistorkis and Fasciola parasites are capable to induce liver cancer and cirrhosis in humans. Searching literature verifies this issue in this study.
Method: Literature was surveyed using a panel of words including liver fluke, cancer, and cirrhosis.
Results: For fasciolosis, people at risk are estimated at 91.1×106. The global burden is 665,352 DALYs for food-borne trematodes, of which a most important share is attributed to fasciolosis. After infection of human by consuming contaminated vegetables or water, fasciolosis is established and results to proliferation of connective tissue and liver cirrhosis. The clinical manifestations include biliary colic, epigastric pain, fatty food intolerance, nausea, jaundice, pruritus, and right upper-quadrant abdominal tenderness. Regarding opistorchidae family, Opisthorchis viverrini, Clonorchis sinensis and

O. felineus, the number of infected people is estimated 26 million. Up to 700 million are at risk of infection only with O. felineus. Humans are infected by consumption of undercooked fish containing viable metacercariae. The infection induces hepatobiliary involvement, which in the end leads to bile duct cancer, cholangiocarcinoma (CCA), the leading cause of death in Asia. O. viverrini and C. sinensis are known as type 1 carcinogen because of a strong link to CCA. They may cause biliary atresia, cholecystitis, liver fibrosis, including cirrhosis. Mortality rate due to CCA is high and in the endemic areas the incidence of CCA varied from 90-300 per 100,000.

Conclusion: The risk of cancer and cirrhosis by liver flukes is high. At-risk people especially should be aware of the risks of these parasitoses.

Topic 17: Liver Cirrhosis and Complications

No: 2069

Value of ascitic fluid cholesterol to differentiate cirrhotic from non cirrhotic ascites

Syed Abul Foez Foez[1], Salimur Rahman Salimur[2], Nooruddin Ahmad Ahmad[3], Mamun-al-mahtab Mahtab[3]

Bed Hospital, Moulvibazar. Medicine Sylhet-Bangladesh[1], Bangabandhu Sheikh Mujib Medical Hospital Hepatology Dhaka-Bangladesh[2], Bangabandhu Sheikh Mujib Medical University Hepatology Dhaka-Bangladesh[3]

The differential diagnosis of ascites remains a clinical problem. Appropriate management depends on proper diagnosis. To differentiate the cause of ascites various parameters of ascitic fluid were used. The present study was conducted in the Department of Hepatology, Bangabandhu Sheikh Mujib Medical University (BSMMU) to see the 'value of ascitic fluid cholesterol to differentiate cirrhotic from non-cirrhotic ascites'. A total 80 patients with ascites (40- cirrhotic, 40-non cirrhotic) were enrolled who met the inclusion criteria.

Ascitic fluid cholesterol in cirrhotic ascites found much lower than non-cirrhotic ascites. Mean (± SD) cholesterol in cirrhotic ascites is 8.425 ± 5.96 mg/dl, whereas in non-cirrhotic ascites is 87.15 ± 26.05 mg/dl and the difference between two groups is highly significant ($P < 0.001$). At a cutoff level of ascitic fluid cholesterol 29 mg/dl, the sensitivity, specificity, PPV, NPV and diagnostic accuracy is 100 % to differentiate cirrhotic from non-cirrhotic (T.B/Malignancy) ascites. Mean (± SD) ascitic fluid cholesterol in malignant ascites is 83.62 ± 26.32 mg/dl, whereas in tubercular ascites is 90.03 ± 26.14 mg/dl and the difference is not statistically significant ($p > 0.05$). Ascitic fluid cholesterol in cirrhotic patients with CP stage B is 10.44 ± 6.38 mg/dl, whereas in CP stage C it is 7.83 ± 5.86 mg/dl and the result is not statistically significant ($p > 0.05$).

In view of the good diagnostic efficiency, easy availability and cost effectiveness, ascitic fluid cholesterol is an excellent parameter to differentiate cirrhotic ascites.

Topic 17: Liver Cirrhosis and Complications

No: 1057

A prospective study of spleen stiffness & its dependency on body position & probe size in cirrhotic vs. non cirrhotic patients using fibroscan technology

Kerstina Boctor[1], Magdy Elkhashab[2], Marzena Magnes[1]

Toronto Liver Centre Hepatology Toronto-Canada[1], University of Toronto, Toronto Liver Centre Gasteroenterology & Hepatotology Toronto-Canada[2]

Background & aims: In recent years, FibroScan technology has been utilized to assess spleen stiffness measurement (SSM), and its role in predicting presence of esophageal varices in cirrhotic patients. [i,ii,iii,iv] We examined the effect of body position on spleen stiffness by using M and XL-probe; in cirrhotic & non-cirrhotic patients, to test SSM in the Supine (S), & right lateral decubitus (RLD) positions. [v]

Methods: 40 patients (11 cirrhotic, 29 non-cirrhotic) were randomly selected to undergo SSM using M-probe, XL-probe, or both. SSMs were initially completed in all patients utilizing M-probe; if unsuccessful, XL-probe was then used.

Results: Of the 57 SSM conducted, a 73.7 % success rate was achieved. 81.8 % of the cirrhotic patients, had evidence of portal hypertension. 52.3 % of tests were conducted in supine position, while the remaining in RLD.

The mean (and SD) of the SSM in S position was 45.8 kPa, & RLD position, was 33.67(25.54)kPa. The correlation between supine and RLD was 0.65($P = 0.06$) amongst the 9 patients who had SSM in both positions. The adjusted difference between means of SSM in both positions was 11.98 kPa, $P = 0.08$.

Effect of probe size was examined in 15 patients using only M-probe, and 9 patients using only XL-probe; resulting in a corrected SDE for the difference of 10.95 kPa; $z = 0.54$, $P = 0.59$.

Conclusion: SSMs are greater in supine vs. RLD by a coefficient of 0.65. In this subset of patients, using M-probe for SSM resulted in a minimum increase of 10.95 kPa in comparison to that of the XL probe measurements. We plan to further examine this finding in a larger number of patients.

Topic 17: Liver Cirrhosis and Complications

No: 2241

Treatment of refractory ascites

Tarek Korah[1]

Faculty of Medicine, Menoufiya University, Egypt Int. Medicine Menoufiya-Egypt[1]

Refractory ascites is a fluid overload which is unresponsive to sodium-restricted diet, high-dose diuretic treatment (400 mg/day spironolactone and 160 mg/day furosemide), for at least 1 week, or recurs rapidly after therapeutic paracentesis. Once patients become refractory to medical therapy, about 20 % die within 6 months.

Repeated large-volume paracentesis (plus albumin) is the first line of treatment for refractory ascites. For large-volume paracenteses, an albumin infusion of 6-8 g/L of fluid removed can be considered. Aquaretic agents (e.g. vasopressin receptor antagonists) produce solute-free diuresis are the most important aquaretic agents that have been proven useful. However, their clinical utility remains to be defined.

Transjugular intrahepatic portosystemic shunt (TIPS) may be considered in appropriately selected patients. Referral for liver transplantation should be considered for all patients with refractory ascites. Lastly, peritoneovenous shunt has a very little role in treatment, and may be considered for patients with refractory ascites who are not candidates for paracenteses, TIPS, or liver transplant.

Topic 17: Liver Cirrhosis and Complications

No: 1276

Clinical profile and mortality in patients with hepatopulmonary syndrome

Nauman Arif Jadoon[1], Irfan Younis[2], Shahid Sarwar[2], Zeeshan Butt[2]

Ittefaq Hospital Medicine Lahore-Pakistan[1], Mayo Hospital Medicine Lahore-Pakistan[2]

Aim: The aim of our present study was to assess the prevalence and predictors of HPS and prospectively evaluate the effect of HPS on mortality in patients with advanced cirrhosis.
Methods: This study was carried out at Department of Medicine, King Edward Medical University Lahore, Pakistan. Patients with cirrhosis of liver were evaluated for presence of HPS with arterial blood gas analysis and saline bubble echocardiography. All patients were followed for 6 months for complications and mortality.
Results: 110 patients were included in the study. Twenty-nine patients (26 %) had HPS. MELD score was significantly higher ($P < 0.01$) in patients with HPS (18.93 ± 3.51) as compared to that in patients without HPS (13.52 ± 3.3). Twenty two (75.9 %) patients of Child Class C, 5 (17.2 %) patients of Child Class B and 2 (6.9 %) patients of Child Class A had HPS (P 0.03). HPS significantly increased mortality during six month follow up period (HR: 2.47, 95 % CI: 1.10-5.55). Child-Pugh and MELD scores were also associated with increased mortality. HPS was no longer associated with mortality when adjustment was done for age, gender, Child-Pugh, and MELD scores (HR: 0.44, 95 % CI: 0.14-1.41). Both the Child-Pugh and MELD scores remained significantly associated with mortality in the multivariate survival analysis.
Conclusions: HPS indicates advanced liver disease and is associated with mortality, however, it does not have an impact on mortality when adjusted for age, gender and severity of cirrhosis.

Topic 17: Liver Cirrhosis and Complications

No: 1043

Can cirrhosis cause cardiomyopathy

Burcu Cetin Sezgin[1], Ahmet Uyanikoglu[2], Timucin Aydogan[2], Huriye Camlıbel[3], Yusuf Sezen[4], Hasim Nar[2], Turgay Ulas[3], Necati Yenice[2]

Akcakale City Hospital Internal Medicine Sanliurfa-Turkey[1], Harran University Gastroenterology Sanliurfa-Turkey[2], Harran University Internal Medicine Sanliurfa-Turkey[3], Harran University Cardiology Sanliurfa-Turkey[4]

Aim: We, in this study, researched whether there is between cardiomyopathy and cirrhosis relation in compensated and decompensated cirrhosis patients performing echocardiography, EKG and evaluating Troponin I and Pro-BNP levels.
Method: In the study 60 liver cirrhosis patients and 30 healthy volunteer group participated. The participants are divided in 3 groups as compensated (Group 1, n = 30), decompensated (Group 2, n = 30) cirrhosis patients and healty control (Group 3, n = 30). By performing echocardiography of each cases, E/A ratio, LVDD levels and QT prolongation are calculated. In addition Troponin I and Pro-BNP levels are measured by chemiluminesans method in a biochemistry autoanalyser.
Findings: A statistically significant difference is not seen between groups regarding to age and sex (p > 0,05). Pro-BNP levels of Group 2 patients were statistically higher than those of the other groups ($P < 0{,}001$). Also it was higher in Group 1 than that in Group 3 ($P = 0{,}006$). QT prolongation in Group 1 showed a statistically significant difference comparing to Group 3 ($P = 0{,}011$).
Result: Our study showed that Pro-BNP levels and QT prolongation are high in cirrhosis patients and these parameters support cirrhotic cardiomyopathy. Between the groups, Troponin levels, LVDD and E/A ratio were not a significant difference.

Topic 17: Liver Cirrhosis and Complications

No: 1047

Predictors of response and outcome to terlipressin in patients with hepatorenal syndrome

Dr. Vinit Shah[1], Dr. Ashish Kumar[2], Dr. Praveen Sharma[3], Dr. Rinkesh Bansal[2], Dr. Pankaj Tyagi[2], Dr. Naresh Bansal[2], Dr. Vikas Singla[2], Dr. Mandhir Kumar[2], Dr. Piyush Ranjan[2], Dr. Munish Sachdeva[2], Dr. Anil Arora[2]

Sir Ganga Ram Hospital Gastroenterology & Hepatology New Delhi-India[1], Sir Ganga Ram Hospital Gastroenterology and Hepatology New Delhi-India[2], Sir Ganga Ram Hospital Gastroentrology & Hepatology New Delhi-India[3]

Background: Prospective, observational, cohort study to determine factors influencing hepatorenal syndrome (HRS) development, survival and predictors of terlipressin response.
Methods: Cirrhotic patients were diagnosed with acute kidney injury as per (IAC/ADQI) definition, evaluated as per study protocol. Patients with HRS were analysed for factors influencing development, survival and those who received terlipressin were analysed for predictors of response.
Results: 395 consecutive cirrhotics with renal impairment were included. HRS was seen in 85 patients (21.5 %). Median age 54 years (25–86). Males (85.3 %) and females (14.7 %). Median hospitals stay 7 days (1–48). Terlipressin was given to 162 patients, 72 (44 %) patients responded to terlipressin and 90 (56 %) were terlipressin non responders. HRS had worst survival of all AKI types with terlipressin non responders having worst survival as compared to terlipressin responders. Higher MELD score, low serum albumin, presence of SBP and hypotension with inotrope requirement were more significantly associated with HRS/ATN development.Longer duration of hospitalization, higher CTP & MELD score, higher INR, male gender, presence of HE, hypotension with inotropic requirement correlated significantly with response to terlipressin on univariate analysis. Presence of hypotension requiring inotropic support was only factor on multivariate analysis to correlate with terlipressin non response.
Conclusions: Development of HRS is associated with significantly reduced survival than other types of AKI in cirrhotics with especially dismal survival in terlipressin non responders. The terlipressin response rate in our cohort was 44 %. Development of hypotension with inotropic requirement was the single most important predictor of terlipressin non response.

Topic 17: Liver Cirrhosis and Complications

No: 1973

Early pleuricentesis predicts survival in cirrhotics with spontaneous bacterial empyema

Amrish Sahney[1], Ankur Jindal[1], Chetan Kalal[1], Lovkesh Anand[1], Cyriac Abby Philips[1], Shiv Sarin[1]

Ilbs Hepatology New Delhi-India[1]

Background: Spontaneous bacterial empyema (SBEM) is associated with high mortality and occurs in absence of spontaneous bacterial peritonitis (SBP) in one-third of cases. We compared the clinical outcomes of these patients who received early (< 24 h) vs. late (24-72 h) pleuricentesis (EP vs.LP).
Methods: Consecutive cirrhotics with SBEM (pleural fluid neutrophil count ≥ 500 cells/mm3) diagnosed within 72 h of hospitalization were included. Main indications for pleuricentesis were suspected pleural fluid infection and/or symptomatic hydrothorax. Patients were sub-grouped based on defined pleuricentesis interval from hospitalization; and those with concurrent SBP (n = 70) were excluded. Study end-points included in-hospital death and duration of hospitalization.
Results: Of the 140 patients with SBEM,109 werediagnosedwithin72 h(77 %),39(36 %) patients had SBEM without SBP. Overall mortality was significantly lower in SBEM patients without SBP (25 % vs. 52 %, P ≤ .01) compared to those with SBP. Subgroup analysis of SBEM patients without SBP revealed that clinical, demographic and lab profile was comparable in EP and LP group. On multivariate analysis, MELD score > 21, serum creatinine level > 1.5 mg % and LP independently predicted mortality. LP group had longer hospital stay [mean intensive care days (6.5.0 ± 2.14 versus 2.8 ± 2, P ≤ 0.05), ward stay (9.0 ± 2.67 vs6.5 ± 2.0, P ≤ 0.05)] and higher in-hospital mortality compared (41 % versus 10 %, P ≤ 0.05) compared with EP group. Each hour delay in pleuricentasis was associated with 2.5 % increase in mortality after adjusting for MELD score and creatinine levels.
Conclusions: Hospitalized patients with SBEM receiving late pleuricentesis had increase in mortality. Diagnostic pleuricentesis performed < 24 h from hospitalization in cirrhotics with pleural effusion may improve short-term survival.

Topic 17: Liver Cirrhosis and Complications

No: 1046

Risks of venous thromboembolism in patients with liver cirrhosis a nationwide cohort study in Taiwan

Khai Jing Ng[1], Yung-cheng Su[2], Yi-kung Lee[2]

Dalin Tzu Chi Hospital Internal Medicine Dalin-Taiwan[1], Dalin Tzu Chi Hospital Emergency Department Dalin-Taiwan[2]

Background: Various studies attempted to assess risks of venous thromboembolism in liver cirrhosis came out with conflicting results. Furthermore, while Asians were thought to have relatively low incidence of venous thromboembolism, no study regarding the relation between venous thromboembolism and liver cirrhosis has been carried out in Asian countries.
Objective: We investigated the risks of venous thromboembolism among cirrhotic patients in Taiwan to evaluate if there is a higher risk compared to the general population.
Methods: We utilized a National Health Insurance (NHI) claims data sample containing one million beneficiaries. We followed all adult beneficiaries from January 1, 2007 until December 31, 2010 to identify if he or she was diagnosed with venous thromboembolism. We further identified patients with liver cirrhosis and matched each one with ten non-cirrhotic patients based on their high-dimensional propensity scores. Cox regression models were applied to compare the hazard ratios of venous thromboembolism in the matched cohorts.
Results: A total of 757,940 patients were enrolled. After matching, 2,223 cirrhotic patients and 22,230 non-cirrhotic patients were selected. The adjust hazard ratio of venous thromboembolism is significantly increased (1.71; 95 % CI, 1.05–2.78). A subgroup analysis of 293 patients with advanced cirrhosis and 2,930 without liver cirrhosis were further evaluated. The hazard ratio of venous thromboembolism is much higher in the advanced cirrhotic patients. (4.36; 95 % CI, 1.36–14.01).
Conclusion: The risk of venous thromboembolism in cirrhotic Asian patients may be higher compared to the general population, especially in those with advanced stages.

Topic 17: Liver Cirrhosis and Complications

No: 1274

Hyponatremia in decompensated cirrhosis is it associated with more severe disease

Nauman Arif Jadoon[1], Zeeshan Butt[2], Ahmed Shahzad[3], Kamran Mushtaq[3]

Ittefaq Hospital Medicine Lahore-Pakistan[1], Mayo Hospital Medicine Lahore-Pakistan[2], Nishtar Medical College Hospital Medicine Lahore-Pakistan[3]

Aim: The aim of our study was to evaluate whether there is any association between hyponatremia and severity of decompensated cirrhosis.
Methods: Consecutive patients of decompensated cirrhosis presenting at three tertiary care hospitals were included in the study. Hyponatremia was defined as serum sodium levels of < 135 mEq/L. Patients with Child-Pugh Class A and B were considered having mild disease and Class C patients were categorized as having severe disease.
Results: A total of 202 patients were included in the study with male preponderance (53 %). Patients presenting with Child-Pugh Class A, B and C were 16 (6.9 %), 74 (36.6 %) and 114 (56.4 %) respectively. Hyponatremia was present in 37.3 % of the patients. On bivariate analysis, factors associated with severe decompensated cirrhosis (Child-Pugh Class C) were total protein < 6 g/dL (p, 0.002), hemoglobin level < 12 g/dL (p, 0.006), APTT > 35 s ($P < 0.001$), AST > 35 IU (p, 0.03) and serum sodium level < 135 mEq/L. Thrombocytopenia, raised blood urea, raised serum creatinine, and hyperkalemia were not associated with severity of decompensated cirrhosis as was the etiology of cirrhosis (Hepatitis C versus non-hepatisis C). Variables significant in the bivariate analysis were then included in the multivariate logistic regression model. All the variables remained significant except anemia which did not show any association with severity of disease in multivariate analysis.
Conclusion: One third of the patients with decompensated cirrhosis in the present study had hyponatremia which was associated with less severe disease (lower Child-Pugh Class) at presentation.

Topic 17: Liver Cirrhosis and Complications

No: 1158

Demographic and clinic characteristics of cirrhotic patients in sanliurfa Turkey

Ahmet Uyanikoglu[1], Timucin Aydogan[1], Ferzan Aydin[1], Burcu Sezgin[1], Hasim Nar[1], Necati Yenice[1]

Harran University, Medical Faculty Gastroenterology Sanliurfa-Turkey[1]

Objective: To investigate the demographic and clinic characteristics of cirrhotic patients who were followed of Harran University Gastroenterology Clinic.
Material-method: 112 patients followed in the gastroenterology clinic between January2012-July 2014 were analyzed, retrospectively. Patients with newly diagnosed and previously diagnosed with sufficient data of file were included. Defined as patients with decompensated cirrhosis with ascites, patients were evaluated according to Child and MELD scoring.
Results: 65 patients (58 %) were men, mean age were 54.7 ± 15.1 (range 19-89) years. 34(30 %) patients were compensated, 78 (70 %) were decompensated cirrhosis. 35 % of patients were Child A, 41 % B and 24 % C, respectively. 38 patients (36 %) of MELD score was 15 and over. Etiology of patients were 38 (34 %) hepatitis B, 26 (23 %) cryptogenic, 21 (19 %) hepatitis C, 11 (10 %) delta, 5 (4.5 %) Wilson disease, 2 B + C coinfection, 9 (7 %) others (cholestatic, hemocromatozis, cardiogenic, alcholic and otoimmun), respectively. 26 (23 %) patients had a history of variceal bleeding. 14(13 %) patients had comorbid disease. Diabetes mellitus was the most frequent comorbid disease in 8(6 %) patients.
Conclusion: Approximately half of the patients decompensated during follow-up clinic and Child B–C there were liver transplantation candidates and hepatitis B the most frequent etiology. One quarter of the patients were cryptogenic, one ten were delta, there are the relatively high rate in the literature. In one quarter of patients were history of variceal bleeding and the most common concomitant diseases was diabetes mellitus.

Topic 17: Liver Cirrhosis and Complications

No: 1939

Dynamic contrast enhanced MRI (DCE MRI) is a new non invasive modality for accurate prediction of liver cirrhosis

Pik-eu Chang[1], Choon-hua Thng[2], Thong-san Koh[2], Kiat-hon Lim[3], Chee-kiat Tan[1]

Singapore General Hospital Gastroenterology & Hepatology Singapore-Singapore[1], National Cancer Center Oncologic Imaging Singapore-Singapore[2], Singapore General Hospital Pathology Singapore-Singapore[3]

Background/aims: Chronic liver injury leads to accumulation of fibrous tissue in Disse's space. We postulate that the fractional interstitial volume(FIV) measured using dynamic contrast-enhanced MRI(DCE-MRI) estimates the volume of Disse's space and can be used to predict severity of liver fibrosis/cirrhosis. This pilot study aims to evaluate the accuracy of DCE-MRI to predict severity of liver fibrosis in patients with chronic liver disease.
Methods: Chronic liver disease patients undergoing liver biopsy received DCE-MRI and liver stiffness measurement(LSM) via Fibroscan® within 1 month in a prospective study. AUROC of DCE-MRI was compared against Fibroscan® for diagnosis of significant fibrosis(METAVIR ≥ F2), advanced fibrosis(METAVIR ≥ F3) and cirrhosis(F4).
Results: Thirty patients with mean age 48.4 ± 11.4 years and 63.3 % males were recruited. Etiology of liver disease was HBV(47 %), HCV(20 %), NASH(17 %), AIH/PBC(16 %). Eight patients did not complete the study. The remaining 22 were divided into four groups based on liver histology: No/mild fibrosis(23 %), significant fibrosis(30 %), advanced fibrosis(30 %) and cirrhosis(17 %). Mean FIV on DCE-MRI was 8.5 ± 4.2, 9.7 ± 3.8, 10.4 ± 5.7, 19.8 ± 4.9 % and mean LSM was 12.7 ± 5.4, 11.3 ± 5.0, 14.9 ± 6.9, 15.7 ± 4.7 kPa respectively. AUROC for diagnosis of significant fibrosis, advanced fibrosis and cirrhosis by DCE-MRI was 0.65, 0.68 and 0.94 respectively vs. 0.52, 0.64 and 0.68 for Fibroscan®. An optimal FIV value > 12.5 % was 94 % accurate in predicting cirrhosis with 100 % sensitivity and 89 % specificity.
Conclusions: Our results support the hypothesis that FIV measured by DCE-MRI correlates with liver fibrosis stage. DCE-MRI is particularly accurate for the non-invasive diagnosis of liver cirrhosis compared to Fibroscan® but is less discerning for lower stages of liver fibrosis.

Topic 17: Liver Cirrhosis and Complications

No: 1427

Impact of the vasopressin v2 receptor antagonist tolvaptan on renal hemodynamics in cirrhotic patients with ascites a preliminary study

Kazuhisa Nakashima[1], Yasuji Komorizono[1], Katumi Sako[1], Toshihiko Shibatou[1]

Nanpuh Hospital Hepatology Kagoshima-Japan[1]

Background and aim: The Doppler sonographic renal resistance index (RI) is known to be associated with renal hemodynamics in cirrhotic patients with ascites. The vasopressin V2-receptor antagonist tolvaptan is a novel and promising agent for the treatment of hyponatremia and ascites in end-stage liver disease (ESLD). This preliminary study was designed to investigate the impact of tolvaptan on renal hemodynamics in cirrhotic patients with ascites.
Methods: Ten cirrhotic patients with ascites (5 males and 5 females; aged 48–83 years; mean, 67 years) who showed insufficient response to a sodium-restricted diet and a dual-diuretic regimen with oral spironolactone (≧50 mg/day) and oral furosemide (≧40 mg/day) were prospectively included in this study. Tolvaptan was started at a dose of 3.75 mg/day in the inpatient setting as an add-on therapy to the dual-diuretic regimen. Non-responders who did not achieve insufficient weight loss (<1 kg body-weight) at day 7 received 7.5 mg/day tolvaptan. The renal hemodynamics were measured for the Doppler sonographic renal RI before and day14–28 after the administration of tolvaptan.
Results: Seven patients (70 %) achieved sufficient response to tolvaptan. Compared with baseline values, the mean changes in weight loss and RI reduction were 6 kg and 0.04, respectively. Renal RIs were significantly decreased from those before the administration of tolvaptan ($P = 0.001$).
Conclusion: The results of this study must be interpreted with consideration of the important limitations of the relatively small sample size; however, our data indicates that tolvaptan as an add-on therapy to a dual-diuretic regimen improved renal hemodynamics and ascites.

Topic 17: Liver Cirrhosis and Complications

No: 2148

Rifaximin versus placebo in reducing the risk of clinically overt hepatic encephalopathy recurrence in patients having cirrhosis of liver

Ahmad Nawaz[1], Aamir Ghafoor[1], Abbas Khan[1], Hasmat Ullah[1]

Lady Reading Hospital Gastroenterology & Heaptology Peshawar-Pakistan[1]

Background: Hepatic Encephalopathy (HE) is a common complication of cirrhosis of liver. In the pathogenesis of HE ammonia production plays the most important role. Antibiotics help in HE via reducing the ammonia level by eliminating the ammonia-producing colonic bacteria. Rifaximin is minimally absorbed oral antibiotics having broad spectrum antibacterial activity against bacteria of the gut.
Objective: To determine the efficacy of Rifaximin in reducing the risk of clinically overt hepatic encephalopathy recurrence in patients having cirrhosis of liver as compared to placebo.
Methadology: This placebo controlled randomized trial, was conducted in the department of Gastroenterology and Hepatology Department PGMI/LRH, Peshawar, Pakistan. Adult patients having cirrhosis of liver and with history of two or more episode of acute HE in the past 6 months were randomized into either the Rifaximin or placebo group. Rifaximin or placebo was given 550 mg twice daily for 6 months or till the recurrence of acute attack of HE.
Results: A total of 150 patients were enrolled in the study, 75 in each the Rifaximin and the placebo group. The patients in the Rifaximin group have lesser recurrence of the episodes of hepatic encephalopathy (46.17 %) as compared to the placebo group (68.94 %) and the difference was found to be statistically significant.
Conclusion: In this placebo controlled randomized trial, the Rifaximin has shown to reduce the risk of clinically overt hepatic encephalopathy recurrence in patients having cirrhosis of liver as compared to placebo.

Topic 17: Liver Cirrhosis and Complications

No: 1302

Occurrence of anemia in chronic liver disease

Dr. Mohsin Ali Baloch[1], Dr. Saira Baloch[2]

2faculty of Pharmacy University of Sindh, Jamshoro, Pakistan Faculty of Pharmacy University of Sindh, Jamshoro, Pakistan Jamshoro-Pakistan[1], Medical Research Center, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan. Medical Research Center, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan. Jamshoro-Pakistan[2]

Objective: To evaluate the occurrence of anemia in chronic liver disease patients and to detect the abnormalities of RBCs in patients with liver cirrhosis and to find the type of anemia in a patient with chronic liver disease.
Materials and methods: The study was conducted in L.U.H, hospital. Eighty patients were selected in this study from patients coming to department of Medicine OPD. Conclusion The study showed 80 % had anemia which is very common in chronic liver disease, it is concluded that early diagnosis of anemia in chronic liver disease may assist a part in the treatment of patients and prevent morbidity and mortality.

Topic 17: Liver Cirrhosis and Complications

No: 2065

N acetyl cysteine is ineffective in preventing ischemic hepatitis following variceal bleed in cirrhotics interim analysis of a prospective randomized controlled trial

Awinash Kumar[1], Devraja Rangegowda[1], Lovkesh Anand[1], Amrish Sahney[1], Ajeet Bhadoria[2], Chitranshu Vasisth[1], Shiv Sarin[1]

Ilbs Hepatology New Delhi-India[1], Ilbs Research New Delhi-India[2]

Background: Ischemic hepatitis (IH) following variceal bleed in cirrhotics carries ominous prognosis. N-acetylcysteine can be helpful in the prevention of hepatic ischemia by providing cytoprotection against free-radical (oxidant) induced cellular injury.
Aim: To compare the efficacy of N-acetylcysteine in the prevention of development of IH and patient survival. Methods: 190 bleeders presenting to the ILBS were screened; 56 were excluded and 134 were randomized to receive either standard of care plus N-acetylcysteine for 72 h (Group A, n = 66) or only standard of care (Group B, n = 68). Standard of care included I.V. fluids, terlipressin, endotherapy, blood products and antibiotics..IH was defined as an increase in AST of $\geq$ 5 times ULN and bilirubin $\geq$ 1.5 times of baseline in next 24 h. Severity of variceal bleed was calculated by APASL bleeding severity score (Table 1) .
Results: Of the 134 bleeders,20 (14.9 %) developed IH. The IH developed in 8/66 (12.1 %) patients in Gr.A and 12/68 (17.6 %) in Gr.B ($P = 0.37$). Patients who had IH had significantly higher CTP (11.35 $\pm$ 1.59 Vs 10.1 $\pm$ 1.9), MELD (26.5 $\pm$ 10.5 Vs 21 $\pm$ 8.9), lactate (8.4 $\pm$ 3.2 Vs 4 $\pm$ 2.7 mmol/L) LDH (3553 Vs 724 IU/ml), APASL bleeding severity score (4.9 $\pm$ 1.4Vs2.9 $\pm$ 1.5) and lower mean arterial pressure (66.3 $\pm$ 9.7Vs78 $\pm$ 14.5 mmHg). Mortality in Gr A (15/66,22.7 %) and in Gr B (14/68,20.5 %) was comparable and was higher in patients with IH (12/20, 60 % Vs 17/114, 14.9 %) ($P < 0.001$).
Conclusion: IH develops in about 15 % of cirrhotic patients with acute variceal bleed and is associated with a high mortality.N-acetylcysteine therapy does not significantly prevent or ameliorate the development of IH.

Topic 17: Liver Cirrhosis and Complications

No: 1881

Safety and efficacy of therapeutic paracentesis in spontaeous bacterial peritonitis

Hasnain Ali Shah[1], Manzoor Hussain[1], Saadat Ali[1]

Aga Khan University Hospital Section of Gastroenterology, Department of Medicine Karachi-Pakistan[1]

Background: Spontaneous bacterial peritonitis (SBP) is a common complication of cirrhosis and leads to significant morbidity and mortality. A significant proportion of patients with this condition have tense ascites and need therapeutic paracentesis(TP) for symptomatic relief.
Aims: To determine the safety and efficacy of TP in SBP with tense ascites.
Methods: Retrospective analysis of case records of patients with SBP and tense ascites who underwent TP, and comparison with patients who did not undergo therapeutic paracentesis.
Results: Case records of 91 patients with SBP were evaluated. Patients were divided into two groups: A)Paracentesis group (n = 45) and B) No paracentesis group (n = 46). Baseline characteristics of patients in two groups were similar: mean age 53.64 $\pm$ 11.72 vs. 52.70 $\pm$ 11.66 years; hepatic encephalopathy 26/45 (57.7 %) vs. 25/46 (54.3 %); hepatocellular carcinoma 13/45 (28.8 %) vs. 11/45(24.4 %); serum creatinine 1.30 $\pm$ 0.82 vs. 1.62 $\pm$ 1.15 mg/dl; Child-Pugh score 7.14 $\pm$ 1.84 vs. 7.50 $\pm$ 1.95; and MELD score 19.51 $\pm$ 5.3 vs. 21.74 $\pm$ 7.55. Post-paracentesis (48-hr) mean serum creatinine was

1.26 ± 0.79 mg/dl in group A as compared to 1.66 ± 1.20 mg/dl in group B. The incidence of acute kidney injury (AKI) was not different between group A and B: 8/45 (18.1 %) vs. 6/46 (13.3 %) ($P = 0.82$).Hypotension was observed only in 3/45(6.6 %) patients in group A patients.Four week mortality was higher in group B 12/42 (28.57 %)vs. 16/36 (44.44 %) ($P = 0.04$) in group A.
Conclusion: Therapeutic paracentesis is safe in SBP. The occurrence of AKI was not different from the non-paracentesis group and hypotension was an infrequent complication.Four week mortality was in the patients undergoing paracentesis.

Topic 17: Liver Cirrhosis and Complications

No: 2243

Measurement of serum procalcitonin levels for the early diagnosis of spontaneous bacterial peritonitis in patients with decompensated liver cirrhosis

Huiguo Ding[1]

Beijing Youan Hospital Affiliated To Capital Medical University Gi and Hepatology Beijing-China[1]

Background: It is difficult to diagnose spontaneous bacterial peritonitis (SBP) early in decompensated liver cirrhotic ascites patients (DCPs).The aim of the study was to measure serum procalcitonin (PCT) levels and peripheral blood leukocyte/platelet (WBC/PLT) ratios to obtain an early diagnostic indication of SBP in DCPs.
Methods: Our cohort of 129 patients included 112 DCPs (94 of whom had infections) and 17 cases with compensated cirrhosis as controls. Bacterial cultures, ascitic fluid (AF) leukocyte and peripheral WBC/PLT counts, and serum PCT measurements at admission were carried out prior to the use of antibiotics. Receiver operating characteristic (ROC) curves were generated to test the accuracies and cut-off values for different inflammatory markers.
Results: Among the 94 infected patients, 66 tested positive by bacterial culture, for which the positivity of blood, ascites and other secretions were 25.8, 30.3 and 43.9 %, respectively. Lung infection, SBP and unknown sites of infection accounted for 8.5, 64.9 and 26.6 % of the cases, respectively. Serum PCT levels (3.02 ± 3.30 ng/mL) in DCPs with infections were significantly higher than those in control patients (0.15 ± 0.08 ng/mL); $P < 0.05$. We used PCT ≥ 0.5 ng/mL as a cut-off value to diagnose infections, for which the sensitivity and specificity was 92.5 % and 77.1 %. The area under the curve (AUC) was 0.89 (95 % confidence interval: 0.84–0.91). The sensitivity and specificity were 62.8 % and 94.2 % for the diagnosis of infections, and were 68.8 % and 94.2 % for the diagnosis of SBP in DCPs when PCT ≥ 2 ng/mL was used as a cut-off value. For the combined PCT and WBC/PLT measurements, the sensitivity was 76.8 % and 83.6 % for the diagnosis of infections or SBP in DCPs, respectively.
Conclusion: Serum PCT levels alone or in combination with WBC/PLT measurements seem to provide a satisfactory early diagnostic biomarker in DCPs with infections, especially for patients with SBP.

Topic 17: Liver Cirrhosis and Complications

No: 1277

Clinical presentation ultrasound findings and biochemical abnormalities in decompensated cirrhosis a review of 162 patients

Nauman Arif Jadoon[1], Zeeshan Butt[2], Ahmed Shahzad[3], Kamran Mushtaq[3]

Ittefaq Hospital Medicine Lahore-Pakistan[1], Mayo Hospital Medicine Lahore-Pakistan[2], Nishtar Medical College Hospital Medicine Lahore-Pakistan[3]

Objectives: The objectives of our study were to know the clinical presentation, frequency of classical clinical signs, ultrasound findings, and abnormalities in laboratory investigations in patients with decompensated cirrhosis.
Method: 162 consecutive patients with decompensated cirrhosis admitted in Mayo Hospital, Lahore were enrolled in the study. Patients were examined at bedside and presence of classical signs of cirrhosis was noted. Patients were asked about presence of co-morbid conditions. Records of the patients were reviewed and findings on abdominal ultrasound and abnormalities on laboratory investigations were noted.
Results: Sixty percent of 162 patients were male. Hepatic encephalopathy was the most common presentation (46 %) followed by ascites (33 %) and hematemesis (33 %). Twenty four percent patients had malena also. About one third (35 %) of patients were diabetic and one fourth (27 %) hypertensive. Jaundice was the most common clinical sign (55 %) followed by peripheral edema (54 %). Digital clubbing was present in 9 % of patients while palmer erythema in 12 % of patients. Ultrasonography revealed enlarged spleen (> 12 cm) in 56 % of patients and ascites in 62 % of patients. Hepatitis C was the cause of cirrhosis in 82 % of patients while hepatitis B in 9 %. About one third had blood bilirubin levels more than 1.2 mg/dl and a similar proportion had albumin less than 3.4 g/dl. Anemia (Hemoglobin < 12 g/dl) was present in 80 % of patients.
Conclusion: Hepatic encephalopathy is the most common clinical presentation of decompensated cirrhosis. Jaundice and peripheral edema are the most common clinical signs of cirrhosis.

Topic 18: Liver Transplantation

No: 1446

Safety of right lobe living donor liver transplant from donors with gilbert syndrome

Hussien Elsiesy[1], Sara Yousef[1], Khalid Selim[1], Waleed Alhamoudi[1], Mohamed Shagrani[1], Mohamed Al Sebayel[1], Dieter Broring[1], Faisal Abaalkhail[1]

King Faisal Specialist Hospital & Research Center Liver Transplantation Riyadh-Saudi Arabia[1]

Introduction: Donor safety is the most important consideration of living donor liver transplantation (LDLT) evaluation. Some candidates with normal liver function test have isolated indirect hyperbilirubinemia related to Gilbert Syndrome.
Case reports and small case series demonstrated safety of use of donors with Gilbert syndrome. Our aim is to review the donor safety of liver donation from Gilbert and the effect on the recipients.
Method: Between January 2001 and September 2014, 222 LDLT using right-lobe grafts were performed in our hospital. Donors with Gilbert syndrome were defined as those whose serum bilirubin level was greater than 20.5 μmol/L (1.2 mg/dL). Fifteen of 222 (6.7 %)right-lobe LDLT were performed using donors with Gilbert syndrome, data on the age, gender, body mass index (BMI), total and direct bilirubin before donation, post-operative maximum bilirubin (PMB), total liver volume, percentage of remaining liver volume, donor and receipt outcome.
Results: The mean follow up period is 75 months (4-138), the mean age was 25 (18-32), all male, mean BMI was 23 (18-27), mean per-operative total bilirubin was 28 (18-34), mean per-operative direct bilirubin was 6 (1-10), mean PMB total was 85 (50-122), mean PMB direct was 23 (11-45), all has right lobe hepatectomy with a mean

remaining volume of 36 % (30-43). No mortality in the donors, one recipient died of hepatic artery thrombosis.
Conclusion: Right lobe living donor liver transplantation from donor with Gilbert disease is safe for donors with excellent outcome in the recipients.

Topic 18: Liver Transplantation

No: 1730

Outcomes of liver transplantation in patients with hepatitis B and hepatocellular carcinoma the U.S. transplant registry data

Zobair Younossi[1], Maria Stepanova[1], Sammy Saab[2], Aijaz Ahmed[3], Robert Wong[4], Brian Lam[1], Manirath Srishord[5], Chapy Venkatesan[1], Homan Wei[1], Linda Henry[5]

Center For Liver Diseases, Inova Fairfax Hospital Medicine Falls Church-United States[1], Departments of Medicine and Surgery, David Geffen School of Medicine At The University of California At Los Angeles Los Angeles-United States[2], Division of Gastroenterology and Hepatology, Stanford University School of Medicine Stanford-United States[3], Division of Gastroenterology and Hepatology, Alameda Health System-highland Hospital Campus Oakland-United States[4], Betty and Guy Beatty Center For Integrated Research, Inova Health System Falls Church-United States[5]

Background: Hepatocellular carcinoma (HCC) is an important complication of hepatitis B (HBV). HBV remains a major indication for liver transplantation.
Aim: Assess the outcome of HBV transplant recipients with and without HCC.
Methods: All adult liver transplant recipients with positive HBsAg were included from the U.S. Scientific Registry of Transplant Recipients (2004-2013).
Results: Total 2,592 liver transplant recipients with HBV were included (53.5 ± 10.4 years old, 76.5 % male). of these, 676 (26.1 %) had HCC with or without cirrhosis. HBV patients with HCC were older, predominantly Asian, had lower MELD scores, better functional status and shorter inpatient stay (all $P < 0.05$). Inpatient mortality was lower in HBV patients with HCC: 3.74 % vs. 7.16 % ($P = 0.0017$). In follow-up (45 ± 30 months), 18.7 % patients died. One-year mortality was again lower in HBV patients with HCC: 7.4 % vs. 10.9 % ($P = 0.0139$). However, starting second year post-transplant, no difference in mortality was noted (all $p > 0.05$). Three-year mortality was 16.7 %, 5-year 20.9 %, and 7-year mortality 24.9 %. The rates of graft failure were also similar between HCC and non-HCC HBV patients: 4.5 % in 1 year, 7.0 % in 3 years, 8.6 % in 5 years. In multivariate survival analysis, younger age, Asian race and study year were independent predictors of lower mortality, while HCC was not associated with mortality in HBV ($p > 0.05$). Increased risk of graft failure in HBV was associated with younger age and procurement from a non-heart-beating donor ($P < 0.05$), but not with HCC ($p > 0.05$).
Conclusions: In liver transplant recipients with HBV and HCC, the diagnosis of HCC does not impact survival.

Topic 18: Liver Transplantation

No: 2119

Plasmapharesis intravenous immunoglobulin and rituximab successfully treat recurrent progressive familial intrahepatic cholestasis type 2 after liver transplantation

Hussien Elsiesy[1], Faisal Abaalkhail[1], Waleed Alhamoudi[1], Hessah Al Hussaini[2], Mohamed Al Sebayel[1], Dieter Broring[1], Mohammed Shagrani[1]

King Faisal Specialist Hospital & Research Center Liver Transplantation Riyadh-Saudi Arabia[1], King Faisal Specialist Hospital & Research Center Pathology Riyadh-Saudi Arabia[2]

Background: After liver transplantation, antibodies against BSEP receptors can form and bind BSEP receptors causing a picture similar to PFIC-2, this was first described in 2009. Since then, few cases of PFIC-2 recurrence was reported.
Methods: We present two cases with PFIC-2 recurrence after liver transplantation; a 14 years old boy and his 19 years old sister who had received cadaveric liver transplantation in the United states in 2011. In January 2014 they presented with severe itching, high bilirubin, high AST/ALT and high serum bile acid. Virology, Autoimmune screen, Abdominal CT Scan and liver biopsy were negative. Initial liver biopsy on both patients were not conclusive but repeat biopsy of the 14 year-old boy on May 2014 showed recurrence of PFIC2, his anti-BSEP titer was 1: 1200, Treatment regimen for him started by 5 sessions of plasmapharesis every other day with an exchange volume of 1.5, followed by IV immunoglobulin (IVIG), followed by one dose of IV Rituximab 375/m2. His sister's liver biopsy showed PFIC2 recurrence. She started on the same treatment regimen.
Results: Currently, both patients improved clinically and biochemically and still on treatment plan.
Conclusions: PFIC-2 recurrence after liver transplantation occur through an antibody mediated rejection against BSEP receptors and can successfully be treated with plasmapharesis, IVIG and rituximab obviating the need for re-transplantation.

Topic 18: Liver Transplantation

No: 1953

Acoustic radiation force impulse imaging for the prediction of graft fibrosis after liver transplantation

Yukihiro Okuda[1], Kojiro Taura[1], Yoshinobu Ikeno[1], Takahiro Nishio[1], Gen Yamamoto[1], Kazutaka Tanabe[1], Kohei Ogawa[1], Yasuhiro Fujimoto[1], Akira Mori[1], Etsuro Hatano[1], Toshimi Kaido[1], Hideaki Okajima[1], Shinji Uemoto[1]

Graduate School of Medicine Kyoto University Department of Surgery Kyoto-Japan[1]

Background and aim: Graft fibrosis is a common and significant event after liver transplantation. Liver biopsy has been the gold standard for assessing graft fibrosis, however, less invasive method would be ideal. We aimed to evaluate the usefulness of noninvasive liver stiffness measurement by acoustic radiation force impulse imaging (ARFI) for the prediction of graft fibrosis.
Patients and methods: We performed ARFI on 123 consecutive post liver transplant patients (primary diseases: 41 viral hepatitis/cirrhosis, 34 biliary atresia, 24 PBC/PSC, and 24 others) undergoing liver biopsy. Liver stiffness expressed as shear wave velocity (SWV, m/s) as well as routine laboratory test was compared with Metavir fibrosis score (F0-F4).
Results: F≧1 and F≧2 were observed in 91 and 32 patients, respectively. SWV was higher in F≧1 than in F0 as well as in F≧2 than in F≦1 ($P < 0.0001$; $P = 0.02$). The area under the receiver operating characteristic curve (AUROC) of SWV for F≧1 and F≧2 was 0.62 and 0.76, respectively, which were higher than AUROCs of any hematological/biochemistrical parameters. Multivariate analysis identified SWV as one of the significant predictors for both F≧1 and

F≧2. Combination of SWV and hematological/biochemistrical parameters improved diagnostic accuracy for graft fibrosis (AUROC 0.67 for F≧1 and 0.81 for F≧2).
Conclusion: Liver stiffness measurement by ARFI has good accuracy for the prediction of graft fibrosis after liver transplantation.

Topic 18: Liver Transplantation

No: 1176

Liver transplantation

Jie Chen[1], Jingyu Liao[1], Lixin Li[1], Lina Zhu[1], Bei Cai[1], Yi Li[1], Yun Liao[1], Lanlan Wang[1]

West China Hospital of Sichuan University Lab Medicine Chengdu-China[1]

Objectives: Liver function regeneration after liver transplantation (LT) is important for patients' prognosis. In order to establish the laboratory evaluation system for liver regeneration after LT and improve the survival, we analyzed the recovery process of laboratory indexes of LT recipients, and key risk factors causing poor liver regeneration.
Method: 152 LT recipients were tracked from 2001 to 2013. They were divided into two groups: normal and poor liver regeneration after transplantation. We analyzed the difference of liver function recovery process according to their pathogenesis such as liver cancer, liver cirrhosis, both tumor and cirrhosis. Recipient's age, sex, BMI index, pathogenesis, MELD score, Child-Pugh class, donor age, ischemic time, graft source and laboratory assays were analyzed and logistic regression were used to assess the potential risk factors of poor liver regeneration.
Results: For patients with normal regeneration: TB, PT and FIB recovered within a week; PLT, Alb recovered within a month; ALT, AST, GGT need more than one month. For patients with poor regeneration: PT, FIB recovered within a week; TB, Alb recovered within 3 months; others need more than 3 months or almost unstable. Risk factor analysis showed high MELD-score, high concentration of TB and living donor liver transplantation (LDLT) were key factors influencing liver regeneration.
Conclusion: The most sensitive laboratory assays in assessing liver regeneration were TB, FIB and PT. All of the indexes had delayed recovery in patients with poor liver regeneration. High MELD score, high serum TB and LDLT were important factors influencing liver regeneration after transplantation.

Topic 18: Liver Transplantation

No: 1954

Post liver transplant hyperglycaemia requiring insulin treatment is associated with increased risk of new onset diabetes after transplant (nodat)

Chern Hao Chong[1], Long Hua Teh[2], Mark Yeo[3], Seng Gee Lim[1], Yock Young Dan[1], How Cheng Low[1], Guan Huei Lee[1], Maung Aye Thwin[1], Poh Seng Tan[1], Alfred Kow[4], Stephen Chang[4], K.k Madhavan[4], Ganpathi Iyer Shridhar[4], Kieron Lim[1]

National University Hospital Gastroenterology and Hepatology Singapore-Singapore[1], Yong Loo Lin School of Medicine-Singapore[2], National University Hospital Internal Medicine-Singapore[3], National University Hospital National University Centre For Organ Transplantation-Singapore[4]

Background/aims: NODAT is a known complication post-transplant that can increase mortality and morbidity. We aim to look for factors associated with NODAT in cohort of adult liver transplant recipients in National University Hospital Singapore.
Method: We retrospectively analyze patients who have undergone liver transplantation from January 2004 until November 2013 with at least 1 year follow up. Patients' pre transplant fasting sugar, HBA1C, BMI, MELD score, immunosuppression treatment, blood sugar level first 3 days post-transplant and early use of insulin or oral hypoglycemic agent (OHGA) was documented.
Result: A total of 52 previously non-diabetic liver transplant patients completed 1 year follow up. 18/52(35 %) patients developed NODAT. Pre-transplant fasting sugar was noted to be higher in NODAT cohort. Post-transplant blood sugar level significantly higher in NODAT group after intravenous methylprednisolone given ($P < 0.05$). 15 patients required treatment for hyperglycemia of which 7 with insulin and 8 with OHGA.

Patients requiring perioperative insulin treatment has increased risk of progression into NODAT. RR = 4.091 (CI 95 % 2.448–6.838).
Conclusion: The Immediate use of insulin post-transplant to control severe hyperglycemia is a strong predictor for NODAT. We suggest close follow up in this particular patient group.

Topic 18: Liver Transplantation

No: 1083

Positive cross match and older liver grafts are associated with recurrence of primary sclerosing cholangitis after liver transplantation

Walid El Moghazy[1], Bryce Lowry[2], Glenda Meelberg[2], Norman Kneteman[2]

Sohag University Surgery Sohag-Egypt[1], University of Alberta Hpb Surgery and Transplantation Edmonton-Canada[2]

Liver transplantation (LT) is the only therapeutic option for primary sclerosing cholangitis (PSC), however, recurrence of PSC (rPSC) post-LT occurs at rates ranging from 9-47 %. We aimed to define risk factors for rPSC post-LT

A total of 101 liver transplants were done for 94 patients diagnosed with PSC over a period of 20 years at University of Alberta Hospital. The Kaplan–Meier curve was used to calculate survival and Cox's proportional regression hazard model was used to identify risk factors. A P-value of < 0.05 was considered significant.

The mean age of patients at time of transplant was 41 years. The overall patient survival was 81 % during the follow-up period; survival at 1 year was 95 %, at 5 years was 89 % and at 10 years was 85 %. rPSC occurred in 42 patients and overall recurrence free survival was 56 %. The overall graft survival was 76 %; graft survival at 1 year was 89 %, at 5 years was 83 % and at 10 years was 78 %. Univariate analysis revealed that younger recipient age at time of transplant, previous biliary surgery, low serum albumin, positive cross-match, and older donor age are potential predictors of recurrence. Multivariate analysis revealed that positive cross-match (HR = 3.316, 95 % CI (1.021-10.772)), and donor age (HR = 1.043 (1.005-1.082)) are independent predictors of rPSC.

In conclusion, LT remains the best management for end-stage PSC. Positive cross-match and older liver grafts are predictors of recurrence of PSC post-LT.

Topic 18: Liver Transplantation

No: 1480

Graft versus host disease after liver transplantation

Hussien Elsiesy[1], Ibeer Ibrahim[2], Moahemd Al Sebayel[1], Waleed Alhamoudi[1], Rania Alarieh[1], Faisal Abaalkhail[1]

King Faisal Specialist Hospital & Research Center Liver Transplantation Riyadh-Saudi Arabia[1], Alexandria University Gastroenterology Alexandria-Egypt[2]

Introduction: Graft versus host disease (GVHD) is a rare post liver transplantation (LT) complication with high mortality. Since 1988, about 80 cases had been reported with mortality rate of 80-100 %. We describe five cases of GVHD diagnosed over a period of 13 years in a total of 529 Liver transplant recipients (255 deceased donor liver transplant and 276 living-related liver transplant.
Case reports: We are reporting a case series of 5 patients with acute GVHD post LT from May 2001 till June 2013. Four cases were males; age 51-67 (average 59). The indication for liver transplantation was HBV related cirrhosis in two, one with hepatocellular carcinoma, HCV in 2 cases, and AIH. The average MELD Score at the time of transplantation was 18 (14-20). The duration from transplantation until clinical presentation ranged from 8 to 12 weeks. Four cases had diarrhea and pancytopenia, three out of five presented with erythematous skin rashes and one had cytomegalovirus colitis. GVHD was confirmed through skin biopsies, engraftment profile from bone marrow biopsy and sigmoid colon biopsy. Treatment strategies included use of corticosteroids in four cases, and stopping immunosuppression in one case.
Four cases died 27 to 96 days from clinical presentation (average 52 days) and one patient with mild form of GVHD still alive.
Conclusion: GVHD is a rare complication after liver transplantation that needs a high index of suspicion in patients who develop rash, diarrhea or severe cytopenia, there is no consensus on the best treatment regimen; and mortality remains high.

Topic 18: Liver Transplantation

No: 1793

Preoperative estimation of graft weight using portal vein diameter before donor hepatectomy for living donor liver transplantation

Piyush Sinha[1], Kishore Gs Bharathy[1], Senthil Kumar[1], Viniyendra Pamecha[1]

Institute of Liver and Biliary Sciences Hpb Surgery New Delhi-India[1]

Introduction: Accurate estimation of graft weight before donor hepatectomy is warranted for optimal donor selection as well as operative planning. Method using portal vein diameter have been found to be accurate but the results have not been validated widely.
Patients and methods: All donors undergoing right or left hepatectomy at a tertiary care centre in India from,March 2012 to January 2014 were enrolled($n = 69$).Graft weight was estimated using right portal vein diameter(R), left portal vein diameter (L), right anterior and posterior portal vein diameter (RA,RP) according to Lee's formula ($RHLV = SLV \times [R2/(R2 + L2)]$, $LHLV = SLVx[L2/(R2 + L2)]$) and modified Lee's formula($RHLV = SLV \times [(RA2 + RP2)/(RA2 + RP2 + L2)]$, $LHLV = SLV \times [(L2/(RA2 + RP2 + L2)]$.Standard liver volume was calculated using 16 different formula described in the literature. Seven were left hemiliver grafts and 10 patients had segmental branch draining to right portal vein so calculation of modified Lee's formula was not possible. Compared to actual graft volumes, the most accurate method for estimating live-donor graft volume was the Lee's formula and substituting the SLV calculation by the method of Urata and Hashimoto. CT overestimated the graft volume by Mean 54 ± 93.6 ml which was statistically different from the actual graft volume $P < 0.001$.Similarly when modified Lee's formula was used substituting the SLV calculation by the method of Urata and Hashimoto gave the most accurate estimation.
Conclusion: Modified Lee's formula could not be applied in 14 %patients. CT over estimates graft volume while Lee' and modifies Lee's formula give accurate results when SLV is calculated by Urata and Hashimoto Formula.

Topic 19: Metabolic and Genetic Liver Diseases

No: 1671

Liver transplantation for progressive familial intrahepatic cholestasis type 3 (PFIC 3) presenting in the 5th decade of life

Hussien Elsiesy[1], Sarra Yousif[1], Moahemd Shagrani[1], Hussa Al Hussaini[2], Mohamed Al Sebayel[1], Waleed Alhamoudi[1], Faisal Abaalkhail[1]

King Faisal Specialist Hospital & Research Center Liver Transplantation Riyadh-Saudi Arabia[1], King Faisal Specialist Hospital & Research Center Pathology Riyadh-Saudi Arabia[2]

Background: PFIC a rare heterogeneous group of autosomal-recessive disorders that presents during the neonatal period or within the first year of life. PFIC3 generally occurs later presenting either in late infancy, childhood, or even early adulthood.
Case Report: 44-year old gentleman with history of DM and jaundice since childhood due to Dubin- Johnson syndrome without itching, he developed progressive jaundice and intractable itching associated with dark urine and pale stools, over the past 2 years, his total bilirubin was 563 umol/L with high GGT. Serology for viral hepatitis, autoimmune hepatitis, Wilson, alpha 1 antitrypsin and hemochromatosis were negative. Abdominal US showed no bile duct dilatation. MRCP showed Moderate splenomegaly without evidence of primary sclerosing cholangitis (PSC), liver biopsy showed Chronic liver disease (stage II/IV) with finding suggestive of small duct PSC, and Dubin-Johnson syndrome.He was started on hemodialysis for biopsy proven diabetic nephropathy 1 year ago. Progressive familial intrahepatic cholestasis (PFIC) was considered and liver biopsy stained negative for MDR3, and genetic testing revealed a combination of Dubin-Johnson mutations and PFIC-3 mutations. He received Living donor liver transplantation from his daughter on September 16, 2014 and he has an excellent graft function, awaiting living related kidney transplant in 1 week.
Conclusion: To our knowledge, this is the first reported case of liver transplantation for pathologically and genetically confirmed PFIC-3 presenting in the fifth decade of life.

Topic 19: Metabolic and Genetic Liver Diseases

No: 1488

Profile and outcome of metabolic liver disease in under fives with liver related pediatric emergencies in a tertiary care pediatric hepatology centre

Seema Alam[1], Vikrant Sood[1], Bikrant Bihari Lal[1], Rajeev Khanna[1], Dinesh Rawat[1]

Institute of Liver and Biliary Sciences Pediatric Hepatology New Delhi-India[1].

Objective: (i) To study the clinical profile and outcome of metabolic liver disease (MLD) in infants and young children < 5 years presenting as liver related pediatric emergencies.
Methods: All infants and young children less than 5 years of age, admitted between January 2011 and October 2014 with liver related pediatric emergencies were included in the protocol based approach that we follow for MLD at ILBS. Poor outcome was defined as death or liver transplantation within 12 weeks of presentation. The etiological spectrum was studied and the factors affecting outcome were analyzed.
Results: There were 3 children with encephalopathy & liver dysfunction and all of them were diagnosed with gluconeogenetic defect (Fructose 1,6 biphosphatase deficiency, Fbpase). Fructose was removed from the diet and cornstarch was added. With dietary elimination of fructose, all the three children are thriving well with no further encephalopathy and normalized liver functions. of the 5 children admitted with cyclical vomiting, none turned out to be MLD. In 50 children less than 5 years with acute liver failure (ALF), 11 had etiology of MLD: Galactosemia (4), Fructosemia (2), Tyrosinemia (1), Mitochondrial disorders (2), Urea cycle disorder (1) and one of the children with Fbpase also had ALF. Two of the 4 Galactosemia and child with urea cycle defect survived.. Poor outcome was seen in 8 out of 11 acute liver failure. None could be transplanted due to non availability of organ and logistics constraints.
Conclusions: MLD is a common cause of liver related pediatric emergencies and the outcome is poor.

Topic 19: Metabolic and Genetic Liver Diseases

No: 1108

Wilson disease with hepatic presentation in an 8 month old boy

Kuerbanjiang Abuduxikuer[1], Jian-she Wang[2]

Children Liver Center Shanghai-China[1], Jinshan Hospital of Fudan University Liver Center Shanghai-China[2]

Wilson disease is an autosomal recessive disorder of copper deposition that can cause fatal neurological and hepatic disease if not diagnosed and treate. The youngest child with normal liver function reported so far is an 8-month-old Japanese boy with low ceruloplasmin levels. In terms of liver function abnormality, the youngest child ever reported so far is a 9-month-old Korean boy with elevated aminotransferase confirmed by genetic testing. We report an 8-month-old Chinese boy presented with elevated liver enzymes, and low serum ceruloplasmin level. Genetic analysis of ATP7B gene detected two heterozygous mutations (c.3809A > G/p.A874 V and c.2621C > T/p.N1270S) that have been reported to cause WD in the Wilson Disease Mutation Database. Parents screened for the disease causing mutations. Father was heterozygous for the mutation of c.3809A > G/p.N1270S, and mother was heterozygous for c.2621C > T/p.A874 V. Elevated serum aminotransferase in this infant was refractory, but persistent normalization was achieved with zinc therapy. To our best knowledge, this is the youngest patient with elevated liver enzymes ever reported worldwide. We hope that this will raise awareness among pediatricians, leading to earlier diagnosis, timely treatment, and better clinical outcome.

Topic 19: Metabolic and Genetic Liver Diseases

No: 1223

Efficacy of allogeneic mesenchymal stem cell transplantation in patients with Wilson cirrhosis

Murat Kantarcioglu[1], Deniz Torun[2], Hakan Demirci[1], Yildirim Karslioglu[3], Ferit Avcu[4], Hasan Gurel[1], Kadir Ozturk[1], Meral Akdogan Kayhan[5], Sabite Kacar[5], Ali Ugur Ural[6], Sait Bagci[1]

Gulhane Military Medical Academy Gastroenterology Ankara-Turkey[1], Gulhane Military Medical Academy Genetics Ankara-Turkey[2], Gulhane Military Medical Academy Pathology Ankara-Turkey[3], Gulhane Military Medical Academy Hematology Ankara-Turkey[4], Turkiyeyuksek Ihtisas Hospital Gastroenterology Ankara-Turkey[5], Bayindir Hospital Hematology Ankara-Turkey[6]

Background and aims: Wilson's disease is an autosomal recessive genetically inherited disorder of copper metabolism where cirrhosis is the end stage. in these patients liver transplantation can be the only cure. Many studies encourage use of allogeneic bone marrow (BM) derived mesenchymal stem cells (MSCs) for genetic liver diseases. We aimed to assess the efficacy of allogeneic MSC transplantation in these patients.
Patients and methods: 6 male, 4 female patients were transplanted 1x106 BM MSCs/kg, via hepatic artery without immunosuppressive regime. Volunteer donors were all sex-mismatched. MSC expansion was performed in Acibadem Labcell®/Istanbul. Liver biopsies were performed right after MSC transplantation and at 6th month. Histopathology examinations and X, Y chromosome Fluorescein in situ hybridization (X,Y-FISH) tests for tracking allogeneic transplanted MSCs, were performed in liver specimens. Patients were followed up by monthly laboratory tests and radiologic screening.
Results: In all patients no side effects were seen due to MSC transplantation. Throughout follow up period, there were no significant changes in serum seruloplasmin and 24 h urine copper output levels and histopathology examination results between first and second biopsy specimens. However in liver biopsy specimens at 6th month, female donor originated cells in 5 male patients were observed (figure. 1) while there were no male donor originated cells in female patients' liver specimens.
Conclusion: Healthy female donor derived MSCs are of choice for tissue regeneration. Performing MSC tx in greater amount and with repeated administrations seems reasonable.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1194

An open label randomized control study to compare the efficacy of vitamin E versus ursodeoxycholic acid in non diabetic Indian nafld patients

Pathik Parikh[1], Prabha Sawant[1], Meghraj Ingle[1]

Lokmanya Tilak Municipal Medical College and General Hospital, Department of Gastroenterology, Mumbai-India[1]

Aim: The study was carried out to compare the efficacy of Vitamin E versus ursodeoxycholic acid (UDCA) in non diabetic NAFLD patients.
Methods: We randomized 250 non cirrhotic and non diabetic NAFLD patients diagnosed on ultrasound, with raised aminotransferase (ALT) (> 40 IU/L), to receive Vitamin E 400 mg twice a day (Group 1) or UDCA 300 mg twice a day (Group 2) for 52 weeks. Life style

modification to achieve at least 5 % weight reduction and subsequent weight control and regular exercise was advised to both groups. The primary study endpoint was normalization in ALT levels from baseline. Secondary end points were the proportion of patients with reduction in ALT, relative reduction in the NAFLD Fibrosis score (NFS), symptomatic improvement, and tolerability.
Results: 150 patients received UDCA as compared to 100 patients receiving Vitamin E. The treatment groups were comparable at entry with regard to age (44.1 versus 42.4 years), gender (67 % versus 63 % female), risk factors for NASH, hypochondriac pain, serum liver biochemistries and NAFLD Fibrosis score. The primary end point was achieved in 21(14 %) and 19(19 %) of patients in Group 1 and group 2 respectively ($P = 0.2$). The proportion of patients with reduction in ALT (56 % versus 63 %, $P = 0.2$), symptomatic improvement (78 % versus 67 %, $P = 0.058$), reduction in the NFS (44 % versus 47 %, $P = 0.69$) and tolerability (98 % versus 95 %, $P = 0.2$) were similar between Group 1 and Group 2 respectively.
Conclusion: UDCA is an effective and safe alternative to Vitamin E in non diabetic–non cirrhotic Indian NAFLD patients.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1967

Evaluation of serum ferritin as an important predictor of non alcoholic steatohepatitis

Md.zia Hayder Bosunia[1], Salimur Rahman[2], Mamun Al Mahtab[2], Ayub Al Mamun[2], Mohammed Kamal[2], Ahmed Lutful Moben[3], Sheikh Mohammad Noor-e-alam[4], Syed Abul Foez[5], Abu Saleh Md. Sadequl Islam[6], Arfin Akter[7]

Rangpur Medical College Hospita Department of Hepatology Rangpur-Bangladesh[1], Bangabandhu Sheikh Mujib Medical University Department of Hepatology Dhaka-Bangladesh[2], Shahid Sarwardi Medical College Hospital Department of Medicine Dhaka-Bangladesh[3], Shahid Sarwardi Medical College Hospital Department of Hepatology Dhaka-Bangladesh[4], Moulivibazar 250 Bed District Sadar Hospital Department of Medicine Moulivibazar-Bangladesh[5], Shaheed Ziaur Rahman Medical College Hospital Department of Medicine Bogra-Bangladesh[6], Rangpur Medical College Department of Pharmacology Rangpur-Bangladesh[7]

Introduction: Nonalcoholic fatty liver disease (NAFLD) is one of the the most common cause of chronic liver injury which ranging from non NASH fatty liver (NNFL) generally follows a benign clinical course to non alcoholic steatohepatitis (NASH), that may progress to cirrhosis and end-stage liver disease. Differentiation between NNFL and NASH is important as NASH may progress to cirrhosis.Till now liver biopsy plays an important role to diagnose NASH.
Aim: To examine the relationship between serum ferritin and NAFLD severity and find out a non-invasive tool for diagnosis of NASH.
Method: Demographic, clinical, histologic laboratory and anthropometric data were analyzed in 52 adult patients with biopsy proven NAFLD.Those with concurrent liver diseases and co-existing disease that would alter serum ferritin level were excluded.Among 52 patients 25 were diagnosed as NNFL (48.1 %) and 27 were diagnosed as NASH (51.9 %). No fibrosis was found in 4 (7.7 %) patients. Stage 1 fibrosis was found in 41(78.8 %) patients, Stage 2 fibrosis was found in 3 (5.8 %) patients. Stage 3 fibrosis was found in 4 (7.7 %) patients and cirrhosis was not found in any patients.On multiple regression analysis, serum ferritin levels had no significant difference in between NNFL and NASH group.Mean serum ferritin level of total 52 patients was 97.29 μg/dl. Among NNFL and NASH patients mean serum ferritin was 94.9 μg/dl and 99.51 μg/dl ($P = 0.8$).On multiple comparison of serum ferritin value among the different stage of fibrosis found that there was no statistically significant difference.
Conclusion: Serum ferritin level could not predict the stage of underlying NAFLD disease.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 2156

Nonalcoholic fatty liver disease with and without metabolic syndrome—two different disorders yes or no

Angela Peltec[1], Victoria Ivanov[2], Ghenadii Curocichin[3], Vlada Dumbrava[1], Andrei Munteanu[4]

University of Medicine and Pharmacy "nicolae Testemitanu" Internal Medicine, Gastroenterology Chishinev-Moldova[1], Institute of Cardiology Interventional Cardiology Chisinev-Moldova[2], University of Medicine and Pharmacy "nicolae Testemitanu" Genetical Laboratory Chishinev-Moldova[3], University of Medicine and Pharmacy "nicolae Testemitanu" Morphopathology Chisninev-Moldova[4]

Background: The diagnosis of nonalcoholic fatty liver disease (NAFLD) is typically suspected in patients with the metabolic syndrome (MS), but not all patients with the MS will develop NAFLD and not all patients with NAFLD have the MS.
Methods: A cross-sectional study was performed among the 167 patients (mean age: 49,62 ± 9,97 years, age range: 23-73; 85/167–50,9 % females) who had NAFLD. We used ultrasound score as suggestive criteria for NAFLD diagnosis. Alanine aminotransferase (ALT) > 30U/L was defined as elevated ALT. NAFLD Fibrosis Score was calculated for separate patients with and without advanced fibrosis (less -1,455 for fibrosis lees than F2; ≥ -1,455 – fibrosis > F2).
Results: NAFLD with MS was diagnosed in 99/167 (60 %) subjects, while the remaining 68/167 (40 %) did not met the criteria for the MS. NAFLD with elevated ALT were detected in 107 subjects (70/99 –with MS and 37/68 patients without MS). Logistic regression analysis showed that ALT ($P = 0,03$; odds ratios (OR) - 2,02; 95 % CI 1,06-3,85) and advanced fibrosis ($P = 0,001$; OR—3,14; 95 % CI—1,65-5,99) were independent associated with NAFLD with MS. Presents of diabetes mellitus (DM) and impairment fasting glucose ($P = 0,0003$; OR 5,20; 95 % CI 2,14 -12,60) was an independent predictor for fibrosis > 2 in NAFLD patients with MS. Subjects with NAFLD unrelated to the MS didn't present this type of correlation.
Conclusion: In case of NAFLD with MS presents of impairment fasting glucose and diabetes mellitus predict the advantage fibrosis and should be considered in the selection of cases for histological assessment.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1892

Farnesoid X receptor activation improves adipose metabolic dysfunction and liver histology in mouse models of nonalcoholic fatty liver disease

F. Haczeyni[1], L. Poekes[2], V. Barn[1], A. R. Mridha[1], M. M. Yeh[3], N. C.-h. Teoh[1], G. C. Farrell[1]

The Australian National University Medical School Canberra-Australia[1], Catholic University of Leuven Institute of Experimental and Clinical Research Brussels-Belgium[2], University of Washington School of Medicine Seattle-United States[3]

The farnesoid X receptor (FXR) agonist obeticholic acid (OCA) was recently shown to improve nonalcoholic fatty liver disease (NAFLD) activity score in patients, but the protective mechanism remains unresolved due to the complex associations between fatty liver, adipose function and glucose metabolism. We studied the effects of OCA (given orally, 10 mg/kg-diet) on multiple adipose depots, metabolic indices and liver histology in mouse models of NAFLD

Atherogenic diet (23 % fat, 0.2 % cholesterol)-fed wildtype mice develop mild nonalcoholic steatohepatitis (NASH) whereas foz/foz (appetite-dysregulated, obese/diabetic) mice develop severe NASH. As in humans in FLINT study, OCA reduced body weight in wildtype, but not in foz/foz mice. Post-prandial blood glucose was strikingly increased with atherogenic feeding and foz/foz mutation; OCA completely corrected this effect in wildtype mice. Liver mass, steatosis and histology were significantly improved in OCA-treated wildtype mice, but partially in foz/foz mice. OCA prevented excess adiposity in wildtype mice visceral depots. As a reflection, adipose morphometry and the number of adipose crown-like structures were significantly improved with OCA treatment in wildtype (partially in foz/foz) mice. OCA caused a macrophage phenotypic switch from pro-inflammatory to anti-inflammatory in wildtype mice adipose stromal vascular fractions, but pro-inflammatory macrophages remained abundant in foz/foz mice.

In conclusion, FXR activation significantly improved glucose intolerance, visceral adiposity and liver histology in wildtype mice fed a NAFLD/NASH-generating diet, but in obese diabetic foz/foz mice with severer metabolic phenotype, OCA mildly reversed NASH pathology. These metabolic improvements suggest an indirect hepatoprotective mechanism of OCA through improving adipose inflammation and dysfunction in NASH development.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1265

Estimation of normal values of serum transaminases based on liver histology in healthy Asian Indians

Neeraj Saraf[1], Narendra Choudhary[1], Sanjiv Saigal[1], Arvinder Soin[1]

Medanta Medicity Institute of Liver Transplantation Gurgaon,-India[1]

Background: liver biopsy based studies have shown that serum levels of aminotransferases are lower than conventional cut-off of 40 IU/mL in persons with normal histology. There is no histology based data in Indian population.
Aims: to estimate normal values of serum aminotransferases in healthy Indian population with normal liver histology.
Materials and methods: Present retrospective study includes all liver donors who underwent liver donation at our centre and had a pre-operative liver biopsy done for various reasons. All the donors had negative viral markers. Non-alcoholic fatty liver (NAFL) was defined as > 5 % hepatocytes having steatosis and no changes of steatohepatitis.
Results: The study included 331 donors (147 males), age 35.7 ± 10.2 years. NAFL was present in 167(50.4 %). On comparison of male donors with normal histology ($n = 67$) to NAFL ($n = 80$), donors with steatosis had significantly higher age, body mass index, AST, ALT, alkaline phosphatase, gamma-glutamyl transpeptidase, total cholesterol, low density lipoprotein and fasting blood sugar. On comparison of female donors with normal histology and NAFL, females with steatosis had significantly higher body mass index, ALT and triglycerides, however, there was no significant difference regarding other parameters. Ninety fifth percentile of AST and ALT in normal histology donors were 33.8 IU/L and 38.6 IU/L for males, 31 IU/L and 35.2 IU/L for females. Twenty-five donors had lean NAFL (BMI < 23 kg/M2).
Conclusion: Serum aminotransferase values in healthy Asian Indian population with normal histology are provided. Histological NAFL is present in almost half of apparently normal donors. Simple steatosis has different associations in males and females.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1642

Development of fatty liver scoring system for adults patients in Asian population

Cosmas Rinaldi A. Lesmana[1], Levina S. Pakasi[1], Sri Inggriani[2], Maria L. Aidawati[2], Laurentius A. Lesmana[1]

Digestive Disease and Gi Oncology Centre Medistra Hospital Jakarta-Indonesia[1], Department of Radiology Medistra Hospital Jakarta-Indonesia[2]

Objective: to predict the presence of fatty liver in Asian population.
Method: A cross-sectional study was held among medical check-up patients underwent abdominal ultrasound between January and December 2013 in Medistra Hospital, Jakarta. The presence of fatty liver was diagnosed by ultrasound. Logistic regression analyses were undertaken to identify the best combination of risk factors for predicting fatty liver using the backward (likelihood ratio) approach.
Results: 1054 cases were included in this study. Fatty liver was present in 538 (51.0 %) patients. Six predictors were included in the final model, i.e. male sex (score 1.9), age > 35 years (score 2.1), BMI > 25 kg/m2 (score 3.6), TG > 150 mg/dL (score 1.6), HDL < 40 (male) or < 50 (female) mg/dL (score 1.0), and ALT > 35 U/L (score 2.0). On validation, the area under the ROC curve (AUC) of the prediction model was 0.833 (95 % confidence interval = 0.809-0.857). The Hosmer–Lemeshow goodness-of-fit p value was 0.232, which indicated the appropriateness of the logistic regression model to predict fatty liver.
Conclusion: The presence of fatty liver can be predicted using our proposed fatty liver scoring consisting of gender, age, body mass index, triglyceride, HDL-cholesterol, and serum ALT levels.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 2060

Different effect of berberine on two mice models of nonalcoholic fatty liver disease

Haiyan Song[1], Yang Liu[1], Li Zhang[1], Lili Yang[1], Guang Ji[1]

Institute of Digestive Diseases Longhua Hospital, Shanghai University of Traditional Chinese Medicine Shanghai-China[1]

Objective: This study aims to investigate the effect of berberine on nonalcoholic fatty liver disease (NAFLD) and explore the mechanism through intervening two different kinds of NAFLD model.
Methods: Male C57BL/6 mice were fed with methionine and choline deficient (MCD) diet for 6 weeks, and were simultaneously administered intragastrically with berberine (100 mg/kg/d). For another model, Male C57BL/6 mice were fed with high fat diet (60 % calories

from lipid) for 18 weeks. Then berberine was applied in the same way for 4 weeks. Liver histopathology was observed through HE and Oil red O staining of liver sections. Serum biochemical examination was carried out. The level of serum insulin, triglycerides of liver homogenates, and hepatic expression of Aopoc3, NF-E2-related factor 2 (Nrf2) and its target gene were determined.
Results: MCD model presented very low weight of body and liver, while HF diet-induced model increased weight. Berberine decreased the weight of HF model while change little for MCD model. Severe hepatic steatosis, increased lobular inflammation, and elevated serum ALT were demonstrated in both models. Berberine reversed the pathologic change in HF model but changed little in MCD model. Berberine reversed the downregulated insulin level in MCD model as well as the upregulated insulin level in HF model. It increased the expression of Nrf2 and its target gene in both models. It also increased Apoc3 level in HF model but not in MCD model.
Conclusion: Berberine demonstrates differential effect on the NAFLD models due to different mechanism, which may be correlated with its bioactivity.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1614

Asymmetric dimethylarginine (ADMA) levels are increased in nafld patients independent from inflammation and hepatic injury

Salih Boga[1], Ali Riza Koksal[2], Huseyin Alkim[2], Meltem Ergun[2], Mehmet Bayram[2], Gurhan Sisman[3], Muveddet Banu Yilmaz Ozguven[2], Sebnem Tekin Neijmann[4], Canan Alkim[2]

Yale University School of Medicine, Yale New Haven Hospital Department of Digestive Diseases, Department of Liver Transplantation New Haven-United States[1], Sisli Etfal Education and Research Hospital Department of Gastroenterology Istanbul-Turkey[2], Istanbul Education and Research Hospital Department of Gastroenterology Istanbul-Turkey[3], Bakirkoy Dr. Sadi Konuk Education and Research Hospital Department of Bıochemistry Istanbul-Turkey[4]

Background and aim: Cardiovascular disease (CVD) is the most frequent cause of death in nonalcoholic fatty liver disease (NAFLD). Insulin resistance, hepatic dysfunction and chronic inflammation are factors interacting in explaining the increased CVD incidence.
We aimed to evaluate the effects of insulin resistance and inflammation on asymmetric dimethylarginine (ADMA) levels, a novel marker of endothelial dysfunction and a predictor of future cardiovascular events. We also investigated the relationship of these factors to varying degrees of pathologic findings like hepatic steatosis, lobular inflammation, fibrosis and presence of non alcoholic steatohepatitis (NASH).
Patients and methods: Plasma ADMA, high-sensitivity c-reactive protein (hs-CRP), interleukin-6 (IL-6) and homeostasis model assessment of insulin resistance (HOMA-IR) were measured in 70 patients with histologically verified NAFLD (53 with NASH, 17 with Non-NASH) and 12 controls.
Results: ADMA, hs-CRP, IL-6 and HOMA-IR levels were found significantly higher in NAFLD group than the control group and IL-6 and HOMA-IR levels were significantly higher in biopsy proven NASH group than the Non-NASH group while hs-CRP and ADMA levels didn't differ in terms of presence of NASH (Tables 1 and 2).

HOMA-IR had a significant correlation with grade of steatosis and stage of fibrosis. IL-6 had a significant correlation with the grade of steatosis, lobular inflammation and ballooning. The only determinant significantly correlated to ADMA was HOMA-IR.
Conclusion: Our data suggested that NAFLD is associated with endothelial dysfunction and CVD, and this association is independent from inflammatory parameters and histologic level of liver.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 2134

How non alcoholic steatosis influence the postoperative outcome and living donor security after hepatectomy performed for the donation

Angela Peltec[1], Adrian Hotineanu[2], Vlad Brashoveanu[3], Grigorii Ivancov[4], Natalia Taran[5], Elena Moraru[6], Andrei Munteanu[7], Victor Cojocari[8], Vladimir Hotineanu[2], Vlada Dumbrava[1]

University of Medicine and Pharmacy "nicolae Testemitanu" Internal Medicine, Gastroenterology Chishinev-Moldova[1], University of Medicine and Pharmacy "nicolae Testemitanu" Surgery Nb 2 Chisinev-Moldova[2], Clinical Instutute of Fundeni, University "titu Maiorescu" Liver Surgery and Liver Transplantation Bucharest - Romania[3], Clinical Republican Hospital Purulent Surgery Chishinau - moldova[4], University of Medicine and Pharmacy "nicolae Testemitanu" Laboratory of Gastroenterology Chishinev-Moldova[5], Clinical Republican Hospital Intensive Care Unite Chishinev-Moldova[6], University of Medicine and Pharmacy "nicolae Testemitanu" Morphopathology Chishinev-Moldova[7], University of Medicine and Pharmacy "nicolae Testemitanu" Anesteziology and Intensive Care Chishinev-Moldova[8]

Introduction: It is not well defined influence of graft steatosis on the safety of the living donor hepatectomy performed for the donation. The degree of hepatic steatosis in living donor could influence and affect the potential donor recovery after partial hepatectomy.
The aim of this study was to evaluate the impact of minimal macrovezicular steatosis on the postoperative outcome and donor security.
Materials and methods: We examined 7 living liver donors who were divided into two groups depending on the presence of minimal macrovezicular hepatic steatosis in the morphological examination. The groups were analyzed in terms of demographic, anthropometric characteristics, intraoperative evaluation and prevalence of postoperative complications.
Results: Statistically significant differences were found on the body mass index, duration of surgery, ALT level, and time of ALAT level normalization. The prevalence of postoperative complications and the volume of intraoperative bleeding did not influenced by the presence of hepatic steatosis.
Conclusions: Donor graft survival is not affected by macrovezicular minimal hepatic steatosis (less than 30 %). Postoperative outcome does not depend on the presence of minimal, macrovezicular.
hepatic steatosis.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1197

Serum ferritin levels in predicting histological severity in patients with nonalcoholic fatty liver disease in India

Pathik Parikh[1], Jatin Patel[1], Meghraj Ingle[1], Prabha Sawant[1]

Lokmanya Tilak Municipal Medical College and General Hospital, Department of Gastroenterology, Mumbai,-India[1]

Aim: To determine the levels of serum ferritin which predict fibrosis in Indian patients with non alcoholic fatty liver disease (NAFLD).
Methods: The clinical, biochemical, radiologic and histological findings of consecutive adult NAFLD patients accessed at a tertiary care center over a 3-year period were analyzed. Fifty five patients with NAFLD on ultrasound and raised transaminases (> ULN) underwent liver biopsy. Patients were stratified into two groups based on their histological stage steatosis (with or without inflammation) but no fibrosis and NASH with Fibrosis/cirrhosis. Serum ferritin levels were measured at the same time as getting liver biopsy. Fibroscan was carried out in each of these patients. These were compared with 50 age and sex matched controls with normal ultrasound, liver enzymes and no history of alcohol.
Results: Fifty five NAFLD patients diagnosed on ultrasound and with raised enzymes underwent biopsy. Steatosis (with or without inflammation, but no fibrosis/ballooning) was seen in 35 patients, fibrosis/ballooning in 14 patients and cirrhosis in 6 patients. Mean ferritin levels in groups with steatosis and fibrosis/cirrhosis were 39.4 and 72.7 ng/ml respectively ($P < 0.001$). The mean ferritin levels in NAFLD and controls were 51.2 and 35.2 ng/ml respectively ($P < 0.05$). The AUC of serum ferritin at value 48.0 ng/ml is 0.779. The coefficient of correlation between Fibroscan and serum ferritin levels was 0.37.
Conclusion: Serum Ferritin is low in Indian individuals and levels even within apparently normal range indicates fibrosis and cirrhosis. Indians should utilize 48.0 IU/ml as cutoff for fibrosis in NAFLD.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1212

The effect of fatty pancreas on serum glucose parameters in patients with nonalcoholic steatohepatitis

Ahmet Uygun[1], Abdurrahman Kadayifci[2], Hakan Demirci[1], Mutlu Saglam[3], Yusuf Serdar Sakin[1], Kadir Ozturk[1], Zulfikar Polat[1], Yildirim Karslioglu[4], Erol Bolu[5]

Gulhane Military Medical Academy Gastroenterology Ankara-Turkey[1], University of Gaziantep Gastroenterology Gaziantep-Turkey[2], Gulhane Military Medical Academy Radiology Ankara-Turkey[3], Gulhane Military Medical Academy Pathology Ankara-Turkey[4], Gulhane Military Medical Academy Endocrinology Ankara-Turkey[5]

Objective: Fatty pancreas (FP) is related to obesity, and may have some clinical implications on glucose metabolism. The frequency and importance of FP in patients with nonalcoholic steatohepatitis (NASH) is not clear. This study aimed to investigate; the frequency of FP in patients with NASH, and its effects on serum glucose parameters.
Methods: FP was detected and graded by transabdominal ultrasonography (USG) in patients with biopsy-proven NASH and healthy controls. Body Mass Index and waist circumference were recorded, and serum lipids, fasting serum glucose, HbA1c, OGTT-2 h, insulin level, insulin resistance, type 2 diabetes mellitus (DM) and prediabetes rates were detected.
Results: Eighty-four subjects with NASH and 35 healthy controls were enrolled in the study. There was no FP in 41 (48.8 %) of the NASH patients according the study criteria. Forty-three of the NASH patients and 5 of the controls had different grade of fat in their pancreas (51.2 % vs. 14 %, $P = 0.001$). The HbA1c and OGTT 2-h results was significantly higher in NASH patients with FP compared to without ($P = 0.003$ and $P = 0.018$). The rate of both prediabetes and DM was also found significantly increased in NASH patients with FP ($P = 0.004$). The mean waist circumference was higher in patients with FP ($P = 0.027$). Grade of FP by USG showed no effect on study parameters in subgroup analysis.
Conclusion: FP is common in patients with NASH and increases the rate of prediabetes and DM. The coexistence of both NASH and FP has a further impact on glucose metabolism and DM frequency.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1465

Comparison of fibroscan to simple noninvasive screening tools in predicting fibrosis in nafld patients of western India with high risk of liver fibrosis

Pathik Parikh[1], Ravindra Surude[1], Nilesh Pandav[1], Jatin Patel[1], Prabha Sawant[1]

Lokmanya Tilak Municipal Medical College and General Hospital, Department of Gastroenterology, Mumbai-India[1]

Aim: The study is aimed to determine the efficacy of Fibroscan as compared to noninvasive markers, NAFLD Fibrosis Score (NFS), APRI (AST/Platelet ratio) and AAR (AST/ALT ratio) as a screening tool in NAFLD patients with high risk of liver fibrosis.
Methods: This is a single center study carried out in patients attending OPD for dyspepsia and diagnosed as fatty liver on ultrasound. Liver biopsy was advised in diabetics, metabolic syndrome, BMI > 30 kg/m2, raised transaminases and hypothyroidism. Fibroscan, APRI, AAR and NFS were calculated. AUROC, NPV, PPV was calculated for each diagnostic test.
Results: Of 1500 patients screened, 110 with above described risk factors underwent liver biopsy (72 had F Stage 0/1/2 fibrosis, 38 showed stage 3/4 Fibrosis). Diabetes predicted severe fibrosis (stage 3/4) as compared to mild disease. The sensitivity, specificity, PPV, NPV and AUROC for Fibroscan at value 12 kPa was 0.9, 0.8, 0.70, 0.93 and 0.91 respectively for predicting stage 3/4 fibrosis. With increase in severity of liver fibrosis there was step wise increase in Fibroscan values ($P = 0.000038$, Kruskal–Wallis test). The Sensitivity, specificity, PPV and NPV for AAR and NFS at cutoff of 1.5 and 0.676 is 0.8, 1.0, 1.0 and 0.92 and 0.8, 1.0, 1.0 and 0.92 respectively.
Conclusion: Fibroscan, NFS and AAR are simple noninvasive markers of fibrosis that can be utilized as a screening tool in patients with high risk for fibrosis to determine the need for biopsy. The cutoff of Fibroscan for stage 3/4 fibrosis was 12 kPa.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 2066

Association between PNPLA3 i148 m polymorphism and nonalcoholic fatty liver disease (NAFLD) in the Indian continent

Devaraja Rangegowda[1], Shvetank Sharma[2], Chandan Kumar K. N.[1], Awinash Kumar[1], Manoj Kumar Sharma[1], Archana Rastogi[3], Shiv Sarin[1]

Ilbs Hepatology New Delhi-India[1], Ilbs Research New Delhi-India[2], Ilbs Pathology New Delhi-India[3]

Aim: We investigated the genotype frequency of PNPLA3 rs738409 in NAFLD patients and its association with different biochemical and histological features. Methods: A hospital-based cross sectional study was conducted on NAFLD patient attending OPD in New Delhi. Liver biopsy was done in 216 patients. We analysed rs738409 polymorphism by TaqMan assay in all NAFLD patients and assessed its association with biochemical and histological features of NASH.
Results: A total of 310 NAFLD patients were included. Simple fatty liver was seen in 124 patients (40 %) [Mean age 40.9 ± 14, male 73.4 5 %, mean BMI 25.8 ± 5.7 kg/m2, lean 33.3 %]. There were 120 patients (38.7 %) in NASH [Age 38.2 ± 11.8, male 85.8 %, BMI 24.8 ± 5 kg/m2, lean 42 %] and 66 patients (21.3 %) in NAFLD related cirrhosis [Age 52.6 ± 11.3, male 83.3 %, BMI 25.6 ± 4.68 kg/m2, lean 35.2 %]. PNPLA3 genotypes were CC type in 121 (39 %), CG type in 88 (28.40 %) and GG type in 101 (32.60 %) in all NAFLD patients. Prevalence of homozygous (GG) type was 33/124 (26.6 %) in fatty liver, 31/120 (25.8 %) in NASH and 37/66 (56.1 %) in cirrhotic patients (p value < 0.001). There was no influence of PNPLA3 genotypes on clinical as well as histological features in NASH (p value > 0.5). There was also no association between presences of PNPLA3 in lean BMI < 23 kg/m2 versus obese > 23 kg/m2.
Conclusion: GG type was significantly more common in NAFLD related cirrhotic as compared to simple fatty liver and NASH. PNPLA3 rs738409 polymorphism neither correlated with histological features nor with biochemical parameters of NASH.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 2139

Evaluation of serum ferritin in non alcoholic fatty liver disease (NAFLD)

Noha Khalil[1], Mohamed Elbasel[1], Haytham Sameer[2], Dina Hassan[3]

Faculty of Medicine Internal Medicine Cairo-Egypt[1], Elmonira Hospital Internal Medicine Cairo-Egypt[2], Faculty of Medicine Clinical Pathology Cairo-Egypt[3]

Background: Non-alcoholic fatty liver disease (NAFLD) is a clinical condition that comprises a wide spectrum of liver damage, ranging from simple steatosis to steatohepatitis, advanced fibrosis and cirrhosis in patients with normal or elevated serum alanine transaminase enzyme (ALT). NAFLD and non-alcoholic steatohepatitis (NASH) are highly prevalent diseases, and is estimated that a quarter of the adult population currently has NAFLD. Furthermore, 20–30 % of patients with NAFLD will develop NASH that may progress to cirrhosis, end stage liver disease and hepatocellular carcinoma.
Non-alcoholic fatty liver disease (NAFLD) is the build up of extra fat in liver cells that is not caused by alcohol. It is normal for the liver to contain some fat. However, if more than 5 % - 10 % percent of the liver's weight is fat, then it is called a fatty liver.NAFLD tends to develop in people who are overweight or obese or have diabetes, high cholesterol or high triglycerides. Rapid weight loss and poor eating habits also may lead to NAFLD. However, some people develop NAFLD even if they do not have any risk factors.
Methods: The study is a case control study conducted on 50 patients who were diagnosed to have fatty liver assessed by ultrasonography and 25 controlled healthy individuals with matched age and sex. All the study persons underwent full clinical assessment and laboratory investigations including ALT and AST-, serum albumin, prothrombin time and INR, complete blood.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1423

Upregulated expression of de sumo specific protease 3 (SENP3) plays an important role in the progression of non alcoholic fatty liver disease

Yuhan Liu[1], Qing Xie[1], Yan Han[1], Qing Li[1], Shaowen Jiang[1], Rongtao Lai[1], Gangde Zhao[1], Weiliang Tang[1], Simin Guo[1], Xiaogang Xiang[1], Jie Lu[1]

Ruijin Hospital, Shanghai Jiaotong University School of Medicine Department of Infectious Diseases Shanghai-China[1]

Aim: Non-alcoholic fatty liver disease (NAFLD),ranging from non-alcoholic fatty liver(NAFL) to non-alcoholic steatohepatitis(NASH) and fibrosis,has become an increasingly common healthy problem.SENP3,a sentrin/de-SUMO specific protease, plays an important role in spectrum of cellular process. Reports have demonstrated that SENP3 was sensitive to stresses.However stresses such as oxidative stress, lipid accumulation, cytokines, et al., have been known as major factors involved in the development of NAFLD. Thus, the aim of this study was to investigate if and how SENP3 was involved in NAFLD.
Methods: Liver biopsy samples of 20 NAFLD patients and 3 normal controls, obtained from Shanghai Ruijin Hospital from 2012 to 2014,were subject to immunohistochemical staining(IHC) of SENP3 expression. Meanwhile,Sprague–Dawley(SD) rats fed with high-fat diet were utilized as NAFLD animal model to further validate the results found in human.Finally,normal liver cell line (L02) was treated with medium containing oleate and palmitate(oleate/palmitate, 2: 1 ratio) as the cell model to explore the potential mechanism.SENP3 was overexpressed in L02 by transfected with GFP-SENP3 plasmid, and the cellular lipid content was determined by Oil Red O staining.
Results: IHC results showed that intrahepatic level of SENP3 was higher in NAFLD patients than controls; interestingly, SENP3 was found located around fat vacuole. Consistently, elevated expression of SENP3 was also observed in the NAFLD rat model and cell model. Furthermore,the overexpression of SENP3 promoted lipid accumulatio.
Conclusion: Taken these findings together,we report for the first time that upregulated expression of SENP3 in the liver tissue may play an important role in the progression of NAFLD. The potential underline mechanism of SENP3 in NAFLD is still under investigated.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1087

Insulin resistance in nonalcoholic fatty liver disease revalidation of old concept in the new era

Shahinul Alam[1], Utpal Das[1], Nazmul Hasan[1], Jahangir Kabir[1], Dulal Chandra Das[1], Akm Khorshed Alam[1]

Bangabandhu Sheikh Mujib Medical University Hepatology Dhaka-Bangladesh[1]

Aim: Insulin resistance (IR) largely been hypothesized as central in multifactorial pathogenesis of nonalcoholic fatty liver disease (NAFLD). This study aimed to explore the association of IR in NAFLD and nonalcoholic steatohepatitis (NASH).

Methods: We have included 219 patient of NAFLD with sonographic evidence of fatty changes in liver after exclusion of alcohol intake and other causes during the period of June 2012 to July 2014.Liver biopsy was done in 110 patients with elevated ALT of > 30 u/l for male and > 18 u/l for female. IR was measured by homeostatic model assessment of insulin resistance (HOMA-IR2).
Results: Age of the study population was 40.6 ± 10.0 years, male: female was 83: 136, ALT was 54.3 ± 63.2 u/l, AST was 41.5 ± 44.7 u/l and GGT was 49.4 ± 34.5 u/l. According to Asian criteria 57 (25.9 %) were nonobese, 140 (64.1 %) had metabolic syndrome, 164 (74.8 %) were hypertriglyceridemic, 200 (91.3 %) had low HDL and 170 (77.4 %) had high waist. Hypertensive and diabetic was 58 (26.7 %) and 57 (26.1 %) respectively. IR was 1.9 ± 1.3 with the range of 0.4 to 9.3 and only 87 (39.7 %) were above normal.of the 110 biopsied 65 (59.1 %) was NASH. Normal and raised IR was associated with 32 (50.8 %) and 33 (70.2 %) NASH respectively ($P < 0.05$). Correlation between IR and steatosis, ballooning and fibrosis was insignificant except lobular inflammation. IR was similar in NASH (2.2 ± 1.6) and nonNASH (1.9 ± 1.6).
Conclusion: Large number of NAFLD patients had normal IR. IR had inconsistent association with histological activity and fibrosis.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1064

Effect of telmisartan on histological activity and fibrosis of non alcoholic steatohepatitis patient a one year randomized control trial

Shahinul Alam[1], Jahangir Kabir[1], Utpal Das[1], Nazmul Hasan[1], Akm Khorshed Alam[1]

Bangabandhu Sheikh Mujib Medical University Deprtment of Hepatology Dhaka-Bangladesh[1]

Aim: Telmisartan may act in 2 hit pathogenesis of Non-alcoholic Steatohepatitis (NASH). This study was aimed to see the effect of Telmisartan on nonalcoholic fatty liver disease (NAFLD) activity score (NAS) and fibrosis in NASH patient.
Method: The total 50 NASH patients were randomized; 35 of treatment arm treated with Telmisartan 40/80 mg once daily with life style modification and 15 control arm advised for life style modification only for one year. At the end 20 treatments and 10 controls were analyzed. NAS improvement ≥ 2 or NAS improvement ≥ 1 + fibrosis improvement ≥ 1 were considered as histological responder.
Results: Base line NAS, fibrosis, ALT, AST, insulin resistance index, component of metabolic syndrome, age and sex were similar in both group. In treatment and control group NAS improvement at the end of study was 2.15 ± 1.66 and 1.10 ± 0.57 ($P = 0.017$), fibrosis improvement was 0.65 ± 0.93, and—0.30 ± 0.48 ($P = 0.001$). NAS ≥ 2 improved in treatment arm was 13 (65 %) and in control arm was 2 (20 %). Fibrosis score ≥ 1 improved in 8 (40 %) in treatment arm and none in control. Multivariate analysis revealed that, only Telmisartan could improve NAS and fibrosis (p value 0.035; OR = 92.07, CI = 1.39-6106), weight reduction and improvement of metabolic syndrome didn't influence. There were similar minor adverse effects in both groups.
Conclusion: Telmisartan improves histological activity and fibrosis in NASH.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 2231

The resolution of nonalcoholic steatohepatitis after bariatric surgery

Paweł Ziemiański[1], Rafał Marszałek[1], Zbigniew Wierzbicki[1], Maciej Kosieradzki[1], Dariusz Wasiak[2], Agnieszka Ptasińska-perkowska[3], Tomasz Gryczewski[1], Piotr Małkowski[2], Wojciech Lisik[1], Andrzej Chmura[1]

Medical University of Warsaw Department of General Surgery and Transplantology Warsaw-Poland[1], Medical University of Warsaw Department of Surgical and Transplantation Nursing Warsaw-Poland[2], Medical University of Warsaw Department of Transplant Medicine and Nephrology Warsaw-Poland[3]

Aim: The efficacy of bariatric surgery in the treatment of obesity is confirmed. It is believed that after reaching the desired weight loss can be achieved a beneficial effect on the course of a fatty liver disease. The aim of the study was to evaluate the incidence of non-alcoholic statohepatitis (NASH) among obese individuals undergoing bariatric surgery and to determine the impact of bariatric surgery on the liver parenchyma.
Methods: 145 liver biopsies taken during bariatric procedures were analyzed. To determine the impact of bariatric surgery on the liver parenchyma, we compared initial biopsies with those taken after weight loss during abdominoplasty (24 paired biopsies).
Results: Baseline biopsies showed nonalcoholic fatty liver disease (NAFLD) in 83.5 % cases. In this group, steatosis alone (SA) was found in 42 % and NASH in 58 %. Initial mean weight and BMI was respectively 134.0 ± 21.4 kg and 47.4 ± 6.05 kg/m2. There was no difference in the percentage of fat and total fat mass. In controls an expected weight loss (%EWL) was achieved in all cases (mean %EWL 66,9 %). Repeated biopsy showed regression of steatosis in 88,9 % and withdrawal of NASH in all cases. Liver fibrosis was identified in 17 of all patients. After weight loss fibrosis decreased in severity in 6 cases (25 %), remained unchanged in 6 (25 %) and increased in 7 (29 %), including one without fibrosis at first biopsy.
Conclusion: Surgical-induced weight loss is associated with improvement of liver histology, what leads to withdrawal of steatohepatitis.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1448

The epoxyeicosatrienoic acids ameliorated liver inflammation in mice with steatohepatitis by inhibiting the NF kb pathway

Xiaojing Wang[1], Lan Li[2], Hongwu Wang[2], Jianing Luo[3], Fang Xiao[2], Todd Harris[4], Kin Sing Lee[4], Bruce Hammock[4], Xiaoping Luo[5], Qin Ning[2]

Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institute of Infectious Disease Wuhan-China[1], Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institution of Infectious Diseases Wuhan-China[2], University of Toronto Faculty of Arts and Science Toronto-Canada[3], University of California, Davis Department of Entomology and UC Davis Comprehensive Cancer Center California-United States[4], Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department of Pediatrics Wuhan-China[5]

Background and aims: Nonalcoholic steatohepatitis (NASH) may progress to end-stage liver disease and hepatocellular carcinoma. The epoxyeicosatrienoic acids (EETs), the products of cytochrome P450 epoxygenases, are found to have an anti-inflammatory activity. In this study, we investigated the protective role of EETs in methionine-choline-deficient (MCD)-diet induced steatohepatitis in mice and the potential mechanism.
Methods: The C57BL/6 mice have been fed an MCD diet for 6 weeks. TPPU, a soluble epoxide hydrolase (sEH) inhibitor was used to treat the mice. Proinflammatory cytokines were detected by ELISA assay. mRNA of inflammation related moleculars were tested by Realtime-PCR. External EETs were added to THP-1/HepG2 cells stimulated by free fatty acid (oleic acid plus palmitic acid). The NF-kB nuclear translocation of THP-1 cells was examined by laser confocal microscopy.
Results: After TPPU treatment, the levels of liver enzymes (ALT, AST), proinflammatory cytokines (TNF-a, IL-1, IL-6, IFN-γ) as well as related chemokines (IL-8, MCP-1) have been reduced considerably in mice with steatohepatitis. mRNA of inflammation relevant adhesion moleculars (ICAM-1, VCAM-1) was down-regulated, whereas mRNA of peroxisome proliferator-activated receptor (PPAR-α) was elevated. The hepatocyte necrosis, inflammatory cell infiltration and total NF-kB expression in the liver tissue was also dramatically decreased. In vitro, HepG2 and THP-1 co-cultures were stimulated with FFA. After EETs treatment, levels of proinflammatory cytokines from supernatant of the co-cultures were significantly decreased. The NF-kB nuclear translocation induced by FFA was partially inhibited by EETs.
Conclusions: EETs might ameliorate the liver inflammation in mice with steatohepatitis by inhibiting the activation of NF-kB pathway.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 2159

Is hemoglobin level predicted the stage of nonalcoholic fatty liver disease unrelated with the metabolic syndromes

Angela Peltec[1], Victoria Ivanov[2], Ghenadii Curocichin[3], Vlada Dumbrava[1], andrei Munteanu[4]

University of Medicine and Pharmacy "nicolae Testemitanu" Internal Medicine, Gastroenterology Chishinev-Moldova[1], Institute of Cardiology Interventional Cardiology Chisinev-Moldova[2], University of Medicine and Pharmacy "nicolae Testemitanu" Genetical Laboratory Chishinev-Moldova[3], University of Medicine and Pharmacy "nicolae Testemitanu" Morphopathology Chishinev-Moldova[4]

Background: Nonalcoholic fatty liver disease (NAFLD) unrelated to the metabolic syndrome (MS) useful for identifying novel mechanism of hepatic fat accumulation. We perform a prospective study to examine the association between hemoglobin level (Hb) and advanced liver fibrosis.
Methods: A cross-sectional study was performed among the 167 patients (mean age: 49,62 $\pm$ 9,97 years; 85/167–50.9 % females) who had NAFLD. We used ultrasound score as suggestive criteria for NAFLD diagnosis. NAFLD Fibrosis Score was calculated for separate patients with and without advanced fibrosis. Alanine aminotransferase (ALT) $>$ 30 U/L was defined as elevated ALT. Hemoglobin concentration was divided into age- and sex-dependent quintiles to evaluate the association of Hb level with advanced fibrosis.
Results: A total of 99 patients with NAFLD met the criteria for the MS, while the remaining 68 did not. Participants who had NAFLD without MS were younger (47,6 $\pm$ 10,6 vs 51,0 $\pm$ 9,2; $P = 0{,}029$; 95 % confidence intervals (CI) 0,3447-6,4953), with lower BMI (31,03 $\pm$ 5,67 vs 33,97 $\pm$ 5,67; $P = 0{,}0012$; 95 % CI 1,1767-4,7033) with comparable Hb (141,0 $\pm$ 14,9 vs 143,7 $\pm$ 16,8; $P = 0{,}99$) and ALT level (p less than 0,05). After adjusting for advance fibrosis, compared with the lowest quintiles (Hb less than 130 g/L), odds ratios (95 % CI) were: third quintiles (Q3) (Hb 140 - 153 g/L): 0,14 (0,04–0,53) and highest quartile (Q4) (Hb $>$ 153 g/L): 0,10 (0,01–0,61). Q3 Hb level (OR = 2,26; 95 % CI 0,66-7,70) and Q4 Hb level (OR = 2,62; 95 % CI 0,65-10,48) were associated with NAFLD unrelated to the MS with elevated ALT.
Conclusion: Increased hemoglobin in NAFLD without MS were associated with elevated ALT, but not with advanced fibrosis.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1412

Non alcoholic fatty liver disease promotes mhv 3 replication in C3H hen mice

Ting Wu[1], Hongwu Wang[1], Lan Li[1], Aichao Shi[1], Xiaojing Wang[1], Yaqi Wang[1], Weiming Yan[1], Dong Xi[1], Xiaoping Luo[2], Qin Ning[1]

Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department and Institution of Infectious Diseases Wuhan-China[1], Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology Department of Pediatrics Wuhan-China[2]

Background and aims: In view of the increasing trend of non-alcoholic fatty liver disease (NAFLD) in patients with chronic viral hepatitis, it is important to understand the influence of NAFLD on virus replication.
Methods: We used a murine hepatitis virus-3 (MHV-3) induced hepatitis animal model and investigated the impact of NAFLD on virus replication in C3H/HeN mice. Sixty 6-week-old female mice were fed with high fatty diet (HFD) or normal diet (ND) in random. After feeding for 12 weeks, 6 mice in each group were scarified and liver histology was examined, and serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST), fasting lipid profile, fasting blood glucose (FBG), serum insulin were measured. Another 24 mice in each group were injected with 10 plaque forming units of MHV-3 intraperitoneally. Hepatic MHV-3 viral loads were detected by quantitative PCR on day 4, day 8, day 12, and day 16 post infection.
Results: At week 12, enlarged and yellowish liver was evidenced with a great number of lipid droplets deposition histologically in HFD feeding mice. There were significant differences between HFD group and ND group in AST (58.50 $\pm$ 4.66U/L vs. 47.37 $\pm$ 7.84U/L, $P = 0.027$), triglyceride (1.68 $\pm$ 0.19 mmol/L vs. 1.26 $\pm$ 0.08 mmol/L, $P = 0.022$), cholesterol (6.07 $\pm$ 0.06 mmol/L vs. 3.44 $\pm$ 0.60 mmol/L, $P < 0.001$), FBG (7.40 $\pm$ 1.33 mmol/L vs. 4.17 $\pm$ 0.75 mmol/L, $P < 0.001$), and insulin (1.36 $\pm$ 0.52 μg/L vs. 0.50 $\pm$ 0.19 μg/L, $P = 0.005$). MHV-3 viral loads in NAFLD mice were significantly higher on day 4 post infection ($P = 0.002$), and this trend last until day 8 and day 12.
Conclusions: In early period of MHV-3 infection, NAFLD can promote intrahepatic viral replication in C3H/HeN mice.

Topic 20: Non Alcoholic Fatty Liver Disease

No: 1951

Hyperhomocysteinemia in non cirrhotic insulin resistant and obese patients with non alcoholic fatty liver disease

Nikhil Patel[1], Sulabhsinh Solanki[2], Payal Patel[2], Fulkunvarba Zala[2], Kinnari Matroja[3], Chetan Lakhani[4], Sanjay Patel[5], Deepak Amarapurkar[6]

Jivandeep Hospital Gastroenterology Anand-India[1], An Patel Institute Mlt Anand-India[2], An Patel Institute Mlt Anand-India[3], Darpan Laboratory Pathology Anand-India[4], Sanjay Laboratory Pathology Anand-India[5], Bombay Hospital and Medical Research Centre Gastroenterology Mumbai-India[6]

Background: Insulin resistance (IR) and obesity (O) predispose to non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome (MS). These are increasingly recognized with epidemic of obesity and diabetes in India. Recently, hyperhomocysteinemia (HHcy) is recognized to be commonly present in NAFLD adults and might affect course of NAFLD. This study was planned to identify prevalence and importance of HHcy in development of NAFLD in IR-O subjects.
Methods: This observational prospective study was planned on consecutive IR-O children (identified in school health check-up, n = 78, age = 11.4 ± 2.9, males = 57(73 %)) and adults (attending tertiary-care hospital, n = 100, age = 39.6 ± 11.8, males = 67 (67 %)). All underwent anthropometry, blood-pressure measurement, blood sugar, lipids, insulin, liver profile, ultrasonography, homocysteine and tests to rule out viral, metabolic and autoimmune liver disease.
Results: Presence of NAFLD (71.7 % vs. 79 %) or non-alcoholic steatohepatitis (NASH) (44.8 % vs. 54 %) was similar, but HHcy (28.2 % vs. 66 %) and MS (19.2 % vs 68 %) were significantly more in adults than children. In subgroup analysis, in IR-O NAFLD, HHcy was associated with less NASH in both children [5/21(23.8 %) vs. 30/35(85.7 %)] and adults [29/52 (48 %) vs. 25/27 (92.5 %)]. In IR-O children, NAFLD was more in HHcy [21/22(95.4 %) vs. 35/56 (62.5 %)] than in MS [9/15 (60 %) vs. 47/63 (74.6 %)]. In IR-O adults, NAFLD was more in MS [58/68 (85.2 %) vs. 21/32 (65.6 %)] than in HHcy [(52/66 (78.7 %) vs. 27/34 (79.4 %)].
Conclusions: HHcy is important factor in development of NAFLD and NASH in IR-obese patients especially in children.

Topic 21: Other Liver Tumors

No: 1687

Aggressive recurrence of primary hepatic epithelioid haemangioendothelioma (HEHE) after liver transplantation

Hussien Elsiesy[1], Qusay Abdoh[2], Mohamad Almansour[3], Hussa Al Hussaini[4], Mohamed Al Sebayel[1], Waleed Alhamoudi[1], Faisal Abaalkhail[1]

King Faisal Specialist Hospital & Research Center Liver Transplantation Riyadh-Saudi Arabia[1], An-najah National University Gastroenterology Nablus-Palestine[2], King Faisal Specialist Hospital & Research Center Critical Care Riyadh-Saudi Arabia[3], King Faisal Specialist Hospital & Research Center Pathology Riyadh-Saudi Arabia[4]

Introduction: HEHE is a rare neoplasm of vascular origin that that occurs in the liver, UNOS reported a favorable outcome after liver transplantation in 110 patients with 1 and 5 years survival of 80 % and 64 %.
Case report: A 40 year old lady with history of hypertension, presented with three month history of right upper abdominal pain with nausea, vomiting & significant loss of weight associated with scleral icterus and progressive abdominal distension.
Examination revealed jaundice, hepatomegaly and ascites.

Serum bilirubin was 26.5 mg/dl, ALP was 552.

Contrast Computed Tomography (CT) Abdomen and pelvic showed diffuse infiltrative neoplastic process of the liver with a mass effect and stretching of the hepatic and portal veins, in addition to bile duct dilatation.

Viral hepatitis markers were negative and serum Alpha fetoprotein was within reference range.

Liver biopsy was consistent with HEHE, with positive endothelial markers (CD31, CD34 & factor VIII-related antigen)

She underwent living Related Liver transplantation on June 2013, and was discharged after 20 days with normal liver enzymes.

The explanted liver weighed 3222 grams. Gross and microscopic pathology showed (fig 1-7).

Four month later, she presented with severe abdominal pain and ascites with elevated liver enzymes, CT showed numerous variable size non enhancing tumors associated with small amount of ascites. Hepatic veins, artery and portal vein are patent.

Liver biopsy confirmed disease recurrence, she received supportive treatment and unfortunately she died 2 weeks later.
Conclusion: HEHE can have rapid and aggressive recurrence after liver transplantation.

Topic 21: Other Liver Tumors

No: 2107

Prognostic value of CA 19 9 kinetics during gemcitabine based chemotherapy in patients with advanced cholangiocarcinoma

Ban Seok Lee[1], Sang Hyub Lee[1], Dong Kee Jang[1], Kwang Hyun Chung[1], Ji Kon Ryu[1], Yong-tae Kim[1]

Seoul National University College of Medicine Department of Internal Medicine and Liver Research Institute Seoul-Korea, South[1]

Objective: Little is known about prognostic value of CEA/CA19-9 kinetics during chemotherapy in patients with advanced cholangiocarcinoma (CCA). The aim of this study was to evaluate association between change in CEA and CA 19-9 level during gemcitabine-based chemotherapy and survival in patients with advanced CCA.
Method: A total of 236 patients with pathologically-confirmed advanced CCA received gemcitabine-based chemotherapy were reviewed, and 179 were eligible for analysis. Baseline, pre-, and post-treatment (after 2 cycles of chemotherapy) CEA and CA 19-9 values were checked, and survival was compared according to various cutting points of baseline measurement or extent of change of tumor marker level.
Result: Patients with a decrease of ≥ 50 % in CA 19-9 level had better survival than the others (16.0 vs. 9.0 months). However, CEA decline did not predict survival gain. Significant prognostic factors in multivariable analysis included predict survival gain. Significant pro8), distal location of tumor (HR 0.50), and baseline CA 19-9 level ≤ 1000 U/ml (HR 0.53). Subgroup analysis was conducted in 114 patients with pre-treatment CA 19-9 > 37 U/ml and bilirubin ≤ 2 mg/dL. ≥ 50 % decline in CA 19-9 level still showed an independent prognostic significance.
Conclusion: CA19-9 but not CEA kinetics serves as a predictor of better survival in patients with advanced CCA on gemcitabine-based

chemotherapy, and a itabine-based in CA 19-9 level after 2 cycles of chemotherapy may have clinical utility as a early indicator of better response to gemcitabine-based chemotherapy.

Topic 22: Pediatric Gastroenterology

No: 1028

Progressive familial intrahepatic cholestasis at tertiary care centre in Saudi Arabia

Ali Almehaidib[1], Adel Alshahrani[1], Mohaammad Banemai[1], Khaled Alsaleem[1], Wajeeh Aldekhail[1]

King Faisal Specialist Hospital & Research Center Pediatrics Riyadh-Saudi Arabia[1]

Introduction: Progressive familial intrahepatic cholestasis (PFIC) is a rare inherited autosomal recessive disease where patients develop severe cholestasis progressing to biliary cirrhosis and chronic liver failure, usually during the first decade of life.
Aim: To review the clinical presentation, familial involvement and outcome of patients with PFIC in Saudi Arabia.
Methods: A retrospective study for patients who were diagnosed to be PFIC based on gene study between 2000 - 2013.
Results: 48 patients were confirmed by gene test to have PFIC: 5/type 1, 27/type 2, and 16/type 3.

Consanguinity is seen in all patients (100 %) and 31 patients (64 %) having positive family history of liver diseases All PFIC type 1 patients presented with jaundice, poor growth, hepatomegaly, normal hearing and GGT. Diarrhea in 4 patients (80 %) Two patients (40 %) underwent liver transplantation. of the 27 patients with PFIC type2, 24 patients (88 %) with jaundice 22 patients (81 %) and itching 3 patients (11 %),hepatomegaly in 23 patients (85 %), and 6 patients (22 %) with signs of rickets. Biochemically three patients (11 %) have high GGT on presentation and the rest of patients (88 %) had normal GGT and normal cholesterol and 9 patients (33 %) had coagulopathy (INR $>$ 1.3). Fifteen patients (55 %) underwent liver transplantation; three patients (11 %) died.

16 patients with PFIC type 3 presented after 2 years of age, 6 patients (37 %) with only jaundice in 5 patients (31 %) and 4 patients (25 %) with

Topic 22: Pediatric Gastroenterology

No: 1486

Predictors of short term outcome in unoperated biliary atresia or those with unsuccessful portoenterostomy

Seema Alam[1], Nikhil Mehra[1], Bikrant Bihari Lal[1], Rajeev Khanna[1], Dinesh Rawat[1]

Institute of Liver and Biliary Sciences Pediatric Hepatology New Delhi-India[1]

Aims: To evaluate the predictors of short term (90-days) survival in unoperated biliary atresia(BA) cases or those with unsuccessful Kasai portoenterostomy(KPE) who were listed for pediatric liver transplantation(PLTx).
Methods: All unoperated or unsuccessful KPE cases of BA $<$ 2 years presenting between Jan 2011 to July 2014 at the time of listing for PLTx were enrolled. Diagnosis of BA was based on per-operative cholangiogram or liver biopsy. Those with presence of cirrhosis on liver biopsy or evidence of PHTN were not considered for KPE. Success of KPE was defined as bilirubin level $<$ 2 mg/dL at 3 months. Listing for PLTx was done on basis of presence of complications of PHTN—ascites, variceal bleed, hepatic encephalopathy or hepatopulmonary syndrome; or PELD $>$ 14. Clinical and laboratory variables were analysed for prediction of short-term survival at 90 days.
Results: Of the 31 patients waitlisted for PLTx, 8 (25.8 %) died within 90 days. Predictors of mortality at 90 days from the time of listing were CTP, PELD and low platelets. Presence of significant ascites (OR 2.24; 95 % CI 1.26-3.97) and HE (OR 3.59; 95 % CI 1.27-10.17) also predicted poor outcome (Table).
Conclusion: High PELD score and presence of significant ascites, hepatic encephalopathy or low platelets are predictors of 90 days mortality in BA cases.

Topic 22: Pediatric Gastroenterology

No: 1378

A single center pediatric ERCP experience

Canan Alkim[1], Meltem Ergun[1], Huseyin Alkim[1], Ali Riza Koksal[1], Salih Boğa[1], Mehmet Bayram[1], Pinar Sayin[2], Nafiye Urganci[3], Ali Ihsan Dokucu[4]

Sisli Hamidiye Etfal Education and Research Hospital Gastroenterology Clinic Istanbul-Turkey[1], Sisli Hamidiye Etfal Education and Research Hospital Anesthesiology Clinic Istanbul-Turkey[2], Sisli Hamidiye Etfal Education and Research Hospital Pediatric Gastroenterology Clinic Istanbul-Turkey[3], Sisli Hamidiye Etfal Education and Research Hospital Pedatric Surgery Clinic Istanbul-Turkey[4]

Objective: This study was planned for evaluating indications, success rate and results of ERCP done at pediatric patients in our clinic.
Results: Total 20 ERCP sessions were performed on 11 children (4 female, 7 male) aged 12-18 years. ERCP indications were: 5 bile duct stone, 3 hydatid cyst disease, 2 acute recurrent pancreatitis and 1 bile duct obstruction due to hepatocellular carcinoma. In 4 of the 5 patients with pre-procedural common bile duct stone diagnoses, stone was detected and extracted. In the 5th patient stone wasn't seen, biliary sphincterotomy was done. Membrane extraction was done to the hydatid cyst disease patient which presented with mechanical obstruction. 2 cysto-biliary fistula patients were treated by the way of nasobiliary drainage. In one of the acute recurrent pancreatitis patients bile duct stone was detected and extracted. Biliary tree of the second patient was normal. There was a stricture at the head portion of the Wirsung with dilatation distal to the stricture. Pancreatic 5F plastic stent was inserted. Biliary plastic stent was inserted to the hepatocellular carcinoma patient for the palliation of jaundice. Common bile duct stone was the most common (6/11, 54 %) diagnosis reached after ERCP.
Conclusion: ERCP was done for therapeutic indications not for diagnostic purposes. The most common indication for ERCP was bile duct stone in children. These findings are consistent with the literature. The second major indication for ERCP was hydatid cyst disease in our child group, and this is different from the literature. In conclusion, ERCP was a safe and effective therapeutic procedure in children.

Topic 22: Pediatric Gastroenterology

No: 1366

Wider impact of liver disease on young people's lives

Shahreen Bashir[1], Pam Lowe[1], Elizabeth Peel[2]

Aston University School of Languages and Social Sciences Birmingham-United Kingdom[1], University of Worcester Institute of Health & Society Worcester-United Kingdom[2]

Young people living with liver disease in the United Kingdom are currently an under-researched population. Scant attention has been given to the impact of liver disease on a young person's wider life. If we are going to improve patient care and services it is imperative to understand the implications a liver disease diagnosis can have on a person's wider life.

This research project is funded by The Children's Liver Disease Foundation (CLDF) and has explored the lives of young liver disease patients through the use of semi-structured, in-depth interviews. Participants in this research were aged between 14 and 25 years with a range of liver diseases differing in aetiology and onset age.

The project found young people struggled with not being able to play contact sports at school and experiencing disruption to their education through periods of ill health or for hospital visits. Other issues included the impact on intimate relationships and friendships. It was important young people were able to minimise the disruption of treatments or illness to their lives. Participants reported receiving support from many sources including family, friends, health professionals and the CLDF.

Liver disease can impact a young person's wider life and it is important alongside medical treatment young people have access to specialised support services.

Topic 22: Pediatric Gastroenterology

No: 1970

Prevalence and etiology of increased transaminases in asymptomatic school children

Nikhil Patel[1], Sulabhsinh Solanki[2], Payal Patel[2], Priya Patel[2], Sanjay Patel[3], Chetan Lakhani[4], Deepak Amarapurkar[5]

Jivandeep Hospital Gastroenterology Anand-glorioso Islands[1], An Patel Institute Mlt Anand-India[2], Sanjay Laboratory Pathology Anand-glorioso Islands[3], Darpan Laboratory Pathology Anand-India[4], Bombay Hospital and Medical Research Centre Gastroenterology Mumbai-India[5]

Background: In western world, 1-9 % asymptomatic general population has elevated transaminases. The commonest cause is non-alcoholic fatty liver disease(NAFLD), which is prevalent in 15-40 %. In India, there is sparse data on prevalence and etiology of tranaminase elevation. This data is important in view of rising obesity and diabetes. This observational prospective study was planned to determine prevalence and etiology of elevated transaminase in asymptomatic school children.
Methods: 3624 school children [age = 10.1 ± 6.2 years, range = 5-15 years, male = 2229(61 %)] were included. All the students underwent history, examination, anthropometry, ALT, AST, HBsAg, antiHCV, bilirubin and sonography. Those with elevated transaminases (ALT and/or AST) were evaluated for etiology (IgM antiHAV, IgM antiHEV, IgM antiHBc, ferritin, ceruloplasmin, autoimmune hepatitis profile, protein electrophoresis, homocysteine, lipid, insulin, blood sugar and vitamin B12 in all; CT scan/liver biopsy as per need) and reevaluated for liver function tests at 1- and 3-month.
Results: Out of 3624 children, transaminase elevation was seen in 96(2.6 %) children [age = 11.1 ± 6.9 years, male = 68 (70.8 %)]. 6 children with transient elevation were excluded after etiological analysis. Acute transamiinase elevation was seen in 10 (10.4 %): hepatitis A = 7 (7.2 %), hepatitis E = 2 (2.1 %) and undetermined = 1 (1 %). Chronic elevation was seen in 86(89.5 %): NAFLD = 71 (73.9 %), vitamin B12 deficiency/hyperhomocysteinemia = 12 (12.5 %), hepatitis B = 1(1 %), undetermined = 2 (2.1 %). In risk factor analysis, elevated transaminase group had significantly higher obesity [38(39.5 %) vs. 242 (6.8 %)], hyperlipidemia [22 (22.9 %) vs. 23 (0.6 %)], hypertension [15(15.8 %) vs. 203 (5.7 %)] and family history of metabolic syndrome diseases [15 (15.6 %) vs. 290 (8.2 %)]; whereas dietary, activity and viral risk factors were not significant.
Conclusion: NAFLD is commonest cause of elevated transaminases in school children. Risk factors for elevated transaminases were presence or family history of metabolic factors.

Topic 22: Pediatric Gastroenterology

No: 1095

Hepatic granuloma in children a report of 23 cases

Ali Almehaidib[1], Bassel Alshemmeri[1], Sulaiman Almayouf[1]

King Faisal Specialist Hospital Pediatric Riyadh-Saudi Arabia[1]

Introduction: Hepatic granuloma represents a nonspecific reaction to specific antigens and occur in a variety of infectious and non infectious diseases. Previous study from saudi arabia have identified an infectious etiology in 96 % of adults caeses. No data is available in children in Saudi Arabia.
Aim: to evaluate the etiology, and clinical presentation of children with hepatic granuloma in Saudi Arabia.
Method: A retrospective study of all children with hepatic granuloma found in the archives of the Department of Pathology at KFSHRC between 2003 and 2013.The medical records were reviewed for clinical presentations, laboratory and histopathology findings.
Results: Hepatic granuloma was seen in 23 biopsies (14 males) out of 1089 biopsies during 10 years period with a n incidence of 2.11 %. The mean age was 6.6 years.The most common etiologies were: sarcoidosis (22.7 %) primary immunodeficiency,fugal infection and malignancies each accounts for 13 %. Drug reaction and EBV infection each 8.65. and one case of: tuberculosis cryptococcal infection, transient cholestasis, focal nodular hyperplasia and progressive familial intrahepatic cholestasis.
Conclusion: Hepatic granuloma is seen in 2.11 % of liver biopsies in children. Sarcoidosis is the most common cause and infections are not that common in our patients as was reported previously in adults in Saudi Arabia or in children in Iran.

Topic 23: Pregnancy and Liver

No: 1875

Factors associated with mother to child transmission of hepatitis B virus despite immunoprophylaxis

Hong Tang[1], Cui-ping Liu[1], Yi-lan Zeng[2], Min Zhou[2], Em-qang Chen[1], Rong Hu[2], Li Wang[2]

West China Hospital of Sichuan University Center of Infectious Diseases Chengdu-China[1], Public Health Clinical Center of Chengdu Department of Obstetrics Chengdu-China[2]

Objective: This study aimed to assess the risk factors for mother-to-child transmission (MTCT) of hepatitis B virus (HBV) after immunoprophylaxis.
Methods: We enrolled 256 mother–child pairs with positive maternal hepatitis B surface antigen (HBsAg) between January 2010 and June 2013. All children received passive-active immunization after birth. The children were tested for HBsAg at birth and 6-12 months and/or 1-3 years of age. and risk factors for MTCT were assessed using a multivariate logistic regression model.
Results: Among 256 children, 10 (3.9 %) developed HBV infection. All of them were born to hepatitis B e antigen (HBeAg)-positive mothers with high HBVDNA levels (median, 7.36; range, 6.75–8.00 log10 IU/ml). There were 20 mothers receiving antiviral treatment during pregnancy. Maternal viral load decreased from the average of 7.16 log10 IU/ml to 3.08 log10 IU/ml ($P < 0.0001$) at delivery. The multivariate logistic regression analysis showed that high maternal HBV DNA levels (OR for each log10 IU/ml increase, 2.44; 95 % CI, 1.13-5.29, $P = 0.023$) and vaginal delivery (OR = 6.96, 95 % CI, 1.80-26.93, $P = 0.005$) were risk factors for HBV immunoprophylaxis failure.
Conclusion: Additional strategies should be considered for HBeAg-positive mothers with HBV DNA level above 6-7 log10 IU/ml and our study supports cesarean section for infants born to HBsAg-positive mothers.

Topic 23: Pregnancy and Liver

No: 1902

Teratogenesis induced by in utero exposure of trimethoprim sulfamethoxazole in mice

Madeeha Arshad[1]

Punjab University Zoology Lahore-Pakistan[1]

Aims: Antibiotic therapy is the most common therapy for treating the UTIs during gestation. Trimethoprim Sulfamethoxazole (TMP-SMX) is used to treat such infections. During this study, TMP-SMX was tested for its ability to induce developmental defects in mice fetuses.
Methodology: Different concentrations of the drug, 0.00, 4.10, 8.33 and 16.66 μg/g B.W. were administered. The doses were given orally to pups bearing mothers on days 6-12 of gestation, and fetuses were recovered on day 18 of gestation.
Results: Morphologically, fetuses showed abnormalities such as haemorrhages, microphthalmia, limb deformities (shortening of forelimb, forelimbs hyperextensions, drooping wrists, low set arms, hindlimb displacement), hygroma, kyphosis, curved, short tail and fluid filled abdominal cysts. Intrauterine growth retardation with increasing dose was also observed. Fetal resorptions (44.99 %) were noted in dose group 16.66 μg/g. Morphometric observations of fetal body parts like head circumference, eye circumference, forelimb and hindlimb size and tail length demonstrated a significant ($P < 0.005$) decrease with increasing dose in comparison with control. The fetal body weight and CR length were also minimized significantly ($P < 0.005$) in all dose group. Histologically, liver necrosis was observed.
Conclusion: Obtained results showed that TMP-SMX has significant potential to cause congenital defects in developing mice and it is manifested that TMP-SMX must be used with extreme care during organogenesis.

Topic 23: Pregnancy and Liver

No: 1585

The downward spiral of acute fatty liver of pregnancy a case report

Josephine Anne Lucero[1], Farrah Haidee Pedracio[1], Girlie Merdegia[2], Aleth Marie Sia-encinares[3]

University of The Philippines Philippine General Hospital Medicine Manila-Philippines[1], University of The Philippines Philippine General Hospital Nephrology Manila-Philippines[2], University of The Philippines Philippine General Hospital Gastroenterology Manila-Philippines[3]

Background and aim: Acute fatty liver of pregnancy is rare and carries high mortality rates due to the development of acute liver failure and disseminated intravascular coagulation. Its diagnosis may be difficult as it can be confused with viral hepatitis, cholestasis of pregnancy, preeclampsia, and other infectious entities. It is proposed to be due to impaired fetal fatty acid metabolism causing microsteatosis in the liver. Management involves expeditious delivery and supportive care for the mother and child. This case report aims to characterize the presentation of acute fatty liver of pregnancy.
Summary of the case: This is a case of a young Filipino primigravid who developed jaundice in her third trimester of pregnancy. Upon admission, an infectious etiology to the jaundice was initially considered which was treated empirically but quickly ruled out. The patient underwent caesarean section due to fetal death in utero after which her mental status began to deteriorate and her organs began to fail. Acute fatty liver of pregnancy was then considered. She developed acute liver and renal failure, and disseminated intravascular coagulation. Supportive management with plasma transfusions, renal replacement therapy, and mechanical ventilation were given. The patient eventually succumbed to multiple organ failure.
Significance: There is no established therapy to ensure survival in the disease but experimental strategies to treat the complications have been attempted. Immediate diagnosis is crucial to beginning supportive management for acute fatty liver of pregnancy.

Topic 23: Pregnancy and Liver

No: 1371

Changes of serum TH1 TH2 cytokines level in pregnant women with hbv infection after telbivudine treatment

Hongfei Huang[1], Dengming He[1], Quanxin Wu[1], Maoshi Li[1], Xianghua Zeng[1], Yuming Wang[1]

Southwest Hospital, Third Military Medical University Institute of Infectious Disease Chongqing-China[1]

Background and aims: Telbivudine can block mother-to-child transmission, but the influence on Th1/Th2 balance was unknown. We aimed to explore the mechanism in HBV infected pregnant women treated with telbivudine by observing the serum levels of Th1/Th2 cytokines.
Methods: Fifty-four HBeAg-positive pregnancy women were divided into two groups according to ALT levels (18 immune active group and 36 immune tolerant group), and they were given telbivudine at the second or third trimester. ALT, HBV-DNA, HBV makers, Th1 cytokines (IL-2, IFN-γ) and Th2 cytokines (IL-4, IL-6) levels were detected before treatment and before delivery.

Results: In addition to serum HBV-DNA level decreased significantly, ALT and HBeAg disappear or seroconversion rate showed no significant difference between before treatment and before delivery. Both groups showed that Th1 cytokines were high expression, while Th2 cytokines were low expression before treatment and before delivery. There was no significant difference of IL-2, IFN-γ, IL-4, and IL-6 levels between two groups. Before delivery, IL-4 level was elevated in immune active group ($P = 0.014$), but was still in normal range, while IL-2, IFN-γ and IL-6 levels had no significant changes ($P = 0.182$, 0.259 and 0.710). The levels of IL-2, IFN-γ, IL-4 and IL-6 in immune tolerant group also have no significant changes ($P = 0.651$, 0.839, 0.650 and 0.542).
Conclusions: Th1 cytokines are high expression and Th2 cytokines are low expression at the second or third trimester in pregnant women with chronic HBV infection. There is little influence on Th1/Th2 balance in HBV infected pregnant women after a short treatment of telbivudine.

Topic 24: Other viral Hepatitis

No: 1654

Who western pacific regional hepatitis action plan comprehensive action on viral hepatitis

Nick Walsh[1], Kiren Mitruka[2], Eric Wiesen[3], Ying-ru Lo[1]

World Health Organization Hiv, Hepatitis and Sti Unit, Wpro Manila-Philippines[1], United States Centers For Disease Control Division of Hepatitis Atlanta-United States[2], World Health Organization Expanded Program On Immunisation, Wpro Manila-[3]

The countries of the Western Pacific Region bear a disproportionate burden of chronic viral hepatitis. Mortality from viral hepatitis in this Region is equivalent to that of tuberculosis, and three to fourfold higher than for HIV/AIDS. More than half of global hepatitis B related deaths occur in the Western Pacific Region. Hepatocellular carcinoma, 85 % of which is related to chronic viral hepatitis, is the second most common cause of cancer deaths in the Asia–Pacific. China alone accounts for over 50 % of the global liver cancer burden. Infection-related cancers are preventable.

In the Western Pacific, 30 out of 37 countries of the Region have reached the 2012 milestone of reducing the rate of chronic hepatitis B infection among 5-year-old children to < 2 %. Building on this success, and given recent new hepatitis B and C antiviral medicines, there is an opportunity to move beyond immunization to comprehensive action on viral hepatitis to address the high burden of chronic hepatitis B and C.

The Regional Hepatitis Action Plan will provide countries with a policy structure to support the development of strategic national plans on hepatitis. The Action Plan includes region specific viral hepatitis guidance on priority activities and targets on raising awareness, promoting partnerships and mobilizing resources; evidence-based policy and data for action; prevention of transmission; and screening, care and treatment. The draft Regional Hepatitis Action Plan will be presented and discussed.

Topic 24: Other viral Hepatitis

No: 1810

A cross sectional study on intrahepatic cholestasis indicators of viral hepatitis patients

J. Cheng[1], J.b. Wang[2], W.h. Zhang[3], Y. Cao[4], X.x. Yang[5], W. Xie[1], C.y. Zhou[2], N. Li[3], X.x. Geng[5]

Beijing Ditan Hospital Capital Medical University Hepatology Beijing-China[1], China-Japan Union Hospital of Jilin University Hepatology Changchun-China[2], Huashan Hospital Affiliated To Fudan University Hepatology Shanghai-China[3], Guangzhou Eighth People's Hospital Hepatology Guangzhou-China[4], Sichuan Provincial People's Hospital Hepatology Chengdu-China[5]

Aim: Intrahepatic cholestasis (IHC) is common in viral hepatitis patients. Although the patients are clinically asymptomatic, the IHC indicators, alkaline phosphatase (ALP) or gamma glutamyltransferase (GGT), remain abnormal. This study is to investigate the IHC indicators for in-patients with viral hepatitis when they are being discharged, and to explore the correlation between IHC indicators and liver fibrosis.
Materials & methods: It is a multi-center, cross-sectional study. A total of 1000 hospitalized patients with viral hepatitis were recruited from five big hospitals. Demographic characteristics, clinical and laboratory data including IHC indicators and liver fibrosis indicators (hyaluronic acid and type IV collagen) were collected. Chi square and multivariate logistic regression were performed to determine the correlation between abnormal IHC indicators and liver fibrosis.
Results: 998 of 1000 patients were included in the analysis (Table 1). 560 patients (56.17 %) had abnormal IHC indicators at discharge. Comparing to patients with normal IHC indicators, patients with abnormal IHC indicators had significantly more abnormal liver fibrosis indicators (hyaluronic acid and type IV collagen; severer Child-Pugh Classification. both $P < 0.001$). Multivariate analysis showed that patients with abnormal IHC indicators had significantly higher risk to have abnormal liver fibrosis indicators ($P = 0.0236$, OR = 1.542), and higher trend to have higher Child-Pugh Classification ($p > 0.05$, OR = 1.238).
Conclusions: More than half of the patients with viral hepatitis had abnormal IHC indicators at discharge, which are correlated with liver fibrosis in clinical practice. Therefore, monitoring and following up on IHC indicators after discharge are recommended for viral hepatitis patients.

Topic 24: Other viral Hepatitis

No: 1080

Robust chemokine induction in hepatitis a virus infected hepatocytes

Pil Soo Sung[1], Jeewon Lee[1], Woo Jin Chung[2], Eui-cheol Shin[1]

Kaist Graduate School of Medical Science and Engineering Daejeon-Korea, South[1], Keimyung University School of Medicine Department of Internal Medicine Daegu-Korea, South[2]

Background: Acute HAV infection is typically self-limited but accompanied by hepatic inflammation, elevation of liver enzymes, and periportal infiltrates of immune cells in the liver. However, the mechanism of immune cell recruitment to liver in acute HAV infection has not been elucidated yet.
Methods: Eleven serum samples of acute HAV patients and those of age-matched healthy controls were collected and CXCL10, CCL4, and CCL5 levels were determined using cytometric bead array method. Wild-type HM-175 HAV virus was purified from patient with acute HAV infection, and propagated in Huh-7.5 cell lines. After HAV infection to primary human hepatocytes and HepG2 cells, serial cell pellets and culture supernatants were harvested to determine the mRNA and protein level of chemokines. Knocking down important

signal molecules downstream of RIG-like receptors and blocking the effects of IFNs using anti-IFN-antibody were done.
Results: In the serum samples of patients with acute HAV infection, the level of CXCL10, CCL4, and CCL5 was elevated. HAV-infected primary human hepatocytes and HepG2 cells produced minimal IFN-beta but robust IFN-lambda. The levels of CXCL10, CCL4, and CCL5 were markedly increased in the similar pattern with IFN-lambda, but blocking interferon-lambda marginally affected the level of CCL4 and CCL5, and did not affect the production of CXCL10. Knocking down MAVS and IRF3 significantly downregulated the expression of CXCL10, CCL4, and CCL5, suggesting that IFN-independent regulation is critical in production of chemokines in HAV-infected hepatocytes.
Conclusions: HAV-infected hepatocytes produce chemokines robustly, and endogenous type III IFN has minimal effects on the induction of chemokines.

Poster Presentations

Topic 1: Acute on Chronic Liver Failure

No: 1088

Sepsis is rare as acute precipitating event in patients with hbv related acute on chronic liver failure

Hong Shi[1], Jianyun Zhu[1], Xiangyong Li[1], Yutian Chong[1]

The Third Affiliated Hospital of Sun Yat-sen University Department of Infectious Diseases Guangzhou-China[1]

Background/aims: The causes of acute injury in acute-on-chronic liver failure (ACLF) are variable. Sepsis is a common acute precipitating event in some studies. However, the role of sepsis in HBV-ACLF is debatable. The aims of this study were to investigate those acute insult factors in patients with HBV-ACLF, and explore the relation between sepsis with HBV-ACLF.
Methods: ACLF was defined as per the Asian Pacific Association for the Study of the Liver (APASL) criteria. Patients with ALCF were prospectively enrolled from January 2013 to December 2013 and were evaluated for acute insults.
Results: 78 patients with HBV-related ACLF were included in the study. 35 patients (45 %) had known cirrhosis whereas 43 patients (55 %) had chronic hepatitis without cirrhosis as underlying chronic liver disease. HBV flare was the most common precipitating cause of ACLF, occurring 44 patients (56 %). 7 patients received immunosuppressant agents and 5 patients were given chemotherapy, including 1 patient with treatment of pulmonary tuberculosis. Acute viral hepatitis (hepatitis E virus) accounted for 4 patients. Sepsis as precipitating event was just identified in 2 patients, who have ascites with cirrhosis. The cause of acute insult was unknown in 16 patients (20 %). However, 19 patients developed sepsis in the progress of ACLF. Patients with sepsis had a higher 30 days mortality ($\chi^2 = 8.588$, $P = 0.004$).
Conclusions: Sepsis is not a common acute precipitating event in patients with HBV-related Acute on chronic liver failure, but may increase mortality.

Topic 1: Acute on Chronic Liver Failure

No: 2132

A rare cause of liver failure after right hepatectomy partial left lobule rotation

Erdem Karadeniz[1], Şükrü Arslan[1], Ercan Korkut[1], Nurhak Aksungur[2], Gürkan Öztürk[1], Bülent Güvendi[1], Bülent Aydinli[1]

Ataturk University General Surgery Erzurum-Turkey[1], Tekman State Hospital General Surgery Erzurum-Turkey[2]

Introduction: With a better understanding in liver surgery anatomy, liver resections are being performed in many medical centers with an increasing frequency.
Case: A 48-year-old female patient who had received right hepatectomy due to alveolar echinococcoses lesion in the right lobule of the liver in a different medical center was sent to our clinic for a liver transplantation, because she had experienced liver failure on the 6th postoperative day of her surgery. In the abdomen tomography in our clinic, there were limited perfusion defects here and there in the liver parenchyma, common congestion in parenchyma, and the left lobule of the liver was partially rotational. In the laboratory tests of the patient, the findings were as follows: T-bilirubin: 11, D-bilirubin: 6, AST: 256, ALT: 390 INR: 2.1 The patient was operated. It was observed that the left lobule of the liver was rotated towards the place of the right lobule which was taken out, and it was also detected that the vascular structures of the left liver lobule, together with the vena cava, were partially torsioned. The left lobule was taken to its normal anatomic place and the falciform ligament, which was not sutured to the front wall of the abdomen, was sutured.
Result: The problem in our patient in our case stemmed not from the scarcity of the volume, but from a technical deficiency. After right hepatectomy, it is a standard procedure that the left lobule is sutured to the front wall of the abdomen with the help of falciform ligament. The follow-up of such patients require experience.

Topic 1: Acute on Chronic Liver Failure

No: 1478

Complement 5A receptor mediated neutrophil dysfunction is associated with a poor outcome in sepsis patients

Ruonan Xu[1], Fang Lin[1], Zheng Zhang[1], Fu-sheng Wang[1]

Beijing 302 Hospital Research Center For Biological Therapy Beijing-China[1]

Aims: Complement 5a (C5a) has been implicated in the pathogenesis of sepsis through inducing functional impairment of neutrophil; however, the predicting role of C5a receptors as biomarkers for management of sepsis is still lacking. This study investigates the dynamic changes of C5a and C5a receptors (C5aRs) expression on neutrophils and their influences on neutrophil function.
Methods: A total of 19 patients with SIRS and 24 patients with severe sepsis as well as 18 healthy subjects as controls were enrolled in the study. The sequential blood samples were used to analyze C5aRs expression on neutrophils and the effect of C5a on neutrophil function. 28-day survival rate was evaluated to C5aRs expression in these patients.
Results: Sepsis patients displayed low levels of expression of C5aRs on neutrophils as compared with healthy and SIRS subjects, and correlated with the disease severity in these patients. Further analysis indicated that low expression of C5aRs associated with poor survival of sepsis patients. In vitro, addition of C5a significantly reduced C5aRs expression and IL-8 production by neutrophils from sepsis patients.
Conclusions: The diminished expression of C5aRs was associated with functional impairment of neutrophils and was a poor prognosis of sepsis patients. This finding may provide C5aRs expression as early markers to predict the severity of sepsis patients.

Topic 1: Acute on Chronic Liver Failure

No: 1146

'Broken heart' in acute on chronic liver failure

Ennaliza Salazar[1], Chee Kiat Tan[1], George Boon-bee Goh[1]

Singapore General Hospital Gastroenterology and Hepatology Department Singapore-Singapore[1]

Takotsubo cardiomyopathy usually occurs as a result of catecholamine release causing myocardial 'stunning' during physical or emotional stress. Typically, coronary angiogram shows normal or minor coronary artery disease and echocardiogram showing apical ballooning with basal wall hyperkinesia. It usually has good cardiac recovery function within days to weeks. Here we report first case of takotsubo cardiomyopathy in a patient with acute on chronic liver failure.

Topic 1: Acute on Chronic Liver Failure

No: 1006

Clinical observation of plasma exchange in the treatment of liver failure in northeast China

Xu Li[1]

The 1st Hospital of Jilin University Hepatology Changchun-China[1]

Aim: Observation of the clinical efficacy and changes in biochemical parameters of plasma exchange (PE) in the treatment of liver failure .
Method: Retrospective analysis of a total of 46 patients with liver failure which live in our hospital from March 2004 $\sim$ March 2014, and according to the different treatments, they were divided into treatment group and control group, the treatment group' patients were treated with comprehensive treatment in conjunction with plasma exchange treatment, and the patients in control groups were treated with comprehensive treatment. we observated the clinical symptoms and liver function after treatment changes.
Conclusion: (1)After regular treatment, the clinical symptoms of the two groups' patients except disturbance of consciousness had improved, the state of consciousness in patients treated with plasma exchange in treatment 1 d $\sim$ 5 d improved, 10 d $\sim$ 14 d increase; (2) After 10 d $\sim$ 14 d of plasma exchange treatment, AST, ALT decreased, ALB, CHE increased, PTA increased ($P < 0.05$); (3) After 10 d $\sim$ 14 d of comprehensive medical treatment, AST, ALT, GGT decreased, PTA increased ($P < 0.05$); (4) In the treatment group and control group, there was no significant difference in length of stay, and in hospital costs, the treatment group were significantly higher the the others ($P < 0.05$); (5) By the formal After treatment, the prognosis of patients with no significant difference ($P > 0.05$); wishing to effect continuous improvement in the prognosis of patients with liver failure required a short interval continuity of treatment.

Topic 1: Acute on Chronic Liver Failure

No: 1369

Intrahepatic cholestasis in a patient with sickle cell anemia a case report

Talat Ayyildiz[1], Ahmet Tarik Eminler[2], Unal Akcali[3], Saduman Balaban Adim[4], Selim Gurel[2], Macit Gulten[2], Murat Kiyici[2], Kader Irak[2], Enver Dolar[2], Selim Giray Nak[2]

Ondokuz Mayis University Gastroenterology Samsun-Turkey[1], Uludag University Gastroenterology Bursa-Turkey[2], Uludag University Internal Medicine Bursa-Turkey[3], Uludag University Pathology Bursa-Turkey[4]

Objective: Sickle Cell Anemia (SCA) is a disorder that occurs when there is a point mutation in the beta chain of hemoglobin which results in glutamic acid being substituted by valine at position 6. In this case report, we will discuss a rare form of SCA with manifestations of intrahepatic cholestasis.
Case: A 50-year-old male patient was hospitalized with complaints of joint pain in arms and legs and jaundice. He underwent splenectomy after experiencing weakness and splenomegaly in 1982. He was then diagnosed with SCA and thalassemia minor. In July 2010 he experienced yellowing of his eyes and skin. Laboratory workup showed: HbS 39.9 %. Abdominal ultrasonography showed intrahepatic bile ducts were minimally dilated and gallbladder was larger than normal. Extrahepatic bile ducts had normal width.

Other pathologies were ruled out by relevant investigations. Deltacortil therapy was initiated. This therapy did not provide any beneficial effects on clinical picture and the patient was given outpatient supportive treatment. He died 1.5 months after discharge.
Conclusion: Sickle cell intrahepatic cholestasis is often fatal. It involves hepatic ischemia and widespread sickling within hepatic sinusoids. At presentation, lower right quadrant pain, nausea-vomiting, fever, enlarged liver and leukocytosis are present and remarkable jaundice develops afterwards. With considerably high WBC count and bilirubin and LDH values, the case presented here stands out among the other few cases reported in literature. Limited therapeutic options account for the increased risk of mortality associated with this form of the disease.

Topic 1: Acute on Chronic Liver Failure

No: 2225

Protective effects of nicotine against acetaminophen induced hepatotoxicity

Surim Park[1], Jong Won Kim[1], Cae Woong Lim[1], Bumseok Kim[1]

Biosafety Research Institute and Laboratory of Pathology, College of Veterinary Medicine (bk21 Plus Program) Chonbuk National University Jeonju-Korea, South[1]

Aim: Acetaminophen (APAP) is a widely used analgesic and antipyretic drug, when taken at therapeutic doses. However an acute or cumulative overdose of APAP can cause severe liver failure. The mechanism of cell death is initiated by formation of a reactive metabolite, N-acetyl-p-benzoquinone imine (NAPQI), which binds to mitochondrial proteins and promotes mitochondrial dysfunction and apoptosis. Nicotine, a major constituent of tobacco smoke, has been shown to exert anti-inflammatory effects on different cell types and to be beneficial in disorders where inflammation-related mechanisms are involved such as ulcerative colitis and obesity. Furthermore, nicotine has also been shown hepatoprotective effects against liver ischemia/reperfusion injury. In the present study, we investigated the effect of nicotine on APAP induced hepatic toxicity in mice, and elucidated underlying mechanisms.
Methods: Male BALB/C mice (20 g body weight) were intraperitoneally (i.p.) injected with 300 mg/kg of APAP. Thirty minutes after

APAP administration, the animals were treated intraperitoneally with nicotine (1 mg/kg). Two, 4, 8, and 24 h after APAP treatment, mice were sacrificed and blood and liver samples were collected for evaluation of histopathologic changes and hepatotoxicity related metabolism and mechanism.
Results: Nicotine significantly reduced serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels and histopathologic damage in APAP-induced liver injury. Analysis of cell viability by the MTT assay revealed that nicotine directly protects APAP-induced cytotoxicity in hepatocyte. Administration of nicotine alleviated acetaminophen induced hepatic NAPQI protein, APAP-protein adducts formation, and hepatic glutathione (GSH) depletion, demonstrating that reactive metabolite generation was diminished. Furthermore, Nicotine decreased TUNEL-positive apoptosis cells induced by APAP, which was mediated by decreased expression of apoptotic-related protein bax and increased expression of anti-apoptosis related protein bcl2.
Conclusion: These data demonstrated that nicotine has hepatoprotective activity against APAP-induced liver injury by preventing formation of a reactive metabolite NAPQI and apoptosis via increased bcl-2 and decreased bax protein expression.

Topic 1: Acute on Chronic Liver Failure

No: 1386

Previous acute decompensation within one year is associated with higher post 28 day mortality in patients with acute on chronic liver failure

Hee Yeon Kim[1], Tae Yeob Kim[2], Chang Wook Kim[1], Do Seon Song[1], Dong Hyun Sinn[3], Eileen L Yoon[4], Young Kul Jung[5], Heon Ju Lee[6], Young Seok Kim[7], Sang Gyune Kim[7], Ki Tae Suk[8], Dong Joon Kim[8]

College of Medicine, The Catholic University of Korea Internal Medicine Seoul-Korea, South[1], Hanyang University College of Medicine Internal Medicine Seoul-Korea, South[2], Samsung Medical Center Internal Medicine Seoul-Korea, South[3], Inje University Sanggye Paik Hospital Internal Medicine Seoul-Korea, South[4], Korea University College of Medicine Internal Medicine Seoul-Korea, South[5], Yeungnam University College of Medicine Internal Medicine Seoul-Korea, South[6], Soonchunhyang University College of Medicine Internal Medicine Seoul-Korea, South[7], Hallym University College of Medicine Internal Medicine Seoul-Korea, South[8]

Introduction: The aim of the study was to investigate the prognosis of acute on chronic liver failure (ACLF) patients according to the presence of previous decompensation (PD) or the time interval of PD.
Materials and methods: We collected data from 1330 consecutive hospitalized patients with cirrhosis and acute decompensation from January 2013 to December 2013 from 21 academic hospitals in Korea. The study population included 637 patients without PD (type 1), 352 with PD more than one year ago (type 2), and 341 with PD within one year (type 3). Multinominal logistic regression analysis and Kaplan–Meier method with log-rank test were used.
Results: A total of 269 patients (20.2 %) had ACLF either at enrollment or during the 28-day follow-up period; 127 (19.9 %) had ACLF in type 1 patients, 64 (18.2 %) in type 2, and 78 (22.9 %) in type 3. The 28-day, 3-month and 1-year mortality rates were 34, 49, and 50 % in type 1, 27, 35, and 61 % in type 2, and 42, 67, and 80 % in type 3 ACLF patients, respectively. On multinominal logistic regression analysis, 28-day mortality was not associated with type of PD ($P = 0.098$). However, type 3 ACLF was significantly associated with post-28-day mortality (OR 4.1, 95 % CI 1.8-9.1; $P = 0.001$).
Conclusions: The prevalence of ACLF development in cirrhotic patients with acute decompensation was similar irrespective of the presence of PD or the time interval of PD. ACLF patients with different types showed comparable 28-day mortality, but type 3 ACLF patients had highest post-28-day mortality.

Topic 1: Acute on Chronic Liver Failure

No: 1657

Precipitating factor of hepatic encephalopathy and faecal calprotectin concentration

Fauzi Yusuf[1], Azzaki Abubakar[1], Cut Srijuita[1]

Faculty of Medicine, Syiah Kuala University Internal Medicine Banda Aceh-Indonesia[1]

Aim: This study aimed to investigate correlation between precipitating factors of hepatic encephalopathy (HE) and fecal calprotectin (FC) concentration in cirrhotic patients.
Method: This cross-sectional study was conducted in the Zainoel Abidin General Hospital (RSUZA) Total of 38 subjects were consecutively selected from cirrhotic patients visiting our hospital during the period of January–May 2014. Subjects were grouped into two, being group 1 was of subjects with single precipitating factor (either constipation, anemia or electrolyte disturbance) and group 2 was of subjects with two precipitating factors (e.g. constipation and electrolyte disturbance). Patients with diarrhea or gastrointestinal bleeding and patients receiving antiplatelets, antibiotics or proton pump inhibitors (PPI) were excluded. Demographic data, endoscopy and abdominal sonogram findings were recorded. HE was graded based on West Haven criteria along with the result of Number Connection Test (NCT). FC concentration was measured in subjects stools samples collected within 24 h. Hypothesis testing was performed using Fisher's exact test.
Result: The subjects mean age was 52,39 ± 9,18 years and 78,9 % of them were male. The most common etiology of cirrhosis in the study subjects was Hepatitis B Virus (68 %). FC concentration was significantly elevated in subjects with constipation, anemia or electrolyte disturbance ($P < 0.001$).
Conclusion: This study showed that precipitating factors of HE significantly increased FC concentration in patient with liver cirrhosis.

Topic 1: Acute on Chronic Liver Failure

No: 1152

'Broken heart' in acute on chronic liver failure

Ennaliza Salazar[1], Chee Kiat Tan[1], George-boon Bee Goh[1]

Singapore General Hospital Gastroenterology and Hepatology Singapore-Singapore[1]

Takotsubo cardiomyopathy usually occurs as a result of catecholamine release causing myocardial 'stunning' during physical or emotional stress. Typically, coronary angiogram shows normal or minor coronary artery disease and echocardiogram showing apical ballooning with basal wall hyperkinesia. It usually has good cardiac recovery function within days to weeks. Here we report first case of takotsubo cardiomyopathy in a patient with acute on chronic liver failure.

Topic 1: Acute on Chronic Liver Failure

No: 2237

Acute kidney injury in hepatitis B related acute on chronic liver failure without preexisting liver cirrhosis

Zuxiong Huang[1], Chun Lin[1], Jiankai Fang[1], Ning Wang[1], Rui Zhou[1], Chen Pan[1]

Affiliated Infectious Disease Hospital of Fujian Medical University Hepatology Fuzhou-China[1]

Background and aim: Acute kidney injury (AKI) proposed by acute kidney injury network was investigated widely in decompensated liver cirrhosis. AKI was frequently progressive and independently associated with mortality of these patients. However, in Asia–Pacific region, the majority of acute on chronic liver failure (ACLF) is caused by acute severe exacerbation of chronic hepatitis B without preexisting cirrhosis. It is not clear whether it is at similar risk as the patients with underlying cirrhosis.
Methods: We performed a retrospective cohort analysis of hepatitis B-related ACLF patients in Fujian Medical University Affiliate Infectious Disease Hospital from January 2004 through December 2011, and evaluated the occurrence of AKI after admission and its relation with 3-month mortality of ACLF patients.
Results: Total 439 patients of hepatitis B-related ACLF without preexisting cirrhosis were enrolled. At the end of the 3-month follow-up period, 127 patients (28.9 %) died. The median MELD was 26 (11–50) at the time of enrollment, and the incidence of complications in patients who had suffered from was as follows: spontaneous bacterial peritonitis (72.9 %), hyponatremia (53.1 %), hepatic encephalopathy (35.8 %), pulmonary infection (20.5 %), hypokalemia (13 %) and variceal bleeding (9.3 %). Among them 158 patients (36.0 %) developed AKI during hospitalization. ACLF patients with AKI had higher serum creatinine (sCr), bilirubin, INR, MELD score and more complications compared to those patients without AKI ($P < 0.01$), which stated more severe liver failure. Seventy-two (46.5 %) of 158 patients who had developed AKI during hospitalization died compared with only 55 (19.4 %) of 281 patients without AKI at the end of the 3-month follow-up period ($P < 0.001$). Occurrence of AKI and its stage affect 3-months mortality of ACLF patients ($P < 0.001$), and a greater percentage of AKI was found in non-survivors than survivors (56.7 % vs 27.6 %, $P < 0.001$). The cumulative survival of patient with no AKI, AKI stage 1, 2 and 3 was 77.84, 65.46, 41.38 and 27.03 %, respectively. Meanwhile, we adopted a combination of AKIN criteria and sCr $\geq$ 1.5 mg/dL to predict AKIN stage progression. Eighteen patients had progression of AKI during hospital stay: 8 patients with stage 1 progressed to stage 2, 7 patients with stage 1 progressed to stage 3, and 3 patients with stage 2 progressed to stage 3. Patients with AKI stage 1 and sCr $\geq$ 1.5 mg/dL or AKI stage 2 showed a higher possibility of progression to a higher stage compared to patients with AKI stage 1 and sCr $<$ 1.5 mg/dL ($P = 0.040$, $P = 0.034$).
Conclusions: In our study, we observed AKI development was common and associated with increased 3-months mortality in hepatitis B-related ACLF patients without preexisting cirrhosis. Higher initial AKI stage and sCr levels showed a more tendency for AKI progression. The higher AKI stage predicted a worse prognosis. Our findings support the importance of early identification and timely therapy of AKI in hepatitis B-related ACLF patients.

Topic 1: Acute on Chronic Liver Failure

No: 1413

Risk factors for acute liver failure in chronic hepatitis B patients

Yu-jiao Zhang[1], Wen Zheng[2], Bao-rong Chi[1], Jian Sun[2]

The First Hospital of Jilin University Department of Gastroenterology and Hepatology Changchun-China[1], The First Hospital of Jilin University Department of Cardiology Changchun-China[2]

Objective: Acute on chronic liver failure (ACLF) is one of the main causes of death in chronic hepatitis B (CHB) patients. The study was to investigate the risk factors related to the incidence of ACLF in CHB patients.
Methods: A retrospective, case–control study was conducted to included all inpatients with CHB in our department through 2010 to 2013. Multiple logistic regression was performed to identify risk factors associated with ACLF.
Results: Among 1,668 inpatients with CHB, 116 (7.0 %) patients were diagnosed as ACLF. The average age in ACLF group and CHB group were 43.2 ± 12.4 and 45.3 ± 13.5 ($P = 0.58$), respectively. There was higher proportion of male in ACLF group compared with CHB group (64.2 % vs. 45.8 %, $P < 0.01$). Multivariate logistic regression analysis showed that liver-injury drugs usage (odds ratio (OR) = 7.215, 95 % confidence interval (CI): 3.681-17.532), overlapping virus infection (OR = 5.471, 95 % CI: 3.231-13.201), family history of CHB (OR = 4.282, 95 % CI 3.629-7.524), alcohol drinking (OR = 4.127, 95 % CI 1.894-8.654), recent infection (OR = 3.965, 95 % CI 1.857-6.721), mental stress and physical fatigue (OR = 3.017, 95 % CI 1.836-4.571), high HBV load (OR = 2.524, 95 % CI 2.307-3.721) were among the strongest risk factors for the incidence of ACLF, except the history of antiviral therapy (OR = 0.163, 95 % CI 0.085-0.417). From a receiver-operator characteristic plot (mean area under curve of 0.712), the predictive accuracy of the final logistic regression model is considered modest.
Conclusion: These results highlight the importance of the standard management of liver-injury drugs, healthy lifestyle, appropriate mental health counseling and strengthened anti-viral treatment for CHB patients in order to reduce the incidence of ACLF.

Topic 2: Alcoholic Liver Disease

No: 1305

Sarcopenia as a prognostic factor in patients with severe alcoholic hepatitis

Do Seon Song[1], U Im Chang[1], Sang Wook Choi[1], Se Hyun Cho[1], Joon Yeol Han[1], Jin Mo Yang[1]

The Catholic University of Korea Internal Medicine Seoul-Korea, South[1]

Background: Sarcopenia has emerged as an independent predictor of clinical outcomes in a variety of clinical conditions. The aim of this study was to examine the association between the sarcopenia and the early mortality (90-days) or overall survival in the patients with severe alcoholic hepatitis (SAH).

Methods: Eighty-one consecutive patients with SAH (Maddrey's discriminant function (DF) $\geq$ 32) were retrospectively analyzed. Skeletal muscle cross sectional area was measured on a computed tomography (CT) image at the L3 level.
Results: Sixty-six patients were male (81.5 %), and mean age was 49.6 $\pm$ 9.8 years with median follow-up of 7.4 months. Overall 90-day mortality was 30.9 % and 55 patients (67.9 %) had sarcopenia. By univariate logistic regression analysis, presence of infection, hepatic encephalopathy (HE), spleen size, INR, serum creatinine, and leukocyte count were potential risk factors of short-term mortality ($P < 0.1$). However, sarcopenia was not associated with 90-day mortality ($P = 0.125$). By multivariate analysis, INR and HE were independently associated with 90-days mortality. Sarcopenia tended to have association with HE ($P = 0.082$) at the time of admission. Sarcopenic group had shorter overall survival time (47.7 vs. 29.3 months, $P = 0.072$) than non-sarcopenic group, although not statistically significant. GAHS was the most accurate predictive factor for early mortality among DF, ABIC (Age, Bilirubin, INR, Creatinine), Child-Pugh, and Model for end-stage liver disease score (AUROC—0.785).
Conclusions: Sarcopenia is frequent complication in patients with SAH. Sarcopenia is not associated with early mortality. However, sarcopenia is likely to be associated with overall survival and HE, which is important prognostic factor for short term mortality.

Topic 2: Alcoholic Liver Disease

No: 1921

Efficacy of supplementation with vitamin B6 vitamin B12 and folate in patients with alcoholic liver disease

Soon Young Ko[1], Jeong Han Kim[1], Won Hyeok Choe[1], So Young Kwon[1], Hyun Soo Ahn[2], Kwang Pyo Kim[2], Hee Bok Chae[3]

Konkuk University School of Medicine Internal Medicine Seoul-Korea, South[1], Kyung Hee University Applied Chemistry Yongin-Korea, South[2], Chungbuk National University Internal Medicine Cheongju-Korea, South[3]

Background and aims: Although three essential B-vitamins (vitamin B6, vitamin B12, and folate) play a critical role in the methionine metabolic cycle related to the pathogenesis of experimental alcoholic liver disease (ALD), the effectiveness of B-vitamin supplementation is not known in clinical situation. The aims of this study were to identify changes between serum levels of methionine metabolites after 4 weeks of B-vitamin supplementation and determine the relationship between aberrant methionine metabolic cycle and B-vitamin supplementation in patients with ALD.
Methods: At baseline, serum levels of liver function biochemical parameters, B-vitamins (vitamin B6, vitamin B12, and folate), and methionine metabolites (homocysteine, S-adenosylhomocysteine) were measured in 20 ALD patients and 20 healthy subjects. Among these 20 ALD patients, 10 patients (Group A) received 4-week B-vitamin supplementation, which included vitamin B6, vitamin B12, and folate. The other 10 patients (Group B) received 4-week B-vitamin supplementation without folate. Methionine metabolite levels, homocysteine and S-adenosylhomocysteine, were measured using stable isotope dilution liquid mass spectrometry.
Results: Two groups of ALD patients showed an overall improvement in liver function biochemical parameters and B-vitamin levels after 4 weeks of B-vitamin supplementation. Serum homocysteine and S- adenosylhomocysteine levels tended to show reduction in the Group A patients after 4 weeks of B-vitamin supplementation, which included folate ($P = 0.209$ for HCY and $P = 0.038$ for SAH).
Conclusions: Short-term abstinence and B-vitamin supplementation including folate may help improve nutritional status and methionine metabolite levels related to the aberrant methionine metabolic pathway. Efficacy of B-vitamin supplementation may require the regimen including folate supplementation.

Topic 2: Alcoholic Liver Disease

No: 1625

The prevalence of osteoporosis in alcoholic liver cirrhotic patients a preliminary data of multicenter study in Gangwon province South Korea

Daehee Choi[1], Taesuk Kim[1], Jinmyoung Park[1], Moonyoung Kim[2], Soonkoo Baik[2], Kitae Suk[3], Dongjoon Kim[3], Youngdon Kim[4], Gabjin Cheon[4]

Kangwon National University School of Medicine Internal Medicine Chuncheon-Korea, South[1], Yonsei University Wonju College of Medicine Internal Medicine Wonju-Korea, South[2], Hallym University College of Medicine Internal Medicine Chuncheon-Korea, South[3], Gangneung Asan Hospital, University of Ulsan College of Medicine Internal Medicine Gangneung-Korea, South[4]

Background: Although osteoporosis in alcoholic liver cirrhosis(ALC) is clinically important because of a resulting morbidity such as spinal fractures, its real prevalence in Asians remains unknown. The aim of this study is to describe a prevalence of osteoporosis and osteopenia in ALC patients assessed by WHO's criteria, and its affecting factors.
Method: We present the preliminary results of our ongoing prospective multicenter study. During July 2013, to September 2014, Seventy-five ALC patients who admitted at four centers in Gangwon-province were consecutively recruited. Alcohol consumption habits, known risk factors of osteoporosis development through lifestyle questionnaires, laboratory findings, and hormone levels were also conducted.
Results: The Crude prevalence of osteoporosis in ALC patient (29-82 years old) was 21.9 % for men and 12.5 % for women. The data compared with 2008-10 Korean National Health and Nutrition Examination Survey (KNHANES). Standardized prevalence of osteoporosis for persons aged 50 years or more at lumbar spine, femoral neck and total hip was 21.7, 8.6 and 4.3 % in men. The prevalence of osteoporosis in ALC patient (male, > 50 years) higher than that of KNHANES. (21.7 % vs. 7.8 %) Osteoporosis in ALC patient have low BMI (20.2 $\pm$ 2.64 kg/m2 vs. 23.3 $\pm$ 3.77 kg/m2, $P = 0.025$) and high iPTH (50.4 $\pm$ 33.4 pg/mL vs. 32.2 $\pm$ 16.2 pg/mL, $P = 0.022$).
Conclusion: The present study provides the disease-specific reference BMD values at various sites, age & sex-standardized prevalence of osteoporosis in ALC patient in Korea. The absolute BMD of ALC patient was higher to Korean people. We expect to reval a real prevalence and affecting factors of osteoporosis in ALC patients soon.

Topic 2: Alcoholic Liver Disease

No: 1479

Hepatic inflammatory response to ethanol the effect of hepatocytes and macrophages co culture

Veronica Marin[1], Pablo J. Giraudi[1], Claudio Tiribelli[1], Natalia Rosso[1]

Fondazione Italiana Fegato Centro Studi Fegato Trieste-Italy[1]

Macrophage migration inhibitory factor (MIF) is involved in chronic inflammatory disorders. Few information is available about MIF regulation between hepatocytes and macrophages in response to ethanol (EtOH). The aim of this work is to elucidate this aspect.

Co-culture (transwell system) of hepatocytes (HuH7) and differentiated macrophages (THP1 + 100nM PMA) were exposed for 24 h to 25 mM-EtOH; monocultures of each cell type were used as controls (CTRL). Was assessed the gene expression of MIF and its receptor CD74 as well as TNF-α. Moreover the release of MIF was quantified by ELISA.

Data reported in table 1 show that, in hepatocytes monoculture, EtOH induces the up-regulation of TNF-alpha. Furthermore we found that, in terms of gene expression, MIF follows the same trend of increase, even if the amount of released MIF was unchanged. Expression of CD74 was barely detectable in hepatocytes. Conversely, macrophages monocultures exposed to 25 mM-EtOH did not show any changes on the parameters under study.

Interestingly, we observed that in the co-culture system hepatocytes presented a dramatic increase in TNF-alpha gene expression, whereas the opposite happened in macrophages. Moreover, in co-culture both hepatocytes and macrophages increased MIF release, with unchanged gene expression, suggesting a synergic inflammatory response to EtOH. Furthermore, we observed a significant up-regulation of CD74 in co-cultured hepatocytes, confirming that cells respond differently when macrophages are in the system.

In conclusion, EtOH deleterious effect could have hepatocytes as target. Injured hepatocytes may be able to modulate macrophages response, which (once activated) contribute to perpetrate the inflammatory state, increasing MIF production.

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Topic 2: Alcoholic Liver Disease

No: 1618

Predictive factors associated with development and the clinical course of alcohol withdrawal in patients with alcoholic liver disease

Daehee Choi[1], Taesuk Kim[1], Sungchul Park[1], Jinmyoung Park[1], Changdong Kang[1], Sungjoon Lee[1]

Kangwon National University Internal Medicine Chuncheon-Korea, South[1]

Background: Alcohol related diseases including alcohol withdrawal(AW) are still big social and medical problems. However, the studies about clinical factors associated with development and prognosis of AW are lacking. Therefore, the aim of this study was to evaluate the clinical factors associated with AW and hospital courses of AW in patients who were admitted to a general hospital with alcoholic liver disease (ALD).
Method: Our retrospective case–control study was conducted among ALD patients, who were consecutive admitted in a general hospital between January 2008 and October 2013. We divided two groups, AW and non-AW, and analyzed alcohol consumption habits, comorbidities, laboratory findings and hospital courses by medical record.
Results: We analyzed 263 cases out of 534 admitted cases. In AW group, 103 cases were included and median age was 49.5 years old. Presence of previous alcohol withdrawal history ($P = 0.014$), high heart rate (96.5 ± 20.0 bpm vs. 91.4 ± 16.0 bpm, $P = 0.030$), high glucose level (185.1 ± 115.46 mg/dL vs. 144.0 ± 66.9 mg/dL, $P = 0.010$), low pCO2 level (30.9 ± 7.8 mmHg vs. 33.8 ± 6.9 mmHg, 0.029) and high CRP level (2.0 ± 4.3 mg/dL vs. 1.0 ± 0.3 mg/dL, $P = 0.029$) were statistically significant variables between two groups. Multivariate logistic regression analysis demonstrated that heart rate, CRP, and pCO2 were independent risk factors for AW (all $P < 0.050$). In addition, in AW group, more patients needed ICU care and had long hospital stay (23.1 ± 17.7 days vs. 19.2 ± 14.0 days, $P = 0.048$).
Conclusion: Our study shows several clinical data that strongly predict AW development and long hospitalization course of AW patients. Therefore, proper evaluation and treatment is required as soon as they are admitted.

Topic 2: Alcoholic Liver Disease

No: 1859

QT interval prolongation and QRS voltage reduction in patients with liver cirrhosis

Halina Cichoż-lach[1], Agnieszka Kowalik[1], Michał Tomaszewski[2], Emilia Lis[1], Tomasz Lach[3], andrzej Tomaszewski[2], Krzysztof Celiński[1]

Medical University of Lublin Department of Gastroenterology Lublin-Poland[1], Medical University of Lublin Department of Cardiology Lublin-Poland[2], Medical University of Lublin Student of The Second Faculty of Medical University of Lublin Lublin-Poland[3]

Background: Liver cirrhosis is associated with functional abnormalities of cardiovascular system with co-existing ECG abnormalities.
Objectives: The aim was to analyse ECG changes in patients with cirrhosis, to evaluate whether alcoholic aetiology of cirrhosis and ascites impact on ECG changes.
Methods: The study encompassed 81 patients with previously untreated alcoholic cirrhosis (64 patients with ascites- class B and C according to the Child-Pugh classification, and 17 without ascites- categorised as class A), 41 patients with previously untreated HCV cirrhosis (30 patients with ascites - class B and C and 11 without ascites- class A), 42 with alcoholic steatohepatitis and 46 with alcoholic steatosis. Controls consisted of 32 healthy volunteers. The 12-lead ECG recording was performed and selected parameters were measured.
Results: Statistically significantly longer QT and QTc intervals and lower QRS voltage were found in patients with alcoholic and HCV cirrhosis compared to controls. Statistically significant lower QRS voltage was found in subjects with ascites than without ascites. Removal of ascites statistically significantly increased QRS voltage.
Conclusion: In cirrhosis, irrespective of aetiology, ECG changes involved prolonged QT and QTc intervals and reduced QRS voltage. Prolonged QT and QTc intervals were not related to the severity of cirrhosis and the presence of ascites. However, low QRS voltage was associated with the presence of ascites. Removal of ascites reverses low QRS voltage.

Topic 3: Autoimmune Liver Diseases

No: 1564

Epidemiological indicators and clinical outcomes in patients with autoimmune hepatitis in Iran

Mohammad Hossein Somi[1], Morteza Ghojazadeh[2], Mohammad Reza Abdollahi[3], Mehran Rahimi[3], Ahmad Reza Badali[3]

Liver and Gastrointestinal Disease Research Center Internal Medicine Tabriz-Iran[1], Liver and Gastrointestinal Disease Research Center Physiology Tabriz-Iran[2], Liver and Gastrointestinal Disease Research Center Medical Faculty Tabriz-Iran[3]

Aim: Autoimmune hepatitis (AIH) is a chronic liver disease which if not diagnosed quickly and cured properly, in most cases leads to cirrhosis, liver failure and death. The goal of this study which is based on 131 records of AIH patients who referred to Imam Reza hospital and other specialist clinics in Tabriz is to survey treatment outcomes.
Methods: Records of patients were analysed retrospectively between the years 2012-2014. Scores higher than 15 were considered as definitive diagnosis. Information was collected and used for statistical analysis of demographic information, medical history, physical examination, liver function check, electrophoresis, serology tests, pathology and response to treatment.
Results: The mean age was 36.8 ± 8. The most common clinical symptoms were: fatigue, jaundice and menstrual disorder (in women). Among auto antibodies, ASMA in 41.8 % and ANA in 35 % of cases were positive. In non-cirrhotic patients, average grade was 5.5 and average stage was 2. The most used regimen was Prednisone plus Imuran. Therapeutic response was considered based on clinical symptoms, AST, gamma globulin and histologic activity. The average time needed for obtaining the complete response was 10 months varying 12 to 24 months. Beginning of response to treatment and time for remission in cirrhotic patients was longer than non-cirrhotic AIH patients.
Conclusion: According to other epidemiologic studies, it seems that patients in our country from the aspect of age, sex, clinical symptoms and response to treatment are similar to other countries.

Topic 3: Autoimmune Liver Diseases

No: 1198

Autoimmune hepatitis with azathioprine intolerance successfully treated with mycophenolate mofetil a case report

Mehmet Asil[1], Sami Cifci[1], Huseyin Ataseven[1], Murat Biyik[2], Hakki Polat[1], Ali Demir[1]

Necmettin Erbakan University Faculty of Medicine Department of Gastroenterology Konya-Turkey[1], Adiyaman Education and Research Hospital Department of Gastroenterology Adiyaman-Turkey[2]

Introduction: Azathioprine is frequently used in the treatment of autoimmune hepatitis. He we present a patient with autoimmune hepatitis intolerant to azathioprine successfully treated with mycophenolate mofetil.
Case report: A 59 years old female patient was referred to our clinic with the complaints of dizziness and elevated liver enzymes lasting for 3 months. She had diabetes mellitus for 5 years. Laboratory investigations for possible causes of chronic hepatitis were negative except positive test for antinuclear antibody. Histological findings in liver biopsy were compatible with auto immune hepatitis with moderate interface hepatitis and fibrosis. Prednisone 30 mg/day and azathioprine 50 mg/day was started. Patient experienced severe myalgia, nausea and vomiting following administration of azathioprine. The drug is discontinued for a few days but reinstitution of the drug resulted in recurrence of symptoms. Azathioprine was replaced with 6-mercaptopurine but intolerance symptoms developed again. After remission induction with prednisolone alone, mycophenolate mofetil 2x1 g was started as maintenance therapy due to problematic glycemic control and possible risk of long term corticotherapy. She had been on mycophenolate mofetil monotherapy for 1 year and she is still in good health with clinic and biochemical remission.
Discussion: Azathioprine intolerance is not so rare usually causing discontinuation of the drug. Here we present a patient with autoimmune hepatitis intolerant to azathioprine successfully treated with mycophenolate mofetil. There are also studies in the literature where mycophenolate mofetil was found to be effective in autoimmune hepatitis so it can be used as maintenance therapy in patients with azathioprine intolerance.

Topic 3: Autoimmune Liver Diseases

No: 1643

Coexistence of primary biliary cirrhosis with celiac disease case report

Aylin Demirezer Bolat[1], Öykü Tayfur Yürekli[1], Fatma Ebru Akın[1], Mustafa Tahtacı[1], Murat Başaran[2], Hüseyin Köseoğlu[2], Eyüp Selvi[1], Şemnur Büyükaşık[1], Osman Ersoy[2]

Atatürk Education and Research Hospital Gastroenterology Ankara-Turkey[1], Yıldırım Beyazıt University Gastroenterology Ankara-Turkey[2]

Celiac Disease (CD) develops in reaction to diatary gliadine in genetically predisposed patients Primary Biliary Cirrhosis (PBC) is an autoimmune liver disorder with progressive destruction of intrahepatic bile ducts. Both of them are regarded as autoimmune disorders because of predominance in females, frequent autoimmune comorbidities and immune response against autoantigens. Herein we present a PBC patient diagnosed with CD during variceal screening.
Case: 51-year-old male admitted with abdominal pain and weight loss during the last year. Liver enzymes were elevated with marked ALP and GGT increments. Viral serology and ANA were negative, AMA was positive. Abdominal CT showed hepatosplenomegaly and multiple periportal lymphadenopathies. Liver biopsy revealed ill–defined granulomas centered on bile ducts. Lymphocytes, histiocytes and plasma cells were present in the portal tracts. Gastroduodenoscopy revealed scalloping of duodenal folds and mosaic like pattern between pili. Antibodies against tissue transglutaminase (tTg) and Ig A endomysial antibody were positive. Biopsy was consistent with CD modified Marsh Grade 3a.
Discussion: An aberrant intestinal T lymphocyte recruitment to the liver is important for the development of T–cell-mediated hepatic disorders associated with gut inflammation. One of the best examples for this is the frequent coexistence of CD and PBC. Since early diagnosis of both PBC and CD is advantageous, the screening for PBC by AMA in CD patients and that for CD by tTGA and EmA in PBC subjects is suggested.

Topic 3: Autoimmune Liver Diseases

No: 1232

Liver stiffness measurement for prediction of portal hypertension in children with autoimmune hepatitis

Malgorzata Wozniak[1], Jakub Kmiotek[1], Piotr Socha[1], Maciej Dadalski[1], Marek Woynarowski[1]

Children's Memorial Health Institute, Department of Gastroenterology and Hepatology Warsaw-Poland[1]

Objectives: Transient elastography is easily applicable to children with Autoimmune Hepatitis (AIH). Liver stiffness (LS) measurement strongly correlates to the degree of fibrosis on liver biopsy, liver function tests and inflammation in AIH patients. The aim of this study was to evaluate the role of LSM as a predictor of portal hypertension in children with AIH.
Methods: 30 AIH children (M-8; F-22) aged 7-17 years (mean ± SD: 13.7 ± 2.6) were included into the study. LS (E-med) was measured in kPa by FibroScan® (FS). The diagnosis of portal hypertension was based on endoscopy examination showing oesophageal varices, gastric varices or portal gastropathy. Mann–Whitney test was used to compare the results and ROC analysis was done to detect the optimal cut off point for prediction of the portal hypertension.
Results: Portal hypertension was found in 6 (20 %) of subjects (oesophageal varices-6, gastric varices-3, portal gastropathy-4). Liver stiffness expressed by E-med in children with portal hypertension was significantly higher than in those without portal hypertension (44.6; 35.3; 65.2 vs. 5; 4.2; 8.8 [median; q1; q3] $P < 0.001$). ROC analysis showed AUC = 0.98 and the E-med optimal cut off point for detection of portal hypertension was greater than or equal 16.6 kPa with sensitivity (95 % CI) = 1 (0.54 to 1 [97.5 % one-sided CI]) and specificity (95 % CI) = 0.92 (0.73 to 0.99).
Conclusion: We demonstrated that LS measurement may be used as a predictor factor for portal hypertension. AIH children with E-med ≤ 16,5 kPa are unlikely to have portal hypertension.

Topic 3: Autoimmune Liver Diseases

No: 1251

Low serum vitamin d levels are associated with severe histological features and poor response to therapy in patients with autoimmune hepatitis

Cumali Efe[1], Taylan Kav[12], Ersan Ozaslan[12], Tugrul Purnak[12], Mustafa Cengiz[12], Seren Ozenirler[12], Cisel Aydın[12], Narin Nasıroğlu-imga[12], Turan Turhan[12], Daniel S. Smyk[12], Murat Torgutalp[12], Dimitrios P. Bogdanos[12]

Hacettepe Gastroenterology Ankara-Turkey[1]

Background and aim: 25-hydroxyvitamin D (25[OH]D) has an important role in fibrosis progression and inflammatory response in patients with various etiologies of chronic liver disease. However, its influence on autoimmune hepatitis (AIH) has not been investigated.
Materials and methods: Serum 25(OH)D levels were quantified in 68 therapy naïve AIH patients and 34 healthy controls.
Results: Mean serum 25(OH)D levels were significantly lower in AIH compared to healthy controls (16.8 ± 9.2 vs. 35.7 ± 13.6, $P < 0.0001$). According liver histology, mean serum 25(OH)D levels were significantly different in patients with moderate interface hepatitis compared to those with mild or severe interface hepatitis (Figure 1a). Similarly, serum 25(OH) D levels were significantly decreased in each increased step of fibrosis scores (Figure 1b). Low levels of 25(OH)D (< 30 μg/L) were independently associated with advance fibrosis and severe interface hepatitis in AIH patients ($P = 0.014$; odds ratio [OR] = 0.12, 95 % confidence interval [CI], 0.02-0.65 and $P = 0.020$, OR = 0.17, 95 % CI, 0.04-0.76, respectively, Table-1). Severe 25(OH)D deficiency (< 10 μg/L) was also independently associated with interface hepatitis and fibrosis scores in a multiple regression analysis ($P = 0.005$; OR = 0.12, 95 % CI, 0.03-0.53 and $P = 0.022$; OR = 0.15, 95 % CI, 0.03-0.75, respectively, Table-1). Mean serum 25(OH)D levels were lower in non-responders compared to responders (9.2 ± 4.8 v.s 17.1 ± 9.4, $P = 0.015$) and 25(OH)D deficiency was more commonly observed in non-responders than the responders (80 % v.s 43 %, $P = 0.036$).
Conclusions: Low 25(OH)D levels are associated with advance fibrosis and severe inflammation in AIH. Our study suggests that vitamin D may be a potential biomarker that predicts response to therapy and histological features in AIH.

Topic 3: Autoimmune Liver Diseases

No: 2024

Autoimmune hepatitis in Singapore high incidence of drug induced cases

Doreen Siew Ching Koay[1], Ennaliza Salazar[1], Chee Kiat Tan[1], Jason Pik Eu Chang[1], Wai Choung Ong[1], Hang Hock Shim[1], Jing Hieng Ngu[1]

Singapore General Hospital Gastroenterology and Hepatology Singapore-Singapore[1]

Background: Autoimmune hepatitis (AIH) is a chronic progressive inflammatory liver disease that can lead to cirrhosis, hepatic failure and death. Information on AIH in Asia remains scarce. We aimed to describe the clinical characteristics of AIH patients in Singapore.
Methods: Consecutive AIH cases diagnosed between 2008 and 2013 in Singapore General Hospital that fulfilled the simplified AIH diagnostic criteria were included. Drug-induced AIH was defined as patients who fulfilled the simplified AIH criteria but also had identifiable drug aetiology. End of follow up was at death, liver transplantation or the end of study (1st November 2014). Kaplan–Meier curves were used to present survival data.
Results: In total 62 AIH patients were included with male to female ratio of 1: 5. Mean and median ages of presentation were 58 and 56 years respectively. ANA, SMA, SLA and LKM were positive in 93.5, 27.6, 1.7 and 0 % respectively. Cumulative 5-year survival was 89 %. Nearly a quarter (24.2 %) had drug-induced AIH and most (88 %) were caused by traditional Chinese medicine (TCM). Interestingly drug-induced AIH patients were less likely to remain on treatment ($P = 0.002$), and had worse 2-year survival (86 % vs 98 %) compared to other AIH patients.
Conclusion: We report a high proportion of drug-induced AIH secondary to TCM in Singapore. They were less likely to require long term treatment, but had a worse early mortality when compared to other AIH patients. It is prudent that careful drug history, including TCM, is taken for AIH patients in Asia.

Topic 3: Autoimmune Liver Diseases

No: 1538

The benefit of liver biopsy in older patients with primary birialy cirrhosis and autoimmune hepatitis

Yuki Haga[1], Tatsuo Kanda[1], Katsuhiro Hagiwara[1], Reina Sasaki[1], Masato Nakamura[1], Xia Jiang[1], Shin Yasui[1], Makoto Arai[1], Shingo Nakamoto[2], Osamu Yokosuka[1]

Chiba University Department of Gastroenterology and Nephrology Chiba-Japan[1], Chiba University Department of Molecular Virology Chiba-Japan[2]

Aim: To investigate the recent liver biopsy findings of autoimmune liver diseases such as primary biliary cirrhosis (PBC) and autoimmune hepatitis (AIH) and the impact of aging and gender on autoimmune liver diseases in an urban area of Japan.
Methods: Total 259 patients (mean age 56.8 years; male 18 %) who underwent percutaneous liver biopsy for PBC or AIH were included and we analyzed their liver biopsy findings according to age and gender.
Results: In all 259 patients, 49 % and 39 % patients were diagnosed as PBC and AIH, respectively. Among PBC patients aged older than or equal to 65 years, Scheuer stage 4 patients was 18 %. The proportion of PBC Scheuer stage 4 patients aged older than or equal to 65 years tended to be higher than that aged younger than 65 years. The proportion of AIH patients with moderate or severe activity (A2 or A3) in males was higher than in females. From the point of view of fibrosis stage or inflammatory activity grade of the liver, the proportion of AIH patients aged older than or equal to 65 years was similar to that aged younger than 65 years. Although we identified 6 cirrhotic patients older than or equal to 65 years with AIH, 3 of them were male.
Conclusion: Clinician should pay attention for the progression of fibrosis and inflammatory activity of the liver in older patients with autoimmune liver diseases. In clinical daily practice, liver biopsy should be considered in older patients with autoimmune liver diseases to obtain accurate their information.

Topic 3: Autoimmune Liver Diseases

No: 1527

Prevalence and incidence of autoimmune hepatitis

Parisa Ramazanilar[1], Nasrin Taghizadieh[1]

Tabriz University of Medical Sciences Liver An Gastro Intestinal Disease Research Center Tabriz-Iran[1]

Background and aim: Autoimmune hepatitis was first diagnosed in 1940s, although it was known as chronic active hepatitis CCAH before. It's clear that less information is available about this type of hepatitis compared with the other types. This can be due to its low prevalence in comparison with hepatitis B&C, however more researches should be done in this field.
Method: We collected data on the prevalence and incidence of autoimmune hepatitis by searching on the internet. Articles and books that had relative information have been studied and analysed.
Results: Prevalence of autoimmune hepatitis (AIH) was reported between 10–17 per 100000 in Europe and it's the cause of 2.6 % of liver transplantation in USA.It can be estimated that (AIH) has higher prevalence in women rather than men. A study in Shahid Beheshti University indicates that out of 46 (AIH) patients,83 % were women. Statistics show that there are 1248 AIH patients in USA and in China 5520 cases have been reported and in IRAN out of 67503205 people 286 have been reported as (AIH) patients.
Conclusion: (AIH) is not a common type of hepatitis but it's essential that further studies must be done to estimate the prevalence of this disease in our country

Topic 3: Autoimmune Liver Diseases

No: 1537

Severe chronic hepatitis related to tetracycline in a 16 year old female with mixed connective tissue disease and autoimmune cholangitis

Xu Li[1], Yang Gao[1], Huifan Ji[1], Xiaolin Guo[1]

The First Hospital of Jilin University Hepatology Changchun-China[1]

Aims: The term "mixed connective tissue disease" (MCTD) concerns a systemic autoimmune disease typified by overlapping features between two or more systemic autoimmune diseases. But the patient who exists both MCTD and autoimmune cholangitis is very rare.
Methods: A 16-year-old female with a medical history significant for MCTD presented complaining of yellow eyes. She had been diagnosed with MCTD in the context of cutaneous lesions, raised ESR, and high elevated anti-nRNP and anti-Sm eight years earlier, and initially treated with oral steroids then stopped without physician order. One month prior to presentation, oral Tetracycline for acne had been started for 2 weeks. Laboratory tests on admission were significant for PT of 19.7 s; TBIL of 402.8 umol/L; AST of 325U/L; ALT of 261U/L; γ-GT of 136U/L; ALP of 345U/L; ESR 64 mm/1 h; total IgG levels were raised at 40.10 g/L, IgA 6.15 g/L, IgM 2.98 g/L; Anti-nRNP and anti-Sm antibodies was +++, viral hepatitis serologies were normal. Liver biopsy was proceeded and the histopathology demonstrated the features of autoimmune cholangitis with a chronic portal and centrilobular pleomorph hepatitis including lymphocytes, plasmocytes, and eosinophils. These histological features were felt to be consistent with sequelae of a severe chronic hepatitis related to Tetracycline with Mixed connective tissue disease and autoimmune cholangitis. A diagnosis of autoimmune cholangitis (stage II-III) overlap chronic drug-induced hepatitis was made. The patient was started on prednisone 40 mg per day, and liver transaminases improved. At follow up two months later, the patient reported normalization of liver function tests.
Conclusions: Early diagnosis and treatment is helpful for the prognosis of patients.

Topic 3: Autoimmune Liver Diseases

No: 1763

A very rare cause of markedly elevated ca 19 9 autoimmune hepatitis

Ferdane Sapmaz[1], Ismail Hakkı Kalkan[1], Üçler Kısa[2], Sefa Güliter[1]

Kırıkkale University Faculty of Medicine Gastroenterology Kırıkkale-Turkey[1], Kırıkkale University Faculty of Medicine Biochemistry Kırıkkale-Turkey[2]

Carbohydrate antigen 19-9 (CA19-9) is a specific tumor marker of the biliary, pancreatic and gastrointestinal tracts. Autoimmune hepatitis is a chronic immune-mediated liver disorder characterised by female predominance. We report a case of approximately 30-fold increased serum CA19-9 in a 57-year-old woman who was diagnosed with autoimmune hepatitis. She had no evidence of any malignant disease in pancreatobiliary or gastrointestinal tracts. CA 19.9 levels decreased to normal levels with immunosuppressive treatment. Markedly elevated serum CA19-9 levels might be encountered with benign liver diseases such as autoimmune hepatitis.

Topic 3: Autoimmune Liver Diseases

No: 1876

Long term prognosis and clinical features in patients with primary biliary cirrhosis

Keiko Takano[1], Chisato Saeki[1], Ryo Nakagawa[1], Atsushi Hokari[1], Tomohisa Ishikawa[1], Hisao Tajiri[1], Zeniya Mikio[2]

Jikei University School of Medicine Gastroenterology and Hepatology Tokyo-Japan[1], Jikei University School of Medicine Gastroenterology Tokyo-Japan[2]

Aim: We assessed the clinical features at diagnosis, response to treatment (Paris2 criteria), and analyzed correlation with poor outcome (death, transplantation), complication of cirrhosis in patients with PBC.
Methods: In total, 275 PBC patients were enrolled who were treated with ursodeoxycholic acid (UDCA) or combined treatment with bezafibrate (Beza).
Results: A total of 123 patients (44.7 %) responded to UDCA (Group A) and 152 patients (55.3 %) were non-responders. Among non-responders, 80 patients (29.1 %) continued UDCA Monotheraphy (Group B), and 72 patients (26.1 %) were treated combined with Beza. of patients treated with UDCA and Beza, 52 patients (72.2 %) were responders (Group C), and 20 (27.8 %) were non-responders (Group D). The level of ALP was significantly higher in Group B, C, D than in Group A ($P < 0.001$). The total number of poor outcome was 9; 6 patients died and 3 underwent transplantation. A total of 5 dead patients and all patients underwent transplantation were included in Group B and Group D. of patients with development of cirrhosis, 65.2 % were included in Group B and Group D. In the ALP high group (> fourfold the upper limit of normal (ULN)), UDCA non-responders were more frequent ($P < 0.001$). Meanwhile, in the ALT high group (> ULN), UDCA and Beza non-responders were more frequent. ($P < 0.05$). The level of ALT and ALP in patients with poor outcome was significantly high, and ALT levels remained abnormal after treatment in 67 % of all these patients.
Conclusion: Higher ALT and ALP level at diagnosis, sustained high level of ALT are predictors for poor prognosis in PBC.

Topic 3: Autoimmune Liver Diseases

No: 2229

Expression of TGF β1 in patients with autoimmune liver diseases

Ludmila Paigova[1], Karina Raikhelson[1], Vadim Karev[2], Nataly Marchenko[1], Ekaterina Pozenko[1], andrey Kharitiniv[1], Sergey Trotsyuk[1], Nikolay Semenov[1]

North-western State Medical University Named After I. I. Mechnikov Gastroenterology and Dietology Saint-Petersburg-Russia[1], Research Institute of Children's Infections of Federal Medico-biology Agency Pathologic Laboratory Saint-Petersburg-Russia[2]

Introduction: Transforming growth factor-beta1 (TGFβ1) is key event in pathogenesis of hepatic fibrosis. High levels of TGF-β1 have been described in different acute and chronic liver diseases. However, its role in pathogenesis of autoimmune liver diseases (AiLD) and hepatitis C virus (HCV) remains unclear.
Objective: To evaluate expression of mononuclear phagocytes (CD68) and TGF-β1 in hepatic tissue of patients with AiLD, HCV
Materials and methods: We processed liver biopsies for immunohistochemical cell characterization from 49 patients (15 primary biliary cirrhosis (PBC), 12 – autoimmune hepatitis (AIH), 12 – primary sclerosing cholangitis (PSC), 10 – HCV). Expression of TGF-β1 was quantified as percent of positive cells rather CD68 as a whole. Patients with cirrhosis (6 – AIH, 5 – PBC) were also included in study with separate into account the results in cirrhosis and fibrosis stages. Activity scores were similar in all groups (METAVIR A2-A3).
Results: TGF-β1 expression in CD68 + nonparenchymal liver cells was significantly higher in patients with PSC compared with other AiLD (PBC $p > 0.05$, AIG $P = 0.0002$) and HCV ($P = 0.0001$). TGF-β1 expression in patients with HCV was significantly higher compared with PBC ($P = 0.016$). TGF-β1 expression in CD68 + was higher in patients with HCV and cirrhosis compared with non-cirrhotic patients ($P = 0.04$). Increased absolute count of CD68 + cells was higher in patients with HCV compared with AiLD (AIG $P = 0.002$; PBC $P = 0.007$; PSC $P = 0.003$, respectively).
Conclusions: increased expression of TGFβ1 in AIH and PBC patients with cirrhosis confirms it's role in fibrogenesis in AiLD. Increased TGF-β1 in PSC.

Topic 3: Autoimmune Liver Diseases

No: 1374

Analysis of the clinical features in patients with autoimmune liver disease in southwest China

Zhiling Cheng[1]

Department of Infectious Diseases, Southwest Hospital, Third Military Medical University, Chongqing, 3department of Gynecology and Obstetrics, Southwest Hospital, Third Military Medical University Chongqing-China[1]

To analyze the clinical characteristics of autoimmune liver disease patients in southwest China, in order to improve diagnostic accuracy.
Methods: A total of 436 patients with ALD including 211 cases with autoimmune hepatitis (AIH), 145 cases with primary biliary cirrhosis (PBC), autoimmune hepatitis and 80 cases with AIH and PBC overlap syndrome (OS) at the department of infectious diseases, Southwest Hospital, during the past 10 years, were included in our study. The characteristics of general data, clinical manifestation, biochemical indicators, autoantibodies and liver biopsy pathology observation were analyzed.
Results: The majority of patients were female, with an average age 49.7 years old. The clinical manifestations were similar. There were significant different among the 3 groups in ALT, GGT, TBIL ($P < 0.05$). The major autoantibody in the AIH group was ANA, in the PBC group were AMA (especially AMA-M2), but the OS group is characterized of the 3 autoantibody as mentioned. Pathology results confirmed ALD by the manifestations as followed: liver cell degeneration and necrosis, inflammatory cell infiltration, bile duct inflammation and fibrous hyperplasia. Conclusions: Most of ALD patients were female and middle-aged, especially 50 years old women in perimenopausal period, in southwest region of China. Serum biochemical indexes (ALT, GGT), immunoglobulin subtypes, autoantibodies and liver biopsy were essential to distinguish ALD, and combined analysis of them was helpful in diagnosis of ALD.

Topic 3: Autoimmune Liver Diseases

No: 1597

Autoimmune liver diseases is closely correlated to hepatitis B virus infection

Chonghan Nan[1], Zehui Yan[1], Yuming Wang[1]

Southwest Hospital Institute of Infectious Diseases Chongqing-China[1]

Objective: To explore the association between autoimmune liver diseases (AILD) and hepatitis B virus (HBV) infection and provide clinical evidence for the trigger of AILD.
Methods: The clinical data of a total of 447 patients who were diagnosed as AILD were collected and analyzed. The past HBV infection rate of these 447 patients were retrospectly analyzed and were compared with that of 103 833 non-HBV infecting volunteers.
Result: The past HBV infection rate of patients with AILD was 73.2 %, significantly higher than that of the non-HBV infecting volunteers (9.4 %) ($P < 0.001$);and can be observed in three forms of AILD including AIH, PBC, PSC and OS, in which no significant difference ($P > 0.05$), the trigger of some patients of AILD were observed due to HBV serological outcomes.
Conclusion: There is certain association between having been infected with HBV and AILD in our region. Infected HBV may be the trigger of AILD and the seroconversion of HBsAg must have been one of the direct trigger of AILD.

Topic 3: Autoimmune Liver Diseases

No: 1051

Biochemical and histological effectiveness of long term use of fenofibrate for asymptomatic primary biliary cirrhosis

Kazufumi Dohmen[1], Hirofumi Tanaka[1], Masatora Haruno[1], Shinichi Aishima[2]

Chihaya Hospital Internal Medicine Fukuoka-Japan[1], Saga University Pathology & Microbiology Saga-Japan[2]

Background/aims: Ursodeoxycholic acid (UDCA) is the standard option for asymptomatic primary biliary cirrhosis (aPBC). Favourable effects of fibrates have been demonstrated for treating aPBC patients with an incomplete response to UDCA. Among fibrates, the binding activity of fenofibrate to PPAR-α is stronger than that of bezafibrate. The aim of this study was to evaluate the biochemical and histological effects of the long-term use of fenofibrate in patients with aPBC who were refractory to UDCA.
Methods: 13 aPBC patients treated with fenofibrate plus UDCA for more than thirty-six months were involved in this study. Various characteristics of these 13 patients were compared between the time of the initiation of fenofibarate and thirty-six months after the administration of fenofibrate. Liver biopsy examinations for five patients were performed at the administration of fenofibrate and at two and a half years (22–39 months) after the fenofibrate administration. The histological stage was determined using Scheuer's and Nakanuma's classifications.
Results: In the patients treated with UDCA and fenofibrate, the serum alkaline phosphatase (ALP), γ-glutamyl transpeptidase (γGTP) and serum IgM levels decreased from 524.6 $\pm$ 190.8 to 218.7 $\pm$ 74.8 IU/l, 192.7 $\pm$ 87.1 to 29.5 $\pm$ 17.5 IU/l and 391.4 $\pm$ 244.0 to 166.3 $\pm$ 115.3 mg/dl ($P < 0.0001$), respectively. The histological findings of the liver obtained at approximately 2 and a half years after the fenofibrate plus UDCA treatment were more improved compared to that obtained at the initiation of fenofibrate.
Conclusion: Combination therapy with fenofibrate plus UDCA induces significant biochemical and histological improvements in patients with aPBC.

Topic 3: Autoimmune Liver Diseases

No: 1504

Risk factors for liver related mortality in primary biliary cirrhosis patients a deceased case living control study in China

Xuexiu Zhang[1], Lifeng Wang[1], Fu-sheng Wang[1]

Beijing 302 Hospital Research Center For Biological Therapy Beijing-China[1]

Aim: This study was designed to investigate the risk factors for liver-related mortality in Primary biliary cirrhosis (PBC) patients.
Methods: The data of all deceased PBC patients were collected from Beijing 302 Hospital database during the period from 2002 to 2013. The controls were matched to cases by gender, age ($\pm$ 2 years), and index date ($\pm$ 6 months). Potential risk factors were included for evaluation, and odds ratios (OR) and 95 % CIs were estimated using univariate (unadjusted OR, UOR) and multivariate (adjusted OR, AOR) conditional logistic regressions. A cutoff value of risk factor was determined by receiver operator characteristics analysis.
Results: Based on the analysis of data of 126 liver-related deceased PBC cases and 504 controls, we found that hepatocellular carcinoma (HCC), high level of total bilirubin (TBIL), low levels of albumin (ALB) and platelet (PLT), non-response to ursodeoxycholic acid (UDCA), and diabetes mellitus were independently associated with a significant increase in the risk of liver-related mortality in PBC patients ($P < 0.001$). Cutoff values of TBIL and ALB for prediction of poor prognosis were determined as 34.5 g/L and 37.65 μmol/L, respectively; the areas under the receiver operating characteristic curve were 0.759 and 0.770 ($P < 0.001$), respectively.
Conclusions: This study indicates that hepatocellular carcinoma (HCC) and levels of ALB, TBIL, PLT at the initial diagnosis of disease, non-response to UDCA, and diabetes mellitus were all independent risk factors for liver-related mortality in PBC patients.

Topic 3: Autoimmune Liver Diseases

No: 1484

Clinical epidemiology of 1255 inpatients with primary biliary cirrhosis in China

Lifeng Wang[1], Yuanyuan Li[1], Fu-sheng Wang[1]

Beijing 302 Hospital Research Center For Biological Therapy Beijing-China[1]

Aim: Our study is aimed to investigate the clinical epidemiology, especially in a large cohort of Primary biliary cirrhosis (PBC) patients.
Methods: One thousand and two hundreds twenty-five inpatients with PBC were enrolled and followed during the period of 2002 and 2013 in Beijing 302 hospital. Clinical, laboratory parameters were recorded during our follow-up check.
Results: Our data showed there is an significant increase of inpatients with PBC in our hospital. Among the 1255 inpatients, the mean age at diagnosis was 53 $\pm$ 11.2 years. The highest incidence of PBC was observed among 40- to 60-year old inpatients. A total of 1068 inpatients (85.1 %) were symptomatic, and 187 patients (14.9 %) had already developed into decompensated liver cirrhosis. At the time of diagnosis, the most common clinical symptoms were with splenomegaly or splenectomy because of portal hypertension and its related

complications, and 27.3 % of those inpatients with PBC simultaneously suffered from cholecystitis. 256 of patients (20.4 %) in our study were serum AMA negative, statistical analysis showed that there was no significant difference between AMA-negative and AMA-positive PBC inpatients with respect to sex, age, duration of disease, and laboratory parameters in our study. Comparing different biochemical criteria, Paris I was more fit to evaluate the efficacy of UDCA treatment for those patients.

Conclusion: We demonstrates that the burden of new identified PBC in China is increased during the last ten years. Paris criteria appear to be better to predict the efficacy of UDCA treatment.

Topic 4: Basic Science of Hepatology

No: 2216

Expression of tipe2 mRNA in peripheral blood mononuclear cells from hepatocellular carcinoma patients

Li Kong[1], Wei Li[2], Qing-shan Zhang[1], Su-xian Zhao[1], Zhu-jun Zhao[2], Xiao-hua Guo[2]

Third Hospital of Hebei Medical University Department of Hepatology Shijiazhuang-China[1], Third Hospital of Hebei Medical University Department of Experimental Center Shijiazhuang-China[2]

Aim: Hepatocellular carcinoma (HCC) is one of the most common malignant tumors and the third leading cause of cancer death worldwide. The immune system plays an important role in development of HCC. Tumor necrosis factor-α induced protein 8 like-2 (TIPE2) is a novel essential negative regulator of both innate and adaptive immunity and contribute for maintaining immune homeostasis. In this study we investigated the TIPE2 mRNA expression in PBMCs from HCC patients and its relationship with Foxp3, a specific marker of CD4 + CD25 + Foxp3 + regulatory T cell (Treg), and T lymphocyte subsets.

Method: The mRNA expression levels of TIPE2 and Foxp3 in PBMCs were examined by quantitative real-time reverse transcription polymerase chain reaction. T lymphocyte subsets were analyzed by flow cytometry.

Results: The expression of TIPE2 mRNA was significant lower and Foxp3 mRNA was higher in HCC patients than that in health controls. Down-regulated TIPE2 mRNA level was negatively correlated with ALT, AST levels and Foxp3 mRNA expression. Moreover, TIPE2 mRNA expression level was negatively correlated with elevated CD8 + T cell numbers and positively correlated with both decreased CD4 + T cell numbers and CD4 +/CD8 + T cell ratio.

Conclusion: These results indicate that TIPE2 gene may be involved in the tumorigenesis by regulating Foxp3 + Tregs function and T cell response in HCC patients.

Topic 4: Basic Science of Hepatology

No: 1155

Pathological changes in the splenic tissue architecture in of thioacetamide administered rats

Tasleem Akhtar[1], Nadeem Sheikh[1], Muddasir H. Abbasi[2]

University of The Punjab Department of Zoology Lahore-Pakistan[1], Govt. College of Science Wahdat Road Department of Zoology Lahore-[2]

Aims: Exposure to thioacetamide (TAA) is associated with the development of liver cirrhosis in experimental animals. In addition to liver, TAA toxicity has been observed in other organs. Present work was done to investigate the histopathological changes in the spleen of Wistar rats after long-term oral intake of TAA. Spleen plays an important role in iron metabolism and active immune response.

Methods: The dose given to the experimental animals (Rattus norvagicus) was 200 mg/l of TAA in drinking water for 18 weeks when their weight was 150 ± 25 g. Control animals were provided with normal drinking water. After 18 weeks all the animals were sacrificed and spleen was excised and following processing hematoxylin and eosin staining was used to analyze the histopathological changes.

Results: Histopathological analysis showed distortion of the normal architecture, profound congestion of the red pulp being smaller in size and containing macrophages leading to structure alteration of pulp nodules. Lymphoid hyperplasia in the white pulp was also observed.

Conclusion: It is conclusively stated that TAA is also toxic to extrahepatic organs like spleen. Distortion of normal splenic architecture and lymphoid hyperplasia confirms TAA toxicity.

Topic 4: Basic Science of Hepatology

No: 1458

ELK3 modulates non smad pathway of tumor growth factor β (TGF β) induced epithelial mesenchymal transition (EMT) through regulation of EGR 1 expression

Seung Kew Yoon[1], Tian Zhu Li[2], Wonhee Hur[1], Sung Woo Hong[1], Eun Byul Lee[1], Si Hyun Bae[1], Sang Wook Choi[3]

The Catholic University of Korea The Catholic University Liver Research Center & Who Collaborating Center of Viral Hepatitis, College of Medicine Seoul-Korea, South[1], Chifeng University Molecular Medicine Research Center, School of Medical Science Chifeng-China[2], The Catholic University of Korea Department of Internal Medicine, St. Paul Hospital Seoul-Korea, South[3]

One of mechanisms implicated in liver fibrogenesis is the epithelial mesenchymal transition (EMT). ELk3 is a downstream target of the Ras pathway, which plays an important role in cell migration, angiogenesis and tumorigenesis. The C domain of ELK3 has been known to be phosphorylated in vitro by ERK and p38. However, the role of ELK3 in EMT and liver fibrogenesis remains unclear. In this study, we investigated the roles of ELK3 in TGF-β induced EMT model.

We established in vitro EMT model using FL83B cells, AML12 cells and primary hepatocytes, treated with TGF-β1. EMT was determined by expression levels of related markers such as E-cadherin, β-catenin, vimentin and α-SMA. Expression ELK3 and its target Egr-1 was analyzed by immunoblotting in EMT induced cells, CCl4-induced mouse liver fibrotic tissues, and human liver cirrhotic tissues. Cells were transfected with ELK3 siRNA.

The mesenchymal marker expressions increased in EMT induced cells, while decreasing of epithelial markers expression. The expressions of ELK3 and its target EGR1 significantly increased in EMT induced cells, CCl4-induced mouse liver and human cirrhotic liver tissues. Silencing of ELK3 and inhibition of Ras-ELK3 pathway suppressed EMT-related markers. Moreover, ELK3 expression via p38 MAPK phosphorylation was found during EMT progression. Our findings define that ELK3 plays an important role in the progression of liver fibrosis through the regulation of EMT via regulates of MAPK signaling.

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Topic 4: Basic Science of Hepatology

No: 1102

Fucoidan protects hepatocytes from apoptosis while inhibits invasion of hepatoma cells through up regulating mapk dependent cap 43

Yuri Cho[1], Dong Hyeon Lee[1], Jeong-hoon Lee[1], Su Jong Yu[1], Jung-hwan Yoon[1]

Seoul National University College of Medicine Department of Internal Medicine and Liver Research Institute Seoul-Korea, South[1]

Fucoidan may have both protective effect on hepatocyte and inhibitory effect on proliferation of hepatocellular carcinoma (HCC) cells through downregulation of CXCL-12. However, more specific mechanisms of fucoidan's dual effects, which might be the most ideal anti-cancer strategy, remain poorly understood. Therefore, we investigated the effect of fucoidan on invasion and proliferation of HCC cells, and on survival of hepatocytes. Human HCC cells (Huh-7, a well-differentiated HCC cell line and SNU-761, a poorly differentiated HCC cell line) were grown either in a normoxic or hypoxic condition. MTS assay and invasion assay were done to evaluate the antitumor effects of fucoidan. To investigate the mechanisms of tumor inhibitory and the hepato-protective effects, western blottings were performed. Fucoidan suppressed tumor invasion of HCC cells (Huh-7 and SNU-761) in both normoxic and hypoxic condition, but did not inhibit the proliferation of HCC cells. Fucoidan up-regulated the expression of NDRG-1/CAP 43, which is a stress-responsive protein involved in cell growth, differentiation and acts as a tumor suppressor in many cell types, by increasing phosphorylayed-p42/44 mitogen-activated protein kinase (MAPK). Furthermore, fucoidan decreased apoptosis of hepatocyte in both normoxic and hypoxic condition as shown in the protein expressions of phosphorylated- c-Jun NH2-terminal kinase (JNK), caspase-8, and caspase-9. Also, fucoidan suppressed the mobilizations of caspase-8, Fas associated death domain (FADD) into death-inducing signaling complex (DISC). Fucoidan exhibited protective effect on hepatocytes from apoptosis and preferentially inhibitory effect on invasion of HCC cells by up-regulating NDRG-1/CAP 43, which is suggested as a potent tumor-invasion suppressor with hepato-protective effect.

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No: 1666

Propolis components suppresses collagen production and cell proliferation in activated hepatic stellate cells

Tomohiro Ogawa[1], Ryo Hirao[2], Takumi Terada[2], Yasue Yamada[2], Hideyuki Hyogo[3], Norifumi Kawada[4]

Kinki University Center For The Advancement of Higher Education Higashi-hiroshima-Japan[1], Kinki University Department of Biotechnology and Chemistry, Faculty of Engineering Higashi-hiroshima-Japan[2], Hiroshima University Department of Medicine and Molecular Science, Graduate School of Biomedical Sciences Hiroshima-Japan[3], Osaka City University Department of Hepatology, Graduate School of Medicine Osaka-Japan[4]

Introduction: Propolis is a honeybee product and has more than 300 components. We previously have reported the benefit effect of propolis on lipid metabolism and liver injury. However, the each effect of propolis components on liver injury has understood poorly. In this study, we examined the effect of propolis components on activated hepatic stellate cells and liver fibrosis in mice.
Materials and methods: A human stellate cell line LX-2 cells were incubated with propolis (0-0.1 mg/ml) and propolis components (0-0.1 mM), and its effect on collagen synthesis and cell proliferation was examined at the gene and protein expression levels. Live and dead cell staining kit was used for the evaluation of cell proliferation. Apoptosis was measured by caspase-3 activation. Mice on CCl4-induced liver fibrosis were treated with 30 mg/kg of propolis components for 8 weeks, and the liver was histologically investigated. ALT was also measured enzymatically. The expression of inflammation and liver fibrosis-related genes in the liver was measured by real-time PCR.
Results: By the addition of propolis and some propolis components on cultured activated stellate cells, the proliferation was suppressed in a dose-dependent manner, and cell death was induced. We identified some propolis components, which induced cell death severely. Additionally, the expression of genes related to liver fibrosis such as type I collagen genes significantly suppressed in propolis component-treated stellate cells.
Conclusions: Propolis has some antifibrotic components, which suppressed cell proliferation and collagen production in cultured stellate cells, suggesting the inhibitory effect of liver fibrosis by propolis components.

Topic 4: Basic Science of Hepatology

No: 1236

DNA methylome and cancer specific expression change of clustered mirnas in non b non c hepatocellular carcinoma

Takeshi Matsui[1], Masanori Nojima[2], Etsuko Iio[1], Akihiro Tamori[3], Shoji Kubo[4], Ken Shirabe[5], Koichi Kimura[5], Mitsuo Shimada[6], Tohru Utsunomiya[6], Yasuteru Kondo[7], Takahiro Ochiya[8], Yasuhito Tanaka[1]

Nagoya City University Graduate School of Medical Sciences Department of Virology Unit Nagoya-Japan[1], The University of Tokyo Center For Translational Research Tokyo-Japan[2], Osaka City University Graduate School of Medicine Department of Hepatology Osaka-Japan[3], Graduate School of Medicine, Osaka City University Department of Hepato-biliary-pancreatic Surgery Osaka-Japan[4], Graduate School of Medical Sciences, Kyushu University Department of Surgery and Science Fukuoka-Japan[5], The University of Tokushima Department of Surgery Tokushima-Japan[6], Tohoku University Hospital Division of Gastroenterology Sendai-Japan[7], National Cancer Center Research Institute Division of Molecular and Cellular Medicine Tokyo-Japan[8]

Background: Non-B non-C hepatocellular carcinoma (NBNC-HCC) is considered increasing based on increase of nonalcoholic fatty liver disease (NAFLD) in Japan. Molecular biological mechanism should be pursued against this disease structure change.
Aim: To explore critical changes of DNA methylome and related mRNA/micro RNA (miRNA) expression in tumorigenesis of NBNC-HCC.
Methods: Infinium HumanMethylation450 BeadChip Kit (Illumina) and micro 3D-Gene miRNA Oligo Chip (Toray) were applied in 26 pairs of tumor and non-tumor background tissue samples.
Results and plan: Hierarchical clustering of the DNA methylome status demonstrates clear discrimination between tumor and non-tumor samples. While approx. 20 % of CpG islands in promoters were dominantly hypermethylated in the tumor, other regions were

globally hypomethylated in the tumor. The mean difference in methylation levels of total probes was -10.5 % in non-CpG islands, and 0.68 % in CpG islands (tumor vs. non-tumor). Next, we determine the characteristics of hypomethylated sites, and then found several miRNA clusters were markedly hypomethylated (-30 % to -40 %) in tumor tissues (e.g. 14q32.31, 19q13.42). Average methylation level in miRNA coding region were lower than other regions. In detail, 52.8 % of total miRNA probes were significantly hypomethylated, and mean difference in methylation levels were -14.4 % in non-CpG islands, and 0.14 % in CpG islands. Consistent with the hypomethylation tendency, average miRNA expression level was 28.0 % up-regulated. In particular, hypomethylated miRNA clusters (such as 14q32.31), miRNA expression significantly around 50 % to 100 % up-regulated.
Conclusions: The hypomethylated miRNA clusters were associated with cancer-specific miRNA overexpression.

Topic 4: Basic Science of Hepatology

No: 1605

Eupatilin pretreatment for prophylaxis of nonalcoholic steatohepatitis

Dong Hyeon Lee[1], Jung-hwan Yoon[9], Yuri Cho[9], Jung-ju Yoo[9], Minjong Lee[9], Eun Ju Cho[9], Jeong-hoon Lee[9], Su Jong Yu[9], Hyosuk Lee[9]

Department of Internal Medicine and Liver Research Institute Department of Internal Medicine and Liver Research Institute Seoul-Korea, South[1]

The prevailing hypothesis in pathogenesis of nonalcoholic steatohepatitis (NASH) consists of two steps: excessive lipid accumulation and hepatocyte injury by oxidative stress, abnormal cytokines, mitochondrial dysfunction, and/or endoplasmic reticulum (ER) stress. Eupatilin, an extract of Artemisia asiatica Nakai, has been established as an anti-oxidative, anti-inflammatory, and cytoprotective agent. We hypothesized that eupatilin prevents development of NASH by diminishment of liver injury.

The role of eupatilin was evaluated in two hepatocellular carcinoma cell lines and methionine choline-deficient diet-fed C57BL/6 mice. The effects of eupatilin on the development of NASH and its underlying mechanism were assessed by RT-PCR, immunoblot assay, DAPI, and histological examination.

Eupatilin attenuated the palmitic acid-induced lipoapotosis by suppression of ER stress. In animal study, eupatilin decreased the level of Ccl2 and Tnf mRNA, known as inflammatory cytokines. Eupatilin also attenuated the expression of Sod2, whereas restored the expression of decreased Acox1. The nitrotyrosine stained area in mouse liver tissue was suppressed by eupatilin pretreatment. These results proposed that eupatilin alleviated the liver injury by acting as an anti-inflammatory and anti-oxidative agent. In addition, signaling of ER stress and apoptosis were all attenuated in mice treated with eupatilin. These protective effects of eupatilin might lead to the histological improvements of mouse liver tissue. Histological studies showed that euaptilin attenuated the hepatic inflammatory foci and non-alcoholic fatty liver disease activity score (NAS).

These findings suggested that eupatilin is a promising therapeutic agent against development of NASH and its preventative effects may be mediated by suppression of liver injury through diminishment of hepatic inflammation, oxidative stress, and ER stress.

Topic 4: Basic Science of Hepatology

No: 1590

Suppression of calpain expression inhibits invasion of hepatoma cells through down regulation of HIF 1α

Donghyeon Lee[1], Jung-hwan Yoon[9], Yuri Cho[9], Jung-ju Yoo[9], Minjong Lee[9], Eun Ju Cho[9], Jeong-hoon Lee[9], Su Jong Yu[9], Hyosuk Lee[9]

Seoul National University College of Medicine Department of Internal Medicine and Liver Research Institute Seoul-Korea, South[1]

Background: A calpain is one of calcium-dependent, non-lysosomal cysteine proteases expressed ubiquitously in mammals. Although the role of calpain is not fully understood, they have been shown to be active participants in processes such as cell mobility and cell cycle progression. Then, we hypothesized that suppression of calpain expression inhibits proliferation and invasion of hepatocellular carcinoma (HCC) cells.
Methods: In cell culture, SNU761 cells, a poorly differentiated HCC cell line, were treated with control siRNA or calpain specific siRNA. Cell viability, cell migration, apoptosis, and their mechanisms were assessed by using MTS assay, invasion assay, RT-PCR, and immunoblot assay.
Results: Cell proliferation was not influenced by suppression of calpain expression both in normoxia and in hypoxia. On the contrary, decreased expression of calpain attenuated cell invasion under hypoxic condition. However, well known markers of cell invasion, such as MMP9, MMP2, IL-8, CK19, and CAP43, were not suppressed by transfection of calpain specific siRNA under hypoxic condition. Instead of these signals, suppression of calpain expression attenuated hypoxia-inducible factor-1α (HIF-1α). Because following treatment with MG132, one of proteasome suppressants, restored the HIF-1α expression, suppressed by calpain siRNA, enhancement of proteasome activity might be a main mechanism of calpain siRNA to inhibit cell invasion.
Conclusions: In this study, we demonstrate that down regulation of calpain suppressed invasion of HCC cells by enhancement of HIF-1α degradation. Suppression of calpain expression could be used as one of therapeutic options for hypovascular HCC.

Topic 4: Basic Science of Hepatology

No: 1461

RAR related orphan receptor gamma (RORC) contribute to epithelial mesenchymal transition (EMT) progression through regulation of SMAD2 expression

Seung Kew Yoon[1], Sung Min Kim[1], Jung-hee Kim[1], Jung Eun Choi[1], Sung Woo Kim[1], Joon Ho Lee[1], Si Hyun Bae[1], Sang Wook Choi[2]

The Catholic University of Korea The Catholic University Liver Research Center & Who Collaborating Center of Viral Hepatitis, College of Medicine Seoul-Korea, South[1], The Catholic University of Korea Department of Internal Medicine, St. Paul Hospital Seoul-Korea, South[2]

Epithelial mesenchymal transition (EMT) plays a critical role during embryonic development, tumor invasion and fibrogenesis. RAR-related orphan receptor gamma (RORC) is a member of the ROR subfamily of orphan nuclear receptors. RORC has been reported to control the development of thymocytes, and a transcription factor for

the differentiation of Th17 T cells. However, the role of RORC in EMT and fibrogenesis remains unclear. In this study, we investigated the roles of RORC in fibrogenesis in TGF-β induced EMT model.

RORC expression was analyzed by immunoblotting in CCl4-induced mouse liver and human cirrhotic liver tissues. We established in vitro EMT model using FL83B cells treated with TGF-β1. To verify the role of RORC in EMT, we performed knockdown of RORC gene in FL83B cells by lentiviral shRNA vector. Morphological change and E-cadherin and Vimentin expression were determined by microscopy and immunoblotting, respectively.

The RORC expression significantly increased in mouse and human fibrotic liver tissues. During EMT progression, RORC expression increased in TGF-β1 treated cells. E-cadherin was upregulated while vimentin was downregulated in RORC silenced cells. RORC was bound to ROR-specific DNA response elements (ROREs) in the promoter regulatory region of target genes. We showed that Smad2 is a direct target of RORC among putative transcriptional targets. Interestingly, the Smad2 expression decreased in RORC silenced cells. These results suggest that RORC associated with EMT progression leading to liver fibrosis.

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Topic 4: Basic Science of Hepatology

No: 1965

Surveillance of viral dominance in patients with HBV HCV co infection in southern Taiwan 2013 2014

Hung Ting-chun[1], Lee Ching-chien[1], Chen Ching-ju[1], Shen Hui-chuan[1], Wu Li-ching[2], Lin Chun-ching[3]

Chi Mei Medical Center Virology Tainan-Taiwan[1], Chi Mei Medical Center Clinical Pathology Tainan-Taiwan[2], Kaohsiung Medical University Graduate Institute of Natural Products Kaohsiung-Taiwan[3]

Among liver disease caused by the hepatitis virus, HBV and HCV infection are the most prevalent, and also are the major health issues.In our previous study, we survey the correlation of several clinical findings with different HCV genotypes and HBV drug-resistant strains in patients to propose effective prevention strategies for minimizing the consequence of the disease to health. The results show that HCV genotype 2 comprised the greatest proportion (56.9 %), followed by genotype 1b, 6, and 1 (27.6, 12.1, and 3.4 %). The proportions of HBV strains were as follows: YMDD (74.4 %), YIDD (10.7 %), YVDD (9.9 %), and mixed (5.0 %). HCV viral load for each genotypes was found high significant ($p<0.001$).

This study was performed to determine the viral dominance in patients with HBV/HCV co-infection. Total of blood sample of HBV and HCV co-infection patients were collected from outpatient and inpatient department of medical center in southern Taiwan. All serum sample were tested for genotyping, HBV DNA, HCV RNA, hepatitis B surface antigen (HBsAg), anti-HCV antibodies.It is helpful to determine which virus is dominant in co-infected patients.

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No: 1081

BMP 2 restoration rescues the liver fibrosis injuries by attenuating the TGF β1 signaling

Yueh-hua Chung[1], Ying-hsien Kao[2], Tsung-hui Tsung-hui[3], Ting-ya Wang[4], Eton Lin[5], Ming-hong Tai[1]

National Sun Yat-sen University, Kaohsiung 804, Taiwan. Institute of Biomedical Sciences Kaohsiung-Taiwan[1], E-da Hospital, Kaohsiung, Taiwan. Laboratory of Regenerative Medicine, Department of Medical Research Kaohsiung-Taiwan[2], Kaohsiung Chang Gung Memorial Hospital Division of Hepato-gastroenterology Kaohsiung-Taiwan[3], Kaohsiung Chang Gung Memorial Hospital Division of Pulmonary & Critical Care Medicine Kaohsiung-Taiwan[4], Box Hill Hospital, Department of General Medicine Department of Allergy, Immunology Melbourne-Australia[5]

Objective: Transforming growth factor-β (TGF-β) plays a central role in hepatic fibrogenesis. The present study investigated the function and mechanism of bone morphogenetic protein-2 (BMP-2), a member of TGF-β family, in hepatic fibrosis models.
Design: Mouse model of hepatic fibrosis was achieved with bile duct ligation (BDL) or carbon tetrachloride (CCl4) administration. The expression of BMP-2 and other fibrosis-related markers was measured using quantitative RT-PCR and immunoblot assays. Hepatic BMP-2 overexpression was achieved by adenovirus gene delivery. Hepatic stellate cells (HSC-T6) and hepatocytes (Clone 9) were used to study the interplay between BMP-2 and TGF-β1.
Results: BMP-2 expression was significantly decreased during fibrosis progression in both BDL and CCl4 models. After BDL/CCl4 administration induced, the hepatic BMP-2 mRNA and protein levels in mice were down-regulated, whereas TGF-β1 up-regulated. In addition, sera inflammatory markers were significantly raised by BDL or CCl4 administration and reduced by BMP-2 gene delivery. Furthermore, pathological examination showed BMP-2 gene delivery alleviated inflammation and liver injury caused by BDL or CCl4 exposure. The in vitro study demonstrated that exogenous TGF-β1 inhibited BMP-2 expression in both cultured stellate cells and hepatocytes. Additionally, exogenous BMP-2 significantly attenuated the development of fibrosis via suppressed the TGF-β1, TGF-β receptor I, II and downstream signal transduction molecule smad2/3 expression/phosphorylation.
Conclusions: These findings strongly suggest that BMP-2 is involved in the pathogenesis of hepatic fibrosis which is mutually and negatively regulated by TGF-β1. Moreover, BMP-2 gene delivery alleviated the hepatic fibrosis in mice. Thus, BMP-2 supplementation may be a novel strategy for fibrosis prophylaxis and therapeutic agent.

Topic 4: Basic Science of Hepatology

No: 2102

Estradiol activated microrna 23a directly or synergistically with p53 implicated in sex difference in hepatocellular carcinoma development

Fung-yu Huang[1], Danny Ka-ho Wong[1], Wai-kay Seto[1], Ching-lung Lai[1], Man-fung Yuen[1]

The University of Hong Kong Department of Medicine Hong Kong-China[1]

Background: Estrogen (E2) exerts a protective role against hepatocellular carcinoma (HCC) development. We sought to determine the effects of E2 on apoptotic miRNAs expression and explore the possible mechanism underlying apoptosis in HCC.
Methods: Microarray was performed to analyze alteration of apoptotic miRNAs in E2-treated liver cell-line. Expression profiles of selected miRNAs were verified using qRT-PCR. qRT-PCR and Western-blot were used to analyze the alteration of mRNA and

protein levels of genes such as p53, ERα, XIAP and caspase-3/7. Activity of caspase3/7 was measured using a luminescent assay.
Results: After E2 treatment, more than twofold alteration was observed in 25 upregulated and 10 downregulated miRNAs. Expression of miR-23a in p53-mutated male cell-lines was significantly lower than cell-lines with functional p53 (all $P < 0.001$), but not in female cells. p53 activation increased miR-23a expression in p53 +/+ HepG2 cells ($P < 0.0001$ at 12 h. $P < 0.01$ at 24 h), but not in p53-/-Hep3B cells. E2 via ERα could significantly activated miR-23a ($P < 0.001$) and p53 ($P < 0.01$) expression, and thus replenished p53-deficiency SNU387 cells in activation of miR-23a. Moreover, miR-23a mimic and E2 significantly activated miR-23a ($P < 0.001$) and suppressed the expression of its target XIAP ($P < 0.0001$ and $P < 0.01$). Decreasing of XIAP contributes to activation of caspase-3 activity and cell apoptosis. Caspase-3 mRNA was significantly upregulated with E2 and miR-23a mimic treatment ($P < 0.0001$ for E2, and $P < 0.01$ for miR-23a mimic). Treatment of cells with anit-miR-23a increased XIAP expression ($P < 0.001$), and abolished caspase-3 activation ($P < 0.001$).
Conclusions: This study revealed a novel E2-signaling mechanism in regulating miRNAs expression and apoptosis that may contribute to sex difference in HCC development.

Topic 4: Basic Science of Hepatology

No: 1445

Hepatitis B virus x protein impairs alpha interferon signaling through up regulation of suppressor of cytokine signaling 3 and protein phosphatase 2a

Seiji Tsunematsu[1], Atsushi Ito[1], Fumiyuki Sato[1], Katsumi Terashita[1], Yoko Tsukuda[1], Masato Nakai[1], Takuya Sho[1], Goki Suda[1], Kenichi Morikawa[1], Mitsuteru Natsuizaka[1], Koji Ogawa[1], Naoya Sakamoto[1]

Hokkaido University, Graduate School of Medicine Departments of Gastroenterology and Hepatology Sapporo-Japan[1]

Background/aims: Hepatitis B is a major pathogen causing liver cirrhosis and hepatocellular carcinoma worldwide. Although Interferon therapy is one of standard therapies for patient with chronic hepatitis B virus (HBV) infection, its efficacy is limited. Recently it is reported that HBV impair IFN signaling, however the mechanism has not been well clarified. In this study, we aimed to analyze the mechanisms how Hepatitis B virus X protein (HBx) impairs IFN signaling.
Methods: We established HepG2 cells stably expressing HBx (HBx/HepG2) and those transfected with a control empty vector (control/HepG2) by retrovirus-mediated gene transfer. Then we evaluated effects of HBx on IFN signaling. Subsequently we analyzed the expression levels of IFN negative regulators in HBx/HepG2 cells and analyze the mechanism how these factors are induced.
Results: By IFN stimulation, HBx/HepG2 cells showed reduced expression of interferon stimulated genes compared with control/HepG2 cells. Analysis of expression levels of IFN negative regulatory factors showed that HepG2/HBx cells expressed higher levels of suppressor of cytokine signaling 3 (SOCS3) and protein phosphatase 2A (PP2A) compared with control/HepG2 cells. By siRNA knockdown of these factors, HBx/HepG2 cells restored IFN sensitivity. Moreover HBx/HepG2 cells express higher level of phosphorylation of signal transducers and activators of transcription 3 (STAT3) and endoplasmic reticulum stress, inducer of SOCS3 and PP2A respectively.
Conclusion: HBx impairs IFN signaling through increased expression of SOCS3 and PP2A, providing a novel mechanistic insight. It might be a therapeutic target to enhance IFN therapy.

Topic 4: Basic Science of Hepatology

No: 1074

Efficacy of lansoprazole for liver damages by up regulating the hepatic expression of a redox sensitive transcriptional factor NF E2 related factor

Yasunobu Yamashita[1], Takashi Ueyama[2], Yuta Yamamoto[2], Hideyuki Tamai[1], Yoshihiro Tsuruo[2], Masao Ichinose[1]

Wakayama Medical University Second Department of Internal Medicine Wakayama-Japan[1], Wakayama Medical University Department of Anatomy and Cell Biology Wakayama-Japan[2]

Aim: The aim of this study is to investigate efficacy of lansoprazole for liver damage with anti-oxidative stress in the liver.
Methods: Lansoprazole (10 mg/kg – 100 mg/kg) was orally administrated to male Wistar rats for single administration-model. Lansoprazole (30 mg/kg/day) was also subcutaneously administrated for successive 7 days in chronic model. Expression of NF-E2-related factor (Nrf2), Kelch-like ECH-associated protein (Keap1), and heme oxygenase 1 (HO-1) was investigated by RT-PCR, Western blotting and immunohistochemistry. The effect of lansoprazole on the acute hepatic damages made by intraperitoneal administration of thioacetamide (500 mg/kg) was investigated with chronic model.
Results: Up-regulation of mRNAs and immunoreactivities for Nrf2 and HO-1 was observed in a dose-dependent manner. Nuclear translocation of Nrf2 in the hepatocytes was observed in Western blotting and immunohistochemistry. However, Keap1 which sequesters Nrf2 in the cytoplasm under un-stimulated conditions were constant. These results were confirmed in chronic model. Therefore, lansoprazole can induce Nrf2 mRNA expression in the hepatocytes without affecting the level of Keap1, thereby increased free Nrf2 was translocated into the nuclei of the hepatocytes, resulting in the systematic anti-oxidative stress responses in the liver. In fact, hepatic damage was significantly attenuated by treatment with lansoprazole in histology and blood test.
Conclusions: Lansoprazole could attenuate liver damage by up-regulating Nrf2. It is expected efficacy of lansoprazole for liver damage by oxidative stress such as non-alcoholic steatohepatitis (NASH).

Topic 4: Basic Science of Hepatology

No: 2117

Serum trace metals in patients with acute myocardial infarction in sindh Pakistan

Dr. Farzana Chang[1], Dr. Saira Baloch[2], Dr. Muhammad Suleman Pirzado[3]

Department of Pathology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan Department of Pathology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan Jamshoro-Pakistan[1], Medical Research Center, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan. Medical Research Center, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan. Jamshoro-Pakistan[2], Department of Molecular Biology and Genetics, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan Department of Molecular Biology and Genetics, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan Jamshoro-Pakistan[3]

Background: Acute myocardial infarction is one of the most prevalent diseases in developed countries. It is a leading cause of morbidity and

mortality throughout worldwide. The disease occurs when diminished blood supply to the heart, exceeds a critical threshold and overwhelms myocardial cellular repair mechanisms designed to maintain normal operating function and homeostasis which cause myocardial ischemia. Critical myocardial ischemia also occurs due to increased myocardial metabolic demand, decreased delivery of oxygen and nutrients to the myocardium via the coronary circulation, or both. Trace metals (Cu, Mg and Zn) play a vital role in health and disease and their role has been stressed in myocardial infarction before.
Objective: In the present study we have asses the status of serum zinc, copper and magnesium levels in age and sex matched patients with acute myocardial infarction compared with healthy control subjects.
Methods: For the determination of trace metals fifty intravenous blood samples each from referred AMI patients and healthy control subjects were collected and immediately centrifuged to obtain the supernatant liquid, serum for analysis. Trace Metal (Cu, Mg and Zn) were determined by Atomic Absorption Spectroscopy using air-acetylene flame (AAS, Model Varian A-20).
Results: It was observed that serum Mg and Cu concentration were significantly increased whereas; Zn concentration was decreased significantly in patients as compared to the healthy control subjects.
Conclusion: Deficiency levels of trace metals may play a role in the development of AMI. Imbalanced concentrations of trace metals may supposed to contribute in the causes of AMI.

Topic 4: Basic Science of Hepatology

No: 1818

Inhibition of tumor angiogenesis by lentivirus mediated small interference HIF 1β in hepatocellular carcinoma

Sung Hoon Choi[1], Wonseok Kang[2], Seungtaek Kim[3], Do Young Kim[2], Sang Hoon Ahn[2], Kwang-hyub Han[2], Seung Up Kim[2]

Science, Yonsei University College of Medicine Bk21 Plus Project For Medical Science Seoul-Korea, South[1], Institute of Gastroenterology, Yonsei University College of Medicine Department of Internal Medicine Seoul-Korea, South[2], Institute of Gastroenterology, Yonsei University College of Medicine Department of Medical Bioscience Seoul-Korea, South[3]

Background/aim: Dimerization of hypoxia-inducible factor-1 beta (HIF-1β, ARNT) with HIF-1α is involved in various aspects of cancer biology, including proliferation and tumor angiogenesis under hypoxic conditions. We investigated the in vitro mechanism by which silencing of HIF-1β leads to the suppression of tumor cell growth and cellular functions.
Methods: Various hepatocellular carcinoma (HCC) cell lines (Huh-7, Hep3B, and HepG2) were transfected with small interfering RNA (siRNA) against HIF-1β (siHIF-1β) and cultured under hypoxic conditions (1 % O2 for 24 h). The expression levels of HIF-1β, HIF-1α, and angiogenic factors were examined by immunoblotting. Tumor growth was measured using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay, and tumor angiogenesis was measured by invasion, and tube formation in HUVECs.
Results: Under hypoxic conditions, silencing of HIF-1β expression suppressed tumor cell growth and regulated the expression of tumor angiogenesis factor, such as vascular endothelial growth factor, epidermal growth factor. Suppression of tumor angiogenesis was also demonstrated in HUVECs.
Conclusion: Silencing of HIF-1β expression may induce anti-angiogenic effects under hypoxic conditions in HCC cell lines.

Topic 4: Basic Science of Hepatology

No: 2219

Protective effects of s adenosylmethionine against CCL4 and ethanol induced experimental hepatic fibrosis

Feng Zhang[1], Yuzheng Zhuge[1]

Ffiliated Drum Tower Hospital of Nanjing University Medical School Department of Gastroenterology Nanjing-China[1]

Aim: To investigate the effects of S-Adenosylmethionine (SAM) on experimental hepatic fibrosis rats induced by carbon tetrachloride (CCl4) and ethanol and to explore the relevant potential mechanisms.
Method: Fifty eight-week-old male Sprague–Dawley rats were randomly divided into five groups: the normal control group, model control group, SAM-prevented group, treatment control group, and SAM-treated group. Hepatic fibrotic animal model was established with CCl4 diluted in olive oil and being drunk with the 10 % ethanol water. SAM was used for prevention and treatment, respectively. The liver function was detected using an automatic biochemistry analyzer. Histological evaluation was carried out by hematoxylin-eosin (HE) and Masson staining of liver samples.
Results: Serum biochemical assays showed alanine aminotransferase (ALT) was increased and albumin (ALB) was decreased by CCl4 and ethanol, which was suppressed by both preventing and treating use of SAM. Total bilirubin (TB) was not significantly changed in each group. Compared to the normal group, the model control group got significantly higher scores in fatty degeneration, lobular inflammation, and hepatocyte ballooning. and significant improvement was observed in the SAM-prevented group and SAM-treated group, which was consistent with the change of fibrosis scoring in each group. Smad3 was induced by CCl4 and ethanol in the model control group, which was significantly down regulated by preventable and treating use of SAM.
Conclusion: SAM had a protective effect on liver fibrosis of rats induced by CCl4 combined with ethanol and the down-regulation of the expression of Smad3 was involved in the potential mechanisms.

Topic 4: Basic Science of Hepatology

No: 1015

Human amniotic epithelial cell therapy improves survival of d galactosamine induced acute liver failure in mice

Veysel Tahan[1], Roberto Gramignoli[2], Kristin Skvorak[3], Jorge Guzman-lepe[3], Evan Delgado[3], Asli Tahan[4], Kenneth Dorko[3], Mark Hansel[3], Fabio Marongiu[5], Stephen Strom[2]

University of Iowa Hospitals and Clinics Department of Gastroenterology Iowa City, Ia-United States[1], Karolinska Institutet Stockholm-Sweden[2], University of Pittsburgh Department of Pathology Pittsburgh, Pa-United States[3], University of Iowa Faculty of Science Iowa City, Ia-United States[4], University of Cagliari Department of Biomedical Sciences Cagliari-Italy[5]

Human amniotic epithelial cells (hAEC) have been shown to have characteristics similar to pluripotent stem cells and also anti-inflammatory and immunomodulatory effects that may play beneficial roles in acute liver failure (ALF) progression. Our objective was to evaluate the effects of hAEC on D-galactosamine (D-gal) induced ALF.
Methods: 28 C57/B16 mice received D-gal (5 g/kg) intraperitoneally. Six hours later, 2x106[SUP][/SUP]hAECs were injected via the

spleen of 14 D-gal treated mice, whereas the remaining14 D-gal treated mice were injected with saline. Half of the D-gal (n = 7) and half of the D-gal + hAEC (n = 7) treated animals along with seven control mice were sacrificed 48 h after hAEC transplantation to examine the acute effects of D-gal alone and D-gal + hAEC transplant. The remaining seven mice from each group were followed to compare the differences in survival between groups. After spontaneous death or sacrifice blood and liver tissues were collected to evaluate histopathological, biochemical and gene expression parameters.

Results: D-gal treatment caused severe ALF and all mice treated with D-gal only survived less than 5 days. The D-gal + hAEC treated mice, not sacrificed at 48 h, survived more than 2 weeks and were sacrificed for further comparison studies. D-gal treatment increased serum AST, ALT and transforming growth factor-β (TGF-β) and caused deterioration of the inflammatory cytokine balance. hAEC therapy improved all parameters. In conclusion: hAEC therapy improved the survival, liver transaminases, TGF-β and inflammatory cytokine levels in the model. These results suggest that hAEC transplantation may provide an alternative therapeutic option to solid liver transplantation in progressive ALF.

Topic 4: Basic Science of Hepatology

No: 2242

PI3 K AKT MTOR signaling pathway mediates hepatoma cell autophagy induced by hydrogen sulfide

Huiguo Ding[1]

Beijing Youan Hospital Affiliated To Capital Medical University Gi and Hepatology Beijing-China[1]

Background: Gasotransmitter hydrogen sulfide (H2S) plays an important role in the pathogenesis of liver diseases. However, the role of H2S in pathogenesis of hepatocellular carcinoma (HCC) remains unclear. This study aimed to investigate the effect of H2S on hepatoma cell autophagy and its molecular mechanism.

Methods: The two kinds of hepatoma cell lines——HepG2 and HLE cells were used in this study.After transfection with GFP-LC3 plasmids into cells treated with NaHS, an exogenous H2S donor, LC3 punctate dots were tested using fluorescence microscopy. The intracellular double-membrane vesicles of autophagy were observed by transmission electron microscope (TEM). The beclin1 mRNA and atg5mRNA levels were measured by quantitative RT-PCR.The beclin1, atg5 and protein 1 light chain 3II (LC3-II) were respectively assayed by western blotting(WB). WB and immunofluorescence staining were also used to measure the proteins of PI3 K/Akt/mTOR signaling pathway.

Results: The percentage of LC3 punctate dots was clearly increased in HepG2 (64.7 ± 3.15 % vs 8.77 ± 0.89 %, $P < 0.05$) and HLE (47.87 ± 6.93 % vs 7.0 ± 0.52 %, $P < 0.05$) after treatment with NaHS. The intracellular double-membrane vesicles in HepG2 and HLE cells were increased.Furthermore, the autophagy related proteins—beclin 1, atg5 and LC3-II were up-regulated in HCC cells and beclin 1mRNA, atg5 mRNA levels were also increased after treatment using NaHS. The p-PI3 K, p-Akt, and mTOR proteins were reduced. Notably, the autophagy and LC3-II were increased when the cells were treated using rapamycin,the mTOR inhibitor.

Conclusions: Exogenous H2S can promote hepatoma cell autophagy by the inhibition of PI3 K/Akt/mTOR signaling pathway.

Topic 4: Basic Science of Hepatology

No: 2217

S adenosylmethionine suppresses the expression of smad3 4 in activated human hepatic stellate cells via methylating rac1 promoter

Kangqi Bian[1], Feng Zhang[1], Yuzheng Zhuge[1]

Affiliated Drum Tower Hospital of Nanjing University Medical School Department of Gastroenterology Nanjing-China[1]

Aim: To investigate the potential mechanism that S-Adenosylmethionine (SAM) suppresses activated human hepatic stellate cells (HSCs).

Method: Human HSCs LX-2 were cultured with SAM and NSC23766 or transfected with plasmids encoding Rac1 protein or empty expression vector. The proliferation was detected by CCK-8. Cell migration and invasion were tested by the transwell assay. The expression of Rac1 and Smad3/4 was identified by real-time PCR or western blotting. Methylation status of Rac1 promoters was measured by methylation specific PCR.

Results: Both SAM and NSC23766 suppressed the expression of Smad3/4 of LX-2 cells. Overexpression of Rac1 enhanced the proliferation, migration and invasion of LX-2 cells. Compared with the control groups, LX-2 cells transfected with Rac1 plasmids showed a remarkable increase in both Smad3 and Smad4 protein, indicating that Rac1 promoted the expression of Smad3/4 in LX-2 cells. and the result of methylation specific PCR showed that SAM converted the methylation status of Rac1 promoters.

Conclusion: the present study suggested that Rac1 enhanced the expression of Smad3/4 in activated HSCs, which was suppressed by SAM via methylating the promoters of Rac1 to inhibit the expression of Rac1.

Topic 4: Basic Science of Hepatology

No: 2172

Hepatitis A B C serology of university students and young health care workers in tokat region of Turkey

Sener Barut[1], Osman Demir[2], Feyza Yildiz Aytekin[1]

Gaziosmanpasa University Infectious Diseases Tokat-Turkey[1], Gaziosmanpasa University Biostatistics Tokat-Turkey[2]

In Turkey, although hepatitis A vaccine was added to national vaccination schedule in 2012, some of adolescents or young adults remain susceptible to hepatitis A virus (HAV) infection. In this study, hepatitis A, B and C serology was investigated in university students or young health care workers (HCW) who started working recently in Tokat region of Turkey.

Students or HCW's (in the beginning of their work) who admitted to infectious diseases outpatient clinic for health screening or immunoprophylaxis in October–November 2014, were included in the study. HBsAg, anti-HBs, anti-HCV and anti-HAV IgG tests were performed by using an enzyme immunoassay kit.

Seventy students (especially from dentistry school) and 19 health care workers (total 89 subjects) were included in the study. Mean age was 20.17 ± 4.4 years. Only one subject was HBsAg positive whereas all cases were anti-HCV negative. Eighty-one (%92) subjects had anti-HBs antibodies higher than 10 IU/ml. However 62 of 89 subjects were anti-HAV IgG negative. No subjects were vaccinated

against HAV. HAV seropositivity was more frequently seen in older subjects than younger ones (table 1, $P = 0.049$).
Conclusion: In Turkey all infants are being vaccinated against HBV since 1998. Also, catch-up vaccination was applied between years 2004-2008. Our results suggest that high immunity to hepatitis B in university students or young adults were related to favourable results of catch-up vaccination of HBV. However, nationwide HAV vaccination for children was implemented only two years ago (only for infants at the age of 12 months). According to our results, most of adolescents or young adults remain susceptible to HAV.

Topic 4: Basic Science of Hepatology

No: 1093

Alterations in blood cell indices and serological parameters due to toxicity of industrial leachate in Wistar rats

Babar Khawar[1], Zillay Mariam[1], Muddasir Abbasi[1], Tasleem Akhtar[1], Nadeem Sheikh[1]

University of The Punjab Department of Zoology Lahore-Pakistan[1]

Background & aims: Industrial leachate is a brownish color liquid containing various toxic heavy metals and other chemicals of organic and inorganic nature which can house a variety of pathogens. As it drains it pollutes the groundwater table and if used for irrigation purpose represents a major health risk not only to humans but also to local flora and fauna. The purpose of current research work was to analyze the toxicity of leachate in Wistar rats.
Methods: Wistar rats of about 250 g were selected and divided into three groups namely Control, Group 1 & Group 2. Group 1 was given 4 ml/kg leachate while Group 2 received 4 ml/kg of 1: 10 diluted leachate intra-peritoneally. After 24 h of the injection, animals were euthanized and blood was drawn for further studies. Data were analyzed using one way ANOVA.
Results: Serological analysis of both Group 1 and Group 2 showed a significant decrease of various components including Cl- ($P = 0.0023$), K + ($P = 0.0002$), Na + ($P = 0.0001$), total proteins ($P < 0.0001$) and albumin ($P < 0.0001$) when compared against control. Similarly, hematological analysis revealed a significant decrease in WBCs ($P < 0.0001$), RBCs ($P = 0.0001$), Hemoglobin ($P < 0.0001$), Platelets ($P < 0.0001$), and MCHC ($P < 0.0001$) while MCV ($P < 0.0001$) showed a remarkable positive change when compared with control. Hematocrit ($P < 0.0001$) was found to be enhanced significantly in Group 1 but decreased in Group 2 while MCH showed exactly opposite trend to Hematocrit.
Conclusion: Findings of current research confirmed that leachate is a highly toxic industrial effluent which leads to hematological and serological changes in biological systems so there is a need of proper waste treatment prior to disposal.

Topic 4: Basic Science of Hepatology

No: 1691

Effect of metal dust on various serological parameters in workers of cutlery industry in wazirabad Pakistan

Nadeem Sheikh[1], Rabia Mehmood[1], Babar Khawar[1], Muddasir H. Abbasi[1]

University of The Punjab Zoology Lahore-Pakistan[1]

Background and aims: The metal toxicity is related to its route of exposure viz. inhaled, ingested or absorbed via skin. Certain metals are carcinogenic and the workers in metal handling factories are at maximum risk of exposure. Wazirabad city of Pakistan is famous for its cutlery works and extensive metal grinding is in practice over there. The present study was intended to check the effects of metal dust in the workers of cutlery industry of Wazirabad.
Materials and methods: Blood samples of the workers working in metal grinding industry were collected and divided in three experimental groups G-1, G-2, G-3 and compared with two control groups named C-1 and C-2. The experimental groups G-1, G-2 and G-3 were based upon the exposure duration i.e. 1-13, 14-26 and 27-40 years respectively in the metal grinding field, compared against C-1 (from Lahore city) and C-2 (from Wazirabad city). The sera were isolated by spinning the samples at 4000 rpm for 15 min. Serological analysis were carried out using commercially available ready to use kits. Data were analyzed using one-way ANOVA using Graphpad prism 5.
Results: Serological analysis showed significant positive variations in Blood Urea($P = 0.0009$), Serum Creatinine($P = 0.0043$), Bilirubin total($P = 0.0178$), ALT ($P = 0.0026$), ALP($P = 0.0211$), Triglycerides ($P = 0.0357$), Cholesterol ($P = 0.0401$), HDL($P = 0.0198$) and LDL($P = 0.0067$) when compared with the C-1.
Conclusion: Taken together these findings, we can conclude that exposure to the metal dust in the respective industry is potentially impairing the kidney and liver functioning and lipid profile of the workers which may be a serious health concern.

Topic 4: Basic Science of Hepatology

No: 2014

Pathological variations of iron deposition in spleen small intestine and kidneys in response to thioacetamide induced toxicity

Tasleem Akhtar[1], Nadeem Sheikh[1], Muddasir H. Abbasi[2]

University of The Punjab Department of Zoology Lahore-Pakistan[1], Government College of Science, Wahdat Road Department of Zoology Lahore-Pakistan[2]

Aims: Iron is an essential element for virtually every form of life due to its key role in most biological systems and metabolic pathways. Under inflammatory conditions, a diversion of iron traffic occurs from the circulation to storage sites of reticuloendothelial system so as to minimize the availability of this essential element. Liver production of hepcidin inhibits the duodenal absorption of iron and promotes iron sequestration by macrophages, while limiting its recycling. The present study was aimed to investigate the changes in tissue iron contents in extrahepatic organs after thioacetamide induced chronic inflammation.
Methods: Male Wistar rats; 150 ± 25 g were given 0.2 g/L of Thioacetamide in drinking water for 18 weeks, whereas control group received normal drinking water. After that animals were sacrificed and spleen, small intestine and kidney were excised and following processing Prussian blue staining was used to analyze histochemical changes.
Results: Histochemical analysis has shown notable reduction of iron contents in the red pulp of splenic tissue of all experimental animals as compared to control tissue. In white pulp, the cells stained for iron were few macrophages in the mantle zone and in marginal zone, most of them were negative for hemosiderin. While in small intestine and kidney no significant difference in iron contents were found in comparison to control.
Conclusion: These observations show that long-term TAA use significantly reduces splenic iron availability and contributes to the

development of the anemia by minimizing iron availability for erythropoiesis.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 1982

The approach to hydatid cyst perforations our clinical experience

Ercan Korkut[1], Şükrü Arslan[1], Erdem Karadeniz[1], Gürkan Öztürk[1], Nurhak Aksungur[2], Sabri Selçuk Atamanalp[1], Bülent Güvendi[1], Bülent Aydinli[1]

Ataturk University Faculty of Medicine General Surgery Erzurum-Turkey[1], Tekman State Hospital General Surgery Erzurum-Turkey[2]

Introduction: Rupture of the hydatic cyst into the abdominal cavity can lead to abdominal pain, urticaria, anaphylaxis, and even sudden death. In this study, we aimed to share the clinical data, our surgical experience and results of 5 patients with hydatic cysts ruptured into the abdominal cavity and compare with the data in the literature.
Material-method: We analyzed 5 cases who had undergone surgery for ruptured hydatid cysts between January 2010 and October 2014.
Results: Of 5 patients, 4 were male and one was female, with the mean age being 28.6 years. In all patients admitted with the complaint of abdominal pain, findings of peritoneal irritation were present. All patients underwent diagnostic abdominal CT. of ruptured hydatid cysts, 3 were located at the right lobe and 2 were at the left lobe. Mean diameter of the cysts was 14.8 cm (6-20 cm). In one patient ruptured cysts, sized 10 cm and 6 cm were present in 8th and 6th segments of the liver. While all patients were treated by partial cystectomy and tube-drainage procedure, a total of 6 bile duct involvements in 3 patients were repaired primarily. No mortality was detected.
Conclusion: Trauma and elevation of intracystic pressure are encountered among causes of rupture in the literature. The risk factors for rupture are young age of the patient, cyst diameter being over 10 cm, and superficial localization of the cyst. In patients who developed rupture, probability of anaphylaxis should not be overlooked and the operation should be performed at the shortest time available.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 1264

A case of liver cyst with biliary communication successfully treated with deroofing

Atsushi Shimizu[1], Shojiro Hata[1], Daisuke Ito[1], Kaoru Kobayashi[1], Masanori Teruya[1], Michio Kaminishi[1]

Showa General Hospital Digestive Surgery Tokyo-Japan[1]

Aim: Liver cysts with biliary communication are rare. Although standard treatment is not established, careful attention should be paid to avoid postoperative bile leakage in surgical procedures.
Methods: We herein report a case of 74-year-old man having multiple liver cysts with elevated serum liver enzymes. Computed tomography revealed one of the cysts measuring 15 cm in size in right liver compressing intrahepatic bile duct. Discharge from percutaneous transhepatic cyst drainage contained pure bile and subsequential endoscopic retrograde cholangiography showed cyst-biliary communication. Because biliary discharge from the placed drainage tube continued, we conducted operation. Deroofing with wide resection of the cystic wall was performed. Necrotic tissues in the liver cyst were removed after deroofing. Although gross detection of biliary fistula was difficult, air injection to common bile duct from the stump of the cystic duct led us to identify two small biliary fistula nearby coming bubbles from the cyst cavity. After repairing the fistula with suture, intraoperative cholangiography confirmed no bile leakage or biliary stricture. Pathological findings of the cyst wall were consistent with a simple cyst. Postoperative course was uneventful and the patient was discharged from the hospital 13 days after the operation. A year have passed since the operation and no recurrent cyst have been detected with computed tomography.
Conclusion: The technique using air injection to common bile duct may be useful for identifying the biliary fistula during surgical deroofing of liver cysts with small biliary communication.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 1709

Ruptured gas forming pyogenic liver abscess into the peritoneal cavity successfully treated with medical treatment

Soo Hyung Ryu[1], Sung Won Park[1], Won Jae Yoon[1], Jin Nam Kim[1], You Sun Kim[1], Jeong Seop Moon[1]

Seoul Paik Hospital, Inje University College of Medicine Department of Internal Medicine Seoul-Korea, South[1]

Introduction: Gas-forming pyogenic liver abscess (GFPLA) which ruptured into the peritoneal cavity is very rare and the mortality rate is very high, in which surgical treatment is usually needed. Here we present a rare case of ruptured GFPLA accompanied with peritonitis and septic shock, which was fully recovered with only medical treatment.
Case report: A 68-year-old woman visited our hospital with a five-day history of fever and abdominal pain. Her serum glucose level was 601 mg/dl and HbA1c level was 10.9 %. Abdominal CT revealed a 10 cm sized huge liver abscess with gas formation in the right lobe of the liver. Also air bubbles and ascites were noted along right subphrenic area and right paracolic gutter due to leakage from a hepatic abscess. Ultrasound-guided percutaneous catheter drainage (PCD) was immediately performed, and broad spectrum intravenous antibiotics and insulin were given. Later, Klebsiella pneumoniae was isolated from both blood and pus of a liver abscess. Her medical condition deteriorated and progressed into severe metabolic acidosis by sepsis. She underwent continuous renal replacement therapy (CRRT) for three days. The follow-up abdominal CT showed a significant decrease in the size of the abscess cavity and diminished fluid collection and air bubbles of extra-hepatic sites. She was recovered and discharged, and in good health at follow-up.
Discussion: To reduce morbidity and mortality in case of a ruptured GFPLA, adequate antibiotics, good control of blood glucose, and early adequate PCD are mandatory. Surgery should not be delayed if medical treatment with PCD fails.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 1675

Our experience on solid pseudopapillary neoplasm of pancreas (SPN)

Yusuf Kayar[1], Birol Baysal[1], Ali Tuzun Ince[1], Mehmet Sait Bugdaci[1], Ahmet Danalioglu[1], Hakan Senturk[1]

Bezmialem Vakif University Gastroenterology Istanbul-Turkey[1]

Background/aim: SPN is a rare entity. It is almost exclusively seen in females and occurs in the second or third decades of life. Due to very limited number of cases seen, the natural history of the disease is not fully understood.
Aim: To evaluate clinic and histopathologic characteristics as well as the estrogen and progesteron receptor status of the patients.
Methodology: Data of patients with SPN was retrospectively evaluated. Demographic, laboratory, radiological, surgical and pathological features and the immuno-histochemical findings were considered.
Result: Five patients (1.5 %) among 323 patients with pancreas malignancies were diagnosed with SPN. of these, 4 were females and mean age 27 (range: 16–50). CA 19–9 levels were normal in four patients while slightly increased in one (60 U/mL (0–33)). Mean of size of the lesions was 7.6 cm (5-10.3). Immunohistochemical analysis demonstrated that progesteron and estrogen receptors were positive in 80 % and vimentin, β-Catenin, CD10, CD56, p53, Ki-67 index were positive in all of the patients.
Conclusion: Despite patients with SPN have an excellent prognosis after surgical excision, our study draws attention to the hormonal status and receptor variety of SPN, that may be evaluated in many fields such as differential diagnosis and therapy in the future.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 2173

Fasciola hepatica infection at Van Yuzuncu Yil University research hospital

Mahmut Sunnetcioglu[1], Ümüt Yakan[1], Abdussamed Batur[1], Mustafa Kasım Karahocagil[1], Fatih Esmer[1]

1yuzuncu Yil University, Medical Faculty Infectious Diseases and Clinical Microbiology Van-Turkey[1]

Objective: The goal of our study is to determine eosinophile level and antibody rates used in the diagnosis of F. hepatica (FH) and to compare with ultrasound and tomography results.
Materials and methods: Data from 18 patients with fascioliasis who were admitted in the department of Infectious Diseases and Clinical Microbiology of Yuzuncu Yil University Hospital between January 2013 and December 2014 were analyzed retrospectively.
Results: Of the patients diagnosed with fascioliasis, 13 were female and 5 were men. The most common symptom was abdominal pain, nausea, vomiting and the most common clinical finding was abdominal tenderness and hepatosplenomegaly. In all subjects, initial complete clinical history, physical examination findings, routine laboratory results including complete blood count and routine biochemical analysis were recorded. The clinical manifestations was hepatosplenomegaly. Eosinophilia was the most common laboratory finding. No parasite eggs were found in feces. F. hepatica antibodies were investigated in serum samples taken from 18 patients by using the İndirekt Hemaglutinasyon (IHA) method and 6 of these were positive. Abdominal ultrasound (US) examination and computed tomography (CT) was performed in all patients with F. Hepatica infection. The most common radiological findings were typical lesions in the liver. The lesions were subcapsular round or settle around the biliary tract in the liver. In all patients were diagnosed via clinical, laboratory and radiological findings.
Conclusion: With this study, in fasciolozis diagnosis; of the presence of common clinical symptoms, eosinophilia, Fasciola hepatica antibodies and to compare with the radiological findings.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 1823

Eosinophilic peritonitis caused by liver cyst hidatic in a patient receiving maintenance peritoneal dialysis

Sebahat Basyigit[1], Feyza Bora[2]

Kecioren Research and Training Hospital Gastroenterology Ankara-Turkey[1], Yenimahalle State Hospital Nephrology Ankara-Turkey[2]

Hydatid disease is frequently caused by Echinococcus Granulosus. The liver is one of the most commonly infected organs. Peritoneal echinococcosis is a very rare state. Echinococcosis related peritonitis have not been reported in any patients receiving maintenance peritoneal dialysis (PD).

A 56-year-old female maintained PD admitted to our hospital complaining with abdominal pain and fever. On admission, she was febrile, her abdomen was diffusely tender. Laboratory studies revealed the following: white blood cell (WBC) count 13090/mm3 (36 % eosinophil), hemoglobin 11,4 gr/dL, platelet 284000/mm3. The peritoneal fluid showed 5030/mm3 WBC (60 % eosinophil). She had been given empiric intravenous (i.v) antibiotic combinations. One week later, she was stil febril. Ultrasound for tunnel infection were normal. Routine evaluations for bacteria, fungi and mycobacteria were negative. Computerized tomography showed 86x87x66 mm in size multiloculized cystic lesion in the left lobe of liver. There was no cystic formation in the peritoneal cavity. E. granulosus immunoglobulin G was > 200 mg/dl. The patient was diagnosed as hydatid peritonitis and given albendazole 4x500 mg. The patient was offered surgical intervention but declined. After 2 week from starting the albendazol clinical signs was resolved. Decreasing in WBC and eosinophil count in dialysate was observed. Patient was discharged recommending to continue therapy for 3 months.

Parasiter infections should be considered in PD patients who has negative peritoneal culture. The spillage of scolex may occurred during insertion of tenckhoff catheter in PD patients who had intra-abdominal hydatid cyst.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 1978

Detecting biliary tract participation in cyst hydatid surgery treatment a series of 103 cases

Şükrü Arslan[1], Erdem Karadeniz[1], Ercan Korkut[1], Gürkan Öztürk[1], Nurhak Aksungur[2], Sabri Selçuk Atamanalp[1], Bülent Aydinli[1]

Ataturk University Faculty of Medicine General Surgery Erzurum-Turkey[1], Tekman State Hospital General Surgery Erzurum-Turkey[2]

Purpose: In our study, we examined the efficiency of the open biliary duct detection method with the help of a catheter applied to cystic duct in cases treated surgically in our clinic due to hepatic cyst hydatid disease.
Material-method: The patients operated due to cystic duct disease in our clinic between the dates January 2010 and October 2014 were examined retrospectively. The demographic properties and findings in the operations of 103 patients whose biliary tract participations were examined and recorded.

Findings: 56 of the patients were female, and 47 of them were male. The mean age value was 35,3. In 32 of the 103 patients, biliary tract participations were detected directly without any other processes being necessary. In total, 54 biliary tract participations were detected in these 32 patients. Biliary leakage was examined in 71 patients with the help of a feeding catheter applied through the cystic duct by giving pressured physiological saline solution. In 56 of these patients, biliary tract participations were detected which were not previously detected before the process. The 145 biliary tract participations in 56 patients were fixed as primary mode of treatment.
Result: Biliary tract participations are among major problems in cyst hydatid cases and increase morbidity and mortality. The open biliary duct detection by applying cysticostomy with the help of an intraoperative feeding catheter, and giving pressured physiological saline solution is an efficient method in order to decrease the biliary fistula rates.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 2008

Malignant paraganglioma of the common hepatic duct

Hyoun Soo Lee[1], Sang Goon Shim[1], Man Je Park[1]

Samsung Changwon Hospital, Sungkyunkwan University School of Medicine Internal Medicine Changwon-si-Korea, South[1]

Introduction: Paragangliomas are rare extra-adrenal neoplasms of the neural crest origin. The most common extra-adrenal location of these tumours is the retroperitoneum. So far only four cases of paraganglioma of the hepatic bile duct have been reported.
Case report: A 75-year-old man presented with obstructive jaundice for the last two days. He had no symptoms of headache, palpitation or family history of any malignancy. Physical examination revealed moderate icterus. Serum conjugated bilirubin level was 4.7 mg/dL, aspartate transaminase (AST) level was 102 IU/L, alanine transaminase (ALT) level was 73 IU/L and serum alkaline phosphatase (SAP) level was 123 IU/L. A non-contrast enhanced computed tomography scan of the abdomen revealed about 1.3 cm × 1.2 cm heterogeneously enhancing lesion in common hepatic duct with dilatation of intrahepatic duct. He was scheduled for Endoscopic retrograde cholangiopancreatography (ERCP) for confirm of common hepatic duct's lesion. ERCP was done with ballooning. After that, the CHD mass lesion extracted spontaneously from ampulla of vater. The extracted lesion was about 1.5 cm × 1.5 cm × 1.5 cm size and revealed necrotic and edematous change on the surface. The lesion's histopathology revealed a malignant paraganglioma of the bile duct. Therefore we recommended surgical treatment. But the patient and guardian refused due to patient's age and general condition. Presently jaundice was improved and bilirubin was normalized, so we have done supportive care.
Conclusion: We want to report malignant paraganglioma of the common hepatic duct.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 1981

Our surgical results in hydatid cyst disease a series of 214 cases

Şükrü Arslan[1], Ercan Korkut[1], Erdem Karadeniz[1], Gürkan Öztürk[1], Sabri Selçuk Atamanalp[1], Nurhak Aksungur[1], Bülent Güvendi[1], Bülent Aydinli[1]

Ataturk University Faculty of Medicine General Surgery Erzurum-Turkey[1]

Aim: Open surgery, laparoscopic surgery and percutaneous drainage are standard methods of treatment in hydatid cyst disease, which is endemic in Eastern Anatolia Region. In our study, the results of the cases treated surgically with the diagnosis of hepatic hydatic cyst in our department were evaluated.
Material and method: Patients who underwent surgery with the diagnosis of hydatid cyst disease in our center between January 2010 and October 2014 were analyzed retrospectively. The demographic characteristics and operative findings were noted for 214 patients involved in the study.
Results: 121 of the patients were female (mean age: 36.3) and 93 were male (mean age: 35.6). While 196 of 214 patients underwent partial cystectomy and tube drainage, 10 patients were treated with non-anatomic resections, 6 patients with left hepatectomy and 2 patients with left lateral segmentectomy. Hydatidosis was diagnosed in 6 patients, cyst abscess in 5 patients and cyst rupture in 5 patients. In 13 of 196 patients who underwent partial cystectomy, the procedure was performed laparoscopically. During surgery, cysticostomy and control for intracystic bile leakage was performed by the help of a feeding catheter in 71 patients; 56 bile duct involvements were repaired primarily.
Conclusion: For treatment of complicated and multiple cysts, which are not possible to be managed percutaneously, open and laparoscopic methods are preferred. In some patients, segmentectomy and hepatectomy may be needed. Intraoperative detection and repair of bile leaks reduces morbidity.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 2131

Early period results of the first 13 patients to whom we applied laparoscopic surgery in liver cystic hydatic treatment

Erdem Karadeniz[1], Şükrü Arslan[1], Ercan Korkut[1], Nurhak Aksungur[2], Gürkan Öztürk[1], Bülent Aydinli[1]

Ataturk University General Surgery Erzurum-Turkey[1], Tekman State Hospital General Surgery Erzurum-Turkey[2]

Purpose: Open surgery is being slowly replaced by laparoscopic surgery with the improvements in laparoscopic surgery. Our purpose is to share the results of 13 patients whom we treated laparoscopically in our clinic.
Method: Between the years 2010 and 2014, 13 patients who were serologically and radiologically diagnosed as having hydatic cyst, but who could not be treated with percutaneous method received laparoscopy. The surrounding of the cyst was wrapped with sponges that were immersed in savlon solutions. Savlon was injected into the cyst with the Veres injector. After the cystitomy was performed, the contents of the cyst were taken out of the abdomen with a specimen bag or an aspirator.
Findings: 6 of the patients were female, and 7 of them were male. The mean age was 28. There were 16 cysts in total in the patients. 12 of these cysts were located in the right lobule, and 4 of them were located in the left lobule. The diameter of the smallest of the cysts was 5 cm, and the diameter of the biggest was 20 cm. All of the patients received partial cystectomy and tube drainage. The average operation time was 62 min. The average hospitalization time was 4.1 days. No morbidity and mortality were observed in the patients.
Result: The laparoscopic surgery is a method that can be used safely in the liver cyst hydatic treatment in proper cases. It is important that

due care is given while taking out the contents of the cyst to prevent the relapses in the abdomen.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 1335

Indication and outcome of liver resection for giant liver cysts

Hiroki Kajioka[1], Masaru Inagaki[1], Nanako Yasui[1], Kouji Kitada[1], Naoyuki Tokunaga[1], Gou Nishii[1], Masaaki Akai[1], Takashi Nonoshita[1], Kengo Kawada[1], Kenta Isoda[1], Manabu Nishie[1], Ryosuke Hamano[1], Hideaki Miyaso[1], Yosuke Tsunemitsu[1], Shinya Othuka[1], Kazuhide Iwakawa[1], Hiromi Iwagaki[1]

National Hospital Organization Fukuyama Medical Center Surgery Hiroshima-Japan[1]

Introduction: A giant hepatic cyst was basically benign tumor, but it has the malignant potential and sometimes evokes infectious complications. Treatment strategy is controversial.
Methods: We reviewed 8 patients of liver resection for giant hepatic cysts between March 2004 to April 2014.
Results: 4 cases were female and 4 cases male, with an average age of 73 years old (range: 63-83 years old). Chief complaints were abdominal pain in 4 patients, fever in 2, and epigastric distress in 1. Preoperative diagnosis were simple liver cyst in 2 cases, infected cyst in 3, and liver cyst with suspicious of malignancy in 3. Mean diameter of cysts was 12.6 cm (range: 5.5-17 cm). Operative procedures were right trisegmentectomy in 2 cases, left lateral segmentectomy in 2, right lobectomy in 2, extended right lobectomy in 1, and right trisegmentectomy with caudate lobectomy in 1. Mean operation time was 427 min (range: 282-647 min) and mean blood loss was 1134 ml (range: 400-2000 ml). Histopathological examination diagnosed as cystoadenoma in 1 case, but all cases had no malignancy. Mean postoperative hospital stay was 19 days (range: 14-24 days). Postoperative complications developed in 3 cases (i.e.; pancreatitis, portal vein thrombosis, and intraabdominal abscess). 7 cases existed cysts in remnant liver, but no recurrence of giant liver cysts had been detected.
Conclusions: Giant liver cysts always affect the anatomical positions of blood vessels and bile ducts, so the hepatic resection is more complicated. Liver resection is an important option for the treatment of giant liver cyst, but we should care to avoid postoperative complications.

Topic 5: Cystic Disorders of the Liver and Biliary System

No: 1927

Pericholangitic abscess

Sebahat Basyigit[1], Bora Aktas[1], Elif Aktas[2], Yasar Nazligul[1]

Kecioren Research and Training Hospital Gastroenterology Ankara-Turkey[1], Dr. Abdurrahman Yurtaslan Oncology Hospital Radiology Ankara-Turkey[2]

Pericholangitic abscess (PA) is a rare form of liver abscesses which is connected with biliary tree. It has remained radiological diagnosis and its clinical course and treatment approaches have not been defined. With increasing use of radiologic techniques, clinicians began to encounter with PA more often. In our cases patients were treated with ERCP and antibiotherapy. ERCP provide the biliary drenaige and should be considered in the treatment of PA.
Case 1
57-year-old female patient admitted to hospital with right upper quadrant (RUQ) pain and fever. In physical examination there was tenderness in RUQ and her temperature was 38,5 C. Laboratory analysis revelead leukocytosis (15800/mm3), ALT: 18 U/L, AST: 41 U/L, GGT: 118 U/L, ALP: 201 U/L, Total bilirubin: 1,36 mg/dl, D. Bilirubine: 0,3 mg/dl. Her abdominal computerized tomography (CT) showed multiple millimetric PAs (figure). She underwent ERCP procedure and was given cephoperazone 2x1 gr. Her clinical and laboratory signs became normal in one week.
Case 2
63-year-old male patient admitted to hospital with RUQ pain. He had tenderness in RUQ in physical examination. He had history of sump operation. Laboratory analysis showed leukocytosis (15700/mm3), ALT: 225 U/L, AST: 210 U/L, GGT: 209 U/L, ALP: 120 U/L, Total bilirubin: 0,73, D. Bilirubine: 0,33, CRP: 47 mg/dl. His abdominal CT showed dilatation in all bile ducts. In the right lob of the liver, there was a 6 cm diameter PA (Figure 2. He underwent ERCP and was given cephtriaxon 2x1 gr. His clinical and laboratory signs were improved in ten days.

Topic 6: Drugs Herbals and Liver

No: 1214

Young people living with liver disease experiences of taking medication

Shahreen Bashir[1], Pam Lowe[1], Elizabeth Peel[2]

Aston University Languages and Social Sciences Birmingham-United Kingdom[1], University of Worcester Institute of Health & Society Worcester-United Kingdom[2]

Young people living with liver disease in the United Kingdom are currently an under-researched population and scant attention has been given to their experiences of managing their medication. This research project was funded by The Children's Liver Disease Foundation and has explored 33 liver disease patients' experiences of managing medication through semi-structured, in-depth interviews. Participants in this research were aged between 14–25 years with a range of liver diseases differing in aetiology and onset age. They reported taking a variety of medicines ranging from immunosuppressants, steroids and medicines for comorbid conditions. Preliminary findings revealed young people reported accounts of facing various challenges associated with managing medication. Physical challenges included the repulsive taste of liquid medicines, difficulty swallowing large tablets and remembering to take the medicine with them when outside of the home. Social challenges included the stigma of taking medicines in the presence of peers. Some young people reported unfavourable side effects such as unwanted hair growth, hair loss and weight gain. Practical challenges of managing medication included life changes such as introducing meals before taking tablets and organising doses in advance as a management strategy. Not all young people face difficulties in managing medication and young people acquire the responsibility of managing their own medication from their parents at different stages in their life. If we are going to improve services for young liver disease patients it is imperative health professionals understand of the impact of medicine taking on the lives of their patients.

Topic 6: Drugs Herbals and Liver

No: 2221

Low molecular weight heparin combined with warfarin improved survival in patients with tusanqi related hsos

Huimin Guo[1], Yuzheng Zhuge[1]

Nanjing Drum Tower Hospital Department of Gastroenterology Nanjing-China[1]

Background: Hepatic sinusoidal obstruction syndrome (HSOS) is associated with a high mortality because of its severity and lack of effective therapy. In China, it is most commonly induced by herbal medicine containing Pyrrolizidine alkaloid(PA), especially by Gynura segetum duing to misstaking of TuSanQi. Given the paucity of study on HSOS induced by Gynura segetum, the purposes of our study were to investigate the long-term outcome of the treatment for Gynura segetum-related HSOS, and to determine the risk factors related to the progression of the disease.
Methods: Between 2008 and 2013, patients because of HSOS admitted to our department were recruited. Clinical characteristics, laboratory examinations and ultrasound data were collected. All patients, according to be treated with two different therapies, were divided into two groups (A and B). The rates of complete recovery and the mortality were analysised with Chi square test. Logistic regression modeling was performed to determine the predictors of prognosis of complete recover.
Results: 40 patients were collected. Patients ingroup A were treated with diuretic, prostaglandin E1 and tanshinone. Patients in group B were treated with low molecular weight heparin (Fraxiparine) and Warfarin besides the medines used in group A. As a result, complete recovery rate and mortality rate was 63.2 % (12/19) and 15.8 % (3/19) in group B, while which was 28.6 % (6/21) and 71.4 % (15/21) in group A, respectively. There were significant differences between the two groups in terms of the complete recovery rate ($P = 0.03$) and the mortality rate ($P = 0.01$). As a remedial measure, transjugular intrahepatic portosystemic shunt (TIPS) was utilized in one patient in group A and three patients in group B. On logistic regression modeling, anticoagulation therapy with Fraxiparine and Warfarin, early therapeutic intervention and decreased bilirubin concentration in the course of disease were significant predictors of complete recover.
Conclusions: Anticoagulation therapy with low molecular weight heparin and Warfarin may be effective of HSOS resulting from TuSanQi. Early therapeutic intervention and decreased bilirubin concentration in the course of disease may be indicative of a favorable outcome. TIPS may be a remedial treatment for severity cases.

Topic 6: Drugs Herbals and Liver

No: 1995

Artesunate suppresses proliferation and induces apoptosis and autophagic cell death of activated hepatic stellate cells

Yuanwei Pan[1], Jian Ping[1], Lieming Xu[1]

Shuguang Hospital Affiliated To Shanghai University of Traditional Chinese Medicine Institute of Liver Diseases Shanghai-China[1]

Aim: To deal with apoptosis and autophagy of human hepatic stellate cell line (LX-2) induced by artesunate, which is a derivative of Artemisinin, through JNK pathways.
Methods: LX-2 was incubated with artesunate for 4 h, 8 h, 12 h or 24 h. The cell viability was detected for cell counting kit-8. The apoptosis rate was measured by cytometric analysis. The FITC/PI dyeing was observed by using confocal microscope. The expression of cleaved caspase-3, Bcl-2, LC3B, JNK, p-JNK and LC3B were by Western blotting analysis.
Results: Artesunate (10, 20, 40, 60, 80 and 100umol/L) can inhibit the proliferation of LX-2 in a dose-dependent fashion (vs. controls, each $P < 0.01$) and Artesunate (100umol/L) increased about apoptosis rate of LX-2 for two folds of controls ($P < 0.01$). The expression of LC3B, a marker protein of autophagy, was inhibited by SP600125, an inhibitor of JNK (0.6 folds vs. controls, $P < 0.05$) in 24 h. Artesunate, however, increased the expression of p-JNK (1.1 folds vs. controls, $P < 0.01$) and induced express of LC3B protein in 24 h (1.5 folds vs. controls $P < 0.01$). Apoptosis induced by artesunate was observed by fluorescence staining. Artesunate could also induce the expression of cleaved caspase-3 (1.3 folds vs. controls, $P < 0.01$) and decrease the expression of Bcl-2 (0.3 folds vs. controls, $P < 0.01$) in 12 h.
Conclusions: Artesunate can remarkably decrease the viability of LX-2. It can induce autophagy and apoptosis in LX-2. The JNK pathway maybe involved in the process of autophagic cell death and artesunate could up-regulate this signaling pathway.

Topic 6: Drugs Herbals and Liver

No: 1926

Propylthiouracil induced asymptomatic toxic hepatitis

Murat Eser[1], Mithat Eser[2], Sebahat Basyigit[3], Zeliha Asilturk[1], Yasar Nazligul[3]

Kecioren Research and Training Hospital Internal Medicine Ankara-Turkey[1], Gulhane Military Medical Academy Internal Medicine Ankara-Turkey[2], Kecioren Research and Training Hospital Gastroenterology Ankara-Turkey[3]

38-year-old female patient admitted to hospital complained with fatigue. She had no special medical history except Grave's disease. She had been taking propylthiouracil (PTU) 300 mg/day for 1 month. She had no history of another medication, eating mushroom, alcohol consumption, travelling, family history of liver disease. Her physical examination were normal. Laboratory analysis revealed that ALT: 543 U/L, AST: 227 U/L, GGT: 66 U/L, ALP: 136 U/L. Serum levels of bilirubin and albumin,, INR, complete blood count and thyroid function tests were normal. She has been learned to have normal liver function test (LFT) before using PTU from medical records. PTU was discontinued and she has been given methimazole. She was examined for the etiology of abnormal LFT and no specific etiology was detected except PTU related toxic hepatitis. In her follow-up LFT has turned to normal level as shown table 1.

Hepatotoxicity is rare but major side effect of PTU. Its fatality rate has been suggested to be high as 25 %–50 % in the literature. But reported fatality rates are thought to be overestimated, because of the number of both unreported and undiagnosed, asymptomatic cases. The available data are also insufficient to establish if LFT abnormalities are seen in patients taking PTU (1). Because of asymptomatic cases remain nonvisible part of the iceberg and there is no consensus about such cases, here we reported a case of PTU related asemptomatic toxic hepatitis to exemplify the clinical course of such cases

Topic 6: Drugs Herbals and Liver

No: 2005

A peptide based nanofibrous hydrogel for delivering a novel non nucleosidic hbv inhibitor in vitro

W. Wang[1], X.y. Wang[1], Y. Liu[2], X.y. Jiang[2], H.s. Chen[1], L. Wei[1]

Peking University People's Hospital, Peking University Hepatology Institute Hepatology Beijing-China[1], National Center For Nanoscience and Technology Cas Key Lab For Biological Effects of Nanomaterials and Nanosafety Beijing-China[2]

Aim: The development of bioengineering has provided powerful tools in medical fields. Some enzyme-triggered hydrogels can self-assemble into defined structure which useful as the drug delivery systems. Here, we used a novel peptide-based nanofibrous hydrogel (named MI2) for loading GLS4, a member of heteroaryldihydropyrimidines (HAP) compound, which is the first HBV core particle-targeted non-nucleosidic inhibitor developed in China, and investigated the anti-HBV effect of the GLS4-loaded hydrogel (GLS4-MI2) in vitro.
Method: MI2, as a short peptide to construct gelators of nanofibrous hydrogel, was well synthesized and mixed with GLS4 in phosphate buffered saline, and then alkaline phosphatase was added to turn the solution into hydrogel at room temperature. The surface morphology of the hydrogel was observed by transmission electron microscope. Anti-HBV effect was studied by measuring HBV DNA in cell supernatant 7 days after adding PBS, GLS4 solution, blank MI2, GLS4-MI2 into HepG2.2.15 cell line, respectively. The toxicity of the MI2 alone was investigated by measuring the cell viability after co-incubation with HepG2.2.15.
Conclusion: After addition of alkaline phosphatase, the solution became slightly turbid and then turned into translucent hydrogels within 10 min. The hydrogel showed nanofibrous structure with the width of about 10 nm. The HBV inhibition of GLS4 was improved from 30.4 % to 61.0 % after loading GLS4 into hyrogel at the concentration of 10nM/L. MI2 alone has no effect on the cell viability after 48 h co-incubation with HepG2.2.15. The results revealed that the peptide-based nanofibrous hydrogel may be a safe material which can provide an alternative mean to efficiently deliver anti-HBV drugs.

Topic 6: Drugs Herbals and Liver

No: 1531

Misdiagnosis of drug induced liver injury a case report

Xu Li[1], Yang Gao[1], Huifan Ji[1], Xiaolin Guo[1]

The First Hospital of Jilin University Hepatology Changchun-China[1]

Aims: Drug-induced liver injury (DILI) can pose substantial diagnostic, prognostic, and therapeutic challenges to the practicing gastroenterologist.
Methods: A 68-year-old female with a medical history significant for hypertension and diabetes presented complaining of yellow eyes for 2 years, as well as progressively worsening fatigue and pruritus over the last 2 weeks. Her medications included traditional Chinese medicine for diabetes. She also reported obvious abnormal liver function tests one year earlier. A liver puncture was proceeded at a local clinic before admission and the histopathology tend to a diagnosis of vanishing bile duct syndrome. On admission, laboratory results revealed TBil of 115.1 umol/L, AST of 87 U/L, ALP of 643 U/L, γ-GT of 1012 U/L, CA199 of 56.54U/mL, with the remainder of the laboratory tests(autoimmune liver disease related antigen, prothrombin time) within normal limits. Abdominal CT scan demonstrated chronic liver damage and Magnetic Resonance Cholangiopancreatography did not show any abnormities of biliary tract. A liver biopsy was performed and pathologists demonstrated chronic drug-induced liver injury. Besides discontinuation of suspected drugs, reduced glutathione and UDCA were given. The patient was discharged on hospital week #4, at which time her TBil had fallen to 68 umol/L, ALT to 50 U/L, ALP to 198 U/L, γ-GT to 319 U/L, AST had normalized to 35U/L. No recurrence after follow-up hitherto.
Conclusions: Early diagnosis and treatment of drug-induced liver injury can prevent its complications

Topic 6: Drugs Herbals and Liver

No: 1148

Prolonged cholestatic liver disease secondary to methotrexate

Yahya Atayan[1], Yasir Furkan Çağın[1], Mehmet Ali Erdoğan[2], Yılmaz Bilgiç[2], Murat Aladağ[2]

Inönü Üniversity Gastroenterology Malatya-Turkey[1], Inönü Üniversity Gastroenterolog Malatya-Turkey[2]

Drug-induced hepatotoxicity varies from non-specific liver changes to acute fulminant failure, cirrhosis and liver cancer. Methotrexate (MTX) is a folate antagonist which damages the DNA and it is classified as an antimetabolite antineoplastic agent. It may cause acute increase in transaminase enzymes, and on the long-term it may lead to liver fibrosis and cirrhosis. Because liver damage does not correlate with the increase in liver enzymes, it was recommended to obtain a liver biopsy once a cumulative dose of 1.5 grams is consumed (6).In this case report, A 52 year old male patient was diagnosed with rheumatoid arthritis 4 years ago. He was started on MTX tablet, we introduce a case in which hepatic fibrosis and prolonged cholestatic liver disease occurred secondary to prolonged usage of MTX.

Topic 6: Drugs Herbals and Liver

No: 1441

Chronic lead poisoning: hepatologist's perspective

Ananta Shrestha[1], Thupten Lama[1], Akhilesh Kasyap[2], Sneha Karki[3]

Liver Foundation Nepal Hepatology Kathmandu-Nepal[1], Bir Hospital Gastroenterology Kathmandu-Nepal[2], Civil Service Hospital Medicine Kathmandu-Nepal[3]

Background: Chronic lead toxicity causes abnormalities in multiple systems resulting mainly in neurologic, hematological and gastrointestinal symptoms. However, little is known about the impact of lead poisoning on liver.
Methods: Four patients presented with severe abdominal pain requiring hospital admission due to lead poisoning, They were evaluated to assess the biochemical, hematological, and imaging features of the liver as well as gastroenterological system.
Results: Three of them were male. Peripheral blood film revealed basophilic stippling in all four cases and blood lead levels were markedly elevated. Clinical features are shown in table 1. Mild normochromic normocytic anemia, constipation and bloating were

present in all the patients while two of them had intestinal pseudo-obstruction. Mild conjugated hyperbilirubinemia and increased levels of alanine aminotransferase (up to 5 times the upper limit of normal) were in all four patients. Hepato-splenomegaly was seen in two of them. All four patients received Penicillamine and monitored for 3 monthly with blood and urinary lead levels. All four responded to penicillamine and therapy was stopped after blood lead levels were normalized.
Conclusion: The reported cases were referred to hepatologist for deranged liver function tests identified during evaluation of recurrent pain abdomen. Mild anemia, abdominal bloating and features of chronic intestinal pseudoobstruction with mildly deranged liver function test should raise suspicion for lead toxicity. Peripheral blood film was found to be very useful screening tool for detection of chronic lead poisoning. Penicillamine appears to be effective in treating lead poisoning.

Topic 6: Drugs Herbals and Liver

No: 1622

A late hepatotoxicity associated with imatinib mesylate in a patient with gist

Dilek Erdem[1], Talat Ayyildiz[2], Ahmet Bektaş[2]

Medical Park Hospital Medical Oncology Samsun-Turkey[1], Ondokuz Mayis University Gastroenterology Samsun-Turkey[2]

Introduction: Imatinib mesylate is a multifunctional tyrosine kinase inhibitor and used for chronic myeloid leukemia and gastrointestinal stromal tumor (GIST). Only a few cases of imatinib-related hepatotoxicity have been reported in GIST patients. Here, a case of delayed toxicity, imatinib-induced hepatototoxicity, is reported which occurred at 28 weeks of imatinib therapy.
Case: A 59-year-old female patient had a mass (11 x 9 x 6 cm) located between left hepatic lobe and stomach which was subsequently resected. Histopathological examination of the tumor showed a mitotic index of 6 per 50 high-power fields and Ki-67 was under 5 %. Tumor stained positively for CD117, CD34 and SMA and negatively for desmin and was diagnosed as GIST. Treatment with imatinib mesylate 400 mg daily was initiated. Biochemical tests were normal before treatment. She had no history of hepatitis or alcohol use. Elevations in liver function tests were detected at follow-up visits. At 28 weeks of treatment, her laboratory investigations showed a total bilirubin of 0.68 mg/dl, alanine aminotransferase of 481.3 UI/L, aspartate aminotransferase of 341.5 UI/L, alkaline phosphatase of 87 U/L, and international normalized ratio of 1.19. Liver biopsy report included findings of subacute hepatitis consistent with toxic hepatitis. After discontinuation of imatinib, liver enzymes gradually fell and returned to normal before discharge.
Conclusion: Our patient developed hepatocellular toxicity during imatinib therapy. Liver function tests should be monitored closely while using imatinib. It should be kept in mind that in addition to transient and usually asymptomatic LFT elevations, imatinib may cause reactivation of latent chronic hepatitis B infection.

Topic 6: Drugs Herbals and Liver

No: 1250

Long term methotrexate use is not associated with liver stiffness

Ibrahim Hatemi[1], Caner Saygın[2], Didem Uzunaslan[2], Gülen Hatemi[2], Nurhan Demir[1], Sebati Özdemir[1], Abdullah Sonsuz[1]

Istanbul University, Cerrahpaşa Faculty of Medicine Department of Internal Medicine, Division of Gastroenterology Istanbul-Turkey[1], Istanbul University, Cerrahpaşa Faculty of Medicine Department of Internal Medicine, Division of Rheumatology Istanbul-Turkey[2]

Aim: Liver fibrosis could be related to long term methotrexate (MTX) use. Elastography may help to detect patients with increased risk of liver fibrosis. The aim of this study is to evaluate liver stiffness associated with long term MTX use among rheumatoid arthritis (RA) patients.
Methods: We included RA patients with a disease duration of at least 10 years and who had used MTX for at least 5 years ($n = 45$). Control groups were RA patients with a similar disease duration but no MTX use ($n = 9$), healthy control composed of hospital staff ($n = 22$) and hepatitis B related cirrhosis patients with Metavir score ≥ 3 as positive controls ($n = 9$) Fibroscan was carried out by two gastroenterologists who were blinded to the diagnoses of the patients. The liver stiffness levels were compared using ANOVA.
Results: There was no difference in mean liver stiffness level between RA patients who had used MTX (5.1 ± 2.4 kPA), who had not used MTX (5.4 ± 2.2 kPA) and healthy controls (5.2 ± 2.0 kPA) (F2df: 0.05, $P = 0.95$). The mean liver stiffness level was significantly higher among cirrhosis patients (22.8 ± 21.1 kPA) compared to the other groups (F3df: 17.13, $P < 0.0001$). The median cumulative MTX dose was 1402 mg (range 293 - 16625 mg). The mean duration of MTX use was 12 ± 9.4 years.
Conclusion: MTX use over 5 years seems to be safe in terms of liver fibrosis in RA patients. Transient elastography may be a useful method to screen patients who are at risk.

Topic 6: Drugs Herbals and Liver

No: 1032

Nerium oleander novel hepatoprotective plant reversing experimental thiocetamide induced hepatotoxicity

Tasleem Akhtar[1], Nadeem Sheikh[1]

University of The Punjab Department of Zoology Lahore-Pakistan[1]

Aims: The present study was aimed to investigate the protective effect of Nerium oleander leaves extract against liver toxicity induced by thioacetamide. Nerium oleander has historically been considered a poisonous plant. Despite its toxic potential, all parts of plant are reputed as therapeutic agents. Thioacetamide is reported as model hepatotoxicant, prolonged oral intake of this chemical leads to hyperplastic liver nodules, liver cell adenomas, cholangiomas and hepatocarcinomas.
Methods: *Rattus norvagicus*, weighing 150 ± 15 g were divided into three groups ($n = 5$) Con, T1 & T2. Con group was provided with normal drinking water, among the treated groups T1 was given thioacetamide (200 mg/l) in drinking water for 18 weeks and T2 was given thioacetamide (200 mg/l) in drinking water for 18 weeks plus additional 7 days oral intake of Nerium oleander leaves extract.
Results: Serological analysis showed significant decrease in Alanine transaminase ($P = 0.001$), Albumin ($P = 0.005$), total proteins ($P = 0.0007$) and significant increase in Bilirubin level ($P = 0.01$). Histopathological analysis of liver sections of T1 group showed severe toxicity characterized by vascular fibrosis, aggregation of lymphocytes in fibrotic area, degenerated hepatic lobular architecture, hepatopoises, necrotic cells infiltration, increased sinusoidal Kupffer cells density low degree cirrhosis, and mild level of haemorrhage. In T2, Nerium oleander

appeared to reduce the thioacetamide induced toxicity as evidenced by lower degree of hepatic lobular architecture deformation, vascular fibrosis initiating and low degree of hepatocytic necrosis.
Conclusion: Thioacetamide provides the foundation of chronic liver injury whereas Nerium oleander extract have the potential to reverse or at least minimize the liver injury due to its potential hepatoprotective nature.

Topic 6: Drugs Herbals and Liver

No: 1472

Liver injury due to venlafaxine in a patient with depression

Ahmet Dogru[1], Fuat Ekiz[2]

Hatay Antakya State Hospital Department of Psychiatri Psychiatri Hatay-Turkey[1], Hatay Antakya State Hospital Department of Gastroenterology Gastroenterology Hatay-Turkey[2]

Antidepressants are generally prescribed and use in the treatment of depression, anxiety and psychiatric disorders. These durgs are associated with a lot of adverse reactions including hepatotoxicity. Selective serotonin reuptake inhibitors and venlafaksine can cause reversible liver toxicity upon discontinuation of the agent. Herein, we present a case of liver injury due to venlafaxine in a patient with depression. A 27 years old man was consultated to our department because of elevated transaminases. In his history, he has only used venlafaxine 150 m/day for a month due to depression, he mentioned no alcohol consumption and any other drugs. Laboratory tests were as follows alanine aminotransferase: 240 U/L, aspartate aminotransferase: 274 I/U, other biochemical laboratory tests including gamaglutamyltransferase, alkaline phosphatase, bilirubin levels were normal. Serological markers of viral hepatitis (EBV, CMV, Hepatitis A, B,C) were negative. Other etiology of hepatitis (autoimmune, hemochromatosis, Wilson disease, alpha-1 antityripsin deficiency) were excluded. Hepatobiliary ultrasonography was also normal. In these findings, we thought that liver toxicity due to venlafaxine, after discontination the drug two weeks later transaminase levels were normal. Up to now, only one case reported which is hepatotoxicity due to venlafaksine a patient with ulcerative colitis from Turkey. To our knowledge, this is the second case hepatotoxicity due to venlafaxine. In conclusion, physicians should be aware of liver toxicity due to venlafaksine in terms of widespread drug.

Topic 6: Drugs Herbals and Liver

No: 2038

Early monitoring for detection of antitubeculous drug induced hepatotoxicity

Tae Hyo Kim[1], Chang Min Lee[1], Sang Soo Lee[1], Hong Jun Kim[1], Chang Yoon Ha[1], Hyun Jin Kim[1], Woon Tae Jung[1], Ok Jae Lee[1]

Gyeongsang National University Hospital Internal Medicine Jinju-Korea, South[1]

Background/aims: We investigated onset time to develop antituberculous drug induced hepatotoxicity (ADIH) and characteristics according to onset time for hepatotoxicity.
Methods: A total of 1031adult patients to treat with first line antituberculous drugs between February 2009 and January 2013 were enrolled.
Results: of 1031 patients, 108 (10.5 %) developed ADIH occurring on a mean of 39.6 ± 43.7 days after treatment initiation. Especially, 28 (25.9 %) patients developed ADIH within 7 days and 73 (67.6 %) developed within 30 days. The ≤ 30 days group (detected within 30 days) was characterized by higher peak ALT level and a high proportion of patients with maintenance of first line antituberculous drugs compared to the > 30 days group (detected beyond 30 days). In subgroup analysis, the ≤ 7 days group (detected within 7 days) was characterized by higher baseline aspartate aminotransferase (AST) and ALT, a high proportion of patients with maintenance of first line antituberculous drugs, and a high proportion of patients with extrapulmonary tuberculosis compared to the > 7 days group (detected beyond 7 days).
Conclusions: Approximately 70 % of the patients occurred in the first 1 month of antituberculous treatment, associated with continuation of the first line drugs without change of regimen.

Topic 6: Drugs Herbals and Liver

No: 1513

Spectrum of drug induced liver injury in children—concern regarding cases with concomitant hepatotropic viral infection

Nikhil Mehra[1], Bikrant Bihari Lal[1], Rajeev Khanna[1], Dinesh Rawat[1], Seema Alam[1]

Institute of Liver and Biliary Sciences Pediatric Hepatology New Delhi-India[1]

Aims: To study the prevalence and spectrum of Drug induced Liver injury (DILI) in children under 18 years of age.
Methods: From January 2011 to May 2014 children below 18 years of age presenting with liver dysfunction with a history of drug intake were included. Liver injury was classified biochemically as per Hy's law into hepatocellular, cholestatic or mixed. Presence of concomitant hepatotropic viral infection and clinical presentation were recorded.
Results: There were 18 cases of DILI - 12 (66.6 %) were males; 5 (27.8 %) were co-infected with Hepatitis-A. Out of these 10 (55.5 %) cases developed a hepatocellular pattern of injury, whereas 5 (27.8 %) and 3 (16.7 %) had cholestatic and mixed patterns, respectively. Acute liver failure (ALF) is the most common presentation accounting for 7(38.9 %) cases out of which 85 % were hepatocellular. 2 (11.1 %) cases developed hypersensitivity. Most common agents accounting for DILI were ATDs [6 (33.3 %)], followed by alternative medicines [4 (22.2 %)], antiepileptics [AEDs—valproate, phenytoin and clobazam; 4 (22.2 %)] and paracetamol [2 (11.1 %)]. Half of the cases of DILI secondary to ATDs had ALF and none of them had concomitant viral infection. Those with DILI superimposed on hepatitis-A infection 4(80 %) had cholestatic or mixed pattern of liver injury and majority presented with prolonged cholestasis. Alternative medicines were responsible for superimposed DILI in acute hepatitis-A in 60 % of cases.
Conclusion: DILI in children needs a high index of suspicion. In the setting of acute viral hepatitis, usage of alternative medicines may further exacerbate the liver injury.

Topic 6: Drugs Herbals and Liver

No: 1658

The study of the impact of a Chinese medicine compound on cellular immune functions in chronic hbv carriers

Daqiao Zhou[1], Yingjie Chen[1], Jinsong He[1], Guangdong Tong[1], Yufeng Xing[1], Chunshan Wei[1]

Shenzhen Chinese Medicine Hospital Hepatopathy Shenzhen-China[1]

Objective: To study the impact of a Chinese medicine compound of invigorating kidney, strengthening spleen and detoxification (IKSSD) on cellular immune functions in chronic HBV carriers.
Methods: The cases were divided into two groups, 30 cases of chronic HBV carriers in treatment group and 10 cases of healthy volunteers in control group. Chinese medicine compound (IKSSD) and placebo were administered for 48 weeks respectively. The changes of following indexes in peripheral serum were observed: CD4 + CD25 + Treg expression frequency, IL-10, TGF-β, CD4 + , CD8 + T cells and CD4 +/CD8 +.
Results: At baseline, the peripheral serum CD4 + CD25 + Treg expression frequency was obviously higher in treatment group than control group (7.68 % versus 5.72 %), and so were the contents of serum IL-10 and TGF-β ($P < 0.05$). The serum CD3 + and CD4 + T cells expressions in treatment group were more lower than control group (62.94 %, 32.68 % versus 72.28 %, 39.49 %) ($P < 0.05$). The expression of CD8 + T cells was higher than that in control group (29.03 % vs 23.04 %), and the CD4 +/CD8 + ratio was lower than that in control group(1.18 vs 1.77, $P < 0.05$, respectively). After 48-week, the serum CD4 + CD25 + Treg expression frequency and the serum IL-10 and TGF-β contents were obviously decreased in treatment group ($P < 0.05$). The CD3 + and CD4 + T cells expressions in treatment group increased to 67.35 % and 37.22 %, respectively, while the CD8 + T cells expression decreased to 24.41 %, and the CD4 +/CD8 + ratio obviously increased to 1.61($P < 0.05$). The CD4 + , CD8 + T cell expression and the CD4 +/CD8 + ratio were no significant differences between two groups ($P > 0.05$).
Conclusions: A Chinese medicine compound could down-regulate CD4 + CD25 + Treg expression,and regulates the expressions of CD3 + , CD4 + and CD8 + T cells in chronic HBV carriers.

Topic 6: Drugs Herbals and Liver

No: 1656

Case report diltiazem causing cholestasis and hepatoportal sclerosis

Nagaraj Sriram[1], Jayaram Menon[1]

Qeh Gastroenterology Kota Kinabalu-Malaysia[1]

We present a case report of a 31 year old gentleman with background history of Diabetes Mellitus Type 1, CKD 3 (single functioning kidney) who developed Cholestasis after receiving T. Diltiazem. Liver Biopsy showed evidence of hepatoportal sclerosis.

Diltiazem is associated with a low rate of mild and transient elevations in serum aminotransferase levels which are usually asymptomatic. In large case series of drug induced liver injury, calcium channel blockers are rarely mentioned.

Our patient developed asymptomatic cholestasis with elevated transaminases and alkaline phosphatase (250-700 U/L) 4 months after starting on Diltiazem (for proteinuria). However he was never jaundiced. Viral hepatitis screening and autoimmune screening turned out negative. Transabdominal Ultrasound and Endoscopic Ultrasound showed no evidence of biliary obstruction.

Liver biopsy done showed periportal fibrosis, with concomitant perivenular and perisinusoidal fibrosis that may be seen in hepatoportal with no histological changes of portal hypertension.

Liver enzymes has resolved on stopping T. Diltiazem.

Topic 6: Drugs Herbals and Liver

No: 1040

Liver and antiretrovirals what about efavirenz

Nassima Belabas[1], Achour Amrane[1], Mohamed Zeroual[1], Abdelouhab Dif[1]

Laadi Flici (el-kettar) Hospital Department of Infectious Diseases Algiers-Algeria[1]

Introduction: Hepatotoxicity is a significant cause of morbidity and mortality among people living with HIV (PLH).
Objectives: This study assessed hepatotoxicity of efavirenz in 74 outpatients infectious diseases unit.
Materials and methods: Retrospective study from 2008 to 2012 including PLH adults naïve under antiretroviral (ARV) regimen with efavirenz. The parameters studied: alanine aminotransferase (ALT) taking graded with the WHO classification of drug toxicity, metabolic syndrome and liver stiffness measured by Fibroscan.
Results: A total of 74 patients were recruited (52 men/22 women). Mean age (39.95 years-old ± 11.95). 92.3 % were heterosexual. Mean liver stiffness: 5.2 kPa ± 2.9 (2.7 kPa—21.7 kPa) and (10 %) had a liver stiffness between 6 and 11 kPa.
Mean CD4 + T-cell (180.2/mm3 ± 114.7), mean HIV-RNA (5.20 ± log10 copies/ml ± 0.617), mean ALT(27 UI/l ± 18). During the first month of treatment, we report a hypertransaminasemia grade 1 (19 %) and grade 2 (05 %). After 4 years of treatment, mean liver stiffness increased to 5.9 kPa ± 3.1 (2.8–23 kPa) ($P = 0.006$) and 38 % had a liver stiffness between 6 and 11 kPa. We noted four (5 %) cases of metabolic syndrome.
Conclusion: After the start of an efavirenz-based ARV regimen, ALT abnormalities appears to be low and graded moderate but the increase of liver stiffness is significant and should be strictly monitored in PLH.

Topic 6: Drugs Herbals and Liver

No: 1621

Expression of iron metabolism regulatory genes under the influence of fat rich diet and medicinal herbs

Afshan Syed[1], Nadeem Sheikh[1], Afia Farrukh[1]

University of The Punjab Zoology Lahore-Pakistan[1]

There is an elevating trend of using natural herbs as an alternative of synthetic medicines. The purpose behind the current study was to investigate the counter impact of *Nigella sativa* seeds and *Plantago ovata* husk against fat induced inflammation on iron metabolism regulatory genes. Adult (A) and weaning (w) *Rattus norvegicus* of 200 g and 30 g respectively were divided into four groups (n = 10),

depending upon different diets. The group designated as 0 served as negative control and consumed 100 % rat chow, group I was positive control and consumed FRD, II and III were experimental groups and were provided with FRD supplemented with *N. sativa* seeds or *P. ovata* husks respectively. The results obtained by the PCR presented elevated hepatic hepcidin expression in groups W–I, A-I, W-II and A-II while down regulated expression in group W-III and A-III. However, contrasting results were obtained for the transferrin (Tf) and ferroportin-1 (Fpn-1) gene expression analysis. Conclusively, it can be stated that fat induced inflammation leads to iron burdens while *P. ovata* husk lowers the iron levels of the body even below normal range.

Topic 6: Drugs Herbals and Liver

No: 1629

Variations in serum protein profile of adult rats under the effect of *Plantago ovata* and *Nigella sativa* seeds in fat induced inflammation

Afshan Syed[1], Nadeem Sheikh[1]

University of The Punjab Department of Zoology Lahore-Pakistan[1]

The current project involves the counter effect of herbal medicines against fat induced inflammatory response of the *Rattus norvegicus* on the serum protein profile. Forty adult *Rattus norvegicus* 200 g were divided into four groups (n = 10), designated as 0 (negative control), I (positive control), II and III (experimental). Group 0 was fed on diet "A" (100 % rat chow), group I received fat rich diet (FRD) "B" (34 % Rat chow + 33 % Sucrose + 20 % commercially available tea whitener + 13 % water), and group II received diet "C" ("B" + 50 g N. sativa seeds/Kg of "B" and group III was fed on diet "D" ("B" + 50 g P. ovata husks/Kg of "B"). The serum protein fractions of adult rat groups resolved on the 8 % SDS-PAGE scrutinized the protein bands from 54 kDa to 295 kDa against protein marker. The protein fractions of 295 kDa, 246 kDa, 133 kDa and 110 kDa were absents in group A-III, while, protein fraction of 86 kDa was present only in A-II group rat sera. Conclusively, it can be stated that hypoproteinemia is induced in the adult rats under the effect of P. ovata husk supplementation.

Topic 6: Drugs Herbals and Liver

No: 1607

Influence of a Chinese medicine compound prescription of invigorating kidney and strengthening spleen and detoxification on dendritic cells in chronic hbv carriers

Jinsong He[1], Daqiao Zhou[1], Yingjie Chen[1], Guangdong Tong[1], Yufeng Xing[1], Liang Chen[1]

Shenzhen Chinese Medicine Hospital Hepatopathy Shenzhen-China[1]

Objective: To study the influence of a Chinese medicine compound of invigorating kidney, strengthening spleen and detoxification (IKSSD)on Dendritic cells (DC) in chronic HBV carriers.
Methods: The cases were divided in to two groups, 30 cases of chronic HBV carriers in the treatment group and 10 cases of healthy volunteers in the control group. Chinese medicine compoundiption of IKSSD and placebo were administered for 48 weeks, respectively. We observe changes of DC's mature surface markers, allogeneic mixed lymphocyte reaction (MLR) induced by DC and the levels of related cytokines.
Results: In baseline, the expression levels of DC mature surface markers such as HLA-DR, CD86, CD80 and CD1α in the chronic HBV carriers with immune resistance were 61.34, 55.78, 42.63 and 43.17 %, respectively, which were significantly lower than that (90.52, 83.26, 76.81 and 84.90 %) in the control group ($P < 0.01$). Meanwhile, DC inducing MLR ability was inferior, and IL-12 and IFN-γ levels in MLR supernatant were less compared to the healthy people ($P < 0.01$). After treatment, expression levels of DC mature surface markers in the treatment group increased obviously compared to the baseline ($P < 0.01$). DC inducing MLR ability was enhanced distinctly with administration of medication for 48 weeks ($P < 0.01$). At the same time, were presented significantly increases in IL-12 and IFN-γ levels post treatment in the treatment group ($P < 0.01$). Nonetheless, DC inducing MLR ability and IFN-γ levels in the treatment group did not reach that in the control ($P < 0.05$ or 0.01).
Conclusions: For the chronic HBV carriers, the Chinese medicine compound could promote DC mature and enhance DC's immune function.

Topic 7: ERCP and Interventional Hepatology

No: 1856

Our fully covered self expanding metalic stent experience in sclerosing cholangitis patients

Ibrahim Hakki Koker[1], Birol Baysal[2], Ali Tuzun Ince[3], Hakan Şentürk[3]

Okmeydani Research and Education Hospital Gastroenterology Istanbul-Turkey[1], Bezmi Alam Medicine Faculty Gastroenterology Istanbul-Turkey[2], Bezmi Alem Medicine Faculty Gastroenterology Istanbul-Turkey[3]

Background: Fully covered self-expanding metal stents (FCSEMS) are started to be used increasingly as an option in benign biliary stenosis (BBS). FCSEMS provide a better dilation of the bile duct and they are lesser obstructed with sludge than the plastic stents. FCSEMS were not considered in Sclerosing cholangjtis (SC) as an endotherapy strategy for BBS in previous studies.
Aims: Observing the efficacy of FCSEMS in choledochal strictures due to SC.
Patients: Three patients with SC were considered for FCSEMS placements due to choledochal stricture. FCSEMS (Wallflex, Boston Scientific) were available in 10 mm diameter and 80 mm in length used. First patient was male, 60 years old and diagnosed 20 years ago and he had had multiple or single plastic stent exchanges more than 20 ERCP sessions. Then, FCSEMS is placed. In follow up, the patient was clinically stable and did not need a new ERCP stent replacement since 13 months. The second patient had PSC due to Ulcerative Colitis since three years. This patient had a previous choledochal stricture treated by pneumatic dilatation. FCSEMS introduced. After one month, the stent dropped spontaneously. In follow up, he has no complaints. The third patient was a 37 year old male with PSC. He had multiple ERCP sessions with multiple synchronous plastic stent exchange. FCSEMS placed to the main choledochal stricture. He has no drainage problem since three weeks after the FCSEMS.
Conclusions: FCSEMS might be an effective and an easier method in keeping the long term patency of BBS due to SC.

Topic 7: ERCP and Interventional Hepatology

No: 2091

An unusual reason of gi bleeding hemobilia a fearful complication of liver biopsy

Meltem Ergun[1], Aylin Hasanefendioglu[2], Ali Riza Koksal[1], Salih Boga[1], Mehmet Bayram[3], Huseyin Alkim[3], Canan Alkim[4]

Sisli Etfal Education and Training Hospital Gastroenterology Istanbul-Turkey[1], Sisli Etfal Education and Training Hospital Radiology Istanbul-Turkey[2], Sisli Etfal Education and Training Hospital Gastroneterology Istanbul-Turkey[3], Sisli Etfal Education and Training Hospital Gastroenterologu Istanbul-Turkey[4]

Liver biopsy is an important tool for diagnosing and/or staging of liver disease. Although liver biopsy is considered safe, unusual and life threating complications may occur. We herein report a case with hemobilia after liver biopsy.

A 37-year-old male patient presented with hematemesis. He was an IV drug user, he had a history of chronic hepatitis C (untreated), and recently diagnosed with active pulmonary tuberculosis. Liver biopsy was performed at another institution, to staging the liver disease, 10 days ago. We performed upper and lower gastrointestinal endoscopy, stomach was full of blood, but we could not find the lesion. Because of hemoglobin levels continue to fall, we performed endoscopy, 48 h later. Massive bleeding was recognized from the papilla vateri and ERCP was done. A lot of blood and clots were removed from common bile duct and also intrahepatic ducts. Early intervention by angiography and embolization of a portobiliary fistula was performed. The patient was recovered uneventfully from GI bleeding.

Hemobilia is a rare cause of GI bleeding. Patients who had a history of recent liver biopsy, portobiliary fistula may be the reason for bleeding.

Topic 7: ERCP and Interventional Hepatology

No: 1768

Predictive factors that affecting the fluoroscopy time in endoscopic retrograde cholangiopancreatography (ERCP)

Ahmet Tarik Eminler[1], Mustafa Ihsan Uslan[1], Aydin Seref Koksal[1], Erkan Parlak[1]

Sakarya University Gastroenterology Sakarya-Turkey[1]

Introduction: Fluoroscopy time (FT), as it is important for the safety of the patient and the treatment team, in terms of the quality of the process is considered as a parameter. In this study we tried to reveal the factors affecting FT in ERCP.
Materials and methods: The study enrolled 400 patients with a mean age of 59,4 ± 18,4 years. We investigated the effects of demographic characteristics, presentation, disease (stone, trick-distal stenosis, etc.), processing of the specifications (front incision, sphincterotomy, stenting, etc.) on the fluoroscopy time.
Results: The mean fluoroscopy time was found 210 (8-2400) seconds. A multivariate linear regression analysis with the results of the evaluation; operation for biliary complications of transplanted liver (OR = 0.68, $P = 0.01$) and carrying out operations for pancreatic disease (OR = 0.77, $P = 0.04$); and during the process of papillary dilatation (OR = 0.63, $P < 0.001$), processing pancreatic sphincterotomy (OR = 1.03, $P = 0.03$) and stenting pancreatic or biliary system (OR for pancreatic stent = 0.34, $P = 0.03$; for biliary stent OR = 0.40, $P < 0.001$) were found to be independent predictors.
Conclusion: The physicians should anticipate that the FT may be long and should be more careful about prevention methods that can be applied in liver transplantation patients and therapeutic pancreatic procedures.

Topic 7: ERCP and Interventional Hepatology

No: 1377

Diagnostic yield of brush cytology in indeterminate biliary strictures

Ali Riza Koksal[1], Huseyin Alkim[1], Meltem Ergun[1], Salih Boga[2], Mehmet Bayram[1], Banu Ozguven[3], Muharrem Battal[4], Canan Alkim[1]

Sisli Hamidiye Etfal Training and Research Hospital Gastroenterology Istanbul-Turkey[1], Yale University, School of Medicine Gastroenterology New Haven-United States[2], Sisli Hamidiye Etfal Training and Research Hospital Pathology Istanbul-Turkey[3], Sisli Hamidiye Etfal Training and Research Hospital General Surgery Istanbul-Turkey[4]

Aim: The aim of this study was to define sensitivity, specificity and positive and negative predictive values of ERCP brush cytology from indeterminate biliary strictures.
Material-method: We retrospectively analyzed diagnostic yield of brush cytology in indeterminate biliary strictures in our single center, between January 2013 and April 2014.
Results: Cytologic examination of thirty seven sampling was done in 35 patients. The mean age of patients was 63.7 ± 12 years. of cases, 19 were females and 16 were males. Three adenocarcinoma, one high grade dysplasia and one low grade dysplasia were detected at cytological evaluation. Twenty sampling were reported as normal with sufficient material, 3 were reported as insufficient material and 9 were reported as indeterminate. The diagnosis of malignancy was confirmed with other methods in 4 patients. Follow-up data were obtained in 13 out of 18 with malignancy negative patients. Ten of these 13 patients were detected negative for malignancy and 3 were diagnosed malignant with additional examinations. Also, 3 out of 12 patients whose cytological results were insufficient or indeterminate were diagnosed malignant after additional examinations, and the rest 9 patients were found negative for malignancy. In accuracy analysis, the sensitivity of brush cytology was calculated as 57.1 %, specificity 100 %, positive predictive value 100 % and negative predictive value 76.9 %.
Conclusion: In cases with indeterminate biliary strictures, positive predictive value of brush cytology was high; but, negative cytology results do not exclude malignancy. Cases with high suspicion of malignancy must be evaluated with additional examinations.

Topic 7: ERCP and Interventional Hepatology

No: 2135

Subcapsular liver hematom after ercp (endoscopic retrograde cholangiopancreatography) a case report

Şükrü Arslan[1], Ercan Korkut[1], Erdem Karadeniz[1], Nurhak Aksungur[2], Bülent Güvendi[1]

Ataturk University General Surgery Erzurum-Turkey[1], Tekman State Hospital General Surgery Erzurum-Turkey[2]

Introduction: Complications such as pancreatitis, perforation and bleeding may develop during ERCP. However, liver hematoma after the ERCP is reported rarely in the literature.
Case: A 71-year-old male patient who had received ERCP due to choledocholithiasis in another medical center and who had stomachache afterwards was sent to our clinic. At the time of arrival, the laboratory findings of the patient were as follows: AST: 320, Alt: 370, GGT: 100, ALP: 180, Amylase: 90, T-Bilirubin: 4.8, D-Bilirubin: 2.4, Hb: 9.1. In the abdomen tomography, it was detected that the patient had hematoma and perfusion defects in the right liver lobule. We had a conservative approach to the patient for 7 days; however, peritoneal irritation findings were detected in physical examination. In the abdomen tomography, it was detected that the hematoma and perfusion defects in the liver had become wider, and the capsule integrity of the liver was deformed, and the patient was operated. In the operation, wide hematoma and necrosis in the right lobule of the liver were observed; and approximately 200 cc biliary pouch was detected. There was also widespread hemorrhagic liquid in the abdomen. The necrotic material was debrided. The operation area was drained. The patient whose postoperative laboratory findings and clinic findings had become stable was discharged.
Result: In the patients who experience stomachache after ERCP and whose hemoglobin levels are low, the liver hematoma, which is one of the rare complications of the ERCP, must be considered; and it must be confirmed with radiological methods.

Topic 7: ERCP and Interventional Hepatology

No: 1663

Does portal hypertension occur in cowden syndrome an answer to an uncommon presentation

R. Asokkumar[1], Chang Pe[1]

Singapore General Hospital Department of Gastroenterology and Hepatology Singapore-Singapore[1]

Introduction: Cowden syndrome (CS) is an autosomal dominant hamartomatous polyposis syndrome. Ascites related to portal hypertension (PHT) has never been reported in CS patients.
Case report: A 32-year-old female with CS presented to our department for evaluation of ascites. Diagnosis of CS was based on positive PTEN mutation and the presence of multiple gastrointestinal hamartomas, mucocutaneous papillomas, follicular thyroid carcinoma, intellectual impairment, macrocephaly and fibroadenoma. Ascitic fluid analysis revealed a SAAG ratio > 11 suggestive of PHT. No biochemical or imaging features of cirrhosis were present. Radiological imaging showed multiple hepatic hamartomas without portal vein (PV) obstruction. Doppler analyses showed PV flow reversal and a hepatic AVM. Hepatic venous pressure gradient (HVPG) was elevated (12 mmHg). Liver biopsy showed moderate steatosis with bridging fibrosis but no cirrhosis. Ascites was diuretic refractory requiring transjugular intrahepatic portosystemic shunt (TIPS). During TIPS the direct PV pressure was significantly higher (31 mmHg) than HVPG, suggesting presence of non-sinusoidal PHT. Angiography demonstrated a high-flow AVM from the hepatic artery to PV contributing significantly to PHT. Post-TIPS portosystemic gradient was 19 mmHg which decreased further to 8 mmHg after embolization of the AVM. Her ascites improved with decrease in diuretic requirements.
Discussion: PTEN has anti-angiogenic effect by down regulating VEGF expression. Loss of function mutation in PTEN may cause AVM in CS, which are commonly intramuscular and intracranial. Our case is unique with a high-flow hepatic AVM contributing significantly to PHT and ascites which improved after embolization.
Conclusion: We report the first case of PHT in CS due to a hepatic arterioportal malformation. Clinicians should be aware of the potential risks of PHT-related complications in CS.

Topic 7: ERCP and Interventional Hepatology

No: 1778

The study of residual stone rate and risk factors after endoscopic extraction of the common bile duct stones

Dong Hee Koh[1], Jung Eun Choi[1], Juah Jang[1], Se Woo Park[1], Min Ho Choi[1], Hyun Joo Jang[1], Sea Hyub Kae[1], Jin Lee[1]

Hallym University College of Medicine Internal Medicine Hwaseong-Korea, South[1]

Background: Recurrence of common bile duct (CBD) stones after endoscopic stone removal has been reported ranging from 4 to 24 %. Relatively early recurrences suggest that part of the cause of 'recurrent' bile duct stones is failure to remove of stones at the first endoscopic retrograde cholangiopancreatography (ERCP). Placement of endoscopic nasobiliary drainage (ENBD) tube with follow-up cholangiogram has been advocated for improved clearance of fragments in the bile duct. We investigated the rate and risk factor of residual stone after extraction of CBD stones.
Methods: A total of 119 patients with choledocholithiasis who underwent ERCP and CBD stone extraction were recruited in the period 2008 to 2009. An ENBD was placed in the bile duct after the balloon cholangiogram for confirming no residual CBD stone. We underwent follow-up cholangiogram for detect residual stones. We compared the residual stone group with the non-residual stone group.
Results: In 32 of 119 patients (26.9 %), there were residual stones in follow-up cholangiogram. There were no significant differences in demographic and laboratory data between the 2 groups. In sharpness of CBD angulations (129.27 ± 18.74 vs. 137.18 ± 15.91, $P = 0.024$) and multiple CBD stones (4.53 ± 2.83 vs. 2.90 ± 2.15, $P = 0.05$), there were significant differences between 2 groups.
Conclusion: Placement of ENBD tube with follow-up cholangiogram was helpful in angulated CBD or multiple CBD stone for reducing residual stone rate after extraction of CBD stones.

Topic 7: ERCP and Interventional Hepatology

No: 1151

Feasibility of self expandable metal stent for preservation of sphincter of oddi function in patients with common bile duct stones a pilot study

Sungkyu Choi[1], Chunghwan Jun[1], Eunae Cho[1], Doohyun Lee[1]

Chonnam National University Medical School Department of Internal Medicine Gwangju-Korea, South[1]

Background and study aims: The aim of this study was to evaluate the feasibility of self-expandable metal stents (SEMS) for preservation of sphincter of Oddi (SO) function in patients with common bile duct (CBD) stones.
Patients and methods: From February 2014 to July 2014, 10 patients with CBD stones who had small caliber CBD (< 11 mm in diameter)

were enrolled. Endoscopic removal of CBD stones was performed using trans-papillary SEMS without endoscopic sphincterotomy. Achieving complete duct clearance, preserving SO function and procedure-related complications were evaluated.
Results: Trans-papillary SEMS deployment was successfully performed in all patients (100 %, 10/10). The mean age of the patients was 47.3 years; the mean diameter of CBD was 8.8 mm; the mean diameter of stones was 5.6 mm; the mean number of stones was 1.5. In 9 (90 %) patients, stones were removed using a basket without mechanical lithotripsy; in 1 (10 %) patient, stones were removed using mechanical lithotripsy. All SEMS were removed successfully using a polypectomy snare or a rat tooth. All patients showed preserved SO function. There were no significant procedure-related complications.
Conclusions: Trans-papillary SEMS facilitates stone removal in patients with small CBD. This technique appears to be effective in preservation of SO function.

Topic 7: ERCP and Interventional Hepatology

No: 1210

Safety of endoscopic retrograde cholangiopancreatography in pregnancy experience of a single center

Bugra Tolga Konduk[1], Samet Alkan[1], Abdullah Emre Yildirim[1], Ayhan Balkan[1], Sezgin Barutcu[1], Ramazan Erdem Er[1], Murat Taner Gulsen[1]

University of Gaziantep Gastroenterology Gaziantep-Turkey[1]

Aim: In pregnancy, choledocolithiasis is the most common indication for ERCP. Although the second trimester is felt to be the safest time to perform ERCP, often the need arise during the first or third trimester. ERCP has not been validated in pregnants yet. The fetal risk of radiation increases after dose of 100 or 200 mGy. Our aim is to demonstrate ERCP procedure in pregnant patients and to discuss its benefits and risks.
Method: We retrospectively recruited six cholestatic or cholangitic pregnant patients in the last 14 months. The features of our patients are summarized in table 1. All patients were sedated with propofol by the endoscopist. Cannulation was performed using fluoroscopy in 5 and bile aspiration technique in 1 case. Monopolary standard biliary sphincterotomies and balloon extractions were performed in all cases.
Results: The average age of the pregnants was 28.8 years. of cases, 4 (66.6 %) in their second, 1 (16.6 %) in the first and 1(16.6 %) in the third trimester underwent ERCP. The average duration of fluoroscopy was 4 s, cannulation was successful and uneventful in all cases. One patient in her first trimester had a vaginal bleeding three days after the procedure and had an abortus which was found to be related to primary obstetrical problems. The remainder of the patients had normal deliveries and healthy babies. After deliveries, the new-borns were apparently healthy for a period of three months. As a conclusion, ERCP can be performed successfully in pregnancy and has a lower risk than thought.

Topic 7: ERCP and Interventional Hepatology

No: 1579

A new technique for the management of basket impaction gastric band cutter system

Nevin Akçaer Öztürk[1], Burçak Evren Taşdoğan[1]

Numune Research and Training Hospital Gastroenterology Adana-Turkey[1]

Endoscopic retrograde cholangiopancreatography is the first line therapy for choledocholithiasis. In the management of difficult cases with large and multiple stones, mechanical lithotripsy and/or stenting is an alternative treatment option. Impaction of a lithotripsy basket during endoscopic lithotomy is a declared complication and is usually due to the size of the stones and the discrepancy between the size of the stone and the distal bile duct. Our case is a 53-year-old female who underwent an ERCP procedure for choledocholithiasis. In the procedure, the retrievable basket around the stone became impacted and mechanic lithotriptor was inadequate to take out the stone- basket complex. We used a gastric band cutter system to crush the stone and take out the stone-basket complex. Since there were residue stones in the choledocus, stenting was performed. Consequently, the need for surgery and the risk of cholangitis were eradicated. We think that, in such conditions, this technique can be used safely instead of surgery.

Topic 8: Gall Bladder and Biliary Tract

No: 1836

Percutaneous liver biopsy on the diagnosis of cholangiocarcinoma experience of a tertiary gi center

Metin Basaranoglu[1], Nesrin Turhan[2]

Bezmialem University Gastroenterology Istanbul-Turkey[1], Türkiye Yuksek Ihtisas Pathology Ankara-Turkey[2]

Objectives: Diagnosis of cholangiocarcinoma (CC) is a difficult and challenging issue. We investigated our pathology results to define the patients with CC.
Methods: We evaluated our pathology records from 2008 to 2013. In our lab, every year approximately13.000 specimens were examined. All of the materials, 70 % was GI specimens and 7 % was liver origin.
Results: We found 44 patients by using the ICQ code. Any specimen with primer other than pancreas and biliary system which was detected by immunohistochemical stains was excluded from the further analysis. Anyone showed pancreas origin during the clinical and laboratory examinations was also excluded from the study. At the end, we had 19 patients with CC.

Of the 19 patients with CC, one was diagnosed from the operation material, and one from the lymph node biopsy by endosonographic examination and diagnosis confirmed by ERCP brush cytology. The rest of them were diagnosed by percutaneous liver biopsy via the transabdominal ultrasonography or computerized tomography.
Conclusion: Diagnosis of CC is still a challenging issue, and early diagnosis is not possible. Any clinical or lab examination such as tumor markers or radiologic imaging alone was not be found helpful.

Topic 8: Gall Bladder and Biliary Tract

No: 1293

Spontaneous cholecystocutaneous fistula as a rare complication of cholecystitis

Yuriko Takayama[1], Tadatoshi Takayama[1], Masaru Aoki[1], Shintaro Yamazaki[1], Yutaka Midorikawa[1], Akira Kanamoto[1], Masamichi Moriguchi[1], Tokio Higaki[1], Takao Okubo[1], Hisashi Nakayama[1]

Nihon University, School of Medicine Digestive Surgery Tokyo-Japan[1]

Aim (Background): Spontaneous cholecystocutaneous fistula is an extremely uncommon complication of cholecystitis. We here report a case spontaneous cholecystocutaneous fistula as a rare clinical presentation.
Method (Case report): A 69-year-old woman was admitted to our hospital complaining of right quadrant oblique pain, concomitant to the right subcostal mass.
There were previous history, appendectomy for acute appendicitis, right inguinal hernia, hypertension, and hyperlipidemia.

Abdominal ultrasound echo revealed cholecystocutaneous fistula.

Abdominal computed tomography scan and magnetic resonance image showed gallstone and communication between the abscess and the gallbladder. Malignancy could not rule out radiological examinations.

Percutaneous abdominal wall abscess drainage was performed. The top of the drainage tube was fixed in the gallbladder for the communication between the abscess and the gallbladder.1 month later cholecystectomy was performed.

Histopathological analysis revealed chronic cholecystitis with no evidence of malignancy.Postoperative course was uneventful.
Conclusion: We reported the rare case of spontaneous cholecystocutaneous fistula that caused abdominal wall abscess.

Topic 8: Gall Bladder and Biliary Tract

No: 1894

The association between body mass index cholesterolosis and cholecystitis

Kyoung Min Sohn[1], Yeon Ju Jeon[2], Jiwoo Sohn[2], Jai Hoon Yoon[3], Dae Yong Kim[3]

We Want Healthcare Internal Medicine Seoul-Korea, South[1], Medigenlab Medicine Seoul-Korea, South[2], Hallym University College of Medicine Internal Medicine Chuncheon-Korea, South[3]

Obesity is a chronic inflammatory condition and is strongly linked to raised levels of pro-inflammatory factors and may lead to fatty infiltration of multiple internal organs including gallbladder and liver, causing organ dysfunctions. Fatty infiltration of gallbladder leads to chronic inflammation such as cholecystitis and tissue damage. This study was performed to evaluate association of body mass index (BMI) between acute and chronic cholecystitis and cholestrolosis. This retrospective study covered the period from January 2007 to April 2011, We evaluated 1,158 patients who had cholecystectomy. We excluded gallbladder cancer, adenomyomatosis, cholestrolosis without cholecystitis. Finally, we investigated data of total 1,065 patients with cholecystitis. Laboratory test. and clinical data such as age, sex, BMI, height, weight and underlying diseases. We investigated retrospectively acute and chronic cholecystitis, cholesterol polyps, other gallbladder disease such as gallbladder cancer and adenomyomatosis according the histopatholic finding. Parameters included a) acute inflammation, b) chronic inflammation, c) cholesterosis, d) presence of cholesterol polyp. There was a significant difference of BMI between the cholecystitis with cholesterolosis and without cholesterolosis ($P = 0.001$). In patients who had cholecystitis with cholesterolosis, average of BMI was 25.2 kg/m2, In cholecystitis without cholesterolosis, average of BMI was 23.4 kg/m2. Weight, systolic blood pressure, platelet count, glucose, triglyceride, LDL-cholesterol were different in above groups ($P < 0.05$). However, there was no significant difference between acute and chronic cholecystitis according to BMI ($P = 0.05$). BMI was associated with cholesterol related cholecystitstis. We suggest that, BMI could be used as one of predictive factors of cholecystitis in obese patients.

Topic 8: Gall Bladder and Biliary Tract

No: 1301

Coexistence of celiac disease and pancreatic neuroendocrine tumor

Talat Ayyildiz[1], Cınar Yildirim[2], Enver Dolar[3], Omer Yerci[4], Omer Fatih Nas[5]

Ondokuzmayis University Gastroenterology Samsun-Turkey[1], Uludag University Gastroeneterology Bursa-Turkey[2], Uludag University Gastroenterology Bursa-Turkey[3], Uludag University Pathology Bursa-Turkey[4], Uludag University Radiology Bursa-Turkey[5]

Objective: Celiac disease is a disorder of the small intestine which is characterized by crypt hyperplasia, villous atrophy and mucosal inflammation. Its coexistence with other conditions has been described. However, there is only one publication in literature that reported coexistence of celiac disease with a pancreatic neuroendocrine tumor. This report represents the second case with such coexistence.
Case presentation: A 55-year-old female patient admitted to the gastroenterology outpatient clinic with burning sensation in the stomach, weakness and weight loss (3-4 kg) over the previous 3 months. Radiological examination including ultrasonography and comuputed tomography showed a 4 x 3 cm mass in the pancreatic head. Endoscopically, increased granularity of the duodenal mucosa were identified. Subsequent biopsies were consistent with celiac disease. A biopsy material obtained from the pancreatic head lesion showed positive staining with Chromogranin, Synaptophysin, CD56 and CD57 and led to diagnosis of a neuroendocrine tumor.
Conclusion: Celiac disease is often associated with dermatitis herpetiformis, Down syndrome, thyroid disease, enteropathy-associated T-cell lymphoma and autoimmune liver disease. Coexistence of celiac disease and pancreatic neuroendocrine tumors was first emphasized in 2014 by Gundling et al. who suggested a possible link between these two disorders and diffuse G-cell hyperplasia and enterochromaffin cell carcinogenesis. Similarly, celiac disease was diagnosed in our patient with the use of endoscopic biopsy and a well-differentiated endocrine tumor was reported by pathological examination of the resected pancreatic head. We believe that this case merits consideration since it is the second report of such coexistence available in literature.

Topic 8: Gall Bladder and Biliary Tract

No: 1780

Patterns of cholangiographic changes in patients with symptomatic portal cavernoma cholangiopathy

Vivek Saraswat[1], Neetu Soni[2], Nakul Morakhia[1], Samir Mohindra[1], Gaurav Pandey[1], Sunil Jain[2]

Sanjay Gandhi Postgraduate Institute of Medical Sciences Gastroenterology Lucknow-India[1], Sanjay Gandhi Postgraduate Institute of Medical Sciences Radiodiagnosis Lucknow-India[2]

Background: Portal cavernoma cholangiopathy (PCC) refers to biliary tree abnormalities in patients with portal cavernoma. Patients with symptomatic biliary obstruction need non-surgical management.
Objective: Available cholangiographic classifications are inadequate for symptomatic PCC. Cholangiographic changes were evaluated to develop a clinically useful classification for symptomatic PCC.
Patients and methods: Fifteen patients (12 men) with symptomatic PCC underwent MRCP and ERCP for biliary obstruction. Cholangiograms were analyzed for irregular contour, biliary stenosis (number, site, length), prestenotic dilatation and biliary calculi (number, size, site).
Results: Biliary stenosi(e)s (BS) were seen in 93 % patients (multiple in 60 %). 31 BS [17 intrahepatic (IHBS)] included 16 short (< 20 mm) and 15 long stenoses. 70 % of long EHBS (median 43.5 mm) were seen in the extrahepatic biliary system. 77 % of IHBS were short. Mean diameter of prestenotic dilatation, present in 80 %, was 11.2 mm. Biliary calculi, present in 93 %, were located in gallbladder (33 %), EHBD (20 %) or IHBD (40 %).
Conclusions: A novel classification for symptomatic PCC, likely to be helpful in planning management, is proposed.

Topic 8: Gall Bladder and Biliary Tract

No: 1573

Endoscopic extraction of living fasciola hepatica case report

Yasir Furkan Cagin[1], Yahya Atayan[1], Mehmet Ali Erdogan[1], Yılmaz Bilgic[1], Fırat Dagtekin[2], Hulya Aladag[3], Murat Aladag[1]

Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[1], Inonu University Faculty of Medicine Internal Medicine Malatya-Turkey[2], Inonu University Faculty of Medicine Obstetric & Gynocology Malatya-Turkey[3]

Introduction: Fasciola hepatica (FH) is zoonotic liver trematodes. FH is a rare cause of cholestasis. Symptoms of cholestasis may show up abruptly. Sometimes, clinical presentation has a broad spectrum from fever and eosinophilia to vague gastrointestinal symptoms. FH infection was demonstrated by endoscopic retrograde cholangiography (ERCP). We presented the case with a sudden onset of symptoms of cholangitis.
Case: 52 years old male patient admitted with the complaints of abdominal pain and darkening in urine color. The patient has an animal farm. Her scleras were subicteric in physical examination. Laboratory findings were as follows: Leukocyte: 11.700/ul, Eosinophile: %11(%7 <), Hb: 15,1 g/dl, Hct: 45.3 %, MCV: 87.4, Plt: 272000/ul, Sedim: 52 mm/h, INR: 1.0, CRP: 26 mg/dl, AFP: 2.1 IU/ml, AST: 259/ALT: 280 U/L, ALP: 360, GGT: 1025 U/L, T.bil/D.bil: 4.08/2.56 mg/dl, amylase: 81 U/L, lipase: 35 U/L. In abdominal USG; the diameter of the choledoc was 10 mm and there was a hyperechoic lesion without shade in the lumen. Gall bladder was hydropic and the wall was edematous (6 mm). Choledoc was canalized selectively in the ERCP and EST was done. After basket the parasite compatible with Fasciola hepatica was excised. Triclabendazole 10 mg/kg dose was given to the patient for two days. The complaints of the patient reduced to almost zero. Clinical and laboratory values returned to normal.
Conclusion: F. hepatica is one of the parasites that can cause recurrent cholangitis. When eosinophilia and dilatation in the choledoc are detected FH should be thought in the diagnosis.

Topic 8: Gall Bladder and Biliary Tract

No: 1450

Life threatening hemobilia from a ruptured gastroduodenal artery pseudoaneurysm after cholecystectomy

Mara Teresa Panlilio[1], Neil Bacaltos[2], Ramon De Vera[2], Mark Anthony De Lusong[1]

University of The Philippines-Philippine General Hospital Section of Gastroenterology Manila-Philippines[1], University of The Philippines-Philippine General Hospital Department of Surgery Manila-Philippines[2]

Hemobilia from ruptured gastroduodenal pseudoaneursym is a rare condition that is associated with a high mortality rate. Although this is usually associated with chronic pancreatitis, recent biliary tract surgery is also a less recognized risk factor. Early recognition of this entity is important, since prompt angiography and subsequent embolization is effective and safer than surgical ligation.

This is a case of a 37 year-old female presenting with hemobilia, jaundice, and right upper quadrant pain. She was admitted for hemodynamic instability one month post-cholecystectomy and T-tube choledochostomy. Fluid resuscitation, blood transfusion, and Somatostatin drip were started. Upper endoscopy revealed a swollen ampulla with minimal bleeding. Ultrasound suggested hematoma formation and visceral pseudoaneurysm formation. Emergency visceral angiography revealed a large saccular pseudoaneurysm formation at the proximal gastroduodenal artery. There were no arteriovenous malformation or arterioportal shunting. Occlusion of distal common hepatic, proximal hepatic, and gastroduodenal arteries with seven microcoils and two platinum coils was done. The patient had no recurrence of bleeding, and T-tube choledochostomy was removed 2 months post-discharge with no further complications.

The presence of Quincke's triad, hemodynamic instability, and recent abdominal surgery warrants investigation for the presence of an abdominal pseudoaneurysm. When this is suspected, angiography is useful for determining the exact location. In addition, it can save time and prevent the danger of an emergency surgical procedure to locate the source of bleeding without angiography.

Topic 8: Gall Bladder and Biliary Tract

No: 1072

Comparison on gallstone dissolution efficacy between CNU and UDCA according to stone density on CT scan

Jong Jin Hyun[1], Sang Jun Suh[1], Seung Young Kim[1], Sung Woo Jung[1], Young Kul Jung[1], Ja Seol Koo[1], Hyung Joon Yim[1], Hong Sik Lee[1], Sang Woo Lee[1]

Korea University Ansan Hospital Internal Medicine Ansan-Korea, South[1], Department of Internal Medicine, Korea University Ansan Hospital, Ansna-si, Korea

Aim: To compare the dissolution efficacy of ursodeoxycholic acid (UDCA) or a combination of chenodeoxycholic acid (CDCA) and UDCA (CNU) according to stone density on CT scan.
Method: A total of 84 patients (CNU grou$P = 46$, UDCA grou$P = 38$) completed dissolution therapy which was started from December 2010 to March 2014. Partial dissolution of gallbladder stone was defined as reduction in stone volume of > 50 %. Response was defined as complete dissolution or partial dissolution. Dissolution

efficacy was defined as % decrease in the stone volume. Stone density on abdominal CT scan was divided into 4 categories: hypodense, isodense, hyperdense, and calcified.
Results: The baseline age(48.83 ± 14.68 years vs. 53.74 ± 17.72 years), treatment duration(183.17 ± 15.33 days vs. 181.37 ± 14.64 days), and pre-treatment stone size(8.81 ± 4.35 mm vs. 9.72 ± 4.76 mm) were not different between the two groups. Response to therapy was observed in 41.3 %(19/46) and 57.9 %(22/38) of patients after CNU and UDCA treatment, respectively($P = 0.133$). Dissolution efficacy of CNU group and UDCA group was 37.55 ± 44.63 % and 54.98 ± 47.27 %, respectively($P = 0.087$). When only isodense stones were analyzed, response to therapy rose to 80.0 % and 83.3 % with CNU and UDCA treatment, respectively ($P = 0.577$). Dissolution efficacy also increased to 77.34 % and 80.64 % with CNU and UDCA treatment, respectively.
Conclusion: Patients with gallbladder stones that were isodense showed much better response to dissolution therapy with CNU and UDCA showing comparable efficacy. Therefore, CT scan should be performed prior to medication therapy if stone dissolution is intended.

Topic 8: Gall Bladder and Biliary Tract

No: 1452

Prevention of post ERCP pancreatitis for malignant biliary obstruction by performing minor endoscopic sphincterotomy before SEMS insertion

Yu Yi Choi[1], Dae Hwan Kang[1], Hyung Wook Kim[1], Cheol Woong Choi[1], Su Bum Park[1], Su Jin Kim[1], Joon Ho Jeon[1], Sook Kyoung Oh[1]

Pusan National University Yangsan Hospital Internal Medicine Yangsan-si-Korea, South[1]

Background/aims: The aim of performing self-expanding metal stent (SEMS) is to relieve obstruction in patients with unrespectable pancreaticobiliary. Although endoscopic sphincterotomy (ES) decreases the post-ERCP pancreatitis and facilitate stent placements, there are potential complications of bleeding. In this study, we evaluated early post-ERCP complications in patients who underwent minor ES before biliary drainage with SEMS: especially focused on PEP and bleeding.
Patients and methods: We assessed 172 patients with unresectable pancreaticobiliary malignancies who underwent SEMSs with minor ES. According to the data, the etiology of malignancy were cholangiocarcinoma in 92 patients, pancreatic cancer in 50 patients, gallbladder cancer in 11 patients and non-pancreaticobiliary malignancy such as ampullary carcinoma, hepatocellular carcinoma and metastatic cancer in 19 patients.
Results: 143 uncovered SEMSs and 29 covered SEMSs were placed. The frequency of PEP was 5.2 % (9/172). Patients younger than 40 who had PEP and at least 1 pancreatic duct injection were the significant predictors of PEP in univariate analysis. The frequencies of PEP in covered and uncovered SEMSs were 3.4 % and 5.6 % ($P = 0.336$). We found the complication of bleeding in 2 patients who underwent minor ES. But it wasn't fatal bleeding which requires blood transfusion.
Conclusions: Just a few complications of SEMS insertion after minor ES were reported. There was no difference between covered and uncovered SEMS. Therefore it is helpful to perform minor ES before biliary drainage with SEMS for the purpose of reducing the complications of the early post-ERCP.

Topic 8: Gall Bladder and Biliary Tract

No: 1167

Simple predictors of delayed nutritional recovery in patients with acute cholecystitis

Hiroaki Igarashi[1], Hiroshi Nakamura[1], Kiyoshi Tsuchiya[1], Hiroko Yamashita[1], Itsuro Ogata[1]

Kawakita General Hospital Internal Medicine Tokyo-Japan[1]

Background: Acute cholecystitis (AC) is sometimes treated with non-operative measures including fluid intravenous infusion and the administration of antibiotics without oral food intake for several days, and this treatment usually leads to temporary nutritional disorder
Objective: The aim of our study was to determine the predictors of the delay of nutritional recovery from nutritional disorder associated with non-operative treatment for AC
Methods: A total of 64 patients (36 men) with AC were enrolled in this study with mean age 75.2 ± 14.8 years (29-97 years). We defined it as nutritional recovery when the serum albumin level at 10 days after admission was higher than that on admission or ≧3.8 g/dL(normal lowest level). The following variables were determined and evaluated as possible predictors of delayed nutritional recovery: gender; age; the albumin level, C-reactive protein level, and white blood cell count on admission; days of no oral food intake; comorbidity of diabetes; gallbladder drainage performance.
Results: Forty-eight patients showed delayed nutritional recovery and 16 non-delayed recovery. Between these 2 groups, age (78.2 in delayed group; 66.1 in non-delayed), and days of no food intake (7.40; 5.69, respectively) were significantly different. Carrying out multivariable analysis, age ≧75 years, the albumin level on admission ≧3.4 g/dL (but this group did not seem to suffer from malnutrition), and days of no food intake ≧7 days were significant predictors of delayed nutritional recovery.
Conclusions: Old age (≧75 years) and prolonged no food intake period (≧7 days) can predict delayed nutritional recovery in patients with acute cholecystitis. We recommend that patients who meet at least one of these criteria should receive intensive nutritional support.

Topic 8: Gall Bladder and Biliary Tract

No: 1428

Non fluoroscopic endoscopic ultrasound guided drainage for symptomatic large or infected pseudocysts on pancreas

Hyeong Seok Nam[1], Dae Hwan Kang[1], Hyung Wook Kim[1], Cheol Woong Choi[1], Su Bum Park[1], Su Jin Kim[1], Dae Gon Ryu[1], Yu Yi Choi[1]

Pusan National University Yangsan Hospital Internal Medicine Yangsan-si-Korea, South[1]

Background and aim: Traditionally, Endoscopic ultrasound (EUS)-guided transmural drainage is used under fluoroscopy. But Many centers have the separated rooms for fluoroscopic and EUS examination. Our objective was to evaluate the safety and efficacy of EUS-guided drainage for symptomatic large or infected pseudocysts on pancreas without fluoroscopic guidance.

Methods: We reviewed for 7 consecutive patients underwent EUS-guided drainage without fluoroscopy for symptomatic large or infected pseudocysts on pancreas from September 2012 to August 2014. 8 procedures in 7 patients were performed with one or two 7 Fr pigtail stents in lesions.
Results: A total of 8 symptomatic large or infected pseudocysts on pancreas were drained and accessible via the stomach or duodenum. The mean size of lesions was 6.6 cm (range 2.5-11.5) and the mean time spent per procedure was 26 min (range 18-51). Success rate of endoscopic drainage was 87.5 % (7 of 8). Because of poor patient cooperation and small sized cyst (2.5 cm), one patient with infected pseudocyst was performed only aspiration. One 7 Fr pigtail stent was placed in 7 procedures. Two 7 Fr pigtail stents was placed in one patient with infected pancreatic pseudocyst and he required an additional procedure; percutaneous catheter drainage in infected peripancreatic fluid collection. There were no adverse event of the procedure. All patients relieved their symptoms and revealed partial to complete resolution on follow up CT.
Conclusion: Endoscopic ultrasound-guided drainage without fluoroscopic control for symptomatic large or infected pseudocysts on pancreas can be possible, safe and effective procedure.

Topic 8: Gall Bladder and Biliary Tract

No: 2133

Our surgical experiences in biliary tract injuries after cholecystectomy

Şükrü Arslan[1], Erdem Karadeniz[1], Ercan Korkut[1], Nurhak Aksungur[2], Gürkan Öztürk[1], Sabri Selçuk Atamanalp[1], Bülent Aydinli[1]

Ataturk University General Surgery Erzurum-Turkey[1], Tekman State Hospital General Surgery Erzurum-Turkey[2]

Purpose: Our purpose is to share our experiences in diagnoses, treatments and complications of the patients who were operated by us due to iatrogenic biliary tract injury.
Material and method: The patients who were operated upon the diagnosis of biliary tract injury in our clinic between the years 2010-2014 were examined retrospectively.
Findings: 3of the patients were male, and 7of them were female. The mean age was 57.2 (31-80). The 8operations which were performed due to biliary tract injury were laparoscopic, and 2 of these operations were open cholecystectomy. 4 of the patients, who were sent to our clinic by another medical center after postcholecystectomy, had generalized peritonitis and high level of bilirubin at the time of arrival; 3 of them had bile leakage from the drain without peritonitis finding; and 2 of them had high level of bilirubin without bile drainage. In one patient, intraoperative biliary tract injury occurred during the open operation due to acute cholecystitis. The 4 patients who had generalized peritonitis were operated. The other 5 patients received ERCP. In 2 of them, injury in cystic duct and impact calculus in choledoch were detected. Since the calculus could not be taken out with ERCP, these 2 patients were operated. The localizations of the injuries, according to the Strasberg Classification, were in Type-D (4 patients), Type-A (2 patients), Type-E (2 patients) and Type-E4 (2 patients). 5 of the patients received primary repairing to the choledoch over the t-tube; 4of them received hepaticojejunostomy; 1of them received choledochoduodenostomy. Mortality was observed in 2 of patients.
Result: Mortality rate increases in the biliary tract injuries if the injury is detected late and if the case has generalized peritonitis.

Topic 8: Gall Bladder and Biliary Tract

No: 1224

The issue of positive proximal margin after resection for hilar cholangiocarcinoma analysis of 21 cases

Volkan Oter[1], Ilter Ozer[1], Tahsin Dalgıc[1], Cemil Binarbası[1], Murat Ulas[1], Erdal Birol Bostancı[1], Musa Akoglu[1]

Turkiye Yuksek Ihtisas Teaching and Research Hospital Department of Gastroenterological Surgery Ankara-Turkey[1]

Aim: Surgery is the single potentially curative treatment option for Hilar Cholangiocarcinoma (HC). The major goal of surgery is R0 resection, however it may frequently be difficult to achieve negative proximal surgical margin. The aim of this study was to evaluate the margin status of bile ducts, early postoperative results and survival.
Methods: From January 2008 to December 2013, 21 patients with HC who underwent surgical resections. Data of the patients were analysed retrospectively R0 resection rate and status of proximal margin were recorded and early postoperative results and long term survival were analysed.
Conclusion: R0 resection was achieved in 14 (66.6 %) patients, however the remaining 7 patients (33.3 %) had involved margins. In the postoperative period 4 (19 %) patients had wound infection, 1 (4.7 %) had transient hepatic failure, 2 (9.4 %) had intraabdomianl abscesses, and 1 (4.7 %) had bile fistula. Hospital mortality was observed in one patient who had transient hepatic failure and sepsis. The median hospital stay of 22.6 (7–180) days. The 1-,2-, and 4-year overall survival rates of the 21 patients who underwent resection were 76.2, 40 and 10 %, respectively. Median survival of the patients with negative and positive proximal surgical margins were 22 months (11.93–32.06) and 17 months (14.43–19.56), respectively. Two patients with positive margins were still alive with a survival of 17 months and 56 months. Three patients with negative margins were still alive with a survival of 17 months, 29 months and 61 months. Survival of patients with HC is poor even after potentially curative resection. Survival of patients with positive margins seems not worse than those with negative margine.

Topic 8: Gall Bladder and Biliary Tract

No: 1550

Hemobilia following liver biosy in children—two case reports

Małgorzata Wozniak[1], Marek Woynarowski[1], Marta Sybilska[1]

Children's Memorial Health Institute Department of Gastroenterology and Hepatology Warsaw-Poland[1]

Background: Hemobilia is a rare but severe and potentially fatal complication of liver biopsy. The aim of this study is to present the cases of hemobilia diagnosed at Children's Memorial Health Institute in Warsaw.
Results: 2 cases of hemobilia were reported after 2500 standard Menghini needle liver biopsies performed over the period of 16 years (1998-2014).
Case 1: 14 years old girl presented with hematemesis few hours after liver biopsy. USG showed liver hematoma and enlarged gallbladder. Endoscopy showed presence of fresh blood in stomach an duodenum without visible source of bleeding. Scyntigraphy did not show bleeding source. Patient complained on abdominal pain. Hemoglobin concentration decreased and patient required several blood transfusions over the next week. Bilirubin concentration and

GGTP activity temporarily increased. The symptoms resolved within two weeks.
Case 2: 16 years old girl presented with abdominal pain two days after liver biopsy. She was readmitted to the hospital where she presented hematemesis, melena and anemia. Endoscopy showed blood flow from Vater papilla. USG showed markedly enlarged gallbladder filled with bloody fluid. Patient required several blood transfusions and had cholecystectomy due severe abdominal pain and rapidly increasing cholestasis. Symptoms resolved within three weeks.
Conclusion: The risk of hemobilia after standard Menghini needle liver biopsy in our institution is less than 0,1 %. Hemobilia is a life threatening event and requires prolonged hospital therapy.

Topic 8: Gall Bladder and Biliary Tract

No: 1455

Effects of infusion duration of nafamostat mesilate for the prevention of post ERCP pancreatitis study of 24 hr and 8 hr infusion

Sook Kyoung Oh[1], Dae Hwan Kang[1], Hyung Wook Kim[1], Cheol Woong Choi[1], Su Bum Park[1], Su Jin Kim[1], Jae Gyu Shin[1], Yu Yi Choi[1]

Pusan National University Yangsan Hospital Internal Medicine Yangsan-si-Korea, South[1]

Background/aims: Nafamostat mesilate lower the chances of developing post-ERCP pancreatitis (PEP). The appropriate duration of administration is unknown. In this study, we compare the effects of differences in infusion time of nafamostat mesilate for the prevention of PEP: 24-hour and 8-hour infusion.
Patients and methods: We randomly assigned 344 patients who underwent ERCP to either 24-hour of 8-hour infusion group. Nafamostat mesilate 2 mg/hr was infused 30 min before ERCP and lasted for 24 h in 24-hour infusion group. For 8-hour group, nafamostat was infused for 8 h.
Results: Both groups had similar patient demographic characteristics and procedure risk factors for pancreatitis. The total incidence of pancreatitis was 5.5 % (19/334). In details, 11 (6.4 %) out of 172 patients in 24-hour group and 8 (4.7 %) out of 172 patients in 8-hour group ($P = 0.479$). We found no significant difference between the groups in terms of the severity of pancreatitis.
Conclusions: Based on this study, infusion time of nafamostat mesilate wasn't significantly important for the prevention of PEP. 8-hour infusion of nafamostat mesilate is good enough to perform in outpatient clinics for the purpose of the prevention of PEP.

Topic 8: Gall Bladder and Biliary Tract

No: 2130

Gall bladder cancer a series of 6 cases

Ercan Korkut[1], Erdem Karadeniz[1], Şükrü Arslan[1], Gürkan Öztürk[1], Nurhak Aksungur[2], Bülent Aydinli[1]

Ataturk University General Surgery Erzurum-Turkey[1], Tekman State Hospital General Surgery Erzurum-Turkey[2]

Purpose: Our purpose in this study is to share our surgical approach in gall bladder tumors, which are rarely observed.
Method: 6 patients who were operated due to gall bladder tumors between the years 2010 and 2014 were examined retrospectively.
Findings: In this process, 6 patients were operated in our clinic due to gall bladder tumors. All of the patients were female and the average age was 68.5. Four of the patients were suspected after radiological monitoring in the preoperative period and were operated; worked in intraoperative frozen approach, and their pathologies were reported as malign. During the laparoscopic cholecystectomy due to cholelithiasis in a patient, the thickness of the bladder wall was considered as being suspicious, and the process was converted into an open operation. It was observed that the right hepatic artery was invaded by the lesion. Partial resection and reanastomosis was applied to the hepatic artery, and the frozen result was reported as being malign. Another patient was sent to our clinic after laparoscopic cholecystectomy in another medical center upon the detection of gall bladder tumor incidentally. All patients received lymph node dissection and wedge resection that covered the liver segment 5. The pathology of all of the patients was adenocarcinoma.
Result: A second surgery is needed in the cases that are detected incidentally. In patients who are considered as being suspicious after radiological monitoring or intraoperative process, the frozen approach must definitely be applied; and if a malign result is obtained, the tumor surgery must be performed in concurrent session.

Topic 8: Gall Bladder and Biliary Tract

No: 1923

An audit of peri ampullary growth patients in a tertiary hospital of a third world country

Abdul Kafi Asim[1], Prof. Arif Amir Nawaz Arif[2]

Fatima Memorial Hospital, Lahore Gastroenterology Lahore-Pakistan[1], Fatima Memorial Hospital Gastroenterology Lahore-Pakistan[2]

An Audit of patients with Peri-ampullary growth in a tertiary care hospital of a third world country.

Introduction: Periampullary growth is a common finding during ERCP here in subcontinent in patients presenting with either obstructive jaundice or abdominal pain associated with loss of appetite, weight loss and mild off and on fever. Sometimes they also present as a case of gastric outlet obstruction. Pathological diagnosis is essential to guide treatment and prevent more invasive diagnostic workup. Sampling technique is very easily done by taking biopsy during ERCP. Histology of this sample is diagnostic and confirmatory in almost all of these cases. This is important for finding the malignant potential of the growth which is most important step in further panning of these patients.
Objectives: The aim of this study was to find the main causes of Periampullary growth in this part of the world and also to guide our patients properly in further management and also to provide them best facilities available in our setup.
Materials and methods: A retrospective analytical study was designed to study the different causes of ampullary growth in this part of the world by auditing the data available of three years of ERCP done in our hospital. We reviewed all ERCPs performed from January 2012 to October 2014. During a standard ERCP, biopsies were obtained and immediately put in alcohol by the nursing staff for fixation. Subsequently, a dedicated pathologist conducted the histological analysis and classified the samples into different types.

Topic 8: Gall Bladder and Biliary Tract

No: 2077

ERCP without scope and it's safety

Fikret Goren[1], Ibrahim Goren[1], Talat Ayyıldız[1], Ahmet Bektaş[1], Beytullah Yıldırım[1]

Omu Gastroenterology Samsun-Turkey[1]

Biliary endoscopic intervention is necessary without the guidance of scope in some cases, including; emergency situations (biliary pancreatitis, acute obstruction of bile duct) or unavailability, or pregnancy (contraindicated). Once, endoscopist should ensure that bile duct have been cannulated. ERCP without scope is a safe procedure if the endoscopist is experienced.

ERCP without scope have been performed in 21 patients during past three years in our gastroenterology unit. Three of these patients were pregnant presented with colic pain, increase in cholestasis enzymes and biliary duct expansion in the USG. Sphincterotomy was performed and bile duct was stripped with balloon. 6 and 9 mm sized gallstones was extracted in two and a debris drainage was shown in other patient. The pain has been relieved and cholestatic enzymes were reduced in all pregnant women after ERCP. Diagnosis of remaining 18 patients were as follows: biliary pancreatitis in 8 patients, cholangitis in 6 patients and colic pain in 4 patients.

All patients presenting with biliary pancreatitis was edematous pancreatitis. Gallstones (7-12 mm) were extracted after endoscopic sphincterotomy and large amounts of pus extracted with bile sludge in patients with cholangitis. Bile duct could not be cannulated in two patients. Subsequent ERCP under scope revealed sclerosing cholangitis in one of the patients, an an impacted stone in the other. No complications have been noted during procedures. ERCP without scope in high skilled hands is as successful as ERCP under scope.

Topic 8: Gall Bladder and Biliary Tract

No: 1574

Fasciola hepatica case that referred with liver tumor diagnosis

Yasir Furkan Cagin[1], Mehmet Ali Erdogan[1], Yahya Atayan[1], Yılmaz Bilgic[1], Fırat Dagtekin[2], Hulya Aladag[3], Murat Aladag[1]

Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[1], Inonu University Faculty of Medicine Internal Medicine Malatya-Turkey[2], Inonu University Faculty of Medicine Obstetric&gynocology Malatya-Turkey[3]

Introduction: Fasciola hepatica(FH) is zoonotic liver trematodes. In acute phase, clinical presentation has a broad spectrum from fever and eosinophilia to gastrointestinal symptoms. FH arise with clinical presentation that is similar to malignancy. we presented a patient that was diagnosed FH because of eosinophilia and space-occupying lesion.
Case: 44 years old, male patient appealed with abdominal pain, weakness, widespread muscle pain, weight loss. In another center, abdominal USG has been examined and detected a mass in the liver. The patient has been referred with malignancy suspicion. Physical examination was normal. In laboratory tests, leukocyte: 23000/ul, eosinophil: 12972/ul (0-400), %56.4(%7 <), Hgb: 13.6 g/dl, Htc: 42 %, MCV: 85.3, Plt: 307000/ul, sed: 48 mm/h, CRP: 30 mg/dl, AFP: 2.20 ıu/ml, AST: 48U/L, ALT: 79 U/L, ALP: 113, GGT: 49U/L, Tbil/Dbil: 0.44/0.18 mg/dl were detected. In dynamic liver CT, subcapsular heterogenous hypodense areas were observed in right lobe of the liver. FH antibody titer was determined as 1/160. FH diagnosis was thought because of eosinophilia and space-occupying lesion in the liver. Triclabendazole 10 mg/kg dose was given to the patient for a week. Clinical and laboratory values returned to normal.
Conclusion: The purpose of this case presentation is to remind fasciola hepatica in the differential diagnosis of liver mass. By suspecting FH in patients with liver mass, when eosinophilia and masses in the liver are detected FH should be thought in the diagnosis.

Topic 8: Gall Bladder and Biliary Tract

No: 1689

Effects of biochemical parameters on estimation of clinical course in patients with mild acute pancreatitis classified according to Balthazar

Yusuf Kayar[1], Mukaddes Tozlu[1], Birol Baysal[1], Ali Tuzun Ince[1], Ahmet Danalioglu[1], Hakan Senturk[1]

Bezmialem Vakif University Gastroenterology Istanbul-Turkey[1]

Introduction: In acute pancreatitis, supportive treatment is sufficient in most patients but the disease can be life-threatening in 20 %. Therefore the determination of disease severity in advance is very important in estimating the prognosis of the disease.
Aim: The primary aim of this study is to observe the course of the disease according to Balthazar scoring in patients with mild acute pancreatitis. and the second aim is to determine the relationship between changes in biochemical parameters and changes in disease severity.
Methods: This prospective randomized controlled trial included 180 patients with mild acute pancreatitis according to HAPS and Imrie scoring system. The association between changes of severity of disease and changes in laboratory parameters was evaluated on first and third day of admission. The data was analyzed using Mann–Whitney U test and Mc Nemar test. The value of $P < 0.05$ was considered significant.
Results: Of the patients, women 61.7 % and the mean age was 53.86 ± 17(17-92). Etiologically, biliary pancreatitis was observed in 107(59.4 %), idiopathic in 38(21.1) and post-ERCP in 10(%5.6). The tomographies were performed in the first 12 h and 72. hours of admission. The changes in stage of disease is given in the Table-1. There was a close relationship between the stage of disease and the level of CRP, amylase analyzed on first and third day and also the ratio of CRP (Table-2).
Conclusion: of patients with mild acute pancreatitis, only a few progressed to more severe disease. Use of the biochemical parameters is more beneficial and cost effective in prediction of the clinical course and plan the treatment.

Topic 8: Gall Bladder and Biliary Tract

No: 1033

A very rare cause of postcholecystectomy bile leak from cystic stump fasciola hepatica

Mehmet Asil[1], Sami Cifci[1], Murat Biyik[1], Halil I Tasci[2], Huseyin Ataseven[1], Ahmet Tekin[2], Hakki Polat[1], Ali Demir[1]

Necmettin Erbakan University Faculty of Medicine Department of Gastroenterology Konya-Turkey[1], Necmettin Erbakan University Faculty of Medicine Department of Surgery Konya-Turkey[2]

Introduction: Laparoscopic cholecystectomy is commonly used for the treatment of cholelithiasis. Postoperative biliary leaks are not so rare and ERCP is the first choice for the diagnosis and treatment. Here we present a patient with bile leak from cystic stump due to fasciola hepatica obstructing the common bile duct, successfully treated with ERCP.
Case report: A 60 years old female was admitted to a local hospital 1 week ago and laparoscopic cholecystectomy was performed for cholelithiasis. Postoperatively there was biliary drainage from the surgical drain catheter and was referred to our hospital. Abdominal ultrasound showed intraabdominal fluid collection and approximately 1,5 lt of biliary fluid was drained percutaneously. MRCP showed a filling defect in the distal portion of the common bile duct. ERCP was performed which showed filling defects in distal portion of the common bile duct. After endoscopic sfincterotomy, alive fasciola parasites were extracted from the common bile duct. Biliary stenting was performed to treat cystic stump leak. Drainage from the surgical catheter ceased rapidly and she was discharged. 8 weeks later stent was removed.
Discussion: Postcholecystectomy bile leaks are usually due to surgical trauma, but cystic stump leaks are also common particularly in patients with bile duct stones obstructing the common bile duct. In our case it was fascioliasis obstructing the common bile. Although biliary fascioliasis is a very well documented disease, to our knowledge this is the first case in the English literature in which postcholecystectomy biliary leakage from cystic stump is due to fascioliasis.

Topic 8: Gall Bladder and Biliary Tract

No: 1775

Effects of hmg COA reductase inhibitor (statin) on apoptosis in cultured bile duct cancer cells

Jin Lee[1], Eun Mi Hong[1], Se Woo Park[1], Dong Hee Koh[1], Min Ho Choi[1], Hyun Joo Jang[1], Sea Hyub Kae[1]

Hallym University College of Medicine Internal Medicine Hwaseong-Korea, South[1]

Background and aims: Statin activates PPARs and suppresses inflammatory reaction by blocking TNFα and NF-κB production, and the sustained suppression of inflammatory response induces apoptosis in some cancer cells. However, the apoptotic effect of statins has not been evaluated in bile duct cancer cells. Therefore, we performed to demonstrate whether statins induce apoptosis in bile duct cancer cells, and to evaluate the expressional change of proteins associated with apoptosis.
Methods: Common bile duct cancer cells(SNU-1196) and hilar bile duct cancer cells(SNU-245) were cultured on dishes with hydrophilic(pravastatin) or lipophilic(simvastatin) statin treatment. Cell proliferation was measured by MTT assay, Cell cycle analysis was performed by FACS, degree of apoptosis were assessed by Cell Death Detection ELISA assay, and the activity of caspase-3, the key enzyme of apoptosis, were measured by Caspase Colorimetric Assay Kit, and the protein expression of Bcl-2(anti-apoptotic) and Bax(pro-apototic) were evaluated by Western blotting assay following treatment of various concentrations of statins.
Results: In bile duct cancer cells treated with statins during 24 or 48 h, the cell proliferations were significantly suppressed, the apoptosis were significantly increased, G1 population was increased, and the activities of caspase-3 were significantly increased in a concentration dependent manner. In addition, the expressions of Bcl-2 protein were decreased, and the expressions of Bax-2 proteins were increased in a concentration dependent manner.
Conclusions: Statin suppressed the proliferation and induced the apoptosis in bile duct cancer cells. These results support the potential use of statins in association with conventional treatment as anti-neoplastic agents in bile duct cancer.

Topic 9: Haematological Disorders of Liver Disease

No: 1227

Assessment of the effectiveness the treatment of indolent lymphomas with chronic hepatitis C

Sergey Lepkov[1], Irina Subortseva[2], Olga Ettinger[1], Svetlana Kosura[1], Oleg Kolomeitsev[3], Uylia Ryabukhina[3], Alla Kovrigina[4], Gennadiy Storozhakov[1]

Russian National Research Medical University Named After Ni Pirogov Therapy Moscow-Russia[1], National Haematology Research Center Haematology Moscow-Russia[2], Blockhins Cancer Research Center Haematology Moscow-Russia[3], National Haematology Research Center Pathology Moscow-Russia[4]

According to our view hepatitis C-associated indolent lymphoma (ILAC) is lymphoma with different markers of hepatitic C in the blood and 50 % of the tumor cells have expression of viral proteins of hepatitis C determined by immunohistochemistry. 77 ILAC patients and 16 patients with indolent lymphoma with chronic hepatitis C(ILCC) were included in study. Subtypes of lymphoma were: in group ILAC - 70 %(54)- follicular lymphoma, 26 %(20)-marginal zone lymphoma, 4 %(3)-chronic lymphocytic leukemia; in group ILCC-81 %(13)-follicular lymphoma, 19 %(3)-chronic lymphocytic leukemia. In group ILAC 47 %(36) received combination chemotherapy(CC), 53 %(41) received antiviral therapy (AVT). In group ILCC 94 %(15) received CC and 6 %(1) received AVT.
Results: In patients with ILAC complete remission(CR) and partial remissions(PR) were obtained in 96 %(40) - AVT and 92 %(33) - CC, stabilization of disease was in 4 %(1), and progression is not revealed during antiviral therapy, 8 %(3) had treatment failure with polychemotherapy($P = 0.04$). In patients with ILCC CR was obtained in 56 %(9), PR- 25 %(4), treatment without effect was in 12 %(2pts). AVT in 1 patient- without effect.

Duration CR in group ILAC after AVT was from 6 to 118 months (median 36 after CC was from 2 to 230 months(median 19). The duration of CR in patients in the group ILCC from 6 to 96 months(median 27 months). The difference in duration of CR was statistically significant ($P = 0.003$).
Conclusion: In group patients with ILAC AVT-the first line of treatment was more effective than polichemistry.

Topic 9: Haematological Disorders of Liver Disease

No: 1459

Obscure overt gastrointestinal bleeding from jejunal varices

Mara Teresa Panlilio[1], Neil Bacaltos[2], Ramon De Vera[2], Janus Ong[1]

University of The Philippines-Philippine General Hospital Section of Gastroenterology Manila-Philippines[1], University of The Philippines-

Philippine General Hospital Department of Surgery Manila-Philippines[2]

Ectopic varices are portosystemic venous collaterals that are located anywhere other than the gastroesophageal region. Obscure overt gastrointestinal bleeding from ectopic variceal bleeding is rare. This is often associated with hemodynamic instability and high mortality due to difficult pre-operative diagnosis. However, when an accurate diagnosis is made, bleeding is controlled by surgery, with low recurrence.

This report describes a case of a 32 year-old female with recurrent melena from jejunal varices secondary to portal vein thrombosis. She was on prolonged oral contraception and with a history of biliary tract surgery for choledocholithiasis. Initial upper endoscopy revealed large esophageal varices, for which endoscopic variceal ligation was done. However, melena recurred, this time necessitating daily blood transfusion. There was a high index of suspicion for ectopic variceal bleeding after doing endoscopy, which revealed only small esophageal varices. CT angiography confirmed a mural vascular enhancement at a jejunal segment. Intraoperative enteroscopy confirmed the presence of varices with cherry red spots at the hepaticojejunostomy anastomosis. Mesocaval shunt was created. The patient had no bleeding recurrence noted over a 1-year follow-up period.

Ectopic variceal bleeding should be suspected in a patient with portal hypertension, melena without hematemesis, and previous abdominal surgery. Though rare, ectopic variceal bleeding should be considered in patients with portal hypertension presenting with obscure overt gastrointestinal bleeding. Early recognition of this condition is critical to institution of appropriate management, which requires decompression of the portal bed.

Topic 9: Haematologycical Disorders of Liver Disease

No: 1215

Case report klebsiella pneumoniae liver abscesses lead to multiple organ

Wanyu Li[1], Yanjun Cai[1], Yue Qi[1], Na Wu[1]

The First Hospital of Jilin University Hepatology Changchun-China[1]

A case is reported of a man who lived in a country of China, experienced right upper abdominal pain for five days without fever. His past medical history was unremarkable. A mass in liver was found two days later. Comuted tomography scans and Magnetic resonance imaging indicated abscess in right lobe(10.2x9.0 cm), while ultrasonic contrast indicated hepatic carcinoma. Bacteriological investigation of the blood detected Klebsiella pneumoniae, but after the antibiotics,the bone marrow and pleural effusions culture yielded negative results.The mass in the liver demonstrated, by direct and histological examination, to be an abscess. In the course of disease, a large amount of free fluid was found in the right thoracic cavity,furthermore multiple organ failure was diagnoized for the liver failure,renal dysfunction and pancreatic damage. Consequently, antiamoebic drugs combine with physiotherapy were administered, leading to improvement in the patient's condition. Drainage wasn't performed without the liquidation. As is evident from this case, a huge amoebic liver abscess is rare but sometimes maybe misdiagnosed and lead to multiple organ failure.

Topic 9: Haematologycical Disorders of Liver Disease

No: 1476

Seroprevalence of hepatitis B hepatitis C and HIV in patients with hemoglobinopathy patients

Gul Ilhan[1], Fuat Ekiz[2], Can Acipayam[3], Gonul Oktay[1]

Hatay Antakya State Hospital Hematology Hatay-Turkey[1], Hatay Antakya State Hospital Gastroenterology Hatay-Turkey[2], Hatay Antakya State Hospital Pediatric Hematology Hatay-Turkey[3]

Purpose: Thalassemia and sickle cell anemia patients have frequent transfusions. Hepatitis B (HBV), hepatitis C (HCV) and human immunodeficiency virus (HIV) are transmitted infections with blood. The objective of this study is to determine frequency of these infections in our hemoglobinopathy patients.
Materials and methods: We investigated 410 hemoglobinopathy patients. Viral serologies were detected with second-generation enzyme-linked immunosorbent assay method. In 410 patients (116 thalassemia major, 16 thalassemia intermedia, 12 hemoglobin H, 222 sickle cell anemia, 43 sickle-beta thalassemia and 1 Hb SE), there were 258 males and 152 females.
Results: The rate of HBV is 1,2 %, HCV is 3,2 % and HIV is 0 %. Our results shows that transfusion transmitted viral infection prevelance is not high compared to the literature.
Conclusion: Using sensitive screening tests with periodically and right donor selection are very important for preventing these infections in hemoglobinopathy patients who are under high risk.

Topic 9: Haematologycical Disorders of Liver Disease

No: 1225

Clinical characteristics of patients with indolent lymphomas with markers of viral hepatitis C (IL + c) and indolent lymphomas without hepatitis C

Sergey Lepkov[1], Irina Subortseva[2], Olga Ettinger[1], Svetlana Kosura[1], Oleg Kolomeitsev[3], Uylia Ryabukhina[4], Alla Kovrigina[5]

Russian National Research Medical University Named After Ni Pirogov Therapy Moscow-Russia[1], National Haematology Research Center Haematology Moscow-Russia[2], Blockhins Cancer Research Center Haematology Moscow-Russia[3], Blochins Cancer Research Center Haematology Moscow-Russia[4], National Haematology Research Center Pathology Moscow-Russia[5]

Background: Virus-associated IL is distinct group according to WHO classification (2008).
The aim was to identify clinical features of IL + C and IL-C.
Methods: 93 IL + C patients and 146 IL-C patients were included in study. Subtypes of lymphoma: follicular lymphoma 71 % (67); marginal zone lymphoma 22 % (20); chronic lymphocytic leukemia 7 % (6).
Results: We found statistically significant differences in the two groups in age, the prevalence of the disease (stage), extranodal involvement, laboratory parameters, liver cirrhosis. The data presented in the table.
Conclusion: IL with hepatitis C is a separate group of lymphomas with certain clinical, laboratory characteristics.

Topic 9: Haematologycical Disorders of Liver Disease

No: 1729

Spleen size a predictor of variceal bleeding in myeloproliferative disease with portal hypertension

R. Asokkumar[1], Chang Pe[1]

Singapore General Hospital Department of Gastroenterology and Hepatology Singapore-Singapore[1]

Objective: Portal hypertension (PHT) in myeloproliferative disease (MPD) occurs either from spleno-portal venous thrombosis or due to increased portal inflow from MPD. Our study aims to describe the association and outcome of PHT in MPD.
Methods: Records of 18 patients with MPD referred for gastroenterology evaluation at our hospital from 1999–2013 were reviewed. Demographics, presentation, endoscopy, radiology findings and treatment outcomes were analyzed.
Results: Median age at presentation was 52 (range 41–75) years. Main symptoms were abdominal pain (39 %), variceal bleeding (33 %) and thrombocytopenia (22 %). Type of MPD included myelofibrosis (39 %), essential thrombocytosis (27 %), polycythemia rubra vera (22 %) and others (11 %). MPD was diagnosed by positive JAK-2 mutation or bone-marrow analysis. All had splenomegaly with a mean spleen size (SS) of 18.4 ($\pm$ 3.7) cm. All had normal liver function. Mean liver stiffness was 9.6 $\pm$ 3.1 kPa in (11/18) patients who underwent Fibroscan®. Radiological imaging in all showed splenomegaly and collaterals without features of chronic liver disease. Gastroscopy performed in 15 patients showed isolated gastric varices in 6/15 (40 %), isolated esophageal varices in 3/15 (20 %) and both in 4/15 (27 %). Variceal bleeding occurred in 6 patients (33.3 %). Mean SS in variceal bleeders was 21.2 $\pm$ 1.5 cm vs. 16.0 $\pm$ 3.3 in non-bleeders ($P < 0.005$). SS accurately predicted variceal bleeding in MPD with an AUROC of 0.907 (95 % confidence interval 0.730-1.000). SS > 19 cm was predictive of variceal bleeding with sensitivity 100 %, specificity 89 %, PPV 85 % and NPV100 %. During a median follow-up of 5.5 $\pm$ 4.6 years, two died (one from variceal bleeding and other from advanced MPD) and two developed cirrhosis.
Conclusion: This is the first case series in South East Asia describing the association of MPD with PHT. We conclude that MPD with spleen size > 19 cm have increased risk of variceal bleeding and will benefit from endoscopic screening.

Topic 9: Haematologycical Disorders of Liver Disease

No: 2144

Idiopathic intrahepatic cholestasis; an unusual presentation of hodgkin's disease

Hande Atalay[1], Banu Boyuk[1], Muhammet Ates[1], Aslan Celebi[1], Ismail Ekizoglu[1], Arzu Algun Didik[2], Fatih Teker[3]

Gaziomanpasa Taksim Edu.research Hospital Internal Medicine Istanbul-Turkey[1], Gaziomanpasa Taksim Edu.research Hospital Pathology Department Istanbul-Turkey[2], Samsun 19 Mayis Medicine Faculty Medical Oncology Samsun-Turkey[3]

Intrahepatic cholestasis in the form of paraneoplastic phenomena is an uncommon presentation of Hodgkin's lymphoma (HL). Herein we report the diagnosis of mixed type HL related idiopathic intrahepatic cholestasis in a 73-year-old man presenting with jaundice, after the inguinal lymph node biopsy indicative of mixed cellular type HL and liver biopsy consistent with intrahepatic cholestasis, following several diagnostic interventions including surgery for suspected extrahepatic obstructive cholestasis. Our findings emphasize to consider HL-related idiopathic intrahepatic cholestasis as a diagnosis of exclusion in cholestatic jaundice of obscure origin.

Topic 9: Haematologycical Disorders of Liver Disease

No: 1229

Chemotherapy in patients with chronic hepatitis C and indolent lymphomas

Sergey Lepkov[1], Irina Subortseva[2], Olga Ettinger[1], Svetlana Kosura[1], Oleg Kolomeitsev[3], Uylia Ryabykhina[3], Alla Kovrigina[4], Gennadiy Storozhkov[1]

Russian National Research Medical University Named After Ni Pirogov Therapy Moscow-Russia[1], National Haematology Research Center Haematology Moscow-Russia[2], Blokchins Cancer Research Center Haematology Moscow-Russia[3], National Haematology Research Center Patology Moscow-Russia[4]

Background: More than 880 billion people in world are infected with HCV. It is known that HCV is one of the main reason of chronic inflammatory diseases of the liver. HCV is etiologic factor in production of indolent lymphomas(IL) besides chronic inflammatory liver diseases. Chemotherapy in patients with HCV and IL and influence of HCV on increase toxicity of chemotherapy are not well understood.
Methods: Study included 53pts with IL and HCV. Patients were followed from 2000 to 2013 in Cancer Research Center. Patients were screened for HCV(serology and presence of HCV RNA)at diagnosis lymphoma. We investigated variation of load and HCV dynamics transaminases and hematological toxicity of chemotherapy.
Results: 53 patients with IL, have been identified as having positive test for antibodies to HCV. 75 %(40) had positive PCR HCV. Median viral load at start of chemotherapy was 2x10[SUP][/SUP]copies/ml. 53 patients received chemotherapy CHOP/R-CHOP. No patient had decompensated liver disease at baseline. Beginning of therapy, median ALT68 IU/l(28-540), AST-60 IU/l(22-440),GGT 58 IU/l(20-150), alkaline phosphatase(AP)–265 IU/l(150-620).

After 6 cycles chemotherapy complete remission(CR) was achieved in 64 %(33), partial remission(PR)-28 %(15) without effect-8 %(5). After 6 courses of chemotherapy median ALT was 138 IU/l(20-780), AST-79 IU/l(40-440),GGTP-287 IU/l(150-530),AP-297 IU/l (180-540). Positive PCR HCV after chemotherapy was in 96 %(51). Median viral load after chemotherapy was 2.2x10[SUP][/SUP]copies/ml. 14 %(7) had hepatocellular insufficiency after polychemotherapy, it was cause of death in 4 %(2).

The duration of complete response was 22 months(6 - 230).
Conclusion: Chemotherapy leads to reactivation HCV in majority of patients with lymphoma and hepatitis C markers. Chemotherapy can cause severe hepatocellular insufficiency.

Topic 10: Hepatic Surgery

No: 1694

Risk factors for and outcomes of open conversion after laparoscopic minor hepatectomy initial experience at a single institution

Brian Goh[1], Chung Yip Chan[9], Jen San Wong[9], Victor Lee[9], Ser Yee Lee[9], Peng Chung Cheow[9], Pierce Chow[9], London Ooi[9], Alexander Chung[9]

Singapore General Hospital Hepatopancreatobiliary and Transplantation Surgery Singapore-Singapore[1]

Background: Laparoscopic liver resection has been increasingly adopted world-wide as a result of the rapid advancement in surgical techniques and equipment. This study aims to determine the risk factors for and outcomes of open conversion after laparoscopic minor hepatectomy (LMH) based on a single center multi-surgeon experience.
Methods: This is a retrospective review of the first 147 consecutive LMH performed between 2006 to April 2014 at a single institution.
Results: LMH were performed for malignancy in 114 (77.6 %) patients of which hepatocellular carcinoma (n = 82) and colorectal metastases (n = 16) were the most common pathologies. The median tumor size was 25, range (6-150) mm. Forty-one (27.9 %) patients had cirrhotic livers and 18 (15.7 %) had fibrotic livers. Eighty-four patients (57.1 %) underwent resection of ≤ 1 segment and 37 (25.2 %) had resections involving postero-superior segments. Fifty patients (44 %) had concomitant surgery in addition to LMH. Twenty (13.6 %) procedures required open conversion and the most common reason was for bleeding (n = 12). Twenty-five patients (17 %) experienced postoperative complications. Univariate analyses demonstrated that only individual surgeon experience and institution experience were risk factors for open conversion. Open conversion was associated with increased intra-operative blood loss, increased intra-operative blood transfusion, increased postoperative morbidity and longer postoperative stay.
Conclusions: Individual surgeon and institution experiences were important risk factors of open conversion after LMH. Open conversion after LMH resulted in poorer outcomes compared to procedures successfully completed laparoscopically.

Topic 10: Hepatic Surgery

No: 1762

Associating liver partition and portal vein ligation for staged hepatectomy (alpps) single center experience in Santiago de chile

Sebastián Uribe-echevarría[1], Mario Uribe[1], María Ignacia Zapata[2], Ernesto Muñoz[2], Carlos Mandiola[3], Luis Paqui[1], Pamela Romanque[2]

Hospital Del Salvador Surgery Santiago-Chile[1], Faculty of Medicine, University of Chile Physiopathology Santiago-Chile[2], Hospital José Joaquín Aguirre Surgery Santiago-Chile[3]

Background: Metastases from colorectal cancer (CRC) are the first cause of liver tumors. Curative resection is amenable in only 15 % of the patients. A main cause for ineligibility for complete resection is insufficient future remnant liver volume (RLV). Associating liver partition and portal vein ligation for staged hepatectomy (ALPSS) procedure has been recently introduced as an alternative for liver volume augmentation in cases with small RLV and high risk of liver failure. We retrospectively analyzed our experience with ALPPS in order to evaluate the application of the procedure.
Methods: Patients referred to the Hepatobiliary Surgery team at Hospital del Salvador from 2011 to 2013 were included in the study, according to eligibility criteria. Volume gaining after ALPPS was followed-up with CT-scan. The volumetric parameters evaluated include RLV, total liver volume (TLV) and RLV/TLV ratio. Liver and systemic functions were evaluated through routine exams. Biopsies were obtained from ligated and non-ligated segments.
Results: 10 ALPPS procedures were performed during the period studied. A significant volume increase was achieved with ALPPS, allowing curative liver resection in all patients. The preoperative RLV to body weight ratio was < 0.5 with RLV range from 198-430 cc (303.3 ± 79.1). After ALPPS the RLV increased up to 179.7 % (35.3-179.7 %), with final RLV of 556.5 ± 172.2. The time required to achieve liver augmentation was shorter compared with other procedures (14 to 40 days), which decrease the risk of recanalization and the chances of increasing the size of metastases. Selection of candidates and morbidity/mortality rates are parameters that will require a careful interdisciplinary assessment.

Topic 10: Hepatic Surgery

No: 2040

Evaluating the effect of hemolysis on indocyanine green (ICG) retention

Hui-chuan Shen[1], Li-ching Wu[1], Wan-ching Lin[1], Ting-chun Hung[2]

Chimei Medical Center Clinical Pathology Tainan-Taiwan[1], Chimei Medical Center Virology Tainan-Taiwan[2]

Indocyanine green (ICG) is a fluorescent dye that for determining metabolic detoxification and hepatic function, especially in preoperative evaluation of the patient with liver disease. But the hemolytic samples are a common and unfavorable occurrence in laboratory practice, as they are often considered unsuitable for Indocyanine green (ICG) retention test. This study examines the effect of hemolysis on Indocyanine green retention test. Hemolysis was caused by adding distilled water to blood to give hemoglobin concentrations of 0.1 to 0.8 g/dL and a rating by technologists of 1 to 4 + hemolyzed. ICG concentrations was measured by Abbott Ci8000 auto- analyzer. The bias of hemolysis ranging from 1 + to 4 + are 5.6, 5.6, 36.1 and 306 % respectively. Measurement uncertainty of the result is 16.4 %. The study shows that hemolysis as influence and interference factor, especially in 3 + to 4+ hemolyzed, and no effective in mild hemolysis.

Topic 10: Hepatic Surgery

No: 1932

The pilot experience of laparoscopic irreversible electroporation for liver cancers adjacent to large vessels

Kai-wen Huang[1]

National Taiwan University Hepatitis Research Center Taipei-Taiwan[1]

Irreversible electroporation (IRE) is a novel, non-thermal ablation technique that uses high-voltage current to induce irreversible disruption of cell membrane integrity. We present the initial safety and efficacy experience with IRE in the treatment of Liver cancers adjacent bilateral portal vein or hepatic veins via laparoscopic approach.

The prospective study was performed at National Taiwan University Hospital in 2012. 7 consecutive patients (4 male, 3 female), age 43-77, with hepatocellular carcinoma of 3-4 cm in diameter (3.5 cm in mean), were treated by IRE. Average ECOG grade was 0.6

(range 0-2). ASA class was 3 in all patients. All procedures were performed under ultrasound guidance. Clinical examination and laboratory assay were performed at baseline, 6 h, 1st to 7th day after procedure. Any adverse effect was recorded intra- and post-operatively.

9 technically successful ablations were performed in the 7 patients. No mortalities occurred at 30 days. Intraoperative transient hypertension occurred with 1 treatment (1/9). No patients had prolonged hypertension after completion of IRE. No intra-operative arrhythmia occurred in these patients, and there was no other evidence of adjacent organ damage related to the procedure. Complete target tumor ablation verified by followed-up abdominal contrast-enhanced image. During 12 months follow-up in mean, no local recurrence was noted.

IRE is a feasible and safe modality for treating liver cancers by laparotomic, laparoscopic or percutaneous approach in our experience. The heat sink effect results from nearby vessels will be diminished by non-thermal ablation of IRE. Further larger scale, prospective randomized trials are needed to confirm our findings.

Topic 10: Hepatic Surgery

No: 1322

Anesthesia for biliary atresia

Nasrin Taghizadieh[1], Mahin Seyedhejazi[2]

Tabriz University of Medical Sciences(liver & Gi Research Center) Liver & Gi Research Center Tabriz-Iran[1], 'tabriz University of Medical Sciences Anesthesia Tabriz-Iran[2]

Aim: Biliary Atresia is a rare but sever biliary disease that affects newborn babies. It causes prolonged jaundice (>2 weeks). First observations of biliary atresia were made by Burns, who in 1817 described jaundice and acholic stools in infants with an "incurable state of the biliary apparatus. Treatment involves a surgical operation as early as possible to minimize liver damage.

Material and methods: For anesthesia intravenous or inhalational induction may be used. Nitrous oxide is avoided to prevent bowel distension. A nasogastric tube also helps to decompress the stomach. Maintenance fluids should contain 2.5 % dextrose in Ringer lactate to avoid hypoglycemia.. Blood sugar monitoring should be done at least after induction and at the end of the surgery. Generally, there is a little blood loss and blood replacement is not necessary. However, warm blood is replaced as soon as the loss exceeds 10 % of the estimated blood volume.

Monitoring is usually done with an ECG, pulse oximeter, noninvasive blood pressure and body temperature. Ventilation should be controlled and end tidal gases monitored for oxygen, carbon dioxide and volatile anesthetic agents. Postoperative analgesia is with intravenous opioids or epidural drugs.

Conclusion: Anesthesia for babies with biliary atresia follows the same general principles of anesthesia as for neonates and infants. The degree of liver dysfunction and the drug's ability to bind to plasma proteins are important variables in determining drug kinetics in patients with liver disease.

Topic 10: Hepatic Surgery

No: 1468

Analysis of grade c bile leakage complication after hepatectomy

Nanako Yasui[1], Masaru Inagaki[2], Hiroki Kajioka[2]

National Hospital Organization Fukuyama Medical Center Surgery Fukuyama-Japan[1], National Hospital Organization Fukuyama Medical Center Hepato-biliary-pancreatic Surgery Fukuyama-Japan[2]

Purpose: Bile leakage is one of troublesome complications after hepatectomy and sometimes needs surgical interventions. We analyzed the incidence of Grade C bile leakage after hepatectomy according to International Study Group of Liver Surgery definition and its outcome.

Methods: We reviewed 331 hepatectomy cases between March 2003 and September 2014.

Results: Grade C bile leakage occurred in three cases(0.9 %). Indications of hepatectomy were hepatocellular carcinoma in all cases and anatomical resections were performed in all cases (i.e.: posterior sectionectomy, left hemihepatectomy, and S4 segmentectomy). Mean operation time was 450 min (371 ~ 535 min) and mean blood loss was 2600 ml (1900 ~ 3500 ml). We always performed bile leakage test and could not detect any bile leakage in all cases. Endoscopic or percutaneous biliary drainage was done in every case, but they were not effective, so we decided reoperation. Bile leakage optimized in 1 day, 15 days and 171 days after surgery. One case was a late onset bile leakage. Mean interval between endoscopic or percutaneous biliary drainage and reoperation was 90 days (66 ~ 133 days). Surgical procedures included hepatectomy in 2 cases and hepaticojejunostomy in one case. Recurrence of bile leakage occurred in one case at 18 days after reoperation and needed further treatments.

Conclusions: Bile leakage after hepatectomy needs a long-term treatments and sometimes requires surgical interventions. Surgical interventions were effective in 2 cases, but we should make a careful decision for reoperation.

Topic 10: Hepatic Surgery

No: 1186

Advantage of preoperative percutaneous transhepatic portal embolization for hilar bile duct cancer

Masaru Inagaki[1], Nanako Yasui[1], Hiroki Kajioka[1], Koji Kitada[1], Naoyuki Tokunaga[1], Hiromi Iwagaki[1]

National Hospital Organization Fukuyama Medical Center Surgery Fukuyama-Japan[1]

Introductions: Percutaneous transhepatic portal embolization before operation is recommended in small for size remnant liver, avoiding liver failure in periopeative period. Some cases of hilar bile duct cancer need an extended hepatectomy due to the extensive bile duct invasion.

Methods: We reviewed hilar bile duct patients in our institution from March 2003 to September 2014.

Results: 3 cases needed preoperative percutaneous transhepatic portal embolization. One was male and two were female. Every case needed right trisegmentectomy at the preoperative evaluation. Retention rate of preoperative cyanine tests at 15 min were 18.6, 2.5, and 12.8 %. Complication after percutaneous transhepatic portal embolization was fever in all cases (max temperature: 37.8 ~ 39.4 °C). Liver function test elevated slightly (max AST: 24 ~ 35 IU/l, max ALT: 20 ~ 63 IU/l, max total bilirubin: 1.2–1.9 mg/dl). Resection rate of liver before percutaneous transhepatic portal embolization was 75.3 ± 0.6%. Resection rate of liver after percutaneous transhepatic portal embolization decreased to 69.3 ± 3.1%. Right trisegmentectomy with or without portal

reconstruction were performed as scheduled in all cases. Mean interval between percutaneous transhepatic portal embolization and operation was 20.7 days. Mean max total bilirubin levels after operation was 4.8 mg/dl (3.8–6.0 mg/dl). Complications after operation evoked in all cases (i.e.: Intraabdominal abscess, leakage of hepaticojejunostomy, and cholangitis). Mean hospital stay was 52 days (31–92 days). Grade A liver failure according to ISGLS criteria at Day 5 after operation occurred in two cases, but both cases were not fatal.

Conclusions: Preoperative percutaneous transhepatic portal embolization in hilar bile duct cancer patients is safe and considered as a recommended approach, avoiding a postoperative liver failure.

Topic 10: Hepatic Surgery

No: 2236

Bronchiolltis obliterans organizing pneumonia after orthotopic liver transplantation

Ramin Farajpour[1], Ali Ghavidel[2], Shiva Farajpour[3], Mohammadhosein Soomi[2], Mehdi Farhoodi[4]

Student Research Committee of Tabriz Medical University Faculty of Medicine Tabriz-Iran[1], Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences Tabriz-Iran[2], Vice Chancellor For Research and Technology of Tabriz Medical University Nsrcc(neuroscience Research Center) Tabriz-Iran[3], Nsrcc(neuroscience Research Center) Nsrcc(neuroscience Research Center) Tabriz-Iran[4]

Bronchiolitis obliterans organizing pneumonia (BOOP) has been described after bone marrow, lung, heart–lung, and renal transplantation, but rarely after orthotopic liver transplantation (OLT). We report a case of BOOP after OLT to emphasize BOOP as an under diagnosed and treatable cause of nonresolving pneumonia, which may not be preventable by maintenance low-dose prednisone. A 25-year-old woman was hospitalized for dyspnea and cough 5 years after OLT. Among his medications were tacrolimus and prednisone. Physical examination was significant for lung crepitations and bilateral leg edema. Chest x-ray revealed bilateral infiltrates. Computed tomography (CT) of the chest demonstrated bilateral diffuse infiltrates with areas of sparing and nodularities.

Bronchoscopy was normal and bronchoalveolar lavage was negative. Lung biopsy was performed and demonstrated serpiginous plugs of fibroblastic tissue filling the alveolar spaces, focal fibrosis of some alveolar septa, and reactive pneumocytic hyperplasia consistent with BOOP.

Methylprednisolone was continued with clinical improvement and weaning from the ventilator.

Topic 10: Hepatic Surgery

No: 1278

Consideration of the postoperative chemotherapy after the surgical resection for colorectal cancer liver metastasis

Hiroshi Maeno[1], Masako Noumi[1], Tatsuya Okamoto[1], Syuji Nagao[1], Syunji Kawamoto[1]

Fukuoka Tokusukai Medical Center Surgery Kasuga-Japan[1]

Background/aims: In the recent years, the postoperative adjuvant chemotherapy of colorectal cancer has improved survival rate. Simultaneously, the radical resection cases are also increasing.
There are many reports showed surgical resection for liver metastasis of colorectal cancer if excision will be possible is good treatment results.

However, it is carrying out by operator's decider in many cases after hepatectomy from the colorectal cancer. We consider adjuvant chemotherapy after hepatectomy of the colorectal cancer that an argument is required about the right or wrong. We considered the hepatectomy of the colorectal cancer in our hospital, and examined the usefulness of postoperative adjuvant chemotherapy.

Methodology: We performed that comparison examination with postoperative adjuvant chemotherapy after a hepatic resection this time to 40 cases (synchronous liver metastasis 26 cases and metachronous liver metastasis 14 cases) except surgical death performed the colorectal cancer hepatic resection cases in our hospital from April, 2005 before March, 2014.

Results: There was no significant difference about the profiles or perioperative factors neither synchronous liver metastasis nor metachronous groups. There was significant difference in the point of adjuvant chemotherapy commencing time for the hepatectomy case in the synchronous liver metastasis ($P = 0.0002$). But, there was no significant difference prognosis ($P = 0.19$). There was no significant difference a prognosis in the hepatectomy group of metachronous liver metastasis ($P = 0.56$).

Conclusions: In our hospital, postoperative adjuvant chemotherapy was not relating to prognosis for the hepatectomy of the colorectal liver metastasis. This examination was few number, we think the further future cases needs a pile and inquiring.

Topic 10: Hepatic Surgery

No: 1045

Establishment and validation of SSCLIP scoring system to estimate survival in hepatocellular carcinoma patients who received curative liver resection

Ming-hua Zheng[1], Sha Huang[1], Gui-qian Huang[1], Gui-qi Zhu[1], Wen-yue Liu[1], Jie You[2], Ke-qing Shi[1], Xiao-bo Wang[3], Han-yang Che[4], Guo-liang Chen[5], Jian-feng Fang[6], Yi Zhou[7], Meng-tao Zhou[7], Martin Braddock[8], Yong-ping Chen[1]

The First Affiliated Hospital of Wenzhou Medical University Department of Infection and Liver Diseases, Liver Research Center Wenzhou-China[1], The First Affiliated Hospital of Wenzhou Medical University Department of Oncological Surgery Wenzhou-China[2], Wenzhou Central Hospital Intensive Care Unit Wenzhou-China[3], The Second Affiliated Hospital of Wenzhou Medical University Department of Hepatobiliary Surgery Wenzhou-China[4], Jinhua People's Hospital Department of General Surgery Jinhua-China[5], Shaoxing People's Hospital, Shaoxing Hospital of Zhejiang University Department of Hepatobiliary Surgery Shaoxing-China[6], The First Affiliated Hospital of Wenzhou Medical University Department of Hepatobiliary Surgery Wenzhou-China[7], Astrazeneca R&d Global Medicines Development Loughborough-United Kingdom[8]

Aim: There is no prognostic model that is reliable and practical for patients who have received curative liver resection (CLR) for hepatocellular carcinoma (HCC). Here, we aim to establish and validate a Surgery-Specific Cancer of the Liver Italian Program (SSCLIP) scoring system for those patients

Method: 2215 patients who underwent CLR with suspected HCC from five separate tertiary hospitals were screened. Univariate and multivariate Cox proportional hazards regression analyses were

performed and corresponding independent predictors were identified. The SSCLIP was constructed by adding these predictors to the original Cancer of the Liver Italian Program (CLIP). In both training and validation cohorts, 12-month and 36-month prognostic performances of the SSCLIP were compared against existing models. Survival distributions of different risk levels of the SSCLIP were also assessed.

Result: Four independent predictors were identified and added to construct the SSCLIP, including age (HR = 1.075, 95 % CI 1.019-1.135, $P = 0.009$), albumin (HR = 0.804, 95 % CI 0.681- 0.950, $P = 0.011$), prothrombin time activity (HR = 0.856, $P = 0.020$) and microvascular invasion (HR = 19.852, 95 % CI 2.203 -178.917, $P = 0.008$). In both training and validation cohorts, 12-month and 36-month prognostic performances of the SSCLIP were significantly better than those of the original CLIP, model of end-stage liver disease-based CLIP, Okuda and Child-Turcotte-Pugh score (all $P < 0.05$). The stratification of risk levels of the SSCLIP showed a great ability to differentiate patients with different outcomes.

Conclusion: A novel SSCLIP to predict survival of HCC patients who received CLR based on objective parameters provides a refined prognosis algorithm.

Topic 10: Hepatic Surgery

No: 1888

A rare infectious complication after LDLT; pyogenic spondylodiscitis caused by methicillin resistant staphylococcus aureus (MRSA)

Joo Seop Kim[1], Doo Jin Kim[1], Hyoung Su Kim[2], Jang Yong Jeon[1]

Hallym University Surgery Seoul-Korea, South[1], Hallym University Internal Medicine Seoul-Korea, South[2]

Methicillin-resistant Staphylococcus aureus (MRSA) infection frequently complicates the postoperative course of liver transplant recipients. It has been well described that MRSA associated bacteremia, pneumonia and surgical site infection are common. But, MRSA infection manifesting as pyogenic spondylodiscitis is very rare. To our knowledge, pyogenic spodylodiscitis due to MRSA in lumbar spine after living donor liver transplantation (LDLT) has not been previously reported. Here, we report a 50-year-old man who developed pyogenic spondylodiscitis caused by MRSA after LDLT. Our patient underwent LDLT for HBV related cirrhosis using modified right lobe. Immnosuppressive treatment was administered with basiliximab, tacrolimus, corticosteroids and mycophenolate mofetil. He discharged on postoperative 28th day with uncomplicated course. At one week after discharge the patient was readmitted for abdominal pain and high fever. Bile leakage at the anastomosis site was found by endoscopic retrograde cholangiopancreaticography (ERCP) and managed successfully with endoscopic nasobiliary drainage (ENBD). The culture of drained fluid showed MRSA and the patient was treated with vancomycin for 4 weeks, and resulted in resolution of the infection. However, one month later the patient presented with severe back pain. At this time, MRI showed massive spondylodiscitis of lumbar 2-3 spine and paraspinal abscess formation. Our patient was treated by surgical debridement and primary bone graft. MRSA was cultured from the abscess specimen. Postoperatively, the patient received intravenous vancomycin for 2 weeks and revealed satisfactory outcome without any neurological sequelae. Presently the patient is followed up without rejection and other complications.

Topic 10: Hepatic Surgery

No: 1692

Prognostic factors after liver resection for multifocal hepatocellular carcinoma

Brian Goh[1], Pierce Chow[1], Jin Yao Teo[1], Chung Yip Chan[1], Jen San Wong[1], Peng Chung Cheow[1], Alexander Chung[1], London Ooi[1]

Singapore General Hospital Hepatopancreatobiliary and Transplantation Surgery Singapore-Singapore[1]

Background: Presently, the role of liver resection (LR) for multifocal hepatocellular carcinoma (HCC) remains controversial. However in many regions world-wide, LR remains the only treatment modality available to such patients which offers the possibility of long-term cure. To determine the outcomes and prognostic factors of patients with multifocal HCC after LR.

Methods: This is a retrospective analysis of 110 patients who underwent potentially curative LR for pathologically proven multifocal HCC between 2000 to 2011.

Results: The median age was 64 (range, 18-84) years and there were 88 males (80.0 %). Sixty-one patients underwent a major hepatectomy and the overall postoperative mortality was 1.8 %. Sixty-eight patients had liver cirrhosis of which 58 were Child's A and 10 were Child's B. The 1- and 5-year overall survival (OS) was 82 % and 44 % respectively. The corresponding 1- and 5-year recurrence-free survival (RFS) was 57 % and 19 %, respectively. Multivariate analysis demonstrated that number of nodules (> 3) and presence of microvascular invasion were associated with RFS. Number of nodules (> 3), margin positivity, Child-Pugh status and presence of microvascular invasion were independent prognostic factors of OS.

Conclusions: LR followed by treatment of recurrences may result in reasonable long term survival and should be considered in a selected group of patients with multifocal HCC. Number of nodules (> 3), margin positivity, Child-Pugh status and presence of microvascular invasion but not tumor size were independent predictors of OS. These findings have potential implications on the AJCC staging for multifocal HCC.

Topic 11: Hepatitis B

No: 2099

Potential renal protective effect of telbivudine in patients with chronic hepatitis B infection compared to other antivirals

Vibhakorn Permpoon[1]

Bumrungrad International Hospital Digestive Disease (g-i) Center Bangkok-Thailand[1]

Background: At Bumrungrad International (BI) Hospital, seven licensed medications have been used for treatment of HBV infection. While nephrotoxicity from some medications have been of concern, recent evidence suggested potential renal protective effect of Telbivudine. This study is aimed to comparatively explore potential effects of Telbivudine and other medications (Lamivudine, Adefovir, Tenofovir, Entecavir, Pegylated Interferon α-2a, and Pegylated Interferon α-2b) on renal function measured by estimated glomerular filtration rate (e-GFR).

Methods: This retrospective study utilized clinical information from medical records of 1,065 CHB patients who were treated with the

above medications at BI Hospital between 1 January 2008 and 31 December 2013.

Patient demographic and clinical variables including creatinine, eGFR (MDRD), HBV viral load, AST, ALT, urine protein, and MELD score were analysed. The last observation carried forward was used. Analysis of covariance model with treatment was used to test the difference in eGFR between Telbivudine and other antivirals. Means were calculated using the least square method.

Results: The interim analysis identified 966 of CHB patients treated with at least one of the 7 antivirals and had complete medical records. Telbivudine was used in 176 cases (18.22 %), of which 81 cases (46 %) were combined with other antivirals.

Baseline least square mean eGFR were 95.42 vs 95.64 mL/min/1.73 m[SUP]2[/SUP]; $P = 0.6885$. Renal function steadily improved in Telbivudine group but declined in non-Telbivudine group, with statistically significant difference shown at 12 months after treatment ($P = 0.0087$).

Conclusions: Potentially superior renal protective effect of Telbivudine to other antivirals for chronic hepatitis B infection exists and starts after twelve months.

Topic 11: Hepatitis B

No: 1180

Comparison of HBeAg seroconversion rate among HBeAg positive chronic hepatitis B patients treated with LDT and ETV using propensity score matching methods

Youde Liu[1], Jinping Liu[1], Zhegzhong Hua[1], Yucui Liu[1], Jiguang Yu[1], Zhiqiang Zou[1]

Yantai Infectious Disease Hospital Hepatology Yantai-China[1]

Aim: To compare the HBeAg seroconversion among HBeAg-positive CHB patients treated with either telbivudine or entecavir using propensity score matching (PSM) balanced covariates between the groups.

Methods: Clinical data were retrospectively analyzed among 212 cases of HBeAg-positive CHB patients enrolled between December 2009 to May 2014 in our hospital receiving either telbivudine (Sebivo, 600 mg/day), or entecavir (Baraclude, 0.5 mg/day). PSM function of SPSS software was conducted to reduce confounding bias between the groups.and then survival analysis was performed for the matched data.

Results: Among the 212 patients of follow-up, 152 cases were receiving entecavir treatment, while 60 cases receiving telbivudine treatment. The 2-year cumulative incidence of HBeAg seroconversion in telbivudine treatment group and the entecavir group were 41.7 % and 8.0 %, respectively, and the 4-year cumulative incidence of HBeAg seroconversion rates were 45.8 % and 18.2 %, respectively (Log Rank test $\chi^2 = 23.254$, $P < 0.0001$) (Figure 1, before match).

After the match, the 2-year cumulative incidence of HBeAg seroconversion in telbivudine treatment group ($n = 56$) and entecavir treatment group ($n = 56$) were 28.6 % and 14.8 %, respectively, and the 4-year HBeAg seroconversion cumulative incidence were 42.0 % and 39.3 %, respectively (Log Rank test $\chi^2 = 4.469$, $P = 0.035$) (Fig. 1 after match).

Cox regression analysis showed that telbivudine treatment, low baseline HBeAg levels are independent predictors for HBeAg seroconversion in CHB.

Conclusion: HBeAg seroconversion incidence is higher in HBeAg-positive CHB patients receiving telbivudine than patients receiving entecavir.

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Topic 11: Hepatitis B

No: 1333

Therapeutic effects of telbivudine and entecavir in hepatitis B virus related liver cirrhosis

Cheng-kun Liu[1], Cheng-hung Chien[1], Rong-nan Chien[1], Chih-lang Lin[1]

Chang Gung Memorial Hospital Liver Resarch Unit Keelung-Taiwan[1]

Aim: To compare the long-term effectiveness of telbivudine (LdT) and entecavir (ETV) in HBV-related liver cirrhosis patients, and to evaluate change in renal function post-LdT treatment.

Method: This open-label, observational study enrolled HBV-related liver cirrhosis patients treated with anti-viral agents for > 1 year between December 2007 and April 2011.

Results: Of the 142 eligible patients (mean age, 52 years), 57 received LdT 600 mg q.d. and 85 received ETV 0.5 mg q.d.. Mean treatment duration was 51 months. The table shows proportion of patients achieving ALT normalization and undetectable serum HBV DNA. Eight patients in LdT and five patients in ETV group developed hepatocellular carcinoma after 1 year of treatment (hazard ratio, 2.1; 95 % confidence interval, 0.6–6.8). Renal function was analyzed at baseline and post-treatment in 93.0 % (53/57) patients receiving LdT. On LdT treatment, 24.5 % (12/49) patients showed significant improvement in eGFR with a change in chronic kidney disease (CKD) stage. This improvement was prominent in patients with baseline CKD stage 2 (mean eGFR increase: 1.34 mL/min/1.73 m[SUP]2[/SUP]/year) and stage 3 (mean eGFR increase: 4.27 mL/min/1.73 m[SUP]2[/SUP]/year).

Conclusion: LdT and ETV are effective for long-term treatment of HBV-related liver cirrhosis. Patients with CKD stages 2 and 3 showed the greatest improvement in eGFR with LdT treatment.

Topic 11: Hepatitis B

No: 1290

Comparison of the efficacy of tenofovir and entecavir for the treatment of nucleos(t)ide naive patients with chronic hepatitis B

Sang Goon Shim[1]

Samsung Changwon Hospital, Sungkyunkwan University School of Medicine Internal Medicine Changwon-si-Korea, South[1]

Background/aims: An important goal in the treatment of chronic hepatitis B virus (HBV) infection is to prevent hepatocellular carcinoma and liver cirrhosis by suppressing HBV replication. Tenofovir and entecavir are effective viral suppression compounds, but comparative data is scant, especially in Korea. This study compared tenofovir and entecavir concerning efficiencies and side effects.

Methods: We retrospectively reviewed data of nucleos(t)ide-naïve patients with chronic HBV infection. Independent variables reflecting virological response were evaluated and the decline in serum HBV DNA levels and side effects between tenofovir- and entecavir-treated patients were compared at treatment week 12, 24, and 48.

Results: At the end of 48 weeks, there was no statistical difference in the induction of undetectable levels of HBV DNA between the entecavir (82.5 %) and tenofovir (69.2 %) groups. Entecavir was more effective in reducing serum HBV DNA levels at 24 weeks of treatment (serum HBV DNA decline of 5.53 and 4.95 log10 units for entecavir and tenofovir respectively, $P = 0.044$), but the rate of decline was similar at other weeks. There was no difference between two groups in terms of side effects and discontinuance of treatment due to side effects.
Conclusions: Tenofovir is not significantly different from entecavir in virologic response and tolerability in treatment of chronic HBV.

Topic 11: Hepatitis B

No: 1464

The efficacy and safety of telbivudine or tenofovir disoproxil in pregnancy for prevention of mother to child transmission of hepatitis B virus

Hf Huang[1], Yq Zhang[1], Qx Wu[1], Jn Li[2], Ym Wang[1]

Southwest Hospital, Third Military Medical University Department of Infectious Diseases Chongqing -China[1], Southwest Hospital, Third Military Medical University Department of Gynecology and Obstetrics Chongqing -China[2]

Background and aims: This study was to evaluate the efficacy and safety of telbivudine (LdT) and tenofovir (TDF) as monotherapy or combined treatment in HBeAg-positive pregnant women with high viral load for preventing mother-to-child transmission (MTCT) in an open-labeled study.
Methods: The 355 HBeAg-positive pregnant women with HBV DNA > 10[6]IU/mL enrolled were treated with antiviral therapy from 24-32 weeks of gestation(308 in LdT group, 23 in TDF group, 24 in TDF + LDT group, the latter with a switch therapy from ETV + ADV or LAM + ADV due to pregnancy). All infants were vaccinated with recombinant HBV vaccine and hepatitis B immune globulin (HBIG) according to standard immunoprophylaxis procedure. MTCT rate was determined by HBsAg and HBV DNA detection in 6 months after birth.
Results: Significantly lower HBV DNA levels were noted in all the enrolled mothers when delivery. The rate of HBsAg positive and HBV DNA detectable in infants at 6 months was 0 % in each group. The incidence of undetectable cord blood HBV DNA levels has no significantly difference among the three groups (LdT group, 99.2 %; TDF group, 100 %; LdT + TDF group, 100 %; P > 0.05). No severe adverse events, including blood creatine kinase (CK) and estimated glomerular filtration rate (eGFR), or complications were observed in all the mothers and infants.
Conclusions: LdT and TDF monotherapy or their combo-therapy were equally effective and well-tolerated in HBeAg positive and high viral load mothers as well as their infants on short term follow up, and they were associated with significant reduction of MTCT.[SUP][/SUP][SUP][/SUP]

Topic 11: Hepatitis B

No: 1160

Association between age and seroconversion in initial HBV patients

Sheng-hao Yun[1]

Lanzhou Military Region General Hospital Infectious Disease Lanzhou-China[1]

Aim: To explore whether seroconversion is associated with age in anti-viral treatment.
Methods: 102 patients were divided into four groups according to their ages (< 20 years old, 20-40 years old, 40-60 years old, and > 60 years old, 26 per group), and were given antiretroviral therapy by telbivudine 0.6 g/day. According to the guidelines of chronic hepatitis B prevention and treatment, these treatments are all effective in antiviral therapy. Subsequently, these patients were treated for consecutive 192 weeks and then followed up for another 192 weeks to observe the association of age and seroconversion in antiretroviral therapy.
Results: RVR in the four groups were 100 %, 98 %, 90 %, 75 %, respectively, whereas EVR were 100, 95, 88, 69 %, respectively. The antigen conversion rates were 82, 4, 37, 23 %, respectively.
Conclusion: For antiviral therapy using telbivudine, the seroconversion is closely associated with the patient's age: younger age indicates better response in antiviral treatment. Therefore, it is highly recommended that for patients with evidence of resistance to treatment, it is better to commence the virus treatment at their younger stage, for achieving better treatment effect and better prognosis.

Topic 11: Hepatitis B

No: 2193

The relationship between fibrosis level and blood neutrophil to lymphocyte ratio in inactive hepatitis B carriers

Bulent Yilmaz[1], Faden Hayrunnisa Aydin[2], Guray Can[1], Zeynep Senturk[2], Berna Ustuner[2], Hasan Yilmaz[3], Murat Ozturkler[3], Emir C. Roach[4], Ugur Korkmaz[1], Mevlut Kurt[1], Altay Celebi[3], Omer Senturk[3], Sadettin Hulagu[3]

Aibu Educational Hospital Gastroenterology Bolu-Turkey[1], Kocaeli University Internal Medicine Kocaeli-Turkey[2], Kocaeli University Gastroenterology Kocaeli-Turkey[3], Cleveland Clinic Pathobiology Cleveland-United States[4]

Introduction: Neutrophil–lymphocyte ratio (NLR) has been used as a simple, affordable, and easily accessible marker to predict prognosis in a variety of inflammatory and neoplastic diseases. However, there are few studies investigating their role in patients with hepatitis B. The aim of this study was to investigate the relationship between NLR and liver fibrosis in patients who were being followed as inactive hepatitis B carriers.
Materials and methods: The study included 78 patients who were followed for 1 year as inactive hepatitis B carriers. Liver biopsy was performed and the fibrosis scores of the histological activity index were assessed according to the Metavir scoring system. The patients were divided into two groups on the basis of the fibrosis scores: those with a score below 2 and those with a score above 2. The NLR of patients was calculated from blood samples taken at the same time as the biopsy.
Results: Histopathologic analysis of 78 patients showed that 41 (53 %) had fibrosis grade 0-1 and 37 (47 %) patients had fibrosis grade greater than 2. NLR was found to be statistically significantly lower in the group with fibrosis grade of at least 2 (1.51 ± 0.61 vs. 1.79 ± 0.64, $P = 0.043$). Biochemical and hematological data were found to be similar in both groups. Spearman correlation analysis showed a negative correlation between the fibrosis score and NLR ($r = -0.279$, $P = 0.013$).

Conclusion: In inactive hepatitis B carriers, the histological activity index and NLR were found to be correlated negatively. NLR can be used as a predictor of fibrosis in combination with other noninvasive markers.

Topic 11: Hepatitis B

No: 2161

Spontaneous vaccine escape mutation in inactive hepatitis B carriers and its important

Faden Hayrunnisa Aydin[1], Omer Senturk[2], Murat Sayan[3], Ugur Korkmaz[2], Hasan Yilmaz[2], Murat Ozturkler[2], Fatma Gecgel[2], Altay Celebi[2], Sadettin Hulagu[2]

Kocaeli University Internal Medicine Kocaeli-Turkey[1], Kocaeli University Gastroenterology Kocaeli-Turkey[2], Kocaeli University Microbiology Kocaeli-Turkey[3]

Introduction: The essential problem during oral antiviral therapy of chronic hepatitis B, is a primary or compensatory development of drug resistance mutation and, also it can be seen naturally in patients with KBH. On the other hand, another problem is typical HBsAg escape mutation and antiviral-drug-associated potential vaccine escape mutation (ADAPVEM), related oral antiviral, caused by overlapping of pol and S genes in HBV genome organization. In this study, our aim is to evaluate pattern and frequency of typical HbsAg escape mutation and naturally developed oral antiviral resistance.
Materials and methods: Patients with HbsAg positive, HBV DNA was less than 2000 during 6 months followup, normal AST and ALT level were included study. HBV S gene mutation was detected by DNA sequence method.
Results: S(superficial) gene mutation was detected in 4 of 32 patients, performed genotype analysis in our study. 193. aa position anti-HBV vaccine mutation and immune system escape mutation were detected in 3 (9 %) and 1 (3 %) patients, respectively.
Discussion: S gene mutation was detected in 4 patients in our study (Table). Detected mutation was anti-HBV vaccine escape mutation. This result revealed that, naturally vaccine escape before the treatment can be seen. This issue can be important in terms of public health.

Topic 11: Hepatitis B

No: 1258

Several factors could be considered when applying the liver stiffness by transient elastography in HBV infected patients

Young Kul Jung[1], Sang Jun Suh[1], Hyung Joon Yim[1]

Kumc Ansan Hospital Internal Medicine Ansan-Korea, South[1]

The aim of this study is to compared with transient elastography and other invasive fibrosis marker, and to investigate several factors influencing the liver stiffness measurement (LSM) in chronic hepatitis B patients. Two hundred twenty eight patients with CHB patients who underwent liver biopsy and TE in the same time were recruited from January 2008 to December 2013. 159 (69.7 %) of them were Male, and mean age was 41.9 years old. Mean of AST and ALT were 114.9 IU/L and 165.1 IU/L, respectively. Platelet count was 1.75 x 10[SUP][/SUP] cell/uL. 102 (44.7 %) patients had HBeAg positivity. In liver Biopsy, 39 patients (17.1 %) had F0-1, 57 (25.0 %) had F2, 76 (33.3 %) had F3, and 56 (24.6 %) had F4, respectively. In view of the significant fibrosis (F4), TE showed significantly good estimate of liver fibrosis, and corresponding area under the ROC curves of LSM was 0.733 that showed slightly good estimate value compared with APRI (0.468) and FIB-4 (0.641). Among the lower ALT patients corresponding area under the ROC curves of LSM was 0.804, and among HBeAg negative patients corresponding area under the ROC curves of LSM was 0.755. The cutoff LSM values for $> F2$, $> F3$, and F4 were 6.9, 8.5, and 10.1 kPa, respectively. TE has good estimate performance for liver stiffness and fibrosis compared with AFRI and FIB-4 in chronic hepatitis B patients. ALT and HBeAg could influence liver stiffness. So, different cutoff LSM values may be applied in chronic hepatitis B patients.

Topic 11: Hepatitis B

No: 1205

Study of hepatitis B markers in patients with rheumatoid arthritis

Yukitomo Urata[1]

Tsugaru General Hospital, United Municipalities of Tsugaru Department of Rheumatology Gosyogawara-Japan[1]

Objectives: To investigate variations in levels of anti-hepatitis B surface (anti-HBs) and anti-hepatitis B core (anti-HBc) antibodies, which are recognized as factors affecting reactivation of hepatitis B, in patients with rheumatoid arthritis (RA) and to identify factors associated with decreases in these antibodies.
Subjects: One hundred thirty-nine patients with RA complicated by hepatitis B (102 women; mean age, 67.2 years; disease duration, 8.7 years).
Methods: Anti-HBs levels, anti-HBc levels, other hepatitis B markers, and clinical indices were measured at the time of enrollment and 1 year thereafter. Patients whose antibody levels at 1 year after enrollment were lower than those at the time of enrollment were assigned to the decrease group. Multivariate analysis was then performed to identify factors associated with decreased antibody levels.
Results: After 1 year of follow-up, both anti-HBs and anti-HBc levels were significantly decreased (445 $\rightarrow$ 430 mIU/mL, $P = 0.0001$ and 6.0 $\rightarrow$ 5.1 S/CO, $P < 0.0001$, respectively). Based on multivariate analysis, the only factor significantly associated with decreased anti-HBc levels was anti-HBc levels at the time of enrollment ($P = 0.0062$; odds ratio [OR], 0.71; 95 % confidence interval [CI], 0.52-0.91). The use of steroids was not significantly related to a decrease in anti-HBs levels ($P = 0.0077$; OR, 4.5; 95 % CI, 1.48-14.88). The prednisolone-equivalent steroid dose was 2.8 mg/day in the decrease group.
Conclusion: Over the course of RA, both anti-HBs and anti-HBc levels decrease significantly. Administering a low steroid dosage does not decrease anti-HBs levels.

Topic 11: Hepatitis B

No: 1668

Evolutionary patterns of hepatitis B virus quasispecies under lamivudine treatment and its impact on relapse

Jianning Jiang[1], Baojian Wang[1], Minghua Su[1], Xiaoli Wu[1], Ailian Lu[1], Shaohua Zhong[1], Shihua Li[1], Yanxiu Liang[1], Rong Xie[1], Yanyan Mo[1], Peng Liang[1]

The First Affiliatel Hospital of Guangxi Medical University, Nanning Infectious Disease Department Nanning-China[1]

Objectives: To investigate the evolution of hepatitis B virus (HBV) Polymerase (P) region quasispecies (QS) in CHB patients who stopped lamivudine treatment after meeting end-point criteria of 2008 APASL guideline and its impact on relapse.
Materials and methods: 43 patients with chronic hepatitis B were receiving lamivudine (25 initial treatment, 18 retreatment). All patients stopped lamivudine after meeting end-point criteria of 2008 APASL guideline and were followed up. Serum specimens were taken at baseline and liver biopsy specimens were taken at therapeutic end-point. Full-length hepatocyte cccDNA were amplified with HBV cccDNA special primers by Rolling circle amplification. Serum HBV rcDNA and hepatocyte cccDNA P gene were amplified and cloned. The HBV P region was sequenced at the average of 27 clones per sample (2322 total from both groups).
Results: QS complexity of hepatocyte cccDNA P region in the patients without relapses was statistically lower than that with relapse ($P = 0.03$) at stopping point. In the retreatment patients group, QS complexity of hepatocyte cccDtNA P region in the patients without relapses was statistically lower than that with relapse ($P = 0.006$) at stopping point. QS complexity of hepatocyte cccDNA P region in retreatment patients group was statistically higher than in initial treatment group at stopping point ($P = 0.021$). QS complexity of HBV rcDNA P gene were not significantly different between the patients with and without relapses.
Conclusion: Characteristics of HBV hepatocyte cccDNA P gene QS evolution at therapeutic end-point contribute to the prediction of relapse.

Topic 11: Hepatitis B

No: 2155

The evaluation of HBV prevalence in children

Selma Tosun[1], Erhun Kasirga[2]

Izmir Bozyaka Research and Education Hospital Infectious Diseases Izmir-Turkey[1], Celal Bayar University The School of Medicine Pediatric Gastroenterology Manisa-Turkey[2]

Aim: In this study we aimed to evaluate HBV seroprevalence of a group of primary school children who were vaccinated according to universal vaccination programme.
Methods: HBV serology of the primary school students with low socioeconemic status, who were born in 1996 to 2004, in Manisa was tested by EIA method. An AntiHBs titer of ≤ 9 IU/mL was considered as negative, while a titer of ≥ 10 IU/mL was considered positive.
Results: A total of 353 children were included in the study. None of the children who were born in 2000-2004 had HBsAg positivity, but two children who were born between 1996 and 1999 had HBsAg positivity. Besides, the rate of the AntiHBs titer more than the protective level was significantly higher in children born between 1996 to 1998 than the other group ($P = 0.000$). The reason for that difference is commented to be due to the catch-up HBV vaccination of the children born in 1996-1999.
Conclusion: The efficacy of universal HBV vaccination was quite high in decreasing HBsAg positivity. We think that booster vaccination 7-8 years after the universal HBV vaccination may be beneficial in increasing the antibody response.
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** We thank all health staff that contributed to the different stages of our study.

Topic 11: Hepatitis B

No: 1825

Decline of HBVDNA load correlate with increase of Th17 treg immunity in chronic hepatitis B patients during long term treatment with combining lamivudine and adefovir dipivoxil

Jing You[1], Huaie Liu[1], Ruyi Zhang[1], Shaofeng Rao[1], Lin Zhuang[2], Hongying Chen[1], Jia Wei[3], Xia Feng[4], Zhiwen Duan[1], Hong Dai[1], Weibo Yang[1], Hutcha Sriplung[5], Alan Geater[5], Virasakdi Chongsuvivatwong[5], Sijia Ma[6], Yanhua Che[7], Junhua Huang[8], Shaoming Yan[9], Ting Shen[1], Hemin Chen[1]

The First Affiliated Hospital of Kunming Medical University Department of Infectious Diseases Kunming-China[1], The Third People's Hospital of Kunming Department of Hepatology Kunming-China[2], The Fourth Affiliated Hospital of Kunming Medical University Department of Hepatology, Kunming-China[3], The First Affiliated Hospital of Kunming Medical University Department of Laboratory Medicine Kunming-China[4], Prince of Songkla University, Epidemiology Unit, Faculty of Medicine Hat Yai-Thailand[5], Kunming Medical University Kunming-China[6], The First People's Hospital of Kunming Department of Medicine Kunming-China[7], The Yunnan General Hospital of The Chinese People's Armed Police Forces Department of Infectious Diseases Kunming-China[8], The Third People's Hospital of Yunnan Province Department of Internal Medicine Kunming-China[9]

Background/aims: Antiviral treatment with combining Lamivudine(LAM) and Adefovir dipivoxil(ADV) has significantly improved the outcome of chronic hepatitis B virus(HBV) infection and with a lower resistance risk than single of them. To investigate dynamic fluctuations of serum viral load and Th17/Treg immunity of chronic hepatitis B patients and their correlation during long-term LAM + ADV therapy.
Patients and methods: Sixty-one patients received LAM(100 mg/day) plus ADV(10 mg/day) therapy. Serum HBVDNA load was measured by Real-Time-PCR, and the levels of cytokines and Th17 and Treg T-cells by flow cytometry during 260 weeks of the treatment. Multilevel modelling was used to analyze the relationship between these variables.
Results: Of the 61 patients, all HBeAg positive and with detectable HBVDNA, the majority(82.0 %) had serum levels of HBVDNA over 107 copies per milliliter. Th17/Treg cytokines producing T-cells were significantly lower in chronic hepatitis B patients as compared with normal individuals. HBV viral load dropped sharply during the first two weeks. In 45.9 % and 78.7 % patients, the level became undetectable from week 24 and 48, respectively. Using pre-therapy level as the reference, a significant increase in Th17/Treg T-cells and serum cytokine levels were found from week 12. These parameters and Th17/Treg balance steadlly improved throughout the 260 weeks. Multilevel analyses showed that the level of decrement of HBVDNA load was associated with the increment of Th17/Treg activities only in the later period (12-260 week).
Conclusion: Decline of HBVDNA load correlate with increase of Th17/Treg immunity in chronic hepatitis B patients during a long-term treatment with combining Lamivudine and Adefovir dipivoxil.

Topic 11: Hepatitis B

No: 1992

Evaluation of the effect of universal hepatitis B vaccination among children on the prevalance of hepatitis B virus

Selma Tosun[1], Erhun Kasirga[2]

Izmir Bozyaka Research and Education Hospital Infectious Diseases Izmir-Turkey[1], Celal Bayar University The School of Medicine Pediatric Gastroenterology Manisa-Turkey[2]

Aim: The aim of this study is to determine the change in HBV seroprevalance among children born before and after the universal vaccination initiated in our country in 1998.
Method: The study group was composed of primary school students from the center of Manisa province. Blood was taken from the students and HBsAg and antiHBs were examined through EIA method. Those having ≤ 9 IU/mL of AntiHBs titer were considered as negative while those having ≥ 10 IU/mL of AntiHBs were regarded as positive.
Results: The number of students in the study was 4111 and 51.7 % of them (n = 2125) were males, while 48.3 % of them (n = 1986) were females. It was determined that the rate of HBsAg positivity in children born before the universal HBV vaccination (between 1994 and 1998) was 1.2 %, however this rate was 0.15 % in those born after the vaccination program (between 1999 and 2006) ($P = 0.0000$). AntiHBs positivity was 51 % and 51.3 % in children, respectively.
Conclusion: As a result, universal HBV vaccination applied in our country for 16 years reduced HBsAg positive statistically significantly during the childhood period in our study group. In the study,it was observed that the mothers of 91 % (20/22) of the children having HBsAg positive had also HBsAg positive; therefore all pregnants should have HBsAg examination and the immunization of the babies of carrier mothers should not be neglected.
* We would like to thank public health specialist, Assistant Professor Dr.Serol Deveci, who made the statistical evaluations.

** We thank all health staff that contributed to the different stages of our study.

Topic 11: Hepatitis B

No: 1529

Antiviral efficacy of entecavir versus entecavir plus adefovir for hepatitis B virus rta181 v t mutants alone

Myung Jin Oh[1]

Cha University School of Medicine Department of Internal Medicine Gumi-Korea, South[1]

Background: Hepatitis B virus (HBV) rtA181 V/T mutants developed by long-term nucleos(t)ide analogues therapy are known to confer cross-resistance for other nucleos(t)ide analogues, except entecavir (ETV). In practice, rtA181 V/T mutants might show an association with incomplete response, despite rescue therapy with ETV. The aim of this study was to investigate antiviral efficacy of ETV alone and in combination with adefovir (ADV) as rescue therapy for HBV rtA181 V/T mutants alone.
Methods: A total of 30 patients who received ETV (1.0 mg/day) monotherapy or ETV plus ADV (10 mg/day) therapy over 48 weeks against HBV rtA181 V/T mutants without other concomitant mutants between April 2008 and October 2011 were enrolled. The subjects were divided into the ETV group (n = 16) and the ETV + ADV group (n = 14). Virological, biochemical, and serological response after 48 weeks of rescue therapy were investigated retrospectively.
Results: No significant difference in baseline characteristics, including serum HBV DNA (4.8 ± 1.7 vs. 4.1 ± 1.8log10 IU/mL) and HBeAg positivity (93.8 vs. 100 %) was observed between the two groups ($p > 0.05$). Virological response at 48 weeks showed complete virological response (62.5 vs. 42.9 %), partial virological response (6.3 vs. 28.6 %), non-response (25.0 vs. 28.6 %), and virological breakthrough (6.3 vs. 0 %), respectively ($P = 0.278$). No significant difference in mean reduction of serum HBV DNA and biochemical response rates was observed between both groups, respectively (4.3 ± 2.9 vs. 4.1 ± 1.8log10 IU/mL; $P = 0.294$, 88.9 vs. 100 %; $P = 1.000$). In addition, no significant difference in HBeAg loss or seroconversion was observed between the two groups (26.7 vs. 28.6 %; $P = 1.000$).
Conclusions: As rescue therapy for HBV rtA181 V/T mutants alone, ETV monotherapy was as effective as ETV + ADV therapy at 48 weeks.

Topic 11: Hepatitis B

No: 1437

Association between alcohol drinking and hepatitis B related hepatocellular carcinoma is not modified by genetic polymorphisms of ADH1B and ALDH2

Jessica Liu[1], Hwai-i Yang[1], Mei-hsuan Lee[2], Chin-lan Jen[1], Sheng-nan Lu[3], Li-yu Wang[4], San-lin You[1], Chien-jen Chen[1]

Academia Sinica Genomics Research Center Taipei-Taiwan[1], National Yang Ming University Institute of Clinical Medicine Taipei-Taiwan[2], Changgung Memorial Hospital Department of Gastroenterology Kaohsiung-Taiwan[3], Mackay College of Medicine Mackay College of Medicine Taipei-Taiwan[4]

Background and aims: The role of genetic polymorphisms on ADH1B and ALDH2 in individuals with chronic hepatitis B is unclear. This study aims to examine the role of two ADH1B and ALDH2 polymorphisms on predicting alcohol drinking, and also aims to look at the interaction between these polymorphisms and alcohol drinking on the risk of HCC among those with chronic hepatitis B.
Methods: A total of 3824 individuals with chronic hepatitis B were enrolled in this study. Two SNPs, rs1229984 (ADH1B) and rs671 (ALDH2) were genotyped as a part of a genome-wide association study of the 3824 individuals in the cohort using the Affymetrix Axiom Genome-wide CHB1 Array.
Results: Among 3824 individuals, there were 602 cases of HCC, and 3222 non-HCC controls. The frequencies of the mutant rs1229984 (ADH1B) T allele and rs671 (ALDH2) A allele were 72.9 % and 28.8 % in the cohort, respectively. For the prediction of alcohol drinking, only individuals who carried both SNPs were significantly less likely to become alcohol drinkers (OR [95 % CI] = 0.23 [0.13-0.42]). Alcohol drinking was the main predictor of increased HCC risk, with drinkers experiencing two to three fold increased risk of HCC compared to non-drinkers. Further carrying mutant alleles for rs1229984 (ADH1B) and rs671 (ALDH2) did not additionally affect rates of HCC.
Conclusions: This study found that the association between alcohol and hepatocellular carcinoma was not further modified by single nucleotide polymorphisms on ADH1B and ALDH2.

Topic 11: Hepatitis B

No: 2053

Hepatitis pathway from the patients' perspective

Zeliha Kocak Tufan[1], Rahmet Guner[1], Mehmet A. Tasyaran[1]

Yildirim Beyazit University, Ankara Ataturk Training & Research Hospital Infectious Diseases & Clinical Microbiology Department Ankara-Turkey[1]

Objective: Chronic hepatitis B (CHB) and C (CHC) are seen frequently and can be silent for a long time, show up with major complications afterwards. Proper& periodic follow up as well as monitoring the treatment and compliance of the patient to the therapy are extremely important. The profile of the patients affects the coordination, which is the cornerstone for this pathway. We aimed to define characteristics of our patients and evaluate their perspective on disease.
Methods: The study was conducted in a tertiary care university hospital. All CHB and CHC patients applied to our hepatology department during March-June 2014 were included. A questionnaire which includes detailed questions about their perspective and the follow up was prepared to be fulfilled by the patients.
Results: A total of 128 patients were included; demographic variables were given in Table 1.Answers to the treatment pathway were given in Table 2. The answers to the questions about the knowledge and perspective of the patients' on their disease were given in Figure 1 and Figure 2.
Conclusion: More than half were under therapy, mainly within their 5 years of treatment. Although a significant proportion of the study group seem to be aware of their disease and importance of the treatment, dose skip was stated to be as high as 20 %. According to these results, seen by the same hepatologist is very important for the patients, which should be taken into account in regulation of the outpatient departments. Another result is that the patient's education and meetings has to focus on the importance of the strict obey to treatment.

Topic 11: Hepatitis B

No: 2085

Two cases of telbivudine induced peripheral neuropathy

Kamuran Türker[1], Betül Taş[2], Nejat Sebzeci[1], Fatma Ekşi Polat[1], Bilge Özdemir[3]

Bağcılar Training and Research Hospital Infectious Diseases Istanbul-Turkey[1], Bağcılar Training and Research Hospital Dermatology Istanbul-Turkey[2], Bağcılar Training and Research Hospital Microbiology Istanbul-Turkey[3]

Chronic hepatitis B (CHB) is a major health problem worldwide. Several nucleos(t)ide analogues (NAs) have been developed over the past decade, and administration of NAs has played a crucial role in the treatment of CHB. Successful treatment of chronic hepatitis B (CHB) often requires long-term oral nucleoside/nucleotide agents which can be associated with viral resistance, patient non-compliance and adverse effects.

Telbivudine is a new synthetic nucleoside analogue and is a bioavailable L-nucleoside with specific anti-HBV activity in vitro. Telbivudine is one of the more potent options available. It is also one of the few drugs in the treatment of CHB under FDA pregnancy Category B. In a clinical trial, telbivudine alone in patients with 2000 people, 5 people showed peripheral neuropathy, occurs only 0.3 %. Combining telbivudine and interferon also runs the risk of severe peripheral neuropathy.

We report here the two cases of telbivudine-induced neuropathy in patients with CHB.

Case 1:

A fifty-eight year old woman who had carpal tunnel syndrome ten months after the receiving telbivudine therapy.

She was diagnosed as having chronic HBV infection proven by positive HBsAg, HBeAg positive, antiHBeAB negative, antidelta Ab negative, HBV-DNA 7796 IU/mL, AST: 17 U/L, ALT: 25 U/L liver biopsy score HAİ: 9/18 stage 3/6 at the beginning of the therapy.

Case 2:

He was sixty seven year old man who had lower extremity sensory neuropahty eleven months after the begining of therapy. He had HBsAg positive, HBeAg positive, antiHBeAB negative, antidelta Ab negative, HBV-DNA 17700 IU/mL, AST: 39ALT: 44 U/L liver biopsy score HAİ: 9/18 stage 4/6.

Topic 11: Hepatitis B

No: 1481

Telbivudine therapy in patients with chronic hepatitis B infection real life experience from Turkey

Mehmet Bayram[1], Meltem Ergun[1], Ali Riza Koksal[1], Salih Boga[1], Huseyin Alkim[1], Canan Alkim[1]

Sisli Hamidiye Etfal Training and Research Hospital Gastroenterology Istanbul-Turkey[1]

Aim: Telbivudine is effective in the treatment of chronic hepatitis B virus (HBV) infection. We investigate the efficacy and adverse effects of telbivudine treatment in patients with chronic hepatitis B (CHB) in real life clinical settings.
Methods: HBeAg-positive and HBeAg-negative adult CHB patients, with HBV DNA $>$ 2000 IU/ml and histologic activity index $\geq$ 6 or fibrosis $\geq$ 2 were started on telbivudine 600 mg once a day. We retrospectively analyzed patients' demographic characteristics, histopathologic data, viral loads, ALT and creatine phosphokinase (CK) levels and adverse effects in the treatment duration.
Results: Sixty-seven patients (38 female) with mean age (range) of 41.2 (24–61) were enrolled the study in Sisli Etfal Education and Research Hospital between 2011 and 2014. 97 % of them were HBeAg negative at baseline. The median follow-up period was 15 months (range 6-30 months). Undetectable HBV DNA rates were 58, 81 and 84 % at week 12, 24 and 48 respectively. We detect virologic breakthroughs in 5 (7 %) patients.

CK level elevations were observed in 19 (28 %) patients; fortunately only six (9 %) of them were suffering muscle soreness. Treatment was discontinued in symptomatic patients. Also peripheral neuropathy was detected in another patient; the drug was switched as well.
Conclusion: Telbivudine appears effective for the treatment of chronic hepatitis B, Roadmap concept may improve clinical outcomes in patients with suboptimal antiviral response. Adverse effects may be problematic for some patients; therefore clinicians should be alert in this regard.

Topic 11: Hepatitis B

No: 1972

Association between neutrophil to lymphocyte ratio mean platelet volume and severity of liver fibrosis in patients with chronic hepatitis B

Alpaslan Tanoglu[1], Ergenekon Karagoz[2], Asım Ulcay[2], Vedat Turhan[2], Muammer Kara[1], Yusuf Yazgan[1]

Gata Haydarpasa Training Hospital Gastroenterology Istanbul-Turkey[1], Gata Haydarpasa Training Hospital Infectious Disease Istanbul-Turkey[2]

Aim: Although being an invasive method, liver biopsy is the gold-standard technique to predict the severity of liver fibrosis. Nowadays, noninvasive parameters are utilized to estimate liver fibrosis. We aimed to investigate the relationship between the severity of fibrosis and neutrophil to lymphocyte ratio (NLR) and mean platelet volume (MPV) in chronic hepatitis B (CHB) patients.
Method: 95 consecutive biopsy-proven naïve CHB cases were included in the study. The patients were separated into two groups based upon the fibrosis score (according to ISHAC score): F0, F1were included in the Group 1, whereas F2, F3, F4 were included in the Group 2. The complete blood count variables and other routine biochemical parameters were tested. Data analyses were carried out using SPSS 15 software.
Results: Of the 95 patients, 76 (80 %) were male and 19 (80 %) were female.The mean age of the patients was 39.93 years. Fibrosis scores of 59 cases (62.2 %) were less than 2, whereas 36 cases (37.8 %) had fibrosis scores greater than or equal to 2.There was a significant difference between these two groups for NLR(2.38 ± 0.96 and 1.64 ± 0.6, $P < 0.001$). There was also a significant difference between these two groups for MPV (8.13 ± 1.2 and 8.77 ± 1.4, $P < 0.05$). We compared the ROC curves for the diagnostic performance of NLR and MPV in identifying fibrosis in CHB and area under the curve values for these variables were 0.206 and 0.671, respectively.
Conclusion: Significantly lower levels of NLR and higher levels of MPV in CHB patients with significant fibrosis were determined. In the light of our results, NLR and MPV can be defined as independent predicting factors for predicting severity of hepatic fibrosis.

Topic 11: Hepatitis B

No: 1547

Kinetics of hepatitis B surface antigen with nucleo(s)tide analogues

Özlem Kandemir[1], Neslihan Demir[1], Onur Gültekin[1], Sibel Ünlü[2]

Mersin University, Faculty of Medicine Clinical Microbiology and Infectious Diseases Mersin-Turkey[1], Mersin Toros Hospital Clinical Microbiology and Infectious Diseases Mersin-Turkey[2]

Aim: We aimed to determine serum hepatitis B surface antigen (HBsAg) levels in patients with chronic hepatitis B (CHB) virus infection during nucleo(s)tide analogues therapy.
Methods: HBsAg was quantified by Elecsys HBsAg II assay (Roche Diagnostics) at baseline and during antiviral therapy (weeks12, 24 and 48) in HBeAg positive ($n = 21$) and negative patients ($n = 10$) treated with nucleo(s)tide analogues.
Results: A total of 31 patients with CHB and a mean age of 41 years, of which 20 were male, were included in this study. When all cases were considered, decline in the level of HBsAg was not significant in 12th and 24th weeks of the treatment, however it was significant in the 48th weeks of the treatment ($P = 0{,}015$). The decline in the level of HBsAg in HBeAg positive cases was significant all terms ($P = 0{,}008$, $P = 0{,}046$, $P = 0{,}001$ respectively). In addition the decline in the level of HBsAg in 3 cases with HBeAg seroconversion was more with respect to those without seroconversion. The decline in the level of HBsAg has never been significant in the HBeAg negative patients. A positive correlation was found between the initial ALT level and the decline in the HBsAg levels ($r = 0{,}394$, $P = 0{,}028$).
Conclusion: This preliminary study has shown us that a significant decline in the level of HBsAg in HBeAg positive cases may be the harbinger of seroconversion. In addition a positive correlation was found between high levels of ALT and decline in the levels of HBsAg. This suggests that HBsAg decline might be linked to increased immunological activity.

Topic 11: Hepatitis B

No: 2022

Characterization of the dynamics of hbv resistances and genetic diversity from longitudinally antiviral therapy treated patients with next generation sequencing

Yoon-seok Chung[1], Hui-seong Kim[1], Hyo-jin Yang[1], Hyun Park[1], Byeong-sun Choi[1], Chun Kang[1]

Division of Aids, Center For Immunology and Pathology, Korea National Institute of Health Kcdc Chungju-si-Korea, South[1]

HBV drug resistance testing is routinely performed prior to antiretroviral treatment. Long durations of therapy are required and often lead to the emergence of drug resistance. Next-generation sequencing (NGS) technologies allow the rapid and cost-effective acquisition of thousands to millions of short DNA sequences from a single sample. Here, we presented data of the clinical samples to obtain insights in sensitivity, accuracy and the putative impact of minority variants on resistance interpretation. The thirty two specimens from 8 patients on polymerase were performed from specimen for whom resistance testing was longitudinally collected for about 10 years. For deep sequencing, the PCR products were used for Nextera XT® library preparation and sequenced using Illumina's Hiseq 2500 sequencing system. Bioinformatics analyses were performed using an automated customized pipeline. The dynamics of lamivudine, adefovir-resistant variants were complex and differed among patients as results of evolving differences in variant fitness. NGS analysis revealed successive waves of selection of HBV population with single and multiple amino acid substitution. In addition to, G-to-A hypermutaion mediated by apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like family to cytidine deaminases was estimated to be present in 0.6 % of polymerase gene. NGS detected low-prevalence HBV variants with lamivudine, adefovir, entecavir, G-to-A hypermutation with a sensitivity not previously possible. Substitutions conferring HBV resistances to antiviral agents exist as a passage of treatments are much more complex and heterogeneous than previously thought and thus far unknown amino acid substitutions.

Topic 11: Hepatitis B

No: 1962

Predicting factors about liver histology in inactive chronic hepatitis B patients

Mehmet Ibis[1], Nazik Okumuş[2], Mehmet Arhan[1], Güldal Yilmaz[3], Kenan Hızel[4], Selahattin Unal[1]

Gazi University Gastroenterology Ankara-Turkey[1], Gazi University Internal Medicine Ankara-Turkey[2], Gazi University Pathology Ankara-Turkey[3], Gazi University Infectious Disease Ankara-Turkey[4]

Introduction: Hepatitis B virus (HBV) infection is known to affect two billion people in worldwide. Chronic HBV infection results in hepatic inflammation and fibrosis is caused by cirrhosis and hepatocellular carcinoma.

Asymptomatic HBsAg-negative chronic hepatitis B is difficult to distinguish with the inactive HBV carrier patients. There is no cut-off level for determination of each phases separately.

Liver fibrosis in patients with inactive carriers phase is minimal or absent and progression is not visible. Decision of treatment in this patients is very strictly related to liver fibrosis score.

In this study we were investigated predicting factors about liver fibrosis in inactive carriers.

Materials/methods: Retrospectively 80 patients liver biopsy had been applied and HBV DNA < 10 5, ALT level were normal, following 10 years or at least 35 years old, HBe Ag negative were admitted. Totally 60 women and 20 men patients and mean age were 50.6 years old.

Laboratory parameters ALT, AST, albumin, MPV (mean platelet volume), platelet counts, HBV DNA level, RDW (red cell distribution width), patient age, liver steatosis ratio were compared with liver fibrosis score and histologic activity.

Results: After evaluation of the fibrosis and histologic activity we were decided to treat 23 patients according to chronic HBV infection. It was not able to start treatment without biopsy in these patients. Our aim were to determine any correlate parameters between liver histology and especially MPV, RDW, HBV DNA level in inactive HBV carriers patients without liver biopsy. There were not any correlate parameters predicting liver histology in inactive chronic HBV patients.

Topic 11: Hepatitis B

No: 1535

Association between il12a il1b and il17a gene polymorphisms and hbeag seroconversion in chronic hepatitis B patients who received entecavir treatment

Junqiu Wu[1], Dengming He[1], Zehui Yan[1], Maoshi Li[1], Shiqi Tao[1], Cheng Xu[1], Yuming Wang[1]

Southwest Hospital, Third Military Medical University Institute of Infectious Disease Chongqing-China[1]

Background and aim: Host genetic factor is one of important reasons for different response of antiviral treatment in chronic hepatitis B. IL-12, IL-1β and IL-17 play an important role in immune to HBV. IL12A rs568408, IL1B rs1143623, and IL17A rs8193036 are association with many diseases. The study aimed to observe the association between IL12A, IL1B and IL17A gene polymorphisms and HBeAg seroconversion in chronic hepatitis B patients who received entecavir treatment.

Methods: IL12A rs568408, IL1B rs1143623, and IL17A rs8193036 were genotyped using the MGB-TaqMan SNP genotyping assay in 109 HBeAg-positive chronic hepatitis B patients who had received entecavir treatment. After 24 months, 29 cases achieved HBeAg seroconversion (response) were assigned as the case and the remaining 80 cases were assigned as the control. SNPstats was applied to analyze the association between IL12A rs568408, IL1B rs1143623, and IL17A rs8193036 and HBeAg seroconversion.

Results: IL-12A rs568408 was associated with HBeAg seroconversion (OR 3.72, 95 % CI 1.34-10.32, $P = 0.012$). GA genotype achieved higher HBeAg seroconversion rate than GG genotype. However, we didn't observe the significant association between IL1B rs1143623 (OR 1.99, 95 % CI 0.72-5.44, $P = 0.17$) and IL17A rs8193036 (OR 1.54, 95 % CI 0.32-7.33, $P = 0.60$) and HBeAg seroconversion.

Conclusion: IL-12A rs568408 was significantly associated with HBeAg seroconversion in HBeAg-positive chronic hepatitis B patients who received entecavir treatment.

Topic 11: Hepatitis B

No: 2157

Efficacy of tenofovir in hepatitis B patients who non response to pegylated interferon treatment

Şükran Köse[1], Mustafa Kemal Çelen[2], Tuba Kiş[1], Süheyla Serin Senger[1], Erol Avşar[3]

Tepecik Training and Research Hospital Clinic of Infectious Diseases and Clinical Microbiology Izmir-Turkey[1], Dicle University School of Medicine, Department of Infectious Diseases Diyarbakir-Turkey[2], Academic Hospital Department of Gastroenterology Istanbul-Turkey[3]

Introduction: Chronic hepatitis B is a major health problem worldwide and also for our country. Pegylated interferon (PEG-IFN) or antiviral agents such as lamivudine, telbivudine, adefovir, tenofovir and entecavir are used for treatment of chronic hepatitis B. Potent antivirals such as tenofovir provide treatment alternative in patients who are non-responsive after PEG-INF use.

The purpose of our study was to determine the response rates of tenofovir treatment in 56 patients who were unresponsive to PEG-IFN treatment.

Materials and methods: Fifty six non-responsive cases diagnosed with chronic hepatitis B who had a history of 48-week PEG-INF use were included in the study. The cases were treated with 245 mg/day tenofovir disoproxil fumarate (TDF). HBsAg, anti-HBs, HBeAg, anti-HBe and HBV-DNA were checked before TDF treatment; liver biopsies were conducted before treatment to determine the HAI and fibrosis scores. Biochemical and virological response status of the patients in the first month, third month, sixth month, first year and second year were evaluated.

Results: Of the patients 21 (37.8 %) were female and the mean age was 40.3 (18-63). Thirty six of the cases (64.2 %) were HBeAg-positive. The biochemical response (BR) was 100 % and rapid virological response (RVR) was 14.2 % in the first month; BR was 100 %, early virological response (EVR) was 19.6 % in the third month; BR was 100 %, VR was 58.9 % in the sixth month, BR was 95.8 %, VR was 98.2 % in the first year; and BR was 96.7 %, VR was 99.2 % in the second year. Virologic breakthrough was reported in two(3.5 %) of patients, with no potentially resistance-associated mutations identified to date.

Topic 11: Hepatitis B

No: 1830

Long term outcomes of hepatitis B virus related cirrhosis treated with nucleos(t)ide analogues

Chao-hung Hung[1], Chien-hung Chen[1], Tsung-hui Hu[1], Sheng-nan Lu[1], Chuan-mo Lee[1], Jing-houng Wang[1]

Kaohsiung Chang Gung Memorial Hospital Division of Hepato-gastroenterology, Department of Internal Medicine Kaohsiung-Taiwan[1]

Objectives: We aimed to evaluate the outcomes of chronic hepatitis B (CHB) patients with cirrhosis who received long-term nucleos(t)ide analogues (NUCs) therapy.
Methods: A total of 546 consecutive cirrhotic patients receiving entecavir (n = 359), telbivudine (n = 104) or tenofovir (n = 83) for CHB between January 2007 and December 2013 were enrolled. Evaluation of hepatocellular carcinoma (HCC) incidence and overall survival was performed by Kaplan–Meier method and Cox proportional hazards analysis.
Results: During a median follow-up of 39 months (IQR, 26–47 months), 56 (10.3 %) patients developed HCC and 14 (2.6 %) patients died. These outcomes were not associated with different antivirals use. Multivariate Cox proportional hazards analysis showed that age (hazard ratio (HR) 1.04; 95 % confidence interval (CI) 1.01-1.07; $P = 0.015$), statin use (HR 3.49; 95 % CI 1.59-7.66; $P = 0.002$), platelet count (HR 0.99; 95 % CI 0.98-1.00; $P = 0.047$) and variceal bleeding history (HR 7.91; 95 % CI 3.63-17.23; $P < 0.001$) were independent factors for HCC development. As regards to survival, Child-Pugh B/C (HR 3.15; 95 % CI, 1.07-9.26; $P = 0.037$) and platelet count (HR 0.98; 95 % CI 0.97-0.99; $P = 0.016$) were independent factors. Despite no difference in deteriorating renal function (serum creatinine increase 0.5 mg/dL from baseline) among three antivirals groups, estimated glomerular filtration rate (eGFR) significantly increased in patients receiving telbivudine ($P = 0.047$), but decreased in those receiving tenofovir ($P < 0.001$) at year 2.
Conclusions: Long-term NUCs therapy does not guarantee against the HCC development and mortality in CHB-related cirrhotic patients. Careful HCC surveillance is necessary in patients with old age, statin use, low platelet count and variceal bleeding history.

Topic 11: Hepatitis B

No: 1313

The correlation between ALT level and gene expression of HBV infection

Jinglan Jin[1], Ruihong Wu[1], Junqi Niu[1]

The First Hospital, Jilin University Hepatology Changchun-China[1]

OBJECTIVES: To analyse the correlation between the ALT level and gene expression intensity.
Methods: Total of 84 individual's sample was collected: acute hepatitis (AH) (9 cases), chronic HBV infection (67 cases) and healthy controls (N) (8 cases). Chronic HBV infection was further divided according the level of alanine aminotransferase (ALT) into chronic hepatitis (CH) (ALT > 40U/L) (39 cases) and chronic HBV carrier (CA) (ALT < 40U/L) (28 cases). Total RNA was extracted from peripheral blood mononuclear cells (PBMCs). Whole-genome gene expression array was performed using Human HT-12v4 chip purchased from Illumina, Inc. (San Diego, CA, USA) and operated according to the manufacturer's protocols with minor modifications.
Results: The gene expression level and ALT level by Spearman correlation test identified significant correlation in 397 genes: 161 positively and 236 negatively correlated genes These genes were enriched in immune response, antigen processing and presentation, MHC I receptor activity and proteolytic activity and proteasome activity function class. In chronic hepatitis group, IFITM3 and GBP-1 expression were positively correlated with ALT level (ALT > , < , = 200U/L). On the whole gene set level, 67 genes were selected to be positively correlated with ALT level (cor. value ≥ 0.5). The major classes of theses genes are interferon stimulated genes (ISGs) (ATF5, GBP1, GBP5, IFI27, IFITM2, IFITM3, OASL, STAT1, GCH1), antigen processing and presentation (FCGR1A, FCGR1B, HLA-F, PSME2) and cytokine (chemokine) and receptors (IL-27, IL15RA, CXCL-9).
Conclusions: To some extend, ALT level is positively correlated with immune response intensity, just like IFITM3, GBP1 and FCGR1A are highly positively

Topic 11: Hepatitis B

No: 1262

Adefovir entecavir combination rescue therapy for previous chronic hepatitis B treatment failure; 3 years data

Jeong Han Kim[1], Soon Young Ko[1], Won Hyeok Choe[1], So Young Kwon[1]

Konkuk University Internal Medicine Seoul-Korea, South[1]

Background: Before tenofovir (TDF) become available in Korea, entecavir (ETV) and adevovir (ADV) combination has been most potent regimen for chronic hepatitis B (CHB) patients failed to achieve response with rescue therapy for resistance. We aimed to analyze efficacy of ADV-ETV combination therapy for such patients.
Methods: We retrospectively reviewed medical records of CHB patients treated ADV-ETV combination as rescue therapy for resistance. Only patients who did not respond with prior rescue therapy other than ADV-ETV combination were enrolled. Virologic response (VR) was defined as undetectable HBV DNA level.
Results: Total 48 patients were enrolled for analysis. Male patients were 41 (85.4 %) and mean age were 48.2 years. Cirrhotic patients were 12 (25.0 %) and hepatocellular carcinoma patients were 3 (6.3 %). Most patients were HBeAg positive (47, 97.9 %) and mean HBV DNA level was 6 Log10 copies/ml. Initial treatment agents were lamivudine (LMV) in 41 patients (85.4 %), clevudine (CLV) in 6 patients (12.5 %) and ETV in 1 patient (2.1 %). Prior rescue therapies were ADV monotherapy in 13 patients, ETV monotherapy in 15 patients, LMV-ADV combination in 35 patients, CLV-ADV combination in 3 patients and pegylated interferon in 3 patients. VR rates were 6.5 % (3/46) at 6 month, 18.6 % (8/43) at 12 month, 26.7 % (8/30) at 24 month and 52.9 % (9/17) at 36 month.
Conclusions: ADV-ETV combination is not enough for CHB patients who were refractory to rescue therapy. More potent regimen such as ETV-TDF combination is warranted.

Topic 11: Hepatitis B

No: 1175

Kinetics of hepatitis B surface antigen decline during 3 years of telbivudine treatment in hepatitis B e antigen negative patients in Changzhou China

Xiao-gang Zhang[1], Long-gen Liu[1], Ze-yu Huang[1]

Third People Institute of Liver Diseases Changzhou-China[1]

Background: The ideal end points of therapy in HBeAg-negative chronic hepatitis B patients(CHB) is HBsAg loss and development of anti-HBs but infrequently achievable. Long-term telbivudine therapy might be beneficial from the decline in serum HBsAg levels in HBeAg-negative chronic hepatitis B patients. **Aim:** To assess the impact on serum HBsAg levels in HBeAg-negative chronic hepatitis B patients receiving long-term treatment of telbivudine.
Methods: We retrospectively quantitatively assessed serum HBsAg levels during 3 years of telbivudine treatment in 42 patients (25 HBeAg-positive and 17 HBeAg-negative)who maintained undetectable serum hepatitis B virus (HBV) DNA.
Results: Telbivudine treatment progressively reduced serum HBsAg levels (mean ± SD) from baseline(298.3 ± 183.9 ng/mL) to treatment week 24 (219.9 ± 145.9 ng/mL), treatment year 1(200.3 ± 125.9 ng/mL), and treatment year 3(131.3 ± 84.7 ng/mL) in 17 HBeAg-negative patients ($P < 0.01$); HBsAg reduction rate of HBeAg-negative CHB patients treated with telbivudine was higher than HBeAg-positive(88.2 % vs 76.0 %,$P < 0.05$); During the first year of treatment, three patterns of HBsAg decline were observed: rapid (50 %) in 10 patients, slow (20 %) in 28 patients, and steady levels i[SUP][/SUP]n 4 patients. 4 of 10 patients with rapid HBsAg decline versus none of 28 patients with steady HBsAg levels achieved HBsAg loss at year 3 ($P < 0.01$), and 2 of 4 development of anti-HBs; all cases with HBsAg loss was HBeAg-negative, none of HBeAg-positive.
Conclusion: In patients who have effective suppression of viral replication during long-term telbivudine treatment, a rapid decline in serum HBsAg levels during the first year may have a greater likelihood of achieving HBsAg clearance in HBeAg-negative patients than those in HBeAg-positive patients.

Topic 11: Hepatitis B

No: 2160

Relationship between histopathologic features and serum complement level for in ative hepatitis B carriers

Omer Senturk[1], Faden Hayrunnisa Aydin[1], Ugur Korkmaz[1], Altay Celebi[1], Sadettin Hulagu[1]

Kocaeli University Gastroenterology Kocaeli-Turkey[1]

Introduction: Chronic hepatitis B can cause chronic liver disease, cirrhosis, hepatocellular carcinoma. Although viral determinants and other laboratory tests use in diagnosis and followup, those tests do not show liver damage. In our study, we aim to find relationship between their histopathologic features and complement levels for inactive HBV carrier.
Materials and methods: Seventy patients, who were inactive HBV carriers, HBsAg positive, HBV DNA less than 2000 IU/ml during 12 months followup, normal AST and ALT level, included in our study. Liver biopsy and complements tests were performed to evaluate. Severe fibrosis and lower degree of fibrosis were seen in 31 and 39 patients, whom their complement levels were measured (mg/dL).
Results: Complement levels of severe fibrosis and lower fibrosis group were C4 = 20 ± 5, C3 = 112 ± 16 and C4 = 24 ± 7, C3 = 120 ± 22, respectively. C4 level is lower in severe fibrosis group rather than lower fibrosis group ($P = 0.014$). However, there was no correlation in C3 level. C4 level was detected as a diagnostic tool in ROC analysis (figure).
Conclusion: Negative correlation was seen inbetween serum complement levels and fibrosis level. Complement C4 levels may be important to evaluate severe fibrosis in the inactive hepatitis B carriers.

Topic 11: Hepatitis B

No: 1171

Quasispecies characteristics of CPG islands and inhibitory guanosine rich oligodeoxynucleotides differ across spectrum of hepatitis B virus infection

Yuan Xue[1], Su-yuan Huang[1], Ming-jie Wang[1], Zhi-tao Yang[1], Xin-xin Zhang[1]

Ruijin Hospital, Shanghai Jiaotong University, School of Medicine Department of Infectious Diseases, Institute of Infectious and Respiratory Diseases Shanghai-China[1]

Background: Unmethylated cytosine-phosphate-guanosine oligodeoxynucleotides (CpG), which is the ligand of Toll-like receptor 9, can trigger immune responses. It was reported recently that guanosine-rich oligodeoxynucleotides (ODN) within hepatitis B virus (HBV) genomes can inhibit the function of HBV-CpG. Objective Our present study aimed to investigate the characteristics of CpG islands and HBV-ODN in full-length genomes of HBV quasispecies (QS) from patients with different clinical outcomes of HBV infection.
Methods: Thirty-five patients diagnosed with acute on chronic liver failure (ACLF, n = 7), acute hepatitis B (AHB, n = 8), asymptomatic HBV carriers (ASC, n = 10), or chronic hepatitis B (CHB, n = 10), were enrolled. Full-length HBV genomes were amplified by PCR, and a total of 523 clones were sequenced and analyzed.
Results: Absence of CpG island I was more common in HBV genotype C, and CpG island III was longer in genotype C compared to genotype B. For HBV genotype B, CpG island III of ACLF group was shorter compared to ASC group ($P < 0.01$), while its QS heterogeneity was high. Further study showed that the frequency of triple mutations (G1896A/A1762T/G1764A) in HBV-ODN was significantly higher in ACLF group (31/60 clones) compared to the other three groups. For genotype C, CpG island III of ACLF group was longer compared to the other three groups ($P < 0.01$), while its QS heterogeneity was low. The frequency of mutations (G1896A/A1762T/G1764A) was not different among ACLF, ASC and CHB groups.
Conclusions: QS characteristics of CpG islands and HBV-ODN differ across spectrum of HBV infection. The relevance to the clinical outcomes and its mechanism need to be further investigated.

Topic 11: Hepatitis B

No: 2180

The relationship between fibrosis level and blood neutrophil to lymphocyte ratio in inactive hepatitis B carriers

Bulent Yilmaz[1], Hayrunnisa Aydın[2], Guray Can[1], Zeynep Senturk[2], Berna Ustuner[2], Hasan Yilmaz[2], Murat Ozturk[2], Emir Roach[3], Ugur Korkmaz[1], Mevlut Kurt[1], Altay Celebi[4], Omer Senturk[4], Sadettin Hulagu[4]

Abant Izzet Baysal University Izzet Baysal Training and Research Hospital Gastroenterology Bolu-Turkey[1], Kocaeli University Internal Medicine Kocaeli-Turkey[2], Cleveland University Pathobiology

Cleveland-Turkey[3], Kocaeli University Gastroenterology Kocaeli-Turkey[4]

Aim: Neutrophil–lymphocyte ratio (NLR) has been used as a simple, affordable, and easily accessible marker to predict prognosis in a variety of inflammatory and neoplastic diseases. The aim of this study was to investigate the relationship between NLR and liver fibrosis in patients who were being followed as inactive hepatitis B carriers.
Materials and methods: The study included 78 patients who were followed for 1 year as inactive hepatitis B carriers. Liver biopsy was performed and the fibrosis scores of the histological activity index were assessed according to the Metavir scoring system. The patients were divided into two groups on the basis of the fibrosis scores: those with a score below 2 and those with a score above 2. In both groups, demographic data such as sex, age, and BMI were similar.
Conclusion: Histopathologic analysis of 78 patients showed that 41 (53 %) had fibrosis grade 0–1 and 37 (47 %) patients had fibrosis grade greater than 2. NLR was found to be statistically significantly lower in the group with fibrosis grade of at least 2 (1.51 ± 0.61 vs. 1.79 ± 0.64, $P = 0.043$). Other biochemical and hematological data were found to be similar in both groups. No correlation was found between laboratory values and NLR. In addition, there was no correlation between NLR with histologic activity. Spearman correlation analysis showed a negative correlation between the fibrosis score and NLR ($r = -0.279$, $P = 0.013$). In inactive hepatitis B carriers, the histological activity index and NLR were found to be correlated negatively.

Topic 11: Hepatitis B

No: 1096

Comparative study of telbivudine and pegylated interferon α 2a optimization therapy for e antigen positive chronic hepatitis B patients

Yufeng Gao[1]

The Second Affiliated Hospital of Anhui Medical University The Department of Hepatopathy Hefei-China[1]

Aim: To compare the efficacy of telbivudine and pegylated interferon α-2a optimized therapy for E antigen-positive CHB patients. Methods 85 patients initially treated by telbivudine monotherapy and 54 patients initially treated by pegylated interferon α-2a monotherapy were enrolled in the present study. At 24 weeks the patients were treated with an optimized plan. For patients in telbivudine group with HBV DNA higher than 1000 copies/ml, a combined therapy using adefovir dipivoxil will be provided; for patients in pegylated interferon α-2a group with HBV DNA higher than 10[SUP]5[/SUP] copies/ml or HBsAg level higher than 20000 IU/ml, a combined therapy using lamivudine will be considered. Treatment efficacy in both groups will be observed at 12, 24, 36, and 48 weeks.
Result: At 12, 24, 36, and 48 weeks, the ALT normalization rate in telbivudine treatment group was significantly higher than pegylated interferon α-2a treatment group ($P < 0.05$), while their HBV DNA negative rates, e antigen negative rates, e antigen seroconversion rates were not significantly different between two groups ($p > 0.05$). E antigen seroconversion rates of the two groups at 48 weeks were 28.2 % and 29.6 %, respectively; in both groups, patients with HBV DNA levels less than 1000 copies/ml at 12 weeks can get higher E antigen seroconversion rate at 48 weeks (36.4 % vs 43.5 %); S antigen negative conversion rate at 48 weeks in pegylated interferon α-2a treatment group was 9.3 %, significantly higher than telbivudine group ($P < 0.05$).
Conclusion: Optimization therapy using Telbivudine and pegylated interferon α-2a can achieve similar virologic response rates and E seroconversion rates at 48 weeks.

Topic 11: Hepatitis B

No: 1911

Renal function during 2 years treatment with telbivudine in patients over 50 years old—a "fresh" study sub analysis (CLDT600AGR01)

Konstantinos Mimidis[1], Ioannis Ketikoglou[2], Maria Raptopoulougigi[3], Konstantinos Kaligeros[4], Ioannis Elefsiniotis[5], Nikolaos Antonakopoulos[6]

University Hospital of Alexandroupolis 1st Department of Internal Medicine Alexandroupolis-Greece[1], Ippokrateio Hospital Department of Internal Medicine Athens-Greece[2], Aristotle University Medical School 2nd Medical Department Thessaloniki-Greece[3], Sismanogleio Hospital 2nd Department of Internal Medicine Athens-Greece[4], General & Oncology Hospital Athens "agioi Anargyroi" University Internal Medicine Clinic Athens-Greece[5], Novartis Hellas Medical Department Athens-Greece[6]

Introduction: Renal function monitoring during HBV treatment is of growing importance as documented in the latest international guidelines.
Aims: To analyze renal function evolution in CHB patients over 50 years of age, under Telbivudine monotherapy.
Methodology: We report here a sub-analysis of an ongoing real-life study in CHB. 90 HBeAg positive and negative, nucleos(t)ide-naive patients from 6 Greek tertiary Hepatology centers were followed-up for 2 years under Telbivudine monotherapy. 27 of these patients were > 50 years of age at start of study enrollment. Renal function was assessed by both serum creatinine and eGFR (Cockroft-Gault, MDRD4, CKD-EPI).
Results: Renal function was significantly improved over time with the following outcomes:

Serum creatinine; mixed-model regression analysis showed a significant decrease of 0.07 mg/dl at year 2 compared to baseline ($\beta = -0.02$, SE = 0.009, $P = 0.021$).

Estimated GFR; significant increase at year 2 of 8.7 ml/min/1.732 (Cockcroft-Gault), 8.6 ml/min/1.732 (MDRD4) and 9.1 ml/min/1.732 (CKD-EPI) vs. baseline, with respective mixed-model regression analyses as following: ($\beta = 3.05$, SE = 1.30, $P = 0.02$), ($\beta = 3.06$, SE = 1.30, $P = 0.019$), ($\beta = 1.92$, SE = 0.88, $P = 0.029$).

Nine (9/27) patients from the same subgroup (> 50y) had baseline GFR (C-G) 60–90 ml/min/1.73m^2. Five of these patients (5/9) (66.7 %) had GFR over 90 ml/min/1.73m^2 at two years.

Six (6/27) patients had baseline GFR (C-G) 60-80 ml/min/1.73m2. Three of these patients (3/6) (50 %) had GFR over 90 ml/min/1.73m2 at two years.
Conclusions: Renal function was significantly improved after 24 months treatment with telbivudine in the challenging subgroup of patients over 50 years old, adding to the growing literature of this renoprotective effect.

Topic 11: Hepatitis B

No: 1270

Single nucleotide polymorphism of HLA DPA1 is associated with treatment response to pegylated interferon in thai patients with HBeAg negative chronic hepatitis B

Umaporn Limothai[1], Srunthron Akkarathamrongsin[2], Yong Poovorawan[2], Pisit Tangkijvanich[1]

Chulalongkorn University Research Unit of Hepatitis and Liver Cancer, Department of Biochemistry, Faculty of Medicine Bangkok-Thailand[1], Chulalongkorn University Center of Excellence In Clinical Virology, Faculty of Medicine Bangkok-Thailand[2]

Objectives: Recent genome-wide association studies (GWAS) have showed that single nucleotide polymorphisms (SNPs) in the human leucocyte antigen (HLA) genes are associated with spontaneous HBV clearance. In this study, we investigated the association of the SNP HLA-DPA1 (rs3077) with treatment response to pegylated interferon (PEG-IFN) in patients with chronic hepatitis B (CHB).
Methods: We analyzed data from a randomized study comparing efficacy of PEG-IFN monotherapy (group 1) versus combination with entecavir (group 2) in Thai patients with HBeAg-negative CHB. All patients were treated for 48 weeks and followed-up for 48 weeks to assess virological response (VR, HBV DNA level < 2,000 IU/mL). DNA extracted from blood samples was analyzed for the SNP rs3077 by real-time PCR with TaqMan probes.
Results: 63 patients in each group were enrolled. There was no significant difference in VR between groups 1 and 2 (41.3 % vs. 38.1 %, $P = 0.856$). The distribution of CC, CT and TT genotypes of rs3077 was 73 (57.9 %), 43 (34.1 %) and 10 (8.0 %), respectively. Baseline ALT, HBV DNA and HBsAg levels were comparable with respect to rs3077 genotypes (CC and non-CC). Patients with CC genotype, in comparison to those with non-CC genotype, had significantly higher VR (49.3 % vs. 26.4 %, $P = 0.009$) and HBsAg clearance (11.0 % vs. 1.9 %, $P = 0.035$). In multivariate analysis, CC genotype was an independently factor associated with VR (odds ratio 2.8, 95 % confidence interval: 1.2–6.6, $P = 0.017$).
Conclusion: The SNP rs3077 was independently associated with treatment response to PEG-IFN in Thai patients with HBeAg-negative CHB.

Topic 11: Hepatitis B

No: 1288

Effectiveness of several simple and noninvasive models in assessing liver fibrosis in patients with chronic hepatitis B

Xianghua Zeng[1], Cheng Xu[1], Yuming Wang[1]

Southwest Hospital Third Military Medical University Department of Infectious Diseases Chongqing-China[1]

Aims: Liver biopsy and transient elastography, as the two major methods to evaluate liver fibrosis, still has some limitations. Our research intended to screen for several simple noninvasive models composed of serum markers, and compare their diagnostic value in diagnosing liver fibrosis with chronic hepatitis B (CHB).
Methods: 262 patients with CHB who received biopsy, laboratory tests and liver stiffness measurement (LSM), were included. The receiver operating characteristic (ROC) curves and area under ROC (AUROC) were used for analyzing the results of models, including age-platelet (PLT) index (API), aspartate transaminase (AST) to alanine aminotransferase (ALT) ratio (AAR), AST to PLT ratio index (APRI),γ-glutamyl transpeptidase (GGT) to PLT ratio index (GPRI), GGT-PLT- albumin index (S index), age-AST-PLT-ALT index (FIB-4) and age-AST-PLT-ALT-international normalized ratio (INR) index (Fibro-Q).
Results: The AUROC of S index, GPRI, FIB-4, APRI, API, Fibro-Q, AAR and LSM for predicting significant liver fibrosis was 0.726 ($P < 0.001$), 0.726 ($P < 0.001$), 0.621 ($P = 0.001$), 0.619 ($P = 0.001$), 0.580 ($P = 0.033$), 0.569 ($P = 0.066$), 0.495 ($P = 0.886$) and 0.757 ($P < 0.001$), respectively. S index and GPRI had the highest correlations with LSM (r = 0.516, r = 0.516, respectively). When combining LSM with S index and GPRI, the AUROC were 0.753 and 0.740, respectively.
Conclusion: Among the various markers, S index and GPRI showed the best diagnostic value of significant liver fibrosis, and were the robust predictive models of significant liver fibrosis with CHB in primary care or developing countries where FibroScan was unavailable.

Topic 11: Hepatitis B

No: 1279

The association of interferon gamma induced protein 10 (ip 10) polymorphism and treatment response to pegylated interferon in patients with HBeAg negative chronic hepatitis B

Umaporn Limothai[1], Srunthron Akkarathamrongsin[2], Yong Poovorawan[2], Pisit Tangkijvanich[1]

Chulalongkorn University Research Unit of Hepatitis and Liver Cancer, Department of Biochemistry, Faculty of Medicine Bangkok-Thailand[1], Chulalongkorn University Center of Excellence In Clinical Virology, Faculty of Medicine Bangkok-Thailand[2]

Objectives: Interferon-gamma induced protein-10 (IP-10) plays an important role in liver inflammation in chronic hepatitis B (CHB). Recent data have shown an association between single nucleotide polymorphism (SNP) G201A in promoter region of the IP-10 gene and disease progression in chronic hepatitis B. However, the importance of the SNP in predicting treatment response to pegylated interferon (PEG-IFN) in patients with CHB is unknown.
Methods: We analyzed data from a randomized study comparing efficacy of PEG-IFN monotherapy (group 1) versus combination with entecavir (group 2) in Thai patients with HBeAg-negative CHB. All patients were treated for 48 weeks and followed-up for 48 weeks to assess virological response (VR, HBV DNA level < 2,000 IU/mL). DNA extracted from blood samples was analyzed for the SNP G201A by RFLP.
Results: 63 patients in each group were enrolled. There was no significant difference in VR rates between groups 1 and 2 (41.3 % vs. 38.1 %, $P = 0.856$). The distribution of GG, GA and AA genotypes of G201A was 93 (73.8 %), 32 (25.4 %) and 1 (0.8 %), respectively. Baseline serum ALT level was significantly higher in patients with non-GG genotype compared to patients with GG genotype. However, other baseline characteristics, as well as VR and HBsAg clearance rates, were not significantly different according to the SNP genotypes (GG and non-GG).
Conclusion: The SNP G201A was associated with baseline ALT level but was not associated with treatment response to PEG-IFN in patients with HBeAg-negative CHB.

Topic 11: Hepatitis B

No: 1189

The prediction value of serum hbsag and hbeag in hbeag seroconversion after nucleoside analogue therapy

Meijie Shi[1], Huanming Xiao[1], Baoyu Xie[1], Yajun Zeng[2], Xiaoling Chi[1]

Guangdong Provincial Hospital of Chinese Medicine Hepatology Guangzhou-China[1], Guangzhou University of Chinese Medicine Hepatology Guangzhou-China[2]

Aim: To assess the prediction value of hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg) in HBeAg seroconversion in chronic hepatitis B (CHB) patients receiving nucleoside analogue agents.

Methods and patients: A case–control study was conducted, in which 90 chronic hepatitis B patients were enrolled and treated with telbivudine or entecavir. Among the subjects, 30 patients underwent HBeAg seroconversion, and 60 patients were set as the control. The levels of HBsAg, HBeAg, ALT, and HBV DNA were measured at baseline and 12, 24 and 48 weeks after treatment. An evident decrease in the HBeAg level, but not the HBsAg level, was observed during nucleoside analogue treatment. The accuracy of serum HBsAg and HBeAg for the prediction of HBeAg seroconversion was analyzed using non-conditional logistic regression and receiver operating characteristic (ROC) curve.

Results: No direct correlation was found between HBsAg and HBeAg seroconversion; however, the mean decline in serum HBeAg levels at 24 weeks and HBeAg level at baseline level were associated with HBeAg seroconversion. The serum HBeAg reduction at week 24 from baseline predicted HBeAg seroconversion (area under curve 0.780) better than HBeAg at baseline (area under curve 0.678). Using a cutoff of 172 for HBeAg reduction at 24 weeks, the sensitivity/specificity for HBeAg seroconversion was 60 %/88.3 %.

Conclusion: This study suggests that serum HBeAg reduction at week 24 from the baseline could be a predictor of HBeAg seroconversion of naive HBeAg-positive CHB patients receiving telbivudine or entecavir.

Topic 11: Hepatitis B

No: 1985

Alopeciae due to antiviral usage

Kamuran Türker[1], Betül Taş[2], Serdar Altınay[3], Ebru Taş[4], Nejat Sebzeci[1]

Istanbul Bağcılar Training and Research Hospital Infectious Diseases Istanbul-Turkey[1], Istanbul Bağcılar Training and Research Hospital Dermatology Istanbul-Turkey[2], Istanbul Bağcılar Training and Research Hospital Pathology Istanbul-Turkey[3], Kütahya Dumlupınar University Faculty of Medicine Gastrology Kütahya-Turkey[4]

Chronic HBV infection is one of the most important unresolved health problems in the world. Chronic HBV infection affects more than 350 million people worldwide with many more individuals having evidence of prior HBV infection, overall representing approximately one-third of the world's population. Every year about one million people die due to complications of HBV.

Antiviral drugs can resolve hepatitis B treatment more effective and less drug adverse effect than before using agent such as interferons.

Tenofovir disoproxil belongs to a class of antiretroviral drugs known as nucleotide analogue reverse transcriptase inhibitors (NRTIs), which block reverse transcriptase, a crucial virus enzyme in human immunodeficiency virus 1 (HIV-1) and hepatitis B virus infections. Tenofovir potently blocks HBV replication has been suggested to have antiviral efficacy superior to that of lamivudine.

Alopeciae usually has known as a drug advers effect to interferon therapy. Herein we reported a case with androgenetic alopeciae due to usage of tenofovir(TNF) treatment.

Case:

A twenty two-year old woman who had androgenetic alopeciae just after the receiving of the TNF therapy.

She was diagnosed as having chronic HBV infection proven by positive HBsAg, HBeAg positive, antiHBeAB negative, antidelta Ab negative, HBV-DNA 1,1 × 109 IU/mL, AST: 27 U/L, ALT: 37 U/L liver biopsy score HAİ: 6/18 stage 2/6 at the begining of the TNF 245 mg/day oral therapy in 28.05.2014. After beginning of TNF therapy she had presented progressive hair loss, with the appearance of an androgenetic form alopeciae especially in temporal area of the scalp.

Her antiviral therapy switched entecavir 0.5 mg/day oral.

Topic 11: Hepatitis B

No: 1669

What is the role of alanine aminotransferase level and liver biopsy for antiviral therapy decision in hbeag negative chronic hepatitis B with HBV DNA level between 104 and 105 copies ml

Derya Seyman[1], Dilara Inan[2], Kaya Suer[3], Figen Sarigul[1], Özlem Elpek[4], Aycin Ozdemir[5], Ayla Ozcan[6], Senay Dodanli[1], Tulin Temizkan[1]

Antalya Education and Research Hospital Department of Infectious Diseases and Clinical Microbiology Antalya-Turkey[1], Akdeniz University Medical Faculty Department of Infectious Diseases and Clinical Microbiology Antalya-Turkey[2], Near East University Department of Infectious Diseases and Clinical Microbiology Lefkoşe-Cyprus[3], Akdeniz University Medical Faculty Department of Pathology Antalya-Turkey[4], Antalya Atatürk State Hospital Department of Infectious Diseases and Clinical Microbiology Antalya-Turkey[5], Akdeniz University Medical Faculty Department of Clinical Microbiology Antalya-Turkey[6]

Background: In HBeAg-negative chronic hepatitis B(CHB) patients with normal ALT and HBV DNA level between 104 and 105copies/ml, the presence or absence of active hepatitis are incompletely understood so far.

The aim of this study are to determine grade of hepatic inflammation and fibrosis by liver biopsy in HBeAg negative patients with HBV DNAlevel between 104 and 105copies/ml and also whether ALTlevel is a parameter for histological changes or not.

Methods: Patients with HBeAg negative CHB admitted to three regional hospital were included in the study. Patients with HBV DNA level between 104 and 105copies/ml were performed liver biopsy. Significant histology was defined as fibrosis stage ≥ 2 or necroinflammation grade ≥ 4 according to Ishak scoring system.

Results: 60 patients with HBV DNAlevel between 104 and 105copies/ml were included. Thirty of these patients agreed to liver biopsy and the liver biopsy results of 27patients were included for evaluation. Significant histology was found in 18patients. The ALT level in twelve of these patients was normal and high in six patients. In patients with grade ≥ 4; there was not statistically significant difference between patients with normal ALT and elevated ALT($P = 0.36$). the ALT level isn't always a reliable marker for the presence and absence of histopathologic damage.

Conclusions: Patients with HBV DNA level between 104 and 105 copies/ml could not be accepted as the inactive carrier group or HBeAg negativeCHB patients. These patients are borderline group for antiviral therapy decision. Guidelines do not recommend directly antiviral therapy. Therefore, these patients should be performed liver biopsy, regardless of ALT level.

Topic 11: Hepatitis B

No: 1024

Tenofovir may show comparable safety and antiviral efficacy for treatment naïve Korean hepatitis B patients under 50 years as well as over 50 years in age

Myung Jin Oh[1], Jung Gil Park[1]

Cha University School of Medicine Department of Internal Medicine Gumi-Korea, South[1]

Background: Tenofovir is used as a first-line nucleotide analogue for chronic hepatitis B. A recent epidemiologic study reported that the seroprevelance of HBsAg was a distinct difference, based on age of 50 years in Korea. Thus, the aim of our study is to compare safety and antiviral efficacy of tenofovir between treatment-naïve Korean patients below 50 years and patients above 50 years in age.
Methods: From Dec. 2012 to Nov. 2013, a total of 40 treatment-naïve patients who received tenofovir therapy over 24 weeks were enrolled. The enrolled patients were divided into younger group (20 years old $\leq$ age $<$ 50 years old, n = 21) and older group ($\geq$ 50 years in age, n = 19), respectively. The selected subjects were retrospectively investigated for virological response, serological response, biochemical response, and adverse events at 24 weeks.
Results: No significant difference in baseline characteristics was observed ($P < 0.05$). Virological response at 24 weeks showed complete response (57.1 % vs. 63.2 %), and partial response (42.9 % vs. 36.8 %), respectively ($P = 0.755$). Mean decline of serum HBV DNA at 24 weeks was not significantly different between the two groups (6.3 ± 1.8log10 IU/ml vs. 6.2 ± 1.6log10 IU/ml; $P = 0.503$). The rate of loss or seroconversion of HBeAg did not differ between both groups (8.3 % vs. 11.1 %; $P = 1.000$). In addition, no statistical difference in normalization of serum ALT was observed (68.8 % vs. 71.4 %; $P = 1.000$). Adverse events including pruritus, dyspepsia, and alopecia were not significantly different in the two groups (9.5 % vs. 15.8 %; $P = 0.654$).
Conclusions: Tenofovir may show comparable safety and antiviral efficacy for treatment-naïve Korean hepatitis B patients under 50 years as well as over 50 years in age.

Topic 11: Hepatitis B

No: 2073

The association between serum hepcidin and hepatic fibrosis levels in patients with chronic hepatitis B

Hakan Cam[1], Seyithan Taysı[2], Ediz Tutar[3], Muhammet Cemil Savas[4]

Aksaray State Hospital Gastroenterology Aksaray-Turkey[1], Gaziantep University Medical Faculty Biochemistry Gaziantep-Turkey[2], Gaziantep University Medical Faculty Pathology Gaziantep-Turkey[3], Gaziantep University Medical Faculty Gastroenterology Gaziantep-Turkey[4]

Introduction and aim: Iron metabolism disorders have been defined in progression of chronic hepatic diseases at various levels. It has been reported that hepcidin hormone, which is produced in liver and is the main regulator of iron metabolism, has an important role in the progressive hepatic disease. We aimed to evaluate the correlation between serum hepcidin level as well as hepatic fibrosis score, which has been revealed by liver biopsy, and iron deposition in liver in patients with chronic hepatitis B (CHB.
Method: A total of 149 cases (126 CHB, and 23 healthy controls) were enrolled in the study. Percutaneous liver biopsy was performed in all CHB patients. Fibrosis, HAI, and liver iron amount were determined in biopsy samples. Serum hepcidin levels, liver function tests, and serum iron parameters of all patients were measured. CHB patients were compared in all parameters within the group between subgroups as well as in biochemical measurements with the control group.
Results: Serum hepcidin level was defined markedly lower in CHB patients than the control group ($P < 0.001$). Increased iron deposition was detected in the liver of 26 CHB (20.6 %) patients. Patients were divided into a total of 6 subgroups according to fibrosis stages. There was a significant correlation with negative direction between hepcidin level, fibrosis stage and HAI (respective p values 0.007 and 0.05). No statistically significant difference was detected between mean levels of hepcidin and fibrosis stage. Number of patients was increased by forming 3 subgroups according to fibrosis stage, like mild, moderate, and severe. Groups were compared within themselves. Statistically

Topic 11: Hepatitis B

No: 2194

Effect of nucleos(t)ide analogues on renal function in patients with chronic hepatitis B

Mehmet Ata Çevik[1], Beytullah Yildirim[2], Fikret Gören[2], Ibrahim Gören[2], Talat Ayyildiz[2], Ahmet Bektaş[2]

Ondokuz Mayis University, Medical Faculty Department of Internal Medicine Samsun-Turkey[1], Ondokuz Mayis University, Medical Faculty Department of Gastroenterology Samsun-Turkey[2]

Aim: Chronic hepatitis B patients (CHB) treated with nucleos(t)ide analogues have potential nephrotoxicity. The aim of this study was to assess the relationship between glomerular filtration rate (GFR) and antiviral drugs.
Materials and methods: Two hundred and forty-nine CHB patients, who had been followed at least 6 months, were enrolled in this study. The subgroups of patients were 81 of entecavir (ETV), 70 of lamivudine (LAM), 85 of tenofovir (TDF) and 13 of telbivudine (LDT). HBV DNA (PCR), ALT, AST, albumin, Ca, creatinine and phosphorus levels were evaluated in pre-treatment and third, sixth, twelfth, twenty-fourth, and last month of follow up.
Results: The average observation times were 47.8 ± 22.3 months in the ETV group, 37.05 ± 23.8 months in the LAM group, 35.1 ± 16.8 months in the TDF group, and 16.5 ± 6.54 months in the LDT group. The differences between last and initial values of GFR were -4.4(-16.4/27) ml/min (4.2 %) in the ETV group, -0.8(-12/36) ml/min (2.2 %) in the LAM group, -7.7(- 13/40) ml/min (8.5 %) in the TDF group, and -1.5(-10/16) ml/min (2.1 %) in the LDT group. The differences in groups of ETV ($P < 0.0001$) and TDF ($P < 0.0001$) were statistically significant. The rate of HBV DNA negativity for ETV and TDF were found similar in naive patients.
Conclusion: The treatment of TDF and ETV may cause to decrease of GFR values. There were no statistically meaningful values LAM and LDT.

Topic 11: Hepatitis B

No: 1042

The acceptability of screening for human immunodeficiency virus hepatitis C and B virus infections among pregnant women results of a survey in a testing center in algiers

Nassima Belabas[1], Mohamed Zeroual[1], Naima Ihaddadene[1], Abdelouhab Dif[1]

Laadi Flici (el-kettar) Hospital Department of Infectious Diseases Algiers-Algeria[1]

Objective: To definite the epidemiological characteristics and the acceptability of screening for HIV/HBV/HCV infections among pregnant women in a testing center (TC).
Methods: Cross-sectional survey using a standardized questionnaire on all pregnant women who received HIV/HCV/HBV serology and syphilis every working day between 13/10/2011 and 23/01/2012 (73 days) in a TC.
Results: These are 62 pregnant women married an Algerian national. The average age was 29 years (range 18 -44 years) and 49 consultants were jobless. The mean gestational age was 14 weeks (range 03-35 weeks). The reason for the visit was part of a perinatal assessment in all cases. The prescribed statement was incomplete in 12 cases (19 %). Thirty-nine women (63 %) underwent testing before the current pregnancy as part of a premarital assessment in 25 cases, a perinatal assessment in 12 cases, another health check or following a voluntary approach in 01 case each. After the consultation, all the women agreed to be tested for the infections and 55 women (89 %) agreed to continue the serological surveillance until the third trimester. Twenty-nine consultants (47 %) reported that their husband had already practiced the test as part of a premarital assessment in 22 cases. HIV seroprevalence was (4.83 %), HBV (3.22 %), HCV (0 %) and syphilis (1.61 %) with notably 02 HIV-HBV coinfection.
Conclusion: The practice of testing for a marriage project raises the couples' awareness for other indications of STI screening. The routinely offered screening during the perinatal consultation is well accepted by pregnant women.

Topic 11: Hepatitis B

No: 1988

Comparison of one year therapeutic response rate of four oral antiviral in chronic hepatitis B patients with initial low HBV DNA level

Alpay Ari[1], Sebnem Calik[1], Bengisu Ay[1], Banu Karaca[1], Meltem Avci[1], Selma Tosun[1]

Izmir Bozyaka Teaching and Research Hospital Infectious Disease and Clinical Microbiology Izmir-Turkey[1]

Aim: It was aimed to comparison of one year therapeutic response rate of four oral antiviral in chronic hepatitis B patients with initial low (< 107 copies/ml) HBV DNA level.
Methods: Patients with chronic hepatitis B infections who were given oral antiviral due to defined hepatic inflammation symptoms and findings were included since June 2007 that the date of HBV DNA PCR test became available. Patients with HCV, HIV, delta coinfections, decompansation symptoms and high initial HBV DNA were excluded. Ninety three patients entecavir, tenofovir, lamivudin and telbivudin were given 18, 18, 34 and 23 respectively. Therapeutic response defined as undetectable HBV DNA.
Findings: Eleven patient HBeAg positive and initial HBV DNA mean was 1712151 ± 2424747 copies/ml. At the end of one year, therapeutic response rates for tenofovir, entecavir, lamivudine and telbivudine were %94, %89, %88 and %87 respectively and statistically similar.
Results and conclusion: In low initial viral load,all four oral antviral drugs provide similar response rate in chronic hepatitis B patients.

Topic 11: Hepatitis B

No: 1849

Occult hepatitis B virus infection in Egyptian hepatitis C patients prevalence and impact on hepatocellular carcinoma development

Ibrahim Baghdady[1], Sabry Shoeib[2], Ehab Abdelatty[3], Ashraf Dala[2], Emad Eed[4], Ashraf Zytoon[5]

Faculty of Medicine, Menoufia University Hepatology Menoufia-Egypt[1], Faculty of Medicine, Menoufia University Internal Medicine Menoufia-Egypt[2], Faculty of Medicine Menoufia University Hepatology Menoufia-Egypt[3], Faculty of Medicine, Menoufia University Bacteriology Menoufia-Egypt[4], Faculty of Medicine, Menoufia University Radiology Menoufia-Egypt[5]

The aim of the work is to study the prevalence of OBI among HCV-positive Egyptian patients and its impact on HCC development.
Patients & methods: The study included 100 HCV positive patients. Blood sample was withdrawn for AST, ALT, albumin, bilirubin, PT % and AFP. Diagnosis was done clinically, by abdominal ultrasonography and by assessing viral markers (HBsAg, HBsAb, HBcAb and qualitative PCR for HBV-DNA). HCC lesions were further confirmed by triphasic CT and AFP.
Results: Out of 100 examined HCV patients, only 16 patients (16 %) had Occult Hepatitis B (OBI). HCC were significantly more common in Dually infected patients (OBI/HCV) (31 %) than HCV monoinfected patients (7 %) ($P = 0.01$). AST/platelet ratio is significantly higher among OBI/HCV than HCV patients ($P = 0.03$).
Out of the 100 chronic HCV patients, only 11 patients (11 %) had HCC. Presence of OBI was significantly more common in HCV patients with HCC 45 %) than in HCV patients without HCC (12 %) ($P = 0.01$). All HCV patients with HCC had shrunken liver (100 %) which was significantly more common than HCV patients without HCC (58 %) ($P = 0.0001$). On doing multiple logistic regression analysis of risk factors of HCC, we found that OBI and presence of shrunken liver are independent risk factors of HCC ($P = 0.04$ and 0.03 respectively).
Conclusion: Occult HBV infection may influence the outcome of HCV infection leading to more hepatic fibrosis and development of HCC. The persistent HBV infection may have a critical role in the development of HCC in HBsAg-negative patients. So, occult HBV should be considered and evaluated by more sensitive PCR among HCV-infected patients.

Topic 11: Hepatitis B

No: 1586

Should we take into account the history of hyperthyroidism during interferon alpha treatment

Deniz Ozkaya[1], Esma Yuksel[1], Gunnur Mungan[1]

Md Infectious Disease Izmir-Turkey[1]

Objective: We presented a patient with HBV Infection, developed Autoimmune thyroiditis during the Interferon-alpha treatment.
Case: 30 year-old female patient had been followed since 2004 due to HBV infection. In the liver biopsy performed in March 2012, Hystologic Activity index: 7/18 and Stage: 1/6 were found. The liver enzymes and thyroid hormone levels were normal. Pegylated interferon alpha-2a (PEG-IFN) was started to the patient. At the 3rd month of treatment, ALT: 50 IU/L, HBV-DNA: 1.00 + 8 IU/ml were

determined and the patient was considered as refractory primer. PEG-IFN therapy was switched to tenofovir. After the PEG-IFN therapy, chills, weakness, palpitations, irritability, difficulty in walking, loss of weight (12 pounds in 2 weeks) and hair loss symptoms began. In blood examination, it was found as FT3: >32.55 pg/ml (2.00- 4: 40), FT4: >7.77 ng/dL (0.93- 1.70), TSH: <0.005 mIU/ml (0: 27 to 4: 20), thyroglobulin: >300 ng/ml Anti TPO (anti-M): 176.54I/ml (0-35) respectively. Thyroid ultrasonography and scintigraphy, and laboratory results were consistent with Autoimmune thyroiditis. Thyromazol (methimazole) and dideral treatment was given for Graves. This patient's symptoms improved with treatment and thyroid function is normal. Antiviral treatment was continued during this period. A survey conducted retrospectively, the patient's laboratory tests revealed hyperthyroidism and she had not used any treatment.
Conclusion: Consequently, even if thyroid function is normal at the beginning of PEG-IFN treatment, especially in patients with a past history of hyperthyroidism should be monitored for autoimmune thyroiditis. Autoimmune markers should be investigated in all patients before PEG-IFN treatment.

Topic 11: Hepatitis B

No: 1221

The role of serum HBSAG and traditional chinese medicine syndromes in predicting significant fibrosis in chronic hepatitis B patients

Xiaoling Chi[1], Meijie Shi[1], Huanming Xiao[1], Yubao Xie[1], Guangjun Tian[1], Junmin Jiang[1], Gaoshu Cai[1], Shuduo Wu[1], Jiezhen Chen[1], Pengtao Zhao[1], Chaozhen Zhang[1]

Guangdong Provincial Hospital of Chinese Medicine Hepatology Guangzhou-China[1]

Aim: To evaluate the predictive value of HBsAg and Traditional Chinese Medicine (TCM) syndromes for hepatic fibrosis in Chronic Hepatitis B (CHB) patients.
Methods: The clinical and pathological data of 709 CHB patients with ALT less than 80 IU/L were collected from April 2009 and October 2012.In the enrolled patients, 281 out of 709 have serum HBsAg levels. Area under receiver-operator curve (AUC) was used to determine the diagnostic accuracy of simple tests for significant fibrosis (Scheuer stage, $F \geq 2$).
Results: Among the 281 patients with serum HBsAg levels, 122 (43.42 %) were HBeAg(+), 159 (56.58 %) were HBeAg(-) and significant fibrosis was confirmed in 201 (71.35 %) patients. By logistical regression analysis, HBsAg, AST, ALB, PLT were identified as predictors for significant fibrosis. The Logistic regression model above resulted in the highest AUC (0.771), followed by APRI (0.736), and FIB-4 (0.725). However, the logistic regression model was comparable with the other two panels (both $P > 0.05$). Using an optimal cut-off of 0.699, the logistic regression model showed an sensitivity of 72.5 % and an specificity of 70 % in predicting significant fibrosis. Moreover, stage of fibrosis was highest in the patients with Liver depression and Spleen deficiency accompanied with dampness-heat stagnancy ($F > 2$ accounted for 63.88 %).
Conclusion: This study clearly suggest that serum HBsAg indeed provides a distinct predictive value for significant fibrosis. Furthermore, TCM syndrome typed liver stagnation and spleen deficiency accompanied with dampness-heat stagnancy was associated with fibrosis severity in CHB patients with ALT less than 80 IU/L.

Topic 11: Hepatitis B

No: 1700

The comparison of therapeutic response between entecavir and tenofovir in the treatment naïve patients with chronic hepatitis B

Sung Won Park[1], Soo Hyung Ryu[1], Dae Young Kim[1], Yun Ho Lee[1], Song I Bae[1], Won Jae Yoon[1], Jin Nam Kim[1], You Sun Kim[1], Jeong Seop Moon[1]

Seoul Paik Hospital, Inje University College of Medicine Department of Internal Medicine Seoul-Korea, South[1]

Background and aims: Entecavir (ETV) and tenofovir disoproxil fumarate (TDF) are effective oral antivirals in the treatment of chronic hepatitis B (CHB) with high genetic barriers against resistance. Our aim is to compare the effectiveness of ETV and TDF in nucleoside-naïve CHB patients.
Patients and methods: We retrospectively analyzed clinical and laboratory data of 53 patients treated with ETV and 40 patients with TDF from October 2008 to November 2014. Complete viral response (CVR) was defined as undetectable serum HBV DNA (< 50 copies/mL; the detection limit of real time PCR assay of HBV DNA).
Results: There was no significant differences in baseline characteristics such as age, gender, disease, HBeAg positivity, serum ALT and HBV DNA levels between both groups. Median treatment duration was 34 (range; 15-71) months in ETV and 18 (range; 12-22) months in TDF group. The cumulative rates of CVR at 6 months, 12 months, and 24 months in ETV group were 35.8, 60.4, and 81.1 %, respectively. The cumulative rates of CVR in TDF at 6 months, 12 months, and 24 months were 42.5, 67.5, and 75.6 %, respectively (P = NS). The cumulative rates of ALT normalization at 6 months, 12 months, and 24 months in both groups were similar, 67.9 % vs. 55.0 %, 84.9 % vs. 91.2 %, and 91.4 % vs. 95.6 %, respectively (P = NS). HBeAg seroconversion rates at 1 year were similar in both groups (28 % in ETV, 21 % in TDF).
Conclusion: ETV and TDF showed similar viral and chemical responses in treatment-naïve CHB patients during follow-up periods.

Topic 11: Hepatitis B

No: 1757

AST ALT RATIO (AAR) is not useful to predict the degree of fibrosis in chronic viral hepatitis patients

Ahmet Tarik Eminler[1], Talat Ayyildiz[2], Kader Irak[3], Murat Kiyici[3], Selim Gurel[3], Macit Gulten[3], Selim Giray Nak[3], Enver Dolar[3]

Sakarya University Gastroenterology Sakarya-Turkey[1], Ondokuz Mayis University Gastroenterology Sakarya-Turkey[2], Uludag University Gastroenterology Bursa-Turkey[3]

Introduction: Noninvasive tests of hepatic fibrosis are primarily used for staging of fibrosis in patients with chronic liver disease. Several

studies have also evaluated the accuracy of combinations (or ratios) of these measures.

Aims & methods: The aim of the present study was to investigate the relationship between five noninvasive models AST/ALT ratio (AAR), AST to PLT ratio index (APRI), Bonacini cirrhosis discriminant score (CDS), age-PLT index (AP-ind) and King's score and the degree of hepatic fibrosis determined by biopsy in patients with chronic hepatitis B and C patients. Total 380 patients with viral hepatitis (237 chronic hepatitis B and 143 chronic hepatitis C) were retrospectively analyzed.Five noninvasive models were compared between the low and high fibrosis groups.

Result: There was a statistically significant difference between the high and low fibrosis group of the both viral hepatitis patients according to AP-ind (4.49 ± 2.35 vs 2.41 ± 1.84; $P < 0.001$ in hepatitis B and 4.83 ± 2.25 vs 2.92 ± 1.88; $P < 0.001$ in hepatitis C); APRI (1.00 ± 1.17 vs 0.47 ± 0.39; $P < 0.001$ in hepatitis B and 1.01 ± 1.01 vs 0.41 ± 0.29; $P < 0.001$ in hepatitis C); CDS (4.53 ± 1.90 vs 3.58 ± 1.30; $P < 0.001$ in hepatitis B and 4.71 ± 2.03 vs 3.42 ± 1.49; $P < 0.05$ in hepatitis C) and King's score (24.31 ± 3.14 vs 7.65 ± 6.70; $P < 0.001$ in hepatitis B and 24.82 ± 2.55 vs 8.33 ± 7.29; $P < 0.001$ in hepatitis C). According to AAR we found no significant difference between the fibrosis groups of the both viral hepatitis patients (0.78 ± 0.31 vs 0.74 ± 0.34; $P = 0.082$ in hepatitis B and 0.91 ± 0.40 vs. 0.85 ± 0.27; $P = 0.25$ in hepatitis C).

Conclusion: There was not any significant relationship between the degree of hepatic fibrosis and AAR score.

Topic 11: Hepatitis B

No: 2012

Expression and purification of active recombinant reverse transcriptase domain of human hepatitis B virus polymerase

Dipendra Raj Pandeya[1]

Nepalese Army Institute of Health Sciences Biochemistry Kathmandu-Nepal[1]

Introduction: Hepatitis B virus polymerase plays a critical role during HBV life cycle, and polymerase/reverse transcriptase (RT) activities are critical for HBV-pol during viral replication.

Method: To investigate RT domain of human HBV polymerase, a 5′ end Polyhistidine tagged RT DNA (304-693 amino acids) of HBV-pol was successfully expressed in Escherichia coli. Recombinant RT was purified in native condition employing Ni–NTA affinity column. The recombinant plasmid pT7-RT was purified with Qiagen Midiprep DNA-dependent DNA polymerase activity (DDDP) and reverse transcriptase/RNA dependent DNA polymerase activity (RDDP) were monitored by the synthesis of DNA using poly (dA)·oligo (dT) 12–18 and poly (rA)·oligo (dT) 12–18 as template-primer (Amersham Biosciences Corp.).

Result: Purified RT showed a stable reverse transcriptase activity and a much stronger DNA polymerase activity, compared to RT expressed in rabbit reticulocyte lysate coupled transcriptase-translation system. The purified RT was a stable protein and showed a low selective polymerase activity. Computer modeling results also indicated that RT domain banded to nucleotide substrate in a loose mode.

Conclusion: Employing the approach in this work, a functional RT domain of human HBV-Pol was achieved in *E.coli* expression system. The availability of this recombinant protein in pure form should facilitate the antibody preparation and detailed analysis of the structure and mechanism of RT domain. Large quantity of functional HBV-RT was also required in high throughout screening assay for potential inhibitors development.

Topic 11: Hepatitis B

No: 1201

Tuberculosis lymphadenitis during pegylated interferon alfa and ribavirin therapy for patient coinfected with hepatitis B virus and hepatitis C virus

Dilara Inan[1], Gülay Ozbilim[2]

University of Akdeniz, Faculty of Medicine Infectious Diseases Antalya-Turkey[1], University of Akdeniz, Faculty of Medicine Pathology Antalya-Turkey[2]

The causative role of IFN-based antiviral therapy in exacerbating tuberculosis infection remains controversial; the possible mechanisms are as yet unclear. Clinical and laboratory studies have shown that the hepatitis B virus (HBV) and hepatitis C virus (HCV) interact with each other and affect immune responses. We present the case of 48-year-old woman with chronic hepatitis B and C virus coinfection, who developed dry cough, chest pain, and dysphagia after receiving 29 weeks of pegylated interferon alfa-2a and ribavirin treatment. Physical examination of the patient's painful, bilateral cervical, paratracheal and supraclavicular lymph node enlargement were found. Lymph node biopsy showed that granulomatous lymphadenitis of uncertain etiology with tuberculoid-type granulomas. Treatment for HBV/HCV coinfection were completed total 48 weeks. Two weeks later antituberculous treatment was started. During the third month of treatment, acute hepatic flare due to HBV developed. Tenofovir was started for treatment of chronic hepatitis B. The outcome of antituberculosis therapy was favourable and completed after 9 months. Virological suppression was obtained for both viruses. At 6 months after pegylated interferon alfa-2a and ribavirin therapy, a sustained virological response was achieved for HCV. A maintained undetectable HBV DNA was achieved under tenofovir therapy. This is believed to be the first case report of virologic response from coinfection of HBV/HCV and tuberculosis treated concurrently with antiviral and antituberculous agents.

Topic 11: Hepatitis B

No: 1558

Effectivity of oral antivirals used in chronic hepatitis B and effects on kidney function

Mustafa Kemal Celen[1], Celal Ayaz[1], Irem Akdemir[2], Berivan Tunca[3], Tunga Barcin[4], Ilker Alakus[2], Salih Hosoglu[1]

Dicle University Hospital Infectious Diseases Diyarbakir-Turkey[1], Batman State Hospital Infectious Diseases Batman-Turkey[2], Kiziltepe State Hosptial Infectious Diseases Kiziltepe-Turkey[3], Mardin Park Hospital Infectious Diseases Mardin-Turkey[4]

Background: Chronic hepatitis B (CHB) is an important disease involving 350 million people worldwide. Long term use of oral antiviral drug in the treatment of CHB requires close monitoring of renal functions. In present study the efficacy of treatment and renal functions were evaluated in patients taking oral antiviral therapy for 52 weeks.

Methods: In this study, entecavir 0.5 mg (n = 30, group 1), tenofovir 245 mg (n = 31, group 2), telbivudine 600 mg (n = 28, group 3) and lamivudine 100 mg (n = 31, group 4) using 120 HBeAg-negative patients were evaluated, retrospectively. There was no impairment of earlier kidney function in any of the patients treated in Dicle

University Hospital between 2009-2013. All patients were treatment-naive patients.
Results: Dermographic values of patients were similar before the treatment. Virological response after 52 weeks (HBVD to < 300 copies/mL) was as follow: group 1: 93.3 %, group 2: 93.5 %, group 3: 89.2 %, and group 4: 77.4 %. HBsAg loss did not occur in any of the patients. The average rate of GFR and serum creatinine level at the beginning of the treatment were compared with average rate of GFR and and serum creatinine level at week 52.
Conclusions: In patients, TDF and ETV indicated the most effective viral suppression. Serum creatinine levels were shown to not be directly related to changes in GFR rate. Especially in group-3, a decline was not observed in the rate of GFR at week 52 compared with baseline. The present study once again emphasized the need for close monitoring.

Topic 11: Hepatitis B

No: 1782

Epidemiological characteristics and clinical features on HIV co infection with hbv and or HCV

Jing You[1], Xiaoli Zhang[2], Honying Chen[1], Xia Feng[3], Lin Zhuang[4], Haibin Wang[4], Zhiwen Duan[1], Hong Dai[1], Yanhua Che[5], Sijia Ma[6], Junhua Huang[7], Shaoming Yan[8], Ruyi Zhang[1], Shaofeng Rao[1]

The First Affiliated Hospital of Kunming Medical University Department of Infectious Diseases Kunming-China[1], The First Affiliated Hospital of Kunming Medical University Department of Infectious Diseases, Kunming-China[2], The First Affiliated Hospital of Kunming Medical University Department of Laboratory Medicine Kunming-China[3], The Third People's Hospital of Kunming Department of Hepatology Kunming-China[4], Faculty of Medicine, Prince of Songkla University Epidemiology Unit Songkla-Thailand[5], Kunming Medical University Kunming-China[6], The Yunnan General Hospital of The Chinese People's Armed Police Forces Department of Infectious Diseases Kunming-China[7], The Third People's Hospital of Yunnan Province Department of Internal Medicine Kunming-China[8]

Background/aim: To explore the epidemiological characteristics and clinical features of HIV and co-infection with HBV and/or HCV in HIV/AIDS patients.
Patients and methods: Six hundred and ninety patients with HIV/AIDS were analyzed retrospectively for the epidemiological data and their clinical items including biochemical, viral and immunocal features.
Results: Of the 690 HIV/AIDS patients, the majority (55.94 %) were AIDS. The rate of HIV/HCV co-infection (26.52 %) was higher than that of HIV/HBV co-infection (10.29 %). The average age 41.05 ± 13.06 years old. Young adults (539) accounted for the majority (78.12 %). The farmers and migrant workers were the majority (78.12 %). Sexually transmitted was the main transmitted way in HIV, HIV/HBV and HIV/HBV/HCV group (82.93 %, 84.50 %, 69.23 %; respectively). Intravenous drug use was the main transmitted way in HIV/HCV group (62.84 %). The incidence of tuberculosis, venereal disease and kaposi's sarcoma had significant differences in the four groups ($P < 0.05$). HIV/HBV, HIV/HCV, HIV/HBV/HCV group had mildly or moderate liver function damage. HIV/HBV/HCV had lowest CD4 + T lymphocyte count ($P < 0.05$). HIV group had a lowest HIV RNA level. HIV/HBV/HCV had a highest HIV-RNA level. HBV-DNA load and HCV-RNA load of HIV/HBV/HCV group were respectively higher than HIV/HBV and HIV/HCV group ($P < 0.05$).
Conclusion: Co-infection with HBV and/or HCV would increase the incidence of opportunistic infections and tumors. Co-infection with HBV and/or HCV would increase HIV-RNA load level. HIV/HBV/HCV co-infection would increase HBV-DNA and HCV-RNA load level. HIV/HBV/HCV co-infection would aggravate the damage of cellular immunity.

Topic 11: Hepatitis B

No: 2191

Naturally developing hbv polimerase and superficial gene variants in inactive hepatitis B carriers

Omer Senturk[1], Faden Hayrunnisa Aydin[2], Murat Sayan[3], Ugur Korkmaz[1], Hasan Yilmaz[1], Murat Ozturkler[1], Zeynep Senturk[2], Altay Celebi[1], Sadettin Hulagu[1]

Kocaeli University Gastroenterology Kocaeli-Turkey[1], Kocaeli University Internal Medicine Kocaeli-Turkey[2], Kocaeli University Microbiology Kocaeli-Turkey[3]

Introduction: The most serious problem in the oral antiviral treatment of chronic hepatitis B is the primary and compensatory development of drug resistance mutation naturally seen in inactive hepatitis B carriers. In this study, our aim is to evaluate the frequency and pattern of naturally developing oral antiviral drug resistance and typical HbsAg escape mutation in inactive chronic hepatitis B carriers.
Material and method: In this study, total 91 patients including HbsAg positive, HBV DNA is less than 2000 IU/ml during 12 months followup (screening at every 6 month) and normal AST and ALT level. HBV pol gene mutation was detected by DNA sequencing method.
Results: HBV DNA was detected in the serum of 32/91 (35 %) patients.Oral antiviral related naturally developing compensatory resistance mutation was detected in 53 %(17/32) of patients.Primary drug resistance mutation was not detected in any patients. Compensatory drug resistance mutation was seen in 82 %(14/17) of patients against to lamivudine and adefovir. Also compensatory telbuvidine resistance mutation was detected in 29 % (5/17)of them.
Discussion: In this presenting study, secondary drug resistance mutations were detected in 149, 214, 215, and 238. position of HBV polimerase gene and in 91. position for lamivudine, adefovir and telbuvidine, respectively. These mutations repair HBV viral replication.Besides these viral replication repair mutations were seen in treatment sensitive patients, oral antiviral treatment success can be affected by similar mutation at other clinical phases.

Topic 11: Hepatitis B

No: 2114

A clinical study on anti HBV DC inducing therapy in the HBeAg positive chronic hepatitis B virus carriers

Bang-fu Wu[1], Jiang-ying Yang[1], Yong Liu[2], Xuan-qin Wang[2], Xiang-hua Huang[2], Zheng-sheng Xiao[2], Xue-song Li[2], Ming Yang[2], Tuo-pu Wu[1]

Guangzhou Pubang Bio-immunological Tech Research Institute Tech Department Guangzhou-China[1], Southern Medical University

Renkang Hospital Gastroenterology and Hepatology Center Dongguan-China[2]

Aims: To observe the clinical efficacy of the anti-HBV-dendritic cells(DC) inducing therapy combined with telbivudine in the HBeAg positive chronic hepatitis B virus(HBV) carriers.
Methods: 31 male and 19 female HBeAg positive chronic HBV carriers were recruited in the study. Patient's median age was 28 years (from 17 to 42 years). All patient's ALT was normal. The anti-HBV-DC inducing agent which been an admixture of hepatitis B vaccine, rhGM-CSF and BCG polysaccharide nucleic acid was injected hypodermically to the patient once every two weeks for 18 practices applications totally. Telbivudine was taken 600 mg daily. Quantitative HBVM(TRFIA) and HBVDNA were evaluated at week 0, 12, 24 and 36.
Results: At week 12, 24 and 36, the HBVDNA negative conversion rate were 6.00 %(3/50), 20.00 %(10/50) and 48.00 %(24/50), the HBeAg negative conversion rate were 0.00 %(0/50), 4.00 %(1/50) and 12.00 %(6/50), the HBeAb positive conversion rate were 2.00 %(1/50), 6.00 %(3/50) and 18.00 %(9/50), the HBeAg seroconversion rate was 0.00 %(0/50), 2.00 %(1/50) and 12.00 %(6/50), and the HBsAb positive conversion rate were 38.00 %(19/50), 70.00 %(35/50) and 90.00 %(45/50). The HBsAg negative conversion was none. The mild abnormal ALT was observed in two patients at week 12, in four patients at week 24 and in three patients at week 36. The rate of adverse effect was 36.67 %. The adverse effect include fever, headache, ache all over, bellyache, urticaria and hives, dyspnea, and tumefaction ache in the injection site.
Conclusions: The anti-HBV-DC inducing agent can induce the subcutaneous immature DC become to mature DC, and restart the immune responses against HBV. The anti-HBV-DC inducing therapy can be considered as an efficient approach for HBeAg(+) chronic HBV carriers.

Topic 11: Hepatitis B

No: 1632

A comparison of renal safety of telbivudine entecavir and tenofovir treatment in chronic hepatitis B patients a single center large "real life" cohort study

Tsung-hui Hu[1], Kuo-chin Chang[1], Po-lin Tseng[1], Ming-tsung Lin[1], Chao-hung Hung[1], Yi-hao Yen[1]

Chang Gung Memorial Hospital-Kaohsiung Medical Center Department of Internal Medicine Kaohsiung-Taiwan[1]

Aim: To compare the nephrotoxicity among chronic hepatitis B (CHB) patients treated with tenofovir (TDF), telbivudine (LdT), or entecavir (ETV).
Method: We performed a retrospective cohort study of 587 CHB patients primarily treated with TDF (n = 170), LdT (n = 184) and ETV (n = 233) for at least 1 year. Renal function was assessed by the change of serum estimated glomerular filtration rate (eGFR) yearly, along with serum phosphate, urine phosphate, total protein and microalbumin.
Results: The mean eGFR level decreased in TDF group significantly after a mean treatment duration of 17 months (92.2 to 85.6 ml/min/1.73 m[SUP]2[/SUP], $P < 0.001$), but increased in LdT group after mean treatment of 32 months (86.1 to 95 ml/min/1.73 m[SUP]2[/SUP], $P < 0.001$). There was no significant change in ETV group after a mean of 44 months (80.5 to 82.1 ml/min/1.73 m[SUP]2[/SUP]). By multivariate analysis, only pre-existing renal insufficiency (odds ratio, 6.184; 95 % CI 2.762–13.845; $P < 0.001$) and diabetes mellitus (odds ratio, 2.567; 95 % CI 1.111–5.933; $P = 0.027$) were independent predictors for renal function progression. There was no significant difference in serum phosphate, urine phosphate, total protein and microalbumin level after 2 year of treatment.
Conclusion: Telbivudine has the best renal reserve comparing to ETV and TDF. Long-term use of ETV is safe in renal function. The clinical physicians have to be alert to the deterioration of renal function in TDF treatment, especially in patients with comorbidity.

Topic 11: Hepatitis B

No: 1206

Estimation of alt fluctuation in the past 10 years by non invasive test

Takashi Taida[1], Makoto Arai[1], Yuki Haga[1], Tatsuo Kanda[1], Fumio Imazeki[2], Osamu Yokosuka[1]

Chiba University Gastroenterology Chiba-Japan[1], Chiba University Safety and Health Organization Chiba-Japan[2]

Background: Most HBV carriers show the normal liver function, then evaluating liver function has not been undertaken enough. Therefore, we often care HBV carriers at outpatient without the information of liver function in past.
Methods: For 116 HBV carriers who were observed in our hospital for more than 10 years, we classified their ALT fluctuation for 10 years to 5 groups (0: ALT levels kept normal for 10 years, 1: for 5 to 9 years, 2: for 3 to 4 years, 3: for less than 2 years, 4: ALT levels did not keep normal). Normal ALT level was defined as 30 IU/L or less. We analyzed the relation between the pattern of ALT fluctuation for past 10 years and liver function (ALT, HBV-DNA, HBsAg, HBV genotype, platelet count, age, gender) including the value of FibroScan® retrospectively.
Result: Patients included 54 men and 62 women and their mean age was 53.9 ± 13.6 (21-81) years old. The numbers of genotype (A/B/C) were 6/16/66. The number of cases in group 0, 1, 2, 3, and 4 were 36, 20, 18, 18, and 24, respectively. The factors related to groups were analyzed by univariate analysis. Age, gender, hepatic hardness, ALT and HBV-DNA were extracted. In multivariate analysis, ALT fluctuation in the past 10 years were estimated by HBV-DNA ($P = 0.000$), hepatic hardness ($P = 0.026$) and gender ($P = 0.000$).
Conclusion: Only non-invasive tests can estimate ALT fluctuation in the past 10 years. It is very useful to evaluate HBV carriers who did not undertake efficient follow-up.

Topic 11: Hepatitis B

No: 1878

Entecavir plus adefovir or entecavir plus tenofovir for patients with chronic hepatitis B resistant to neucleot(s)ide analogues

Jung Gil Park[1], Soo Young Park[2], Young Oh Kweon[2], Won Young Tak[2], Se Young Jang[2], Soo Hyun Lee[2], Yu Rim Lee[2], Won Im[3], Hyun Young Woo[3], Jung Heo[3]

Cha University, Gumi Cha Medical Center Internal Medicine Gumi-Korea, South[1], School of Medicine, Kyungpook National University Internal Medicine Daegu-Korea, South[2], School of Medicine, Pusan National University Internal Medicine Pusan-Korea, South[3]

Background & aims: The consensus is little about the optimal management of patients with chronic hepatitis B (CHB) who

developed drug resistance. As multiple drug resistance has been emerging, more potent combination of drugs is needed to investigate.
Methods: We enrolled 258 patients with compensated CHB who developed nucleot(s)ide analogues resistant mutations during nucleot(s)ide analogues medication for 2 years. Among these patients, 58 were treated with a combination of entecavir plus adefovir (ETV + ADV group) and 36 were treated with a combination of entecavir plus tenofovir (ETV + TDF group).
Results: Baseline serum DNA level of ETV + ADV group tends to higher than ETV + TDF group. After adjustment by propensity score, the rate of complete virologic response (CVR, serum HBV DNA < 300 copies/mL) was significant greater in the ETV + ADV than in the ETV + TDF group in 12 months (39 %vs. 67 %, $P = 0.018$ at 3 months; 44 %vs.72 %, $P = 0.017$ at 6 months; 47 %vs.86 %, $P < 0.001$ at 9 months; 56 %vs.89 %, $P = 0.002$ at 12 months). The rate of CVR was significantly increased in ETV + TDF group ($P = 0.009$, HR = 2.177, CI = 1.210–3.917) and decreased in patients with high baseline serum DNA level ($P = 0.010$, HR = 0.714, CI = 0.553–0.921) in multivariate analysis.
Conclusions: In patients with CHB who developed drug resistance, combination therapy with ETV + TDF was superior to ETV + ADV in achieving CVR. We suggest more potent combination therapy was needed in patients who developed drug resistance. Further large-scale prospective study is needed for delineation of these results.

Topic 11: Hepatitis B

No: 1184

Long term efficacy of entecavir monotherapy for partial virologic response to entecavir in treatment naïve chronic hepatitis B patients

Byung Seok Kim[1], Han Na Choi[1], Sun Mi Kang[1], Si Hye Kim[1], Joon Seok Park[1], Chang Hyeong Lee[1]

Catholic University of Daegu School of Medicine Department of Internal Medicine Daegu-Korea, South[1]

Background/aim: The optimal management of patients with partial virologic response (PVR) to entecavir (ETV) is currently not well established. The aim of this study was to evaluate the long-term efficacy of ETV monotherapy in treatment-naïve chronic hepatitis B (CHB) patients with PVR to ETV therapy.
Methods: 364 treatment-naïve CHB patients treated with ETV for at least 48 weeks and had continuous ETV monotherapy for over 96 weeks were included. PVR was defined as a decrease in serum hepatitis B virus (HBV) DNA of more than 2 log10 IU/mL from baseline but detectable HBV DNA by real-time PCR assay at week 48.
Results: Fifty-two of 364 patients (14.3 %) showed PVR. Among them, 41 patients had continuous ETV monotherapy for over 96 weeks (mean follow-up duration, 42.6 ± 18.7 months). The mean age was 49.3 years, and 22 patients (55 %) were men. 36 patients (90 %) were HBeAg-positive, and 13 patients (32.5 %) had cirrhosis. 40 of 41 patients (95 %) achieved a virologic response (VR, HBV DNA < 20 IU/mL) during prolonged ETV monotherapy (mean duration, 25.3 ± 14.2 months). The cumulative probabilities of VR at weeks 144, 192, 240, 288 from initial treatment were 92.7, 95.1, 95.1 and 97.6 % respectively. VR rate was 97.2 % (35/36) in HBeAg-positive patients. In HBeAg-negative patients, 100 % (5/5) achieved VR. By multivariate analysis, HBeAg positivity ($P = 0.047$) and high baseline HBV DNA level ($P = 0.000$) were independently associated with delayed virologic response. No one developed genotypic resistance to ETV during follow-up.
Conclusions: Long-term ETV monotherapy is effective for achieving VR in treatment-naïve CHB patients with PVR to ETV.

Topic 11: Hepatitis B

No: 1336

Telbivudine versus lamivudine for antiviral prophylaxis in chronic hepatitis B patients undergoing cytotoxic chemotherapy

Wei-ting Ou[1], Hsien-chung Yu[1], Wei-chih Sun[1], Ping-i Hsu[1]

Kaohsiung Veterans General Hospital Department of Medicine Kaohsiung-Taiwan[1]

Aim: To investigate the efficacy of antiviral prophylaxis of lamivudine and telbivudine in chronic hepatitis B (CHB) patients receiving cytotoxic chemotherapy for malignant diseases.
Method: This retrospective cohort study included 78 CHB patients positive for hepatitis B surface antigen, receiving chemotherapy and antiviral prevention for hepatitis B flare with either telbivudine (n = 45) or lamivudine (n = 33). Antiviral agents were withdrawn 6 months after discontinuing chemotherapy. Liver function and hepatitis B virus (HBV) DNA level were assessed at baseline and every 3-6 months. Genotypic resistance was measured in all patients with viral breakthrough (defined as reappearance of HBV DNA from undetectable level or > 1 log IU/mL than nadir).
Results: Baseline characteristics were comparable between the cohorts. Table 1 describes treatment outcomes. No patient with baseline HBV DNA ≤ 2000 IU/mL or treatment duration $\leq$ 12 months experienced viral breakthrough. HBV DNA > 2000 IU/mL, HBV DNA negativity at month 6, and use of rituximab/steroid based chemotherapy regimen were significant factors related to viral breakthrough ($P < 0.01$ for all). Multivariate analysis identified rituximab/steroid use as the sole factor related to viral breakthrough (hazard ratio = 22.13, 95 % confidence interval = 2.25-217.27, $P < 0.01$; cumulated rate of viral breakthrough, 25, 25, and 63 % at 6, 12, and 18 months, respectively).
Conclusion: Telbivudine and lamivudine achieved similar efficacy and safety for antiviral prophylaxis in CHB patients on chemotherapy.

Topic 11: Hepatitis B

No: 1940

Association of hepatitis B virus infection and glomerulonephritis in Taiwan a population based case controlled study

Sheng-shun Yang[1], Chiao-wei Huang[1], Cheng-heng Lin[2], Kuo-hsiung Shu[3], I-da Lu[1], Chung-hsin Chang[1], Hong-zen Yeh[1]

Taichung Veterans General Hospital Division of Gastroenterology, Department of Internal Medicine Taichung-Taiwan[1], Taichung Veterans General Hospital Department of Medical Research Taichung-Taiwan[2], Taichung Veterans General Hospital Division of Nephrology, Department of Internal Medicine Taichung-Taiwan[3]

Background: Hepatitis B virus (HBV) related glomerulonephritis (GN) is usually under-diagnosed due to lack of pathological confirmation.

Aims: By case-controlled study, we investigate the relationship between HBV infection and GN development from National Health Insurance Research Database (NHIRD).
Methods: Adult patients had at least twice diagnosis of HBV between 2000 and 2010 were enrolled, excluding hepatitis C and end stage renal disease. Four insured subjects without HBV diagnosis for each HBV patient during the same period were sampled for controls matched by age, gender, and Charlson Comorbidity Index (CCI) status. GN development defined as at least three consecutive GN diagnosed at outpatient setting in one year, or at least once on admission.
Results: 35,746 patients were included, of them 597 were diagnosed of GN in HBV group (1.7 %), and 1,786 in non-HBV group (1.2 %). The incidence of GN was significantly higher in HBV group (aOR 1.23, 95 % CI 1.12 $\sim$ 1.35) after adjusting age, gender and CCI status. Incremental year (aOR 1.06 per year) and male (aOR 1.18, 95 % CI 1.09 $\sim$ 1.28, $P = 0.0001$) are independent factors for GN development. Diabetes mellitus, malignancy, rheumatologic disease are risk factors for secondary GN. The occurrence of GN is significantly higher for male patients age 20-34 (OR 1.61, 95 % CI 1.28 $\sim$ 2.03, $P < 0.001$) and age 35-49 (OR 1.52, 95 % CI 1.31 $\sim$ 1.77), while no difference for patients age above 50 in HBV group compared with non-HBV counterpart.
Conclusions: HBV infection is a significant independent risk factor for the development of GN in adult Taiwanese, male HBV-infected subjects age 20-49 are at the highest risk.

Topic 11: Hepatitis B

No: 2031

Alanine transaminase level influences obstetric outcome in maternal carriers of hepatitis B surface antigen

T.T. Lao[1], T.K.W. Cheung[1], L.W. Law[1], V.W.S. Wong[2], H.L.Y. Chan[2], T.Y. Leung[1]

The Chinese University of Hong Kong Obstetrics & Gynaecology Shatin-Hong Kong[1], The Chinese University of Hong Kong Medicine & Therapeutics Shatin-Hong Kong[2]

Aim: To examine obstetric outcome in relation to elevated alanine transaminase (ALT) among asymptomatic mothers with positive antenatal screening for hepatitis B surface antigen (HBsAg) to clarify if elevated ALT at < 20 weeks is a significant pregnancy prognosticator
Methods: 255 asymptomatic mothers with positive antenatal screening for HBsAg were recruited with liver function test done at < 20 weeks gestation. Obstetric outcome was compared between mothers with and without elevated ALT (> 40 IU/L), using t test and Chi square test as appropriate.
Results: Among the 23 (9 %) women with elevated ALT, there was significantly increased incidence of nulliparity (60.9 % versus 34.5 %, $P = 0.012$), antepartum haemorrhage (26.1 % versus 9.9 %, $P = 0.019$), and preterm birth (17.4 % versus 5.6 %, $P = 0.030$), but no difference in pregnancy-induced hypertension (8.7 % versus 5.2 %, $P = 0.476$), prelabor rupture of membranes (4.3 % versus 3.0 %, $P = 0.724$), gestational diabetes mellitus (8.7 % versus 18.9 %, $P = 0.225$), cesarean delivery (26.1 % versus 20.3 %, $P = 0.511$), or male infants (39.1 % versus 49.6 %, $P = 0.339$). The mean infant gestational age (38.1 $\pm$ 2.7 weeks versus 39.0 $\pm$ 1.9 weeks, $P = 0.039$) and birthweight (2942 $\pm$ 571 g versus 3162 $\pm$ 453 g, $P = 0.031$) were significantly lower.
Conclusion: Elevated ALT before 20 weeks gestation was associated with increased antepartum haemorrhage and preterm birth, which together would have resulted in the reduced gestational age and lower mean birthweight in the offspring.

Topic 11: Hepatitis B

No: 1044

Comparison of the efficacy of entecavir lamivudine adefovir dipivoxil and telbivudine in treating nas naive patients in China

Zongping Han[1], Chaoyu Xu[2], Yujia Zhu[2]

The Fifht Affiliated Hospital of Sun Yat-sen University Department of Geriatrics Zhuhai, Guangdong-China[1], The Eighth Affiliated Hospital of Guangxi Medical University Department of Infectious Disease Guigang-China[2]

Objective: To compare the effectiveness of entecavir(ETV), lamivudine(LAM), adefovir dipivoxil(ADV) and telbivudine(LDT) monotherapy in nucleos(t)ide analogs(NAs) naïve patients with median quantities of HBV-DNA (mqHBV-DNA).
Methods: A total of 355 patients who completed 144 weeks of LAM (n = 151), ADV (n = 72), LDT (n = 50) or ETV (n = 82) monotherapy were prospectively studied. The effectiveness data of the four NAs groups were collected and analyzed.
Results: Serum HBV DNA levels decreased from commencement of antiviral therapy in the four groups, especially in ETV group, from week 12 (2.46 $\pm$ 0.43 log10 IU/ml) to 96 (1.99 $\pm$ 0.68 log10 IU/ml) were the statistically lowest (all $P < 0.05$). The rates of undetectable HBV DNA in LAM, ADV, LDT and ETV were statistically different at week 12 ($P = 0.011$), 24 ($P = 0.021$), 36 ($P = 0.002$). However, no differences were found at week 48($P = 0.039$), 72($P = 0.102$), 96($P = 0.650$), 144($P = 0.475$). The median time from baseline to achieving-undetectable HBV DNA of LAM, ADV, LDT and ETV groups were 9.9 (2.0–28.0), 9.90(4.1–36.2), 11.9(1.5–32.1) and 2.45(0.8–23.8) weeks respectively ($P < 0.001$). The proportion of antiviral drugs altered were statistically different in LAM (48.30 %, 73/151) > LDT (18.0 %, 9/50) > ADV (15.2 %, 11/72) > ETV (6.1 %, 5/82) ($P < 0.001$). The rates of complete viral response in ETV(95.1 %,78/82) > LDT (82.0 %,41/50) > ADV(70.8 %,51/72) > LAM 46.3 %,70/151, $P < 0.001$) and viral breakthrough in LAM(33.7 %,51/151) > ADV(26.3 %,19/72) > LDT(24.0 %,12/50) > ETV(8.53 %,7/82)($P = 0.017$) were statistically different at the end of follow up.
Conclusion: ETV monotherapy was more potent and faster in HBV DNA suppression and showed lower viral breakthrough in NAs naive patients.

Topic 11: Hepatitis B

No: 1559

Reactivation of occult hepatitis B infection without marked immunosupression and spontaneous seroconversion

Abdurrahim Sayilir[1], Yavuz Beyazit[1], Serkan Torun[1], Nurgül Şaşmaz[1]

Turkiye Yuksek Ihtisas Teaching and Research Hospital Gastroenterology Ankara-Turkey[1]

Background: Occult Hepatitis B virus infection can be defined as the presence of HBV-DNA in liver tissue and/or blood in the absence of serum HBsAg. We present a case of Occult Hepatitis B reactivation without marked immunosupression.

Case: A 58 years old man who has known coronary artery disease was consulted four days after successful coronary artery bypass surgery for abnormal liver enzymes. Laboratory profile showed elevated levels of ALT 203, AST 144, LDH 736U/L, total bilirubin 2.38 mg/dL, direct bilirubin 1.05 mg/dL. Other laboratory tests within normal range. Viral hepatitis panels showed HBsAg (negative), Anti-HBc IgM (negative), Anti-HBcIgG positive, Anti HAV IgM (negative), anti HCV (negative) and HCV-RNA PCR negative. Two units of packed red blood cells and fresh whole blood were given the patient intraoperatively. Blood donors were negative for HbsAg. Fifteen days after operation his liver chemistry was fully returned to normal range. Outpatient follow up of the patient was continued. Seven months after operation ALT and AST mildly raised again (70 and 48 IU/L respectively). This time his viral profile was changed and HBsAg (positive), Anti-HBcIgG (positive), Anti-HBcIgM (positive), HBV-DNA (PCR)119 IU/ml, AntiHBe(positive) and HBeAg(negative). At the end of one-year follow-up, his liver enzyme levels were normal and DNA was negative. HBsAg seroconversion was observed.
Conclusion: In immunocompetent patient, reactivation of occult HBV is not reported yet. When the balance between virus and host have turned in favor of the virus, reactivation can be possible. This case showed that Occult Hepatitis B may have reactivated in immunocompetent patient.

Topic 11: Hepatitis B

No: 1355

The diagnostic accuracy of transient elastography in liver fibrosis staging in patients with chronic hepatitis B a meta analysis

Y Li[1], Zz Wang[1], Ys Huang[2], F Sun[2], Sy Zhan[2], Xe Liu[1], H Zhuang[1]

Peking University Health Science Center Department of Microbiology and Infectious Disease Center Beijing-China[1], Peking University Health Science Center Department of Epidemiology and Biostatistics Beijing-China[2]

Objectives: Transient elastography (TE) is a non-invasive method for staging liver fibrosis. A meta-analysis was performed to assess the performance of TE for diagnosing fibrosis in patients with chronic hepatitis B (CHB) and to explore the effect of ALT levels on the diagnostic accuracy of TE.
Methods: Medline, Embase, Cochrane library, Chinese database CNKI and Wanfang Data were searched (Jan, 2003 to Nov, 2014). Data were extracted to calculate true/false positive, true/false negative of diagnostic results of TE in CHB patients for fibrosis stage $F \geq 2$, $F \geq 3$ and $F = 4$ with liver biopsy (LB) as a reference standard. The hierarchical summary receiver operating characteristic (HSROC), bivariate model, and subgroup analyses were performed to evaluate the diagnostic accuracy of TE. QUADAS tool was used to assess the quality of studies.
Results: Nineteen literatures were included in the meta-analysis. The summary sensitivity of TE for staging fibrosis $F \geq 2$, $F \geq 3$ and $F = 4$ was 0.807 (95 % CI 0.749-0.853), 0.841 (95 % CI 0.740-0.907) and 0.860 (95 % CI 0.804-0.903), respectively, and the summary specificity was 0.834 (95 % CI 0.773-0.882), 0.864 (95 % CI 0.813-0.903) and 0.880 (95 % CI 0.836-0.913), respectively. No significant differences were found between ALT < 2 upper limit of normal (ULN) and ALT ≥ 2 ULN groups on the performance of TE for detecting fibrosis $F \geq 2$, $F \geq 3$ and $F = 4$, respectively.
Conclusion: TE performs well to diagnose fibrosis in CHB patients. With the use of TE, LB could be reduced and the monitoring of progression of liver fibrosis in CHB patients will become more convenient.

Topic 11: Hepatitis B

No: 1142

Immunofluorescence detection of hepatitis B core antigen in formalin fixed or frozen sections of liver biopsies from chronic hepatitis B patients in Bangladesh

Ruksana Raihan[1], Shahina Tabassum[2], Mamun Al Mahtab[3], Afzalun Nessa[2], Munira Jahan[2], Mohammad Kamal[4], Sheikh Mohammad Fazle Akbar[5], Julio Cesar Aguilar[6]

Aimst University Unit of Microbiology Kedah-Malaysia[1], Bangabandhu Sheikh Mujib Medical University Department of Virology Dhaka-Bangladesh[2], Bangabandhu Sheikh Mujib Medical University Department of Hepatology Dhaka-Bangladesh[3], Bangabandhu Sheikh Mujib Medical University Department of Pathology Dhaka-Bangladesh[4], Toshiba General Hospital Department of Medical Sciences Tokyo-Japan[5], The Center For Genetic Engineering and Biotechnology Department of Biomedical Research Havana-Cuba[6]

Aims: Immunostaining of HBcAg is useful in characterizing CHB, specially HBeAg-negative patients who are difficult to be distinguished from inactive carriers.
Methods: The study compared indirect immunofluorescence(IIF) from formalin fixed paraffin blocks with frozen section of normal saline preparations in detecting HBcAg. Patients were grouped into HBeAg-positive and negative and HBcAg was detected using polyclonal rabbit anti-HBcAg.
Results: Out of 70, 8(11.4 %) were HBeAg-positive and 62(88.57 %) HBeAg-negative. All 8 HBeAg-positive tested HBcAg-positive by IIF. 55(88.7 %) HBeAg-negative were HBcAg-positive and 7(11.29 %) were HBcAg-negative. Comparison between frozen section and formalin fixed paraffin block preparation for IIF from 30 subjects showed, 22(84.62 %) HBeAg-negative were HBcAg-positive by both methods. Among the 4 HBeAg-positive cases, all were HBcAg-positive.
Conclusion: Results suggest that formalin fixed liver tissues can be used to detect HBcAg in CHB, as compared to the frozen section of liver tissues, providing additional benefit in studying previously analyzed biopsies.

Topic 11: Hepatitis B

No: 2192

Hbsag Anti Hcv Anti Hiv 1 2 and syphilis seroprevalence in healthy volunteer blood donors in eastern marmara region Turkey

Mustafa Altindis[1], Mehmet Koroglu[1], Birsen Mutlu[2], Tayfur Demiray[3], Idris Sahin[4], Canan Kulah[5], Umit Ozcelik[6]

Sakarya Uni School of Medicine Medical Microbiology Sakarya-Turkey[1], Kocaeli University Infection Disease Kocaeli-Turkey[2], Sakarya Training and Research Hospital Medical Microbiology Sakarya-Turkey[3], Düzce University Medical Microbiology Duzce-Turkey[4], Zonguldak Be Uni Medical Microbiology Zonguldak-Turkey[5], Sakarya Training and Research Hosp Blood Center Sakarya-Turkey[6]

Determination of Six-year seropositivity rates of microbiologic screening tests obtained among volunteer blood donors in blood centers in Eastern Marmara Region(Kocaeli, Zonguldak, Sakarya, and Duzce) and comparison of the results according to years and cities.

This retrospective study included 150,787 volunteer blood donors admitted to four blood centers (Kocaeli; 99000, Zonguldak: 23377, Sakarya: 18025, Duzce: 10385) between years January'2009 and October'2014. Each sample from volunteer donors was tested for HBsAg, anti-HCV, and anti-HIV 1,2 by chemiluminescence microparticular enzyme immunoassay (CMIA) method. The screening for syphilis is tested by nontreponemal carbon slide test for the first three years, and then by CMIA-based treponemal test (Architect Syphilis TP; Abbott) for the last there years of 150,787 healthy volunteer blood donors, 140536 (93.2 %) were male and 10251 (6.8 %) were female. Out of all donors, 2019 (1.33 %) was found to be positive for at least one screening test. Seropositivity rates for HBsAg, Anti-HCV antibody, anti-HIV1,2, and syphilis were 1340(0.8 %), 578(0,38 %), 38(0,0025 %), and 63(0,004 %), respectively.

A significant decrease was observed in HBsAg and anti-HCV positivity by year. The rate for regional HBsAg positivity was low compared to general population rates reported by The National Viral Hepatitis Society.

Topic 11: Hepatitis B

No: 1905

Clinical significance of serum ferritin in patients with chronic hepatitis B hepatitis B virus related cirrhosis and hepatocellular carcinoma

Ying Li[1], Wei Zhang[1], Tianbai Shen[2], Kun Li[2]

Long-hua Hospital Affiliated To Shanghai University of Traditional Chinese Medicine Liver Department Shanghai-China[1], Traditional Chinese Medicine Shanghai-China[2]

Background: Chronic hepatitis B virus (HBV) infection is one of the common chronic infectious diseases in the world. In the current study, there are more than half a million infected individuals die from HBV-related liver cirrhosis or hepatocellular carcinomas (HCC) each year.

Aim: The present study determined the levels of serum ferritin in patients with chronic hepatitis B, hepatitis B virus-related cirrhosis and hepatocellular carcinoma, and aimed to investigate the relationship between serum ferritin and liver damage, the progression of liver cirrhosis and hepatoma.

Methods: 38 patients with chronic hepatitis B virus, 37 patients with cirrhosis secondary to HBV, 45 HBV-related hepatocellular carcinomas and 50 healthy subjects were included in the study. All the patients with a data concerning age, sex, serum ferritin level, Child-Pugh score, serum biochemical indicators and serum tumor markers were enrolled.

Results: The results revealed that the level of SF in HCC patients was significantly higher than those in patients with cirrhosis (244.6 vs 121.3, $Z = -1.94$, $P = 0.052$) and CHB (244.6 vs.211.6, $Z = -2.14$, $P = 0.033$) (Figure 1). The levels of Serum ferritin also differed significantly according to the Child-Pugh classification B vs A. $P = 0.028$ (Figure 2). Serum ferritin was associated with the oral Child-Pugh classification($r = 0.22$, $P = 0.01$), ALT($r = 0.24$, $P = 0.008$), AST($r = 0.28$, $P = 0.002$), GGT($r = 0.38$, $P < 0.001$), AFP($r = 0.27$ $P = 0.003$), CA50($r = 0.3$, $P = 0.01$), CA199($r = 0.29$, $P = 0.001$).

Conclusions: In summary, serum ferritin level was associated with HBV-related inflammation and fibrosis. and these findings suggest that ferritin may involved in the initiation and progression of hepatitis B virus-related cirrhosis and hepatocellular carcinoma.

Topic 11: Hepatitis B

No: 1679

The knowledge of healthcare workers about the prevention of mother to child transmission of hepatitis B virus in a second state hospital in Turkey

Gule Aydin[1], Zerrin Asci[1]

Afyonkarahisar Zubeyde Hanim Obstetrics % gyneacology and Pediatrics Hospital Clinical Microbiology and Infectious Diseases Afyonkarahisar-Turkey[1]

Introduction: This questionaire was designed to investigate the knowledge awareness of obstetrics & gynaecology and pediatrics hospital staff on the prevention of mother-to-child transmission (PMTCT) of hepatitis B virus (HBV).

Method: 30 male, 90 female totally 120 healthcare workers, aged between 22-60 years (the mean age was 37,8), were invited to complete a questionnaire regarding PMTCT of HBV. A self administered questionnaire, included the clinical implications of HBV serologic markers and PMTCT preventive measures for both pregnant women and infants, was applied to the healthcare workers who accepted to fill out.

Results: Overall, 90 % of participants correctly determined the positive hepatitis B surface antigen (HBsAg) as infectious, but up to 45 % mistakenly considered the presence of anti-HBe and/or anti-HBc with negative HBsAg as infectious. In total, 70 % respondents knew that pregnant women should be screened for HBV infection, and 75 % realized that infants of HBsAg-positive mothers should be injected with hepatitis B immunoglobulin and vaccine. On the other hand, with the available immunoprophylaxis, 35 % participants mistakenly believed caesarean section may prevent HBV mother-to-child transmission, and only 13 % correctly answered that newborns of HBsAg positive mothers may be breastfed.

Conclusion: In conclusion, all healthcare workers must be educated about the diagnosis and management of hepatitis virus B infection during pregnancy. Their knowledge is reinforcing the need of continuous medical education programs.

Topic 11: Hepatitis B

No: 2035

Comparing efficacy of tenofovir monotherapy and tenofovir based combination therapy in antiviral drug resistance chronic hepatitis B patients

Kyu Sik Jung[1], Beom Kyung Kim[1], Ki Tae Yoon[2], Young Seok Kim[3], Seung Up Kim[1], Jun Yong Park[1], Do Young Kim[1], Kwang-hyub Han[1], Sang Hoon Ahn[1]

Yonsei University College of Medicine Department of Internal Medicine Seoul-Korea, South[1], Pusan National University School of Medicine Department of Internal Medicine Yangsan-Korea, South[2], Soonchunhyang University College of Medicine Department of Internal Medicine Cheonan-Korea, South[3]

Background: We aimed to compare clinical efficacy between tenofovir (TDF) monotherapy versus TDF-based combination therapy as rescue therapy for chronic hepatitis B with resistance to antiviral agents.

Methods: A total of 434 consecutive CHB patients treated with TDF monotherapy or TDF-based combination therapy (TDF plus entecavir, lamivudine or telbivudine) as rescue therapy for resistance to antiviral agents were analyzed. Complete virological response (CVR) and biochemical response were defined as undetectable HBV-DNA

(detection limit 20 IU/mL) and normalization of alanine aminotransferase level, respectively. Cumulative incidence rates of CVR was assessed using Kaplan–meier method.
Results: At the time of rescue therapy, the median HBV DNA and ALT level were 3.52 log IU/mL and 28 IU/mL. During follow-up (median 17.1 month), cumulative incidence rates of CVR at 18 months did not differ between patients with TDF monotherapy and those with TDF-based combination therapy (94.9 vs. 92.6 %) among patients with only lamivudine resistance (n = 235). Similar results were maintained (90.5 vs. 89.0 %) among patients with multidrug-resistant CHB (n = 199; lamivudine + entecavir [n = 88], lamivudine + adefovir [n = 77], and lamivudine + adefovir + entecavir [n = 34])(both $p > 0.05$). In a subgroup analysis of 385 patients with at least 12 months of rescue therapy, there were no significant differences of CVR (95.7 vs. 93.9 %, $P = 0.570$) and biochemical response (85.8 vs. 84.0 %, $P = 0.627$) between patients with TDF monotherapy and those with TDF-based combination therapy.
Conclusions: TDF monotherapy revealed similar efficacy compared with TDF-based combination therapy as rescue therapy in CHB with resistance to antiviral agents, including multidrug-resistant strains. Further studies with longer follow-up duration are required to validate these results.

Topic 11: Hepatitis B

No: 1596

Predictors of fatigue in chronic hepatitis B patients

Sang Bong Ahn[1], Jun Bong Kim[1], Tae Kyun Kim[1], Young Kwan Jo[1], Byoung Kwan Son[1], Yun Ju Jo[1], Seong Hwan Kim[1], Young Sook Park[1], Dong Hee Koh[2]

Eulji University College of Medicine Gastroenterology Seoul-Korea, South[1], Hallym University College of Medicine Gastroenterology Dongtan-Korea, South[2]

Background: Fatigue is an important determinant of quality of life in patients with chronic hepatitis B. The aim of the present study was to assess the extent to fatigue symptoms and predictors of fatigue in chronic hepatitis B.
Methods: We evaluated clinical characteristics including sex, age and laboratory findings from 120 chronic hepatitis B patients. Fatigue was evaluated using questionnaire of Brief Fatigue Inventory, Multidimensional Fatigue Scale and critical flicker frequency.
Results: Forty-five patients (37.5 %) patients complain the severe degree of fatigue. Presence of cirrhosis ($P = 0.02$), total bilirubin ($P = 0.01$) and platelet count ($P = 0.05$) is associated with Brief Fatigue Inventory score. Age is associated with fatigue score ($P = 0.003$) and critical ficker frequency ($P = 0.001$). Multidimensional Fatigue Scale score is associated with critical flicker frequency.
Conclusion: In patients with chronic hepatitis B, age, cirrhosis, bilirubin, platelet count and critical flicker frequency were associated fatigue symptoms.

Topic 11: Hepatitis B

No: 2184

Severe hepatic flare and HBeAg seroreversion in two patients with HBeAg positive chronic hepatitis B developing after discontinuation of oral antiviral therapy one year after hbeag seroconversion

Ayse Batirel[1], Sabahat Aktas[1], Yasemin Zeytin[1], Serdar Ozer[1]

Kartal Dr.lutfi Kirdar Training and Research Hospital Infectious Diseases and Clinical Microbiology Istanbul-Turkey[1]

Aim: According to EASL 2012 and APASL 2012 guidelines, the recommended treatment end-point for HBeAg-positive chronic hepatitis B (CHB) patients is 12 more months after sustained HBeAg-seroconversion is achieved. In AASLD 2012 guideline, continuation of antiviral therapy at least 6 months after HBeAg-seroconversion and undetectable HBV-DNA levels are achieved in those patients, but close-monitorization for relapse/flare after cessation of therapy are recommended. We aimed to present two HBeAg-positive CHB patients with severe hepatic flares whose antiviral therapy with entecavir were stopped 12 months after HBeAg-seroconversion.
Patients & methods: HBeAg-positive CHB patients who achieved HBeAg-seroconversion and continued to receive antiviral therapy for 12 more months, and who had hepatic flare after cessation of therapy were included.
Results: A total of 52 HBeAg-positive CHB patients were under follow-up in our viral hepatitis polyclinic for a median duration of 18 months. Only two (4 %) patients had HBeAg-seroconversion during entecavir therapy. Oral antiviral therapy with entecavir was continued for 12 more months after HBeAg-seroconversion. As serum HBV-DNA levels remained undetectable during this period and the patients didn't want to continue therapy lifelong, antiviral therapies were discontinued according to guideline recommendations. They were closely followed-up at 3-month intervals after cessation of therapy. Both of them experienced a hepatic flare and HBeAg-seroreversion. Treatment was restarted. Demographic, laboratory and treatment data of the patients are summarized in Table 1.
Conclusion: The patients whose antiviral therapy are discontinued after HBeAg-seroconversion should be closely monitorized for hepatic flares. Lifelong therapy may be reasonable in such HBeAg-positive CHB patients similar to HBeAg-negative ones in order to avoid hepatic flares.

Topic 11: Hepatitis B

No: 1672

Entecavir and tenofovir treatment in cirrhosis due to hepatitis B

Fatma Ebru Akın[1], Aylin Demirezer Bolat[1], Öykü Tayfur Yürekli[1], Mustafa Tahtacı[1], Eyüp Selvi[1], Naciye Şemnur Büyükaşık[1], Osman Ersoy[2]

Atatürk Education and Research Hospitol Gastroenterology Ankara-Turkey[1], Yıldırım Beyazıt University Medical School Gastroenterology Ankara-Turkey[2]

Aim: We present our treatment results of cirrhotic patients with entecavir or tenofovir.
Material-methods: Patients diagnosed with cirrhosis due to hepatitis B between 2009 and 2013 and received at least 1 year of entecavir or tenofovir are included in this analysis. Liver and kidney function tests, AFP levels, blood counts, anti HBs and anti HBe status, HBV DNA levels were evaluated at the beginning and at 3-6-12 th months and at the last visit. Patients' MELD and Child-Pugh scores were calculated both at the beginning of the treatment and the last visit. Patients were evaluated in terms of cirrhosis decompansation, complications and side effects.

Results: 24 patients (18 male) were included in this retrospective analysis.18 patients were receiving tenofovir while 6 were receiving entecavir. Patients' demographic data and lab. Results at the beginning of the treatment are shown in table-1. 22 were antiviral näive. Mean follow-up was 27 ± 14 months. HBV DNA decreased below 300 copy/ml in 88.9 % of tenofovir and 83.3 % of entecavir treated patients. ALT normalization could be achieved in 94.4 % of tenofovir treated and 100 % of entecavir treated patients. Increase in Child-Pugh score had been noted only in one patient in tenofovir group. Increase in MELD score in 16.7 % of both entecavir and tenofovir treated patients. One patient both from entecavir and tenofovir treatment groups had developed HCC in 12th month of the treatment. Complication rates were similar between the groups.

Tenofovir and entecavir treatment can be considered safe and effective in patients with cirrhosis due to Hepatitis B.

Topic 11: Hepatitis B

No: 1038

Epidemiological characteristics of people living with human immunodeficiency virus co infected with hepatitis B virus in an infectious diseases unit an overview

Nassima Belabas[1], Mohamed Zeroual[1], Naima Ihaddadene[1], Abdelouhab Dif[1]

Laadi Flici (el-kettar) Hospital Department of Infectious Diseases Algiers-Algeria[1]

Objective: To describe the epidemiological characteristics of people with a positive HIV status and carriage of HBsAg in our unit.
Materials and methods: Retrospective study compiling patients monitored and treated for HIV-HBV co-infection in an infectious diseases unit on a ten-year period (January 2004 - May 2014). The socio-demographic characteristics and the main modes of transmission were identified through a review of medical records.
Results: Among the 477 people living with HIV (PLH), we collected 07 patients with HIV-HBV co-infection (01.46 %). We noted two cases of HIV-HBV- Hepatitis C Virus (HCV) co-infection (28.5 %). They were 07 men with a mean age of 40 years (26-47 years). (57.1 %) patients were sub-Saharan African and (28.6 %) patients of Algerian nationality. (71.4 %) patients were married and (57.1 %) were unemployed. Modes of transmission were: multiple sexual partners in (71.4 %), homosexuality in (14.3 %). The mode of contamination has not been detected in (14.3 %). The discovery of HBV seropositivity was made along with a positive HIV test in (71.4 %) ordered for clinical signs of HIV infection, as part of a family screening (14.3 %) or premarital balance in one case (14.3 %).
Conclusion: The prevalence of HIV-HBV co-infection (01.46 %) is below that reported in HIV-HCV co-infection in the same unit (04.6 %). The diagnosis of these sexually transmitted infections (STIs) is made at an advanced stage of the disease so it is important to intensify the actions of their screening.

Topic 11: Hepatitis B

No: 1249

Comparison of histopathological fibrosis stage with fibroscan findings in chronic hepatitis B

Ibrahim Hatemi[1], Nurhan Demir[1], Kadri Atay[1], Ayşe Merve Çelik[1], Selver Işık[1], Nuray Kepil[2], Sibel Çetin[2], Sebati Özdemir[1], Abdullah Sonsuz[1]

Istanbul University, Cerrahpaşa Faculty of Medicine Department of Internal Medicine, Division of Gastroenterology Istanbul-Turkey[1], Istanbul University, Cerrahpaşa Faculty of Medicine Department of Pathology Istanbul-Turkey[2]

Aim: In Turkey health insurance system reimbursement of chronic hepatitis B treatment is limited. Beneath the virological and biochemical activity histopathological activity also should be proven defined as fibrosis level ≥ 2 and histological activity index (HAI) ≥ 6. As a result biopsy is required in all chronic hepatitis B patients before treatment. If it would be possible to prove the fibrosis stage by a non-invasive method, biopsy would not be necessary. The aim of this study is to investigate the capacity of fibroscan to differentiate the patients with histopathological fibrosis stage 0–1 and ≥ 2.
Methods: Fibroscan investigation is done in 24 chronic hepatitis B patients by the same investigator. For each patient at least 10 appropriate measurements are done. Histological fibrosis score was categorized by modified Ishak score.
Results: The mean age was 39.5(range 19–56) in 16 male and 5 female patients. E(kPa) levels are shown in the table. Fibrosis stage and liver stiffness were correlated (Pearson 0.002), There was no correlation between the stiffness (E) and HAI. There was no difference between the groups with fibrosis stage 1 and 2.
Conclusion: Fibrosis stage and liver stiffness measured by fibroscan are correlated. The median E level is 6.6 in patients with a fibrosis stage less than 2. There is no difference in E level in patients with the stage 0–1 and stage 2.

Topic 11: Hepatitis B

No: 1255

Efficacy of entecavir and telbivudine in hbeag positive chronic hepatitis B patients

Mingxing Huang[1], Zongping Han[2]

The Fifht Affiliated Hospital of Sun Yat-sen University Department of Infectious Disease Zhuhai-China[1], The Fifht Affiliated Hospital of Sun Yat-sen University Department of Geriatrics Zhuhai-China[2]

Objective: To analyze the efficacy of entecavir and telbivudine on HBeAg positive chronic hepatitis B (CHB) in China.
Methods: A total of 259 patients with HBeAg positive CHB who completed 72 weeks of entecavir (group ETV, ETV 0.5 mg once per day, 161 cases) and telbivudine (group LDT, LDT 600 mg once per day, 98 cases) monotherapy were prospectively studied. The biochemical response rate, complete virological response rate and serologic response rate in the two groups were observed after treatment at 4,12, 24, 48 and 72 weeks.
Results: The biochemical response rate had no significant differences between the two groups at 4, 12, 24, 48 and 72 weeks (all $P > 0.05$). The levels of HBV-DNA in the two groups were significantly lower at 4th week and were much lower in group ETV than that in group LDT after 24 weeks (all $P < 0.05$). However, the complete virological and serologic response rates showed no significant differences between the two group at different weeks (all $P > 0.05$).
Conclusions: ETV monotherapy was more potent and faster in HBV DNA suppression in NAs naive patients with HBeAg positive.

Topic 11: Hepatitis B

No: 1358

Multicenter observational study of reactivation of hepatitis B virus caused by chemotherapy with sorafenib

Junji Furuse[1], Masafumi Ikeda[2], Shunsuke Kondo[3], Masatoshi Kudo[4], Seijin Nadano[5], Yukio Osaki[6], Takashi Kumada[7], Kazuyoshi Ohkawa[8], Masashi Mizokami[9]

Kyorin University School of Medicine Medical Oncology Mitaka-Japan[1], National Cancer Center Hospital East Hepatobiliary and Pancreatic Oncology Kashiwa-Japan[2], National Cancer Center Hospital Hepatobiliary and Pancreatic Oncology Tokyo-Japan[3], Kinki University School of Medicine Gastroenterology and Hepatology Osaka-Japan[4], National Hospital Organization Shikoku Cancer Center Gastroenterology Matsuyama-Japan[5], Osaka Red Cross Hospital Gastroenterology Osaka-Japan[6], Ogaki Municipal Hospital Gastroenterology Ogaki-Japan[7], Osaka Medical Center For Cancer and Cardiovascular Diseases Hepatobiliary and Pancreatic Oncology Osaka-Japan[8], National Center For Global Health and Medicine The Research Center For Hepatitis and Immunology Ichikawa-Japan[9]

Aim: Sorafenib chemotherapy is reported to be associated with a high frequency of liver dysfunction, and it has been suggested that the liver dysfunction might have an influence on the risk of reactivation of hepatitis B virus (HBV). The aim of this prospective study was to investigate the incidence of HBV reactivation among patients receiving chemotherapy with sorafenib and the clinical outcomes of these patients.
Methods: The patients were seropositive for HBsAg [sAg(+)] or seronegative for HBsAg and seropositive for HBcAb and/or HBsAb [c/sAb(+)] were enrolled in this study. HBV DNA was measured monthly until 12 months after the completion of sorafenib treatment. HBV reactivation was defined as a tenfold or greater increase of the HBV DNA titer.
Results: A total of 52 patients [sAg(+), 29; c/sAb(+), 23] were enrolled, including 50 with hepatocellular carcinoma and 2 with renal cell carcinoma. Among the 29 sAg(+) patients, HBV reactivation occurred in 10 patients (34.5 %), although the HBV DNA level was restored to the baseline level without any treatments in all patients. Among the 23 c/sAb(+) patients, HBV reactivation occurred in 2 patients (8.7 %); one of these two patients showed return of the viral DNA titers to the baseline level without any antiviral therapy. None of the patients in this series showed elevation of the serum transaminase levels or any signs of fulminant hepatitis.
Conclusion: The incidence of HBV reactivation during chemotherapy with sorafenib was not too high, and none of the patients in this study developed clinically significant HBV reactivation.

Topic 11: Hepatitis B

No: 1758

Prediction of significant fibrosis and necroinflammation via non invasive fibrosis markers among a specific patient population with chronic hepatitis B

Ismail Hakkı Kalkan[1], Ferdane Sapmaz[1], Sedat Kaygusuz[2], Serdar Gül[2], Pınar Atasoy[3], Sefa Güliter[1]

Kırıkkale University Faculty of Medicine Gastroenterology Kırıkkale-Turkey[1], Kırıkkale University Faculty of Medicine Infectious Disease Kırıkkale-Turkey[2], Kırıkkale University Faculty of Medicine Pathology Kırıkkale-Turkey[3]

Introduction: We aimed in our study to investigate the predictive ability of non-invasive markers of hepatic fibrosis as potential alternatives to liver biopsy in a specific chronic hepatitis B (CHB) patient group in whom liver biopsy is recommended for treatment decision.
Material & methods: The medical records of 123 patients with a diagnosis of HBeAG (-) CHB who have ALT < 1-2xULN and HBV-DNA between 2000 and 20000 IU/ml and underwent a liver biopsy. Non-invasive fibrosis markers (AST-platelet ratio index (APRI), FIB-4) were calculated for each patient based on previously described formulas. Diagnostic adequacy of these indices for significant fibrosis and histological activity index (HAI) was evaluated by receiver operating characteristic curve analysis (ROC).
Results: APRI and FIB-4 were correlated with significant fibrosis ($r = 0.297$, $P = 0.001$ and $r = 0.274$, $P = 0.002$, respectively) and significant HAI ($r = 0.217$, $P = 0.01$ and $r = 0.275$, $P = 0.002$, respectively). Further analysis with ROC showed that AUROCs for predicting significant fibrosis and HAI were 0.729 ($P < 0.001$) and 0.714 ($P < 0.001$) for APRI while they were 0.693 ($P = 0.001$) and 0.690 ($P < 0.001$) for FIB-4. Comparison of ROC curves didn't show statistically meaningful difference between APRI and FIB-4 in the terms of predicting of significant fibrosis ($P = 0.3$) or significant HAI ($P = 0.4$).
Conclusion: Our results suggest that APRI and FIB-4 may be beneficial to predict significant liver fibrosis and HAI in CHB patients, and potentially reduce the requirement of liver biopsies.

Topic 11: Hepatitis B

No: 2026

Accumulation of platelets in the liver may be an important contributory factor to liver injury in chronic hepatitis B virus infection

R. Huang[1], H.Y. Wu[2], R. Su[3], G.Y. Wang[4], Y. Liu[5], X.M. Yan[4], Y.L. Xiong[4], J. Xia[4], C. Wu[4]

Nanjing Drum Tower Hospital Clinical College of Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine Department of Infectious Diseases Nanjing-China[1], Nanjing Drum Tower Hospital, Nanjing University Medical School Department of Pathology Nanjing-China[2], Nanjing Drum Tower Hospital, Nanjing Medical University Department of Infectious Diseases Nanjing-China[3], Nanjing Drum Tower Hospital, Nanjing University Medical School Department of Infectious Diseases Nanjing-China[4], Nanjing Drum Tower Hospital, Nanjing University Medical School Department of Laboratory Medicine Nanjing-China[5]

Aims: To clarify whether an accumulation of platelets in the liver contributes to liver injury and fibrosis in chronic hepatitis B virus (HBV) infection.
Methods: Fifty liver tissue samples were obtained from patients with chronic HBV infection. Seventeen healthy liver tissue samples were included as control. The platelets (marked by CD61) and nonspecific inflammatory cells (CD68 + macrophages and monocytes) in the liver tissues were identified by immunohistochemistry. The degrees of hepatic inflammation and fibrosis of liver fibrosis were graded using the modified histology activity index described by Scheuer.
Results: Patients with chronic HBV infection had a significantly more extensive CD61 + platelets in the liver tissues compared to healthy controls ($P < 0.001$). Patients with chronic HBV infection with higher inflammatory grading (G) scores had more CD61 + platelets in their livers compared to those with lower scores ($P < 0.05$). However, no

association between liver platelets and fibrotic staging (S) scores was found in the patients ($P > 0.05$). The platelets in the liver tissues were strongly positively correlated with the nonspecific inflammatory cells such as CD68 + macrophages ($r = 0.625$, $P < 0.0001$) and MAC387 + monocytes ($r = 0.780$, $P < 0.0001$). The platelets in the liver tissues of patients with chronic HBV infection were also positively correlated with alanine transaminase ($r = 0.325$, $P = 0.023$) and total bilirubin levels ($r = 0.292$, $P = 0.042$).
Conclusions: The accumulation of platelets in the liver may be involved in hepatic injury of chronic HBV infection. Platelets may take part in the pathogenesis of the liver injury in chronic HBV infection through the mechanism involving the nonspecific inflammatory cells such as macrophages and monocytes.

Topic 11: Hepatitis B

No: 1069

Tenofovir therapy in chronic hepatitis b patients who failed previous nucleoside analogues treatment

Kozielewicz Dorota[1], Halota Waldemar[1]

Collegium Medicum Nicolaus Copernicus University Department of Infectious Diseases and Hepatology Bydgoszcz-Poland[1]

Aim: Tenofovir (TDF) is considered as the first line therapy in chronic HBV patients regardless of their HBeAg status. The study presents the results of TDF treatment in patients who failed previous nucleoside analogues antiviral therapy.
Material: 29 patients (21 male) aged 20–81 years were included into the study. Mean ALT activity was 60 U/l. All patients had fibrosis confirmed by liver biopsy and HBV DNA load between 102 and 107 IU/ml. 15 patients were HBeAg-positive. Previously 15 subjects received lamivudine monotherapy (LAM arm) and 14 patients lamivudine and then entecavir (LAM → ETV arm) treatment. All patients received 12 months TDF treatment. HBV DNA clearance at month 3,6,12 was the primary endpoint in the study while anti-HBe seroconversion and ALT normalisation were secondary endpoints.
Results: At month 3 of the TDF therapy all patients had at least 1log10 reduction of HBV DNA concentration. After 3, 6 and 12 months of therapy, HBV DNA was undetectable in 60, 73 and 73 % of LAM arm and 14, 42 and 60 % of LAM → ETV arm patients, respectively. None of patients in both groups achieved anti-HBe seroconversion. ALT activity decreased from 71 at baseline to 28 U/l at month 12 in LAM arm and from 50 to 18 U/l in LAM → ETV arm, respectively.
Conclusions: HBV DNA clearance in patients treated with TDF occurred faster in those with previous exposure to lamivudine monotherapy than in those exposed to combined lamivudine and entecavir treatment, but finally the rates of HBV DNA negative patients and ALT activity in both groups were similar.

Topic 11: Hepatitis B

No: 1041

Profile of infected consultants by hepatitis B virus and hepatitis C virus experience a free testing center

Nassima Belabas[1], Achour Amrane[1], Mohamed Zeroual[1], Xavier De La Tribonniere[2], Fatma Zohra Aissat[1], Abdelouhab Dif[1]

Laadi Flici (el-kettar) Hospital Department of Infectious Diseases Algiers-Algeria[1], Montpellier Hospital Patient Education Unit Montpellier-France[2]

Objective: To determine the epidemiological characteristics of the population using the detection of hepatitis B virus (HBV) and hepatitis B virus (HCV) and those with seropositivity to HBV or HCV, and the prevalence of infection with HBV or HCV in a free Testing Center (FTC) for human immunodeficiency virus (HIV) infection, viral hepatitis B and C, and syphilis.
Patients and methods: We conducted a descriptive study at our FTC. The variables considered were: socio-demographic characteristics of consultants, risk behaviors, patterns of use of tests for HBV and HCV, seroprevalence of the 02 virus.
Results: (29 117) people were screened between 2002 and 2013. The age of consultants was between 25 and 49 years (64.4 %) with a sex ratio (1.63). (57.7 %) were single and consultants (60.4 %) without occupation. The reason for testing was part of a health check (36.5 %), premarital check-up (26.1 %), a risk situation (17.9 %) or following a voluntary approach for no apparent reason (19.5 %). The prevalence of HBsAg and anti-HCV antibodies increased respectively (3.98 %) and (1.32 %) in 2002 (3.04 %) and (1.07 %) in 2013 on 12 years, the overall positivity rates were respectively (2.78 %) and (1.32 %). In 2013 (77 %) of those tested got their results back. (70 %) consultants have benefited from counselling. Co-infection with HIV was noted in (0.14 %) [(03) HIV-HCV co-infection, (02) HIV-HBV co-infected and (01) HIV-HBV-HCV-syphilis co-infection) .
Conclusion: The activity of our FTC was stable between 2006 and 2012 tended to increase since 2013 reflecting increased vigilance of the population to these infections.

Topic 11: Hepatitis B

No: 1356

Multicenter observational study of reactivation of hepatitis B virus caused by chemotherapy for solid tumors

Junji Furuse[1], Masafumi Ikeda[2], Shunsuke Kondo[3], Masatoshi Kudo[4], Seijin Nadano[5], Yukio Osaki[6], Takashi Kumada[7], Kazuyoshi Ohkawa[8], Masashi Mizokami[9]

Kyorin University School of Medicine Medical Oncology Mitaka-Japan[1], National Cancer Center Hospital East Hepatobiliary and Pancreatic Oncology Kashiwa-Japan[2], National Cancer Center Hospital Hepatobiliary and Pancreatic Oncology Mitaka-Japan[3], Kinki University School of Medicine Gastroenterology and Hepatology Osaka-Japan[4], National Hospital Organization Shikoku Cancer Center Gastroenterology Matsuyama-Japan[5], Osaka Red Cross Hospital Gastroenterology Osaka-Japan[6], Ogaki Municipal Hospital Gastroenterology Ogaki-Japan[7], Osaka Medical Center For Cancer and Cardiovascular Diseases Hepatobiliary and Pancreatic Oncology Osaka-Japan[8], National Center For Global Health and Medicine The Research Center For Hepatitis and Immunology Ichikawa-Japan[9]

Aim: The aim of this prospective study was to investigate the incidence of reactivation of hepatitis B virus (HBV) among patients with solid tumors (ST) receiving first-line chemotherapy and the clinical outcomes of these patients.
Methods: The patients with ST receiving first-line chemotherapy who were seropositive for HBsAg [sAg(+)] or seronegative for HBsAg and seropositive for HBcAb and/or HBsAb [c/sAb(+)] were enrolled in this study. HBV DNA was measured at the commencement of the first-line chemotherapy, and at least 3, 6 and 12 months after

completion of the first-line chemotherapy. HBV reactivation was defined as a tenfold or greater increase of the HBV DNA titer.
Results: A total of 379 patients [sAg(+), 35; c/sAb(+), 344] were enrolled in this study. The median period of measurement of HBV DNA was 79 days (range, 5-379 days). Among the 35 sAg(+) patients, HBV reactivation occurred in 10 patients (28.6 %). Among the 344 c/sAb(+) patients, HBV reactivation occurred in 7 patients (2.0 %). Four of the seven patients of the c/sAb(+) group showed return of the viral DNA titers to the baseline level without any antiviral therapy. None of the patients in this series showed elevation of the serum transaminase levels or any signs of fulminant hepatitis.
Conclusion: The incidence of HBV reactivation in ST patients who were was rather low, and none of these patients enrolled in this study developed clinically significant HBV reactivation, presumably as a result of periodic measurement of the HBV DNA titer and prompt and appropriate management of HBV reactivation.

Topic 11: Hepatitis B

No: 1187

Predictive factors of sustained remission after discontinuing antiviral therapy in patients with HBeAg positive chronic hepatitis B multi center experience

Baek Gyu Jun[1], Sae Hwan Lee[1], Hong Soo Kim[1], Sang Gyune Kim[2], Young Seok Kim[2], Boo Sung Kim[2], Soung Won Jeong[3], Jae Young Jang[3], Young Don Kim[4], Gab Jin Cheon[4]

Soonchunhyang University College of Medicine, Cheonan Hospital Department of Internal Medicine Cheonan-Korea, South[1], Soonchunhyang University College of Medicine, Bucheon Hospital Department of Internal Medicine Bucheon-Korea, South[2], Soonchunhyang University College of Medicine, Seoul Hospital Department of Internal Medicine Seoul-Korea, South[3], University of Ulsan College of Medicine Department of Internal Medicine Gangneung-Korea, South[4]

Background/aim: Optimal timing of oral antiviral therapy cessation in patients with HBeAg-positive chronic hepatitis B is controversial. The aim of this study was to identify factors to predict virological relapse after stopping antiviral therapy in patients with HBeAg positive chronic hepatitis B.
Methods: Medical records of 56 patients with HBeAg-positive who discontinued antiviral therapy (24 entecavir, 23 lamivudine, and 9 adefovir with lamivudine) were analyzed retrospectively. Virological relapse was defined as an increase in serum HBV DNA to $>$ 2000 IU/ml. Biochemical relapse was defined as a rise of alanine aminotransferase (ALT) $>$ 80 IU/ml. Predictive factor was assessed using time to event analysis.
Results: Between sustained remission group and virologic relapse group, there was no difference in median baseline HBV DNA level ($P = 0.297$), baseline ALT ($P = 0.083$), median duration of sera-negative ($P = 0.146$), or consolidation therapy ($P = 0.211$). Time to first undetectable HBV DNA during treatment was shorter in sustained response group compared to relapse group (5.7 $\pm$ 4.4 months vs. 13.4 $\pm$ 13.5 months, $P = 0.012$). Cumulative relapse rates at 3, 6, 12, and 18 months were 12.5, 30.4, 43.2, and 49.3 %, respectively. Seventeen (30 %) patients who experienced virologic relapse resumed antiviral drugs. Consolidation period ($>$ 18 months, $P = 0.020$) and virological response (HBV DNA $<$20 IU/mL) at 6 months during antiviral therapy ($P = 0.017$) were significant predictors for virologic relapse in multivariate analysis.
Conclusions: Consolidation time more than 18 months and virologic response at 6 months during antiviral therapy were associated with sustained remission in patients with HBeAg positive chronic hepatitis B after stopping antiviral therapy.

Topic 11: Hepatitis B

No: 1799

PEG interferon a 2A upregulates CD74 expression in patients with chronic hepatitis B

Wenting Li[1]

Anhui Provincial Hospital Infectious Disease Hefei-China[1]

Aim: To investigate the molecular mechanism involved in the anti-HBV effect of Peg-interferon a-2a.
Methods: 52 HBV-infected patients treated with Peginterferona-2a for at least 1 year were enrolled in this study. Blood samples were collected at the time of initiation of Peg-interferon a-2a, 6 month and 12 month of treatment. 20 HBV carriers were included as control. The mRNA and protein expression of CD74 in monocytes from the blood sample were evaluated by RT-PCR and western-blot, respectively.
Results: the patients who reached a viral response at 12 month of treatment showed high levels of CD74 compared with HBV carriers and patients did not respond to Peg-interferon a-2a ($P < 0.05$, respectively). Surprisingly, there was no significant difference in the mRNA and protein expression of CD74 between patients did not respond to Peg-interferon a-2a at 6 month of treatment and HBV carriers, while prolonged Peg-interferon a-2a treatment enhanced the expression of CD74 in these patients only when they reached a viral response at 12 month of treatment (Fig. 1).
Conclusions: The antiviral efficacy of Peg-interferon a-2a may be related to its effects of up-regulation of CD74.

Topic 11: Hepatitis B

No: 1990

Distribution of subjects with acute viral hepatitis in adult age group

Selma Tosun[1], Ebru Dik[1], Meltem Avcı[1], Irem Altas[1]

Izmir Bozyaka Research and Education Hospital Infectious Diseases Izmir-Turkey[1]

Aim: The aim of this study is to evaluate the acute viral hepatitis subjects admitted to hospitals in the last decade.
Method: The evaluation has been made through the current documents of acute viral hepatitis subjects from in and out-patients admitted to the Hospital between 2003 and 2013.
Results: It has been observed that 369 subjects were diagnosed by acute viral hepatitis. Of these subjects, 123 of them (33.3 %) had acute HAV infection, while 228 of them (61.2 %) had acute HBV infection; and 19 of them (5 %) were undiagnosed. Considering their distribution according to age, it was defined that acute HAV infection was mostly observed in 21–25 and the HBV infection was observed in 26–40 age groups. It was also determined that in most of the acute HBV cases, there was a suspicious intercourse or another family member with HBsAg positive. Among the followed up subjects, there was no death due to hepatitis or a complication due to HBV.
Conclusion: When the data were evaluated, it was determined that HBV infection still sustains its importance for adults and contact through index subject (intercourse and horizontal contact) is of importance in terms of transmission. Since adult HBV vaccination is not sufficient in our country, there are still subjects with acute HBV. It has been observed that acute HAV subjects accounts for half of the acute viral hepatitis subjects, and they are mostly found in the group of young adults.

Topic 11: Hepatitis B

No: 1110

IL 21 promotes hepatitis B virus antigen specific CD8 + cytotoxic t lymphocytes response in chronic hepatitis B patients

Jie Li[1], Wanhua Ren[1], Jiao Zhang[1], Guoqing Han[1], Zhi Chen[2]

Shandong Provincial Hospital Affiliated To Shandong University Department of Infectious Disease Ji'nan-China[1], The First Affiliated Hospital, School of Medicine, Zhejiang University State Key Laboratory For Diagnosis and Treatment of Infectious Diseases Hanhzhou-China[2]

IL-21 has been demonstrated to play a pivotal role in controlling chronic viral infections. However, little is known about the regulation role of IL-21 on CD8 + cytotoxic T lymphocytes (CTL) in HBV infections. In the present study, serum IL-21 level in chronic hepatitis B (CHB) patients with various disease statues and healthy subjects, as well as the potential association between IL-21 and major clinic indexes were examined. Peripheral blood mononuclear cells (PBMC) isolated from CHB patients were simulated with anti-IL-21 antibody or recombinant IL-21, respectively. The frequency of hepatitis B core antigen (HBcAg)-specific IL-21-secreting CD4 + T cells and CD8 + cytotoxic T lymphocytes were characterized by flow cytometric. Our data indicated that serum IL-21 level was significantly higher in CHB patients than in healthy controls and chronic asymptomatic HBV carrier and increased serum IL-21 concentration was positively associated with serum HBV DNA and HBeAg load. Also, exogenous IL-21 increased the HBcAg-stimulated activation of CTL while anti-IL-21 antibody significantly decreased the frequency of CTL in CHB patients. Our findings imply that IL-21 has a direct functional impact on HBV antigen specific IFN-γ+CD8 + T cells in chronic HBV infections.

Topic 11: Hepatitis B

No: 1510

Impact of nucleos(t)ide analogues treatment and intrahepatic viral loads on the post operative recurrence among patients with hepatitis B virus related hepatocellular carcinoma

Tetsuya Hosaka[1], Fumitaka Suzuki[1], Masahiro Kobayashi[1], Yushin Sorin[1], Taito Fukushima[1], Yusuke Kawamura[1], Hitomi Sezaki[1], Norio Akuta[1], Yoshiyuki Suzuki[1], Satoshi Saitoh[1], Yasuji Arase[1], Kenji Ikeda[1], Mariko Kobayashi[2], Hiromitsu Kumada[1]

Toranomon Hospital Hepatology Tokyo-Japan[1], Toranomon Hospital Research Institute for Hepatology Tokyo-Japan[2]

Aim: The aim of this study is to compare hepatocellular carcinoma (HCC) recurrence after curative treatment with or without nucleos(t)ide analogues (NUCs) treatment in terms of intrahepatic hepatitis B virus (HBV) viral loads.
Methods: We conducted a retrospective cohort study of 307 patients who underwent surgical resection or local ablation for primary HCC. We categorized these patients into three groups as following; group A (n = 68) consisted of patients who received NUCs after HCC treatment, group B (n = 103) of NUCs before and after HCC treatment, and control (n = 136) of no antiviral treatment. Moreover, patients in group B were dichotomized into two subgroup by serum preoperative hepatitis B core-related antigen (HBcrAg) levels (group B-high HBcrAg, or group B-low HBcrAg) because HBcrAg was a surrogate marker of intrahepatic covalently closed circular DNA pools.
Results: Cumulative recurrence-free survival rates (RFS) were higher in group A and B than control (group A vs. control: $P = 0.005$). There was no difference in RFS between group A and B. Divided group B into two subgroup as described above, cumulative RFS were significantly higher in patients of group A or group B-low HBcrAg than control (group B-low HBcrAg vs. control: $P < 0.001$). RFS in group B-high HBcrAg was similar to control. Multivariate Cox model showed that predictive factors of HCC recurrence were multi-nodules, Child-Pugh B cirrhosis, hepatitis B e antigen positivity, and NUCs treatment (group A and group B-low HBcrAg).
Conclusion: Patients with high HBcrAg levels were likely to develop HCC recurrence after curative treatment in spite of continuing NUCs treatment before primary HCC.

Topic 11: Hepatitis B

No: 1651

Efficacy of peg interferon in treatment experienced patients with chronic hepatitis B

Yue-li Xiong[1], Peng Hu[1], Hong Ren[1]

Institute For Viral Hepatitis, Department of Infectious Diseases, The Second Affiliated Hospital of Chongqing Medical University Chongqing-China[1]

Background and aim: High prevalence of relapse after treatment cessation was reported in chronic hepatitis B patients in China, especially in nucleot(s)ide analogues (NUCs)-experienced patients. Retreatment for these patients remains unsolved. The aim of this study was to evaluate the efficacy of Peg-interferon in these patients.
Methods: 55 treatment-experienced and HBeAg positive patients were enrolled in this study (31 NUCs-experienced patients, 18 interferon-experienced patients and 6 combination-experienced patients). 34 patients received Peg-interferon and 21 were retreated with interferon.
Results: In all patients who received Peg-interferon, 52.9 % (18/34) treatment-experienced patients achieved virological response, 35.3 % achieved HBeAg loss and 32.3 % developed anti-HBe. Further analysis showed that patients with Peg-interferon for 48 weeks achieved higher virological response (80 %), HBeAg loss (50 %), HBeAg seroconversion (45 %) and HBsAg loss (5 %) than those of patients with Peg-interferon for less than 48 weeks (14.3, 14.3, 14.3 % and 0 respectively), and also than those of patients with interferon (42.9, 42.9, 38.1 % and 0 respectively). Conclusions: Retreatment with Peg-interferon was effective in treatment-experienced patients with chronic hepatitis, and showed higher rates of virological response, HBeAg loss and seroconversion.

Topic 11: Hepatitis B

No: 1350

Occult HBV infection and its association with hepatocellular carcinoma in the community based long term follow up reveal cohort

Hwai-i Yang[1], Jessica Liu[1], Chia-lin Chang[1], Chin-lan Jen[1], Mei-hsuan Lee[2], Hui-han Hu[1], Chien-jen Chen[1]

Academia Sinica Genomics Research Center Taipei-Taiwan[1], National Yang-ming University Graduate Institute of Clinical Medicine Taipei-Taiwan[2]

Aim: Occult hepatitis B virus infection (OBI) is a challenging topic in viral hepatitis, and community-based data has seldom been reported. We investigated the characteristics of OBI in our community-based long-term follow-up REVEAL cohort.
Methods: Among 19,665 participants seronegative for HBsAg at study entry, serum HBV DNA levels in 170 newly-developed HCC cases, as well as 284, 209, and 230 healthy controls that were anti-HCV-seronegative, anti-HCV-seropositive with undetectable HCV RNA, and anti-HCV-seropositive with detectable HCV RNA were assayed respectively, using the COBAS AmpliPrep/COBAS TaqMan HBV test.
Results: The prevalence of OBI in baseline serum samples was 10.0 % in participants who developed HCC during follow-up, and 7.3 % in those who did not develop HCC. When viral load was taken into account, 2.4 % of HCC cases had serum HBV DNA levels $\geq$ 20,000 IU/mL, compared to only 0.3 % of healthy controls. Using participants with undetectable levels of HBV DNA ($<$ 20 IU/mL) as a reference, the gender-age-adjusted odds ratio (95 % CI) of developing HCC was 1.21 (0.63-2.32) and 16.72 (2.85-98.01), respectively, for participants with serum HBV DNA levels of 20- $<$ 20,000 IU/mL and $\geq$ 20,000 IU/mL. Among participants with both HBsAg- and anti-HCV-seronegativity, we found that female gender, increasing age, elevated ALT levels, alcohol consumption, and serum HBV DNA levels $\geq$ 20,000 IU/mL were significantly associated with increased HCC risk.
Conclusion: Our study suggests that HBsAg-seronegative subjects who have high levels of HBV DNAs are still at substantial risk of developing HCC. Further experimental efforts are needed to delineate the causes of OBI with high viral loads.

Topic 11: Hepatitis B

No: 1077

Cost effectiveness analysis of antiviral therapies in patients with HBeAg positive chronic hepatitis B in China

C. Zhang[1], W.x. Ke[1], Y.h. Gao[1], S.d. Zhou[1], L. Liu[1], X.h. Ye[1], Z.j. Yao[1], Y. Yang[1]

Guangdong Pharmaceutical University, School of Public Health, Department of Epidemiology and Biostatistics and Guangdong Key Lab of Molecular Epidemiology, Guangzhou-China[1]

Aims: To estimate the cost-effectiveness of antiviral treatments lamivudine (LAM), adefovir (ADV), telbivudine (TBV), entecavir (ETV) for patients with HBeAg (+) chronic hepatitis B (CHB) in China.
Methods: A Markov model was used to simulate the lifetime health benefits and costs associated with the antiviral treatments. From the perspective of Chinese health care, relative model parameters were largely derived from Chinese population studies. Two different drug sale prices (Chinese-made drugs and imported drugs) were assessed in scenario analysis. Probabilistic sensitivity analysis and one-way sensitivity analysis were used to explore model uncertainties.
Results: In the base-case analysis, the most quality-adjusted life years was obtained with ETV when compared with LAM, ADV, and TBV. ADV was the least cost and effective treatment as the reference therapy, whereas the ETV strategy was the most cost-effective option, followed by TBV and LAM. Entecavir costs the least additional $7600 to gain 1 additional quality-adjusted life year (QALY) for Chinese-made drug and $9100 for imported drug over other therapies, respectively. The projected 10-year cumulative incidences of decompensated cirrhosis, hepatocellular carcinoma and mortality for ETV were 4.3, 4.8 and 33.7 %, respectively, which were significantly lower than those of rest strategies. In probabilistic sensitivity analyses, ETV was the preferred option at a threshold of $18,924 per QALY.
Conclusions: In patients with HBeAg (+) CHB, entecavir is a cost-effective option compared with other therapies for CHB.

Topic 11: Hepatitis B

No: 1693

HBV DNA level not liver stiffness value could predict significance liver fibrosis in hbeag negative chronic hepatitis B patients who got liver biopsy

Surat Praneenararat[1], Naichaya Chamroonkul[1], Pimsiri Sripongpun[1], Samornmas Kanngurn[2], Roongrueng Jarumanokul[3], Teerha Piratvisuth[1]

Faculty of Medicine, Prince of Songkla University Internal Medicine Songkhla-Thailand[1], Faculty of Medicine, Prince of Songkla University Pathology Songkhla-Thailand[2], Faculty of Medicine, Prince of Songkla University Immunology Songkhla-Thailand[3]

Background: Thirty percent of HBe antigen negative chronic hepatitis B patients who underwent liver biopsy base on recommendation, had significance liver histology and candidate for treatment. However, the rest to them got less benefit from this high risk procedure. Finding out the parameters that can predict significant liver histology to avoid unnecessary liver biopsy is our aim.
Object: To find predictors of significant liver histology in treatment naïve CHB HBeAg-ve patients age $\geq$ 40 years HBV DNA level - $\geq$ 2,000 IU/mL and or elevated alanine aminotransferase level 1-2 times of ULN.
Material and method: Twenty-two patients were prospectively included in the study. Clinical and laboratory parameters including age, gender, underlying disease, family history of cirrhosis or hepatocellular carcinoma, BMI, HBV DNA level, HBsAg level, liver function test, complete blood count, AST-to-platelet ratio index and transient elastography. Liver histology was reviewed by single hepato-pathologist using Metavir and HAI score.
Results: Significant liver inflammation was found in 5/22(23 %) and associated with lower BMI and higher alkaline phosphatase. Seven patients (32 %) had significant liver fibrosis which associated with lower age. On multivariate analysis, only HBV DNA level $>$ 5.5 log IU/mL could predict significant liver fibrosis (odd ratio 28.012, 95 % CI, 1.631–481.240, $P = 0.022$) and its sensitivity, specificity, positive predictive value and negative predictive value were 71.4, 93.3, 83.3 and 87.5 % respectively.
Conclusion: HBV DNA level $>$ 5.5 log IU/mL could predict significant liver fibrosis in treatment naïve HBeAg-negative CHB patients indicated for liver biopsy.

Topic 11: Hepatitis B

No: 1959

Combination of age and hepatitis B surface antigen levels in predicting hbv relapse after cessation of entecavir treatment

Chien-hung Chen[1], Chuan-mo Lee[1], Chao-hung Hung[1], Tsung-hui Hu[1], Jing-houng Wang[1], Sheng-nan Lu[1]

Kaohsiung Chang Gung Memorial Hospital Division of Hepatogastroenterology, Department of Internal Medicine Kaohsiung-Taiwan[1]

Background & aims: To investigate the incidence and useful predictors of hepatitis B virus (HBV) relapse after discontinuing entecavir treatment.
Patients and methods: A total of 244 chronic hepatitis B (CHB) patients [80 HBeAg-positive and 164 HBeAg-negative patients], who were treated with entecavir previously and had post-treatment follow-up for at least 12 months were recruited. All patients fulfilled the stopping criteria of the APASL 2012.
Results: The 2-year post-treatment virological and clinical relapse rate was 42.7 % and 36.4 %, respectively in HBeAg-positive patients, and 3-year virological and clinical relapse rate was 66.6 % and 53.2 %, respectively in HBeAg-negative patients. Cox regression analysis revealed that age, HBV genotype C and higher baseline HBsAg levels in HBeAg-positive patients and age and end-of-treatment HBsAg levels in HBeAg-negative patients were independent factors for virological and clinical relapse. In HBeAg-positive patients, the post-treatment HBV relapse risk further increased with the presence of age of 40 years and HBsAg level of 4,500 IU/mL at baseline ($P < 0.001$). In HBeAg-negative patients, combing age (< 55 years) and HBsAg level (< 190 IU/mL) at the end of treatment could predict the lowest post-treatment HBV relapse rate (3 years: 16 %). In 29 HBeAg-negative cirrhotic patients, an HBsAg of 190 IU/mL could predict virological relapse ($P < 0.001$). There was significant difference in terms of HBsAg decline from end of treatment to month 12 between patients with and without HBsAg loss after cessation of entecavir treatment.
Conclusions: The combination of age and HBsAg levels was a useful predictor to guide the timing of cessation of entecavir treatment.

Topic 11: Hepatitis B

No: 1246

Inactive HBsAG carrier state a single center experience

Sebati Özdemir[1], Muharrem Coşkun[1], Erkan Çağlar[1], Gürhan Şişman[1], Emine Köroğlu[1], Ibrahim Hatemi[1], Nuray Kepil[2], Abdullah Sonsuz[1], Murat Tuncer[1], Hakan Şentürk[3]

Istanbul University, Cerrahpaşa Faculty of Medicine Department of Internal Medicine, Division of Gastroenterology Istanbul-Turkey[1], Istanbul University, Cerrahpaşa Faculty of Medicine Department of Pathology Istanbul-Turkey[2], Bezmialem Vakif University Department of Internal Medicine, Division of Gastroenterology Istanbul-Turkey[3]

Aim: Inactive HBsAg carrier state is defined as persistently serum HBsAg positivity for 6 months, serum HBV-DNA level < 2,000 IU/ml, and normal serum aminotransferases levels. In this study we investigated the serologic, biochemical and histopathological features of inactive HBsAg carriers.
Methods: Research data were obtained from 633 patients with inactive HBsAg carrier. The orderly observed 509 cases (324 males; 185 females) (mean age: 47.3.5 ± 13.7 yr, range: 16-62 yr) were followed-up every 6 months for a period of 2 to 19 years (mean: 10.32 ± 4.43 yr).
Results: Serum HBV-DNA level was found > 2,000 IU/ml in 48 cases in the follow-up period. A liver biopsy was performed in 37 cases with elevated serum aminotransferases levels and HBV-DNA levels of > 2,000 IU/ml. In 34 of these patients mild or moderate chronic hepatitis was detected in the histopathological examination. One of them had inactive cirrhosis. 19 patients were started on antiviral therapy. In 8 cases, HBsAg became negative, and all 8 patients developed anti-HBs. In the follow-up period none of the cases developed hepatocellular carcinoma.
Conclusion: According to the findings of our study, in this country inactive HBsAg carrier state has a benign course and there is no need for routine liver biopsy. However, these patients should be continued follow-up in terms of both serum aminotransferases and HBV-DNA elevations.

Topic 11: Hepatitis B

No: 1809

The effects of tenofovir and entecavir therapy in the development of osteoporosis

Kamil Özdil[1], Resul Kahraman[1], Evren Kanat[1], Turan Çalhan[1], Abdurrahman Şahin[1], Haci Mehmet Sokmen[1]

Umraniye Research and Education Hospital Gastroenterology Istanbul-Turkey[1]

This study was carried out between 2011 and 2014. The ages of the patients ranged from 19 to 67, 78 (48.8 %) males and 82 (51.2 %) of 160 patients were women (patients 32 Tenofovir, 12 entecavir using patients and 112 control group) were included in the study. Drug group compared to the control group and there is no statistically significant difference between the mean age of the patients ($P = 0.955$; $p > 0.05$).There is no statistically significant difference in gender distribution of patients with entecavir and tenofovir group ($p > 0.05$). When the drug groups after treatment than before treatment, total spine T score evaluated changes seen in the tenofovir group compared to pre-treatment level is statistically significant ($P = 0.019$). According to the pre-treatment rate of osteoporosis (5.9 %), increase in post-treatment (23.5 %) was significant. In Entacavir group after treatment compared to pre-treatment levels of total spine T-score was not statistically significant change ($P = 0.368$). There were no differences in osteoporosis from baseline in the control group ($p > 0.05$). When classified level of the group with HBV DNA levels greater than 10^9 HBVDNA; changes seen after treatment compared to before treatment, total spine T-score was statistically significant ($P = 0.013$).

While no cases of osteoporosis in pre-treatment, post-treatment increase (30.8 %) was significant. HBVDNA level lower than 10^9 groups; there was no statistically significant change compared to the total spine score ($P = 0.122$). In the classification made by the fibrosis level, there is no statistically significant difference. In conclusion, in patients with tenofovir treatment in this study has increased the incidence of osteoporosis.

Topic 11: Hepatitis B

No: 1560

Long term outcomes of tenofovir therapy in the cases with chronic HBV

Murat Aladag[1], Hulya Aladag[2], Yilmaz Bilgic[1], Murat Harputluoglu[1], Mehmet Ali Erdogan[1], Yasir Furkan Cagin[1],

Yahya Atayan[1], Oğuzhan Yildirim[1], Yuksel Seckin[1], Melih Karincaoglu[1]

Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[1], Inonu University Faculty of Medicine Gynecology Malatya-Turkey[2]

Introduction and objective: In the present study, we aimed to retrospectively evaluate viral suppression rates and efficacy and safety of drug in chronic hepatitis B cases receiving Tenofovir.
Material and method: The study comprised of a total of 400 chronic hepatitis B patients that have been receiving Tenofovir between 2008 and 2014. We compared HBV-DNA, ALT, AST, HBsAg, Anti-HBs, HBeAg, and Anti-HBe levels on the 1st, 3rd, 6th, 9th and 12th months and thereafter at 6-month intervals.
Results: On the 6th month of treatment, complete response was obtained in 264 (66 %) patients (HBV-DNA negative), partial response was obtained in 72 (18 %) patients, and inadequate response was obtained in 64 (16 %) patients. It was observed that negativity of HBV-DNA has reached to 98 % on the 12th month of treatment, whereas the negativity of HBV-DNA was 99.5 % on the 2nd year of treatment and 99.5 % on the 3rd, 4th, 5th and 6th years of treatment. Only two cases had HBV-DNA positivity at the level of 200 copy/ml. Disappearance of HBsAg was determined in 38 (9.5 %) cases in the 6th year of treatment. It was observed that Anti-HBs developed in 14 (3.5 %) of these cases. No side effect that requires discontinuation of treatment was determined over the course of 6-month treatment period.
Conclusion: In conclusion, it was observed that none of the patients receiving Tenofovir therapy for Chronic Hepatitis B developed resistance over the course of 6-month treatment period. As the result, it was concluded that Tenofovir can be used with high efficacy and safety and no resistance in the cases with chronic HBV.

Topic 11: Hepatitis B

No: 1636

Changes of hepatitis B surface antigen levels in chronic hepatitis B patients with telbivudine treatment for more than 2 years

Hsien-chung Yu[1], Kung-hung Lin[1], Ping-i Hsu[1]

Kaohsiung Veterans General Hospital Department of Medicine Kaohsiung-Taiwan[1]

Aim: To investigate the kinetics of quantification of hepatitis B surface antigen (qHBsAg) in chronic hepatitis B (CHB) patients receiving telbivudine (LdT) for more than 2 years and determine the factors related to significant qHBsAg decline.
Method: This retrospective study included CHB patients receiving LdT as initial therapy for more than 2 years. The qHBsAg level was checked at baseline, third, sixth month and every 6 months thereafter from stored serum retrospectively. Rapid qHBsAg decline was defined by achieving qHBsAg decline > 0.5 log IU/mL from baseline at third month. The early qHBsAg decline was achieving qHBsAg decline > 0.5 log IU/mL from baseline in 12 months. The significant qHBsAg decline was defined as achieving qHBsAg decline > 1 log IU/mL from baseline.
Results: This study enrolled 143 patients. Treatment outcome is shown in table 1. Multivariate analysis revealed that rapid qHBsAg decline (risk ratio, 0.059, 95 % confidence interval, 0.023-0.155, $P < 0.001$) was the sole factor related to significant qHBsAg decline. The cumulative rates of significant qHBsAg decline in patients who achieved rapid qHBsAg decline were 68 % and 74 % in 1 and 2 years, respectively. In contrast, for patients without rapid qHBsAg decline, the cumulative rates of significant qHBsAg decline were only 3 % and 5 % in 1 and 2 years.
Conclusion: Rapid qHBsAg decline more than 0.5 log IU/mL at third month was related to significant qHBsAg decline in future implying the suitable patients for long-term telbivudine-based therapy in this group.

Topic 11: Hepatitis B

No: 1228

Correlation of serum hbs antigen and aminotransferase levels with liver histopathology in viral hepatitis

Ayşe Nur Değer[1], Filiz Özyiğit[2], Özlem Altuntaş Aydin[3], Özlem Arik[4], Berciş Imge Uçar[5], Hayat Kumbasar Karaosmanoğlu[3]

Dumlupinar University Medicine Faculty Department of Pathology Kutahya-Turkey[1], Dumlupinar University Medicine Faculty Department of Pharmacology Kutahya-Turkey[2], Haseki Eğitim Ve Arş Hastanesi Department of Microbiology Istanbul-Turkey[3], Dumlupinar University Medicine Faculty Department of Biostatistics Kutahya-Turkey[4], Dumlupinar University Medicine Faculty Department of General Surgery Kutahya-Turkey[5]

Liver biopsy plays a key role in the evaluation of chronic liver diseases. Since it provides an information on fibrosis and also helps to assess the histology and the progress of the disease. However, liver biopsy has some disadvantages. Presented study was designed to assess the liver damage in viral hepatitis with noninvasive methods and to investigate the correlation of these parameters with histopathological findings in order to avoid the large number of liver biopsies.
Methods: 12 patients diagnosed with chronical hepatitis B were included in the study. HBsAg and aminotransferase (ALT and AST) levels in blood samples and histopathological examination in liver biopsy samples were determined. Correlation between the biochemical parameters in serum and histopathological index (HAI) and fibrosis scores in liver biopsy samples of the patients were investigated using Spearman's Rho Correlation Test.
Results: Serum ALT and AST levels were positively correlated with HAI in liver biopsy samples whereas a negative correlation was found between serum HBsAg levels and the fibrosis scores in liver biopsy samples of the patients.
Conclusion: Liver biopsy is currently considered as the most precise procedure for evaluating the degree of liver inflammation and staging of fibrosis. However, present study suggested that elevated serum aminotransferase levels can provide an information about the increased HAI while elevated serum HBsAg levels may suggest the diminished fibrosis scores. Noninvasive methods may have a remarkable value in followup of the progress of the disease in patients with viral hepatitis in order to decrease the liver biopsy numbers.

Topic 11: Hepatitis B

No: 1122

Risk factors of HBV reactivation in patients underwent hematopoietic stem cell transplantation in HBV endemic area

Eunae Cho[1]

Chonnam National University Internal Medicine Gwangju-Korea, South[1]

Background and aim: The aim of this study is to investigate the rate and risk factors for HBV reactivation in patients undergoing hematopoietic stem cell transplantation (HSCT).
Methods: A total of 506 patients who underwent HSCT from January 2008 to December 2013 were analyzed retrospectively.
Results: Reactivation rate of HBV in patients underwent HSCT was 4.15 % (21/506). Subgroup analysis showed reactivation rate of HBV in patients with occult HBV infection was 5.85 % (10/171). In univariate analysis for risk factors of HBV reactivation, initial detectable HBV DNA ($P = 0.004$), age (> 60) ($P = 0.012$), recipient HBsAg (+) before SCT, ($P = 0.004$) recipient HBsAb (-) before SCT ($P = 0.005$), recipient HBcAb (+) before SCT ($P = 0.013$), and donor HBsAg (+) ($P < 0.001$) were associated with reactivation of HBV. In multivariate analysis, significant risk factors of HBV reactivation in patients underwent HSCT were old age (≥ 60) ($P = 0.032$) and donor HBsAg (+) ($P = 0.026$). Subgroup analysis showed risk factor for reactivation of HBV in patients with occult HBV infection was only old age (≥ 60) ($P = 0.031$).
Conclusion: Reactivation rate of HBV in all patients undergoing HSCT was 4.2 %. In patients with occult HBV infection, it was 5.85 %. Old age (> 60) and donor HBsAg (+) were risk factors for reactivation in patients with patients underwent HSCT. Preemptive antiviral treatment may be needed in older patients with occult HBV infection undergoing HSCT.

Topic 11: Hepatitis B

No: 1696

Sequence characters of HBV from China and adjacent countries and relationships of BCP PreC mutation between clinical status

Qian Zhao[1], Hongmei Li[1], Tao Shen[1]

Institute of Basic and Clinical Medicine, the First People's Hospital of Yunnan Province Molecular Biology Department Kunming-China[1]

Heterogeneous of HBV is an important viral parameter in predicting disease progression and therapeutic outcome. Thus, we collected 1148 Chinese and 952 adjacent countries' HBV sequences from GenBank. C/B and C/B/D were dominant genotypes in China and its adjacent countries, respectively. Adrq+ and adw2 were dominant serotypes. In addition to ATG, ATA, ACG, GTG, CTG, TTG, ATG and AGT were also discovered as initiation codons, however, whether or not a mutation in the start codon in the pre-S2 region has an impact on survival and replication of HBV remains to be determined. The -major stop codons of S-ORF were TAA and TGA in B2 and C2 subgenotype, respectively. Divergence between five sub-genotypes (B3, B5, B7, B8, and B9) was less than 4 %. The B3, B5, B7, B8, and B9 sub-genotypes might be reclustered into quasi-subgenotype B3.A statistical significance of the BCP double mutation was observed between CHB and ASHB ($P < 0.05$) as well as between ACHB and HCC ($P < 0.05$). The mutation difference in pre-C was remarkably significant between HCC and LCHB ($P < 0.01$); it was also significant between ACHB and HCC ($P < 0.05$) and between AHB and ASHB ($P < 0.05$). There were significant differences for both the BCP double mutation and the pre-C mutation between type B and C. The information is critical for the future prevention and therapy of HBV infections.

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*Li HM was contribute the same as Zhao Q.

#Shen T is the corresponding author.

Topic 11: Hepatitis B

No: 1328

Efficacy of lamivudine in patients with chronic hepatitis or cirrhosis due to HBV infection

Aliye Soylu[1], Umit Bilge Dogan[2], Deniz Duman[3], Sule Poturoglu[4], Can Dolapcıoglu[5], Serdal Cakmak[6], Isa Sevindir[6], Osman Cavit Ozdogan[3]

Bakirkoy Dr Sadi Konuk Research and Training Hospital Gastroenterology Istanbul-Turkey[1], Mustafa Kemal Faculty of Medicine Gastroenterology Hatay-Turkey[2], Marmara University Faculty of Medicine Gastroenterology Istanbul-Turkey[3], Haseki Research and Training Hospital Gastroenterology Istanbul-Turkey[4], Kartal Research and Training Hospital Gastroenterology Istanbul-Turkey[5], Bakirkoy Dr. Sadi Konuk Research and Training Hospital Gastroenterology Istanbul-Turkey[6]

Aim: To compare the efficacy of lamivudine (LAM) which is widely available in our market in patients with chronic hepatitis or cirrhosis due to HBV infection.
Materials and methods: We divided the study population into 2 groups as cirrhosis and hepatitis patients. Treatment response was accepted as HBV-DNA negativity which was defined as HBV DNA < 20 IU/ml. We compared the 2 groups in response to the HBV-DNA levels at initial visit, 3rd, 6th and 12th months of therapy.
Results: There was no difference regarding the gender distribution of patients with cirrhosis [111 (71 male)] and chronic hepatitis [175 (118 male)]($P = 0.546$). The initial HBV-DNA level was higher in patients with cirrhosis (2488719.7 ± 9476104.397 IU/ml) than hepatitis (2447848.86 ± 8115349.76 IU/ml) ($P = 0.0001$). The rate of HBV-DNA negativity at the 3rd month of therapy was higher in cirrhotics (48.1 %) than the hepatitis group (31.75 %) ($P = 0.019$). There was no difference in the rates of patients who became HBV-DNA negative at 6th (cirrhosis 68.32 %, hepatitis 68 %; $P = 0.963$) and the 12th months (cirrhosis 87.74 %, hepatitis 81.61 %) ($P = 0.176$) of therapy between the 2 groups(figure-1). Those patients who tested positive for HBV-DNA at the 3rd month of therapy remained the same throughout their course at the 6th and 12th months with regard to their HBV-DNA distributions (Table-1).
Conclusion: Our finding of superior HBV-DNA suppression rates at the 3rd month of therapy in cirrhotics may be attributable to their higher initial HAI scores. However, prolonged treatment with LAM yielded similar results in both groups reaching up to 80 % efficacy at 12 months of therapy.

Topic 11: Hepatitis B

No: 2227

Is soluble urokinase plasminogen activator receptor new non invasive marker in patients with chronic hepatitis B infection

Arif Mansur Cosar[1], Gurdal Yilmaz[2], Iftihar Koksal[2]

Ktu Gastroenterology Trabzon-Turkey[1], Ktu Infectious Diseases and Clinical Microbiology Trabzon-Turkey[2]

Background: Liver biopsy is usually used to assess the extent of necroinflammatory activity and fibrosis and to diagnose cirrhosis in chronic viral hepatitis. It is the main predictor of disease outcome in chronic hepatitis infection. Although liver biopsy is the gold standard for the assessment of fibrosis, it has several disadvantages, such as poor patient compliance, sampling error, limited usefulness for dynamic surveillance, and poor intra- and inter-observation concordance. Biomarkers are being developed as alternatives to liver biopsy for predicting liver fibrosis in patients with chronic hepatitis. We evaluated the association of serum levels of soluble urokinase plasminogen activator receptor (suPAR) with the severity of liver fibrosis in patients with chronic hepatitis B (CHB) infection.
Methods: Serum suPAR levels were assessed in 164 patients (96 female and 68 male, with a mean age of 48.3 ± 12.7) with CHB and 82 healthy volunteers (45 female and 37 male, with a mean age of 44.7 ± 8.9). Liver biopsy was performed in all patients with CHB and serum samples were kept at -80 oC until analysis. During two years study period, liver fibrosis scores obtained via liver biopsy (Metavir scoring system) and serum suPAR levels were compared.
Results: Liver fibrosis score were F0 in 9.8 %, F1 in 25.6 %, F2 in 31,1 %, F3 in 20.7 %, and F4 in 12.8 % of patients with CHB. Serum suPAR value were determined 2.5 ± 0.6 in F0, 2.4 ± 0.8 in F1, 2.9 ± 1.8 in F2, 4.2 ± 1.4 in F3, 5.8 ± 2.7 in F4, and 2.3 ± 0.9 ng/mL in healthy volunteers. Although mean suPAR levels in patients with F0, F1 and F2 fibrosis were not different, they were significantly increased at higher stages of liver fibrosis (F3 and F4, $P < 0.001$). Serum suPAR values had a high diagnostic specificity and sensitivity to differentiate non/mild/moderate fibrosis (F0-F2) from severe fibrosis (F3/F4) with an area under curve of 0.798 ($P < 0.001$).
Conclusions: According our results, serum suPAR levels may a new biomarker usable diagnostic accuracy for prediction of severe liver fibrosis as noninvasive marker.

Topic 11: Hepatitis B

No: 2080

Week efficacy of telbivudine in chronic hepatitis B

Aylin Calica Utku[1], Nazan Tuna[1], Oguz Karabay[1]

Sakarya University Training and Research Hospital Infectious Diseases and Clinical Microbiology Sakarya-Turkey[1]

Aim: Telbivudine(LDT) is an orally administered nucleoside analogue for use in the treatment of chronic hepatitis B(CHB). We evaluated efficacy of LDT on week 52 in CHB patients.
Methods: A total of 58 patients diagnosed with CHB and who were treated with LDT from November 2011-November 2014 in the Sakarya University Training and Research Hospital were evaluated retrospectively. On week 52 of treatment, patients with LDT therapy successful(PLTS) and patients with LDT therapy unsuccessful(PLTU) were compared. HBeAg seroconversion rates and HBsAg loss of the patients were evaluated.
Results: The characteristics of 58 patients treated with LDT are given in Table 1. On week 52 of the treatment, the LDT treatment was changed in 10 patients(17.2 %) with HBV-DNA > 50 IU/mL. The characteristics of PLTS and PLTU are given in Table 2. Statistically significant difference was found HBeAg positivity ($P = 0.006$) and previously received interferon therapy ($P = 0.05$) between PLTS and PLTU. HBeAg clearance and seroconversion, HBsAg clearance was not observed in any patients treated with LDT on week 52.
Table 1: Characteristics of patients treated with LDT.
Table 2: Characteristics of PLTS and PLTU.
Conclusions: Suppression of HBV replication is the main therapeutic goal in the treatment of CHB patients. According to results; LDT was not effective in 17.2 % of patients and HBeAg clearance and seroconversion, HBsAg clearance was not observed in any patients treated with LDT on week 52. Treatment with LDT was not considered a suitable option in HBeAg-positive and previously received interferon therapy patients. This issue needs to clarify in a study with big number of patients.

Topic 11: Hepatitis B

No: 1208

The durability of efficacy and predictor after three years nucleos(t)ide analog off treatment in chronic hepatitis B patients

Ching-chung Lin[1], Tsang-en Wang[1], Ming-jong Bair[1], Chih-jen Chen[1], Cheng-hsin Chu[1], Ming-jen Chen[1], Chia-yuan Liu[1], Shee-chan Lin[1], Horng-yuan Wang[1], Shou-chuan Shih[1]

Mackay Memorial Hospital Internal Medicine Taipei-Taiwan[1]

Background: Lamivudine, telbivudine and entecavir are the first-line drugs covered by Taiwan national health insurance for 3 years to chronic hepatitis B patients, but the optimal duration of treatment is still unclear. We wanted to detect the chronic hepatitis B treatment cessation durability and the predictors between clinical relapsers and non-relapsers.
Methods: In this retrospective cohort study, total 210 chronic hepatitis B patients who had HBeAg + or HBeAg- were completely treated for 3 years by nucleos(t)ide analog. There were 102 patients keeping therapy, and the other 88 patients selected stopping drugs and followed for one year. The efficacy analysis was by HBeAg seroconvertion, HBV DNA clearance, virus breakthrough, clinical relapse and liver decompensation. The predictors of durability were evaluated by ALT, liver fibrosis severity, HBV DNA and drugs differences.
Results: 88 patients (18 lamivudine, 21 telbivudine and 51 entecavir) were recruited. There was no difference in clinical relapse rate among lamivudine, telbivudine and entecavir(37.5 % vs. 38.1 % vs. 33.3 %; $P = 0.908$), and there was no any liver decompensated patient occurred. In baseline clinical characters, there were no differences between clinical relapse group and non-relapse group including age, gender, cirrhosis, prior treatment, HBV DNA, pretreatment ALT and HBeAg. There was significant difference between clinical relapse group and non-relapse group in the third year serum ALT level (37.5 U/L vs. 27.7 U/L; $P = 0.044$).
Conclusion: Three year nucleos(t)ide analog off-treatment with an overall 35.2 % one year relapse rate, and the third year low normal ALT serum level might be a predictor of durability of efficacy.

Topic 11: Hepatitis B

No: 2112

Research of effectiveness of tenofovir used in treatment of chronic hepatitis B infection on bone mineralization

Derya Beslenti[1], Ayhan Akbulut[1], Müge Özgüler[2], Affan Denk[1], Mehmet Ozden[1], Kutbettin Demirdağ[1]

Fırat University Infectious Diseases and Clinical Microbiology Elazıg-Turkey[1], Elazıg Training and Educational Hospital Infectious Diseases and Clinical Microbiology Elazıg-Turkey[2]

Two billion individuals worldwide have exposed to hepatitis B virus (HBV) and 350 millions of them are chronically infected with HBV. Risk of chronicity is about 2-5 % in adult age. Pegylated-interferons with immunomodulatory and antiviral effects and oral antiviral agents are used today for treatment of chronic hepatitis B. Oral antiviral agent tenofovir: Inhibits HBV polymerase activity, DNA chain terminates after introduced into the DNA. In HIV patients, a reduction in bone mineral density was determined under the treatment of tenofovir. In this study; it was aimed to investigate the effect on bone mineralization with tenofovir in chronic HBV infection patients.

Thirty patients who were admitted to Clinical Microbiology and Infectious Diseases Clinic of Fırat University Hospital and who was started tenofovir treatment admitted to this study. Patients lumbar spine were performed with DEXA measurements before the treatment and the 1st, 2nd and 3rd year of the treatment. The decrease in bone mineral density was found to be statistically significant in T and Z scores which was measured initiation and 3rd year of treatment. A significant relationship was found between Vitamin D and reduction in the bone mineralization.

As a result; There was a decrease in bone mineral density in patients who was chronic hepatit B and who was treated with tenofovir ($P < 0.05$). Because of these side effects, HBV infected patients who were treated with tenofovir should be followed periodically and vitamin D supplementation should be done who was needed.

Topic 11: Hepatitis B

No: 1332

Hepatitis B virus x protein sensitizes trail induced hepatocyte apoptosis by inhibiting E3 ubiquitin ligase A20

Hang Zhang[1], Gongying Chen[1], Yan Wang[1], Ningtong Zhuang[1], Songxue Wang[1], Liyun Shi[1]

Hangzhou Normal University School of Medicine Hangzhou-China[1]

Hepatitis B virus (HBV) infection can lead to hepatocyte death and liver damage which may eventually develop cirrhosis and liver cancer. However, the molecular mechanism underlying hepatocyte death during HBV infection has not been well defined. Herein we report that hepatitis B virus X protein (HBx) renders hepatocytes more susceptible to TNF-related apoptosis-inducing ligand (TRAIL)-induced apoptosis. Increased sensitivity to TRAIL was associated with HBx-induced upregulation of miR-125a, which in turn gave rise to the repression of its putative target gene A20. Importantly, the defective expression of A20 led to the decreased K63-linked polyubiquitination of caspase-8, promoting the recruitment of Fas-associated death domain (FADD) and caspase-8 to the death-inducing signaling complex (DISC), and thereby facilitating HBx-mediated apoptotic signaling in hepatocytes. Thus, we show for the first time that HBx-driven miR-125a/A20 axis plays a critical role in regulating the cell death signaling and suggest a unique function for HBx during hepatocyte injury. MiR-125a and A20 could serve as novel diagnostic markers or therapeutic targets for mitigating HBV-induced hepatic damage and dysfunction.

Topic 11: Hepatitis B

No: 1282

Reduction of hepatitis B core related antigen by long term nucleoside nucleotide analogue therapy and its correlation with intrahepatic HBV DNA reduction

Danny Wong[1], Malgorzata Kopaniszen[1], Wai-kay Seto[1], James Fung[1], Ivan Hung[1], John Young[1], John Yuen[1], Vincent Ngai[1], Man-fung Yuen[1], Ching-lung Lai[1]

The University of Hong Kong Medicine Hong Kong-Hong Kong[1]

Objective: We aimed to investigate the reduction of hepatitis B core-related antigen (HBcrAg) in patients with long term nucleoside/nucleotide analogue (NA) therapy.
Methods: Forty-three patients (median age: 43 years, range: 24–63 years) who had been on continuous (median follow-up duration: 10 years; range 5–12 years) NA therapy, including lamivudine, adefovir, telbivudine, entecavir, and tenofovir, were recruited. All patients had liver biopsies at baseline and at the last follow-up. HBcrAg (detection limit: 3 log U/mL) were measured using a Lumipulse HBcrAg assay (Fujirebio, Japan). Intrahepatic total HBV DNA (ihHBV-DNA) and covalently closed circular DNA (cccDNA) were assayed by real-time PCR.
Results: At baseline, the median levels of HBcrAg, ihHBV-DNA, and cccDNA were 6.7 log U/mL, 286 copies/cell, and 7.3 copies/cell, respectively. Baseline level of HBcrAg correlated positively with that of ihHBV-DNA ($r = 0.568$, $P < 0.0001$), and cccDNA ($r = 0.559$, $P < 0.0001$). At the time of last biopsy, 12 (28 %) patients had undetectable HBcrAg (median: 3.8; range: < 3–5.7 log U/mL). All patients had detectable ihHBV-DNA (median: 0.35 copies/cell), and 21 (49 %) patients had undetectable cccDNA. The median logarithmic reductions of HBcrAg, ihHBV-DNA, and cccDNA were 2.7 log U/mL, 2.81 log copies/cell, and 2.94 log copies/cell, respectively. There was a positive correlation between the logarithmic reduction of HBcrAg and ihHBV-DNA ($r = 0.550$, $P < 0.001$) and cccDNA ($r = 0.419$, $P = 0.005$).
Conclusion: The marked reduction of HBcrAg, together with the reduction in ihHBV-DNA and cccDNA, further supports the effectiveness of long-term nucleoside/tide analogue therapy in potentially eradicating HBV from chronic carriers.

Topic 11: Hepatitis B

No: 2017

Evaluation of the hepatitis B virus exposure of the children of HBsAg positive mothers

Selma Tosun[1], Asli Keles[1], Altan Gokgoz[1], Alpay Ari[1], Hulya Bayik[2]

Bozyaka Research and Education Hospital Infectious Diseases Izmir-Turkey[1], Bozyaka Research and Education Hospital Pediatrics Izmir-Turkey[2]

Aim: The aim of this study is to obtain the HBV exposure of the children of HBsAg positive mothers from the current records and to evaluate this exposure through the data obtained from the subjects.
Method: By making face-to-face interview with the HBsAg positive subjects observed in Viral Hepatitis Polyclinic, it was detected whether any examination was made in order to learn the HBV exposure of children. Also,the results of the examinations, and the vaccination

application of the children were questioned;and the results obtained were evaluated along with the current examination results.
Results: The study included 79 women subjects aged between 18 and 69. When the data were evaluated, it was found out that among the first children of HBsAg positive mothers, HBsAg positivity and the rate of being immunized by the virus exposure was higher. It was also determined that the mothers behaved attentively for their children to be examined for HBV and the rate of vaccination of children was high.
Discussion: In this study, it was observed that the HBV exposure of HBsAg positive mothers' children was high and the case was more apparent especially for the first children. The rate was found to be lower for the subsequent children. It was considered that this case might be related to the fact that mothers' HBsAg status is not known during the first pregnancy. Thus, evaluation of pregnants in terms of HBsAg and an appropriate immunization (vaccination + HBIG) of the infants during birth in case of positivity is of great importance.

Topic 11: Hepatitis B

No: 1753

Acute hepatic flair case report

Berivan Tunca[1], Mustafa Kemal Çelen[2]

Kiziltepe State Hospital Infectious Diseases Diyarbakir-Turkey[1], Dicle University Hospital Infectious Diseases Diyarbakir-Turkey[2]

Case: 31 year old male came with jaundice and weakness at 10.10.2014. His complaints were started 2 weeks ago. In his laboratory results; HBsAg: positive, HBeAg: positive, ALT: 2326 U/L, AST: 1410 U/L, Total bilirubin: 3.2 mg/dl, Direct bilirubin: 1.71 mg/dl, Albumine: 3.8 g/dl, platelet: 234700/uL, INR: 1.22, PT: 14.6sn, Anti-Delta: negative, HBV-DNA: $>$ 1.7x10^8 IU/mL. When we questioned his story we learned that he had started using Tenofovir Disoproksil Fumarat at 2010. His laboratory results were; HBeAg: positive,ALT: 45 U/L, HBV-DNA $>$ 10^7 IU/mL and in liver biopsy fibrosis stage was 2 before the treatment. After the sixth month HBV-DNA level become unmeasurable and he used this treatment for 4 years until May 2014. He decided to cut his treatment of his own accord because he was bored of using drugs. We hospitalized the patient and started Tenofovir immediately. We also give 1000 cc %5 dextrose 1*1 iv, multivitamin complex peroral during his hospitalization and vitamin K for three days. On the day seventeen his bilirubin levels have reached the highest level (Total bilirubin: 24.44 mg/dl, Direct bilirubin: 19.8 mg/dl) and the other laboratory results were; ALT: 884 U/L, AST: 1072 U/L, INR: 1.1, PT: 14.4 sn, Albumine: 3.2 g/dl, platelet: 188000/uL. After that day he started to heal and he was discharged on the 31th day.
Discussion: With this case report we want to emphasize the importance of patient compliance during oral antiviral treatment. Our patient was using his drugs for four years and when he decided to stop his treatment he faced with flare. This situation is especially important for patients with Hbeag positivity like our patient.

Topic 11: Hepatitis B

No: 2071

Hepatitis B e antigen negative chronic hepatitis in Bangladeshi patients

Farjana Majid[1], Ahmed Lutful Moben[2], Mamun Al Mahtab Mahtab[3], Salimur Rahman Rahman[3], Munira Jahan[4], Shahina Tabassum[4]

Taerunnessa Medical College Virology Dhaka-Bangladesh[1], Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh Medicine Dhaka-Bangladesh[2], Bsmmu Hepatology Dhaka-Bangladesh[3], Bsmmu Virology Dhaka-Bangladesh[4]

Hepatitis B virus (HBV) causes a spectrum of liver diseases including acute hepatitis, chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma. Hepatitis B e antigen negative chronic hepatitis (e- CHB) with detectable levels of HBV DNA in serum has been reported in cases from Asia. Outcome and treatment also influenced by the HBeAg status among these patients. The present study was designed to evaluate the HBeAg status of CHB patients. A cross sectional study was conducted between July'2010 to June'2011. A total of 200 serologically diagnosed CHB patients were enrolled for the study. Data was analyzed by SPSS. Among the total study population, HBeAg positive CHB patients were 74 (37 %) and HBeAg negative patients were 126 (63 %). Among the HBeAg negative patients, viral load was less and patients were significantly older. The mean viral load of HBeAg positive and HBeAg negative was 6.40 ± 2.042 [log10(copies/ml)] and 2.83 ± 2.55 [log10 (copies/ml)] respectively. HBV DNA was a more reliable indicator of the presence of virus than HBeAg, and was detected in 98.65 % (73/74) HBeAg positive carriers, and in 66.67 % (84/126) HBeAg negative patients. HBeAg negativity is more prevalent among the CHB patients in Bangladesh.

Topic 11: Hepatitis B

No: 1451

Hepatitis B virus reactivation in lymphoma patients with rituximab therapy

Atsushi Suetsugu[1], Hisashi Tsurumi[1], Yuhei Shibata[1], Takurou Matsumoto[1], Nobuhiko Nakamura[1], Masahito Shimizu[1], Hisataka Moriwaki[1]

Gifu University Graduate School of Medicine Department of Gastroenterology Gifu-Japan[1]

Backgrounds/aims: Hepatitis B virus (HBV) reactivation after rituximab combination chemotherapy in HBsAg negative patients with non- Hodgkin lymphoma is reported. In this study, the frequency of HBV reactivation in patients who were receiving rituximab chemotherapy was examined.
Methods: Between January 2004 and December 2012, 338 patients received treatment with rituximab. HBsAg was performed in all patients. A total of 329 HBsAg-negative patients with non -Hodgkin lymphoma were treated with rituximab chemotherapy. HBsAb and/or HBcAb tests were performed in 169 patients. HBsAb,HBcAb and serum HBV-DNA were measured in patients who were occurred HBV reactivation.
Results: Of the 169 patients, 50 (29.6 %) were HBV carriers. HBV reactivation occurred during or after rituximab chemotherapy in two patients (4.0 %). Two patients who developed HBV reactivation were HBcAb positive, and one of two people were also anti-HBs positive. In these two patients, the pretreatment HBV-DNA was not detected. Entecavir administration was started when HBV DNA became positive, and serum HBV-DNA became negative within 1 to 4 months.
Conclusion: HBV reactivation occurred in patients who had been HBsAg negative and HBcAb positive. In addition, HBV reactivation

occurred at under and after treatment of rituximab chemotherapy, but entecavir administration reduced the serum HBV-DNA level and ALT level. Attention should be paid to HBV reactivation in all patients with past as well as chronic HBV infection during and after rituximab therapy.

Topic 11: Hepatitis B

No: 1820

Heart transplantation and B hepatitis

Sabiye Akbulut[1], Kamuran Cumhur Değer[2], Aziz Serkan Senger[2], Mustafa Duman[2]

Kartal Koşuyolu High Specialty Education and Research Hospital Department of Gastroenterology Istanbul-Turkey[1], Kartal Koşuyolu High Specialty Education and Research Hospital Department of Gastroenterological Surgery Istanbul-Turkey[2]

Introduction: Heart transplantation is the gold standard therapy for patients who have end stage heart failure and less than 1 year life expectancy. Tests for hepatitis should be made before heart transplantation and prophylactic antiviral treatment should be guaranteed. In this case we present a HBV reactivation under immunosuppressive treatment patient who did not take prophylactic therapy before heart transplantation.
Case report: Orthotropic heart transplantation for dilated cardiomyopathy was performed to patient H.A (51,M) in 2010. In the blood analyses, HbsAg + , HBV DNA (-), AST 12 IU, ALT 23 IU was measured before cardiac transplantation. Hepatitis B prophylaxis had not begun to the patient before transplantation. Tacrolimus and methyl prednisolone were administered to the patient after transplantation. The blood tests revealed HbsAg(+), HBV DNA 4.172.532 copy/ml, AST 71 IU/mL, ALT 113 IU/mL. Lamivudine 100 mg tablet had given once daily. On the 6th month of the treatment HBV DNA was negative so that lamivudine therapy was continued. On the 3rd year of the therapy HBV DNA was 37.300.000 IU, so lamivudine treatment was interrupted because of drug resistance. Subsequently Tenofovir 245 mg tablet had begun once daily. 24th week of this last treatment HBV DNA was negative and the Tenofovir treatment is still going on.
Conclusion: HBV reactivation is one of the important factors that affect survival after cardiac transplantation. It is recommended to give more potent antiviral agents like entekavir or tenofovir instead of lamivudine to whom will take lifetime immunosuppressive agents like cardiac transplantation patients.

Topic 11: Hepatitis B

No: 2064

A randomized study comparing efficacy of peginterferon alpha 2b monotherapy versus combination with entecavir in HBeAg negative chronic hepatitis B

Pisit Tangkijvanich[1], Salyavit Chittmittraprap[1], Kittiyod Poovorawan[2], Yong Poovorawan[3]

Faculty of Medicine, Chulalongkorn University Biochemistry Bangkok-Thailand[1], Faculty of Medicine, Chulalongkorn University Medicine Bangkok-Thailand[2], Faculty of Medicine, Chulalongkorn University Pediatrics Bangkok-Thailand[3]

Background: The combination therapy of peginterferon (PEG-IFN) and a potent antiviral drug might improve the response in patients with chronic hepatitis B (CHB). The aim of this study was to compare the efficacy of PEG-IFN plus entecavir (ETV) and PEG-IFN alone in Thai patients with HBeAg-negative CHB.
Methods: 126 treatment-naïve patients with HBeAg-negative CHB were randomly assigned to PEG-IFN alpha-2b (group 1) or combination of PEG-IFN alpha-2b and ETV for 48 weeks (group 2). Virological response (VR) was defined as HBV DNA level < 2,000 IU/mL at week 96.
Results: There were 63 patients in each group. At baseline, no difference between groups 1 and 2 was observed with respect to sex, mean age, ALT level, HBV DNA level (5.5 vs. 5.4 log IU/mL) and HBsAg level (3.4 vs. 3.5 log IU/mL). At week 48, rates of undetectable HBV DNA were significantly higher in group 2 than group 1 (87.3 % vs. 41.3 % $P < 0.001$). However, rates of HBsAg decline below 10 IU/mL were comparable between groups 1 and 2 (20.6 % vs. 11.1 %, $P = 0.222$). At week 96, there was no difference in VR rate between groups 1 and 2 (41.3 % vs. 38.1 %, $P = 0.856$). HBsAg clearance was found in 6 (9.5 %) and 3 (4.8 %) in groups 1 and 2, respectively ($P = 0.491$).
Conclusions: The combination therapy leaded to a higher rate of HBV DNA suppression during treatment. However, both regimens were comparable on the basis of off-treatment viral suppression and HBsAg clearance. Thus, combination of PEG-IFN and ETV had no additional therapeutic effect compared to PEG-IFN alone.

Topic 11: Hepatitis B

No: 1518

Continuous entecavir for treatment naïve chinese chronic hepatitis B patients in the real world setting the seven year results

Yuk Fai Lam[1], Wai-kay Seto[1], James Fung[1], Ching Lung Lai[1], Man Fung Yuen[1]

Queen Mary Hospital Medicine Hong Kong -Hong Kong[1]

Background: There is paucity of data on uninterrupted entecavir for treatment-naïve chronic hepatitis B (CHB) beyond 6 years.
Methods: Treatment–naïve Chinese CHB patients were treated continuously with entecavir for up to 7 years. The cumulative rates of HBV DNA undetectability, alanine aminotransferase (ALT) normalization, hepatitis B e-antigen (HBeAg) seroconversion, virological breakthrough, hepatitis B surface antigen (HBsAg) reduction and genotypic resistance to entecavir were determined. HBV DNA levels were measured by Roche Taqman real time PCR assay. Resistance profile was determined by line probe assay (LiPA, Innogenetics NV, Gent, Belgium). Serum HBsAg levels were performed using Elecsys HBsAg II assay (Roche Diagnostics, Gmbh, Mannheim).
Results: 222 Chinese CHB patients (median age 45 years, 70.7 % male) were recruited. 222, 188, 173, 170, 167,162 and 160 patients were followed up for 1, 2, 3, 4, 5, 6 and 7 years respectively. The cumulative rate of HBV DNA undetectability, ALT normalization, HBeAg seroconversion (90 patients were HBeAg positive at baseline) were 98.7, 98.3, 90.2 % up to year 7 respectively. The cumulative rate of virologic breakthrough was 8.3 %. Entecavir signature mutations were found in 2 patients. The cumulative rate of entecavir resistance up to 7 years was 1.2 %. The median rate of HBsAg reduction over 6 years of treatment was 0.095 log IU/ml/year. 15.2 and 7.9 % patients had HBsAg levels less than 200 and 100 IU/mL at the last follow-up. 2 patients developed HBsAg seroconversion at year 2 and 6 respectively. There were no serious adverse events reported.

Conclusion: Prolonged,uninterrupted entecavir therapy is an effective and safe treatment for CHB patients.

Topic 11: Hepatitis B

No: 2123

Evaluation of il 10 levels in patients diagnosed with chronic hepatitis

Müge Ozguler[1], H.handan Akbulut[2], Ayhan Akbulut[3]

Elazıg Training and Education Hospital Infectious Diseases and Clinical Microbiology Elazıg-Turkey[1], Fırat University Medical Faculty Immunology Elazıg-Turkey[2], Fırat University Medical Faculty Infectious Diseases and Clinical Microbiology Elazıg-Turkey[3]

Objective: One of the most important steps playing a role in chronic hepatitis B pathogenesis is cytokine discharge and one of cytokines with anti-inflammatory characteristic is interleukin 10. In the present study, it was aimed to examine interleukin 10 levels in patients with chronic hepatitis B.
Material-methods: Sixty three patients, who have not received any antiviral treatment with chronic hepatitis B disease were included in the study. Serum IL-10 level was investigated by enzyme-linked immunosorbent assay (ELISA) method. In control group, 25 healthy individuals with similar age mean to patient population were included. Control and patient groups were compared and data were statistically analyzed.
Results: IL-10 levels of 25 patients with HBV DNA levels between 2000-20000 IU/ml were compared with those of 25 subjects in the control group, and the level in chronic hepatitis B group was determined statistically significantly higher ($P < 0.05$). IL-10 levels of 38 patients with HBV DNA > 20000 IU/ml were statistically significantly higher than those in the control group. When chronic hepatitis B patients were compared among themselves, it was determined that IL-10 levels were increased as HBV DNA levels were increased. Also when IL-10 levels of HBeAg positive patients were compared with those of negative patients, statistically insignificant decrease was observed.
Conclusion: It is believed that decreasing IL-10 levels by various methods would have significant contributions in disease progression and treatment. Moreover, IL-10 level may be an important marker in HBeAg seroconversion and evaluation of treatment response.

Topic 11: Hepatitis B

No: 1741

Liver biopsy results in HBeAg negative chronic HBV patients with normal alt levels and HBV viral load between 10.000 and 100.000 copy ml

Emin Altiparmak[1], Selim Demirci[1], Ahmet Yozgat[1], Murat Aliyazicioglu[1], Ersan Ozaslan[1], Tankut Koseoglu[1], Ahmet Teoman Erten[1], Faruk Cetin[1], Enver Uner[1], Akif Altınbas[1]

Ankara Numune Education and Research Hospital Gastroenterology Ankara-Turkey[1]

Introduction: Prevalence of HBV infection varied from 0.7 to 9.9 % from west to eastern region of Turkey. Anti-viral medication is still started base on liver biopsy results world wide. However, it is still dilemma whether the chronic HBV patients with normal ALT lower than 100.000 copy/mL should undergo liver biopsy. Therefore, we aimed to investigate the liver biopsy results of these patients, in what ratio of our patients were eligible for HBV therapy based on the current guidelines.
Material-method: Totally 89 patients, over 18 years old, with the diagnosis of HBeAg negative chronic HBV within normal ALT levels, but HBV DNA value greater than 10.000 copy/mL and lower than 100.000 copy/mL undergoing liver biopsy were included into the study, retrospectively. None of the patients had evidence of cirrhosis.
Results: The mean age was 45.9 ± 12.1 and 53.9 % of were male. The laboratory investigation revealed as: mean ALT 21.6 ± 6.9 IU/L, AST 20.9 ± 5.1 IU/L, platelet 223.237 ± 62.500 ×109/L. According to the hystopathologic examinations of the liver biopsies by using ISHAK scoring system: 73 % of HBV patients had HAI value lower than 6 points, and the rest were greater; however, 36 % of them had fibrosis value ≥ 2 points. Only three of our patients had 4 points for presence of fibrosis based on liver biopsy.
Discussion: According to our treatment rules of health ministry for chronic HBV infections, only ones have ≥ 2 fibrosis levels and/or ≥ 6 points of HAI can take anti-viral drugs. So, 36 % and 4.4 % of our patients underwent HBV treatments due to fibrosis and HAI values, respectively.

Topic 11: Hepatitis B

No: 1989

Evaluation of chronic hepatitis B patients's clinic variability on follow up

Alpay Ari[1], S.ayten Coskuner[1], Ebru Dik[1], Meltem Zencir[1], Irem Altaş[1], Asli Keles[1], Ummugulsum Altin[1], Sebnem Calik[1], Selma Tosun[1]

Izmir Bozyaka Teaching and Research Hospital Infectious Disease and Clinical Microbiology Izmir-Turkey[1]

Aim: To evaluation of chronic hepatitis B patients's clinic variability on follow up.
Methods: Patients who were admitted to Infectious Disease Clinic since June 2007 that the date of HBV DNA PCR test became available were evaluated. Patients with HCV, HIV, delta coinfections, decompensation symptoms and admittance less than two times in a year were excluded. Patients categorized according to their initial and the end of HBV DNA and ALT levels as inactive carrier group (G1), normal ALT with high HBV DNA group(G2), high ALT and low HBV DNA group (G3) and high ALT with high HBV DNA group (G4) and cirhosis group (G5). HBV DNA values above 10000 copies/ml and ALT values above 40 U/L were considered high.
Results: Sixtyfive of 928 included patients were had HBeAg positivite and mean follow up time was 39 ± 22 mounts. At the beginning of the follow up 569 (%61,3), 134 (%14,4), 78 (%8,4), 140 (%15), and 7 (% 0,75) patients were considered in G1, G2,G3,G4 and G5 respectively, Pegileinterferons, oral antivirals and preemptive oral antivirals in immunsupressive situations were given to the 16, 113 and 14 patients respectively. HBsAg loss was seen %3.6 of patients. Serious complications of chronic hepatitis B infection such as cirrhosis (%0.75) and HCC (% 0.1) were seen relatively rare in this group, clinic courses of disease had shown broad spectrum from HBsAg loss (%3.7) to activation of disease (%2.9).
Conclusion: Patients with chronic hepatitis B have to be closely monitored clinical variability in follow up.

Topic 11: Hepatitis B

No: 2062

Long term risk factors of mortality in hepatitis B virus related decompensated cirrhosis on lamivudine entecavir and tenofovir therapy in real life clinical practice a multicentre retrospective study

Mehmet Demir[1], Seyfettin Köklü[2], Yaşar Tuna[3], Murat Taner Gülşen[4], Aydın Şeref Köksal[5], Muhammet Cem Kaçkar[6], Cem Aygün[7], Şahin Çoban[8], Kamil Özdil[9], Huseyin Ataseven[10], Ebru Akın[11], Tuğrul Pürnak[12], Ilhami Yüksel[13], Hilmi Ataseven[14], Mehmet Ibiş[15], Beytullah Yıldırım[16], Işılay Nadir[17], Metin Küçükazman (uzman)[18], Erdem Akbal[19], Osman Yüksel[8], Ömer Başer[3], Erhan Alkan[3], Özlem Baykal[20]

Mustafa Kemal Üniversity Gastroenterology Hatay-Turkey[1], Hacettepe Üniversity Gastroenterology Ankara-Turkey[2], Akdeniz University Gastroenterology Antalya-Turkey[3], Gaziantep University Gastroenterology Gaziantep-Turkey[4], Yuksek Ihtisas Hospital Gastroenterology Ankara-Turkey[5], Süleyman Demirel University Gastroenterology Isparta-Turkey[6], Fırat University Gastroenterology Elazig-Turkey[7], Dıs Kapı Education and Research Hospital Gastroenterology Ankara-Turkey[8], Umraniye Education and Research Hospital Gastroenterology Istanbul-Turkey[9], Selcuk University Gastroenterology Konya-Turkey[10] Ataturk Education and Research Hospital Gastroenterology Ankara-Turkey[11] Numune Education and Research Hospital Gastroenterology Ankara-Turkey[12] Etlik Education and Research Hospital Gastroenterology Ankara-Turkey[13] Cumhuriyet University Gastroenterology Sivas-Turkey[14] Gazi University Gastroenterology Ankara-Turkey[15] Ondokuz Mayıs University Gastroenterology Samsun-Turkey[16] Fatih University Gastroenterology Ankara-Turkey[17] Keçiören Education and Research Hospital Gastroenterology Ankara-Turkey[18] Ankara Education and Research Hospital Gastroenterology Ankara-Turkey[19] Süleyman Demirel Universit Gastroenterology Isparta-Turkey[20]

Background: The aim of this study was to determine the risk factors of mortality in patient with hepatitis B virus related decompensated cirrhosis on lamivudine, entecavir and tenofovir therapy in real-life clinical practice.
Methods: We performed a retrospective analysis of data from 137 adult patients with chronic HBV infection who were diagnosed with cirrhosis, beginning in 2005, at 18 centers throughout Turkey. We collected data on patient demographics and baseline characteristics.
Results: The study included 137 patients with hepatitis B virus related decompensated cirrhosis (age: 57 ± 8 years; 66 % male). Mean follow-up duration was 32.3 ± 14.7 months. Fourty-eight patients received lamivudin, 45 patients received tenofovir and 44 patients received entecavir. Levels of HBV DNA < 50 IU/ml were achieved in 79, 93, and 93 % of patients receiving lamivudine, tenofovir or, entecavir, respectively. Twenty-nine (21 %) patients died. Univariate analysis showed that higher age, history of variceal bleeding, lamivudine treatment, hyponatremia (Na < 125 mEq/L), serum creatinine > 1 mg/dl, total bilirubin > 3 mg/dl, platelets count < 100 000/mm3, detectable HBVDNA, CTP score > 10 and MELD score > 20 score were risk factors for mortality. In multivariate analysis, hyponatremia (Na < 125 mEq/L), detectable HBVDNA, CTP score > 10 and MELD score > 20 score were significantly associated with long-term mortality.
Conclusion: These data suggest that the baseline hyponatremia, CTP score, MELD score and detectable HBVDNA when under antiviral treatment were significant risk factors of long-term mortality.

Topic 11: Hepatitis B

No: 1238

Efficacy and safety of telbivudine and entecavir for HBeAg positive chronic hepatitis B

Xiaomei Wang[1], Baijun Li[1], Mingxiang Zhang[1]

The Sixth Hospital of Shenyang Gastroenterology Shenyang-China[1]

Aim: To retrospectively analyze the efficacy and safety of telbivudine and entecavir in patients with previously untreated HBeAg-positive chronic hepatitis B.
Methods: A retrospective collection of HBeAg-positive chronic hepatitis B untreated patients in our hospital was conducted between 2010 to 2012, treated by either telbivudine or entecavir. Among them, 62 cases were enrolled in LDT group (48 males), with an average age of 45.9 ± 10.7 years old; their HBV DNA is 5.8 ± 1.1 l og10 copies/ml, and ALT level is 83.6 ± 66.5U/L. The telbivudine group was treated with telbivudine tablets (Sebivo, Beijing Novartis Pharmaceutical Co., Ltd.), once per day, 600 mg each time, for continuous 72 weeks. For ETV group, there were 66 patients (42 males), with an average age of 45.9 ± 7.9, HBVDNA3.8 ± 0.9log10copies/ml, ALT level was 75 ± 59.8U/L. Patients in entecavir group will be treated with entecavir tablet (Baraclude, Sino-American Shanghai Squibb Pharmaceuticals Ltd.), 0.5 mg/day, for continuous 72 weeks.
Results: For anti-virus effects, HBVDNA negative conversion at 12 weeks, 24 weeks in LDT group is higher than ETV group (43.5 vs 25.8 %, $P < 0.05$; 75.8 vs54.5 %, $P < 0.05$), however, at 72 weeks, both two groups have no significant different (79 vs 83.3 %, $p > 0.05$). For HBeAg seroconversion effects, the conversion incidence has no significant difference at 12 and 24 weeks of treatment (6.4 vs 6.1 % $P > 0.05$ at 12 weeks; 14.5 vs 10.5 %, $P > 0.05$ at 24 weeks), whereas telbivudine treatment has higher seroconversion indicence than entecavir treatment group when treated for 72 weeks (35.5 vs 22.7 %, $P < 0.05$). For biochemical response, ALT normalization rate in both groups at each timepoint has nonstatistical.

Topic 11: Hepatitis B

No: 1835

Off therapy durability of response to telbivudine therapy in chronic hepatitis B patient in Bangladesh

Mohammad Izazul Hoque[1], Abdur Rob Sarkar[2], Arup Kumar Roy[2]

Comilla Medical College Hepatology Comilla-Bangladesh[1], Comilla Medical College Gastroenterology Comilla-Bangladesh[2]

Background: Telbivudine is a potent oral antiviral agent and induces rapid inhibition of hepatitis B virus (HBV) DNA replication and high rate of HBeAg seroconversion. Data on durability of efficacy following Telbivudine off-treatment is limited. The aims of the study was to analyze the sustained off-treatment response of Telbivudine.
Methods: This prospective study was done in the department of Gastroenterology and Hepatology, Comilla medical college, Bangladesh from July 2010 to December 2013 after approval from institutional ethical committee. 42 patients of CHB with normalised ALT, undetectable HBV DNA and HBeAg seroconversion who got telbivudine therapy for at least 48 weeks were included in the study. Patients were followed at 6 months interval for one year for virological (Serum HBV DNA > 2000 IU/ml) and clinical relapse (serum

HBV DNA > 2000 IU/ml and ALT > 2 × ULN). Clinical assessment, ALT, HBsAg, HBeAg, Anti HBe, HBV DNA and abdominal ultrasonography were done in each visit.
Result: Among 42 patient 30 (71 %) were male, 12 (29 %) were female. At 24 and 48 weeks of Telbivudine off-treatment, 42 and 39 patients were evaluated respectively. During follow up no patient developed decompansation or HCC. Virological relapse and Clinical relapse found in 16(38 %) and 11(25 %) patient respectively at 24 weeks. 24(62 %) and 15(38 %) patient out of 39 patients experienced virological and clinical relapse respectively at 48 weeks. HBeAg reversion found in 1 out of 9 patient at 48 weeks. No patient experienced HBsAg seroconversion during the follow up.
Conclusion: Most CHB patient maintained telbivudine-induced sustained response and sustained HBeAg seroconversion.

Topic 11: Hepatitis B

No: 1401

Influence of tenofovir on the renal functions in the treatment of hbv infection

Murat Aladag[1], Yilmaz Bilgic[1], Murat Harputluoglu[1], Yahya Atayan[1], Yasir Furkan Cagin[1], Mehmet Ali Erdoğan[2], Oğuzhan Yildirim[2], Yuksel Seckin[2], Melih Karincaoglu[2]

Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[1], Inonu University Gastroenterology Malatya-[2]

Aim: The present study aimed to evaluate renal functions in the cases that received tenofovir.
Material and method: A total of 255 cases [85 females and 170 males with a mean age of 43 (18-84) years] that received tenofovir therapy were evaluated. Cases that had received therapy for shorter than six months were not enrolled in the study. Regular renal function monitoring included urea and creatinine levels, and glomerular filtration rate (GFR) was calculated using CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula. An increase in creatinine level higher than 0.5 mg/dl or decrease in GFR below 50 mL/min was defined as renal function involvement.
Results: The study comprised 255 cases that fulfilled the criteria. of the cases, 170 were male and 85 were female. The mean duration of treatment was 44 (6-64) months. The mean GFR remained over 50 ml/min over the course of study period; although GFR decreased under 50 ml/min in the second year of treatment in three elder patients with comorbid diabetes mellitus. None of the patients developed renal function impairment that requires discontinuation of treatment. Comparing 12th, 24th and 36th-month urea, creatinine and GFR levels of the patients, no statistically significant difference was observed.
Conclusion: As with all antiviral agents, tenofovir as well may display nephrotoxic effect by causing tubular injury; however, such an injury was not determined in any of the cases in our clinic. It was concluded that, close monitoring of renal functions during treatment is necessary for both the course of treatment and patients' health in the elder patients with comorbidities.

Topic 11: Hepatitis B

No: 1703

Can early viral response at 1 month predict complete viral response at 1 year in patients with chronic hepatitis B treated with tenoforvir disproxil fumarate

Soo Hyung Ryu[1], Sung Won Park[1], Dae Young Kim[1], Yun Ho Lee[1], Song I Bae[1], Won Jae Yoon[1], Jin Nam Kim[1], You Sun Kim[1], Jeong Seop Moon[1]

Seoul Paik Hospital, Inje University College of Medicine Department of Internal Medicine Seoul-Korea, South[1]

Background and aims: Tenofovir disoproxil fumarate (TDF) induces significant virological and biochemical responses in early periods. However, it is unclear whether this early viral response (EVR) at 1 month can predict complete viral response (CVR) at 1 year in patients with chronic hepatitis B (CHB) treated with TDF.
Patients and methods: We retrospectively analyzed clinical and laboratory data of 40 patients (16 chronic hepatitis and 24 liver cirrhosis; 26 male and 14 female; mean age 50.7 years; 22 HBeAg positive and 18 HBeAg negative) treated with TDF 300 mg once daily therapy for over at least 12 months (median 18 months; range 12-22 months). EVR at 1 month was defined as HBV-DNA < 2,000 copies/mL or more than 4 log HBV DNA decrease and CVR at 1 year was defined as under 50 copies/mL of HBV DNA (the detection limit of real time PCR assay of HBV DNA).
Results: Baseline ALT and HBV DNA levels were 108 (range; 33-740) IU/L and 2.4 × 6 log HBV DNA (range; 3.4 × 4 log −2.8 × 9 log) copies/mL, respectively. The cumulative HBV DNA loss (< 50 copies/mL) rates at 6 months, 12 months, and 18 months were 42.5, 67.5, and 75.0 %, respectively. EVR at 1 month were noted in 19 patients, among them, 17 patients achieved CVR at 1 year. In other hands, of 21 patients without EVR at 1 month, only 12 patients acquired CVR at 1 year ($P = 0.025$).
Conclusions: EVR at 1 month can predict CVR at 1 year during TDF treatment in CHB patients.

Topic 11: Hepatitis B

No: 1509

Influence of entecavir on hepatic function of chronic hepatitis B for the first 12 weeks

Mingxing Huang[1], Zongping Han[2]

The Fifth Affiliated Hospital of Sun Yat-sen University Department of Infectious Disease Zhuhai-China[1], The Fifth Affiliated Hospital of Sun Yat-sen University Department of Geriatrics Zhuhai-China[2]

Objective: To investigate the influence of entecavir on hepatic function chronic hepatitis B for the first 12 weeks.
Methods: A total of 60 patients treated with entecavir and hepatinica (Group A: 38 cases) 0.5 mg qd and only hepatinica (Group B 22 cases) were determined by Alanine aminotransferase(ALT),Aspartate aminotransferase (AST) and HBV DNA levels before and after 4, 8, 12 weeks.
Results: Symptom and objective sign in both groups patients were fundamental relief and showed no significant (P > 0.05). The ALT of Group A showed great higher than Group B at 4 weeks ($P < 0.01$),while the ALT of Group A showed great significant lower than Group B at 12 weeks($P < 0.05$),the rebound rate of ALT and AST in Group A were increased prominently and showed great significant higher than Group B at 4 weeks($P < 0.01$).O1),HBV DNA level in Group A showed great significant lower than Group B at 4,8,12 weeks ($P < 0.01$).
Conclusion: Entecavir may have short fluctuation in ALT and AST in the patients with chronic hepatitis B at the first three months.

Topic 11: Hepatitis B

No: 1760

Evaluation of the effect of telbivudine therapy on renal functions in patient with chronic hepatitis B

Cemal Bulut[1], Nesrin Ata[1], Çiğdem Ataman Hatipoğlu[1], Esra Kaya Kılıç[1], Sami Kınıklı[1], Ali Pekcan Demiröz[1]

Ankara Training and Research Hospital Infectious Diseases and Clinical Microbiology Ankara-Turkey[1]

Objectives: Telbivudine is a new antiviral that provides effective and sustained viral suppression in patients with compensated chronic hepatitis B infection. Currently available five oral antiviral agents are all primarily eliminated through renal route. Unlike other nucleotide and nucleoside analogues, renal toxicity is uncommon in telbivudine. In addition, some recent trials reported that telbivudine therapy was also associated with a significant improvement in eGFR levels of patients. In this study we aimed to evaluate the renal functions of patients with CHB during telbivudine therapy.
Methods: One hundred seventy-three CHB patients on telbivudine therapy were followed in our clinic between January 2012 and October 2014. Among them Patients with 15 month of duration of therapy were included to the study. All patients were followed up at 3 months interval. Serum creatinin levels and eGFR were recorded. eGFR was calculated according to CKD-EPI formula. SPSS 15.0 was used for statistical analysis.
Results: Total 79 patients (40 male and 39 female) were included to the study. Mean age of patients was 39.8 $\pm$ 11.3 year (18-64 years). Mean duration of therapy was 24 month (16-32 month). Mean serum creatinin and eGFR values were 0.96 mg/dl and 89.17 mL/min/1.73m2. Serum creatinin and eGFR values were shown in graph.1. When first and last serum creatinin and eGFR values were compared statistically significant improvement were detected in both last values ($P = 0.000$ and $P = 0.006$ respectively).
Conclusion: I n our study group telbivudine therapy was associated with an improvement of renal function. Further comprehensive studies are needed to establish mechanism of telbivudine in renal function improvement.

Topic 11: Hepatitis B

No: 1764

Liver biopsy in hepatitis cases blinded or ultrasonography guided

Husnu Pullukcu[1], Erkan Kismali[2], Tansu Yamazhan[1], Meltem Tasbakan[1], Oguz Resat Sipahi[1], Sercan Ulusoy[1]

Ege Utf Infectious Diseases Izmir-Turkey[1], Ege Utf Radiology Izmir-Turkey[2]

Aim: Despite developments in the diagnostic methods liver biopsy is still the golden standard in the evaluation of liver histology. In this retrospective study we evaluated our liver biopsy cohort in terms of side effects and complications.
Materials and method: Clinical and demographic data of the cases who were performed liver biopsy between 2009-14 were entered into SPSS 13 program. Chi square test performed for comparisons and a p value of < 0.05 was considered as significant.
Results: A total of 430 cases (156 female, 274 male, aged 44.30 $\pm$ 13.33 (Min: 18–max: 72) who were performed liver biopsy between 2008-14 were included in the study. 185 cases were performed blinded biopsy whereas others were performed ultrasonography guided biopsy. Twenty-four cases were performed two biopsies the first blinded and the second ultrasonography guided. Evaluation of the groups in terms of side effect/complication and pain are in table 1. Severe pain, inadequate portal space and any unintended result was significantly more in blinded biopsy.
Conclusion: Despite the disadvantages of requiring ultrasonography and experienced radiologist, ultrasonography guided biopsy is an easier intervention. Patient comfort and pathologic material seems to be better in ultrasonography guided biopsy.

Topic 11: Hepatitis B

No: 1682

Comparison of the efficacy of tenofovir and entecavir for the treatment of nucleos(t)ide naive chronic hepatitis B patients

Nesrin Turker[1], Bahar Ormen[1], Tuna Demirdal[1], Pınar Ozdemir Sen[1], Sevinc Arslan[1], Serap Ural[1], Ilknur Vardar[1]

Izmir Katip Celebi University Ataturk Training and Research Hospital Department of Infectious Diseases and Clinical Microbiology Izmir-Turkey[1]

Aim: In this study we evaluated the treatment response of 85 treatment naive chronic hepatitis B (CHB) patients treated with either tenofovir disoproxil fumarate or entecavir at our clinic and compared their efficiencies.
Materials and methods: This retrospective study enrolled 62 patients treated with tenofovir and 23 patients treated with entacavir at our clinic from January 2008 to September 2014. Sociodemographic data, biochemical and serological tests, biopsy scores at the initiation of the therapies were recorded. Hepatitis B serologic markers and HBV DNA levels were assessed every 12 weeks. Treatment outcomes of the two dugs were analyzed.
Results: The sociodemographic status and mean duration of the therapy were similar in two groups. Fifty six patients in tenofovir group and 20 patients in entecavir group were underwent percutaneous liver biopsy. Stage of fibrosis was $\geq$ 2 in 76,7 % of the tenofovir group and 73,9 % of the entecavir group. HBV DNA suppression ($<$ 20 IU/mL) at week 24, 48 and 96 in tenofovir group was 37 %, 82,2 % and 93,5 % respectively.. HBV DNA suppression at week 24, 48 and 96 in entecavir group was 34 %, 86,9 % and 95,6 %. HBeAg seroconversion was seen in 9 patients in tenofovir group and only one patient in entecavir group. HBsAg seroconversion was seen in only one patient in the entecavir group. No serious side effect was seen in both groups.
Conclusion: Both drugs are similar in terms of antiviral activity, side effects and compliance in naive CHB patients.

Topic 11: Hepatitis B

No: 1846

Partial virologic response does not translate into similar outcomes for lamivudine entecavir and tenofovir in treatment naive chronic hepatitis B patients

Ender Gunes Yegin[1], Osman Cavit Ozdogan[2]

Izmir Bozyaka State Hospital Gastroenterology Izmir-Turkey[1], Marmara University Faculty of Medicine Gastroenterology Istanbul-Turkey[2]

Aim: Partial virological response (PVR) definition was proposed due to its clinical relevance of higher risk of subsequent treatment failure, resulting in the recommendation to modify the regimen to enhance long-term outcomes. Whether this rationale can be applied to all nucleos(t)ide analogues (NA) is not clear. The aim of this study was to evaluate the long-term efficiencies of lamivudin (LAM), entecavir (ETV), and tenofovir (TDF) monotherapies in NA-naive CHB patients in routine clinical practice, and to analyze PVR influence on therapeutic outcomes.
Methods: We retrospectively studied 150 treatment-naive CHB patients receiving LAM, ETV or TDF monotherapies between February 2001 and July 2013.
Results: Sixty-nine LAM, 35 ETV, and 46 TDF patients, with a median duration of 19.5 (6-147) months treatment were analyzed. PVR at 24 weeks was encountered at similar rates among three NAs (LAM 33.3 %, ETV 35 %, TDF %32.4 %, $P = 0.981$). For all three NAs, patients with higher baseline viral load or HBeAg-positive status achieved less often PCR negativity by weeks 24 and 48. PVR at 24 weeks was the independent risk factor for VBR (HR: 3.09, 95 % CI 1.09-8.74, $P = 0.034$), while majority of ETV and TDF partial responders achieved and maintained VR with prolonged monotherapy, except only one ETV patient experienced VBR.
Conclusion: Management strategy for LAM treatment should include adaptation of regimen according to PVR as an on-treatment response parameter due to its relation with unacceptably high VBR probability. Similar conclusion should not be directly translated to high genetic barrier to resistance drugs, ETV and TDF.

Topic 11: Hepatitis B

No: 1873

Comparison of the efficacy of entecavir and tenofovir in treatment naïve chronic hepatitis B patients

Hyoung Su Kim[1], Joo Seop Kim[1], Ji Won Park[1], Sung Eun Kim[1], Ki Tae Suk[1], Myoung Kuk Jang[1], Sang Hoon Park[1], Dong Joon Kim[1], Myung Seok Lee[1], Choong Kee Park[1]

Hallym University Medical Center Digestive Disease Center Seoul-Korea, South[1]

Backgound/aims: There were limited studies directly comparing the efficacy of entecavir (ETV) and tenofovir disoproxil fumarate (TDF). This study was aimed to compare the efficacy of ETV and TDF in treatment-naïve chronic hepatitis B (CHB).
Method: A total of 345 treatment-naïve CHB patients were enrolled in a multicenter retrospective cohort; treated with ETV (n = 200) vs. TDF (n = 145) for 12 months.
Results: The study population was male dominant (63.5 %) with 46.9 ± 11.5 years. Thirty six percent (125/345) had cirrhosis and 58.8 % were positive for hepatitis B e antigen (HBeAg) at baseline. Hepatitis B virus (HBV) DNA and ALT levels were 6.64 ± 1.28 log10 IU/mL and 198.6 ± 318.4 IU/L, respectively. Two groups showed no difference in baseline characteristics. During the 12 months, HBV-DNA levels were similarly suppressed in both groups (ETV vs. TDF; -5.11 vs. -5.24 log10 IU/mL, $P = 0.582$). At month 12, both groups showed no difference in the complete virologic (CR), serologic and biochemical response. In multivariate analysis, HBV-DNA levels (RR, 0.458; 95 % CI, 0.315-0.664; $P < 0.001$) and HBeAg negativity (RR, 3.855; 95 % CI, 1.551-9.579; $P = 0.004$) were independent factors for CR. Even in HBeAg positive subgroup with a higher HBV-DNA levels (> 6 log10 IU/mL), the type of antivirals was not an independent factor for CR, although HBV-DNA levels were more strongly suppressed by TDF than ETV (ETV vs. TDF; −5.91 vs. −5.98 log10 IU/mL, $P = 0.025$).
Conclusion: Although TDF suppress more effectively HBV-DNA levels than ETV in HBeAg positive CHB with a higher HBV DNA,both ETV and TDF may show comparable antiviral efficacy in treatment naïve CHB during the first year.

Topic 11: Hepatitis B

No: 1380

The performance of CXCL9 and ip 10 in predicting virological response in patients with chronic hepatitis B undergoing peginterferon alfa 2A therapy

I-cheng Lee[1], Yi-hsiang Huang[1], Chien-wei Su[1], Yuan-jen Wang[2], Teh-ia Huo[1], Han-chieh Lin[1]

Taipei Veterans General Hospital Division of Gastroenterology Taipei-Taiwan[1], Taipei Veterans General Hospital Health Care Center Taipei-Taiwan[2]

Background & aims: Our recent pilot study showed a potential role of chemokine CXCL9 in predicting treatment response in chronic hepatitis B (CHB) patients. The aim of this study was to compare the performance of CXCL9 and IP-10 in predicting HBsAg decline and virological response (VR) at 6 months after the end of treatment (EOT) in CHB patients undergoing peginterferon alfa-2a (PegIFN) therapy.
Methods: Consecutive 68 CHB patients receiving PegIFN with available samples for testing serial HBsAg, CXCL9 and IP-10 levels were enrolled. VR was defined as HBeAg seroconversion combined with viral load < 2000 IU/mL in HBeAg-positive (n = 35), and viral load < 2000 IU/mL in HBeAg-negative patients (n = 33).
Results: Five (14.3 %) HBeAg-positive and 15 (45.5 %) HBeAg-negative patients achieved VR at 6 months after EOT. For prediction of VR, the area under the receiver operating characteristic curve of CXCL9 and IP-10 were 0.552 and 0.586, respectively, in HBeAg-positive patients; and 0.781 and 0.500, respectively, in HBeAg-negative patients. CXCL9 and IP-10 offered minimal effect on VR in HBeAg-positive patients, whereas in HBeAg-negative patients, baseline CXCL9 level, but not IP-10, significantly correlated with HBsAg decline at week 12 as well as VR at 6 months after EOT. Combining baseline CXCL9 level, HBV viral load, and on-treatment HBsAg decline at week 12 had good performance in predicting VR in HBeAg-negative patients (PPV = 85.7 %, NPV = 100 %).
Conclusions: In addition to baseline HBV viral load and on-treatment HBsAg decline, pre-treatment CXCL9 might serve as a useful marker to predict VR in HBeAg-negative CHB patients undergoing PegIFN therapy.

Topic 11: Hepatitis B

No: 1036

Efficacy and safety of tenofovir disoproxil fumarate + lamivudine combination in the treatment of chronic hepatitis B results of a cohort in an infectious diseases unit

Nassima Belabas[1], Achour Amrane[1], Mohamed Zeroual[1], Naima Ihaddadene[1], Abdelouhab Dif[1]

Laadi Flici (el-kettar) Hospital Infectious Diseases Department Algiers-Algeria[1]

Aims: To evaluate efficacy and safety of treatment with Tenofovir disoproxil fumarate (TDF) + lamivudine (3TC) in chronic hepatitis B (HBV).
Materials and methods: a retrospective study of patients with chronic hepatitis B CHB treated with TDF + 3TC for at least 06 months during (May 2010-April 2014) in an infectious diseases unit. The biological parameters studied: HBV DNA serum markers of HBV, alanine aminotransferase (ALT), serum calcium, phosphorus, creatinine clearance Cockcroft-Gault equation and liver stiffness (Fibroscan).
Results: Thirty-four adults were included, median age 44.5 years. Sex ratio = 3.57. TDF + 3TC were prescribed second line in (37.5 %). 75 % patients were infected with mutant HBV. At baseline, paraclinical parameters were: mean HBV DNA: 5.39. 106 IU/mL, median ALT: 40 IU/L, median creatinine clearance: 106 ml/min, median proteinuria: 0.075 g/24 h, median serum calcium: 95.5 mg/L and median serum phosphorus: 38 mg/mL. The mean liver stiffness was 10 kPa.The undetectable levels of HBV DNA (< 300 copies/ml) was noted at 6 months (M6) treatment (94 %) (n = 34), and (100 %) since M9 (n = 31) to M48 (n = 09). There is a HBsAg seroconversion and HBeAg seroconversion in (01 case) each. At M48, median ALT 26 IU/L, the mean loss of serum calcium.
18.3 mg/L ± 2.7, that of phosphorus: -3.4 mg/mL ± 7.8 and creatinine clearance: 0.22 ml/min ± 3.4. The median proteinuria: 0.15 g/24 h. The mean liver stiffness: 7.4 kPa. No stopping treatment because of secondary effect (s) was noted.
Conclusion: This study shows long period of virological control on TDF + 3TC with a good safety profile.

Topic 11: Hepatitis B

No: 2168

Use of non invasive tests to predict liver fibrosis in chronic hepatitis B

Murat Biyik[1], Ilker Polat[2], Sami Cifci[1], Ramazan Ucar[3], Ismail Baloglu[3], Mehmet Asil[1], Huseyin Ataseven[1], Ali Demir[1], Hakki Polat[3]

Necmettin Erbakan University Gastroenterology Konya-Turkey[1], Afyonkarahisar City Government Hospital Internal Medicine Afyon-Turkey[2], Necmettin Erbakan University Internal Medicine Konya-Turkey[3]

Introduction: Chronic hepatitis B infection is an important health issue around the world. Nowadays percutaneous liver biopsy is the golden standard to show the liver fibrosis. There has been a considerable rise in the number of non-invasive diagnosis tests to detect the phase of the fibrosis without the operation of biopsy because the liver biopsy is an invasive method. In this research our aim was to evaluate the efficiency of the several indirect indicators (AAR, APRI, Fibro-Q, CDS, API, FIB-4, Pohl score) of the liver fibrosis in CHB patients.
Material and method: In the research follow-up chronic hepatitis patients of was observed. The datas of the patients entered into the SPSS 15.0 and non-invasive markers (AAR, APRI, Fibro-Q, CDS, API, FIB-4, Pohl score) were calculated.
Result: A total number of 300 patients consisting of 132 women were considered in this research. Sensitivity, specificity and predictive values' percentage are shown by the 95 % percent confidence levels. In CHB's the detection of obvious fibrosis for the scores of AAR, APRI, Fibro-Q, CDS, API, FIB-4, Pohl score the area under the ROC curve are as follows: 0.602, 0.727, 0.78, 0.692, 0.77, 0.614, 0.773.The sensitivity/specificity values of AAR, APRI, Fibro-Q, CDS, API, FIB-4, are as follows (65%/57.5 %; 70 %/62 %; 75 %/75 %; 75 %/66 %; 75 %/76 %.)
Discussion: According to results of the research it was thought that the indexes of Fibro-Q, API, FIB-4 can be good indicators to detect the obvious fibrosis in CHB patients. But there is a need to make extensive researches to evaluate these non-invasive tests.

Topic 11: Hepatitis B

No: 1670

Effect of antiviral monotherapy on renal functions in chronic hepatitis B patients

Yusuf Kayar[1], Birol Baysal[1], Ahmet Danalioglu[1], Mukaddes Tozlu[1], Orhan Kocaman[1], Ali Tuzun Ince[1], Hakan Senturk[1]

Bezmialem Vakif University Gastroenterology Istanbul-Turkey[1]

Introduction: The nucleotide and nucleoside analogues are the antiviral agents used primarily in the treatment of chronic hepatitis B (HBV). Tenofovir induced nephrotoxicity was reported in patients with HBV and HIV co-infection in some previous studies. Nephrotoxicity due to tenofovir monotherapy in patients with HBV mono-infection is not clear yet.
Aim: In this study we examined the development of nephrotoxicity secondary to using antiviral agents.
Materials and methods: One-hundred and fifty six patients on antiviral treatment for HBV infection were included. Patients' age, gender, disease duration, duration of treatment and pre- and post-treatment creatinine levels were documented. Comparisons were made in terms of changes in creatinine levels between the groups.
Results: Of the patients. 64 were female (%41) and the mean age was 50,1(19-82). The number of patients under treatment of lamivudine, telbivudine, entecavir and tenofovir were 48, 29, 31 and 48 respectively. In total group, mean duration of the disease was 74,2 months (3-360) and mean duration of the treatment 21,7 months (3-120). Groups were similar in terms of age, gender, disease duration, initial creatinine levels and duration of treatment. In all patients, the mean pre-treatment level of creatinine was 0,78 mg/dL and post-treatment 0,76 mg/dL. There was no significant difference in the levels of creatinine between groups of lamivudine, telbivudine, entecavir and tenofovir.
Conclusion: In antiviral monotherapy of HBV, there is no difference between lamivudine, telbivudine, entecavir and tenofovir in terms of nephrotoxicity.

Topic 11: Hepatitis B

No: 1125

Hepatitis B and hepatitis C prevalence in patients with gastric adenocarcinoma

Burak Suvak[1], Ahmet Cumhur Dülger[1], Özgür Kemik[2], Enver Aytemiz[3], Mehmet Taşdemir[4]

Hepatology Yuzuncu Yıl University Van-Turkey[1], Surgical Oncology Yuzuncu Yıl University Van-Turkey[2], Internal Medicine Nizip State Hospital Gaziantep-Turkey[3], Internal Medicine Muş State Hospital Muş-Turkey[4]

Purpose: The presence of viral hepatit markers including HbS Ag and anti-HCV has been proposed as predictor of chemotherapy-related liver complications in patients with gastric adenocarcinoma. However, there are limited data on the prevalence of hepatitis B and hepatitis C in patients with gastric adenocarcinoma. We therefore conducted the current study to determine the prevalence of both hepatitis B and C in chemotheraphy candidates with gastric adenocarcinoma.
Materials and methods: 198 consecutive adult naive patients (70 female, mean age 61 ± 13.2) with gastric adenocarcinoma examined by ELISA device by Cobas 601 device (Roche, Germany). Results of hepatitis B antigen (HbS Ag) and anti-HCV antibody (anti- HCV) were recorded at SPSS. On the other hand, 1062 (560 female, mean age 48 ± 14.4) control subjects were tested for HbS Ag and anti-HCV by the same method.
Results: In cancer group, seven patients (3.5 %) had HBS Ag seropositivity and one (0.5 %) had anti-HCV seropositivity. In control group, 61 patients (5.7 %) tested positive for HBS. Five patients (0.6 %) had a positive result for anti-HCV. There were no statistical difference between control subjects and cancer group ($p > 0.005$).
Conclusion: These data highlight acceptably rates of hepatitis B and hepatitis C in patients with gastric adenocarcinoma. On the other hand, our region is considered as an intermediate endemic area for hepatitis B infection and have a low prevalence for hepatitis C. In the U.S. population, both of and HBV and HCV were not associated with gastric adenocarcinoma.

Topic 11: Hepatitis B

No: 1266

Kinetics of quantitative serum hbsag decline during seven years of nucleos(t)ide analogue therapy in chronic hepatitis B patients

Cheng-yuan Peng[1], Hsueh-chou Lai[1], Wen-pang Su[1], Chia-hsin Lin[1], Po-heng Chuang[1], Sheng-hung Chen[1]

China Medical University Hospital, Division of Hepatogastroenterology, Department of Internal Medicine, Taichung,-Taiwan[1]

Aim: To study the kinetics of quantitative HBsAg (qHBsAg) decline in treatment-naive chronic hepatitis B (CHB) patients receiving long-term nucleos(t)ide analogue (NA) therapy.
Methods: CHB patients receiving continuous NA therapy for over 7 years (Y) were enrolled. On-treatment serum ALT was monitored every 1-3 months (M) and serum qHBsAg (Abbott Architect HBsAg QT assay) and HBV DNA were monitored at baseline, 3, 6, 12 M and annually thereafter during treatment.
Results: Seventy (39 HBeAg-positive and 31 HBeAg-negative) patients received NA therapy (ETV: 41, ADV: 13, LAM- > ETV: 16) for a mean duration of 98.0 ± 14.0 M. The on-treatment undetectable HBV DNA (< 60 IU/mL) and HBeAg loss/seroconversion rates were 90, 94.3, 97.1, 98.6 and 100 %, and 20.5 %/5.1 %, 30.8 %/10.3 %, 41 %/10.3 %, 46.2 %/10.3 %, and 53.8 %/15.4 % at 3 through 7Y, respectively. At each time point, the qHBsAg levels were significantly higher in HBeAg-positive patients than HBeAg-negative patients. The mean annual qHBsAg decline over 7Y was 0.108 log IU/mL (HBeAg-positive: 0.096 versus HBeAg-negative: 0.12). The median decline was significant from baseline-to-3 M, 4Y-to-5Y, 5Y-to-6Y, and 6Y-to-7Y for both HBeAg-positive and -negative patients. One HBeAg-positive patient lost HBsAg at 90 M of therapy. The independent predictor for achieving qHBsAg level < 200 IU/mL at 7Y (n = 16) was either baseline qHBsAg < 1000 IU/mL or a decline from baseline in qHBsAg > 1.0 log IU/mL at 3 M of therapy (OR: 6.981, 95 % CI: 1.573-30.983, $P = 0.0106$).
Conclusion: qHBsAg levels decline significantly early after starting therapy and at 4 through 7Y of therapy. Low baseline qHBsAg levels or rapid decline from baseline at 3 M of therapy predicts HBsAg levels below 200 IU/mL at the end of 7Y.

Topic 11: Hepatitis B

No: 1638

A follow up study on the efficacy of telbivudine for hepatitis B virus infected Taiwanese patients after living donor liver transplantation

Kuo-hua Lin[1], Ping-yi Lin[2], Chih-jan Ko[1], Chia-en Hsieh[1], Yao-li Chen[1]

Changhua Christian Hospital Department of General Surgery Changhua-Taiwan[1], Changhua Christian Hospital Transplant Medicine & Surgery Research Centre Changhua-Taiwan[2]

Aim: The purpose of this study is to examine the safety and/or efficacy of telbivudine in hepatitis B virus (HBV) infected patients after living donor liver transplantation (LDLT).
Method: This was a cross-sectional retrospective study. Patients who had received LDLT, 4 weeks before screening visit and with documented chronic hepatitis B virus infection were enrolled. HBV DNA levels were monitored at week-24 of treatment. For patients with detectable HBV DNA after 24 weeks of therapy, treatment modification should be considered. HBV DNA was monitored every 6 months to assure continued response.
Results: During the study period, 18 patients (mean age, 55.52 years; range, 40-68 years) received telbivudine and 23 patients received entecavir after LDLT. Mean eGFR were significantly higher in telbivudine group than entecavir group at 9 month (85.66 mL/min vs. 66.69 mL/min; $P < 0.05$; Figure 1) and 12 month (88.87 mL/min vs. 66.18 mL/min; $P < 0.05$). The mean levels of creatinine were significantly lower in the telbivudine group at month 12 as shown in figure 1. AST, ALT, and FK-506 levels were comparable between groups.
Conclusion: In this study, we measured renal function and clinical parameters in 18 patients received telbivudine after LDLT. Serial changes of eGFR and creatinine levels in patients were demonstrated. With this preliminary finding, we suggest that it is essential to conduct a further study to clarify the mechanisms of telbivudine in renal function.

Topic 11: Hepatitis B

No: 1443

Hepatitis B prevalence among Syrian immigrants in Turkey

Ahmet Cumhur Dülger[1], Bülent Çolak[2], Mustafa Sağcan[3], Kürşat Türkdoğan[4], Çetin Kotan[5]

Yuzuncuyil University Faculty of Medicine Hepatology Van-Turkey[1], Kilis State Hospital Gastroenterology Kilis-Turkey[2], Kilis State Hospital Internal Medicine Kilis-Turkey[3], Bezmi Alem University Faculty of Medicine Gastroenterology Istanbul-Turkey[4], Yuzuncuyil University Faculty of Medicine General Surgery Van-Turkey[5]

Abstract body: According to the World Health Organization, of the estimated 400 million persons infected with HBV worldwide. Prevalence in the general Turkish population is close to 4 %, but data in Syrian refugees is limited. Our goal was to examine HBV prevalence in Syrian refugees who resident in the Syrian border of Turkey, city of Kilis.
Methods: A total of 251 consecutive Syrian refugee patients (130 female; aged 18-75 years) were seen from September 2013 to October 2014 and were studied via individual chart reviewed using a case report form. HBV infection was defined by positive hepatitis B surface antigen (HBs Ag) or HBV DNA PCR. Control subjects were selected from patients seeking primary care at gastroenterology clinic of Yuzuncuyil university in Van city, where located in the Iranian border of Turkey.
Results: Of these 251 patients, 28 patients (11.1 %; 13 female) had positive HBs Ag. of the 1062 screened control subjects (550 female), 61 (5.7 %; 31 female) patients tested positive for HBs antigen. There were no statistically significant differences in regards to age and sex profile between refugees vs. control subjects. There was a statistically significant difference between Syrian immigrants and control subjects in terms of HBs antigen seropositivity ($P < 0.005$).
Conclusions: In the current study, HBV prevalence in Syrian refugees seeking routine primary care was 11.1 %, which was over double the prevalence for native Turkish citizens at 5.7 %. Syrian immigrants should be screened for hepatitis B infection promptly.

Topic 11: Hepatitis B

No: 1337

An observational study to compare the estimated glomerular filtration rate of telbivudine in chronic hepatitis B patients with or without cirrhosis 2 year follow up data

Ming-shun Wu[1], Fat-moon Suk[1], Gi-shih Lien[1]

Wan Fang Hospital Department of Internal Medicine Taipei-Taiwan[1]

Aim: Effectiveness of traditional therapies for chronic hepatitis B (CHB) with cirrhosis, such as tenofovir, is often limited by side effects of nephrotoxicity and deteriorated renal function. This prospective cohort study assessed the estimated glomerular filtration rate (eGFR) of telbivudine therapy in CHB patients under daily practice setting.
Method: Adult CHB patients with/without liver cirrhosis received 600 mg telbivudine per reimbursement guidelines. The primary and secondary endpoints were change from baseline in serum hepatitis B virus (HBV) DNA and eGFR rates, respectively, assessed at weeks 52 and 104 of treatment.
Results: Of the 64 patients eligible for the analysis, including 20 cirrhotic and 44 noncirrhotic patients, only 18 met the super-responder criteria. Treatment was switched to entecavir 0.5 mg daily in 4 of 5 patients reporting muscle pain. HBV DNA was undetectable in 78.1 % and 87.5 % patients at weeks 52 and 104, respectively. The eGFR improved from 95.3 ± 34.4 mL/min/1.73 m[SUP]2[/SUP] at baseline to 98.57 ± 29.4 mL/min/1.73 m[SUP]2[/SUP] at week 104 in cirrhotic patients. In noncirrhotic patients, eGFR improved from 102.2 ± 37.1 mL/min/1.73 m[SUP]2[/SUP] at baseline to 123.22 ± 45.6 mL/min/1.73 m[SUP]2[/SUP] at week 104. Despite virologic breakthrough in 9 patients, eGFR improved from baseline (94.17 mL/min/1.73 m[SUP]2[/SUP]) to week 104 (102.8 mL/min/1.73 m[SUP]2[/SUP]) after add-on therapy with adefovir.
Conclusion: Irrespective of super-responder status, 1-year telbivudine treatment exhibited effectively controlled antiviral response in nearly 80 % CHB patients. Additionally, eGFR levels improved in both cirrhotic and noncirrhotic patients along with patients receiving telbivudine and adefovir combination treatment for 2 years.

Topic 11: Hepatitis B

No: 1903

Analyzing the mutation pattern of multi drug resistant hepatitis B virus during entecavir rescue therapy

Bora Jin[1], Young Eun Chon[2], Beom Kyung Kim[2], Seung Up Kim[2], Jun Yong Park[2], Do Young Kim[2], Kwang-hyub Han[1], Seungtaek Kim[2], Sang Hoon Ahn[1]

Yonsei University College of Medicine Brain Korea 21 Plus Project For Medical Science Seoul-Korea, South[1], Yonsei University College of Medicine Institute of Gastroenterology, Department of Internal Medicine Seoul-Korea, South[2]

Background and aims: Analyzing the mutation pattern of multi-drug resistance is important in treatment of CHB. However, evolution pattern of multi-drug resistant during ETV rescue therapy has been rarely studied
Methods: Eight CHB patients with LAM- and ADV-resistant mutations showing partial virological response to ETV and subsequent ETV + ADV therapy were enrolled. Mutation pattern was investigated. Direct sequencing, multiplex RFMP, and clonal analysis were compared for clinical decision of antiviral therapy. The binding affinity of TDF was investigated by molecular modeling.
Results: LAM- and ETV-resistant mutations increased but ADV-resistant mutations slightly decreased at the end of ETV therapy. LAM- and ADV-resistant mutation increased but ETV-resistant mutations decreased at 12 month of ETV + ADV therapy. All mutations detected by direct sequencing revealed identical results in the respective analyses by clonal analysis and multiplex RFMP. Clonal analysis detected 85.7 % mutations which RFMP did not. However, none of the mutations exceeding 40 % of total clones by clonal analysis were missed by multiplex RFMP. The binding affinities of TDF with rtM204 V/I + rtA181T/V mutant or rtM204 V/I + rtN236T mutant were both strong, but the latter showed minutely decreased affinity due to rtN236T.
Conclusions: The clonal evolution of multi-drug resistant HBV revealed the selection of LAM-resistant (± ETV-resistant) HBV during ETV rescue therapy, and the main reason for suboptimal response might be LAM-resistance (± ETVresistance) which predominated over ADV resistance. Multiplex RFMP showed high sensitivity for detecting LAM resistant(± ETV-resistant) mutations. The potent drug TDF showed strong binding affinity in multi-drug resistant HBV regardless of their co-location.

Topic 11: Hepatitis B

No: 1898

Can mean platelet volume predict hbv dna negativity in patients on antiviral treatment for chronic hepatitis B

Zeynal Dogan[1], Murat Kekilli[1]

Ankara Education and Research Hospital Gastroenterology Ankara-Turkey[1]

Objective: Patients with chronic hepatitis B (CHB) infection are still at an increased risk for developing cirrhosis and hepatocellular carcinoma (HCC) in the world. The targets of treatment with nucleos(t)id analogues in patients with CHB are suppressing inflammation and decreasing hepatitis B related conditions such as cirrhosis, ascites, variceal bleeding, encephalopathy and HCC. Decreasing serum HBV DNA levels indicate the success of treatment in patients with CHB. Mean platelet volume (MPV) is known as a sign of inflammation. In this study, we want to evaluate whether MPV values will decrease by suppressing of hepatitis B virus infection with nucleos(t)ids at the time of HBV DNA negativity.
Methods: A total of 99 patients with CHB infection who were on antiviral treatment were recruited in the study. There were 47 male and 52 female. The mean age was 52.67 ± 11.95. Complete blood test, MPV and other laboratory tests were reviewed before antiviral treatment. Patients were on treatment with tenofovir or entecavir or lamivudine. Fibrosis scores were between 1 and 3. The mean HBV DNA was 6.43 ± 1.37 logcopy/mL. Baseline characteristics of patients before antiviral treatment are seen in Table 1. MPV and other laboratory features were noted at the time of achieving HBV DNA negativity. The mean time for achieving HBV DNA negativity was 18.60 ± 1.13 month.
Results: The MPV values were significantly lower at the time of achieving HBV DNA negativity than before treatment values ($P < 0.001$) (Table 2).
Conclusion: Our results suggest that MPV may predict HBV DNA negativity in patients on antiviral treatment.

Topic 11: Hepatitis B

No: 1009

Comparison of telbivudine and entecavir treatment of nucleoside analogues naïve chronic hepatitis B for 144 weeks

Chaoyu Xu[1], Zongping Han[2], Yujia Zhu[1]

The Eighth Affiliated Hospital of Guangxi Medical University Department of Infectious Diseases Guigang-China[1], The Fifth Affiliated Hospital of Sun Yat-sen University Department of Geriatrics Zhuhai-China[2]

Objective: To evaluate the clinical efficacy and safety of telbivudine (LdT) versus entecavir (ETV) for patients with nucleoside-analogues naïve chronic hepatitis B.Methods This retrospective study including Gruoup LdT(101 patients, treated with LdT 600 mg once daily)and Group ETV(112 patients,treated with ETV 0.5 mg once daily)were investigated in our follow-up clinic for 144 weeks. Some useful indicators were determined at weeks 12, 24, 36, 48, 72, 96, 144 and others were determined at the end of follow-up.
Results: Quantitative HBV-DNA and the rate of undetectable HBV DNA differ significantly between the two groups at weeks 12,24, 36(all $P < 0.05$),but did not differ significantly at weeks 48,72,96,144(all $P > 0.05$). The median time of HBV-DNA negative conversion were differ significantly (LdT 22.6(11.5-91.0)V.S ETV 11.7 (4.1-51.0) weeks, $P < 0.001$). Creatine kinase in Group LdT consisted of nineteen cases (18.8 %) were more than two times upper limit normal, while only five in Group ETV (4.5 %) ($x^2 = 10.754$,$P = 0.001$). Serum ALT normalization rate(LdT: 94.1 % V.S. ETV: 98.2 %, $P = 0$,111),HBeAg seroconversion rate(LdT: 26.5 % V.S. ETV 16.1 %,$P = 0.062$) and the rates of complete viral response(LdT: 88.1 % V.S. ETV: 94.6,$P = 0.087$) were did not differ significantly.
Conclusion: ETV has a faster and higher suppression of HBV-DNA replication and lower CK leves in NAs naive patents with CHB when compared to telbivudine.

Topic 11: Hepatitis B

No: 1200

Different dynamics of HBV related antigen during entecavir treatment

Makoto Arai[1], Takashi Taida[2], Yuuki Haga[2], Tatsuo Kanda[2], Fumio Imazeki[2], Osamu Yokosuka[2]

Chiba University Gastorenterology Chiba-Japan[1], Chiba University Gastroenterology Chiba-Japan[2]

Background: Treatment of nucleotide analogue (NA) can improve the prognosis of patients with hepatitis B virus (HBV). The elimination of covalently closed circular DNA (cccDNA) of HBV in the liver is the final goal of hepatitis B treatment, but is rarely achieved. HBV surface antigen (HBsAg) and HBV related antigen (HBcrAg) have been reported to reflect cccDNA in the liver. In this study, we evaluated the values of HBsAg and HBcrAg during over 4 years of NA treatment.
Patients and methods: All patients undertook entecavir treatment for over 4 years. Patients with the breakthrough of HBV DNA against treatment were excluded for further analysis. 51 patients (Male 22, Female19) were analyzed and their mean age was 50.5 years old. Averaged period of NA treatment was 72.1 ± 17.8 months. 22 patients with HBeAg showed the seroconversion of HBeAg during treatment. Evaluation of HBsAg and HBcrAg was performed twice a year.
Results: Five patients (9.8 %) showed less than 1.9 log IU/mL of HBsAg and 20 patients (37 %) showed less than 3.0 log U/mL of HBcrAg at 60 months after the start of treatment. Before treatment, there was no factor to predict for HBsAg < 1.9 and HBcrAg < 3.0 by Cox regression model, but the value of HBcrAg at 6 months after the start of treatment was only a predictive factor for it (Odds ratio 7.5, 95 % CI 1.1-50.0, $P < 0.05$).
Conclusion: It is difficult to achieve the enough decrease of HBsAg and HBcrAg by NA treatment, which might show that the clearance of cccDNA in the liver is difficult by NA treatment.

Topic 11: Hepatitis B

No: 1897

Cirrhosis is not mandatory for the development of hepatitis B related hepatocellular carcinoma

Abu Saleh Md. Sadequl Islam[1], Salimur Rahman[2], Mamun Al Mahtab[2], Humayun Sattar[3], Sheikh Mohammad Fazle Akbar[4], Ayub Al Mamun[2], Md. Rafiqul Islam[5]

Shaheed Ziaur Rahman Medical College Hospital Medicime Bogra-Bangladesh[1], Bangabandhu Sheikh Mujib Medical University Hepatology Dhaka-Bangladesh[2], Bangabandhu Sgeikh Mujib Medical University Immunology Dhaka-Bangladesh[3], Toshiba General Hospital Medical Sciences Tokyo-Bangladesh[4], Shaheed Ziaur Rahman Medical College Medicine Bogra-Bangladesh[5]

Background: Hepatocellular carcinoma (HCC) is the fifth most common cancer and the third most common cause of cancer death worldwide. The etiological agent of HCC is known in more than 90 % of cases, in South East Asia, hepatitis B is the most common cause. Cirrhosis is an almost invariable precursor to HCC, except in chronic hepatitis B.
Objective: To find out the relationship of cirrhosis with the development of hepatitis B-related hepatocellular carcinoma.
Materials and methods: This observational study was carried out in the Department of Hepatology, BSMMU from January 2012 to December 2013. The diagnosis of HCC was confirmed by pathological examination or AFP elevation (400 ng/ml) combined imaging (CT/MRI) and diagnosis of cirrhosis was made clinically on the basis history, clinical examination and laboratory investigations including imaging or pathological examination after exclusion of hepatitis C virus infection (Anti HCV + ve) and significant alcohol intake (> 20 gm/day).
Results: A total 44 patients were included in this study.Maximum (50 %) patient's ages were belonged to 35-54 years. Cirrhosis was 79.5 % (n = 35) and no cirrhosis was found 20.5 % (n = 9). The difference was statistically significant ($P = 0.001$) among the two groups. Among cirrhosis group, Child –Pugh A, B and C was 6.8 % (n = 3), 31.8 % (n = 14) and 40.9 % (n = 18) respectively.
Conclusion: We can conclude that cirrhosis may be an independent risk factor for hepatitis B virus related HCC and also shows that inactive carriers are still at risk of HCC.Therefore surveillance for HCC should be standard care for all patients with cirrhosis and also in hepatitis B patients without cirrhosis.

Topic 11: Hepatitis B

No: 1942

With a1574t mutation hbv c type chronic hepatitis B patients have the tendency of spontaneous HBEAG seroconversion

Guangjun Song[1], Henghui Zhang[1], Ruifeng Yang[1], Huiying Rao[1], Bo Feng[1], Lai Wei[1]

Peking University People's Hospital Peking University Hepatology Institute Beijing-China[1]

Background: The association of HBV pre C/C and nearby region mutations with the spontaneous HBeAg seroconversion in chronic hepatitis B patients during immune active phase is increasingly recognized.
Methods: Enrolling criteria: HBV C type chronic hepatitis B; HBeAg positive, HBsAb negative; HBV DNA higher than 1 × 105 IU/ml; ALT 2–10 ULN, followed up for 76 weeks without antiviral therapy. The pre C/C and nearby region were amplified by PCR, then the products were cloned and 30clones were selected randomly each patient for sequencing.
Results: 45 HBV C type chronic hepatitis B patients were enrolled. 6 patients attained spontaneous HBeAg seroconversion (A group). 11patients were randomly selected from the remainders (B group). 6 mutations of baseline HBV DNA had significant difference between these two groups. A1479G (D → G) mutation clones/no mutation clones, A group: B group; 60/120: 233/97 ($X2 = 66.2$;$P = 0.001$; OR = 0.21, 95 % CI: 0.14-0.31); A1574T (T → S) A group: B group; 92/88: 60/270 ($X2 = 60.4$;$P = 0.001$; OR = 4.71, 95 % CI: 3.14-7.05); G1613A (D → N) A group: B group; 43/137: 112/218 ($X2 = 5.6$;$P = 0.018$; OR = 0.61, 95 % CI: 0.41–0.92); G1862A (V → I) A group: B group; 54/126: 43/287 ($X2 = 21.8$;$P = 0.001$; OR 2.86, 95 % CI: 1.82-4.50); G1896A (W → termination codon) A group: B group; 49/131: 18/312 ($X2 = 48.4$;$P = 0.001$; OR = 6.48, 95 % CI: 3.64-11.55); C1913G (P → A) A group: B group; 59/121: 42/288 ($X2 = 29.5$;$P = 0.001$; OR = 3.34, 95 % CI: 2.13-5.24).
Conclusion: HBV C type CHB patients during immune active phase, with the mutations A1574T, G1862A, G1896A and/or C1913G have the tendency of spontaneous HBeAg seroconversion, but with the mutations A1479G and/or G1613A the possibility of spontaneous HBeAg seroconversion decreases.

Topic 11: Hepatitis B

No: 1581

Serum concentrations of asymmetric dimethyl arginine in chronic hepatitis B patients

Zerrin Asci[1], Nese Demirturk[2], Serap Demir[3], Bugra Koca[4], Nurhan Dogan[5]

Zubeyde Hanim Obstetrics & Gynecology and Pediatrics Hospital Infectious Disease Afyonkarahisar-Turkey[1], Medical Faculty Kocatepe University Infectious Disease Afyonkarahisar-Turkey[2], Medical Faculty Mersin University Nephrology Mersin-Turkey[3], Medical Faculty Kocatepe University Biochemistry Afyonkarahisar-Turkey[4], Medical Faculty Kocatepe University Biostatistics Afyonkarahisar-Turkey[5]

Aim: Asymmetric dimethylarginine (ADMA) is an endogenous nitric oxide synthase (NOS) inhibitor. In the body, NOS's function is to synthesize nitric oxide from L-arginine in vascular endothelium. Almost the 90 % of ADMA has been metabolised by dimethylarginine dimethylaminohydrolase in liver. The studies on clinical perspectives of ADMA have been continued and there are enough proof for ADMA's role in several diseases. The aim of the study was to investigate serum concentrations of ADMA in chronic active hepatitis B patients and inactive hepatitis B carriers.
Method: The study was performed with three groups. The groups consisted of 27 patients suffering from chronic active hepatitis B (CHB) as were 27 patients inactive hepatitis B carriers and 28 healthy volunteers. Serum concentrations of ADMA was assessed by ELISA method, using WuhanEIAab commercial kit. Absorbance reading was held in TrinityBiotechCaptia Reader. Analysis of variance, Shapiro–Wilk test and Kruskal–Wallis H test were used to calculate statistics.
Conclusion: Serum concentrations of ADMA were found 521,1 ± 95,9 ng/ml, 517,6 ± 108,9 ng/ml and 524,8 ± 133,4 ng/ml in CHB group, inactive HBV carriers group and healthy volunteers, respectively. It wasn't significantly different between groups. So that, there wasn't a correlation between the clinical score of patients and concentrations of ADMA. The data are presented in the Table. Limited studies on ADMA in hepatitis conducted with alcoholic hepatitis and hepatitis C which obtained different results. In chronic hepatitis B patients, as known pathological changes in liver, there are still many unknowns. and there are almost no studies about hepatitis B and ADMA.

Topic 11: Hepatitis B

No: 1012

TGF β1 Il 23 pathway is up regulated in patients with acute on chronic hepatitis B liver failure and is associated with disease severity and survival

Xueping Yu[1], Ruyi Guo[1], Desong Ming[2], Yong Deng[3], Milong Su[2], Chengzu Lin[1], Julan Lin[1], Zhenzhong Lin[1], Zhijun Su[1]

The First Hospital of Quanzhou Affiliated to Fujian Medical University Department of Infectious Diseases Quanzhou-China[1], The First Hospital of Quanzhou Affiliated to Fujian Medical University Department of Clinical Laboratory Quanzhou-China[2], The Second People's Hospital of Pingxiang Department of Infectious Diseases Pingxiang-China[3]

The TGF-β1/IL-23 pathway plays an important role in the progression of bleomycin-induced pulmonary fibrosis in mice. However, the involvement of the TGF-β1/IL-23 pathway in cytopathic process in hepatitis B virus (HBV) related acute-on-chronic liver failure (ACLF) remains unclear. The levels of TGF-β1, IL-9, IL-10, IL-17, IL-22, IL-23, IL-31, IL-33 and IL-35 measured by enzyme-linked immunosorbent assay (ELISA) were compared in chronic hepatitis B (CHB, n = 17), ACLF (n = 18) and normal control subjects (NC, n = 18). Disease severity in patients with ACLF was assessed using the MELD and Child-Pugh scores. Serum TGF-β1 levels were strongly positively correlated with IL-31 in all subjects, and both of them were positively correlated with IL-17, IL-22 and IL-33. In CHB and ACLF patients, serum levels of TGF-β1 and IL-31 were both increased significantly compared with NC and inversely correlated with ALB levels, but positively correlated with TBil and AFP levels. ACLF patients showed the highest levels of TGF-β1 and IL-31 which were positively correlated with Child-Pugh scores but not with MELD scores. Furthermore, recovery from CHB was associated with decreased TGF-β1 and IL-31 levels. More importantly, serum levels of TGF-β1 and IL-31 were markedly up-regulated in ACLF non-survivors, and IL-31 displayed the highest sensitivity and specificity (85.7 % and 100.0 %; respectively) in predicting non-survival of ACLF patients. In summary, the TGF-β1/IL-23 pathway might be involved in the pathogenesis of ACLF, which is correlated with the extent of liver injury, disease severity and survival of ACLF patients, as well as the recovery of liver injury in CHB.

Topic 11: Hepatitis B

No: 1340

HBV related liver cancer enhances notch ligand genomic abnormality and represents poor prognosis

Kazunori Kawaguchi[1], Masao Honda[1], Naoki Oishi[1], Taro Yamashita[1], Rika Horii[1], Mariko Yoshida[1], Kuniaki Arai[1], Tatsuya Yamashita[1], Yoshio Sakai[1], Eishiro Mizukoshi[1], Shuichi Kaneko[1]

Kanazawa University Gastroenterology Kanazawa-Japan[1]

Introduction: HBV or HCV infection is a major factor of liver cancer, though these virus pathogens represent different mechanism of liver carcinogenesis. We had reported that genomic alterations in liver cancer were associated with expression profile in AFP producing hepatoma cells and Notch related gene, Jagged1 was contributed. Recent reports showed that liver cancer enhanced Notch signal transduction and Hippo signaling related genes affected Notch activity, and furthermore HBV-X protein was closely associated with Jagged1 expression. Thus we assessed Notch signal related genomic change in HBV infected cells and HBV-related liver cancer clinical samples. Methods: We evaluated Jagged1 genomic copy number of HepG2 and HBV infected HepG2.2.15 or HepG2.2.15.7 cells using RTD-PCR (TaqMan Copy Number Assays) and measured cccDNA copy numbers and cellular HBVDNA levels in these cells. We evaluated the Jagged1 copy number variations in genomic DNA of surgical resected liver cancer samples and compared the outcome of the therapy with comparing HBV (n = 32) or HCV (n = 51) infection background.
Results: We could observe significant Jagged1 genomic amplification in HepG2.2.15 or HepG2.2.15.7 compared with HepG2 cells, suggesting HBV infection cause further Notch signal abnormality. HBV-related liver cancer clinical samples showed significant elevated Jagged1 genomic copy number amplification and furthermore represented significant poor survival than HCV-related liver cancer samples.
Conclusion: HBV-related liver cancer demonstrated Notch related genome amplification and results in shorter survival indicating malignant character of liver cancer by Notch activation.

Topic 11: Hepatitis B

No: 1199

Antiviral drug utilization and costs for inpatients with chronic hepatitis B in Guangzhou China

Yanhui Gao[1], Shudong Zhou[1], Weidong Jia[2], Guangming Xiao[2], Yueping Li[2], Junguo Zhang[1], Weixia Ke[1], Chi Zhang[1], Yi Yang[1]

School of Public Health and Guangdong Key Lab of Molecular Epidemiology, Guangdong Pharmaceutical University Department of Epidemiology and Biostatistics Guangzhou-China[1], Guangzhou Eighth People's Hospital Department of Hepatology Guangzhou-China[2]

Objective: To describe antiviral drug utilization and its costs in inpatients with chronic hepatitis B (CHB) virus infection in Guangzhou, China.
Methods: We conducted a retrospective cohort study of inpatients with HBV in the largest specialized infection hospital in Guangdong province from 2008 to 2012. Person-time proportion of antiviral drug utilization among inpatients with CHB, cirrhosis and hepatocellular carcinoma (HCC) and utilization proportion of antiviral drugs including Interferon (IFN), lamivudine (LAM), adefovir dipivoxil (ADV), entecavir (ETV) and telbivudine (LdT) among antiviral treated inpatients were computed. Average annual antiviral costs per person were estimated in RMB 2012 at discounting rate of 5 % per year.
Results: 9615 records from 7337 inpatients were included. Person-time proportion of using antiviral medications was 50.12 % for CHB, 59.42 % for cirrhosis and 45.05 % for HCC, and was steadily ascending from 43.98 to 63.98 %. Person-time utilization proportion for IFN dropped from 54.67 to 27.92 % from 2008 to 2012, while proportions for ETV and LAM increased (11.08 to 31.71 %, 13.45 to 28.38 % respectively). Average annual antiviral costs per person during hospitalization were as follows: CHB, 1534.44 RMB; cirrhosis, 1232.44 RMB and HCC, 856.23 RMB, which accounted for 25.62, 12.35 and 6.78 % of all drug expenditures of inpatients, and increased over time.
Conclusions: The overall proportion of antiviral drug utilization and its costs for inpatients increased annually. Utilization of primary antiviral agents changed from IFN to predominantly LAM and ETV over time. Long-term standard treatments with high efficacy and low resistance antiviral drugs are vital and critical for CHB patients in Guangzhou, China.

Topic 11: Hepatitis B

No: 1998

Evaluation of hepatitis B virus infection among the parents of the individuals having HBsAg positive

Selma Tosun[1], Altan Gokgoz[1], Asli Keles[1], Alpay Ari[1]

Izmir Bozyaka Research and Education Hospital Infectious Diseases Izmir-Turkey[1]

Aim: The aim of this study is to evaluate the Hepatitis B virus infection among the parents of the individuals having HBsAg positive by using the current results of the examination and the information from a face-to-face questionnaire.
Method: By making a face to face interview with the subjects having HBsAg positive followed up in Izmir Bozyaka ERH Viral Hepatitis Polyclinic, the exposure of their parents to HBV was evaluated.Moreover, the examination results at hand were assessed as well.
Results: The study included 79 women subjects aged between 18 and 69.It was determined that in terms of their mothers, 49 of the subjects(62 %) had HBsAg positive,4 of them(5 %) were immune, and 16 of them(20 %) did not receive any HBV examination. In terms of their fathers; it was observed that 5 of the subjects(6 %) had HBsAg positive, 32 of them (40,5 %) were immune, and 26 (33 %) did not have any examination.
Discussion: It was determined that mothers of 62 % of the HBsAg positive subjects as well had HBsAg positive, but mothers of 20 % were not examined at all. Furthermore, it was found out that the relatives from the mother's family had chronic HBV infection,cirrhosis and HCC. It was also detected that fathers had a lower HBsAg positive,but had a much higher natural immunity as compared to mothers. It was observed that vertical transmission was dominant and immunization possibility was higher in men even if the incidence of exposure to virus was high.Therefore,all pregnants should have HBsAg examination during their pregnancy period.

Topic 11: Hepatitis B

No: 1164

Efficacy of tenofovir rescue therapy for drug resistant chronic hepatitis B patients one year multicenter experience in Korea

Baek Gyu Jun[1], Sae Hwan Lee[1], Hong Soo Kim[1], Sang Gyune Kim[2], Young Seok Kim[2], Boo Sung Kim[2], Soung Won Jeong[3], Jae Young Jang[3], Young Don Kim[4], Gab Jin Cheon[4]

Soonchunhyang University,cheonan Hospital Internal Medicine Cheonan-Korea, South[1], Soonchunhyang University,bucheon Hospital Internal Medicine Bucheon-Korea, South[2], Soonchunhyang University, Seoul Hospital Internal Medicine Seoul-Korea, South[3], University of Ulsan College of Medicine Internal Medicine Gangneung Asan Hospital-Korea, South[4]

Background/aim: To investigate the efficacy of tenofovir (TDF)-based rescue therapy for patients with drug-resistant chronic hepatitis B in Korea.
Methods: In this retrospective cohort study, 76 patients received TDF with or without nucleoside analogue more than 12 months were analyzed. Suboptimal response was defined as serum HBV-DNA level above 60 IU/mL during prior rescue therapy. Multi-drug resistance was defined as two or more drug resistance-related mutations were confirmed by mutation detection assay. The relationship between baseline characteristics and virologic response (HBV DNA < 20 IU/mL) at month 12 were evaluated using logistic regression analysis.
Results: Fifty-five (72 %) of patients were suboptimal responders to prior rescue therapy. Twenty-six (34 %) of the subjects had multidrug resistance and 21 had adeforvir (ADV) resistant mutation. Forty-two (55 %) of the subjects received combination therapy with nucleoside analogues. Cumulative virologic response was achieved in 58 (76 %) patients at 12 months. Virologic response at month 12 was not significantly different between TDF monotherapy and combination group ($P = 0.098$) and between presence of ADV-resistance and not ($P = 0.987$). Reductions of serum HBV DNA level at month 12 were -4.49 ± 1.67 log10 IU/mL in monotherapy group and -3.97 ± 1.69 log10 IU/mL in combination group ($P = 0.18$). In multivariate analysis, female ($P = 0.032$), low baseline HBV-DNA level ($P = 0.013$), and TDF monotherapy ($P = 0.046$) were predictive factors for virologic response at month 12.
Conclusions: Combination with nucleoside analogues was not superior to TDF monotherapy and ADV-resistant mutation was not related with virologic response during TDF rescue therapy in patients with drug-resistant chronic hepatitis B.

Topic 11: Hepatitis B

No: 1824

The results of 5 years of lamivudine therapy in chronic hepatitis B

Kadri Atay[1], Emre Durcan[1], Berna Yurttaş[1], Ibrahim Hatemi[1], Billur Canbakan[1], Sebati Özdemir[1], Abdullah Sonsuz[1]

Istanbul University, Cerrahpaşa Faculty of Medicine Department of Internal Medicine, Division of Gastroenterology Istanbul-Turkey[1]

Aim: Due to the rules of medical insurance reimbursement of Turkey that changed recently, we used to start lamivudine therapy obligatorily in chronic hepatitis B patients who had the level of HBV-DNA load (<2.000.000 IU/mL). We retrospectively analyzed the results of our lamivudine therapy experience of 5 years.
Methods: We analyzed the data of chronic hepatitis B patients who had lamivudine therapy and had at least 1 year of follow-up period in our outpatient department. The patients who had hepatitis C, hepatitis delta, autoimmune liver disease, and alcoholic liver disease were excluded.
Results: A total of 195 patients (63 females, 132 males; mean age: 51.2 ± 13.1) with chronic hepatitis B were included in this study. In 51 % of these patients the initial medication was lamivudine. These rates for tenofovir, entecavir, telbivudine and pegylated-interferon were 21, 22, 2, 4 % respectively. In the lamivudine group HBV-DNA level was undetectable at the sixth months in 35.5 % of the patients. The rates of undetectable DNA level at the 12th and at the 18th months were 80 and 90 % respectively. The rate of the patients who were still on lamivudine therapy were 91, 86, 81, 70, 56 % at 1th to 5th years of treatment.
Conclusion: The rate of undetectable HBV-DNA level for lamivudine was %80 at the first year of the treatment. The rate of patients who had continued lamivudine was % 56 at the fifth years of treatment. In nearly half of the patients the medication has been changed due to lamivudine resistance.

Topic 11: Hepatitis B

No: 1203

No detectable resistance to tenofovir disoproxil fumarate in HBeag + and hbeag patients with chronic hepatitis B after eight years of treatment

Amoreena Corsa[1], Yang Liu[1], John Flaherty[2], Patrick Marcellin[3], Michael Miller[1], Kathryn Kitrinos[1]

Gilead Sciences Clinical Virology Foster City-United States[1], Gilead Sciences Clinical-Liver Diseases Foster City-United States[2], Hospital Beaujon, University of Paris Dept of Hepatology Clichy-France[3]

Aim: Evaluate chronic hepatitis B (CHB) patients who qualified for resistance surveillance over 8 years of tenofovir disoproxil fumarate (TDF) treatment.
Methods: Patients in Studies GS-US-174-0102 (HBeAg-) and GS-US-174-0103 (HBeAg +) were randomized 2: 1 to receive TDF or adefovir dipivoxil for 48 weeks followed by open-label TDF through year 8. Virologic breakthrough (VB) was defined as confirmed HBV DNA >1 log10 from nadir or viremia after <400 copies/mL. Population sequencing of HBV pol/RT was attempted for all TDF-treated patients at baseline and, if viremic, annually, at discontinuation, or FTC addition.
Results: Over years 1-2, 9-11 % of patients qualified for genotypic analysis mostly for viremia (≥73 %) without VB. Over years 3-8, <4 % of patients qualified for testing mostly for transient HBV DNA increases. Forty-one VB episodes occurred throughout the study, with most (n = 29, 70 %) associated with nonadherence to study medication. of the VB patients with an opportunity to resuppress, 56 % (22/39) achieved HBV DNA resuppression (<400 copies/mL). Across patients, 36 % had no sequence changes compared to baseline, 29 % had polymorphic site changes, 7 % had conserved site changes, and 28 % were unable to be genotyped. There was no accumulation of conserved site changes and none associated with TDF resistance.
Conclusions: The percentage of subjects qualifying for genotypic analysis declined over time. VB was associated with nonadherence to study medication and HBV DNA resuppression. No accumulation of conserved site changes or evidence of TDF resistance was observed. These results support long-term TDF use for CHB treatment.

Topic 11: Hepatitis B

No: 2013

Serum cytokine chemokine profiles during the natural course of chronic hepatitis B

G.y. Wang[1], R. Su[2], Y. Liu[3], R. Huang[4], X.m. Yan[1], Y.l. Xiong[1], J. Xia[1], Z.h. Sun[2], B. Jia[2], C. Wu[1]

Nanjing Drum Tower Hospital, Nanjing University Medical School Department of Infectious Diseases Nanjing-China[1], Nanjing Drum Tower Hospital, Nanjing Medical University Department of Infectious Diseases Nanjing-China[2], Nanjing Drum Tower Hospital, Nanjing University Medical School Department of Laboratory Medicine Nanjing-China[3], Nanjing Drum Tower Hospital Clinical College of Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine Department of Infectious Diseases Nanjing-China[4]

Aims: To investigate the serum cytokine/chemokine profiles during natural course of chronic hepatitis B (CHB).
Methods: Eighty-two CHB patients and 10 healthy individuals were enrolled and classified according to definitions of the natural phases of CHB. Specifically, the patients were categorized into immune tolerance (IT), HBeAg-positive hepatitis (EPH), HBeAg-negative hepatitis (ENH) and inactive carrier (IC). Seventeen cytokines/chemokines were determined with the Human Magnetic Cytokine/Chemokine Bead Panel.
Results: Four cytokine/chemokines were significantly different in various immune phases of chronic HBV infection. Serum IL-10 and IP-10 levels were significantly elevated in EPH and ENH groups as compared with the IT, IC and HC groups (all $P < 0.01$). However, IL-10 and IP-10 levels were similar between the EPH and ENH groups (all $P > 0.05$). MIP-1β levels increased in the EPH group as compared with IC and HC groups (all $P < 0.01$). However, they were not significantly elevated in the ENH group. MCP-1 levels were significantly decreased in the IT group compared to EPH, IC, ENH and HC groups (all $P < 0.05$). Furthermore, the IL-10, IP-10 and MIP-1β levels were significantly positively correlated with serum ALT levels ($r = 0.446$, $P < 0.001$; $r = 0.432$, $P < 0.001$; $r = 0.246$, $P = 0.026$, respectively). Other cytokines/chemokines including IFN-γ, sCD40L, IL-1RA, IL-5, IL-6, IL-8, IL-17A, IL-12p40, IL-12p70, IL-15, MIP-1α, TNF-α and TNF-β were not significantly changed in various immune phases of CHB.
Conclusions: The IL-10, IP-10, MIP-1β and MCP-1 varied significantly in different phases of CHB and were correlated with ALT levels. These cytokines/chemokines may play an important immune regulation role in the immune clearance of chronic HBV infection.

Topic 11: Hepatitis B

No: 1409

Alteration of intrahepatic cccDNA levels in patients with HBeAg positive chronic hepatitis B treated with pegylated interferon

Natthaya Chuaypen[1]

Faculty of Medicine, Chulalongkorn University Biochemistry Bangkok-Thailand[1]

Background: Coverlently closed circular DNA (cccDNA) is the template for hepatitis B virus (HBV) replication. The aim of this study was to determine changes in intrahepatic cccDNA in patients with HBeAg-positive chronic hepatitis B (CHB) during 48 weeks of pegylated interferon (PEG-IFN).
Method: 22 patients with HBeAg-positive CHB were enrolled. HBV genotype was performed by PCR and direct sequencing methods. Paired liver biopsies from before and at the end of treatment were analyzed for cccDNA by real-time PCR. Serum quantitative HBsAg was measured by a commercially available assay.
Results: All patients in this study were infected with HBV genotype C. Virological response at 24 weeks post treatment, defined as HBeAg seroconversion and HBV DNA less than 2,000 IU/mL was achieved in 7 (32 %) patients. Mean cccDNA level at the end of treatment (0.61 copies/cell) was significantly lower than the corresponding pre-treatment level (0.75 copies/cell, $P < 0.01$). The mean cccDNA decline in responders was significantly higher than in non-responders (0.25 vs 0.097 copies/cell, $P = 0.03$). Changes in intrahepatic cccDNA were positively correlated with the reduction of serum HBsAg levels ($R2 = 0.55$, $P < 0.01$).
Conclusion: PEG-IFN therapy in patients with HBeAg-positive CHB led to decreases in intrahepatic cccDNA, which was significantly higher in responders than in non-responders, and correlated well with reduced HBsAg level.

Topic 11: Hepatitis B

No: 1702

Evolutionary patterns of hepatocyte hepatitis B virus cccDNA basal core promoter and precore quasispecies and its impact on relapse in chronic hepatitis B patients with lamivudine treatment

Jianning Jiang[1], Xiaoli Wu[1], Minghua Su[1], Baojian Wang[1], Ailian Lu[1], Shaohua Zhong[1], Shihua Li[1], Yanxiu Liang[1], Rong Xie[1], Yanyan Mo[1], Peng Liang[1]

The First affiliated Hospital of Guangxi Medical University Infectious Disease Department Nanning-China[1]

Aim: To investigate the evolution of HBVcccDNA basal core promoter and precore(BCP/PreC)region quasispecies (QS)in hepatocyte after meeting the endpoint criteria of 2008 APASL guideline and its impact on relapse in CHB patients with lamivudine (LAM) treatment.
Methods: Liver biopsies were percutaneous needle biopsies in 43 CHB patients received LAM treatment(25 patients with initial treatment, 18 with NAs retreatment who had received LAM initial treatment) who had met the endpoint criteria of 2008 APASL guideline and were followed up,including 22 relapsed patients,21 patients without relapse.BCP/PreC region of HBV cccDNA was cloned into plasmid and transformed into competent cells. 23 positive clones on an average (a total of 999)per sample were sequenced randomly.
Results: (1) In all patients,QS complexity of BCP/PreC region in relapsed patients was higher than patients without relapse(0.7193 ± 0.1480VS0.6925 ± 0.2959,$P = 0.716 > 0.05$),it was also higher in initial treatment patients than that in retreatment patients(0.7623 ± 0.1632VS0.6298 ± 0.2797,$P = 0.084 > 0.05$),but there were no significant different.(2)In initial treatment patients,QS complexity of BCP/PreC region in relapsed patients was lower than patients without relapse(0.7230 ± 0.1243VS0.8047 ± 0.1936,$P = 0.219 > 0.05$),there was no significant different.(3)In retreatment patients,QS complexity of BCP/PreC region in relapsed patients was higher than patients without relapse(0.7381 ± 0.1752VS0.5216 ± 0.3305,$P = 0.108 > 0.05$),there was no significant different.
Conclusions: In CHB patients with LAM treatment who had met the endpoint criteria, the QS complexity of HBV cccDNA BCP/PreC region after meeting the endpoint criteria were not significantly associated with relapse.

Topic 11: Hepatitis B

No: 2109

The safety and therapeutic efficacy evaluation for human umbilical cord mesenchymal stem cells transplantation combined with plasma exchange in patients with liver failure caused by hepatitis B virus

Hongliang He[1], Wenxiong Xu[2], Jianguo Li[2], Hong Deng[2], Guoli Lin[2], Zhiliang Gao[2]

Affiliated Provincial Hospital of Anhui Medical University Department of Infectious Diseases Hefei, Anhui-China[1], Third Affiliated Hospital of Sun Yat-sen University Department of Infectious Diseases Guangzhou, Guangdong-China[2]

Background: To evaluate the safety and therapeutic efficacy of human umbilical cord mesenchymal stem cells (UC-MSCs) transplantation combined with plasma exchange (PE) for patients with liver failure caused by Hepatitis B virus (ACLF).
Methods: 5 cases of ACLF were recruited and received conventional treatment plus 2000 milliliter plasma exchange (every 3 days, 3 times). Meantime taken i.v UC-MSCs transplantation slowly for 30 min (1×105/Kg, once a week, 4 times), the first two times is taken after plasma exchange. Participants were followed until the week 12 study visit. Primary outcome measures such as adverse reactions (including body temperature and allergy), occurrence of complications and survival time were observed at different time points. Secondary outcome measures were examined as follows: biochemical indexes such as alanine aminotransferase (ALT), albumin (ALB), total bilirubin (TBIL), prothrombin time international normalized ratio (INR), clinical symptom including appetite, debilitation and MELD scores were also detected.
Results: Fever and plasma allergic reactions were observed in two patients, no serious adverse reactions and complications occurred in 1-12 weeks. At 12 weeks, there were 4 cases still survived in 5 cases and three patients were discharged. Two weeks after treatment, the symptoms improved. 12 weeks later, symptoms had significant improvements in 3 cases. At 1 week after UC-MSCs combined with PE, the level of ALT, AST, TBil, INR and MELD scores were declined in all cases. The level of ALB were significantly increased at $1 \sim 4$ weeks and had temporarily gone down by the end of week 8. At the 12th week, the level of ALB resumed rise.

Topic 11: Hepatitis B

No: 2143

Impact of adherence to antiviral therapy and outcomes in patients with chronic hepatitis B infection

Qian Qiu[1], Yan Li[2], Xiaowan Duan[2], Li Pan[1], Likun Yang[2], Yu Chen[2], Li Wang[1], Zhongping Duan[2]

Institute of Basic Medical Sciences Chinese Academy of Medical Sciences Epidemiology Beijing-China[1], Beijing You'an Hospital of Capital Medical University Infectious Disease Beijing-China[2]

Aim: Adherence is essential for the long-term nucleoside/nucleotide analogues (NAs) therapy for chronic hepatitis B (CHB) patients in clinical practice. This study was to evaluated the adherence of the two most commonly used NAs in China, ADV and ETV, and the associated effectiveness.
Methods: A retrospective cohort of 2494 NA naïve CHB outpatients were enrolled between January 1, 2009 and December 31, 2012. Demographic characteristics, routine biochemical and virological index and antiviral prescription were collected from electronic database. Medication possession rate (MPR) was used to evaluate adherence. The virological response and HBeAg seroconversion was estimated by Kaplan–Meier analysis. Cox regression was used to evaluate the impact of adherence on virologic response.
Results: The median duration of treatment was 39 months, with the MPR of 0.87 ± 0.22. For HBeAg (+) patients with ETV, the virologic response rate at 24th month was 80.8 % among those with good adherence, 18.6 % and 27.1 % higher than those with moderately and poor adherence, respectively ($P = 0.0013$). For HBeAg(+) patients with ADV, higher virologic response was also observed among those with good adherence even though the difference was not significant ($P = 0.1798$). After adjusted other factors associated with treatment effectiveness, good adherence was still observed to be associated with higher virologic response (HR = 2.14, 95 % CI 1.53-3.00; $P < 0.0001$). The same tendency was observed for HBeAg (-) patients.
Conclusions: Adherence seems to be an independent factors associated with virologic response. Attention should be paid to increase adherence during NAs therapy to increase treatment effectiveness in clinical practice.

Topic 11: Hepatitis B

No: 1503

Impaired function of cd4 + t follicular helper (tfh) cells associated with hepatocellular carcinoma progression

Yiqiong Jia[1], Lifeng Wang[1], Fu-sheng Wang[1]

Beijing 302 Hospital Research Center For Biological Therapy Beijing-China[1]

Aims: CD4 + T follicular helper (Tfh) cells have been demonstrated to be involved in the development and prognosis of tumors. Our study aimed to investigate the functional role of Tfh cells in human hepatocellular carcinoma (HCC).
Methods: A total of 89 HCC patients with hepatitis B virus (HBV) infection, 25 HBV-relative liver cirrhosis (LC) patients, and 20 healthy controls were randomly enrolled. Flow cytometric analysis, immunohistochemical staining, and relative function (i.e., cytokine secretion, B cell maturation) assays were used to analyze the properties of CXCR5 + CD4 + T. In addition, the correlation between the frequency of CXCR5 + CD4 + T cells and overall or disease-free survival rates was analyzed using the Kaplan–Meier method.
Results: The frequency of circulating CXCR5 + CD4 + T cells was significantly decreased in HCC patients compared with HBV-relative liver cirrhosis (LC) patients and healthy controls, and the decrease in circulating CXCR5 + CD4 + T cells correlated with disease progression. The proportion of infiltrated CXCR5 + CD4 + T cells was significantly decreased in tumor regions compared with nontumor regions. Furthermore, compared with healthy controls, the function of circulating CXCR5 + CD4 + T cells in HCC was impaired, with reduced IL-21 secretion and dysfunction in promoting B cell maturation. Importantly, follow-up data indicated that a decreased frequency of circulating CXCR5 + CD4 + T cells was also associated with reduced disease-free survival time in HCC patients.
Conclusions: Impairment of Tfh cells influence the development of HBV-associated HCC. Decreased CD4 + T follicular helper cells represent a potential prognostic marker and serve as a novel therapeutic target for HCC patients.

Topic 11: Hepatitis B

No: 1983

Noninvasive markers for fibrosis in chronic hepatitis B substitution for biopsy

Fatih Saygili[1], Nuretdin Suna[1], Erkin Oztas[1], Hale Gokcan[1], Ufuk Baris Kuzu[1], Zeki Mesut Yalin Kilic[1], Sabite Kacar[1], Meral Akdogan[1], Ertugrul Kayacetin[1]

Turkiye Yuksek Ihtisas Research and Education Hospital Gastroenterology Ankara-Turkey[1]

Chronic Hepatitis B is an important public health problem in Turkey. It is the most common reason for development of cirrhosis and hepatocellular carcinoma. The diagnosis depends on serologic markers, but in order to assess the histologic activity and the degree of fibrosis, liver biopsy is crucial. According to the rules of social security system in Turkey the initiation of therapy depends on the findings observed in liver biopsy. However liver biopsy is a highly invasive procedure with complications up to death even if it is very rare. Noninvasive markers and scoring systems to assess liver fibrosis have been widely suggested and studied in the literature. In our study we have evaluated 396 patients with chronic hepatitis B and investigated the correlation between histopathologic findings in liver biopsy and previously described scores such as APRI, Fib-4, AAR, FibroQ, LOC index, FI score, King score and GUCI. These scores were calculated at the time of biopsy. Correlation analysis with ROC curves were performed. Among 9 scoring systems only APRI and Fib-4 scores showed correlation with liver biopsy with 0,69 and 0,71 AUROC levels respectively. Positive predictive value of these scores are 82 % and 79 % and negative predictive values are 91 % and 94 % respectively. These findings suggest that these scoring systems are most valuable for ruling out fibrosis. However correlation analysis suggest that we still don't have any scoring system that is highly reliable and can replace liver biopsy. Further studies should be conducted for novel alternative scoring systems to replace biopsy.

Topic 11: Hepatitis B

No: 2011

Increase in regulatory b cells and interleukin 10 in immune reactive phase of chronic hepatitis B virus infection

R. Su[1], Y. Liu[2], R. Huang[3], G.y. Wang[4], X.m. Yan[4], Y.l. Xiong[4], J. Xia[4], Z.h. Sun[1], B. Jia[1], C. Wu[4]

Nanjing Drum Tower Hospital, Nanjing Medical University Department of Infectious Diseases Nanjing-China[1], Nanjing Drum Tower Hospital, Nanjing University Medical School Department of Laboratory Medicine Nanjing-China[2], Nanjing Drum Tower Hospital Clinical College of Traditional Chinese and Western Medicine, Nanjing University of Chinese Medicine Department of Infectious Diseases Nanjing-China[3], Nanjing Drum Tower Hospital, Nanjing University Medical School Department of Infectious Diseases Nanjing-China[4]

Aim: To investigate regulatory B cells (Bregs) and serum interleukin 10 (IL-10) in different immune phases of chronic hepatitis B (CHB)
Methods: Fifty-three CHB patients and 10 healthy controls were enrolled. The patients were divided into three groups, namely immune tolerant phase (IT), immune reactive phase (IA) and inactive HBV carrier state (IC) based on HBeAg status, HBV DNA load and alanine aminotransferase (ALT) levels. The frequencies of Bregs (defined as CD24hiCD38hi B cells) in the peripheral blood were measured by flow cytometry. IL-10 levels were determined with the Human Magnetic Cytokine/Chemokine Bead Panel on the MAGPIX instrument.
Results: The frequencies of Bregs were significantly different in various immune phases of chronic HBV infection. Compared to immune tolerant phase (4.768 ± 2.424 %), the frequencies of Bregs were significantly elevated in the immune reactive phase (7.780 ± 3.427 %, $P = 0.010$). The levels of IL-10 in serum were also elevated significantly in immune reactive phase (22.533 ± 24.811 pg/ml) as compared with IT (0.689 ± 1.342 pg/ml, $P < 0.001$), IC (0.306 ± 1.115 pg/ml, $P < 0.001$) and HC group (0.003 ± 0.009 pg/ml, $P < 0.001$). The frequencies of Bregs positively correlated with ALT ($r = 0.316$, $P = 0.012$) and IL-10 levels ($r = 0.282$, $P = 0.025$). In addition, IL-10 levels were also positively correlated with ALT levels ($r = 0.715$, $P < 0.001$).
Conclusions: The frequencies of Bregs and IL-10 levels varied in different phases of chronic HBV infection and were significantly elevated in immune reactive phase. Bregs and IL-10 may play some important role in modulating the immune responses of CHB.

Topic 11: Hepatitis B

No: 1512

Evaluation of different oral antiviral therapies for chronic hepatitis B infection in non cirrhotic patients

Neslihan Yücel Demir[1], Elif Sahin Horasan[1], Gulden Ersoz[1], Ali Kaya[1]

University Hospital Infectious Diseases Mersin-Turkey[1]

The aim of this study was to evaluate the efficacy of different oral antiviral therapies for Chronic Hepatitis B (CHB) infection in non-cirrhotic patients.

We retrospectively analysed data from 206 CHB patients treated with oral antiviral at Mersin University Hospital.

The mean age of the cohort was 42 years, 62 % were male. This study included 206 patients, 30 (14.6 %), 12 (5.8 %), 90 (43.7 %) and 74 (35.9 %) of 206 patients used lamivudine, telbivudine, entecavir and tenofovir, respectively. Virological response (VR) ratios to lamivudine, telbuvidine, entecavir and tenofovir were detected as 52.2 %, 100 %, 71.1 %, 75.4 %, respectively at the end of first year. Although HBeAg seroconversion was not detected in group using lamivudin and telbivudine, it was found in groups using entecavir (18.4 %) and tenofovir (30.7 %). While HBsAg seroconversion was not determined in groups using lamivudine, telbivudin and entecavir, it was found 1.3 % in group using tenofovir. VR and HBeAg seroconversion were found 50 % and 19.4 % for entecavir in patients being HBeAg positive, respectively. On the other hand, these values were found 62.5 % and 33.4 % for tenofovir, respectively. VR was found 87.2 % for entecavir and 82.2 % for tenofovir in HBeAg(-) patients. While HBsAg seroconversion was not observed with entecavir, it was found 2.2 % with tenofovirentecavir and tenofovir were highly effective for treatment CHB patients.

Topic 11: Hepatitis B

No: 2206

Sustained virological response in dual infection of chronic hepatitis B and C virus

Hasan Ozkan[1], Xheni Deda[1], Cagdas Kalkan[1], Ali Tuzun[1], Fatih Karakaya[1], Necati Ormeci[1], Abdulkadir Dokmeci[1]

Ankara University Gastroenterology Ankara-Turkey[1]

Background/aims: Dual hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are common in HBV or HCV endemic areas. In general, the prevalence is around 10–20 % in patients with chronic HBV infection and 2–10 % of anti-HCV-positive patients to have markers of HBV infection. Still there is limited information about the treatment of HBV/HCV co-infection. Determination of the dominant virus before the treatment is important. The purpose of our study is to asses the effect of combinated Peg-INF alpha, ribavirine and oral antiviral therapy in patients co-infected with hepatitis B and C.
Materials and methods: Total 1688 viral hepatitis B and C infected patients that were followed by a single center between 1998 and 2014. There were 1217 CHB and 471 CHC. Average age was 51,7 years. 13 cases were female and 19 cases were male. Patients were eligible for inclusion in the study if they had a positive test for HCV antibody or HCV RNA and positive test for HBsAg or HBV DNA. Patients were followed until death, liver transplantation or end of the study. All of patients were followed and controlled every six months. In these visits we examined HBsAg, AntiHBs, HBV DNA PCR, Anti HCV, HCV RNA PCR, ALT, AST, Total and direct bilirubine.
Results: There were 32 patients HBV + HCV coinfected in 1217 HBV infected patients (2.5 %) and 7 HBV + HCV coinfection in 471 HCV infected patients (6,7 %) in our study. There were 3 HBV + HCV active, 15 active HBV + HCV inactive, 5 active HCV +inactive HBV, 8 inactive HBV + inactive HCV, and 1 patients had triple infection HBV + HCV + HDV with a total of 32 patients. Among the patients that have HCV infection, 3 of them died because of cirrhosis and HCC and 1 of them died because of renal failure. We investigated 1,688 viral hepatit B and C infected patients, 32 of them were HBV and HCV co-infected; the ratio of them was 1.9 %. Our patients were treated as seen in
Conclusion: In endemic regions HBV + HCV coinfection is calculated to be higher. HBV and HCV coinfection was found 1.9 % in our patients. HBV and HCV coinfection is more serious than in patients that carry only one of the viruses. Complications of viral hepatitis like, fulminant hepatic failure, cirrhosis, HCC ratio are detected to be higher among the patients that have co-infection. It is important to determine the type of the dominant virus in order to form the treatment way. It has been reported that combination treatment with Peginterferon plus Ribavirine in HBV/HCV co-infected patients have similar results as in patients who have only HCV infection. Prospective controlled studies in different patients groups.

Topic 11: Hepatitis B

No: 1498

Healthy child birth in spite of entecavir treatment

Sabiye Akbulut[1], Kamuran Cumhur Değer[2], Aziz Serkan Senger[2], Sinan Yol[2]

Kartal Koşuyolu High Specialty Education and Research Hospital Department of Gastroenterology Istanbul-Turkey[1], Kartal Koşuyolu High Specialty Education and Research Hospital Department of Gastroenterological Surgery Istanbul-Turkey[2]

Aim: B hepatitis is a complex process for each mother and fetus in pregnancy. Entecavir is a guanosine nucleoside analogue with selective activity against HBV. Entecavir's FDA pregnancy category is C and this drug is not recommended during pregnancy. In this case we report a pregnant patient that used Entecavir without the knowledge of its side effects and consequent a healthy childbirth.
Case report: A female patient 34 years old had diagnosed chronic hepatitis B four years ago. HbsAg + , AntiHbe + , HBVDNA 4.022.382 copies/ml were in blood test. Liver biopsy result was fibrosis 2 according to the Ishak score and Entecavir therapy had begun 0.5 mg. HBV DNA was negative in the 24th week of the therapy. On the 3rd year of the therapy the patient had become pregnant. Her therapy had been continued during the first 8 weeks. When she came to control after this 8 week, Entecavir treatment was discontinued. Antiviral drugs were offered to the patient that could be used during pregnancy but she denied using any of them. At the end of 39 week she gave birth to a healthy child. Postpartum on the 3rd month control HBV DNA level was 46.500 IU and she accepted to continue therapy with interrupting breastfeeding.
Result: Treatment and surveillance of chronic hepatitis B is important particularly in pregnant woman. We report here a healthy child birth although the patient had used Entecavir therapy unknowingly in the first trimester. There is a need of more studies to state the confidence of Entecavir therapy during pregnancy.

Topic 11: Hepatitis B

No: 1128

Interferon therapy reduced incidence of hepatocellular carcinoma and mortality in chronic hepatitis B patients

Chun-jen Liu[1], Yi-chun Yeh[2], Pei-jer Chen[1], Mei-shu Lai[2]

National Taiwan University College of Medicine Graduate Institute of Clinical Medicine Taipei-Taiwan[1], National Taiwan University College of Public Health Graduate Institute of Epidemiology and Preventive Medicine Taipei-Taiwan[2]

Aim: The efficacy of interferon (IFN) therapy for chronic hepatitis B (CHB) in mitigating the incidence of end-stage liver diseases or mortality has not yet been substantiated. This study was to evaluate the effects of IFN treatment on HCC development and mortality, and use untreated or lamivudine (LAM) treatment groups as controls.
Methods: A total of 355 patients who completed 144 weeks of LAM (n = 151), ADV (n = 72), LDT (n = 50) or ETV (n = 82) monotherapy were prospectively studied. The effectiveness data of the four NAs groups were collected and analyzed. This nationwide cohort study identified patients diagnosed with CHB from the National Health Insurance (NHI) program from years 2004 to 2010 in Taiwan. Patients who underwent IFN/PEG-IFN treatment were matched with properly controlled, untreated and LAM treated patients. We then assessed the outcomes regarding the occurrence of HCC, liver-related mortality, and overall mortality. We employed a Cox proportional hazards model based on inverse probability treatment weighting or propensity score matching to estimate adjusted hazard ratios (HR) and 95 % confidence intervals (CIs).
Results: NHI database included a total of 630,592 CHB patients in study period. Among these patients, 365,567 CHB patients met the inclusion criteria, including 351,960 untreated, 2,747 with IFN/PEG-IFN, and 10,860 with lamivudine. Patients receiving IFN/PEG-IFN treatment presented significant reduction in HCC incidence (HR, 0.25; 95 % CI, 0.18-0.36), liver-related mortality (0.11; 0.06-0.22), and all-cause mortality (0.09; 0.05-0.15) than untreated patients. Interestingly, though both IFN/PEG-IFN and LAM therapies reduced HCC incidence equally, IFN/PEG-IFN treatment provided a greater decrease in liver-related mortality (0.37; 0.18-0.77) and all-cause mortality (0.26; 0.15-0.45) than LAM treatment.
Conclusions: Our results demonstrate the efficacy of anti-HBV interferon therapy in reducing the incidence of HCC and mortality in the long-term follow-up of a large population.

Topic 11: Hepatitis B

No: 1542

Evaluation of the efficacy of lamivudine versus telbivudine in the treatment of naive hepatitis B e antigen (HBeAg) negative chronic hepatitis B patients

Şükran Köse[1], Melda Türken[1], Süheyla Serin Senger[1], Bengü Gireniz Tatar[1], Başak Göl Serin[1]

Yenişehir Training and Research Hospital Infectious Disease and Clinical Microbiology Izmir-Turkey[1]

Background: Chronic hepatitis B is a globally highly prevalent disease, leading to serious consequences if not properly treated.
The Aim: The purpose of this study is to evaluate the efficacy of lamivudine versus telbivudine in the treatment of naive hepatitis B e antigen (HBeAg) - negative chronic hepatitis B patients, using the one year period results from Izmir, Turkey.
Method: Study population was composed of 60 patients with low viral load (HBV DNA: 104-107 copy/ml), naive HBeAg-negative chronic hepatitis B who were followed up in outpatient clinic regularly. Twenty-five patients received telbivudine 600 mg/day (group 1) and 35 patients received lamivudine 100 mg/day (group 2). The biochemical and virological response rates of both group were examined at 12th, 24th and 48th weeks, and were compared in each period. According to international guidelines, virological responses at 12th weeks were assessed as a 2 log reduction of HBV DNA. HBV DNA negativity at the 24th and 48th weeks were evaluated as virological responses. Hepatitis B surface antigen and antibody (HbsAg and HBsAb) were assessed after one year of treatment.
Results: In group 1, virological responses at 12th, 24th and 48th weeks were 100, 84 and 92 %, respectively. Virological responses' results of group 2 were 94, 88 and 80 %, respectively. But there was no difference in ALT normalization (96 % versus 97 %) between the two groups. HBsAg loss has not detected in any of the patients.
Conclusions: Among patients with HBeAg-negative chronic hepatitis B, telbivudine demonstrated greater HBV DNA suppression with less resistance than did lamivudine at the 48th weeks.

Topic 11: Hepatitis B

No: 1477

Impaired anti fibrotic activity of natural killer cells is dependent on hepatic stellate cells derived TGF β and engulf in liver cirrhosis with chronic HBV infection

Juanjuan Zhao[1], Zheng Zhang[1], Fu-sheng Wang[1]

Beijing 302 Hospital Research Center For Biological Therapy Beijing-China[1]

Aims: The present study aims to identify the role of NK cells in liver cirrhosis with chronic HBV infection and relevant mechanisms.
Methods: We comprehensively characterized frequency, phenotypes, function and the relevant mechanisms of peripheral and intrahepatic NK cells in 50 chronic hepatitis B (CHB) patients and 68 HBV-associated LC patients as well as 35 healthy subjects (HC).
Results: Both peripheral and intrahepatic NK cell frequencies in LC and CHB patients were significantly decreased as compared with those in HC subjects. NK cells also expressed lower levels of TRAIL, activation markers, activation receptors and granzyme and perforin and higher levels of inhibitory receptors in LC patients than those from CHB patients, thus displaying the decreased CD107a and interferon (IFN)-γ production and reduced killing capacity against hepatic stellate cells (HSCs). The immunohistochemical staining showed that NKp46-positive cells were more enriched in the α-SMA-negative area in livers from LC patients. In vitro, HSCs-derived TGF-β potentially suppressed NK cytolytic activity, and blockade of TGF-β significantly enhanced NK cell-derived CD107a and IFN-γ production. Importantly, HSCs had increased ability to engulf NK cells from LC patients in vitro. Finally, NK cell cytolytic activity was also correlated negatively with liver fibrosis scores in HBV infected patients, which is further confirmed by the longitudinal follow-up of LC patients.
Conclusions: Our data indicate that the anti-fibrotic activity of NK cells was impaired partially dependent on HSC-derived TGF-β and cellular ingestion, which further associated with liver fibrotic progression in chronic HBV infection patients.

Topic 11: Hepatitis B

No: 2174

Alopecia areata; a rare complication of tenofovir disoproxil fumarate in chronic hepatitis b

Güray Can[1], Mevlüt Kurt[1], Emrah Poşul[1], Bülent Yılmaz[2], Uğur Korkmaz[2], Fatma Akdağ[3], Hatice Can[1]

Abant Izzet Baysal University, Faculty of Medicine Department of Gastroenterology Bolu-Turkey[1], Bolu Izzet Baysal State Hospital Department of Gastroenterology Bolu-Turkey[2], Abant Izzet Baysal University, Faculty of Medicine Department of Internal Medicine Bolu-Turkey[3]

Aim: Being used in treatment of HIV and chronic hepatisis B (CHB), Tenofovir disoproxil fumarate (TDF) is a nucleotide analogue having a high genetic barrier. The most common side effects of tenofovir are nausea, vomiting, diarrhea, asthenia, renal toxicity like acute renal failure and rarely abdominal pain and hepatotoxicity. In literature, only fourteen TDF caused alopecia cases have been reported and all of these cases had a HIV infection. There are no cases that have been reported in CHB. In this report, we presented an alopecia case caused by TDF in CHB infection.
Case: 44-years old male patient who has no chronic illness on his history applied to our clinic with weakness nearly 5 months ago. In his biochemistry tests, nearly threefold increase on his transaminases was determined. HBsAg and antiHBe were positive. There were no risk factors for Hepatit B except for HBsAg positivity of his brother. HBV-DNA level was 11,627,045copy/ml. Hepatitis activity index and fibrosis score were reported 14/18 and 4/6 respectively. TDF was started. Transaminases regressed to normal range in the first month of the treatment. Hair loss was appeared in the sixth week of the treatment on the patient, who has no other drug usage. There were no alopecia history of him and his relatives. It was evaluated by the dermatologist as alopecia areata and zinc-magnesium oxide-sulphate complex and fluocortolone pivalate were started to the patient. TDF was switched to entecavir.
Conclusion: Alopecia may arise in many situations. It should be considered that alopecia can be seen as the side effect of TDF.

Topic 11: Hepatitis B

No: 1422

Concomitant nonalcoholic fatty liver disease may not influence fibrosis severity in patients with chronic hepatitis B

Ruhua Li[1], Youfu Zhu[2], Jinlian Yang[1], Yan Wang[2]

Southern Medical University Department of Hepatobiliary Surgery,zhujiang Hospital Guangzhou-China[1], Southern Medical University State Key Laboratory of Organ Failure Research, Guangdong Provincial Key Laboratory of Viral Hepatitis Research, Dept.infectious Diseases, Nanfang Hos Guangzhou-China[2]

Aim: To identify the impact of concomitant nonalcoholic fatty liver disease (NAFLD) on the development of hepatic fibrosis in patients with chronic hepatitis B (CHB).
Method: We recruited 428 cases of CHB or CHB and NAFLD patients with available liver biopsy diagnosis from a tertiary hospital from Jan. 2009 to Dec. 2012. Patients having complete record of demographic and laboratory data were included for this study. After randomly matched by age and gender, they were divided into: group A with only CHB ($n = 129$); or group B with CHB and coexistent NAFLD ($n = 43$). Steatosis was graded with Brunt scoring system; necroinflammatory activity and fibrosis were evaluated with Scheuer scoring system.
Result: Histological evaluation of groups A and B was illustrated in Table 1. The two groups were comparable in age, gender, necroinflammatory activity, steatosis, HBeAg status, HBV DNA, ALT, AST, ALB, TBIL and DBIL. Fibrosis severity of entire group or different age-subgroups was the same between A and B, and was associated with necroinflammatory activity in both groups (A: $r = 0.620$, $P < 0.001$; B: $r = 0.800$, $P < 0.001$). In group B, steatosis was neither associated with fibrosis severity ($P = 0.898$) nor HBV DNA level ($P = 0.728$); while among the patients whose HBV DNA levels were lower than 108 IU/ml, steatosis had negative association with HBV DNA level ($r = -0.507$, $P = 0.012$). Necroinflammatory activity was associated with HBV DNA level only in group A ($r = 0.184$, $P = 0.037$).
Conclusion: Our result implies that concomitant NAFLD may not significantly affect the fibrosis severity of patients with CHB.

Topic 11: Hepatitis B

No: 1713

Evolutionary patterns of hepatitis B virus quasispecies under lamivudine treatment and its impact on relapse

Jianning Jiang[1], Baojian Wang[1], Minghua Su[1], Xiaoli Wu[1], Ailian Lu[1], Shaohua Zhong[1], Shihua Li[1], Lanxiu Liang[1], Rong Xie[1], Yanyan Mo[1], Peng Liang[1]

The First affiliated Hospital of Guangxi Medical University, Nanning Infectious Disease Department Nanning-China[1]

Objectives: To investigate the evolution of hepatitis B virus (HBV) Polymerase (P) region quasispecies (QS) in CHB patients who stopped lamivudine treatment after meeting end-point criteria of 2008 APASL guideline and its impact on relapse.
Materials and methods: 43 patients with chronic hepatitis B were receiving lamivudine (25initial treatment,18 retreatment). All patients stopped lamivudine after meeting end-point criteria of 2008 APASL guideline and were followed up. Serum specimens were taken at baseline and liver biopsy specimens were taken at therapeutic end-point.Full-length hepatocyte cccDNA were amplified with HBV cccDNA special primers by Rolling circle amplification. Serum HBV rcDNA and hepatocyte cccDNA P gene were amplified and cloned. The HBV P region was sequenced at the average of 27 clones per sample (2322 total from both groups).
Results: QS complexity of hepatocyte cccDNA P region in the patients without relapses was statistically lower than that with relapse (0.351 vs 0.532, $P = 0.030$)at stopping point. In the retreatment patients group, QS complexity of hepatocyte cccDtNA P region in the patients without relapses was statistically lower than that with relapse (0.714 vs 0.398, $P = 0.006$) at stopping point.QS complexity of hepatocyte cccDNA P region in retreatment patients group was statistically higher than in initial treatment group at stopping point(0.556 vs 0.362, $P = 0.021$). QS complexity of HBV rcDNA P gene were not significantly different between the patients with and without relapses(0.363 vs 0.386, $P = 0.815$).
Conclusion: Characteristics of HBV hepatocyte cccDNA P gene QS evolution at therapeutic end-point contribute to the prediction of relapse.

Topic 11: Hepatitis B

No: 1344

The utility of VWF AG as a marker and vitro score in predicting of liver fibrosis stage in patients with chronic hepatitis B

Şahin Çoban[1], Hakan Akıncı[1], Mevlüt Hamamcı[1], Fatih Karaahmet[1], Serta Kılınçalp[1], Yusuf Coşkun[1], Zahide Şimşek[1], Yusuf Üstün[1], Elife Erarslan[1], Ilhami Yüksel[1]

Diskapi Yildirim Beyazit Education and Research Hospital Gastroenterology Ankara-Turkey[1]

Background and aim: Van Willebrand factor (vWF) is an important adhesive protein for both platelet adhesion and aggregation.We aim to assess if vWF-Ag is able to predict different fibrosis stages in patients with chronic hepatitis B.
Methods: A total of 130 chronic hepatitis B patients who underwent biopsy and 30 healthy controls were enrolled consecutively into the study between January 2013 and May 2014. We assessed stage of fibrosis according to Metavir, and measured vWF-Ag using elisa kit (ELISA, Assaypro, St. Charles, MO). Patients with co-infected with HCV, delta virus, and/or human immunodeficiency virus, other autoimmune liver disease, hepatocellular carcinoma, liver transplantation, metabolic liver diseases, cardiopulmonary and/or renal failure, active infections, diabetes mellitus were excluded. Histological assessment of the liver and laboratory analysis of vWF-Ag were done in groups and compared with each other. Laboratory parameters including AST, ALT, GGT, ALP, platelets, bilirubin, albumin, cholesterol and HBV-DNA were taken prior to liver biopsy. We also calculated VITRO score, a new score: vWF-Ag/thrombocytes for prediction of fibrosis.
Results: Descriptive parameters were comparable in both groups. AST and GGT levels were higher in patient group than controls. In patient group, platelets count was less than control group, $P < 0.05$. The mean level of vWF was 2,6 IU/mL in patients group and 2,4 IU/mL in control group, $P > 0.05$. The patients were divided into

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No: 1882

The value of fibrotouch in diagnosis of hepatic fibrosis in CHB patients and influencing factors

Longfeng Jiang[1], Jun Li[1], Yaping Han[1], Ping Shi[1], Yao Liu[1]

The First Affiliated Hospital With Nanjing Medical University Department of Infectious Diseases Nanjing-China[1]

Objective: To evaluate the value and influencing factors of transient elastography (FibroTouch) in predicting liver fibrosis in patients with chronic hepatitis B (CHB).
Methods: Thirty CHB patients in the first affiliated hospital with nanjing medical university from October 2013 to January 2014 were enrolled in this study. Transient elastography (Fibrotouch) was applied in measuring the liver stiffness values of all patients.Liver biopsy was performed on the same period as FT.
Results: The average stiffness (kPa) of FibroTouch for each group was 4.1 ± 0.7, 7.4 ± 2.5, 12.0 ± 5.2, 18.0 ± 4.7, respectively. To compare the result of statistical analysis, the difference of stiffness among liver fibrosis groups is significant ($P < 0.001$). Stiffness had a significant direct correlation with liver fibrosis ($r = 0.806$, $P < 0.001$). The AUROCs of Stiffness for predicting moderate and advanced fibrosis were 0.902 and 0.931, respectively.The cutoff value for significant advanced liver fibrosis was stiffness ≥ 7.80, the sensitivity was 80 %, the specificity was 93.3 %, the positive predictive value was 82.2 % and the negative predictive value was 92.3 %.For advanced fibrosis,the cutoff value was stiffness ≥ 13.71, the sensitivity was 81.3 %, the specificity was 91.7 %, the positive predictive value was 71.4 %, and the negative predictive value was 95.7 %.According to the result of Logistic regression analysis,ALB,PLT,AST and TBIL are not the significant clinical factors which may affect the result of stiffness values in certain range.
Conclusion: Transient elastography (FibroTouch) is a promising non-invasive method for the detection of fibrosis in CHB patients.

Topic 11: Hepatitis B

No: 1442

The effect of tenofovir on serum phosphor concentrations in chronic HBV

Murat Aladag[1], Yilmaz Bilgic[1], Murat Harputluoglu[1], Yahya Atayan[1], Mehmet Ali Erdoğan[1], Yasin Furkan Cagin[2], Oğuzhan Yildirim[2], Yuksel Seckin[2], Melih Karincaoglu[2]

Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[1], Inonu University Gastroenterology Malatya-[2]

Introduction and aim: In the present study, we investigated incidence and severity of adverse events on renal functions in the patients with chronic hepatitis B virus infection and receiving Tenofovir.
Material-Method: Files of a total of 255 cases [85 females and 170 males with a mean age of 43 (18-84) years] that received Tenofovir therapy were evaluated. The patients were questioned in terms of existing comorbidities, medications, and presence of renal disease and the results were recorded by interviewing the patients. Serum phosphor, calcium and creatinine values of the cases, as well as routine biochemical parameters, were recorded and investigated.
Results: The mean duration of treatment was 2.3 years. of the hypertensive cases, 30 have been receiving ARB/ACE group medications, 20 cases have been receiving calcium channel blockers, and others have been receiving various antihypertensive drugs. Baseline serum creatinine level before Tenofovir therapy was 0.7 mg/dl. An elevation of 0.5 mg/dl or higher in creatinine levels over the course of follow-up period was considered significant. The mean baseline serum calcium level was 9.34 mg/dl and the mean baseline phosphor level was 3.4 mg/dl; minimal decrease in phosphor level was determined in 50 (25 %) of 200 cases, of which 35 were male and 15 were female.
Discussion and conclusion: Decrease was determined in phosphate levels in 25 % of the cases. In conclusion, using Tenofovir in the treatment of chronic viral hepatitis is not only effective but also safe; however, we agreed that probability of hypophosphatemia should be kept in mind in elder patients with comorbid conditions.

Topic 11: Hepatitis B

No: 1435

Safety and reliability of tenofovir therapy in pregnancy and lactation period

Hulya Aladag[1], Murat Aladag[2], Yilmaz Bilgic[2], Murat Harputluoglu[2], Mehmet Ali Erdoğan[2], Yasin Furkan Cagin[3],

Yahya Atayan[3], Oğuzhanm Yıldırım[3], Yuksel Seckin[3], Melih Karincaoglu[3]

Inonu University Faculty of Medicine Gynecology Malatya-Turkey[1], Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[2], Inonu University Gastroenterology Malatya-[3]

Objective: In the present study, we aimed to evaluate the findings in the pregnant patients treated in our clinic for HBV between 2008 and 2014.
Material and method: The present study comprised 40 women with a mean age of 27 years, who were being treated in our clinic between 2008 and 2014 for chronic viral hepatitis B. Tenofovir was commenced at a daily dose of one tablet in the cases with HBV-DNA level higher than 6 log. Hepatitis B vaccine was administered in one extremity and hepatitis B hyperimmunoglobulin was administered in the other extremity within the first 12 h following delivery. Hepatitis vaccine continued to be administered on the 1st and 6th months after delivery. The women were advised to breastfeed their children.
Results: Mothers developed no adverse event that requires discontinuation of therapy or dose reduction. It was observed that Anti-HBs titers studied in the first year after birth was at least 100 IU/ml in all of the infants. Hepatitis panels demonstrated no sign of viral activation. It was observed that HBV-DNA levels decreased as of the 3rd month of treatment as compared to the baseline in the mothers that gave birth, and HBV-DNA was found negative in 80 % of the cases after the 6th month of treatment and in 98 % of the cases on the 12th month.
Conclusion: It was observed that tenofovir therapy is effective and safe when used in pregnant women with chronic HBV infection. It was concluded that tenofovir therapy is safe also in the lactation period.

Topic 11: Hepatitis B

No: 1244

Effect of il 28 b polymorphisms on the natural course of hbv infection

Nese Demirturk[1], Nevil Aykin[2], Figen Cevik[2], Bugra Koca[3], Nurhan Doğan[4], Tulay Koken[5]

Kocatepe University Infectious Disease and Clinical Microbiology Afyonkarahisar-Turkey[1], Yunus Emre Hospital Infectious Disease Eskisehir-Turkey[2], Kocatepe University Mediacal Biochemistry Afyonkarahisar-Turkey[3], Kocatepe University Biostatistics Afyonkarahisar-Turkey[4], Kocatepe University Medical Biochemistry Afyonkarahisar-Turkey[5]

The aim of the study was to evaluate the effectiveness of IL 28B rs12979869 polymorhisms in assessing the outcomes of HBV infection.

The study was designed prospectively. The subjects were randomly selected among patients admitted to the Infectious Disease polyclinics of Kocatepe University Medical Faculty and Yunus Emre Hospital. The patients were divided into three groups; group 1, chronic hepatitis B; group 2, inactive HBV carrier state; group 3 HBsAg negative, anti-HBs and anti-HBcIgG positive therefore immune subjects. All subjects were genotyped for the IL 28B promoter single nucleotide polymorphism rs 12979860 at position 3176 C/T.

Totally 99 patients were included in the study. There were 43 (43.4 %), 34 (34.4 %) and 22 (22.2 %) subjects in group 1, group 2 and group 3, respectively. The distribution of IL 28B promoter single nucleotide polymorphism rs12979860 at position 3176 C/T observed in patients by group is shown in table 1. CT (48.8 %) is the most common genotype in group 1 while CC (47.1 and 63.6 %, respectively) is the most common genotype seen in group 2 and in group 3. No differences were observed between the groups in terms of allel distribution ($p > 0.05$).

In conclusion; we found that IL 28B rs12979860 genotype and C/T allele distribution were not distinct in patients with different stage of HBV infection. Therefore IL 28B rs12979860 gene polymorphisms are not effective on the natural course of HBV infection.

Table 1: IL28 B rs12979860 C/T allele polymorphisms distribution.

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No: 1004

CCL20 a potential predictor of significant liver fibrosis in chronic hepatitis B

Xianghua Zeng[1], Maoshi Li[1], Yuming Wang[1]

Southwest Hospital Third Military Medical University Department of Infectious Diseases Chongqing-China[1]

Background and aim: Significant liver fibrosis is one of the indications for antiviral treatment in patients with chronic hepatitis B (CHB). Since CCL20 has turned out to be a potential driver of inflammation and fibrosis in alcoholic hepatitis, however, the association of CCL20 with the severity of fibrosis in CHB is yet unclear. We aim to explore the value of serum CCL20 level in predicting the occurrence of significant liver fibrosis.
Study: CCL20 serum level was assessed in 88 patients with chronic hepatitis B (CHB) by enzyme-linked immunosorbent assay and compared with biopsy-proven histologic stage of liver fibrosis and noninvasive liver fibrosis markers, including FibroScan and aspartate transaminase to platelets ratio index (APRI). The receiver operating characteristic (ROC) curve was used for analyzing the results and determining cut-off values.
Results: Serum CCL20 level was strongly associated with the histologic stage of liver fibrosis ($r = 0.406$, $P = 0.014$), and significantly increased at higher stages of liver fibrosis (F2/F3/F4, $P < 0.0001$). The value of CCL20 had a high diagnostic specificity (84.6 %) and sensitivity (73.7 %) to differentiate significant fibrosis (F2/F3/F4) from none or mild fibrosis (F0/F1), the corresponding area under ROC (AUROC) was 0.7236 ($P = 0.0001$). When combining CCL20 with liver stiffness measurement (LSM), the diagnostic accuracy was significantly improved (AUROC = 0.8471, $P = 0.001$). CCL20 serum level was also strongly correlated to the noninvasive fibrosis markers, APRI ($r = 0.621$, $P < 0.0001$) and LSM ($r = 0.871$, $P < 0.0001$).
Conclusions: Serum CCL20 level was a robust predictive marker of significant liver fibrosis, and might be further used to differentiate various stages of liver fibrosis in CHB.

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No: 1839

Clinical outcome and predictor for relapse after cessation of oral antiviral treatment in chronic hepatitis B patients prospective observational cohort study

Kyu Sik Jung[1], Jun Yong Park[1], Young Eun Chon[1], Hyon-suk Kim[2], Wonseok Kang[1], Beom Kyung Kim[1], Seung Up Kim[1], Do Young Kim[1], Kwang-hyub Han[1], Sang Hoon Ahn[1]

Yonsei University College of Medicine Department of Internal Medicine Seoul-Korea, South[1], Yonsei University College of Medicine Department of Laboratory Medicine Seoul-Korea, South[2]

Background: Little is known about stopping rules of nucelos(t)ide analog (NA) treatment for chronic hepatitis B (CHB).
Methods: A total of 164 consecutive CHB patients who met cessation criteria of NA treatment by APASL guideline were enrolled in this prospective cohort. Fifty-one patients were excluded by exclusion criteria, 113 patients (45 HBeAg-positive and 68 HBeAg-negative CHB), who stopped NA treatment, remained for statistical analysis. Relapse was defined as reappearance of HBV-DNA > 2000 IU/mL after stopping NA treatment.
Results: Within 1 year after NA treatment, relapse occurred in 26 (57.8 %) of 45 HBeAg-positive patients with median time of 219 (IQR 77-397) days and in 37 (54.4 %) of 68 HBeAg-negative patients with median time of 215 (IQR 55-376) days. Among the patients with relapse, 8 (30.8 %) HBeAg-positive patients had a biochemical relapse (ALT elevation > 2XUNL) and 19 (51.4 %) HBeAg-negative patients did. In multivariate analysis, age > 40 years (OR, 10.959; 95 % CI, 2.211-54.320; $P = 0.003$) and pretreatment HBV-DNA > 2X106 IU/mL (OR, 9.285; 95 % CI, 1.545-55.795; $P = 0.036$) were identified as independent risk factor for relapse in HBeAg-positive patients, and age > 40 years (OR, 6.690; 95 % CI, 1.314-34.057; $P = 0.022$) and end of treatment HBcrAg level > 3.7 log IU/mL (OR, 3.751; 95 % CI, 1.187-11.856; $P = 0.024$) were selected in HBeAg-negative patients. During follow up, hepatic decompensation or HCC did not occur and HBV-DNA suppression was achieved in by retreated after relapse in both groups.
Conclusions: Our data suggested that clinical outcome after stopping antiviral agents was favorable despite relatively high relapse rate, suggesting that discontinuation of NA might be considered carefully considering individual risk factors.

Topic 11: Hepatitis B

No: 1615

Quality of life in patients with chronic hepatitis B

Şükran Köse[1], Gülgün Akkoçlu[1], Başak Göl Serin[1]

Yenişehir Training and Research Hospital Infectious Disease and Clinical Microbiology Izmir-Turkey[1]

Background: Quality of life is an expression of individual well-being, and is a statement of subjective satisfaction in different domains of life. Even though, quality of life contains family, work-life, and socio-economic conditions, it also includes the difference between the reality and the targets, expectations, hopes, and dreams of the individual, i.e. the satisfaction and the perception of well-being of the individual at daily life.
Aim: In this study, the purpose was to evaluate the quality of life of patients with inactive hepatitis B (HBV) infection and chronic hepatitis B patients.
Method: Study population was composed of inactive HBV and chronic hepatitis patients, who were followed up in outpatient clinic. They were asked to complete a questionnaire form, questioning for age, gender, and educational level, and Short Form 36 (SF-36) Quality of Life questionnaire for determining quality of life.
Results: Quality of life scores were found substantially similar across patients with inactive hepatitis B infection and chronic HBV patients. While emotional disability and depression were detected significantly more in chronic hepatitis B patients, no physical disability was detected significantly. Emotional disability and depression were detected more in women. Physical disability was detected more in elderly patients and in patients with comorbid diseases.
Conclusion: Since comorbidity of psychiatric disorders, anxiety, and mood disorders is high, the active participation of psychiatry in follow up and treatment stage of chronic hepatitis patients is essential and important. Through detection of disabilities in quality of life of patients, it is considered that early resolution of problems in daily life and treatment compliance will increase.

Topic 11: Hepatitis B

No: 1329

Long term follow up outcome of non antiviral therapy in patients with chronic hepatitis B

Guangdong Tong[1], Yufeng Xing[1], Hongyan Wang[1], Chunshan Wei[1], Sinuan Chen[1], Haihong Tang[1], Yingjun Zheng[1], Daqiao Zhou[1]

Shenzhen Hospital of Traditional Chinese Medicine Hepatology Shenzhen-China[1]

Objective: The relationship between progression of chronic hepatitis B (CHB) and serum alanine aminotransferase(ALT) without antiviral therapy has been reported. We performed a long-term cohort study to elucidate the incidence of liver cirrhosis (LC), hepatocellular carcinoma (HCC) after non- antiviral therapy patients with CHB were treated with anti-inflammatory and hepatoprotective therapy (AIHPT).
Methods: A total of 2748 patients, 362 cases were non-antiviral therapy (male 292, female 70), in which 199 cases were HBeAg-positive. The study began (1993-1998) were followed up until December 2010, with a median follow-up period of 8 years (range 2-17 years). Patients underwent blood and clinic controls every 3 to 12 months. The patients were treated with the Glycyrrhizic acid and Bicyclol whenever ALT elevated. The Kaplan–Meier cumulative incidence was used to estimate associated outcomes.
Results: HBV-DNA seroclearance occurred in 57 patients (15.7 %, 1.987 per 100 person-years). LC cumulative incidence of patients with HBV-DNA seroclearance declined significantly ($P = 0.018$). HBeAgseroconversion occurred in 74 patients (37.2 %, 5.906 per 100 person-years). LC and HCC cumulative incidence in patients with HBeAg seroconversion descented significantly (LC, $P = 0.001$; HCC, $P = 0.015$).
Conclusions: For Patients without antiviral therapy that accepted AIHPT,the incidence of LC or HCC reduced significantly after HBV-DNA or HBeAg seroconversion. This finding can be used as reference for the evaluation of antiviral treatment effect.

Topic 11: Hepatitis B

No: 1237

Virologic response and safety of tenofovir vs. entecavir in treatment naïve chronic hepatitis B patients

So Young Kwon[1], Hyung Min Yu[1], Jeong Han Kim[1], Won Hyeok Choe[1]

Konkuk University Hospital Internal Medicine Seoul-Korea, South[1]

Background/aims: This study aimed to evaluate the antiviral response and safety of TDF vs. ETV in treatment-naïve CHB patients.
Methods: We performed a retrospective cohort study of treatment naive CHB patients who were treated with TDF or ETV. We analyzed virologic, biochemical and serologic responses at 3, 6, and 12 months.
Results: A total of 107 patients (TDF group 49, ETV group 59) were included. Baseline characteristics were similar between the 2 groups. The estimated proportion of complete virologic response in the TDF or ETV group was 44.9 vs. 39.7 % at 6 months and 89.6 vs. 83.2 % at 12 months, respectively ($P = 0.991$). Viral breakthrough was not observed in both groups. One patient in the TDF group and 2 patients in the ETV group experienced HBeAg loss, respectively ($P = 0.657$). High HBV DNA level at baseline was a significant negative predictor of virologic response by Cox regression analysis ($P = 0.007$). The safety profile was similar between the 2 groups. There was no case with serious adverse event.
Conclusions: Both TDF and ETV are effective for achieving complete virologic response and have a favorable safety profile in treatment-naïve CHB patients. High viral load at baseline is a negative predictive factor of complete virologic response.

Topic 11: Hepatitis B

No: 2029

Relationship between alanine transaminase level and hepatitis B viral activity in maternal carriers of hepatitis B surface antigen

T.T. Lao[1], T.K.W. Cheung[1], L.W. Law[1], V.W.S. Wong[2], H.L.Y. Chan[2], T.Y. Leung[1]

The Chinese University of Hong Kong Obstetrics & Gynaecology Shatin-Hong Kong[1], The Chinese University of Hong Kong Medicine & Therapeutics Shatin-Hong Kong[2]

Aim: The relationship between elevated alanine transaminase (ALT) level before 20 weeks gestation (> 40 IU/L) with maternal characteristics and hepatitis B virus (HBV) activity was examined in 255 asymptomatic mothers with positive hepatitis B surface antigen (HBsAg) identified through routine antenatal screening.
Methods: Following recruitment from the antenatal clinic, the mothers were assessed before 20 weeks gestation with blood drawn for liver function test (LFT), hepatitis B envelope antigen (HBeAg) status, and HBV DNA levels. Those with elevated ALT were compared with those with normal ALT for maternal characteristics and HBV activity.
Results: There was 23 (9 %) mothers with elevated ALT. There was no difference in mean(± SD) maternal age (31.4 ± 3.1 versus 32.4 ± 4.3 years), height (159.0 ± 5.8 versus 158.4 ± 8.8 cm), body mass index (22.6 ± 3.3 versus 22.2 ± 3.6 kg/m2); or serum levels of albumin (39.3 ± 2.7 versus 38.8 ± 2.7 g/L), bilirubin (7.0 ± 4.4 versus 6.0 ± 2.7 μmol/L), or alkaline phosphatase (53.9 ± 16.7 versus 46.6 ± 11.1 IU/L), or HBV DNA detection (82.6 % versus 67.6 %); but the HBV DNA level (5.717 ± 3.128 versus 3.113 ± 2.853 log10 copies/mL, $P < 0.001$) and incidence of HBeAg positivity (65.2 % versus 25.4 %, $P < 0.001$) were significantly higher in mothers with elevated ALT.
Conclusion: The 9 % of asymptomatic HBsAg carrier mothers with elevated ALT could not be identified by maternal characteristics, and their LFT results were similar except for the elevated ALT, but they had with higher HBV DNA levels and incidence of HBeAg positivity.

Topic 11: Hepatitis B

No: 1976

Pegylated interferon alfa 2a induced cutaneous lichen planus at the antecubital fossa after vein puncture for blood sampling

Abdullah Emre Yildirim[1], Bugra Tolga Konduk[1], Ayhan Balkan[1], Murat Taner Gulsen[1]

Gaziantep University Faculty of Medicine Gastroenterology Gaziantep-Turkey[1]

Introduction: Lichen planus (LP) is an inflammatory disease which is characterized by papular skin eruptions over the extremities, genitalia, hair follicles and mucous membranes. LP has been associated with viral infections such as HBV and HCV, medications and vaccinations. It is suggested that interferon-α is among the offending medicines for LP. We encountered a 25-year-old woman in whom cutaneus LP developed after starting Peginterferon-alpha 2a (Peg-INF α-2a) treatment for HBV infection.
Case report: A 25 year-old female applied to our clinic. She has been treated with Peg-INF α-2a 180mcg/week for HBV for 6 month. During the interferon treatment she noticed a few pruritic lesions in both proximal forearms around the antecubital vein which arose after blood sampling. Her physical examination revealed a few slightly elevated violaceous erythemas with white streaks and scales on her bilateral forearms close to antecubital fossa. Skin biopsy taken from these lesions revealed lichenoid dermatitis with epidermal hyperplasia, hyperkeratosis, acanthosis and band-like cellular infiltration with dilated small vessels in the upper dermis. Peg-INF α-2a was not discontinued and the patient was recommended to avoid scratching, use mild soaps and emollients. Her skin symptoms improved and lesions completely resolved in two weeks after she was started on topical steroids, 0.1 % triamcinolone-acetonide ointment.
Discussion: Immune treatment of HBV with Peg-INF α-2a can trigger LP-like cutaneous and mucosal eruptions. The relationship between Peg-INF α-2a and LP is not well established. This is the first case of a local LP-like reaction around the antecubital vein after the blood sampling associated with Peg-INF α-2a administration.

Topic 11: Hepatitis B

No: 2211

Prevalence of hepatitis B virus infection in western China epidemiological survey results of general adult population in Mianyang

Yuanji Ma[1], Enqiang Chen[1], Taoyou Zhou[1], Yulin Ji[2], Ping Yuan[3], Hong Tang[1]

West China Hospital of Sichuan University Center of Infectious Diseases Chengdu-China[1], West China Hospital of Sichuan University Department of Respiratory and Critical Care Medicine Chengdu-China[2], Sichuan University West China School of Public Heath Chengdu-China[3]

Objectives: Though the global epidemiology of hepatitis B virus (HBV) infection has been changing rapidly over the last two decades, HBV infection remains a serious public health problem in overpopulated Asia–Pacific countries, especially in China. This study aimed to determinate the prevalence of current or past infection of HBV, and its risk characteristics in generaladult population in Mianyang city, a

demonstration area of infectious disease established by Chinese government.
Methods: A cross-sectional survey was performed between January 2010 and December 2012; and all participators completed a questionnaire, and donated blood voluntarily for HBV serologic markers and biochemical parameters.
Results: A total of 301,574 participators were analyzed in this study, and positive-HBsAg was detected in 6.79 % (20,507/301, 574)of them, and 65.6 % of those positive-HBsAg participators were with positive HBeAg. There were 281,067 subjects with negative HBsAg, and positive anti-HBc (35.06 %) was detected in 98, 570 out of them. The main risk characteristics of positive HBsAg were HBV family history, unvaccination, male gender, and lower levels of education (all $P < 0.05$).
Conclusion: The prevalence of HBsAg is relative lower among adult subjects in this region. Expanding the HBV vaccination coverage and improving the individual education may further reduce the rate of HBV infection in this region.

Topic 11: Hepatitis B

No: 1871

The role of genotype and mutants of hbv in patients of hepatocellular carcinoma with hepatitis C and occult hepatitis B

Wei-lun Tsai[1], Jin-shiung Cheng[1], Kwok-hung Lai[1], Hoi-hung Chan[1], Ping-i Shu[1]

Kaohsiung Veterans General Hospital Department of Gastroenterology Kaohsiung-Taiwan[1]

Background: HBV coinfected with chronic hepatitis C subjects were found to increase the risk to develop advanced liver disease later in their life. In chronic HBV patients, some virological factors such as genotype C, preS deletion and core promoter/precore mutations are found to increase the risk of HCC. However, little was known about the role of the virological risk factors of HBV in chronic HCV patients with occult HBV.
Methods: One hundred and eighty one HBsAg-negative, HCV-Ab positive HCC patients (group A), 153 HBsAg-negative, HCV-Ab positive chronic hepatitis patients (group B), and 20 HCC subjects with both positive HBsAg and HCV-Ab (group C) were enrolled. The preS, core promoter/precore region and S gene were amplified by nested PCR and direct-sequenced. Viral phylogenetic analysis was also performed.
Results: The occult HBV infection was found for 20.4 % (37/181) in the group A, and 34.0 % (52/153) in group B. In addition, the genotype C ($P = 0.019$), BCP mutations ($P = 0.004$), 1858 mutation ($P < 0.001$) and 1896 mutation ($P = 0.032$) were more common in chronic HCV patients with HCC. PreS1 deletion ($P = 0.033$), BCP ($P = 0.014$) and precore 1896 mutation ($P = 0.008$) were more common in chronic HCV patients with overt than occult HBV.
Conclusion: In patients with chronic HCV and occult HBV infection, HBV genotype C, BCP 1858 and 1896 mutations seemed to be associated with the development of HCC.

Topic 11: Hepatitis B

No: 1908

Clinical characteristics and outcome of hepatitis B virus related hepatocellular carcinoma in children adolescents and young adults in Japan

Tomoko Takano[1], Satoko Hosono[2], Hitoshi Tajiri[1], Hideo Tanaka[2]

Osaka General Medical Center Pediatrics Osaka-Japan[1], Aichi Cancer Center Research Institute Epidemiology and Prevention Nagoya-Japan[2]

Aims: Hepatocellular carcinoma (HCC) rarely occurs in children and adolescents. The aims of this study were to investigate the clinical characteristics and outcome of HBV-related HCC in children, adolescents and young adults.
Methods: This observational study included 546 patients with chronic HBV infection which was diagnosed during childhood from 1989 to 2013 in Japan. Only the observational data until the age of 30 years were included.
Results: There were 11 cases of HCC in the 546 subjects. Ten of the 11 were males and the median age at diagnosis of HCC was 15 years (range, 9-25). Most cases with HCC achieved HBe Ag seroconversion, had a slight elevation of ALT and low values of HBV-DNA. Liver cirrhosis was present in 5 of the 11 cases. All cases tested had an elevation of α-fetoprotein. Three cases received interferon therapy that failed to cease sustained hepatitis in all of them. Seven of the 11 with HCC died within one year of the diagnosis. All of the fatal cases had no follow up when HCC was found. The incidence of HCC was estimated to be 0.27 %/year among the present subjects with childhood-onset HBV infection.
Conclusion: This study showed 11 cases of HCC in the 546 subjects with annual rate of 0.27 %. Patients with HCC were more likely males, after achievement of HBe Ag seroconversion and carrying low viral loads. Education of young patients and cooperation among medical staffs may be needed for lifelong follow-up of patients with childhood-onset HBV infection.

Topic 11: Hepatitis B

No: 2210

The serum anti HBS levels among children aged 15 and younger who received routine hepatitis b vaccination during infancy in Mianyang city a typical city of southwest China a cross sectional study

Fang He[1], Yuanji Ma[1], Yulin Ji[2], Juying Zhang[3], Enqiang Chen[1], Hong Tang[1]

West China Hospital of Sichuan University Center of Infectious Diseases Chengdu-China[1], West China Hospital of Sichuan University Department of Respiratory and Critical Care Medicine Chengdu-China[2], Sichuan University West China School of Public Heath Chengdu-China[3]

Background: Hepatitis B virus (HBV) prevalence has been declined remarkably in children due to nationwide universal vaccination program for HBV in China. However, the persistence of immune response against HBV infection and the optimal time when a booster vaccination should be performed remain to be elucidated. This study aimed to assess the persistence of antibody to hepatitis B surface antigen (anti-HBs) levels in a representative population aged 15 and younger who received routine hepatitis B vaccination in Mianyang City, a typical city of southwest China.
Methods: A cross-sectional study was conducted in 2011 and 1526 children aged 15 and younger who received 3-dose 5 μg hepatitis B vaccine series during infancy but didn't receive a booster vaccination later were enrolled. The serum anti-HBs levels were measured by time-resolved immunofluorometric assay.

Results: Of the 1526 children, the mean age was 8.2 ± 4.1 years and 739 children were male. Along with the increase of ages, the median anti-HBs level, the rates of anti-HBs level ≥ 10 mIU/mL and the rates of anti-HBs level ≥ 100 mIU/mL declined remarkably in the early period and reached a low level at the age of 3 years, and then remained relatively stable. The median anti-HBs level, the rates of anti-HBs level ≥ 10 mIU/mL and the rates of anti-HBs level ≥ 100 mIU/mL in children aged 1 and 2 years were much higher than that in children aged 3 to 15 years ($P < 0.05$, respectively). The total rate of anti-HBs level ≥ 10 mIU/mL was 60.9 % with median anti-HBs level of 23.0 mIU/mL. Children whose anti-HBs were positive (anti-HBs level ≥ 10 mIU/mL) were younger than those anti-HBs negative (anti-HBs level < 10 mIU/mL) children (7.8 ± 4.3 years versus 8.8 ± 3.7 years, $P = 0.000$).
Conclusions: The immunity against HBV infection was gradually weakened in the early ages of children aged 15 and younger who received 3-dose hepatitis B vaccine series during infancy in China. Higher doses of hepatitis B vaccines for infants, repeated vaccination or additional booster vaccination for some children at or before the age of 3 years should be performed in order to get much more powerful immunity to HBV.

Topic 11: Hepatitis B

No: 2158

Histopathological evaluation in inactive hepatitis B carriers

Faden Hayrunnisa Aydin[1], Omer Senturk[2], Ugur Korkmaz[2], Berna Ustuner[2], Hasan Yilmaz[2], Murat Ozturkler[2], Altay Celebi[2], Sadettin Hulagu[2]

Kocaeli University Internal Medicine Kocaeli-Turkey[1], Kocaeli University Gastroenterology Kocaeli-Turkey[2]

Introduction: Immune reaction against to virus in the natural course of HBV infection can be evaluated in 5 phase. Seventy percent of the patients are in the immune tolerance phase and it can last lifetime. In a small group of HBV infected patient histologic activity can be intense despite to normality of transaminase and they can develop cirrhosis or HCC. Considering HBV DNA and transaminase level monitoring this small group of patients still remains challenging. In this study we evaluated necessity of additional histologıc investigation to virologıc and biochemical monitoring for detecting the cirrhosis and hcc developers in immune tolerance phase.
Materials and methods: A total of 91 patients in immune tolerance phase followed up for 12 months with 6 months interval and patients whose HbsAg positive, HBV DNA levels below 2000 IU/mL,normal AST, ALT levels included to study. Patients underwent liver biopsy with a 16 gauge needle. Histopathological evaluation was performed according to Ishak scoring system.
Results: In our study, moderate-to-severe liver fibrosis (fibrosis score of 3-4, according to Ishak) was detected 2 of every 5 inactive HBsAg carriers. Thirty-seven percent of 59 HBV DNA negative (< 50) patient has moderate to severe fibrosis in liver biopsy.
Conclusion: These results suggest that the only biochemical and serological evaluation may not always enough in patients with inactive HBsAg carriers. As chronic HBV infected patients this group of patients also may need for histopathological examination. More prospective studies are needed to answer the question which patient requires histopathologic evaluation and should it be invasive.

Topic 11: Hepatitis B

No: 2187

The evaluation of some hematological parameters at patients with chronic inactive hepatitis B virus infection

Ilknur Erdem[1], Rıdvan Kara Ali[1], Şenay Elbasan[1], Mustafa Doğan[1]

Namık Kemal University, Faculty of Medicine Infectious Disease Tekirdağ-Turkey[1]

Introduction: Hematological disorders may occur during hepatitis B and C virus infections, such as aplastic anemia, granulocytopenia, thrombocytopenia or even pancytopenia. In this retrospective study was aimed to investigate whether there is a relationship with some hematological parameters in patients with chronic inactive hepatitis B virus (HBV) infection.
Patients and methods: One hundred thirty-seven patients with chronic inactive HBV infection and 74 apparently healthy individuals who were HBsAg and antiHCV negative as a control group were enrolled in the present study. Complete blood count was performed for each patient.
Results: In our case group there were 78 males and 59 females. Patients' age ranged from 19 to 74 years(with an average age of 47). of the control group, 38 were male and 36 were female, the age ranged from 23 to 59 years(with an average age of 28). Anemia was detected in 11.6 % of the case group, and 10.8 % of controls ($p > 0.05$). Thrombocytopenia was detected in 4.3 % of the case group, and 2.5 % of controls ($p > 0.05$). The white cell count was within the normal limit for all the patients.
Conclusion: This study showed that there were no statistically significant differences between the prevalence of anaemia and thrombocytopenia among chronic inactive HBV carriers and control groups.

Topic 11: Hepatitis B

No: 1143

Detection of hepatitis B core antigen in hepatocytes of chronic hepatitis B patients comparison between indirect immunofluorescence and immunoperoxidase methods

Ruksana Raihan[1], Shahina Tabassum[2], Mamun Al Mahtab[3], Afzalun Nessa[2], Munira Jahan[2], Mohammad Kamal[4], Sheikh Mohammad Fazle Akbar[5], Julio Cesar Aguilar[6]

Aimst University Unit of Microbiology Kedah-Malaysia[1], Bangabandhu Sheikh Mujib Medical University Department of Virology Dhaka-Bangladesh[2], Bangabandhu Sheikh Mujib Medical University Department of Hepatology Dhaka-Bangladesh[3], Bangabandhu Sheikh Mujib Medical University Department of Pathology Dhaka-Bangladesh[4], Toshiba General Hospital Department of Medical Sciences Tokyo-Japan[5], Center For Genetic Engineering and Biotechnology Department of Biomedical Research Havana-Cuba[6]

Aims: Identification of HBcAg in hepatocytes may be used to detect viral replication in patients with mutant HBV variants unable to produce HBeAg and thus help in therpeutic decision-making.
Methods: Study was undertaken to compare between indirect immunofluorescence(IIF) and indirect immunoperoxidase(IIP) methods for detecting HBcAg in 70 CHB patients.
Results: Out of 70, 8(11.4 %) were HBeAg-positive and 62(88.57 %) HBeAg-negative. All HBeAg-positive tested HBcAg-positive by both IIF and IIP methods. Among 62 HBeAg-negative, 55-(88.7 %) were HBcAg-positive by IIF and 51(82 26 %) by IIP methods. There was

positive correlation between viral load and HBcAg detection. This was more evident in HBeAg-negative; their HBcAg expression increased with increasing HBV DNA level.
Conclusion: HBcAg can be detected using IIF from formalin fixed paraffin block preparation and also IIP, as an additional marker for active viral replication, although IIF has higher capacity of detection.

Topic 11: Hepatitis B

No: 1183

Durability of HBeAg seroconversion of telbivudine as monotherapy and as combination therapy with adefovir dipivoxil for chronic hepatitis B patients with high alt level a prospective multicenter cohort study

Yang Ding[1], Chong Zhang[1], Qiuju Sheng[1], Mingxiang Zhang[2], Feng Wu[3], Baojun Song[4], Weili Zhu[5], Jingyan Wang[1], Lilan Shi[1], Xiaoguang Dou[6]

Sheng Jing Hospital of China Medical University Infectious Diseases Shen Yang-China[1], Shenyang Infectious Disease Hospital Infectious Diseases Shen Yang-China[2], Dalian Infectious Disease Hospital Infectious Diseases Da Lian-China[3], Fushun Infectious Disease Hospital Infectious Diseases Fu Shun-China[4], Benxi Infectious Disease Hospital Infectious Diseases Ben Xi -China[5], Sheng Jing Hospital of China Medical University Infectious Diseases Shen Yang-China[6]

Objective: To evaluate the long-term antiviral efficacy of telbivudine (LdT) administered as monotherapy and as combination therapy with adefovir dipivoxil (ADV) for HBeAg-positive chronic hepatitis B(CHB) patients with high ALT level, and investigate the correlation between durability of HBeAg seroconversion following long-term therapy and virological and serological responses.
Methods: HBeAg-positive naïve CHB patients with ALT $> 3 \times$ ULN and HBV DNA > 105 copies/ml were enrolled to receive oral LdT (600 mg/d). HBV DNA will be assessed by COBAS®Taqman for every 24 weeks. LdT monotherapy was still in patients with HBVDNA undetectable, and ADV (10 mg/d) was added to an ongoing LdT therapy in patients who had detectable HBV DNA at week 24 and viral rebound during treatment. Consolidation therapy was continued for more than 2 years after HBeAg seroconversion and total course was more than 3 years. LdT treatment was stopped and they were followed-up for more than 1 years.
Results: A total of 233 patients were enrolled. LdT monotherapy cases were 169, combination therapy cases with LdT and ADV were 27, Changing to other therapies cases were 22, dropout cases were 15. The rates of HBV DNA undetectable at week 24, year 1, 2 and 3 were 86.3 % (201/233), 98.3 % (229/233), 92.3 % (215/233) and 84.1 % (196/233), respectively. The HBeAg loss rates at year 1, 2 and 3 were 55.9 % (128/229), 60.0 % (129/215) and 63.8 % (125/196), respectively. The HBeAg seroconversion rates at year 1, 2 and 3 were 45.9 % (105/229), 52.6 % (113/215) and 57.1 % (112/196), respectively. The rate of patients with durability of HBeAg seroconversion was 75.9 % (66/87).

Topic 11: Hepatitis B

No: 1789

The efficacy of lamivudine treatment in naive chronic hepatitis B patients

Ayhan Balkan[1], Ramazan Erdem Er[1], Abdullah Emre Yıldırım[1], Buğra Tolga Konduk[1], Samet Alkan[2], Sezgin Barutçu[1], Murat Taner Gülşen[1]

Gaziantep University Faculty of Medicine Gastroenterology Gaziantep-Turkey[1], Gaziantep University Faculty of Medicine Internal Medicine Gaziantep-Turkey[2]

Aim: According to our previous national health care system, lamivudine or telbivudine treatment should be initiated in the naive chronic hepatitis B (CHB) patients with low viral load. We aimed to investigate the success of lamivudine treatment in the end of the first year.
Methods: We retrospectively recruited 125 naive CHB patients on lamivudine therapy. We recorded biopsy results, demographic, biochemical, serological and virological values at baseline and 3[SUP]rd[/SUP], 6[SUP]th[/SUP] and 12[SUP]th[/SUP] months of treatment. Virological response was defined as undetectable HBV DNA (< 20 IU/mL).
Results: Of patients, 81 were male (65 %), and the mean age was 42 ± 13. Mean histological activity index (HAI) was 4.55 ± 2.16, and fibrosis was 2.65 ± 0.90 in 114 patients who had biopsy results. The initial mean HBV DNA level was 5.52×10[SUP]6[/SUP] IU/mL. Seroconversion was observed in only 3 (18.75 %) of 16 HBeAg (+) patients While baseline median ALT value was 36 U/L, following values were 28 U/L, 25 U/L and 24 U/L, respectively. Virological response rate of patients by months is summarized in table 1.
Conclusion: Lamivudine treatment for naive CHB patients continues to be effective for the first 6[SUP]th[/SUP] months, and if continued to be treated until 12[SUP]th[/SUP] month, this efficiency can increase.

Topic 11: Hepatitis B

No: 1773

Audio and visual complications and management of those in chronic HCV patients used telapravir + pegylated interferon alpha + ribavirin

Coşkun Yildiz[1], Deniz Ozkaya[2], Sedat Erten[1], Esma Yuksel[2], O.burcak Binicier[1], Z.betul Pakoz[1]

Md Gastroenterology Izmir-Turkey[1], Md Infectious Disease Izmir-Turkey[2]

Introduction: We presented audio and visual complications and their management in patients with Chronic HCV infection treated with Pegylated Interferon-alpha (PEG-IFN) + Ribavirin + Telaprevir.
Case: PEG-IFN + ribavirin were given during 48 weeks to 58 year-old woman with Chronic HCV infection. During the treatment period, HCV RNA didn't disappear and it was 8.57 ± 2 IU/ml at the 52th week. Because HCV RNA remained high level, the therapy protocol was changed with triple therapy including Telapravir. At the 10th day of treatment, hyperaesthesia against to light and noise, vomiting, nausea, headache, pruritus in rectum and ulcers on the earlobe and oral mucosa were identified.

In physical examination of eyes, bilateral conjunctivitis and dry eye were diagnosed. Whereas the ear, throat and nose examinations were normal except for earlobe ulcer. Because all the symptoms and signs decreased with the symptomatic therapy, Telaprevir was not stopped. Photophobia and conjunctivitis completely improved after completing Telaprevir treatment.

Virological response developed at the end of treatment. One month later completing triple treatment, HCV RNA was found as negative. In control examination at the third month completing treatment, there weren't any pathological findings except for minimal

forgetfulness and blurred vision in the left eye. Other signs and symptoms completely healed.
Results: Although Telaprevir, PEG-IFN and Ribavirin therapy increased sustained response in chronic HCV infection, they may cause several side effects. In terms of side effects, patients should be monitored and palliative treatment should be provided.

Topic 11: Hepatitis B

No: 1593

Outcome of tenofovir treatment in chronic hepatitis B patients in real life practice

Jong Seok Ju[1], Hae Jin Shin[1], Ki Dae Kim[1], Eaum Seok Lee[1], Seok Hyun Kim[1], Byung Seok Lee[1], Heon Young Lee[1]

Chungnam National University School of Medicine Internal Medicine Daejon-Korea, South[1]

The aim of this study was to evaluate the biochemical response and virological response to tenofovir in Korean chronic hepatitis B patients at one year after treatment. Total of 122 patients with chronic hepatitis B who were treated with tenofovir for at least 12 months were enrolled. We measured ALT levels, HBeAg, anti-HBe, HBV DNA, serum creatinine and phosphorous at the time of admission and at three months intervals. The biochemical response rate and virological response rate at one year after treatment in naïve patients were 41.7 % and 85.4 %, respectively. After one year treatment the virological response rates in the high baseline viral load group and low baseline viral load group were 14.3 %, 52.9 %, respectively ($P = 0.014$). The results of the analysis of native patients according to the initial HBeAg serostatus after 12 months, the virological response rates of HBeAg-positive group and the HBeAg-negative group were 27.3 %, 73.3 %, respectively ($P = 0.003$).

High virological response rate at one year after treatment showed association with initial low HBV DNA titer and initial negative HBeAg status. In this study nephrotoxicity due to tenofovir was not reported.

Topic 11: Hepatitis B

No: 2129

The examination of mutations created by pegylated interferon alpha and oral antivirals used in the treatment of chronic hepatitis B on HBsAg gene and polymerase gene

Elif Sargin Altunok[1], Sila Akhan[1], Murat Sayan[2]

Kocaeli University Medical Faculty Infectious Diseases and Clinical Microbiology Kocaeli-Turkey[1], Kocaeli University Medical Faculty Pcr Unit, Clinical Laboratory Kocaeli-Turkey[2]

The Hepatitis B Virus has high mutation frequency due to having a high replication capacity and not having error correction capability in reverse transcription. In this study, it is aimed to examine the mutations created by the oral antivirals used in chronic hepatitis B (CHB) treatment on pol gene and S gene and to specify the development of drug resistance in long terms and the results it may cause. Secondly, it is aimed to determine whether the quantitative HBsAg (qHBsAg) titers are early markers for detecting drug resistance or not.

This study was carried out with 94 patients between 2009 and 2014 years. Correlation analyses were performed with monitoring qHBsAg levels and HBsAg-S/Co and HBV DNA levels of the patients. HBV DNA sequencing analysis was done at the patients developing breakthrough pre and during the treatment.

It was monitored that at HBeAg positive patients having severe fibrosis qHBsAg levels were lower. It was seen that in the correlation analysis, a statistically significant middle level correlation existed between the initial qHBsAg and HBV DNA levels. It was concluded that the efficiency of qHBsAg levels on making diagnosis is at a good degree to distinguish inactive HBsAg carriers and HBeAg negative CHB patients and the cutoff value was determined as 2188 IU/mL. It was concluded that values in terms of HBsAg-S/Co cannot be used for monitoring the treatment. In the analyses made, primer drug resistance mutation during the naive period was determined in two patients and naturally developed ADAPVEM pattern was determined in two patients.

Topic 11: Hepatitis B

No: 1207

Relationship between e antigen seroconversion and improved liver histology in patients treated by telbivudine for chronic hepatitis B

Yue Qi[1], Qinglong Jin[1], Junqi Niu[1]

First Hospital of Jilin University Hepatology Changchun-China[1]

Aim: To observe the histological changes and E antigen seroconversion rates in patients treated with telbivudine for 5-year, and to analyze their relationship.
Methods: For patients receiving telbivudine treatment, their virological, serological, immunological, and histological results were obtained at baseline, or treated for 6 months, 2 years, and 5 years. For patients with decreased viral load less than 21 og then treated for 6 months, adefovir will be added for treatment.
Results: A total of 28 patients aged between 20-40 were included in the present study. After the treatment for two years, 9 cases showed e antigen seroconversion, after five years, another 5 cases showed e antigen seroconversion.82.1 % of patients showed improved fibrosis and inflammation levels after treatment for two years, and for complete virus response patients, 89.5 % of them showed improved fibrosis, and 94.7 % showed improvement in inflammation score; for patients with partial response, 66.7 % of them showed improvement in inflammation score, and 55.6 % have improvement in inflammation score. For patients with e antigen seroconversion, 77.8 % of them have improvement in fibrosis score, and 88.9 % showed improvement in inflammation score; for patients without seroconversion, 84.2 % of them showed improved fibrosis score, 78.9 % showed improved inflammation score. For 5 patients with prolonged treatment to 5 years, 60 % of them showed improvement in inflammation and fibrosis score, and 20 % have progress in fibrosis score.
Conclusion: Telbivudine treatment for two years could improve liver tissue in the majority of the patients; when prolonging the treatment, those patients without improvement may also get e antigen seroconversion.

Topic 11: Hepatitis B

No: 1173

Does insulin resistance affect the response of chronic B hepatitis to pegylated interferon treatment

Emel Ahishali[1], Can Dolapcioglu[1], Mehmet Sayiner[2], Resat Dabak[2]

Dr. Lutfi Kirdar Kartal Education and Research Hospital Department of Gastroenterology Istanbul-Turkey[1], Dr. Lutfi Kirdar Kartal Education and Research Hospital Department of Family Medicine Istanbul-Turkey[2]

Aim: To investigate the effect of insulin resistance on response of chronic B hepatitis to pegylated interferon treatment.
Method: "Homeostasis Model Assessment" (HOMA) was performed to determine the insulin resistance before pegylated interferon treatment. Treatment responses, demographical features, HBVDNA levels, ALT values, HBeAg states, histological findings, body mass indexes (BMI), abdominal circumferences, glucose, insulin, HOMA scores and type of pegylated interferon treatment were statistically compared in patients with and without insulin resistance.
Results: A total of 21 patients with 17 males (81 %) were included in the study. Before treatment, all patients had BMIs lower than 30 and 8 patients (62 %) had insulin resistance. At the end of treatment, response was seen in 11 patients (52.4 %). There was no statistically significant difference between patients with and without pretreatment insulin resistance in means of age, sex, HBVDNA level, ALT level, HBeAg status, histopathological grade and type of pegylated interferon treatment. No statistically significant difference was detected for treatment response at the end of treatment between patients with and without pretreatment insulin resistance. BMI, insulin, glucose and HOMA scores of patients with pretreatment insulin resistance were found to be significantly high compared to patients without pretreatment insulin resistance ($P < 0.05$). Abdominal circumference of patients with pretreatment insulin resistance was found to be higher than it was in patients without pretreatment insulin resistance, but this finding was not statistically significant.
Conclusion: This study shows that presence of pretreatment insulin resistance has no effect on response to pegylated interferon treatment in chronic B hepatitis.

Topic 11: Hepatitis B

No: 1740

Relationship between serum levels of angiotensin converting enzyme histopathologic activity and fibrosis in chronic hepatitis B infection

Ahmet Tay[1], Fatih Albayrak[2], Hakan Dursun[2], Ayse Albayrak[3]

Erzurum Region Training and Research Hospital Internal Medicine Erzurum-Turkey[1], Ataturk University Gastroenterology Erzurum-Turkey[2], Ataturk University Infectious Diseases Erzurum-Turkey[3]

Introduction and purpose: The liver biopsy is the gold standard for follow-up of liver fibrosis in patients with chronic hepatitis B (CHB), but it is a difficult procedure because of that is invasive. In the study it was aimed to detect Angiotensin Converting Enzyme (ACE) levels in serum samples of patents with CHB infection and to investigate the relationship between ACE levels and Ishak fibrosis score in liver biopsy and fibrosis.
Materials and methods: We enrolled 54 patients who admitted to Erzurum Regional Training and research Hospital Department of Gastroenterology.
Results: Of the patients, 44 (81.5 %) had mild fibrosis (Ishak score > 2), and 17 (31.5 %) had low histological activity index (HAI score < 6), 37 (68.5 %) had high HAI (HAI score > 6).There was no any patient with HAI score > 12. of the patients, 6(11.1 %) had fibrosis 0, 32 (59.25 %) had fibrosis 1, 6 (11.11 %) had fibrosis 2, 9 (16.67 %) had fibrosis 3, 1 (1.85 %) had fibrosis 5,and no patient had fibrosis 4 or 6. There was no statistically any significance ($P = 0.244$) between fibrosis groups and serum ACE levels. A multiple linear regression analysis was performed and only HAI score was identified as an independent predictor for serum ACE level ($P = 0.050$).
Conclusion: In our study, it was found that serum ACE level was significantly correlated with the HAI score in patients with CHB. In patients with CHB, serum ACE levels may be useful as an indicator of inflammation.

Topic 11: Hepatitis B

No: 1182

Microrna profiling to identify chronic hepatitis B individuals at risk of liver disease progression

Behnaz Riazalhosseini[1], Rosmawati Mohamed[2], Zahurin Mohamed[1]

University Malaya Pharmacology Kuala Lumpur-Malaysia[1], University Malaya Medicine Kuala Lumpur-Malaysia[2]

Aim: Hepatitis B infection (HBV) is a global health problem with 1 million deaths annually. Individuals with chronic HBV are at risk of progression to cirrhosis and hepatocellular carcinoma (HCC). MicroRNAs (miRNAs) have been shown to play a vital role in the host immunity by regulating host-viral connection. In this pilot study, we aim to investigate the micro RNA expression profile in individuals with chronic HBV infection and to assess whether any association exist with susceptibility to liver disease progression.
Methodology: We employed an Affymetrix Gene Chip miRNA 3.0 Array, to provide a universal miRNA coverage. We compared a panel of microRNAs in two groups of chronic HBV patients with and without cirrhosis or HCC to find the aberrantly microRNAs expression. Differential expression in micro RNAs with p-values of less than 0.05 and a fold change of greater than 2 with 95 % reproducibility were considered significant. The results of this microarray revealed 8 differently expressed microRNAs that were either down regulated (2 miRNAs) or up regulated (6 miRNAs) in expression between chronic HBV patients with and those without cirrhosis +/HCC .
Conclusion: The results of our study show that microRNAs can be used to distinguish chronic HBV patients who are at risk of progression to cirrhosis +/HCC. Profiling of micro RNAs may serve as a biomarker to identify chronic HBV individuals susceptible to liver disease progression.

Topic 11: Hepatitis B

No: 1286

Influence of hepatic inflammation on fibroscan in diagnosing fibrosis with chronic hepatitis B

Xianghua Zeng[1], Dengming He[2], Yuming Wang[1]

Southwest Hospital Third Military Medical University Department of Infectious Diseases Chongqing-China[1], The 88th Hospital of Chinese Pla Liver Disease Diagnosis and Treatment Center Tai'an-China[2]

Hepatic inflammation had a great impact on FibroScan. This study aimed to investigate the influence of inflammation histologically on FibroScan in the diagnoses of liver fibrosis. Three hundred and twenty-five patients with chronic hepatitis B, who received liver biopsy and liver stiffness measurement (LSM), were included. According to Scheuer scoring system, liver fibrosis and inflammation were divided into five different stages (S0 $\sim$ S4) and grades

(G0 ~ G4). LSM correlated positively with fibrosis stage and inflammatory grade ($P < 0.001$). LSM in the same fibrosis stage increased along with inflammatory grade. In different grades of inflammation (G0/G1/G2/G3), the area under receiver operating characteristic curves of FibroScan in diagnosing significant fibrosis (S2 ~ S4) was 0.8267 ($P < 0.001$), 0.6956 ($P < 0.001$), 0.709 ($P = 0.0012$) and 0.6947 ($P = 0.137$), respectively. FibroScan showed a good diagnostic value of significant liver fibrosis, but was influenced by hepatic inflammation seen in biopsy.

Topic 11: Hepatitis B

No: 1721

Sequence characters of HBV from China and adjacent countries and relationships of Bcp PreC mutation with clinical status

Qian Zhao[1], Hongmei Li[2], Tao Shen[3]

Institute of Basic and Clinical Medicine,the First People's Hospital of Yunnan Province;kunming Medical Colledge Molecular Biology Department Kunming-China[1], Institute of Basic and Clincal Medicine,the First People's Hospital of Yunnan Province;kunming University of Science and Technology Molecular Biology Department Kunming-China[2], Institute of Basic and Clincal Medicine,the First People's Hospital of Yunnan Province Molecular Biology Department Kunming-China[3], Institute of Basic and Clinical Medicine, the First People's Hospital of Yunnan Province, Kunming 650032, Yunnan Province, China
*Contribution equivalent as Zhao Q
Corresponding author

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Aim: Heterogeneous of HBV is an important viral parameter in predicting disease progression and therapeutic outcome. Thus, to understand the sequence characters of HBV is very necessary.
Method: 1148 Chinese and 952 adjacent countries' HBV sequences from GenBank were collected. MEGA 5.1,Bioedit and SPSS17.0 softwares were used to analyse.
Results: C/B and C/B/D were dominant genotypes in China and its adjacent countries, respectively. Adrq + and adw2 were dominant serotypes. In addition to ATG, ATA, ACG, GTG, CTG, TTG, ATG and AGT were also discovered as initiation codons. The major stop codons of S-ORF were TAA and TGA in B2 and C2 subgenotype, respectively. Divergence between five sub-genotypes (B3, B5, B7, B8, and B9) was less than 4 %. A statistical significance of the BCP double mutation was observed between CHB and ASHB ($P < 0.05$) as well as between ACHB and HCC ($P < 0.05$). The mutation difference in pre-C was remarkably significant between HCC and LCHB ($P < 0.01$); it was also significant between ACHB and HCC ($P < 0.05$) and between AHB and ASHB ($P < 0.05$). There were significant differences for both the BCP double mutation and the pre-C mutation between type B and C.
Conclusion: Whether or not a mutation in the start codon in the preS2 region has an impact on survival and replication of HBV remains to be determined.The B3, B5, B7, B8, and B9sub-genotypes might be reclustered into quasi-subgenotype B3.The relationships of BCP and preC mutation and clinical status is critical for the future prevention and therapy of HBV infections.

Topic 11: Hepatitis B

No: 1298

Add on pegylated interferon alpha 2a therapy in entecavir treated patients with chronic hepatitis B

Hideyuki Tamai[1], Yoshiyuki Mori[1], Shuya Maeshima[1], Junya Nuta[1], Naoki Shingaki[1], Yoshimasa Maeda[1], Kosaku Moribata[1], Yosuke Muraki[1], Hisanobu Deguchi[1], Izumi Inoue[1], Takao Maekita[1], Mikitaka Iguchi[1], Jun Kato[1], Masao Ichinose[1]

Wakayama Medical University Second Department of Internal Medicine Wakayama-Japan[1]

Background/aim: Entecavir is the first-line nucleoside analog for patients with chronic hepatitis B in Japan, but it requires long-term administration. The aim of the present study was to assess the safety and efficacy of adding pegylated interferon alpha-2a (PEG-IFN-alpha-2a) to entecavir.
Methods: Seventeen patients with chronic hepatitis B were treated by the addition of PEG-IFN-alpha-2a to entecavir. PEG-IFN-alpha-2a at 90 microgram was administered subcutaneously once per week for 48 weeks. Entecavir was continued after PEG-IFN-alpha-2a therapy. Four patients were HBe antigen-positive. Fifteen patients had genotype C virus, and 2 patients had genotype B virus. Viral response was assessed after 24 weeks from the end of PEG-IFN-alpha-2a therapy and considered present if the HBs antigen level was lower than 50 % of baseline.
Results: One patient (6 %) discontinued due to arrhythmia. HBe antigen disappearance was seen in 1 patient (25 %). Although no HBs antigen disappearance occurred, HBs antigen levels decreased to less than 100 IU/mL in 4 patients (24 %). The viral response rate was 59 % (10/17). On univariate analysis, the alanine aminotransferase level was the only significant pre-treatment factor associated with viral response. The time of previous entecavir therapy, HBs antigen level, and interleukin-28B polymorphism were not significant factors. of the on-treatment factors, log-reduction of the HBs antigen level at week 12 was a significant predictive factor for viral response (AUC 0.829, $P = 0.025$).
Conclusions: Adding low-dose PEG-IFN-alpha-2a to entecavir is safe but has limited efficacy. Log-reduction of the HBs antigen level at week 12 may become a useful predictor for viral response.

Topic 11: Hepatitis B

No: 1259

Retrospective evaluation of HBeAg anti hbe antibody status liver histology and alt concentrations in adult treatment naive patients with chronic hepatitis B disease

Bülent Albayrak[1], Hakan Dursun[1], Fatih Albayrak[1], Serkan Cerrah[1], Nihat Okçu[1]

Ataturk University, Medical Faculty Department of Gastroenterology Erzurum-Turkey[1]

Chronic hepatitis B (CHB) is a dynamic disease with complex course. Unstable characteristic structure of the virus and patient-related factors result in different patterns encountered during the course of chronic hepatitis B disease. The aim of the present study is to determine general characteristics of CHB patients in the Eastern Anatolian region, to obtain information on progression of the disease via laboratory, histopathological and clinical findings, and to help with further treatment planning.

A total of 167 patients with chronic hepatitis B disease were retrospectively recruited in the study. Patients were evaluated by being divided into groups according to HBeAg status, Anti HBe antibody status, Alanine aminotransferase (ALT) concentration, histological activity index (HAI) and fibrosis status. Whilst 51 patients were HBeAg-positive, 116 patients were HBeAg-negative (Anti HBe antibody-positive). There was statistical difference between the groups in terms of mean age. No statistical difference was determined between ALT, HAI and fibrosis groups in terms of age and viral load.

We conclude that many CHB patients with ALT < ULN have significant liver inflammation or fibrosis and that liver biopsy is necessary to assess liver damage and should be used to assess the need for anti-viral therapy.

Topic 11: Hepatitis B

No: 2154

The efficacy of booster vaccination in universally HBV vaccinated children

Selma Tosun[1], Erhun Kasirga[2]

Izmir Bozyaka Research and Education Hospital Infectious Diseases Izmir-Turkey[1], Celal Bayar University The School of Medicine Pediatric Gastroenterology Manisa-Turkey[2]

Aim: In this study, we aimed to evaluate the efficacy of booster vaccination 7-8 years after the universal HBV vaccination after birth.
Methods: HBV serology of two groups of the students, who were born in 1996 to1999, and in 2000 to 2004, in primary school in Muradiye province of Manisa, Turkey, was tested by EIA method. The reason for allocating the age groups into two in such a way was that children born in 1999 or earlier had received a booster dose in 2006. Those with AntiHBs titer $\leq$ 9 IU/mL were regarded as negative, 10-49 IU/mL: positive, $\geq$ 50 IU/mL: highly positive.
Results: A total of 192 children were included in the study. The rate of the AntiHBs titer less than the protective level was significantly higher in children born between 2000 to 2004 than those who were born between 1996 and 1999 ($P = 0.000$). Highly positive titer of AntiHBs was significantly more frequent in children who were born between 1996 and 1999. The reason for that difference is commented to be due to the catch-up HBV vaccination of the children born in 1996-1999. None of the children had HBsAg positivity.
Conclusion: The efficacy of universal HBV vaccination was quite high in decreasing HBsAg positivity. We think that booster vaccination 7-8 years after the universal HBV vaccination may be beneficial in increasing the antibody response.
* We would like to thank public health specialist, Assistant Professor Dr.Serol Deveci, who made the statistical evaluations.

** We thank all health staff that contributed to the different stages of our study.

Topic 11: Hepatitis B

No: 1327

Efficacy of telbivudine and lamivudine in patients with chronic hepatitis B

Aliye Soylu[1], Umit Bilge Dogan[2], Sule Poturoglu[3], Can Dolapcıoglu[4], Serdal Cakmak[5], Deniz Duman[6], Elif Yorulmaz[7], Isa Sevindir[5], Osman Cavit Ozdogan[6]

Bakirkoy Dr Sadi Konuk Research and Training Hospital Gastroenterology Istanbul-Turkey[1], Mustafa Kemal Faculty of Medicine Gastroenterology Hatay-Turkey[2], Haseki Research and Training Hospital Gastroenterology Istanbul-Turkey[3], Kartal Research and Training Hospital Gastroenterology Istanbul-Turkey[4], Bakirkoy Dr. Sadi Konuk Research and Training Hospital Gastroenterology Istanbul-Turkey[5], Marmara University Faculty of Medicine Gastroenterology Istanbul-Turkey[6], Bağcılar Research and Training Hospital Gastroenterology Istanbul-Turkey[7]

Aim: The efficacies of lamivudine (LAM) that has been prescribed for many years and telbivudine (TBV), a relatively new drug in the market and which we prescribed to treatment-naive patients with chronic Hepatitis B virus (HBV) infection, is compared.
Materials and methods: We enrolled 346 patients with chronic HBV infection who received LAM or TBV therapy for a minimum of one year. We compared the 2 groups regarding the initial HBV-DNA levels, HAI and fibrosis scores together with the treatment responses at the 3rd, 6th and 12th months of therapy.
Results: Treatment response were not different between groups at the 3rd month of therapy ($P = 0.058$) (Table-1). The number of patients who were HBV-DNA positive at the 3rd month but turned to be HBV-DNA negative at the 6th month of therapy were significantly less in LAM group compared to the TBV group (36.5 % vs. 50.7 %, respectively ($P = 0.070$). The rate of HBV-DNA negativity at the 12th month in LAM group was lower than that of the TBV group (62.4 % vs. 92.2 % respectively, $P = 0.0001$) (Table-2).
Conclusion: Although, both antivirals have similar efficacy in the first 3 months, TBV is found to be superior in the following months of treatment. Similar HBV-DNA levels were achieved at the 3rd month of treatment despite the higher initial HBV-DNA with LAM patients who proved more rapid viral response with LAM. By contrast, sustained and long-lasting efficacy is attributable to TBV since greater HBV-DNA drops were observed in long term treatment with TBV.

Topic 11: Hepatitis B

No: 2049

Anxiety and depression in chronic hepatitis patients a multi center study

Rahmet Guner[1], Zeliha Kocak Tufan[1], Nurcan Baykam[2], Cemal Bulut[3], Yunus Gurbuz[4], Kenan Hizel[5], Ediz Tutuncu[4], Gorkem Ugurlu[6]

Yildirim Beyazit University, Ankara Ataturk Training & Research Hospital Infectious Diseases & Clinical Microbiology Department Ankara-Turkey[1], Hitit University, Faculty of Medicine Infectious Diseases & Clinical Microbiology Department Corum-Turkey[2], Ankara Training & Research Hospital Infectious Diseases & Clinical Microbiology Department Ankara-Turkey[3], Ankara Yildirim Beyazit Training & Research Hospital Infectious Diseases & Clinical Microbiology Department Ankara-Turkey[4], Gazi University, Faculty of Medicine Infectious Diseases & Clinical Microbiology Department Ankara-Turkey[5], Yildirim Beyazit University, Ankara Ataturk Training & Research Hospital Psychiatry Ankara-Turkey[6]

Objectives: There are 350million estimated numbers of chronic-hepatitis-B (CHB) and 180million chronic-hepatitis-C (CHC) patients worldwide. Depression and anxiety may effect the quality of life of these patients and also the disease progression. Here we aimed to evaluate the depression and anxiety levels of our CHB&CHC patients. Methods: CHB and CHC patients, who had been followed in

five different tertiary care hospitals were included. Beck's Depression Inventory (BDI) and State-Trait Anxiety Inventory (STAI TX I&II) were used to define the anxiety and depression of the patients. Treatment status and co-morbidities were also recorded.
Results: Mean-age was 45; 47 % male. BDI: Fifty five patients filled out the questionnaire. The average Beck Depression score was 13.8 points, indicating a mild depression in patients on average. The split of severity of depression can be found in the figure 1. STAI TX I: The current anxiety level was low in 82 % of the participants, none of them felt immediate-severe-anxiety. The average immediate-anxiety score was 23, which is equivalent to a low anxiety level (Figure 2). STAI TXII: Fifty-four patients filled out the questionnaire. The average general-anxiety score was 57 which is equivalent to a severe anxiety level (Figure 3).
Conclusion: Almost half of the patients (45 %) presented with a mild to moderate level of depression according to the BDI. The majority of patients (82 %) proved a low level of anxiety on the immediate anxiety test, while the general anxiety test showed 55 % had a severe level of anxiety. The treatment pathway of these patients should include psychiatric management as well.

Topic 11: Hepatitis B

No: 2147

Effect of hepatic b virus infection on liver metastases in colorectal cancer

Shilei Xu[1], Jianrong Liu[2], Kunpeng Hu[1], He Huang[1], Zhicheng Yao[1]

Third Affiliated Hospital of Sun Yat-sen University General Surgery, Guangzhou-China[1], Third Affiliated Hospital of Sun Yat-sen University Transplantation Icu, Guangzhou-China[2]

Objective: To investigate the influence of hepatic B virus on liver metastases in colorectal cancer.
Methods: We retrospectively analyzed 70 colorectal cancer patients in our hospital during Jan. 2003 to Jan. 2013, who were divided into infected group (30 cases) and non-infected group (40 cases). The incidence of liver metastases and survival time were compared using the Kaplan–Meier method.
Results: The incidence of liver metastasis was 21 %(13/112) in the infected group and 13 %(15/114) in the non-infected group(-$P < 0.01$).No significant difference was observed between these two groups with the survival time. In the infected group, the median survival time was 34 months (4-34 months), while the non-infected group 9 months (3-22 months).
Conclusions: The HBV virus infected decrease the risk of colorectal cancer liver metastases. But no impact on the survival.

Topic 11: Hepatitis B

No: 1390

Efficacy of "entecavir" in the treatment naïve chronic hepatitis B patients

Can Dolapcioglu[1], Emel Ahishali[1], Aziz Kural[1], Resat Dabak[2]

Dr.lutfi Kirdar Kartal Research and Training Hospital Gastroenterology Istanbul-Turkey[1], Dr.lutfi Kirdar Kartal Research and Training Hospital Family Medicine Istanbul-Turkey[2]

Objective: Pharmaceutical agents with a high antiviral efficacy and a broad range of genetic barrier has been proved successful in the treatment of chronic hepatitis B (CHB), an important health issue globally. The efficacy of "entecavir" was evaluated in the treatment-naïve CHB patients admitted to our Gastroenterology Unit.
Methods: Treatment-naïve CHB patients that received "entecavir" for one year or more were evaluated. Those with decompensated liver cirrhosis and/or hepatocellular carcinoma were excluded. HBV DNA negativity was accepted as < 300 copies/ml.
Findings: Sixty-three patients (42 male, 21 female) with a mean age of 46.44 ± 11.33 years were included. Sixteen patients had compensated cirrhosis and 11 was positive for HBeAg. Mean duration of treatment was 23.4 ± 12.2 months (range, 12-60 months). Mean pre-treatment HBV DNA was 6.7 ± 1.3 log (range, 5-9 log) and mean ALT level was 130 IU/L. Thirty-nine patients had liver biopsies scored according to the Ishak scoring system. Mean HAI score and fibrosis score was 8.5 ± 2.9 and 2.6 ± 0.9, respectively. At 6 months of treatment, 55 (87.5 %) patients were HBV DNA negative with normal ALT. HBV DNA was 4, 5, and 7 log in 5, 1, and 2 patients, respectively. At 12 months of treatment, 62 (98.4 %) patients were HBV DNA negative with normal ALT. Six patients developed e seroconversion during the first year. None of the patients developed HBsAg loss, biochemical or clinical adverse effects, or treatment resistance. None of the patients required dose reduction.
Conclusion: "Entecavir" is an efficient treatment modality for treatment-naïve CHB patients.

Topic 11: Hepatitis B

No: 1960

Clinical features of chronic hepatitis B patients after stopping nucleos(t)ide analogues

Ping Shi[1], Jun Li[1], Yaping Han[1], Yao Liu[1], Longfeng Jiang[1]

The First Affiliated Hospital With Nanjing Medical University Department of Infectious Diseases Nanjing-China[1]

Objective: To investigate the clinical features of chronic hepatitis B patients after stopping nucleos(t)ide analogues and related factors for hepatitis B relapse.
Methods: We investigated 73 chronic hepatitis B patients who withdrew nucleos(t)ide analogues and analyzed the reasons for withdrawal and related factors for hepatitis B relapse.
Results: Among 73 patients, 10(13.7 %) of them withdrew nucleos(t)ide analogues for economic reason, 15(20.5 %) for poor outcome, 11(15.1 %) for poor compliance and 17(23.3 %) for stable condition. Among patients with total treatment duration more than 24 months, those who stopped entecavir had longer relapse time compared with combination therapy ($P = 0.048$), and lower HBV DNA level while relapsed compared with lamivudine ($P = 0.039$). Among patients who didn't achieve cessation criteria, the correlation coefficient between total treatment duration and relapse time was -0.571($P < 0.001$), and the correlation coefficient between treatment duration after virological response and relapse time was -0.514($P < 0.001$). The COX proportional hazards model analysis showed that total treatment duration was the risk factor for hepatitis B relapse after stopping nucleos(t)ide analogues with patients who didn't achieve cessation criteria.
Conclusion: Most patients stopped nucleos(t)ide analogues without achieving cessation criteria. There was a still high relapse rate among patients in spite of they had achieved cessation criteria. The longer antiviral treatment duration was associated with a short time recurrence with those who didn't achieve cessation criteria.

Topic 11: Hepatitis B

No: 1505

Tenofovir on treatment HBsAg loss in naive HBeAg negative chronic hepatitis B a case report

Celal Ayaz[1], Mustafa Kemal Celen[1]

Dicle University Infection Diyarbakır-Turkey[1]

The aim: Since the licensing of lamivudine in 1999, the treatment of chronic hepatitis B has been revolutionized by the introduction of oral nucleoside and nucleotide analogues (NAs), which act as inhibitors of the HBV polymerase. The effectiveness of the first of these substances was limited by incomplete response and resistance development in many patients, but today, highly potent substances are available that make a reliable and durable suppression of HBV replication, a reduction of necroinflammatory activity in the liver, and even a reversion of liver fibrosis achievable for almost all patients.
Case: A clinical case of a naïve patient with chronic hepatitis HBV-related (CHB) HBeAg negative, treated with Tenofovir (TDF) 300 mg/day. After one years of treatment, as well as it determines rapid, profound and sustained suppression of HBV replication, TDF induced a progressive decline of HBsAg serum level and HBsAg loss, probably through an immune modulator effect. Recent studies have indicated the possible action of TDF on the immune system and specifically it would be able to stimulate Th1 lymphocyte subpopulation by increasing their cytokines production, thus playing a major role in cleaning the HBV infection. This aspect appears to be of much interest in clinical practice, because on-treatment HBsAg rapid decline $>$ 1 log10 IU/mL during the first year of treatment is highly predictive for future HBsAg clearance and CHB resolution.
Conclusion: Is it possible loss of HBsAg first twelve months? Early TDF-induced in a high likelihood of HBsAg loss and may be associated with more profound viral suppression during the first one years of therapy.

Topic 11: Hepatitis B

No: 2145

Effect of HBeAg seroconversion over the liver histology

Can Polat Eyigun[1], Hanefi Cem Gul[1], Ahmet Karakas[1], Cumhur Artuk[1], Ismail Yaşar Avcı[1]

Gmma Infectious Diseases Ankara-Turkey[1]

Aim: The aims of this study were to assess the liver histology after HBeAg seroconversion in patients with chronic hepatits B (CHB) treated with various treatment modality.
Materials and methods: The patients who have HBeAg serocenversion and followed-up as well as treated at our hospital were investigated in this study, retrospectively. Liver biopsies which made before treatment and after seroconversion were dissected. We assessed histological activity by Knodell necroinflamatory score (the top score 18) and fibrosis by Ishak scoring system (the top score 6).
Results: Of 195 patients who were HBeAg positive CHB, 124 patients were occured HBeAg seroconversion during treatment period. of 124 patients, 22 were female, 102 were male and average age of patients was 42.03 (23-75). Liver biopsy were investigated before treatment and these were determined that average of necroinflamatory score was 6,53 (1-14) and fibrosis was 1,69 (0-5). The patients were treated with interferon or various nucleos(t)ide treatment modality. The second liver biopsies of patients who had occured HBeAg seroconversion were investigated. These were determined that average of necroinflamatory score was 3,52 (0-12) and fibrosis was 1,01 (0-5). These findings are not significantly as statistical.
Conclusion: HBeAg seroconversion is not more effective over the liver histology. Loss of HBeAg antigen isn't good criteria for stopping the treatment of CHB. The treatment should be prolonged until HBsAg seroconversion.

Topic 11: Hepatitis B

No: 1528

Long term effectiveness of entecavir therapy in cases with chronic HBV

Murat Aladağ[1], Hulya Aladag[2], Yilmaz Bilgic[1], Murat Harputluoglu[1], Yasir Furkan Cagin[1], Mehmet Ali Erdogan[1], Yahya Atayan[1], Oguzhan Yildirimi[1], Yuksel Seckin[1], Melih Karincaoglu[1]

Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[1], Inonu University Faculty of Medicine Gynecology Malatya-Turkey[2]

Introduction and purpose: In our study, we aimed at retrospectively evaluating the viral suppression, biochemical response rates as well as efficacy and safety of the drug in cases with chronic hepatitis B using Entecavir
Equipment and method: A total of 320 chronic hepatitis B patients using Entecavir, 110 women and 210 men with a mean age of 40 (18-80) were included in the study between the years 2005 and 2013. We compared HBV DNA and biochemical parameters initially at months 3, 6, 12 and subsequently at 6-month intervals.
Results: In the 6th month of therapy, 208 patients (65 %) gave full response (HBV-DNA negative), 60 cases (18,7 %) gave partial response (% 18,7) and 52 cases (16,2 %) gave insufficient response. It was seen that the rate of negative HBV-DNA reached 95,6 % (306/320) at month 12 of therapy and 97,5 % (312/320) in the second year of therapy, and this rate increased in years 3, 4, 5 and 8 to reach 98,4 % (315/320). There was positive HBV-DNA at a level of 200-4000 copy/ml only in 5 cases.At the 8th year, 25 cases (7,8 %) had HBsAg loss. Anti-HBs seroconversion was seen to have developed in 9 cases (2,8 %) among those who had HBsAg loss. During the treatment period of eight years, none of the cases had side effects which required discontinuation of therapy.
Conclusion: During the period of 8 years, none of the patients developed resistance. Consequently, Entecavir therapy was concluded to be an effective, safe and secure treatment agent in chronic HBV cases.

Topic 11: Hepatitis B

No: 1925

Achieving on treatment HBeAg loss significantly reduce clinical relapse after entecavir therapy

Tung-hung Su[1], Chun-jen Liu[1], Hung-chih Yang[2], Chen-hua Liu[1], Shih-jer Hsu[3], Tai-chung Tseng[4], Pei-jer Chen[1], Ding-shinn Chen[1], Jia-horng Kao[1]

National Taiwan University College of Medicine Graduate Institute of Clinical Medicine Taipei-Taiwan[1], National Taiwan University

Hospital Division of Gastroenterology and Hepatology, Department of Internal Medicine Taipei-Taiwan[2], National Taiwan University Hospital, Yun-lin Branch Department of Internal Medicine Yun-lin-Taiwan[3], Buddhist Tzu Chi General Hospital, Taipei Branch Division of Gastroenterology, Department of Internal Medicine Taipei-Taiwan[4]

Aim: Longterm antiviral therapy is associated with prolonged viral suppression. Hepatitis B flare is frequently seen after treatment discontinuation. However, the predictors of clinical relapse in HBeAg-positive patients to stop antiviral therapy remains unclear. Our aim is to identify patients at risk for clinical relapse after antiviral therapy.
Method: We enrolled HBeAg-positive patients who discontinued entecavir monotherapy from a tertiary medical center in Taiwan. The baseline and end-of-treatment (EOT) factors were analyzed to find the predictors for clinical relapse, which was defined as HBV DNA > 2,000 IU/mL with serum alanine aminotransferase (ALT) > 2 times upper limits of normal value.
Results: A total of 186 HBeAg-positive patients received an average of 3 year entecavir therapy was enrolled. The mean age was 42 and 68 % of patients were male. They were followed for 17 months post EOT and 80 patients (43 %) experienced clinical relapse about 10 months post therapy. Significantly more patients achieving on-treatment HBeAg loss in non-relapsers than relapsers (67 % vs. 33 %, $P < 0.001$). Multivariate analysis by Cox proportional hazard model showed HBeAg loss before EOT reduces 66 % risk of clinical relapse (hazard ratio: 0.34, 95 % confidence interval: 0.20-0.58). In patients with HBeAg-loss before EOT, older age, greater ALT level at EOT and shorter consolidation therapy after HBeAg-loss increase the risk of clinical relapse. To increase every 1 month of consolidation therapy may reduce 6 % risk of clinical relapse.
Conclusion: After antiviral therapy, achieving HBeAg-loss and prolong consolidation therapy after HBeAg-loss significantly reduce the risk of clinical relapse off therapy.

Topic 11: Hepatitis B

No: 1598

Efficacy of viral load reduction during chemotherapy in chronic hepatitis B virus infection patients taking nucleosides for chemoprevention

Ming-yao Chen[1], Chun-jen Liu[2], Jia-horng Kao[2]

Taipei Medical University—Shuang Ho Hospital Department of Internal Medicine New Taipei City-Taiwan[1], National Taiwan University Hospital Department of Internal Medicine Taipei-Taiwan[2]

Aim: This study aims to evaluate the serial change of hepatitis B virus (HBV) DNA during chemotherapy in chronic HBV infected patients.
Method: This study included 177 cancer patients with chronic hepatitis B (CHB). Preventive nucleot(s)ide analogue (NUC) therapy was administrated 1 week prior to beginning of chemotherapy, and continued for 6 months after the end of chemotherapy (per APASL guidelines 2012). Serial HBV DNA was monitored.
Results: Of the 177 patients (mean age, 55.2 years), 88 received telbivudine (LdT), while 64 received entecavir (ETV) for chemoprevention. Survival rates were 67 % and 61 % in LdT and ETV group respectively. Fourteen patients were HBeAg-positive. Table 1 shows the mean change in HBV DNA from baseline to each time points. The rates of HBV DNA negativity is described in table 2. There was a trend of slower HBV DNA negativity when the baseline DNA was higher. If HBV DNA was still positive at month-3, DNA negativity rate at month-6, 12 and 18 were 42.9, 60 and 66.7 % in LdT group. HBV DNA negativity rate at month-18 in LdT group was 80 % if HBV DNA was detectable in month-6 and 91.7 % if undetectable DNA at month-6. of the 11 patients who had HBV DNA 6 months after cessation of NUCs, 10 (88.9 %) had reappearance of viral load.
Conclusion: NUCs was effective in HBV reduction during chemotherapy. There was no obvious difference between LdT and ETV. We had to pay attention to the viral relapse after cessation of NUCs after chemotherapy.

Topic 11: Hepatitis B

No: 1784

Increased serum levels of MIF TGF β il 17 and il 23 correlate positively with active viral replication and severity of liver disease in chronic hepatitis B

Jing You[1], Yuanzhi Yan[2], Lin Zhuang[3], Hongying Chen[1], Yanhua Che[4], Sijia Ma[5], Xia Feng[6], Hutcha Sriplung[7], Alan Geater[7], Virasakdi Chongsuvivatwong[7], Junhua Huang[8], Shaoming Yan[9], Ruyi Zhang[1], Shaofeng Rao[1]

The First Affiliated Hospital of Kunming Medical University Department of Infectious Diseases Kunming-China[1], The First Affiliated Hospital of Kunming Medical University Department of Pharmacy Medicine Kunming-China[2], The Third People's Hospital of Kunming Department of Hepatology Kunming-China[3], The First People's Hospital of Kunming Department of Medicine Kunming-China[4], Kunming Medical University Kunming-China[5], The First Affiliated Hospital of Kunming Medical University Department of Laboratory Medicine Kunming-China[6], Prince of Songkla University Epidemiology Unit, Faculty of Medicine Hat Yai-Thailand[7], The Yunnan General Hospital of The Chinese People's Armed Police Forces Department of Infectious Diseases Kunming-China[8], The Third People's Hospital of Yunnan Province Department of Internal Medicine Kunming-China[9]

Background/aims: To investigate the levels of macrophage migration inhibitory factor (MIF), transforming growth factor-β (TGF-β), interleukin-17 (IL-17), interleukin-23 (IL-23) and interleukin-10 (IL-10) and their correlation with viral replication and liver disease in chronic hepatitis B.
Patients and methods: One hundred and twenty-six chronic hepatitis B patients were enrolled the study. 30 normal individuals were as control group. Serum levels of MIF, TGF-β, IL-17, IL-23 and IL-10 were measured using an enzyme-linked immunosorbent assay (ELISA). HBV markers were detected with ELISA. Serum HBV DNA load was assessed with quantitative Real-Time PCR.
Results: Chronic hepatitis B patients had significantly increased serum levels of MIF, TGF-β, IL-17 and IL-23 and decreased IL-10 compared with normal individuals ($P < 0.01$, 0.01, 0.001, 0.001, 0.01, respectively). Univariate analysis showed a similar pattern of the parameters MIF, TGF-β, IL-17 and IL-23 were significantly associated with high viral load, presence of serum hepatitis B e antigen (HBeAg) expression, liver disease severity, and young age at HBV infection, all with $P < 0.01$. In chronic hepatitis B patients, MIF, TGF-β, IL-17, IL-23 and ALT levels were positively correlated (r = 0.629, 0.762, 0.865, 0.891; $P < 0.05$, 0.01, 0.01, 0.01, respectively), IL-10 and ALT was negatively correlated (r = -0.696, $P = <0.01$). Multivariate analysis showed that the levels of increment of MIF, TGF-β, IL-17 and IL-23 were associated with the increment of HBV DNA load and severity of liver disease.

Conclusion: There is a marked correlation between the concentration of MIF, TGF-β, IL-17 and IL-23 and the viral replication and severity of liver disease in chronic hepatitis B.

Topic 11: Hepatitis B

No: 1551

High dose of lamivudine and resistance in patients with chronic hepatitis B

Hamid Wani[1], Saad Alkaabi[1], Manik Sharma[1], Rajvir Singh[1], Anil John[1], Moutaz Derbala[1], Muneera Mohannandi[1]

Hamad Medical Corporation Medicine Doha-Qatar[1]

Background: Lamivudine is the most affordable drug used for chronic hepatitis B and has high safety profile. With the daily dose of 100 mg there is progressive appearance of resistance to lamivudine therapy. In our study we used 150 mg of lamivudine daily as standard dose which warrants further exploration for the efficacy of the drug.
Aims of the study: To assess the efficacy of Lamivudine 150 mg daily on resistance in patients with Chronic Hepatitis B.
Methods: This retrospective study consists of 53 patients of chronic hepatitis B treated with 150 mg of lamivudine daily. The biochemical and virological response to the treatment was recorded at 1, 2, 3, 4, and 5 years period and time of emergence of resistance to the treatment was noted.
Results: The mean age of the patients was 54 years with 80 % being males. The resistance to lamivudine 150 mg daily at 1, 2, 3 and 5 yeas was 12.5, 22.5,37.5 and 60 % respectively, which is much less compared to the standard dose of 100 mg of lamivudine.
Conclusions: Lamivudine is safe and higher dose of 150 mg daily delays the resistance in patients with chronic hepatitis B.

Topic 11: Hepatitis B

No: 1827

A rare side effect of entecavir hepatomegaly and steatosis

Tayibe Bal[1], Yusuf Onlen[1], Selma Ilkay Sahin[1], Vicdan Koksaldi Motor[1], Omer Evirgen[1]

Mustafa Kemal University Medical Faculty Infectious Diseases and Clinical Microbiology Hatay-Turkey[1]

Aim: Hepatomegaly and steatosis is a rare but potentially fatal side effect of nucleoside analogs. We presented the development of hepatomegaly and steatosis in 53 years old man who was treated with entecavir for six years. The aim of this clinical report was to point out a rare side effect of entecavir and to share the applied treatment.
Case: A 53 years old chronic hepatitis B patient who has been treated with entecavir since November 2008 is reported. Preliminary ultrasound of the abdomen revealed a normal liver size. In the fifth years of treatment, ultrasonography showed 163 mm hepatomegaly and steatosis. The liver size increased progressively and in the last ultrasonography the liver size of the patient was 175 mm in diameter. He had no symptoms of lactic asidosis like abdominal pain, shortness of breath, muscle pain or weakness. Physical examination revealed 2 cm hepatomegaly. He was mildly overweight. The serum aminotransferase, bilirubin and blood lipids levels were at normal ranges. By the time this side effect was identified, entecavir was switched to tenofovir. After receiving tenofovir therapy for 3 months, ultrasound of the abdomen showed normal liver size. Therefore, it's very likely that hepatomegaly and steatosis were due to entecavir therapy.
Conclusion: This case highlights the importance of considering hepatomegaly and steatosis as a side effect of entecavir therapy. For the patients developing this potentially fatal side effect of entecavir, switching therapy to tenofovir would be more safe because it's considered that tenofovir cause lesser mitochondrial toxicity.

Topic 11: Hepatitis B

No: 1731

Serum ip 10 level correlates significant fibrosis in chronic hepatitis B

Dilek Yildiz Sevgi[1], Banu Bayraktar[2], Alper Gunduz[1], Banu Yilmaz Ozguven[3], Alper Togay[2], Emin Bulut[2], Nuray Uzun[1], Ilyas Dokmetas[1]

Sisli Hamidiye Etfal Training and Research Hospital Department of Infectious Diseases and Clinical Microbiology Istanbul-Turkey[1], Sisli Hamidiye Etfal Training and Research Hospital Department of Clinical Microbiology Istanbul-Turkey[2], Sisli Hamidiye Etfal Training and Research Hospital Department of Pathology Istanbul-Turkey[3]

Aim: IP-10 expression was correlated with histologic severity and lobular inflammation in patients with chronic hepatitis C virus infection. Limited studies have been done with IP-10's impact on HBV infection in contrast to HCV infection. We evaluated serum IP-10 levels, APRI, AST-to-ALT ratio (AAR) and MPV in chronic hepatitis B (CHB) patients and correlated these data with results from liver biopsies.
Method: The study subjects were patients with chronic HBV infection who had liver biopsy performed between July 2010 and December 2013 at the Department of Infectious Diseases and Clinical Microbiology at Sisli Hamidiye Etfal Research and Training Hospital in Istanbul-Turkey. Healthy volunteers with normal aminotransferases and negative serology for HBV, HCV and HIV were recruited as controls. A total of 76 patients with CHB and 21 controls were recruited into this study. In accordance with Ishak scores, patients were clustered into two groups: (mild fibrosis group F1-F2, and significant fibrosis group F3-F4-F5-F6 respectively 57.7 % and 42.3 %. Statistical analyses were performed using SPSS, version 22.0.
Conclusion: Serum IP-10, MPV values of patients were higher than those of controls ($P < 0.05$). In mild fibrosis group IP-10 and AAR were lower than significant fibrosis group ($P < 0,05$). However there was no significant difference in MPV, APRI, ALT between two groups ($P < 0,05$). (Table 1) IP-10 levels had a high sensitivity and specifity for differentiation of mild and significant fibrosis.

Topic 11: Hepatitis B

No: 1002

Serum hepatitis B surface antigen quantification in the patients with chronic hepatitis B infection

Meryem Demirelli[1], Necla Tulek[1], Fatih Temocin[2], Dogan Yucel[3], F. Sebnem Erdinc[1], Gunay Tuncer Ertem[4]

Ankara Training and Research Hospital Infectious Diseases and Clinical Microbiology Ankara-Turkey[1], State Hospital Infectious

Diseases and Clinical Microbiology Yozgat-Turkey[2], Ankara Training and Research Hospital Medical Biochemistry Ankara-Turkey[3], Ankara Training and Research Hospital Infectious Diseases and Clinical Microbiology Ankara-Turkey[4]

Aim: Recently, quantification of HBsAg in the patients with chronic hepatitis B (HB) has become an attractive issue in both on the predicting natural course of HB infection and treatment response. The aim of the study is to evaluate HBsAg titers in the differentiation of inactive carrier state from other stage of chronic HB and usage in daily practice.
Methods: A total of 145 treatment naïve patients (74 inactive, 71 active HB cases with similar age and gender distribution) followed-up at least six months at our clinic were included in the study. Serum alanine aminotransferases, HBV-DNA levels (Abbott real time quantitative PCR), besides other routine tests were performed and HBeAg situation was recorded in all patients. Quantitative HBsAg was measured with a commercial assay (Elecsys HBsAg II, Roche Diagnostics). The results were compared between inactive carrier stage and others. Correlation of HBsAg titers with age and HBV-DNA levels were analysed by SPSS.
Results: The mean HBsAg titers were significantly lower in inactive carriers (mean ± SD; 3578 ± 5015 IU/ml) than those of active patients (mean ± SD; 28597 ± 64872 IU/ml), than those of HBeAg positive (mean ± SD; 114736 ± 103574 IU/ml) or HBeAg negative patients (mean ± SD; 5524,1 ± 7730,8 IU/ml). Highest HBsAg levels were detected in HBeAg positive patients. In all patients HBsAg titers were well correlated with HBV-DNA levels and negatively correlated with age ($P = 0.001$ and $P = 0.003$ respectively).
Conclusion: Quantification of HBsAg seems to guide at initial evaluation of patients with chronic hepatitis B infection and may provide most accurate identification of stages in a short time when used with other traditional tests.

Topic 11: Hepatitis B

No: 2000

IFNL3 (IL28B) and ifnl4 polymorphisms are not associated with treatment response to pegylated interferon in thai patients with hbeag positive chronic hepatitis B

Umaporn Limothai[1], Srunthron Akkarathamrongsin[2], Yong Poovorawan[2], Pisit Tangkijvanich[1]

Chulalongkorn University Research Unit of Hepatitis and Liver Cancer, Department of Biochemistry, Faculty of Medicine Bangkok-Thailand[1], Chulalongkorn University Center of Excellence In Clinical Virology, Faculty of Medicine Bangkok-Thailand[2]

Objectives: Recent studies have shown an association between single nucleotide polymorphisms (SNPs) in the interferon lambda-3 (IFNL3 or IL-28B) and IFNL4 genes and treatment response in chronic hepatitis C. However, the importance of these SNPs in chronic hepatitis B is unclear. The aim of this study was to investigate whether these SNPs could predict treatment response to pegylated interferon (PEG-IFN) in patients with HBeAg-positive chronic hepatitis B.
Methods: We retrospectively analyzed data of Thai patients with HBeAg-positive chronic hepatitis B treated with PEG-IFN for 48 weeks. The virological response (VR) was defined as HBeAg seroconversion and HBV DNA level < 2,000 IU/mL at week 24 of followed-up. DNA extracted from blood samples was analyzed for the SNPs IFNL3 (rs12979860) and IFNL4 (ss469415590).
Results: A total 95 patients were enrolled in the study (mean age 34 years, male 69.5 %). VR was achieved in 38 (40 %) patients and HBsAg clearance was found in 10 (10.5 %) patients. The distribution of CC, CT and TT genotypes of rs12979860 was 87(91.6 %), 8(8.4 %) and 0(0 %), respectively, while the distribution of TT/TT, ΔG/TT and ΔG/ΔG genotypes of ss469415590 was 88(92.6 %), 7(7.4 %) and 0(0 %), respectively. For rs12979860, 40.2 % of patients with CC genotype versus 37.5 % with CT genotype achieved VR ($P = 0.880$). For ss469415590, 39.8 % of patients with TT/TT genotype versus 42.9 % with ΔG/TT genotype achieved VR ($P = 0.873$). Similarly, there was no association between these genotypes and HBsAg clearance.
Conclusion: The IFNL3 and IFNL4 genotypes were not associated with treatment response to PEG-IFN in Thai patients with HBeAg-positive chronic hepatitis B.

Topic 11: Hepatitis B

No: 1676

The long term outcome of clevudine therapy in naïve patients with chronic hepatitis B

Seok Hyun Kim[1], Eaum Seok Lee[1], Byung Seok Lee[1], Heon Young Lee[1], Jong Seok Ju[1], Ki Dae Kim[1]

Chungnam National University and Chungnam National University Hospital Internal Medicine Daejeon-Korea, South[1]

Aims: There are few studies about the long-term outcome of clevudine in chronic hepatitis B patients. We evaluate the long-term efficacy, viral resistance and safety of treatment with clevudine in naïve patients with chronic hepatitis B(CHB).
Methods: Among clevudine treated 192 patients, 98 patients were excluded due to poor drug compliance, malignancy, decompensated liver cirrhosis, short-term follow up period less than six months and previous medication history of nucleoside or nucleotide analogues or interferon. Serum ALT and hepatitis B virus DNA were analyzed at month 12, 24, 36 and 48. Development of viral breakthrough and myopathy with elevated creatine kinase were also monitored.
Results: From enrolled 94 patients, mean treatment period was 23.8 ± 12.6 months. Cumulative rate of viral response was 70.2, 75.5, 75.5 and 75.5 % at month 12, 24, 36 and 48. Serum ALT normalization rate was 81.2, 88.2, 90.4 and 100 % at month 12, 24, 36 and 48. Total cumulative rate of viral breakthrough for 48 months was 22.3 %(21/94). In treatment period, rate of HBeAg loss and seroconversion were 27.8 %(15/54) and 16.7 %(9/54). Twenty four patients(27.7 %) changed medication due to myopathy with elevated creatine kinase.
Conclusions: Clevudine therapy was effective in a part of patients with CHB up to the 4 years. But we will not recommend clevudine as the first line therapy for CHB because of increasing viral breakthrough and myopathy during long-term use of clevudine.

Topic 11: Hepatitis B

No: 1964

Hepatitis B surface antigen serum titer correlation with hepatitis B virus dna and alanine aminotransferase levels among hepatitis B e antigen negative chronic hepatitis B patients

Mark Lester Sy[1], Jade Jamias[1]

National Kidney and Transplant Institute Internal Medicine Paranaque City-Philippines[1]

Aims: The precise identification of true inactive hepatitis B carrier is difficult and needs serial determination. Hence we correlated the hepatitis B surface antigen titer of untreated Hepatitis B e Antigen (HBeAg) negative patients with their corresponding HBV DNA and alanine aminotransferase (ALT) levels, classified these patients as either inactive carrier or patients in the reactivation phase and finally determined if there was a significant difference in Hepatitis B surface antigen (HBsAg) titer between these groups.
Methods: A cross sectional retrospective study was done. All HBeAg negative Chronic hepatitis B (CHB) patients who had their HBsAg titer, HBV DNA and ALT done at National Kidney and Transplant Institute (NKTI) were obtained and clinical information was abstracted from records. A total of 40 patients were included in the study.
Results: The mean HBsAg titer among untreated HBeAg CHB patients was 3037.04 IU/mL (SD ± 8718.94 IU/mL). HBsAg was found to be directly correlated with HBV DNA ($R = 0.821$, $P = 0 < 0.05$) and serum ALT ($R = 0.654$ $P = 0 < 0.05$). Moreover, mean difference in HBsAg titer between Inactive carrier group (mean 103.72 IU/mL, SD ± 144.25) and reactivation phase group (mean 5690.99 IU/mL, SD ± 11517.39) was significant (p value $= 0 < 0.05$).
Conclusion: HBsAg titer was found to be directly correlated with HBV DNA and ALT. To our knowledge, this is first local study done that supports the concept that HBsAg titer can provide complementary information in differentiating patient as true inactive carrier from those in the reactivation phase.

Topic 11: Hepatitis B

No: 1999

The results related to long term monitoring of the babies of HBsAg positive subjects during pregnancy

Selma Tosun[1], Erhun Kasirga[2], Selda Erensoy[3], Sait Yucebilgin[4]

Izmir Bozyaka Research and Education Hospital Infectious Diseases Izmir-Turkey[1], Celal Bayar University The School of Medicine Pediatric Gastroenterology Manisa-Turkey[2], Ege University The Faculty of Medicine Microbiology Izmir-Turkey[3], Ege University The Faculty of Medicine Gynaecology and Obstetrics Izmir-Turkey[4]

Aim: The aim of this study is to evaluate the long term monitoring data of the babies of HBsAg positive subjects during pregnancy in 1994.
Method: As a result of the examinations, the study included 38 pregnant women determined to have HBsAg positivitiy in 1994.HBV indicators and HBV DNA in the cord blood taken from the babies of pregnants during labor were analyzed and the babies were monitored after applying vaccination during labor and HBIG.The mothers and infants were monitored regularly and the vaccination schedule of the babies were completed.
Results: The study included 38 pregnant women,but 6 of these women did not attend monitoring processes later. It was detected that 4 out of the 32 monitored pregnant women had HBeAg, 28 of them had antiHBe positive and 4 HBeAg positive pregnant women had HBV DNA positivity. In the cord blood 4 infants had HBsAg positive.During the monitoring process, it was determined that HBsAg positivity in 3 of the infants disappeared and all the babies had positive antiHBs beginning from the end of the first month. Only one baby remained as a carrier. Considering all the other children,when they were at the age of 2,one dose of booster was given due to the low/insufficient level of antiHBs.
Conclusion: HBsAg positive pregnants should be defined,and the immunisation and long term monitoring of the infants should not be neglected.

Topic 11: Hepatitis B

No: 2115

A clinical study on anti HBV dc inducing therapy in the HBeAg negative chronic hepatitis B virus carriers

Bang-fu Wu[1], Jiang-ying Yang[1], Yong Liu[2], Xuan-qin Wang[2], Xiang-hua Huang[2], Zheng-sheng Xiao[2], Xue-song Li[2], Ming Yang[2], Tuo-pu Wu[1]

Guangzhou Pubang Bio-immunological Tech Research Institute Tech Department Guangzhou-China[1], Southern Medical University Renkang Hospital Gastroenterology and Hepatology Center Dongguan-China[2]

Aims: To observe the clinical efficacy of the anti-HBV-dendritic cells(DC) inducing therapy combined with telbivudine in the HBeAg negative chronic hepatitis B virus(HBV) carriers.
Methods: 10 male and 4 female HBeAg negative chronic HBV carriers were recruited in the study. Patient's median age was 34 years(from 21 to 52 years). All patient's ALT was normal. The anti-HBV-DC inducing agent which been an admixture of hepatitis B vaccine, rhGM-CSF and BCG polysaccharide nucleic acid was injected hypodermically to the patient once every two weeks for 18 practices applications totally. Telbivudine was taken 600 mg daily. Quantitative HBVM(TRFIA) and HBVDNA were evaluated at week 0, 12, 24 and 36.
Results: At week 12, 24 and 36, the HBVDNA negative conversion rate were 71.43 %(10/14), 85.71 %(12/14) and 92.86 %(13/14), and the HBsAb positive conversion rate were 53.85 %(7/13), 76.92 %(10/13) and 92.31 %(12/13). One patient's HBsAb is always positive before and after the treatment. The HBsAg negative conversion and the HBsAg seroconversion were observed in one patient(7.14 %, 1/14) at week 24 and in two patients(14.29 %, 2/14) at week 36. The mild abnormal ALT was observed in one patient at week 12. The rate of adverse effect was 38.10 %. The adverse effect include fever, headache, ache all over, bellyache, urticaria and hives, dyspnea, and tumefaction ache in the injection site after injected the anti-HBV-DC inducing agent.
Conclusions: The anti-HBV-DC inducing agent can induce the subcutaneous immature DC become to mature DC, and restart the immune responses against HBV. The anti-HBV-DC inducing therapy can be considered as an efficient approach for HBeAg negative chronic HBV carriers.

Topic 11: Hepatitis B

No: 1367

Two year efficacy of the real world "roadmap concept" for lamivudine therapy in chronic hepatitis B patients at songklanagarind hospital

Nopporn Charoenthong[1], Pimsiri Sripongpun[1], Naichaya Chamroonkul[1], Teerha Piratvisuth[1]

Prince of Songkla University Internal Medicine Hatyai-Thailand[1]

Aims: HBV DNA level at week 24 after antiviral treatment in chronic hepatitis B (CH-B) patients is a significant predictor of long-term efficacy, especially in low genetic barrier agent(s). The "Roadmap Concept" of considering add-on therapy for patients who do not achieve an early virological response was introduced in 2007; its aim is to improve the long-term viral suppression rate. This study is to evaluate 2-year efficacy of this approach applied to real-world practice of lamivudine therapy.
Methods: The data of lamivudine-treated CH-B adult patients who were followed up > 2 years at Songklangarind Hospital from 2004 to 2011 were retrospectively analyzed. Patients who received treatment according to the "Roadmap Concept" at week 24 were classified as the "Roadmap Group" and the remaining patients were classified as the "Conventional Group". Treatment outcome was measured at week 96.
Results: Of the 3,551 patients who were diagnosed with CH-B in the hospital database during the study period, 3,298 patients met the exclusion criteria. The remaining 253 patients were included in this study. Seventy-seven patients (30.4 %) were in the "Roadmap Group" and 176 patients were in the "Conventional Group". At week 96, patients in the "Roadmap Group" achieved a significantly higher rate of undetectable virus compared with the "Conventional Group" (83 % vs. 63 %, $P = 0.002$), and less virological breakthrough (17 % vs. 32 %, $P = 0.017$). Biochemical response was also high in the "Roadmap Group" (92 % vs.78 %, $P = 0.066$).
Conclusions: Lamivudine therapy with the application of the "Roadmap Concept" is an effective approach for the treatment of CH-B patients in real-world practice.

Topic 11: Hepatitis B

No: 2179

Transmission routes of hepatitis B virus in istanbul Turkey

Ozlem Altuntas Aydin[1], Hayat Kumbasar Karaosmanoglu[1], Meyha Sahin[1], Gulhan Eren[2], Yesim Kurekci[3]

Haseki Training and Research Hospital Infectious Diseases and Clinical Microbiology Istanbul-Turkey[1], Istanbul Training and Research Hospital Infectious Diseases and Clinical Microbiology Istanbul-Turkey[2], Arnavutkoy State Hospital Infectious Diseases and Clinical Microbiology Istanbul-Turkey[3]

Objective: The aim of this study was to determine the transmission routes of hepatitis B Virus (HBV) in HBV-infected patients in an outpatient clinic in Istanbul, Turkey.
Materials and methods: HBV-infected patients followed by the Infectious Diseases and Clinical Microbiology Outpatient Clinic of Haseki Training and Research Hospital between January 2008 and November 2014 were included in this study. Family members of the HBV-infected patients were checked for HBV infection. These results and epidemiological data were collected retrospectively from case records completed on admission.
Results: Among 221 patients 153 (69.2 %) were men, median age was 39.4 years (range18–68). Four of the patients were coinfected with HDV and only one patient was coinfected with HCV. The probable route of transmission was intrafamilial (original family) in 90 (40.6 %) patients and heterosexual intercourse (interspousal) in 22 (9.9 %) patients. Three patients (1.3 %) had history of blood tranfusion and only one patient had history of injection drug use.
Conclusion: Because of the importance of close contacts for transmission, HBV infection was more prevalent in original family of index cases compared to their spouses. Both parents-to-child and sibling-to-sibling horizontal transmission might be the main route of intrafamilial spread of HBV infection in our patients.

Topic 11: Hepatitis B

No: 1648

Evaluation of lamivudine for the treatment of chronic hepatitis B pre report of real life data from Turkey

Nesrin Turker[1], Bahar Ormen[1], Alpay Ari[2], Necla Tulek[3], Suda Tekin Koruk[4], Ayse Batirel[5], Sila Akhan[6], Saadet Yazici[7], Gulden Ersoz Munis[8], Celal Ayaz[9], Mustafa Kemal Celen[9], Nese Demirturk[10], Safak Kaya[11], Viral Hepatitis Study Group of Turkish Society of Clinical Microbiology[14]

Katip Celebi University Ataturk Training and Research Hospital Department of Infectious Diseases and Clinical Microbiology Izmir-Turkey[1], Bozyaka Training and Research Hospital Department of Infectious Diseases and Clinical Microbiology Izmir-Turkey[2], Ankara Training and Research Hospital Department of Infectious Diseases and Clinical Microbiology Ankara-Turkey[3], Koc University School of Medicine Department of Infectious Diseases and Clinical Microbiology Istanbul-Turkey[4], Dr.lutfi Kirdar Kartal Training and Research Hospital Department of Infectious Diseases and Clinical Microbiology Istanbul-Turkey[5], Kocaeli University School of Medicine Department of Infectious Diseases and Clinical Microbiology Kocaeli-Turkey[6], Medeniyet University Goztepe Training and Research Hospital Department of Infectious Diseases and Clinical Microbiology Istanbul-Turkey[7], Mersin University School of Medicine Department of Infectious Diseases and Clinical Microbiology Mersin-Turkey[8], Dicle University School of Medicine Department of Infectious Diseases and Clinical Microbiology Diyarbakir-Turkey[9], Afyon Kocatepe University School of Medicine Department of Infectious Diseases and Clinical Microbiology Afyon-Turkey[10] Diyarbakirgazi Yasargil Training and Research Hospital Department of Infectious Diseases and Clinical Microbiology Diyarbakir-Turkey[11]

Aim: The aim of this study is to analyze real life data of lamivudine treatment in Chronic hepatitis B (CHB) patients from Turkey.
Materials and methods: This retrospective study enrolled adult patients with CHB treated with lamivudine therapy at 15 centers throughout Turkey from January 1999 to June 2014. Sociodemographic data, biochemical and serological tests, biopsy scores and HBV DNA levels at the time of lamivudine initiation were recorded. Lamivudine treatment outcomes in fourteen years were analyzed.
Results: Totally 527 patients were included, 317 of them were male. Mean age of patients were $43{,}88 \pm 13{,}44$. Mean duration of HBV infection was 7,5 years. Family history was found in 266 (50,47 %) patients. Most of the patients were (80,83 %) HBeAg negative. Mean HBV DNA and ALT levels at the entry were $33511460{,}51 \pm 178130802{,}68$ IU/mL and $83{,}025 \pm 81{,}95$ IU/mL respectively. 417 patients were underwent percutaneous liver biopsy and stage of fibrosis was ≥ 4 in 35 of them. Lamivudine had to change in 293 patients (56 %) (primary nonresponse in 8, partial virological response in 103, viral breakthrough/resistance in 180 and side effect in 2 patients). Among 94 patients tested for YMDD mutation, 19 were positive. Four patients developed HBsAg seroconversion.
Conclusion: Although guidelines recommend potent antivirals with a high barrier to resistance as first line monotherapies, lamivudine can still be one of the most preferred agent in some group of patients

because of its inexpensive cost and excellent safety profile, but close follow up is needed.
*VHSG Members; Huseyin Turgut, Ali Asan, Ozgur Gunal, Kemal Avsar

Topic 11: Hepatitis B

No: 1007

Comparison of the efficacy of tenofovir disoproxil fumarate and entecavir for initial treatment of patient with chronic hepatitis B through 72 weeks in China

Mingxing Huang[1], Hong Shi[2], Xing-hua Li[2], Ye-sheng Jie[2], Yuan-kai Wu[2], Guo-li Lin[2], Yu-tian Chong[2]

The Fifth Affiliated Hospital of Sun Yat-sen University Department of Infectious Diseases Zhuhai-China[1], The Third Affiliated Hospital of Sun Yat-sen University Department of Infectious Diseases Guangzhou-China[2]

Background: Tenofovir disoproxil fumarate (TDF) and entecavir (ETV) have been accepted as the standard treatment drugs for hepatitis B virus (HBV) reactivation. However, comparative research about these two antiviral drugs has not been performed yet in Mainland China. Objective: We aim to compare the efficacy and safety of TDF and ETV initial treatment of chronic hepatitis B (CHB) patients.
Methods: We retrospectively analyzed the efficacy and safety of TDF treatment on 33 CHB patients and of ETV treatment on 65 CHB patients by comparing the HBV DNA levels, HBV DNA undetectable rate, HBV DNA negative conversion multi-factor analysis, alanine amino transferase (ALT) normalization rate, and the adverse event incidence at weeks 4, 12, 24, 36, 48, 72 before and after treatment in each group.
Results: The HBV DNA levels in the ETV group were significantly lower than that in the TDF group at week 4 (95.05 ± 39.49 versus 103.3 ± 80.25 U/L, $P = 0.005$). The differences in HBV DNA levels at the other times between these two treatment groups were not statistically significant. No significant differences were observed with HBV DNA undetectable rate and ALT normalization rate between the two groups ($P = 0.114$, 0.656, respectively). HBV DNA negativity multi-factor analysis showed that the differences in TDF and ETV treatment were not statistically significant ($P = 0.116$).
Conclusion: TDF and ETV treatment both exhibited rapid inhibiting effects on HBV DNA replication in the early phase of naïve CHB patients in Mainland China.

Topic 11: Hepatitis B

No: 1659

A case of prednisolone induced acute flare up of HBV infection in a patient with ocular behcet disease

Ergenekon Karagoz[1], Asim Ulcay[1], Eyup Duzgun[2], Taner Kar[2], Vedat Turhan[1]

Gata Haydarpasa Training Hospital Infectious Diseases and Clinical Microbiology Istanbul-Turkey[1], Gata Haydarpasa Training Hospital Ophthalmology Istanbul-Turkey[2]

Introduction: Hepatitis B virus (HBV) infection is one of the most frequent chronic viral infection which affects the liver around the world with over 400 million people infected. It is known that reactivation of hepatitis B virus is usually observed after chemotherapy or immunosuppressive therapy. Most of these cases have been reported from the fields of oncology and hematology. There have been also some cases reported in patients with rheumatic disease undergoing immunosuppressive therapy and from other fields. We present a case of an inactive 21-year old HBV carrier with acute flare up of HBV after 6 months prednisolone therapy due to ocular Behcet's disease.
Case presentation: A 21 year-old-man visited infectious diseases outpatient clinic with complaints of weakness and fatigue and with elevated liver enzymes.In his history, he had visited the Eye Diseases outpatient clinic in another hospital because of periorbital pain, photophobia and blurred vision. After detailed investigations he was diagnosed as ocular Behcet's disease and metilprednisolone therapy 16 mg 1×3 + cyclosporine 100 mg 2×1 therapy was initiated by opthalmologists. He was an HBV carrier detected 2 year ago; but before receiving steroid treatment, HbsAg positivity was overlooked and antiviral treatment didn't initiated. After 6 months, he visited our hospital for control. In his laboratory tests; AST: 200 U/L,ALT: 370 U/L.The viral panel for HbsAg, AntiHbcIgG,Anti-Hbe, HBV DNA (2.530 IU/ml) was positive. We evaluated this condition as acute hepatitis B caused by HBV reactivation due to immunosuppressive treatment. Lamivudin 100 mg was initiated.
Conclusion: Reactivation of HBV is an important complication which may cause liver failure and even death. Clinicians should screen hepatitis markers in patients who will receive immunosuppressive therapy.

Topic 11: Hepatitis B

No: 1406

Epidemiologic survey of chronic hepatitis B and C in the burmese population of Maryland

Natarajan Ravendhran[1], Sean Byrne[2], Khin Rhupa Maung[3], Jane Pan[3], Dan-tam Phan-hoang[3]

Johns Hopkins Hospital Medicine Baltimore, Md-United States[1], Gilead Sciences, Inc. Medical Sciences Foster City, Ca-United States[2], Hepatitis B Initiative of Washington, Dc Outreach Washington, Dc-United States[3]

EPIDEMIOLOGIC SURVEY OF CHRONIC HEPATITIS B AND C IN THE BURMESE POPULATION OF MARYLAND Ravendhran N[SUP]1[/SUP], Byrne S[SUP]2[/SUP], Maung KR[SUP]3[/SUP], Pan J[SUP]3[/SUP], Phan-Hoang DT[SUP]3[/SUP]Affiliations: 1Johns Hopkins University, Department of Medicine, Baltimore, MD; 2Gilead Sciences, Inc.; 3Hepatitis B Initiative of Washington, DC

Background: According to WHO, an estimated 350 million people are chronically infected globally with CHB with an estimated 1.25 million in the U.S. CHC affects approximately 170 million globally of which three million live in the United States. Studies conducted in Myanmar found that between 10-12 % of the study populations were found to be HBsAg + and 3 % anti-HCV +.
Methods: In this prospective epidemiologic screening survey, patients were screened at community screening events within the Burmese community for both HBV and HCV. HBV status was assessed by screening for HBsAg and anti-HBs. For HCV assessment, patients were screened for anti-HCV and if anti-HCV +, HCV RNA was drawn.
Results: A total of 876 patients were screened over 29 screening events between March 2013 and September 2014. The HBsAg + rate was 4.1 %. 26.1 % required vaccination. 42 % were Female, 33 %

were Male and 4.5 % did not report. 5.3 % were anti-HCV + and 94.5 % were anti-HCV negative. 8 % had a family member with CHB and 3 % had a family member with HCC.
Conclusions: HBsAg positivity rate was less in this population than was reported in Myanmar. The anti-HCV + rate was higher than was reported in Myanmar and was greater than the HBsAg + rate.

Topic 11: Hepatitis B

No: 1070

Hepatitis B and C Virus (HBV and HCV) Prevalence in HIV AIDS Patients which follow in our clinic

Barıs Ertunc[1], Selcuk Kaya[1], Iftihar Köksal[1]

Karadeniz Technical University, School of Medicine Infectious Diseases and Clinical Microbiology Trabzon-Turkey[1]

Objective: We aimed to investigate hepatitis B and C virus (HBV and HCV) prevalance in HIV/AIDS patients.
Methods: HBsAg, anti-HBcIgG and anti-HCV test results of HIV/AIDS patients were screened retrospectively.
Results: HBV and HCV co-infections were seen in 13 (11,3 %) of our patients. The prevalance of HIV + HBsAg, HIV + HCV and HIV + HBV + HCV co-infections were 5.2, 5.2 and 0.9 %, respectively. Anti-HBs and Anti-HBcIgG positivity were seen in 26.9 % of the patients. HBV vaccination was recommended to 23 (20 %) patients therefore Anti-HBs positivity developed in 20 (87 %) of them. Despite triple course of HBV vaccination, two patients had no protective Anti-HBs titers. Anti-HBs negativity was developed in one of seroconverted patients ongoing months.
Conclusion: HBV and HCV co-infections are seen in most of HIV/AIDS patients. Hence progression to cirrhosis are faster than HBV/HCV monoinfected patients, screening them for these infections and follow-up positives would be important. If their immune system allow, protection with HBV vaccination should provide in seronegative patients. Anti-HBs titers should periodically follow in these patients and rapel dose implementation should be done if necessary.

References

1. Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents. http://aidsinfo.nih.gov/guidelines on 5/7/2013.
2. European AIDS Clinical Society (EACS) 2014 guideline. Version 7.02 June 2014.

Topic 11: Hepatitis B

No: 1285

Hepatitis B virus reverse transcriptase mutations in the natural history of chronic hepatitis B

Hu Li[1], Peng Hu[1], Hong Ren[1]

Institute of Viral Hepatitis, Department of Infectious Diseases The Second Affiliated Hospital of Chongqing Medical University Chongqing-China[1]

Background and aims: Naturally occurring mutations in the reverse transcriptase (RT) region of hepatitis B virus (HBV) genome have not been well characterized according to different phases of chronic hepatitis B (CHB). This study aimed to characterize the profiles of naturally occurring mutations of RT region in the natural history of CHB.
Methods: In this cross-sectional study, HBV RT region mutations were determined and analyzed from aspects of RT domains, immune epitopes and its influence (HBsAg "a" determinant and drug resistance) by PCR-clone-sequencing in each phase of CHB.
Results: A total of 575 full-length RT nucleotide sequences were successfully obtained from 28 treatment-naïve subjects. Quasispecies analysis demonstrated that the extents of RT variation were significant different between IT phase and IA, IC phases. The discrepancy was further confirmed by conservation evaluation within RT protein. Finally, 63 amino acid substitutions were found across the study population by the sequences alignment. These mutations' distribution and frequencies were showed significant different in RT domains and immune epitopes. The nucleot(s)ide related mutations (rtI169T, rtA181T, rtS202G) were determined in 8 (1.39 %, 8/575) isolates from two patients (7.14 %, 2/28)and the incidence of isolates with drug resistance mutations were statistically significant between each phase of CHB (IT: 0 %, IA: 3.57 % and IC: 0.65 %, $P < 0.01$).
Conclusion: We well characterized the profiles of naturally occurring mutations within HBV RT region and clearly demonstrated the different mutation patterns at the RT domains and RT immune epitopes. Furthermore, potential impacts on "a" determinant and drug resistance are also significant different in the natural history of CHB.

Topic 12: Hepatitis C

No: 1190

Treatment of chronic hepatitis C in end stage renal disease patients treated by dialysis multicenter experience in Korea

Sang Bong Ahn[1], Byung Kwan Son[1], Dae Won Jun[2], Sang Gyune Kim[3], Sae Hwan Lee[3], Hyun Phil Shin[4], Won Hyeok Choe[5], Ja Kyung Kim[6], Kyu Sik Jung[6], Do Young Kim[6], Jae-jun Shim[7], Soo Young Park[8], Yeon Seok Seo[9], Won Kim[10], Jae Il Chung[11]

Eulji University College of Medicine Gastroenterology Seoul-Korea, South[1], Hanyang University College of Medicine Gastroenterology Seoul-Korea, South[2], Soonchunhyang University Gastroenterology Seoul-Korea, South[3], Kyung Hee University Hospital At Gangdong Gastroenterology Seoul-Korea, South[4], Konkuk University School of Medicine Gastroenterology Seoul-Korea, South[5], Yonsei University School of Medicine Gastroenterology Seoul-Korea, South[6], Kyung Hee University Hospital Gastroenterology Seoul-Korea, South[7], Kyungpook National University Hospital Gastroenterology Daegu-Korea, South[8], Korea University School of Medicine Gastroenterology Seoul-Korea, South[9], Seoul Metropolitan Government Seoul National University Boramae Medical Center Gastroenterology Seoul-Korea, South[10] Sahmyook Medical Center Gastroenterology Seoul-Korea, South[11]

Introduction: Patients with chronic hepatitis C (CHC) underlying disease with ESRD on a dialysis are difficult group to treat and shows higher dropout rate during treatment. The aim of this study was to analyze the treatment outcome in patients with CHC underlying end stage renal disease on a dialysis in Korea.
Methods: Retrospective multi-center studies on thirty-five patients underlying ESRD on a regular dialysis in 13 centers were analyzed. We investigated the tolerability and efficacy of pegylated interferon therapy with or without ribavirin on dialysis patients.
Results: Thirty-five patients (mean age: 45.8 years) were treated with pegylated interferon and ribavirin was prescribed in 19 patients (54 %). Twenty patients (57 %) were genotype 1. Only twenty-two patients finished scheduled course. RVR at 4 weeks was achieved in

24 patients (68 %). EVR and ETR were achieved in 27 patients (77 %). Twenty-three patients (85 %) had SVR among 27 patients who have ETR. Thirteen patients (37 %) dropped out before completion of treatment. However, three patients were PCR negative at the premature termination period, and these patients reached SVR in spite of premature termination. Overall SVR rate 65.7 % in all subjects. Most common side effects were anemia and neutropenia. The patients with ribavirin had higher dropout rate (10 of 19) and higher SVR (13 of 19) compared to the patients without ribavirin. One subject undergone peritoneal dialysis and showed SVR.
Conclusion: HCV treatment underlying ESRD patients are difficult to treat with higher dropout rate. However, despite the high dropout rate, SVR was 65.7 %.

Topic 12: Hepatitis C

No: 1381

Evaluation of the association between il28b polymorphisms and sustained virologic respond in patient with chronic hepatitis C who were followed at akdeniz university infectious disease department

Sevil Yilmaz[1], Aslı Toylu[2], Özden Altiok Clark[2], Dilara Inan[1]

Akdeniz University Infectious Disease Antalya-Turkey[1], Akdeniz University Medical Genetıc Antalya-Turkey[2]

In recent years studies on genetic factors that affect SVR has been started. The most researched in these factors that identified in the IL28B gene on chromosome 19 is single nucleotide polymorphisms. In studies patients who have rs12979860 and rs8099917 major genotype, detected the probability of receiving SVR was high. In this study we aimed to demonstrate the association between IL28B gene polymorphisms and sustained virologic response in patient with chronic hepatitis C.

Forty HCV genotype-1 infected adult patients aged 18-65 who have taken pegIFN + RBV treatment and have followed at least 6 months after the end of therapy were selected.For genotype analysis of patients blood samples were collected after informed consent. The relationship between genotype analysis, pretreatment biochemical and demographic characteristics, monitored features during treatment and SVR were retrospectively evaluated. The most common rs12979860 genotype in patients is CT (60 %), the TT genotype of rs8099917 (57.5 %), respectively.SVR was significantly higher in 12979860 CC genotype compared to non CC. EVR and SVR was significantly higher in rs8099917 TT genotype compared to non TT. Multivariate logistic regression analysis showed a significant association with SVR was observed only with rs8099917 TT genotype and ALT.

In our study we determine the distribution of IL28B genotype of Turkish Society and we showed the datas are compatible with the White race. Before the treatment to predict SVR we think IL28B genotypes may be taken into consideration. However, we must evaluate each patient together with other features that affect SVR and treatment decision for patients must be decided in private.

Topic 12: Hepatitis C

No: 1915

Emerging patterns of spontaneous clearance of high level viremia in chronic hepatitis C

Varun Jain[1], Sonja Marcus[2], Kristel K. Hunt[3], Sheldon T. Brown[3], Norbert Bräu[3]

James J Peters Va Medical Center & Icahn School of Medicine At Mount Sinai Medicine Bronx, NY-United States[1], James J Peters Va Medical Center Bronx, NY-United States[2], James J Peters Va Medical Center & Icahn School of Medicine At Mount Sinai Bronx, NY-United States[3]

Background: In the setting of acute hepatitis C virus (HCV) infection, spontaneous clearance of high-level viremia is common (25-50 %), but it is a rare event in chronic HCV infection.
Methods: This study retrospectively identified all cases of spontaneous clearance of high-level chronic HCV viremia (> 10,000 IU/mL) in a single center between 1997 and 2014 (16 years) and compared patterns of clearance with reported cases in the literature.
Results: Among 2,576 chronically HCV-infected patients seen over these 16 years, 5 (0.19 %) experienced spontaneous clearance in 3 different scenarios: 2 HCV-monoinfected patients after a response-relapse to antiviral therapy, 2 HIV/HCV-coinfected treatment-naive patients with HIV suppression on antiretroviral therapy, and 1 HCV-monoinfected patient two years after liver transplantation. Previous reports of spontaneous clearance of high-level chronic viremia include 16 HCV treatment-naïve HIV/HCV-coinfected subjects with well-controlled HIV infection and 5 patients after liver transplantation as well as 5 treatment-naïve HCV-monoinfected cases and 2 HCV-monoinfected patients following viral non-response to interferon + ribavirin. Clearance following antiviral response-relapse has not been reported previously.
Conclusions: Spontaneous clearance of high-level chronic HCV infection is rare but occurs in distinct patterns: without antiviral therapy, mostly in HIV/HCV-coinfected patients, after liver transplantation, and rarely following antiviral therapy, both with viral non-response and now also viral response-relapse.

Topic 12: Hepatitis C

No: 1756

The impact of overweight and obesity in patients with chronic hepatitis C virus infection in a reference center

Marco Chavez-alfaro[1], Alejandra Martínez-Castellanos[1], Jorge Segura-Ortega[1], Ana Sofía García-Moreno[2], Colin Laverty[3], Laura E. Moreno-Luna[4]

Hospital Civil De Guadalajara Gastroenterology and Hepatology Guadalajara-Mexico[1], Universidad De Guadalajara Clínicas Médicas Guadalajara-Mexico[2], Université De Sherbrooke Université De Sherbrooke Quebec-Canada[3], Universidad De Guadalajara Clinicas Médcias Guadalajara-Mexico[4]

Introduction: Screening of nutritional status for early identification of nutrition-related problems is vital to successful treatment and to prevention of more serious problems in HCV patients. The aim of this study is to report the actual nutritional status and disease severity in patients with HCV infection.
Materials and methods: The study was accepted by the institution's IRB. Patients accepted to participate and gave informed consent. From August 2012 to September 2014 patients were enrolled. A complete clinical history, liver function tests, cytometry, coagulation tests and hepatic ultrasound were performed in the first day of hospitalization. Nutritional status was assessed using anthropometric, dietary and clinical evaluations.
Results: From the 32 patients, 75 % (n = 24) were male, mean age 50 years (range 31 to 78 years), mean MELD 19.5 (6 to 37) and the

Child-Pugh classification was: A 6 % (n = 2), B 28 % (n = 9) and C 65 % (n = 21): The nutritional status was: malnutrition 6 % (n = 2) [(Mild 6 % (n = 2), Moderate < 0 % (n = 0), severe 0 % (n = 0)], normal weight 62 % (n = 20), overweight and obesity 31 % (n = 10) [overweight 12 % (n = 4), pre-obesity 6 % (n = 2), obesity grade 1, 6 % (n = 2), obesity grade 2, 6.25 %(n = 2) and obesity grade 3, (n = 0) respectively].
Conclusions: Obesity and overweight were found even in Child-Pugh C patients. It is five times more common than malnourishment. The impact of overweight and obesity in this group of patients will affect at an immediate future increasing the risk of morbidity and mortality at earlier stages.

Topic 12: Hepatitis C

No: 1847

Sofosbuvir population pharmacokinetics in japanese subjects with chronic genotype 2 HCV infection

Kimberly Garrison[1], Bing Gao[2], Diana Brainard[3], Steven Knox[3], Anita Mathias[1]

Gilead Sciences, Inc. Clinical Pharmacology Foster City-United States[1], Gilead Sciences, Inc. Biostatistics Foster City-United States[2], Gilead Sciences, Inc. Clinical Research Foster City-United States[3]

Background: Sofosbuvir (SOF) + ribavirin (RBV) for 12 weeks led to SVR rates > 95 % in treatment-naïve and treatment-experienced Japanese patients in the Phase 3 trial, GS-US-334-0118. Pharmacokinetic data was collected for Population PK analysis of SOF and its predominant circulating nucleoside metabolite, GS-331007 to examine the relationship between exposure and treatment outcome and compare results to studies in other regions
Methods: Treatment-naïve and treatment-experienced Japanese subjects were enrolled and received SOF 400 mg + RBV for 12 weeks. Plasma PK samples were collected from all subjects (N = 153) at each study visit. Nine subjects participated in an optional intensive PK substudy evaluating steady-state PK over 24-hours. All plasma concentration data was combined and applied to Population PK models for SOF and GS-331007. Exposure estimates were generated for each subject and the effect of covariates on SOF and GS-331007 exposure was evaluated.
Results: SOF exposure in HCV-infected Japanese subjects was similar to subjects administered SOF + RBV ± Peg-IFNα in the overseas Phase 2/3 SOF population. GS-331007 exposure was modestly higher in the Japanese study population; based on Phase 3 safety and efficacy, this finding is not considered clinically relevant. No clinically relevant differences in the PK of SOF or GS-331007 based on age, sex, BMI, cirrhosis status, prior treatment or SVR12 outcome were identified.
Conclusion: SOF exposure was similar and GS-331007 exposure was modestly higher in Japanese subjects compared to those in Phase 2/3 studies in non-Japanese populations. These data support the use of SOF 400 mg for the treatment of GT2 HCV infection in Japanese patients.

Topic 12: Hepatitis C

No: 1062

Never give up fight with hepatitis C

Yasemin Durdu[1], Bülent Durdu[2], Habip Gedik[3]

Eyup State Hospital Infectious Diseases Istanbul-Turkey[1], Bezmialem University Hospital Infectious Diseases Istanbul[2], Bakirkoy Doctor Sadi Konuk Training and Research Hospital Infectious Diseases Istanbul[3]

We want to present a 65 years old patient with hepatitis C with comorbitidies such as Chronic obstructive pulmonary disease (COPD), Diabetes Mellitus type II (DM) and Lung cancer which is in remission for one year.

He was knowing his disease for 2 years, after chemotherapy and radiotherapy for lung cancer, he decided to get the treatment for Hepatitis C. His ALT AST levels were two times higher then the normal level, HCV RNA PCR: 12,169,327 IU/ml, in his total blood count there was no thrombocytopenia, or leucopenia but there was a light anemia (Haemoglobulin (Hgb) level 12 mg/dl). The ultrasonography revealed light hepatomegaly with grade I hepatosteatosis. He was using bronchodialotory treatment for COPD and oral antidiabetics for DM.

He was very willing for the therapy, he was informed for the side effects of the therapy and the outcomes. The treatment has been choosen as PEG interferon alfa 2a 180 mcg and ribavirin as total of 1000 mg. At the beginning the most prominent side effects were fever and anemia. His Hgb level fell down to 9 mg/dl, continue to fall to the level 6,5 mg. Therefore he was transfused 5 times. He also applied to us 3 times with severe pneumonia needing hospitalization. Although with these difficulties he continued to be eager for the therapy. At week 12 HCV RNA level was 3169 IU/ml, the therapy continued and at week 24 the result was negative. He finished the therapy and no relapse has been seen for 6 months, achieving sustained viral response.

Topic 12: Hepatitis C

No: 1738

Population pharmacokinetic analysis of daclatasvir and asunaprevir in non japanese and japanese subjects with hepatitis C virus (HCV) infection

Phyllis Chan[1], Li Zhu[1], Hanbin Li[2], Timothy Eley[1], Marc Bifano[1], Mayu Osawa[1], Takayo Ueno[3], Eric Hughes[1], Malaz Abutarif[1], Brenda Cirincione[1], Frank Lacreta[1], Tushar Garimella[1]

Bristol-myers Squibb Research and Development Lawrenceville, Nj-United States[1], Quantitative Solutions Menlo Park, Ca-United States[2], Bristol-myers K.k. Research and Development Tokyo-Japan[3]

Aim. Population pharmacokinetic (PPK) models were developed for daclatasvir (DCV) and asunaprevir (ASV), a dual regimen approved in Japan, in subjects with chronic HCV infection.
Methods: The non-linear mixed effects PPK models (using NONMEM 7.1.2) for DCV and ASV previously were developed from 11 and 5 studies, respectively, in HCV infected subjects and were then updated with an additional 3 DCV studies and 2 ASV studies. Significant covariates ($P < 0.05$) from univariate screening were included in the full model. The final model was reached by backward elimination ($P < 0.001$). Sensitivity analysis was conducted for Japanese race.
Results: Pharmacokinetics of DCV and ASV were described by a two-compartment model with linear elimination. Absorption was modeled as zero-order release followed by first order absorption for both compounds. An induction effect was identified on ASV CL/F. Inter-individual variability was modest for DCV and ASV CL/F (35.1 % and 41 %, respectively) and DCV V/F (29.5 %) but was large for ASV V/F (148 %). Sex had the highest impact on DCV PK

with females having 28 % higher AUC. Race, baseline and time-varying AST and cirrhosis had the largest impact on ASV PK with 30 %-50 % higher AUCs in Asians and cirrhotics.
Conclusions: The magnitude of estimated covariate effects on DCV PK were small and not clinically meaningful. ASV CL/F decreases with cirrhosis and increasing baseline and time-varying AST indicating an association between hepatic markers and CL/F but has no clinical impact. Sensitivity analysis suggested applicability to allow for evaluation of Japanese subjects.

Topic 12: Hepatitis C

No: 1060

Response guided therapy for hepatitis C virus recurrence on early protocol biopsy after liver transplantation

Hyeyoung Kim[1], Kwang-woong Lee[1], Nam-joon Yi[1], Jaehong Jeong[1], Suk-won Suh[1], Youngrok Choi[1], Hae Won Lee[1], Kyung-suk Suh[1]

Seoul National University College of Medicine Surgery Seoul-Korea, South[1]

Background: Hepatitis C virus (HCV) recurrence after liver transplantation (LT) is universal and progressive. There is a trend of response guided HCV treatment. Here, we report the recent results of response guided therapy for HCV recurrence based on early protocol biopsy after LT.
Methods: We reviewed the patients who underwent LT for HCV related liver disease between 2010 and 2012. Protocol biopsies were done at 3, 6 and 12 months after LT in HCV recurrence. In fibrosis, $\geq$ moderate inflammation on histology or HCV hepatitis accompanying with abnormal liver function test, we treated with pegylated interferon and ribavirin. We adjusted treatment period according to the individual treatment response.
Results: Among 41 HCV related recipients, 61.0 % (n = 25) underwent protocol biopsies more than once and enrolled in this study. The mean follow-up was 37.6 months (range, 20-54 months) after LT. The genotype 1 and 2 were in 56.0 % and 36.0 %. Finally, 28.0 % started HCV treatment after biopsy at post-LT 3 months, 68.0 % at 6 months, and 80.0 % at 12 months (n = 20/25). Rapid or early virological response was 95.0 % (n = 19/20). Except 1 patients on treatment and 5 of incompletion of treatment, 14 patients who finished the treatment all showed end of treatment response (70.0 %, n = 14/20). Sustained virological response was 50.0 % (n = 10/20), and 33.3 % in genotype 1 (n = 4/12) and 75.0 % in non-genotype 1 (n = 6/8) ($P = 0.170$). Overall 3-year survival was 100.0 % in 25 patients who underwent protocol biopsies.
Conclusion: Response guided therapy for HCV recurrence based on early protocol biopsy after LT showed encouraging result.

Topic 12: Hepatitis C

No: 1708

Longterm outcomes of telaprevir based therapy in patients with cirrhotic HCV

Murat Aladag[1], Hulya Aladag[2], Yilmaz Bilgic[1], Murat Harputluoglu[1], Yasir Furkan Cagin[1], Mehmet Ali Erdogan[1], Yahya Atayan[1], Oguzhan Yildirim[1], Yuksel Seckin[1], Melih Karincaoglu[1]

Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[1], Inonu University Faculty of Medicine Gynecology Malatya-Turkey[2]

Introduction and purpose: In this study, we aimed at assessing the long-term outcomes of a telapravir-based triple therapy in cirrhotic patients who responded to the classical dual therapy but had relapses later.
Materials and methods: A total of 24 patients, 15 female and 9 male, with a mean age of 56.4 (22-74) were involved. The patients were started a triple combination therapy. They were assessed heir HCV-RNA measurements at the end of Week 4 and 12. They were examined at Weeks 24, 36, 48, and 72 in the later periods.
Results: Although a drop was seen in the Hb values of 10 of the 24 patients from the first week, their doses of medication were not decreased and 6 of them were given 1-2 units of erythrocyte suspension. HCV RNA that was measured at the end of Weeks 4 and 12 turned out 100 % (24/24) negative in all patients. HCV RNA became positive at Week 24 in a patient who stopped the therapy at Week 17 due to its side effects. HCV RNA measured at Week 24 was negative in 1/24 (95.9 %) patient, at Week 36 in 4/20 (80 %) patients, at Weeks 48 and 72 in 5/20 (75 %) patients. Four of the patients were taken to liver transplantation at Weeks 12, 13, 16, and 18 while their HCV RNAs were negative.
Conclusion: We observed that when telaprevir-based triple therapies are administered in clinics well-organized for hepatitis C treatment, a high rate of eradication can be achieved and sustained for a long time in patients with cirrhotic HCV.

Topic 12: Hepatitis C

No: 1121

Impact of nitazoxanide on sustained virologic response (svr) in Egyptian patients with chronic hepatitis C genotype 4 a double blind placebo controlled trial

Mohamed Kohla[1], Hala El-said[2], Ashraf El_fert[2], Nermine Ehsan[3], Sameera Ezzat[4], Hossam Taha[1]

National Liver Institute Hepatology Shebin El-kom-Egypt[1], National Liver Institute Clinical Biochemistry Shebin El-kom-Egypt[2], National Liver Institute Pathology Shebin El-kom-Egypt[3], National Liver Institute Epidemiology Shebin El-kom-Egypt[4]

Background and aim: Nitazoxanide, approved for treatment of Cryptosporidium parvum and Giardia lamblia, was found to inhibit hepatitis C virus replication in replicon system. The aim of this work is to assess the impact of Nitazoxanide as an add-on therapy to Pegylated Interferon α 2a on Sustained virologic response in a cohort of Egyptian patients with chronic hepatitis C.
Methods: A total of 195 patients were evaluated, 97 patients in the placebo group received placebo, versus 98 patients in the group treated with Nitazoxanide orally at a dose 500 mg twice daily with meals, In all patients, Placebo and Nitazoxanide were given as an add-on therapy to Pegylated Interferon α 2a plus Ribavirin, following a 12-week lead-in phase. Sustained Virologic Response (SVR) to triple therapy was evaluated in the 2 groups. Statistical analysis was done using SPSS software. This trial was registered on www.clinicaltrials.gov with a trial ID NCT01197157 (NEAR trial).
Results: The mean age for patients in the placebo group was 46.5 years versus 45.7 years in the Nitazoxanide group. In the placebo group, 85 patients out of 97 were males (87.6 %), versus 84 patients out of 98 patients (85.7 %) in the Nitazoxanide group.

In the placebo group, 59 patients out of 97 (60.82 %) achieved a Sustained Virologic Response (SVR), compared to 57 patients out of 98 (58.16 %) in the Nitazoxanide group, with a p value of (0.70), which did not show any statistically significant difference.
Conclusions: Our data did not show any significant impact of Nitazoxanide add-on therapy to Pegylated Interferon and Ribavirin on Sustained Virologic Response.

Topic 12: Hepatitis C

No: 1582

Comparative efficacy and tolerability of combination treatment with daclatasvir and asunaprevir versus peginterferon alpha ribavirin based regimens for patients infected with genotype 1b hepatitis C virus

James Signorovitch[1], Keith Betts[1], Yan Song[1], Rachael Sorg[1], Junlong Li[1], Ajay Behl[2], Anupama Kalsekar[2]

Analysis Group, Inc. Health Care Practice Boston-United States[1], Bristol-myers Squibb Virology Gheor Princeton-United States[2]

Objective: To compare the efficacy and tolerability of daclatasvir (DCV) + asunaprevir (ASV) versus peginterferon-alpha/ribavirin (A/R), telaprevir (TVR) + A/R, and boceprevir (BOC) + A/R in treatment-naïve and treatment-experienced patients infected with genotype 1b chronic hepatitis C virus (HCV).
Methods: Systematic literature reviews were conducted to identify randomized trials reporting sustained virologic response (SVR) with studied regimens in patients with genotype 1b HCV. A network meta-analysis (NMA) was conducted in treatment-naïve patients using aggregate data. Matching-adjusted indirect comparisons (MAICs), adjusting for cross-trial differences in patient characteristics, were performed in treatment-naïve and treatment-experienced patients using additional patient-level data from DCV + ASV trials. Outcomes included rates of SVR, anemia, rash, and discontinuation due to adverse events (AEs).
Results: In the NMA, treatment-naïve patients receiving DCV + ASV were significantly more likely to achieve SVR than those receiving TVR + A/R (difference: +18.7 %; 95 % credible interval: 12.3 %-26.1 %), BOC + A/R (+22.7 %; 11.5 %-35.0 %), and A/R (+48.3 %; 41.6 %-53.0 %). In the MAICs, DCV + ASV was associated with significantly higher rates of SVR compared with TVR + A/R (difference: +8.7 %; 95 % confidence interval: 0.2 %-17.3 %), BOC + A/R (+16.5 %; 2.5 %-30.5 %), and A/R (+39.6 %; 30.3 %-48.9 %) in treatment-naïve patients and significantly higher rates of SVR compared with TVR + A/R (+17.0 %; 5.3 %-28.7 %), BOC + A/R (+22.8 %; 6.9 %-38.7 %), and A/R (+57.7 %; 44.0 %-71.4 %) in treatment-experienced patients (the majority of which were relapsers). AE rates were generally lower in patients receiving DCV + ASV versus comparator regimens.
Conclusion: In indirect comparisons among genotype 1b HCV patients, DCV + ASV was associated with a superior efficacy and tolerability profile compared with TVR + A/R, BOC + A/R, and A/R.

Topic 12: Hepatitis C

No: 2046

Frequency of thyroidal dysfunction in chronic hepatitis C sero positives

Dr. Muhammad Imran[1], Prof. Dr. karim Kammeruddin Kammeruddin[1], Dr. Nida Sajid[1]

Baqai Medical University Karachi Pakistan Medicine Karachi-Pakistan[1]

Background: Hepatitis C virus is proving to be a global disease causing serious and debilitating effects on the general health of the public. It has been recognized that hepatitis C manifests itself though hepatic and a variety of extra hepatic diseases. The common two being diabetes mellitus and thyroid dysfunctions. A range of thyroid hormones disturbances are reported in association with hepatitis C infectivity for example Overt and Subclinical hyperthyroidism along with Overt and Subclinical hypothyroidism.
Objective: To determine the relation between Hepatitis C Sero Positivity and Thyroidal Dysfunction.
Methods: We study 274 chronic Hep C sero positive, non cirrhotic cases (Jan 2010–Jun 2014) in OPD of urban Tertiary care hospital (i.e. Baqai Medical University Hospital Nazimabad, Karachi).Out of this, 203 (b/w 20 to 60 years of age) cases were found to be evaluable (i.e. undergone TSH/FT4 evaluation at baseline). TSH was taken according to age groups (i.e. age 20y-54y (0.4-4.2) μIU/ml & 55-87 (0.5-8.9) μIU/ml) & FT4 (all age group) 0.8-2.7 ng/dL.
Results: Thyroid dysfunction was found in 17 patients (8.4 % [n = 203]).The Thyroidal dysfunction among the study group include, One patient with Overt Thyrotoxicosis (5.88 % [n = 17]), 05 with Clinically Hypothyroid (29.41 % [n = 17]) status and 11 cases with Sub-Clinical Hypothyroidism(64.70 % [n = 17]).
Conclusion: An association of thyroid dysfunction and Chronic HCV infection is noted in the study population without known pre-existing thyroidal disease.

Topic 12: Hepatitis C

No: 1797

Safety and rapid prediction of treatment futility of boceprevir with peginterferon ribavirin for Taiwanese treatment experienced hepatitis C virus genotype 1 infected patients

Chung-feng Huang[1], Min-lung Yu[1], Chia-yen Dai[1], Jee-fu Huang[1], Wan-long Chuang[1]

Kaohsiung Medical University Hospital 4 Hepatobiliary Division, Department of Internal Medicine Kaohsiung-Taiwan[1]

The efficacy and safety of the boceprevir-containing triple therapy in Taiwanese treatment-experienced patients remains unclear. After 4 weeks of peginterferon/ribavirin lead-in therapy, patients with cirrhosis or previous null-response received triple therapy for 44 weeks; whereas others received 32 weeks of triple therapy followed by 12 weeks of peginterferon/ribavirin therapy. Patients with HCV RNA > 100 IU/mL at week 12 or with detectable HCV RNA at week 24 of treatment were viewed as futile. One hundred and sixteen patients were recruited; 23 (19.8 %) patients terminated treatment before week 24 due to serious adverse event (SAE, n = 4), adverse event (n = 6), week 12 futility (n = 11), or week 24 futility (n = 2); whereas 93 (80.2 %) patients completed at least 24 weeks of treatment. By using intention-to-treat analysis, the proportion of patients with undetectable HCV RNA at week 4, week 8, week 12, and week 24 was 13.8, 61.5, 75.9, and 79.3 %, respectively. Twenty-one (18.1 %) patients experienced SAE before week 24 of treatment. Multivariate analysis revealed that APRI > 1.5 was the single factor associated with occurrence of SAE (odds ratio: 4.95; 95 % CI: 1.52-18.3; $P = 0.008$). The best viral kinetics in predicting week 12/24 futility was HCV RNA > 3 log IU/mL at week 8 with a positive

predictive value of 85.7 % and an accuracy of 95.5 %. Furthermore, merging the cut-off values of HCV RNA > 7 log IU/mL at baseline and HCV RNA > 6 log IU/mL at week 4 provided the best combing viral kinetics in predicting week 12/24 futility with the PPV.

Topic 12: Hepatitis C

No: 1308

Absence of cross reactivity between telaprevir and boceprevir

Rezzan Harman[1], Elif Sahin Horasan[2]

Konukoğlu Hospital Infectious Diseases Gaziantep-Turkey[1], Mersin University Infectious Diseases Mersin-Turkey[2]

Background: New antivirals for HCV treatment have led to significant improvements in sustained virologic response rates, but have showed to an increase in dermatologic adverse events (DAEs) compared to peginterferon/ribavirin alone. Telaprevir induced eczematous rashes were often observed late in treatment, with 70 % occurring after 4 weeks of treatment. Presented here is a patient with a telaprevir rash observed on the first day of treatment, who had resolution of dermatologic side effects after switching to boceprevir.

Case report: The patient was a 30-year-old woman with chronic hepatitis C- genotip 1b infection for 5 years. She was treatment peginterferon alfa-2b, 100 μg injected subcutaneously once weekly, and ribavirin, 1000 mg orally daily, for 48 week. She was responded well, with an undetectable viral load and improvement in liver function tests at 24 weeks of treatment. Six months after therapy, she had a relapse. The patient was started on treatment for HCV with 750 mg of telaprevir every 8 h, 100 μg peginterferon every week, and 1000 mg ribavirin every day. After 1 days of treatment, the patient developed a maculopapular rash over abdomen. Despite adequate treatment, rash were progressed. Telaprevir was discontinued. It was changed from telaprevir to boceprevir and continued on peginterferon and ribavirin. She did not develop problems and have any cross-reactive side effects clearly associated with boceprevir. After 24 week the treatment, virological response were observed.

Conclusion: In summary, telaprevir, in combination with PEG/riba cause adverse cutaneous reactions. DAEs can be medically managed without HCV treatment discontinuation.

Topic 12: Hepatitis C

No: 2246

Real life safety data of telaprevir containing hepatitis C virus therapy in Turkey the results of peg base cohort

Abdülkadir Dökmeci[1], Mehmet Demir[2], Engin Altıntaş[3], Ömer Evirgen[4], Mevlüt Başkol[5], Reşat Özaras[6], Aysun Yalçı[7], Şener Barut[8], Hasan Özkan[7], Hatice Rahmet Güner[9], Özlem Altuntaş Aydın[10], Ismail Balık[7], Fatih Özdener[11], Seda Erdoğan[11], Necati Örmeci[1]

Ankara University School of Medicine Gastroenterology Ankara-Turkey[1], Mustafa Kemal University School of Medicine Gastroenterology Hatay-Turkey[2], Mersin University School of Medicine Gastrıenterology Mersin-Turkey[3], Mustafa Kemal University School of Medicine Infectious Diseases Hatay-Turkey[4], Erciyes University School of Medicine Gastroenterology Kayseri-Turkey[5], Istanbul University Cerrahpaşa School of Medicine Infectious Diseases Istanbul-Turkey[6], Ankara University School of Medicine Infectious Diseases Ankara-Turkey[7], Tokat Gaziosmanpaşa University School of Medicine Infectious Diseases Tokat-Turkey[8], Yıldırım Beyazıt University Atatürk Training and Research Hospital Infectious Diseases Ankara-Turkey[9], Haseki Training and Research Hospital Infectious Diseases Istanbul-Turkey[10] Roche Pharmaceuticals Clinical Research Istanbul-Turkey[11]

Pegylated interferon and ribavirin (PR) use associates many side effects. Adding telaprevir increases sustained virological response, however it increases the side effects as well. Real-life side effects may be more than clinical trial settings. In this study we aimed to evaluate the safety data of PR and telaprevir treatment in real life clinical practice of Turkish patients.

The study included naïve and treatment experienced patients with chronic hepatitis C (CHC). A total of 149 CHC patients with genotype 1 were given treatment and included into the cohort. Sixty-five naïve patients received PR therapy (Group PR); 15 naïve patients with advanced fibrosis were given PR plus telaprevir (PR + T) (Group Naïve PRT) and 69 relapser patients were given PR + T (Group Naïve PRT).

Any reported side effects in the groups were 82, 87, and 75 % in PR, naïve PRT and relapser PRT respectively.

In PR group, main side affects were asthenia/fatigue (15 %), decreased appetite (8 %), and pruritus (5 %). Main laboratory abnormalities were leukopenia (51 %), anemia (29 %), and thrombocytopenia (17 %).

In naïve PRT group, main side affects were hemorrhoids (27 %), rash (27 %), pruritus (20 %), and nausea (13 %). Main laboratory abnormalities were anemia (60 %), leukopenia (47 %), thrombocytopenia (40 %) and ALT increase (20 %).

In relapser PRT group, main side affects were asthenia/fatigue (15 %), pruritus (20 %), nausea (13 %), hemorrhoids (10 %), and rash (10 %). Main laboratory abnormalities were anemia (38 %), leukopenia (35 %), and thrombocytopenia (16 %).

Although PR and relaprevir containing treatment associates several side effects, severe adverse effects are not frequent. In PR given group, the side effects are non-specific. In patients given telaprevir-containing therapies, side effects of hemorrhoid and rash are noted in 10-25 %. These rates are much lower than those reported in clinical trials.

Topic 12: Hepatitis C

No: 1895

Risk factors for coronary artery diseases in chronic hepatitis C patients receiving interferon based therapy a population based case control study in Taiwan

Ching-sheng Hsu[1], You-chen Chao[1], Hans Hsienhong Lin[1], Chun-jen Huang[2], Pei-shan Tsai[3]

Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation Department of Internal Medicine New Taipei-Taiwan[1], Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation Department of Anesthesiology New Taipei-Taiwan[2], Taipei Medical University Graduate Institute of Nursing Taipei-Taiwan[3]

Background: Although interferon-based therapy (IBT) may reduce the long-term stroke risk in chronic hepatitis C (CHC) patients, several studies have reported an increased risk of lipoprotein profile rebound and coronary artery diseases (CAD) in CHC patients receiving antiviral therapy.

Aim: To identify the risk factors of CAD in CHC patients receiving IBT.

Methods: We conducted a retrospective case control study that followed up 5,760 subjects with a diagnosis of HCV infection selected

from a 10[SUP]6[/SUP] beneficiaries random sample of the Taiwan National Health Insurance Program up to 4 years. Use of IBT was defined as treatment with interferon alfa, pegylated interferon alfa-2a or pegylated interferon alfa-2b for at least 3 months. Risk factors for newly detected CAD were identified by comparison between IBT-treated CHC patients with and without CAD.
Results: The odds ratio (OR) for newly detected CAD was 2.42 for CHC patients with IBT compared to those without IBT (OR = 2.42, 95 % CI = 1.54–3.81, $P < 0.001$). In multivariate analyses, CHC patients who were older (OR = 7.58, 95 % CI = 1.87–30.72, $P = 0.005$), used antidepressant agents (OR = 3.14, 95 % CI = 1.05–9.41, $P = 0.041$), or cardiovascular drugs (OR = 6.22, 95 % CI = 1.01–38.37, $P = 0.049$) had a higher likelihood of CAD when received IBT.
Conclusions: Older age, use of antidepressant agents, or cardiovascular drugs may increase the CAD risk in CHC patients received IBT.

Topic 12: Hepatitis C

No: 1714

Amino acids variations in the NS region of HCV genome were correlated with IFN plus ribavirin combination therapy

Ye Wang[1], Huiying Rao[1], Lai Wei[1]

Peking University Hepatology Beijing-China[1]

Background: It has been reported that prior response to IFN plus ribavirin combination therapy could impact the treatment outcomes of DAAs containing regimens. However, the relationship between amino acid variations in the NS region of HCV genome and IFN plus ribavirin therapy is not clear. In this study, we perform ultra-deep sequencing to investigate the amino acid variation of the active region of DAAs and its correlation to the response to IFN and ribavirin combination therapy in patients with hepatitis C virus genotype 1b.
Methods: We retrospectively analyzed 21 chronic HCV-1b patients (7 with sustained virological response, 7 relapse, and 7 non-response to therapy) treated with PEG-IFNα 2a plus RBV for 48 weeks. The NS3, NS5A and NS5B of HCV genome sequence were amplified and sequenced by ultra-deep sequencing. Frequencies of amino acid variation between baseline and post-treatment were compared.
Results: Several single amino acid variations which have not been reported were closely associated with treatment outcome (L94 M and I407 V in NS3, A406T/E/G/V in NS5A, V85 M/L in NS5B, $P = 0.03$, $P = 0.003$, $P = 0.002$ and $P = 0.04$ respectively). Changes of frequencies of some amino acid variations which have been confirmed as resistance mutations to DAAs were detected, although with no statistical significant (Y93H in NS5A and A338 V in NS5B, $P = 0.27$ and $P = 0.62$ respectively).
Conclusions: Amino acid variations in the NS region of HCV genome were correlated with treatment outcomes of IFN plus ribavirin therapy. IFN plus Ribavirin therapy could cause changes of frequencies of amino acid variations in the NS region.

Topic 12: Hepatitis C

No: 1555

Effect of demographic and baseline disease characteristics on the efficacy and safety of daclatasvir and asunaprevir combination therapy versus telaprevir + pegylated interferon alfa + ribavirin therapy in Japanese patients with HCV genotype 1b infection

Fumitaka Suzuki[1], Yoshiyuki Suzuki[1], Joji Toyota[2], Yoshiyasu Karino[2], Kazuaki Chayama[3], Yoshiiku Kawakami[3], Shigetoshi Fujiyama[4], Takayoshi Ito[5], Yoshito Itoh[6], Etsuko Tamura[7], Hiroki Ishikawa[7], Misti Linaberry[8], Eric Hughes[8], Hiromitsu Kumada[1]

Toranomon Hospital Department of Hepatology Tokyo-Japan[1], Sapporo-Kosei General-hospital Sapporo-Japan[2], Hiroshima University Hiroshima-Japan[3], Kumamoto Shinto General Hospital Kumamoto-Japan[4], Showa University Koto Toyosu Hospital Tokyo-Japan[5], Kyoto Prefectural University of Medicine Kyoto-Japan[6], Bristol-myers Kk Tokyo-Japan[7], Bristol-myers Squibb Research & Development Princeton-United States[8]

Background and aim: Patient characteristics can influence efficacy and safety outcomes with peginterferon/ribavirin (pegIFN/RBV) based regimens. A phase 3 study of the all-oral DCV + ASV combination therapy versus TVR + pegIFN-alfa/RBV demonstrated an overall sustained virologic response (SVR) rate of 89.1 % (non-inferior) and 62.2 % respectively in Japanese patients with HCV genotype 1b infection. The influence of baseline disease characteristics and demographic variables on outcomes from this study was investigated.
Methods: Enrolled patients were treatment-naïve Japanese patients with chronic HCV genotype 1b infection. Patients received DCV 60 mg once daily plus ASV 100 mg twice daily (BID) for 24 weeks, or TVR 3 × 250 mg three times a day for 12 weeks plus pegIFN-alfa plus RBV (24 weeks). For this analysis, SVR at post-treatment week 12 (SVR12) and safety were assessed according to patient demographic and baseline disease characteristics.
Results: Subgroup status including age, gender, BMI, baseline HCV RNA, fibrosis and IL28B genotype did not affect SVR12 response rates with DCV + ASV therapy. SVR12 rates were generally greater across baseline factors in the DCV + ASV therapy arm compared to the TVR arm; particularly for elderly patients (≥ 65 years), non-CC IL28B genotype and despite worsening fibrosis status. DCV + ASV efficacy was unaffected by advanced fibrosis - which decreased TVR therapy efficacy (Table). No clinically meaningful differences in safety outcomes according to baseline subgroup were observed in either arm.
Conclusion: The all-oral combination of DCV + ASV achieved high rates of SVR12 and improved safety outcomes independent of baseline factors compared to TVR + pegIFN-alfa/RBV therapy in Japanese patients with HCV genotype 1b infection.

Topic 12: Hepatitis C

No: 1546

Impact of body mass index (BMI) on svr during treatment of patients with chronic hepatitis C (CHC) with pegylated interferon and ribavirin

Anila Kristo[1], Jonila Cela[2], Nikollaq Leka[3], Eriseld Rapi[1], Jovan Basho[1]

Uhc "mother Teresa" Gastroenterohepatology Tirana-Albania[1], Univerity "a. Xhuvani' Faculty of Medical Science Elbasan-Albania[2], University of Medicine Morfology Tirane-Albania[3]

Introduction: Many host and viral factors at baseline influence response to treatment of CHC patients with standard scheme.
Aim: To evaluate the impact of BMI on HCV standard treatment independently from age and genotype.
Methods: We evaluated 86 patients during period 2008-2012 diagnosed with CHC. All the patients were treated with Peginterferon alfa-2a and Ribavirine (according to body weight and genotype). The primary end point was SVR defined as undetectable HCVRNA level

24 weeks after the end of treatment. We classified the patient in two groups with BMI < 27 (54 patients) and BMI > 27 (30 patients) and then evaluated the rate of SVR and non-SVR in both groups. The percentage of genotypes was; 70 % had genotypes 1 and 4 and 30 % of patients had genotypes 2 and 3. The median age in both groups was similar 42.7 yrs/old in the group with BMI < 27 vs 43. 3yrs/old in the group with BMI > 27, without significant differences between the group (P > 0.05). Statistical analyses were done with t test. $P < 0.05$ was considered statistically significant.
Results: From 86 patients, 84 finished the treatment. Regardless the genotype 58.3 % of patients had SVR and 40.7 % non-SVR. In the group with BMI < 27, 68.5 % of patients had SVR and 31.5 % had non-SVR ($P < 0.001$). In the group with BMI > 27, 60 % of patients had Non-SVR and 40 % SVR ($P = 0.04$).
Conclusion: BMI < 27 is an independent factor on SVR regardless age and genotype. It is very important to optimize BMI before treatment of CHC patients.

Topic 12: Hepatitis C

No: 2036

Pegylated interferon related thyroidal dysfunction in chronic hepatitis C patients

Drnidasajid Sajid[1], Drkarimkammeruddin Kammerudin[1], Drmuhammadimran Imran[1]

Baqaimedicaluniversity Medicine Karachi-Pakistan[1]

Objectives: To assess Pegylated interferon based therapy related thyroidal dysfunction in Chronic hepatitis C patients and to Compare it with those who are hepatitis C Sero positive but have not receive interferon based treatment.
Methodology: It is a Case Control Study in which, 203 patients of Chronic, compensated hepatitis C (130 females, 73 males) were included from Baqai University Hospital Karachi Liver Clinic (b/w Jan 2010–Jun 2014).The participants were checked for thyroid dysfunction at the onset, 17 patients were found to have thyroidal dysfunction in the beginning and were excluded from the total 203 cases, then out of the remaining 186 cases, 101 patients (who were not having T.D initially) opted treatment with pegylated interferon/ribavarin (i.e. Treated group) and the rest (i.e. 85 cases) were taken as Control group.
Results: Thyroid dysfunction was identified in 7 patients giving a frequency of 6.9 %. Out of these 7 patients only one patient is male while the rest are females. The mean age of the patients with thyroid dysfunction was 39.2 ± 7.13 years. Amongst the patients identified with the thyroid dysfunctions, 2 (28.5 %) had Overt hypothyroidism and 5 (71.4 %) had Sub-clinical hypothyroidism. The treatment with combination therapy was significant for development of thyroid dysfunction in patients with hepatitis C ($P = 0.013$) as Compared to Control group in which 85 patients of Chronic hepatitis C who have not developed (T.D) during the Study period.
Conclusion: Thyroidal dysfunction after pegylated interferon/ribavarin treatment in Chronic hepatitis C is Statistically significant with Sub-clinical hypothyroidism is the predominant type in our Study population.

Topic 12: Hepatitis C

No: 1548

Impact of body mass index (bmi) on svr during treatment of patients with chronic hepatitis C (chc) with pegylated interferon and ribavirin

Anila Kristo[1], Jonila Cela[2], Nikollaq Leka[3], Eriseld Rapi[1], Jovan Basho[1]

Uhc "mother Teresa" Service of Gastrohepatology Tirana-Albania[1], University of Medical Science Faculty of Medical Science Elbasan-Albania[2], University of Medicine Department of Morfology Tirane-Albania[3]

Introduction: Many host and viral factors at baseline influence response to treatment of CHC patients with standard scheme.
Aim: To evaluate the impact of BMI on HCV standard treatment independently from age and genotype.
Methods: We evaluated 86 patients during period 2008-2012 diagnosed with CHC. All the patients were treated with Peginterferon alfa-2a and Ribavirine (according to body weight and genotype). The primary end point was SVR defined as undetectable HCVRNA level 24 weeks after the end of treatment. We classified the patient in two groups with BMI < 27 (54 patients) and BMI > 27(30 patients) and then evaluated the rate of SVR and non-SVR in both groups. The percentage of genotypes was; 70 % had genotypes 1 and 4 and 30 % of patients had genotypes 2 and 3. The median age in both groups was similar 42.7ys/old in the group with BMI < 27 vs 43.3ys/old in the group with BMI > 27, without significant differences between the group (P > 0.05). Statistical analyses were done with t test. $P < 0.05$ was considered statistically significant.
Results: From 86 patients, 84 finished the treatment. Regardless the genotype 58.3 % of patients had SVR and 40.7 % non-SVR. In the group with BMI < 27, 68.5 % of patients had SVR and 31.5 % had non-SVR ($P < 0.001$). In the group with BMI > 27, 60 % of patients had Non-SVR and 40 % SVR ($P = 0.04$).
Conclusion: BMI < 27 is an independent factor on SVR regardless age and genotype. It is very important to optimize BMI before treatment of CHC patients.

Topic 12: Hepatitis C

No: 1520

Evaluation of the efficacy and long term post treatment outcomes to interferon free dual oral therapy with daclatasvir and asunaprevir

Hitomi Sezaki[1], Fumitaka Suzuki[1], Yusuke Kawamura[1], Tetsuya Hosaka[1], Norio Akuta[1], Masahiro Kobayashi[1], Yoshiyuki Suzuki[1], Satoshi Saitoh[1], Yasuji Arase[1], Kenji Ikeda[1], Hiromitsu Kumada[1]

Toranomon Hospital Hepatology Tokyo-Japan[1]

Aim: Phase 2 and 3 clinical trials have demonstrated high SVR rates for genotype 1b (GT1b) subjects treated with daclatasvir (DCV) and asunaprevir (ASV) in Japan. The aims of this study were to evaluate the long-term effects to 24-week DCV/ASV therapy in Japanese patients.
Methods: 63 GT1b patients received dual oral treatment for 24 week in our hospital. We evaluated SVR rates at 24 weeks post treatment (SVR24) and changes of albumin, ALT, platelet counts (plt) and AFP levels up to 2 years after the completion of treatment.
Results: 23 males and 40 females were treated, median age (range) was 65 (31-76) years, and 14 % (9/63) had cirrhosis. Baseline parameters (median) were ALT 44 IU/mL, albumin 3.8 g/dL, plt 16.4 × 10[SUP]4[/SUP]/μL, AFP 6 μg/L. Nine patients discontinued this dual therapy, 3 null responders of them needed the addition of peg-interferon/ribavirin to the dual therapy by protocol-defined rules. Overall, 77.8 % of patients achieved SVR24. SVR24 rates with or without NS5A-Y93 resistance-associated variants (RAVs) at baseline

were 12.5 % (1/8) and 87.2 % (48/55), respectively ($P < 0.001$). All of 13 non-SVR patients had Y93 RAVs at virologic failure. At 2 years after the completion of treatment, albumin, ALT, plt and AFP levels significantly improved in comparison with them of baseline in SVR patients and ALT and AFP levels improved in non-SVR patients.
Conclusions: Dual therapy with DCV/ASV achieved high SVR rates and favorable post-treatment outcomes. The presence of Y93 RAVs after virologic failure did not exacerbate their liver function.

Topic 12: Hepatitis C

No: 1272

The comparative efficacy and safety of daclatasvir (DCV) plus asunaprevir (ASV) vs simeprevir (SMV) + pegylated interferon alfa + ribavirin (PR) in previously treated japanese patients chronically infected with hepatitis C virus (HCV) results from a bayesian meta analysis

Kristine R. Broglio[1], Melanie Quintana[1], Anupama Kalsekar[2], Yong Yuan[2], Scott M. Berry[1]

Berry Consultants Llc Research Austin, Tx-United States[1], Bristol Myers Squibb Co Wwheor Princeton, Nj-United States[2]

Purpose: We aimed to determine the comparative efficacy and safety of DCV + ASV and SMV + PR among patients with genotype 1b who were previous nonresponders to PR.
Methods: A systematic review of HCV clinical trials (published 2000-2012) and SMV regulatory documents from US and Japan was conducted. We modeled the endpoints of sustained virologic response 24 weeks following the end of treatment (SVR24), rash, and anemia. We used Bayesian hierarchical models, which included terms for treatment history, HCV genotype, HIV co-infection, country (Japan versus outside Japan), and an interaction term for treatment history and current therapy.
Results: 67 studies were included in the meta-analysis. We additionally include the completed phase III single arm trial of DCV + ASV. The model estimated mean SVR24 rates for DCV + ASV and SMV + PR for previous nonresponder Japanese genotype 1b patients were 79.4 % and 54.3 % respectively. The mean difference in SVR24 rates between the two therapies is 25.2 % (95 % CI = 2.5 %, 42.7 %) and the probability that DCV + ASV is superior is 98.4 %. The model estimated rates for rash are 5.3 % and 33 %, and for anemia 1.6 % and 50.8 %, respectively, for DCV + ASV and SMV + PR, among previously treated Japanese genotype 1 patients. For both safety endpoints, the probability that DCV + ASV is superior is > 99 %. Studies conducted in Japan are estimated to have significantly higher rates of both rash and anemia than outside Japan.
Conclusions: This meta-analysis estimates a high probability that DCV + ASV has superior efficacy and safety than SMV + PR among previously treated patients

Topic 12: Hepatitis C

No: 1907

The significance of change of the mean corpuscular volume (MCV) during treatment of chronic hepatitis C

Eun Young Cho[1], Haak Cheoul Kim[1], Young Bum Cho[1], Min Soo Joo[1], In Hee Kim[2]

College of Medicine, Wonkwang University Department of Internal Medicine Iksan-Korea, South[1], College of Medicine, Chonbuk University Department of Internal Medicine Jeonju-Korea, South[2]

Background/aims: We confirmed that the mean corpuscular volume(MCV) increase was not unusual during the HCV standard treatment and tried to find out the meaning of MCV increase during the HCV treatment.
Methods: The subjects of the study were 178 outpatients who visited University Hospitals in Jeollabuk-do Province because of chronic C viral hepatitis treatment from 2005 to 2010. The medical records of the subjects were analyzed.
Results: The subjects were 99 males and 79 females by gender, and 70 Genotype 1 and 108 Genotype 2 by Genotype. The number of subjects with baseline MCV $\geq$ 100 was 16(9 %), and that with MCV < 100 was 162(91 %), and the group with MCV $\geq$ 100 showed higher APRI(2.73 $\pm$ 1.81 vs. 1.71 $\pm$ 2.86, $P = 0.054$) and lower platelet counts(104.50 $\pm$ 33.19 vs. 163.90 $\pm$ 104.50, $P = 0.000$). The mean MCV values tended to increase during treatment and then decreased after treatment(93.02 $\pm$ 5.36, 96.40 $\pm$ 7.93, 97.11 $\pm$ 6.85, 93.87 $\pm$ 6.54, 92.96 $\pm$ 5.29 in week 0, week 12[$P = 0.000$], week 24[$P = 0.000$], week 48[$P = 0.023$], week 72[$P = 0.225$],respectively). Factors related to sustained virological response(SVR) were younger in age, lower values of HCV RNA, genotype 2, rapid virological response(RVR), and early virological response(EVR). Taken together, in genotype 1, SVR was higher in those whose MCV in week 12 increased by less than 5 than in those with an increase of 5 or more (81.5 % vs. 40.9 %, $P = 0.004$), and in genotype 2, those with baseline MCV < 100 showed higher SVR than those with MCV $\geq$ 100(98.3 vs. 66.7 %, $P = 0.020$).
Conclusions: Megaloblastic change is an indicator reflecting the liver chronicity,and the increase of MCV during treatment has potential as an factor forecasting treatment response.

Topic 12: Hepatitis C

No: 1553

Life quality in patients with hepatitis C and presentation of a structural model

Mohammad Hossein Somi[1], Morteza Ghojazadeh[2], Mehran Rahimi[3], Mohammad Khalafi[3]

Liver and Gastrointestinal Research Center Internal Medicine Tabriz-Iran[1], Liver and Gastrointestinal Research Center Physiology Tabriz-Iran[2], Liver and Gastrointestinal Research Center Liver and Gastrointestinal Research Center Tabriz-Iran[3]

Aim: Hepatitis C is an asymptomatic disease. The quality of life is a major concern in these patients. In this research, we compared quality of life in hepatitis C and healthy people then finally a structural model presented for it.
Methods: This is an analytical study in which a total of 45 patients with confirmed hepatitis C and 90 healthy accompaniers of them were included. A questionnaire composed of Persian translation of SF-36 items and Sweden QOL was used for measuring the HRQOL. Then, data were analyzed using SPSS18 and LISREAL 8.80.
Results: Total adjusted score of HRQOL was 59.18 $\pm$ 4.55 and 73.75 $\pm$ 3.18 in patients versus control group ($P < 0.001$). Age and ALT were 0.22 and -0.10 and had a path coefficient respectively with physical health. Age and co-disease were 0.32 and -0.29 and had a path coefficient respectively with psychological health. Physical health as a mediator accounted for 95 % of the variance and psychological health as a mediator accounted for 81 % of the variance in quality of life.

Conclusion: This study showed that hepatitis C is responsible for great alterations in HRQOL. Every effort is to be made to provide structural models in prediction of quality of life that would play a significant role in resolving of problems.

Topic 12: Hepatitis C

No: 2086

Changing of hepatitis C genotypes in Istanbul

Fatma Ekşi Polat[1], Kamuran Türker[1], Nejat Sebzeci[1], Betül Taş[2], Bilge Özdemir[3]

Bağcılar Training and Research Hospital Infectious Diseases Istanbul-Turkey[1], Bağcılar Training and Research Hospital Dermatology Istanbul-Turkey[2], Bağcılar Training and Research Hospital Microbiology Istanbul-Turkey[3]

Objective: Hepatitis C is divided into six distinct genotypes throughout the world with multiple subtypes in each genotype class. A genotype is a classification of a virus based on the genetic material in the RNA (Ribonucleic acid) strands of the virus. Genotype 1 is the most common type of Hepatitis C genotype in the Turkey and the most difficult to treat. For physicians, knowing the genotype of Hepatitis C is helpful in making a therapeutic recommendation.. Individuals with genotypes 2 and 3 are almost three times more likely than individuals with genotype 1 to respond to therapy with alpha interferon or the combination of alpha interferon and ribavirin. Furthermore, when using combination therapy, the recommended duration of treatment depends on the genotype. For this reason, testing for Hepatitis C genotype is often clinically helpful.
Genotype 1b is mostly found in Europe and Asia and genotype 3a is highly prevalent here in Australia (40 % of cases) and South Asia.
Methods: We enrolled 67 CHC patients that were consecutively admitted to our outpatient hospital from January 2009 to November 2014.
Results: 67 CHC patients included in the study (37 males and 30 females, 55.2 % and 44.8 %) with mean age of 55 years (range 20 - 81). There were big group of patients 47 (70.1 %) had genotype 1. But 16 patients(23.9 %) had genotype 3.
Conclusion: We thought that genotypes of HCV will be change in the near future in İstanbul.

Topic 12: Hepatitis C

No: 1900

First known case of boceprevir induced severe hypokalaemia

Hui Yi, Sara Cheo[1], Wei Lyn Yang[1]

Tan Tock Seng Hospital Department of Gastroenterology & Hepatology Singapore-Singapore[1]

Boceprevir is a first generation NS3/4A protease inhibitor shown to give a higher sustained virologic response in patients with HCV genotype 1 infection. We report on the first known case of boceprevir causing severe hypokalaemia. A 35 year old Chinese Female with (genotype 1a) chronic hepatitis C-related cirrhosis, who had failed to achieve an early virologic response (EVR) with ribavirin and peginterferon alfa-2b, was started on boceprevir, ribavirin and peginterferon in January 2012. At week 31 of treatment, she complained of reduced appetite and some upper respiratory tract symptoms. Blood investigations were done and revealed her serum potassium was 2.5 mmol/L. Her urinary spot potassium was high at 85.3 mmol/L. Other investigations ruled out Fanconi's syndrome or renal tubular acidosis. Our Nephrologist's impression was that of a drug induced tubulopathy. The patient opted to complete her hepatitis C treatment with oral potassium replacement. Her serum potassium levels gradually normalized after boceprevir was stopped and she was successfully weaned off potassium replacement thereafter. A literature search failed to find any previous reported cases of boceprevir, peginterferon alfa-2b or ribavirin causing hypokalaemia. Our patient was not on any other medications at that time, and she had twice previously taken ribavirin and peginterferon alfa-2b for a-12 week period without adverse reaction. The likelihood of boceprevir being the cause of her hypokalaemia is further supported by her serum potassium being normal before boceprevir was started, and then returning to normal after boceprevir was stopped. As such, we believe this is the first report of boceprevir induced hypokalaemia.

Topic 12: Hepatitis C

No: 1549

Elderly and cirrhotic patients without baseline ns5a polymorphisms in HCV genotype 1b have very high sustained virologic responses to daclatasvir plus asunaprevir

Fiona Mcphee[1], Yoshiyuki Suzuki[2], Joji Toyota[3], Yoshiyuki Karino[3], Kazuaki Chayama[4], Yoshiiku Kawakami[4], Hiroki Ishikawa[5], Rafia Bhore[6], Nannan Zhou[6], Dennis Hernandez[6], Patricia Mendez[6], Hiromitsu Kumada[2]

Bms Discovery Virology Wallingford-United States[1], Toranomon Hospital Tokyo-Japan[2], Sapporo Kosei General Hospital Sapporo-Japan[3], Hiroshima University Hiroshima-Japan[4], Bristol-Myers Kk Tokyo-Japan[5], Bristol-Myers Squibb Research and Development Princeton-United States[6]

Aim: The combination of daclatasvir (DCV) plus asunaprevir (ASV) is approved in Japan for treatment of HCV genotype (GT-)1b. Older age and cirrhosis are relatively common among Asian patients. Resistance-associated NS5A polymorphisms (RAPs) to DCV (e.g. NS5A-Y93 and -L31 polymorphisms) have been shown to impact response rates in HCV GT-1b patients treated with DCV + ASV. The effect of RAPs on post-treatment Week-12 sustained virologic response (SVR12) to DCV + ASV was explored in elderly and cirrhotic Asian patients.
Methods: Data were pooled from 5 clinical studies of DCV (60 mg daily) + ASV (200 mg tablet or 100 mg capsule, twice daily) for 24 weeks in GT-1b infected, interferon/ribavirin-naïve and -experienced patients from Asia (Korea, Taiwan, Japan), North/South America, Europe and Australia. SVR12 in patients with versus without baseline Y93H and/or L31 polymorphisms was compared for patients < 65 years and ≥ 65 years old, with and without cirrhosis.
Results: SVR12 and population baseline NS5A sequences were available for 494 Asian (75 % Japanese) and 485 non-Asian patients. NS5A-Y93H and/or -L31 polymorphisms were observed pretreatment in 17.0 % of Asians and 11.7 % of non-Asians. SVR12 rates are shown in the Figure. Responses were lower among those with baseline NS5A-Y93 or –L31 RAPs. By contrast, SVR12 in patients without these RAPs was very high (91-100 %), irrespective of age or cirrhosis, and similar between Asians and non-Asians.
Conclusion: In this pooled analysis, more than 90 % of GT-1b-infected Asian patients without baseline NS5A-Y93 or –L31 polymorphisms achieved a sustained virologic response to DCV + ASV, regardless of age or cirrhosis status.

Topic 12: Hepatitis C

No: 1389

Fat receptor cd36 polymorphism (rs1761667) is associated with the severity of liver damage and liver cirrhosis among HCV infected patients from west Mexico

Omar Lopez-ramos[1], Sonia Roman[1], Karina Gonzalez-Aldaco[1], Erika Martinez-Lopez[1], Rafael Torres-Valadez[1], Maria Elena Trujillo-Trujillo[1], Arturo Panduro[1]

University of Guadalajara Molecular Biology In Medicine Guadalajara-Mexico[1]

Genetic factors and lipid modulation are involved in HCV infection and liver damage. The fat receptor CD36 regulates lipid metabolism and its deficiency is associated to defective lipoprotein secretion, hepatic steatosis and metabolic syndrome. A common single nucleotide polymorphism -31118G > A (rs1761667) in the promoter region of the CD36 gene which reduces its tissue expression has been identified. Aim. To determine the distribution of the CD36 gene polymorphism in a population from West Mexico and analyze its association with liver damage among HCV-infected patients. Methods. In a cross-sectional study, a total of 702 unrelated individuals (native and mestizo) were analyzed for CD36 genotypes (A/A, A/G and G/G) by real-time PCR. For the association of CD36 with liver damage, 235 patients with positive serological diagnosis for chronic HCV infection were included. Lipid biochemical tests and transitional elastography were determined. Results. The distribution of genotypes was concordant with the Hardy–Weinberg Equilibrium in all study groups. The A-allele of CD36 was prevalent in 59.6 % (n = 418) of the total cases and in 73.7 % of native Huicholes (n = 73). The A/A genotype was associated with the severity of liver damage and liver cirrhosis than with the other genotypes (OR = 2.50, 95 % CI 1.04-5.97, $P = 0.03$ and OR = 3.33, 95 % CI 1.20-9.22, $P = 0.01$, respectively). Conclusions. The A-allele of CD36 gene polymorphism was predominant in Mexican native and mestizo populations. The A/A genotype was associated with the severity of liver damage and liver cirrhosis among HCV-infected patients. Thus, CD36 genotype could be a useful genetic marker for liver damage in HCV infection.

Topic 12: Hepatitis C

No: 1641

The relationship between neutrophil to lymphocyte ratio (NLR) and fibrosis level in chronic HCV patients

Ergenekon Karagoz[1], Alpaslan Tanoglu[2], Asim Ulcay[1], Vedat Turhan[1], Muammer Kara[2], Hakan Erdem[1], Yusuf Yazgan[2]

Gata Haydarpasa Training Hospital Infectious Diseases and Clinical Microbiology Istanbul-Turkey[1], Gata Haydarpasa Training Hospital Gastroenterology Istanbul-Turkey[2]

Introduction and objective: The neutrophil to lymphocyte ratio (NLR) is a widely utilized, inexpensive, easily available laboratory marker which is used to predict prognosis of various inflammatory and neoplastic diseases. It is also considered as a prognostic predictor of hepatocellular carcinoma. To date, no study has examined the relationship between NLR and liver fibrosis score in patients with hepatitis C in medical literature. In this study, we aimed to determine the relationship between neutrophil to lymphocyte ratio (NLR) and fibrosis level in chronic HCV patients.

Material-method: This is a retrospective case–control study evaluating 84 naïve chronic HCV-infected cases followed-up in GATA Haydarpasa Training Hospital. Patients were divided into two groups with fibrosis scores of 0–2(Group 1) and 3–6(Group 2)(according to ISHAC) score and we investigated whether NLR has a relationship with the severity of liver fibrosis.

Result: Of the 84 cases, 67 (79.8 %) were male, 17(20.2 %) were female. Fibrosis scores of 27 cases (32.1 %) were $\geq$ 3 while 57 cases had fibrosis scores $<$ 3 (67.9 %).There was a significant correlation existed between fibrosis score and NLR. NLR level was 1,51 $\pm$ 0.63 in patients with fibrosis score 0-2. This was 1.91 $\pm$ 0.91 in patients with fibrosis score 3-6 ($P < 0.05$).

Conclusion: To the best of our knowledge, it was the first study assessing the association between NLR and fibrosis score in patients with chronic hepatitis C. NLR seems to be a useful predictor for severity of liver fibrosis in this patient group. Further studies are required to show the inflammatory status of HCV-infected patients.

Topic 12: Hepatitis C

No: 2164

Association between SNP IL 28b and sustained virological response and its relation with expression of interferon lambda and interferon lambda receptor in liver tissues of chronic hepatitis C patients treated with pegylated interferon α2 and ribavirin

Andri Sanityoso[1], Rino A. Gani[1], Irsan Hasan[1], C. Rinaldi A. Lesmana[1], Juferdy Kurniawan[1], Ening Krisnuhoni[2]

Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo Hospital Department of Internal Medicine, Hepatobiliary Division Jakarta-Indonesia[1], Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo Hospital Department of Anatomic Pathology Jakarta-[2]

Background: SNP IL-28B played an important role in achieving sustained virological response (SVR) among different ethnics in chronic hepatitis C patients and considered potential in predicting treatment response of Pegylated interferon/ribavirin (Peg-IFN/RBV) combination and spontaneous healing in acute hepatitis.

Aim: Understanding association between SNP IL-28B and SVR in chronic hepatitis C treatment and expression of IFN-λ and IFN-λ receptor in liver tissues to evaluate clinical importance of SNP IL-28B examination in treatment through SVR prediction model.

Methods: This study divided into two parts. First, we conducted cross-sectional study in chronic hepatitis C patients who completed Peg-IFN/RBV therapy. The second part was case control study on patients underwent liver biopsy and immunohistochemical staining.

Results: Higher SVR was significantly found in CC allele of SNP IL-28B compared to non CC allele ($P = 0.015$). Higher expression of IFN-λ was found in CC allele compared to non CC allele ($P = 0.018$). On the other hand, there is no significant difference between SVR and expression of IFN-λ ($P = 0.237$) and IFN-λ receptor ($P = 0.237$). We formulated predictor for SVR probability into $P = 1/(1 + e\text{-}y)$; e = 2.7, y = −2.498 + 2.652 (SNP IL-28B) + 2.029 (thrombocytes) for pretreatment and y = −0.223 + 2.621 (RVR) for on-treatment predictor.

Conclusion: SNP IL-28B was important pretreatment predictor in genotype 1 chronic hepatitis C treated with dual therapy. Major allele of IL-28B expressed more IFN-λ and its receptor in response to HCV. Further evaluation study was required to find other possible factors affecting SVR achievement.

Topic 12: Hepatitis C

No: 1106

Treatment efficacy of pegylated interferon plus ribavirin in patients infected with genotype 6 hepatitis C virus in Korea

Sang Hoon Park[1], Myung Seok Lee[1], Jin Woo Lee[2], June Sung Lee[3], Young Seok Kim[4], Young Seok Lim[5], Sook-hyang Jeong[6], Joo Hyun Shon[7]

Hallym University College of Medicine Department of Internal Medicine Seoul-Korea, South[1], Inha University School of Medicine Department of Internal Medicine Incheon-Korea, South[2], Inje University College of Medicine Department of Internal Medicine Goyang-Korea, South[3], Soonchunhyang University College of Medicine Department of Internal Medicine Bucheon-Korea, South[4], Ulsan University College of Medicine Department of Internal Medicine Seoul-Korea, South[5], Seoul National University College of Medicine Department of Internal Medicine Seongnam-Korea, South[6], Hanyang University College of Medicine Department of Internal Medicine Guri-Korea, South[7]

Background and aims: Because of the limited geographic distribution of hepatitis C virus (HCV) genotype 6, there are insufficient data on its response to available treatment. This study was aimed to evaluate the efficacy and safety of peginterferon plus ribavirin for genotype 6 chronic hepatitis C (CHC) patients in Korea.
Methods: Data of patients with genotype 6 CHC who were treated with peginterferon and ribavirin at one regional hospital and 8 Medical College affiliated hospitals in South Korea were reviewed.
Results: There were 22 patients with genotype 6 (age 35-57 years, 41 % male). Among them, data of 10 patients were from the K(G)yeonggi-Incheon Peginterferon Alpha and Ribavirin Effect in CHC Treatment (KIPECT) study group. Subtypes were 6, 6a, 6a/c, and 6c in 1, 3, 1, and 17 patients, respectively. Baseline median ALT level was 82 (19-236) IU/mL, and HCV RNA level was 1,390,000 (185,040-28,844,529) IU/mL. As follow-up loss occurred in 4 patients, a total of 15 patients conformed to the treatment protocol. Among 15 patients who followed the protocol, 8 patients attained sustained virologic response (SVR), 4 patients relapsed, 2 showed null-response, and 1 discontinued treatment with no early virologic response.
Conclusions: Although there existed inconsistent regimens in treatment for patients with genotype 6 CHC, the SVR rate was observed as 53.3 % (8/15). Considering that there has been no consensus in this issue, future studies should seek to clarify issues regarding prevalence, predictors for treatment response and the impact of ethnic and genotypic factors to treatment response in genotype 6 CHC patients.

Topic 12: Hepatitis C

No: 2048

Expression analysis of proteins inducing interferon in chronic hepatitis C patients

Phani Kumar Gumma[1], Soumya Jyoti Choudhury[1], Vijay Kumar Karra[1], Premashis Kar[1]

Maulana Azad Medical College Medicine New Delhi-India[1]

Background & aim: In virus-infected cells, pattern recognition receptors (PRRs) recruits their specific adaptor molecules, mitochondrial antiviral signaling protein (MAVS) and TIR-domain-containing adapter inducing interferon-β (TRIF) which through TRAF6 induce the interferon. This study is designed to quantify TLR3, MAVS, TRIF and TRAF6 proteins from liver biopsies of chronic hepatitis C (CHC) cases.
Materials and methods: Liver tissue from 46 CHC and 12 healthy individuals were studied for the expression levels of TLR3, MAVS, TRIF and TRAF6 proteins using Semi-quantitative Digital Image analysis, after specific detection of these proteins by western blotting followed by immune-detection based chemi-luminance.
Results: CHC group comprised of 39 (84.78 %) treatment naïve patients and 7 (15.22 %) treated patients. Out of these 7 patients, 4 (57.14 %) were non-responders. The TRAF6 expression was raised in CHC (0.234 ± 0.027) compared to healthy (0.212 ± 0.025). TRIF, TLR3 and MAVS were decreased (0.114 ± 0.020, 0.108 ± 0.015 and 0.067 ± 0.012) in CHC compared to healthy individuals (0.142 ± 0.018, 0.182 ± 0.012 and 0.082 ± 0.011). TRAF6 in treated patients (0.244 ± 0.018) expressed less than treatment naïve (0.248 ± 0.017). TRIF, TLR3 and MAVS in treated patients (0.096 ± 0.003, 0.093 ± 0.004 and 0.057 ± 0.009) were significantly less than treatment naïve (0.124 ± 0.018, 0.117 ± 0.011 and 0.073 ± 0.010). TRIF and TLR3 levels were significantly less in non-responders compared to responders (0.095 ± 0.003, 0.092 ± 0.005 and 0.097 ± 0.004, 0.094 ± 0.004). TRAF6 expression was slightly reduced in responders (0.235 ± 0.018) compared to non-responder (0.246 ± 0.021), whereas MAVS expression was raised (0.070 ± 0.003 and 0.053 ± 0.004).
Conclusion: HCV down regulates expression of MAVS and TRIF IN CHC.

Topic 12: Hepatitis C

No: 1124

Retreatment of chronic hepatitis C infection with telaprevir preliminary results in Turkey

Bilgehan Aygen[1], Orhan Yildiz[1], Sila Akhan[2], Mustafa Kemal Celen[3], Onur Ural[4], Suda Tekin Koruk[5], Sukran Kose[6], Fatime Korkmaz[7], Ziya Kuruuzum[8], Nazan Tuna[9], Serpil Taheri[10], Murat Sayan[11], Nazlim Aktug Demir[4], Sua Sumer[4], Elif Sargin Altinok[2]

Erciyes University Infectious Diseases and Clinical Microbiology Kayseri-Turkey[1], Kocaeli University Infectious Diseases and Clinical Microbiology Kocaeli-Turkey[2], Dicle University Infectious Diseases and Clinical Microbiology Diyarbakir-Turkey[3], Selcuk University Infectious Diseases and Clinical Microbiology Konya-Turkey[4], Koc University Infectious Diseases and Clinical Microbiology Istanbul-Turkey[5], Tepecik Training and Research Hospital of Ministry of Health Infectious Diseases and Clinical Microbiology Izmir-Turkey[6], Konya Training and Research Hospital of Ministry of Health Infectious Diseases and Clinical Microbiology Konya-Turkey[7], Dokuz Eylül University Infectious Diseases and Clinical Microbiology Izmir-Turkey[8], Sakarya University Infectious Diseases and Clinical Microbiology Sakarya-Turkey[9], Erciyes University Medical Biology Kayseri-Turkey[10] Kocaeli University Clinical Laboratory, Pcr Unit Kocaeli-Turkey[11]

Background: The use of peginterferon alpha and ribavirin (PegIFN/RBV) in the retreatment of chronic hepatitis C virus infection without sustained virological response to prior PegIFN/RBV treatment has resulted in low success rates.
Aim: To investigate the efficacy and safety of telaprevir (TVR) in combination with PegIFN/RBV in patients infected with HCV genotype 1 and 4 who were previously treated with PegIFN/RBV and failed to achieve SVR. The study was a multi-center, retrospective, cross-sectional study.

Methods: The study included 111 patients: 80 relapsers, 25 null responders, and six partial responders to PegIFN/RBV treatment. The patients were given TVR/PegIFN/RBV for 12 weeks, followed by a 12-week PegIFN/RBV treatment; virological response results were assessed at weeks 4, 12, and 24. Side effects of the combination therapy and rates of treatment discontinuation were investigated.
Results: The mean age of the patients was 56.02 ± 9.96 years and 45.9 % were male. Ninety-one percent of the patients were infected with viral genotype 1, and 69.6 % with interleukin (IL) 28B genotype CT and 20.2 % were cirrhotic. Rapid virological response rate was 92 % in relapsers, 63.6 % in null responders, and 60 % in partial responders ($P = 0.002$). Early virological response rates in those groups were 100, 70, and 100 %, respectively ($P < 0.001$). Virological response at 24th week of treatment was found to be the highest in relapsers (97.3 %); it was 70 % in null responders and 80 % in partial responders ($P = 0.001$). All treatments were discontinued due to side effects in 9.9 % of the patients.
Conclusion: High virological response rates were obtained with TVR/PegIFN/RBV treatment.

Topic 12: Hepatitis C

No: 1373

Combination of pegylated interferon and ribavirin as a prophylactic treatment after liver transplantation for hepatitis C virus single center experience with high virological response

Young Mi Hong[1], Ki Tae Yoon[1], Mong Cho[1], Dae Hwan Kang[1], Hyung Wook Kim[1], Cheol Woong Choi[1], Su Bum Park[1], Jeong Heo[2], Hyun Young Woo[2], Won Lim[2]

Pusan National University Yangsan Hospital Internal Medicine Yangsan-si-Korea, South[1], Pusan National University Hospital Internal Medicine Busan-Korea, South[2]

Background/aims: Pegylated interferon with ribavirin is the most effective therapy for chronic hepatitis C virus (HCV) but its timing, utility and effectiveness after liver transplantation has been difficult to assess. We aimed to evaluate the safety and efficacy of pegylated-interferon and ribavirin as a prophylactic treatment after LT for hepatitis C virus.
Methods: From January 2010 to June 2014, twenty consecutive liver transplantations were performed in 20 HCV-related cirrhotic patients. Among recipients, seven patients with detectable HCV RNA level were started on pegylated interferon plus ribavirin 2- 7 months after LT. Biochemical and virological examinations was analyzed 1, 3, 6, 12, 18 months after initiation of treatment.
Results: Among seven patients, four patients were genotype 1b and three patients were genotype 2. Six patients were finished the treatment and one patient is ongoing treatment (20 weeks). Rapid virological response (RVR) occurred in 42.8 % (3/7) and complete early virological response (c-EVR) was 100 % (7/7). The virological end-of-treatment response (ETR) was 100 %(6/6). Sustained virologic response (SVR) was available for four patients and all patients remained HCV RNA-negative 6 months posttreatment (100 %, 4/4).During the follow-up period, none of the patients died of liver failure, recurrent HCV after virological response, or HCC. Also, none of patients were signs of rejection observed.
Conclusions: Combination therapy with pegylated interferon and ribavirin could conduct valuable role as a prophylactic treatment in recurrent HCV infection post-LT, because it is well tolerated and leads to good results in virological response.

Topic 12: Hepatitis C

No: 1417

Naïve and memory t cells phenotype change in chronic hepatitis C patients with pegylated interferon α with ribavirin treatment

Chia-ju Shih[1], Ya-ling Chiou[1], Wang-sheng Ko[2]

Hungkuang University Biomedical Nutrition Taichung-Taiwan[1], Kuang-tien General Hospital Internal Medicine Taichung-Taiwan[2]

Background: Patients infected with the hepatitis C virus (HCV) may progress toward chronic hepatitis, liver cirrhosis, and liver cancer. The standard therapy for patients of chronic HCV infection is a combination of pegylated interferon-α with ribavirin which have a sustained virological response to 50 to 70 %, but lack an effective predict maker. The T cells expressing the CD45RA isoform are considered a naïve subset. Antigenic stimulation converts T cells from CD45RA to CD45RO + (memory subset). The CD45RO +T cells show immediate response and high lymphokine producing leading to maintenance and up-regulation of immune reactions. Purpose: We collected 30 HCV of patients untreated previously and receive combination of pegylated interferon-α with ribavirin treatment. Blood samples were collected in before treatment, period of treatment (4th, 12th, and 24th week) and after treatment. Results and conclusion: The proportions of CD45RA + T cells were decreased significantly after 12 th week treatment (pretreated: 31.4 % vs. 12 th week: 25.4 %), and the proportions of CD45RO + T cells were increased after 24 th week and 28 th week treatment ($P < 0.05$). The patients with hepatitis C therapy increased CD45RO + T cells significantly, might increase lymphokine production leading to maintenance and up-regulation of immune reactions during and after hepatitis C therapy.

Topic 12: Hepatitis C

No: 2149

Experience of HCV treatment in last two years at ankara numune education and research hospital

Ahmet Yozgat[1], Akif Altıbas[1], Selim Demirci[1], Murat Aliyazicioglu[1], Ahmet Teoman Erten[1], Ersan Ozaslan[1], Tankut Koseoglu[1], Enver Uner[1], Faruk Coskun[1], Emin Altıparmak[1]

Ankara Numune Education and Research Hospital Gastroenterology Ankara-Turkey[1]

Introduction: It is estimated that almost anti-HCV sero-positivity declined to %1 in Turkey in the last decade. Chronic HCV infection is the second most common reason of cirrhosis and hepatocellular carcinoma in our country. New promising treatments against HCV infection are marketing last years. So, in order to determine chronicly HCV infected population, we aimed to investigate our treated HCV patients in the last two years.
Material and method: Totally, 20 chronic HCV patients were treated at Numune Education and Research Hospital in last two years. 12 out of them were naive, 8 of experienced for HCV therapy.
Results: The mean age was 53,6 ± 11,2 and 55 % of were female. All of the patients have genotype 1b virus and three of the 20 patients had cirrhosis. Initial HCV RNA value was 5,5 log. Twelve patient (%60) received peginterferon and ribavirin, 7 patients (%35) received peginterferon ribavirin and telaprevir, 1 patient (%5) received peginterferon ribavirin and boceprevir. Four patients discontinued treatment because of side effect, two of them continues therapy and

14 patients therapy were ended. A patient who discontinued peginterferon ribavirin and telaprevir therapy at 11. weeks is still HCV RNA negative after 18 months of therapy. Twelve patients have reached 6 months after treatment and 10 of them achieved sustained virologic response (SVR). SVR rates were %85,7 and %80 in the group of peginterferon ribavirin telaprevir and peginterferon ribavirin respectively.
Discussion: Our hospital has a high success rate in the treatment of HCV for he last two years, with new treatments this success rate expected to increase.

Topic 12: Hepatitis C

No: 2041

Confirmation and evaluation of elecsys anti HCV ii assay positivities by inno lia HCV score and HCV RNA assays

Banu Bayraktar[1], Mehmet Emin Bulut[1], Gulsah Malkocoglu[1]

Sisli Hamidiye Etfal Research and Training Hospital Clinical Microbiology Istanbul-Turkey[1]

Background: Anti-HCV antibody tests are screening tests that are used for deduction of HCV infection. The positive results of these tests need to be confirmed by a supplementary test such as a line immunoassay. It is also necessary to investigate the presence of active infection with a HCV-RNA test.
Aim: The aim of this study was to evaluate positive results obtained by the Elecsys® Anti-HCV II assay, comparing with the 3rd generation Line Immune Assay (LIA). In addition to this we aimed to investigate the correlation of the HCV-RNA results with Elecsys® Anti-HCV II and LIA tests.
Methods: A total of 356 HCV-positive samples deducted by Elecsys® Anti-HCV II assay on a cobas e 601 platform between April 2014 – November 2014 were included into the study. Repeatedly reactive samples were confirmed by using LIA(INNO-LIA, HCV Score, Innogenetics, Belgium). A total number 95 of samples with reactive anti-HCV results were further tested for the presence of HCV-RNA using the real-time PCR-based COBAS Ampliprep/COBAS TaqMan HCV-RNA assay. The data was analyzed on SPSS 15.
Results: Overall, of the 356 samples reactive for anti-HCV by the Elecsys® Anti-HCV II assay, a total number of 206 (57,9 %) samples were positive, 23 (6,5 %) were indeterminate and 127 (35,7 %) were negative by LIA. The Elecsys s/co values were positively correlated with LIA results. Confirmation rate of LIA was increased with an increase in the s/co values. With a 95 % of confidence interval s/co values <7.8 was associated with a negative LIA result. Among the 356 patient samples with positive anti-HCV results, 95 (26.6 %) were…

Topic 12: Hepatitis C

No: 1695

Triple therapy with telaprevir or boceprevir bezmialem experience

Birol Baysal[1], Yusuf Kayar[1], Mukaddes Tozlu[1], Maged Elshobaky[1], Ahmet Danalıoğlu[1], Orhan Kocaman[1], Ali Ince Tüzün[1], Hakan Şentürk[1]

Bezmialem Vakif University, Faculty of Medicine Department of Gastroenterology Istanbul-Turkey[1]

Introduction: In the last two years, in treatment of genotype 1 related chronic hepatitis C, triple therapy regimens containing telaprevir (TPV) and boceprevir (BOC) were used extensively in our country. However, our knowledge of the response rates in our country is still limited.
Aim: To assess the efficacy of TPV and BOC in treatment of chronic hepatitis C patients infected with genotye 1 virus.
Methods: Patients who have been treated with Peg-IFN + ribavirin + (TPV/BOC), and completed at least 24 weeks of therapy were included in the evaluation. RNA negativity at 24th week of therapy was accepted as on treatment response and persisting of HCV-RNA negativity at post-treatment 24th week as sustained virological response (SVR).
Results: Of the total 56 patients, 52 have completed 6 months of triple therapy. of those, 31 in the TPV group (61.3 % female; age 57 ± 7 years), and 21 in the BOC group (71.4 % female; age 57 ± 8 years). Age, gender, BMI, initial viral load, genotype, ALT, AST, initial fibrosis stage and hematological results were similar in both groups. On treatment response rates were 74.2 % in the TPV and 52.4 % in the BOC group ($P = 0.14$). Because of no patient in BOC group completed post-treatment follow up of 24 weeks, SVR could be evaluated only in the TPV group and was observed in 66.7 % of patients.
Conclusions: On treatment response were observed in about three-quarters of patients in TPV group and half of the patients in BOC group. On treatment response was sustained in 90 % in TPV group.

Topic 12: Hepatitis C

No: 1021

Insulin resistance is associated with elevated serum alpha fetoprotein levels in patients with chronic hepatitis C

Naota Taura[1], Hisamitsu Miyaaki[1], Satoshi Miuma[1], Hidetaka Shibata[1], Takuya Honda[1], Kazuhiko Nakao[1]

Graduate School of Biomedical Sciences Nagasaki University Department of Gastroenterology and Hepatology Nagasaki-Japan[1]

Background: Alpha-fetoprotein (AFP) is a major tumour marker of HCC and is also reported as a factor that reflects the incidence of Hepatocellular carcinoma (HCC) in patients with hepatitis C virus (HCV). Recent studies have discussed the relationship between AFP level and insulin resistance. We investigated whether higher levels of AFP at the time of diagnosis are associated with an increased insulin resistance in patients with HCV.
Methods: A total of 159 HCV patients with chronic liver disease without other risks were evaluated for identify a factor that contributes to elevate serum AFP, including age, sex, alcohol intake, aspartate and alanine aminotransferase levels, bilirubin, albumin, platelet count, homeostasis model assessment as an index of insulin resistance (HOMA-IR) and homeostatic model assessment beta cell function (HOMA-beta) at study entry. Patients were divided into two groups according to the serum AFP level; low AFP group (< 5 ng/ml), and high AFP group (5-20 ng/ml). More than 21 ng/ml of AFP level was excluded.
Results: Multivariate analysis identified the reason that the HOMA-IR [> 2.5: hazard ratio (HR) 3.34, $P = 0.003$] and Platelet (< 145000/micro-l: HR 3.08, $P = 0.008$) was an independent and significant risk factor for the high AFP group. There were significant differences in both whole-body insulin sensitivity index (WBISI) ($P = < 0.001$) between the low AFP group and the high AFP group.

However, delta-insulin/delta-glucose 30 showed no significant difference in two groups.
Conclusions: Our findings suggest that insulin resistance may be associated with an elevated serum AFP level in HCV-infected patients.

Topic 12: Hepatitis C

No: 1783

Assessment of combined serum biomarkers and fibroscan and dynamic computed tomography (CT)

Iftihar Köksal[1], Uğur Kostakoğlu[2], Arif Mansur Coşar[3], Gürdal Yilmaz[1]

Karadeniz Technical University Department of Infectious Diseases and Clinical Microbiology Trabzon-Turkey[1], Kanuni Training and Research Hospital Department of Infectious Diseases and Clinical Microbiology Trabzon-Turkey[2], Karadeniz Technical University Department of Gastroenterology Trabzon-Turkey[3]

Background: Liver biopsy is the gold standard to determine the liver fibrosis in chronic hepatitis patients. Non-invasive tests for hepatic fibrosis include combinations of serum biomarkers (e.g. APRI, Fibrotest, FIB4, AST/ALT ratio, and age/platelet index), and fibroscan (LS). In this study, it is investigated that if non-invasive serum biomarkers and the combination of fibroscan and dynamic computed tomography (CT) could be replaced with liver biopsy in chronic hepatitis C patients and which tests are more beneficial.
Materials and methods: Histopathologic evaluation of liver biopsy samples before the treatment is made with Ishak scoring system. Fibrosis score was recognized as follows: F0–1 no/early stage fibrosis, F2–4 significant fibrosis and F5–6 cirrhosis.
Results: The mean age of the 68 CHC patients that was participated to the study was 46.4 ± 10.7 and 37 of them were male(54.4 %). 21(30.9 %) of the patients had no/early stage fibrosis, 36 of (52.9 %) them were significant fibrosis and 11(16.2 %) them had cirrhosis. There were statistical differences between the results of the non-invasive methods used to detect fibrosis and liver biopsy results ($P < 0.05$) (Table 1). ROC curves of the tests in the prediction of significant fibrosis are plotted in Figure 1. The AUC curves of the Fibroscan, APRI, AAR, FIB-4 and AP to predict significant fibrosis (F2-6) were 0.739, 0.539, 0709, 0.662 and 0.674, respectively (Table 2).
Conclusions: The combinations of tests are more successful in the detection of hepatic fibrosis. As long as AUC < 0.8, with the usage of at least two methods of non-invasive serum biomarkers, CT and fibroscan, reliable results similar with liver biopsy could be achieved.

Topic 12: Hepatitis C

No: 1039

Human immunodeficiency virus hepatitis C virus co infection and obstacles for the initiation of conventional hepatitis C treatment experience of an infectious diseases unit

Nassima Belabas[1], Achour Amrane[1], Mohamed Zeroual[1], Fatma Zohra Aissat[1], Kamel Aknouche[1], Abdelouhab Dif[1]

Laadi Flici (el-kettar) Hospital Department of Infectious Diseases Algiers-Algeria[1]

Objectives: To evaluate the therapeutic particularities and obstacles hindering the initiation of standard therapy for Human Immunodeficiency Virus (HIV)- Hepatitis C Virus (HCV) co-infected patients.
Materials and methods: Retrospective study conducted in an infectious diseases unit on a ten-year period (January 2004-May 2014). We studied the obstacles encountered in the management of HIV-HCV co-infected.
Results: Twenty-two men had HIV-HCV co-infection. Three patients had spontaneous clearance of HCV. Only six men have benefited from the combination Peginterferon-α2a + Ribavrin (PR): (04) patients with SVR, 01 non-responder, 01 early treatment discontinuation due to severe depressive syndrome. Fifteen men were need treatment. (67 %) were over the age of 40 years. Two patients were in detention. We found: (08) injectable drug users, (02) regular drinkers, (02) Sub-Saharan African people, (02) persons in custody and comorbidity such as: epilepsy (01 case), depression (03 cases), metabolic syndrome (02 cases), hypertension (04 cases), dyslipidemia (04 cases). Paraclinical parameters were: HCV RNA $\geq$ 800,000 IU/ml in (47 %), genotype (G)1 in 04 cases and a G4 in 01 case, mean CD4 count: 228/mm3, mean of liver stiffness 12.9 kPa and mean hemoglobin 12 g/dl.
Conclusion: In our study, HIV-HCV co-infection is characterized by the severity of immunosuppression and hepatic fibrosis, an unsatisfactory response to PR and the existence of numerous barriers to care. The introduction of "interferon-free" regimens treatment of HCV is necessary.

Topic 12: Hepatitis C

No: 2067

Studying evolutionary constraints on hepatitis C virus replication via analysis of serine codon usage

Tanvi Khera[1], Richard Brown[1], Thomas Pietschmann[1]

Twincore Centre For Experimental and Clinical Infection Research Institute For Experimental Virology Hannover-Germany[1]

Serine is encoded by two divergent codon types (UCN and AGY) which are non-interchangeable by a single nucleotide substitution. Switching between codon types therefore occurs via intermediate phenotypes or via simultaneous double substitutions. This unique property can be exploited to investigate evolutionary constraints on viral genome mutability. Indeed, previously we have demonstrated divergent restrictions on Hepatitis C virus (HCV) envelope glycoprotein mutability: a subset of codon-switch intermediates can abrogate virion assembly, target cell entry and enhance host recognition. However, whether analogous constraints exist on the mutability of the genes encoding viral replicase complex remains unclear. Therefore, the two non- structural proteins NS3 and NS5B, which are indispensable for RNA replication, were selected for further investigation. Database mining of globally sampled HCV sequence data, comparative sequence alignment of conserved serine residues and phylogenetic analyses revealed multiple examples of serine-serine codon switching and low-level detection of codon switching via intermediates, occurring at both the inter- and intragenotypic level. These analyses informed the generation of a mutant panel of NS3 and NS5B reporter viruses, enabling in vitro characterization of mutational phenotypes. Bioinformatic characterization of deleterious mutations on disruption of putative RNA secondary structures will be performed. Long term passage and deep sequencing of attenuated mutants to demonstrate reversion or acquisition of compensatory mutations will also be performed, in addition to in vivo confirmation via infection of uPA-SCID mice.

These studies will elucidate the mutational constraints operating on the HCV genome, which help shape the global diversity of this medically important pathogen.

Topic 12: Hepatitis C

No: 1353

The association between genetic variations in PNPLA3 gene (rs738409) and severity of liver fibrosis in Thai patients with chronic hepatitis C

Rattanaporn Kiatbumrung[1]

Faculty of Medicine, Chulalongkorn University Biochemistry Bangkok-Thailand[1]

Background: Patatin-Like phospholipase domain containing protein 3 (PNPLA3) rs738409 (C > G) polymorphism has been associated with disease progression in nonalcoholic fatty liver disease. However, the role of the polymorphism in patients with chronic hepatitis C (CHC) is less clear.
Methods: 200 Thai patients with CHC and 200 healthy controls were included in this study. The polymorphism of rs738409 was detected by allelic discrimination using real-time PCR with TaqMan probes. Liver fibrosis was assessed by transient elastography.
Results: The frequency of CC, CG and GG genotypes of rs738409 in the CHC group was 111 (55.5 %), 76 (38 %) and 13 (6.5 %), respectively. In the control group, the corresponding genotypes were 91 (45.5 %), 88 (44 %) and 21 (10.5 %). The frequency of non-CC (CG and GG) was significantly higher in the control group than in the CHC group (odds ratio 0.71, 95 % confidence interval: 0.5-0.99, $P = 0.046$). There was no difference in mean stiffness score between CHC patients with CC and non-CC genotypes (15.0 ± 11.9 vs. 13.9 ± 10.0 kPa, $P = 0.564$). In addition, the frequency of advanced fibrosis (defined as a stiffness score of > 9.5 kPa) was comparable between patients with CC and non-CC genotypes (32.4 % and 31.5 %, respectively, $P = 0.884$).
Conclusion: The rs738409 polymorphism was associated with the risk of HCV infection, but was not associated with the severity of liver fibrosis in Thai patients with CHC.

Topic 12: Hepatitis C

No: 1914

The effect of pegylated interferon and ribavirin combination therapy for chronic hepatitis C infection in elderly patients

Dilek Yildiz Sevgi[1], Ahsen Oncul[1], Alper Gunduz[1], Ahmet Sanli Konuklar[1], Banu Bayraktar[2], Aziz Ahmad Hamidi[1], Nuray Uzun[1], Ilyas Dokmetas[1]

Sisli Hamidiye Etfal Training and Research Hospital Department of Infectious Diseases and Clinical Microbiology Istanbul-Turkey[1], Sisli Hamidiye Etfal Training and Research Hospital Department of Clinical Microbiology Istanbul-Turkey[2]

Aim: In elderly patients with chronic hepatitis C virus (HCV), especially those over 60 years, liver fibrosis is accelerated and the incidence of HCC is increased. Limited studies have been done for evaluating the efficacy and safety of treatment in this population. We investigated the efficacy and safety of interferon-alpha2a or alpha2b plus ribavirin treatment in elderly patients with chronic HCV infection.
Methods: Patients with genotype 1 chronic HCV infection who recieved pegylated interferon-alpha2a or alpha2b plus ribavirin treatment between January 2007 and December 2012 at the Department of Infectious Diseases and Clinical Microbiology at Sisli Hamidiye Etfal Research and Training Hospital in Istanbul-Turkey were enrolled in the study. Subjects were classified into two groups; group 1: patients aged 18-60 years and group 2: $\geq$ 60 years. The primary end point was a sustained virologic response (HCV RNA level of < 25 IU per milliliter) at week 24 (SVR24) after the end of therapy.
Results: 87 patients were enrolled in the study. Patients who could not achieve SVR24 had higher HCV RNA levels (p: 0.012) and were older (p: 0.005). ALT, AST, platelet levels and APRI were not associated with SVR24. (Table 1 and 2)
Conclusion: We conclude that the efficacy of pegylated interferon plus ribavirin combination therapy in elderly patients was inferior to those in younger patients.

Topic 12: Hepatitis C

No: 1913

A comparison of abbott realtime HCV genotype ii and versant lipa 2.0 line probe assays for hepatitis C virus genotyping

Chen-hua Liu[1], Cheng-chao Liang[2], Chun-jen Liu[1], Chih-lin Lin[3], Tung-hung Su[1], Hung-chih Yang[1], Pei-jer Chen[1], Ding-shinn Chen[4], Jia-horng Kao[1]

National Taiwan University Hospital Internal Medicine Taipei-Taiwan[1], Far Eastern Memorial Hospital Internal Medicine Taipei-Taiwan[2], Taipei Municipal Hospital, Ren-ai Branch Internal Medicine Taipei-Taiwan[3], Academia Sinica Genomics Research Center Taipei-Taiwan[4]

Aims: Correct identifying the genotype/subtype of hepatitis C virus (HCV) is important when designing the treatment strategies. We compared the accuracy of HCV genotyping/subtyping among various commercial tests, which are influenced by the sensitivity and the nature of sequence polymorphisms in target subgenomic regions.
Methods: 255 patents with HCV genotype 1, 2, 3, or 6 infection (154 HCV monoinfection; 49 HCV/HBV dual infection; 52 HCV/HIV dual infection) were enrolled. Two commercial genotyping assays (VERSANT-LiPA 2.0 and Abbott RealTime HCV GT II) were compared, taking phylogenetic analyses by direct sequencing at 5′ untranslated region (5′UTR) and non-structural 5B region (NS5B) as the reference standard.
Results: Compared to direct sequencing, the concordance rates for genotypes were 99.2 %, and 99.6 %, and those for subtype 1a/1b were 96.1 % and 96.1 % by VERSANT-LiPA 2.0 and Abbott RealTime HCV GT II assays. One test was indeterminate due to low viral load (744 IU/mL) and 4 tests failed subtyping due to intermediate viral load (4720-62000 IU/mL) by Abbott RealTime HCV GT II assay. The concordance rates were comparable between patients with dual and monoinfection.
Conclusions: Abbott RealTime HCV GT II and VERSANT-LiPA 2.0 assays are accurate to detect HCV genotypes 1, 2, 3 and 6 and subtypes 1a/1b.

Topic 12: Hepatitis C

No: 2018

First week HCV RNA level under the pegylated interferon and ribavirin treatment predicts sustained virological response

Mehmet Bayram[1], Alirıza Köksal[1], Hüseyin Alkım[1], Salih Boğa[1], Meltem Ergün[1], Osman Özdoğan[1], Engin Altınkaya[1], Canan Alkım[8]

Sisli Etfal Training and Research Hospital Gastroenterology Istanbul-Turkey[1]

Objective: This study was planned to investigate whether the decrease in the HCV RNA levels at the 1st week of combined pegylated interferon and ribavirin treatment of naive genotype 1 hepatitis C (HCV) patients were predicting sustained virological response (SVR).
Materials and methods: Fifty two patients were enrolled into the study. HCV RNA levels were measured at the baseline, 1st, 4th and 12th weeks of treatment.
Results: Thirty four patients achieved SVR which basal, 1st week and 4th week HCV RNA levels were log 5.57, log 3.65 and log 1.92 respectively. Eighteen patients couldn't achieve SVR which basal, 1st week and 4th week HCV RNA levels were log 6.22, log 5.45 and log 3.84 respectively ($P < 0,05$). Patients were distributed in two groups according to the amount of decrease in HCV RNA levels at the 1st week as less or more than 1.5 log. There were 20 patients with $\geq$ 1.5 log decrease in the HCV RNA levels at the 1st week. These patients were named as very rapid virological response (VRVR) patients. All patients (100 %) with VRVR were achieved SVR. In only 14 (44 %) of the 32 patients without VRVR, SVR were achieved. In 16 (84 %) of the 19 patients with rapid virological response (RVR) and 33 (79 %) of the 42 patients with early virological response (EVR), SVR were achieved.
Conclusions: A $\geq$ 1.5 log decrease (VRVR) in HCV RNA levels of HCV patients at the 1st week of combined pegylated interferon and ribavirin treatment predicts SVR very strongly.

Topic 12: Hepatitis C

No: 1677

Physicians how much they know and how much aware of the chronic hepatitis C a study with questionnaire

Yusuf Kayar[1], Ahmet Danalioglu[1], Nuket Bayram Kayar[2], Birol Baysal[1], Hakan Senturk[1]

Bezmialem Vakif University Gastroenterology Istanbul-Turkey[1], Bagcilar Education and Traditional Hospital Family Medicine Istanbul-Turkey[2]

Introduction: Hepatitis C virus seroprevalence was reported as an average of 3 % across the world and 0.9 % in our Country. One of the reasons for the inadequate diagnosis and treatment of hepatitis C is inadequate knowledge and awareness of physicians.
Aim: The aim of this study is to measure the level of knowledge and awareness of physicians about chronic hepatitis C infection.
Method: 125 family physicians and 76 internal medicine specialists working in Istanbul were included in the study. The participants were requested to complete questionnaire at the same meeting.
Results: Of the physicians, mean age was 30.9 $\pm$ 7.1 years (range 23-45) and 84(42 %) male. Four of physicians (2 %) had chronic hepatitis C and 12(6 %) had never the test. Physician of 17 (8.4 %) had chronic hepatitis C in relatives.
Answers to questions were as follows: HCV can be transmitted by sexual contact 89 %. The maternal transmittion is possible 74 %. Sharing of shaving materials may cause transmittion % 69. In addition, the physicians answered as HCV can transmitted by kissing (17 %), by using the same toilet (3 %), by working in the same environment (4 %). Positive family history of hepatitis C and specialties of physicians were not significant factors to increase the awareness of hepatitis C infection. Physicians between 23-28 age were significantly less aware of hepatitis C.
Conclusion: The knowledge and awareness of physicians about hepatitis C infection are not enough to effectively prevent the transmission of infection and to catch the patients who need therapy. So attention should be given to screening programs and the training of physicians in primary care.

Topic 12: Hepatitis C

No: 1315

Characterization of resistance in HCV genotype 1b infected Japanese and western patients treated with an interferon and ribavirin free regimen of ombitasvir and abt 450 ritonavir

Tami Pilot-matias[1], Gretja Schnell[1], Rakesh Tripathi[1], Thomas Reisch[1], Jill Beyer[1], Preethi Krishnan[1], Liangjun Lu[1], Teresa Ng[1], Lino Rodrigues-jr[2], Carolyn Setze[3], Xinyan Zhang[3], Coleen Hall[3], Regis Vilchez[4], Christine Collins[1], Christophe Hezode[5], Kazuaki Chayama[6], Hiromitsu Kumada[7]

Abbvie Clinical Virology North Chicago, Il-United States[1], Abbvie Clinical Development North Chicago, Il-United States[2], Abbvie Clinical Statistics North Chicago, Il-United States[3], Abbvie Medical Affairs North Chicago, Il-United States[4], Hospital Henri Mondor, Ap-hp, Universite Paris-est Hepatology and Gastroenterology Creteil-France[5], Hiroshima University Gastroenterology and Metabolism Hiroshima-Japan[6], Toranomon Hospital Hepatology Tokyo-Japan[7]

Aim: Two phase 2 studies, M12-536 in Japan (N = 75) and PEARL-I in US/EU (N = 181), assessed the efficacy of regimens containing NS5A inhibitor ombitasvir and NS3/4A inhibitor ABT-450 (identified by AbbVie and Enanta) dosed with ritonavir (ABT-450/r) in HCV GT 1b-infected patients. Analyses were conducted to assess prevalence of pre-existing resistance-associated variants (RAVs) at baseline and treatment-emergent RAVs after virologic failure (VF) in Japanese compared with US/EU patients.
Methods: Population sequencing was performed on the NS3/4A and NS5A genes from available baseline samples. In patients who experienced VF, population sequencing was performed on the first sample after VF with HCV RNA $\geq$ 1000 IU/mL. A phylogenetic analysis was conducted to evaluate the genetic relatedness of GT1b sequences by geographic region.
Results: NS5A-Y93H was the most prevalent RAV at baseline, present in 5.4 % (4/74) Japanese and 7.4 % (13/176) US/EU patients; NS3/4A RAVs were rare at baseline. Six patients across both studies experienced VF; RAVs present after VF were D168 V (N = 5) and Y56H + D168A (N = 1) in NS3; Y93H (N = 3), P58S + Y93H (N = 2), and L28 M + R30Q + Y93H (N = 1) in NS5A. Pre-existing NS5A-Y93H was present in 0/1 Japanese and 2/5 US/EU patients who experienced VF, while SVR was achieved by 4/4 Japanese and 11/13 US/EU patients with pre-existing NS5A-Y93H. Phylogenetic analysis of NS3 and NS5A sequences did not show evidence of geographic clustering.
Conclusions: Baseline and treatment-emergent RAVs in NS3/4A and NS5A were similar across both Japanese and US/EU studies. The

presence of RAVs including NS5A-Y93H prior to treatment was not predictive of failure.

Topic 12: Hepatitis C

No: 1303

Efficacy and safety of peginterferon lambda 1a with or without daclatasvir compared with peginterferon alfa 2a each in combination with ribavirin in treatment naive patients with chronic hepatitis C virus genotype 2 or 3 infection

Graham Foster[1], Kazuaki Chayama[2], Wan Long Chuang[3], Hugo Fainboim[4], Martti Farkkila[5], Adrian Gadano[6], Giovanni Battista Gaeta[7], Christophe Hezode[8], Yukkiko Inada[9], Jeong Heo[10], Hiromitsu Kumada[11], Sheng-nan Lu[12], Patrick Marcellin[13], Christophe Moreno[14], Stuart Roberts[15], Simone Strasser[16], Alexander Thompson[17], Joji Toyota[18], Seungwoon Paik[19], John Vierling[20], Anna Zignego[21], David Cohen[22], Fiona Mcphee[22], Megan Wind-rotolo[22], Subasree Srinivasan[22], Matthew Hruska[22], Heather Myler[22], Simon Portsmouth[22]

Queen Mary's University of London Hepatology London-United Kingdom[1], Hiroshima University Hiroshima-Japan[2], Kaohsiung Medical University Hospital Kaohsiung-Taiwan[3], University of Buenos Aires Buenos Aires-Argentina[4], University of Helsinki Helsinki-finland[5], Hospital Italiano De Buenos Aires Buenos Aires-Argentina[6], Universita De Studi Di Napoli Naples-Italy[7], Chu Henri Mondor Créteil-France[8], Saga University Saga-Japan[9], Pusan National University School of Medicine Busan-Republic of Korea[10] Toranomon Hospital Tokyo-Japan[11] Kaohsiung Chang Gung Memorial Hospital and Chang Gung University Kaohsiung-Taiwan[12] Hospital Beaujon Clichy-France[13] Université Libre De Bruxelles Brussels-Belgium[14] Alfred Hospital Prahran-Australia[15] Royal Prince Alfred Hospital Sydney-Australia[16] St Vincent's Hospital Melbourne-Australia[17] Sapporo Kosei General Hospital Sapporo-Japan[18] Sungkyunkwan University School of Medicine Seoul-Republic of Korea[19] Baylor College of Medicine Houston-United States[20] Universita Di Firenze Florence-Italy[21] Bristol-myers Squibb Research & Development Wallingford-United States[22]

Aim: This study evaluated the efficacy and safety/tolerability of peginterferon lambda-1a (Lambda) + ribavirin (RBV) + placebo (PBO) and Lambda + RBV + daclatasvir (DCV; potent, pangenotypic NS5A inhibitor) compared with peginterferon alfa-2a (Alfa) + RBV in treatment-naive patients with HCV genotype (GT) 2 or 3 infection.
Methods: This was an international, multicenter, double-blind, phase 3 trial with noninferiority design. Patients were randomized 2: 2: 1 to receive 24 weeks of Lambda + RBV + PBO, 12 weeks of Lambda + RBV + DCV, or 24 weeks of Alfa + RBV. Interim analyses at posttreatment Week 12 were performed.
Results: Overall, 874 patients were treated: Lambda + RBV + PBO, n = 353; Lambda + RBV + DCV, n = 349; Alfa + RBV, n = 172. Patients were 65 % White and 33 % Asian, 57 % male, with a mean age of 47.3 years; 52 % were infected with GT 2 (6.3 % cirrhotic) and 48 % with GT 3 (8.7 % cirrhotic). For both HCV genotypes, patients were well-matched across groups for baseline HCV RNA levels and < i>IL28B </i > CC/non-CC genotype. Lambda + RBV + DCV met the criteria for noninferiority and superiority to Alfa + RBV (Table). SVR12 rates with Lambda + RBV + DCV were 90 % for GT 2 and 75 % for GT 3 (43 % in cirrhotic patients; failures were primarily relapses). Lambda + RBV + DCV was associated with lower incidences of flu-like symptoms, cytopenic abnormalities, and dose reductions and discontinuations due to adverse events compared with Alfa + RBV.
Conclusion: The 12-week regimen of Lambda + RBV + DCV achieved superiority to Alfa + RBV in treatment-naive patients with GT 2 or 3 infection, was highly efficacious in GT 2 patients regardless of baseline characteristics, and was associated with an improved tolerability and safety profile compared with Alfa + RBV.

Topic 12: Hepatitis C

No: 2222

Pilot study to determine the efficacy and safety of combining boceprevir with peginterferon alfa 2b and ribavirin in treatment naive patients with genotype 4 chronic hepatitis C infection

Ibrahim Mostafa[1], Mona Hassan[2], Azza M.ibrahim[3], Ossama Khalafalla[4], Fayza Essawy[2], Amr Abdelazem[1], Mohamed Elrefaiy[1], Mostafa Ibrahim[1]

Theodor Bilharz Research Institute Gastroenterology and Hepatology Giza-Egypt[1], Theodor Bilharz Research Institute Clinical Pathology Giza-Egypt[2], Cairo University -faculty of Medicine-Kasr El Aini Teaching Hospital Clinical Pathology Cairo-Egypt[3], Cairo University -faculty of Medicine-Kasr El Aini Teaching Hospital Clinical Chemistry Cairo-Egypt[4]

Aim: To assess the efficacy and safety of Boceprevir (BOC) in combination with peginterferon (PEG) alfa-2b +Ribavirin (RBV) compared to PEG alfa-2b +RBV in previously untreated adult subjects with chronic hepatitis C(CHC) genotype 4 patients.
Methods: Phase III, prospective, open label, and randomized, controlled, parallel group clinical trial. 40 previously untreated adult subjects with chronic hepatitis C(CHC) genotype 4 infection, we randomly assigned in a 1: 1 ratio to Arm A, received PEG alfa-2b 1.5 μg/kg once per week (QW) subcutaneously (SC) plus weight-based dosing (WBD) of ribavirin 15 mg/kg/day (800 to 1400 mg/day) for 48 weeks. Arm B, received 4 weeks PEG alfa-2b 1.5 μg/kg (QW) subcutaneously plus weight-based dosing (WBD) of ribavirin 15 mg/kg/day (800 to 1400 mg/day) followed by receiving Boceprevir (BOC) 800 mg three times per day in combination with peginterferon alfa-2b (PEG) + ribavirin (RIB) for 44 weeks.
Results: The proportion of patients who achieved early response (undetectable HCV RNA or $\geq$ 2 log reduction at week 8) was higher in Arm B (BOC) (95 %, 19/20) than in Arm A (SOC) (89.5 %, 17/19) while week 12 response was (100 %, 20/20) for Arm B and (100 %, 19/19) for Arm A.
Conclusion: The addition of Boceprevir after 4 weeks of lead-in therapy with PEG2b/R to naive patients infected with genotype 4 Chronic Hepatitis C infection leads to higher rate of undetectable HCV RNA or $\geq$ 2 log reduction at week 8 and similar rates at week 12 compared with patients given only PEG alfa-2b/R

Topic 12: Hepatitis C

No: 2047

Detection of ns5b c316 n—a resistant mutation to sofosbuvir in treatment naïve genotype 1b HCV infected patients using ultra deep sequencing

Ye Wang[1], Huiying Rao[1], Lai Wei[1]

Peking University Hepatology Institute Beijing-China[1]

Background: The C316 N mutation has been reported as the variant to impact the activity of certain NS5B-palm-targeting non-nucleoside

polymerase inhibitors. Baseline N316 polymorphism was associated with treatment failure of the newest NS5B polymerase inhibitor sofosbuvir.
Aim: We aimed here to investigate whether this substitution pre-existed in treatment naïve genotype 1b HCV infected patients, and whether treatment of PegIFN plus RBV would impact the mutation frequencies.
Methods: NS5B polymorphism deep sequencing was performed with an average coverage of 2000 in 24 genotype 1b HCV infected patients both at baseline and after receiving therapy of PegIFN plus RBV for 48 weeks.
Results: C316 N polymorphism was detected in 19 out of 24 patients (79.2 %) at baseline, within mutation frequencies from 6.2 % to 93 %. The prevalence was much higher than 12 % in the Europe as reported by previous studies. When the treatment-outcome was considered, no difference was found between patients who achieved SVR and who didn't (75 % vs 81.3 %, $P = 1.00$). Treatment of PegIFN plus RBV for 48 weeks didn't cause changes of frequencies of this mutation.
Conclusion: NS5B substitution C316 N associated with treatment failure was identified with a quite high prevalence in this study. The detection of this mutation should be considered when patients in Asian receiving treatment of sofosbuvir in the near future.

Topic 12: Hepatitis C

No: 1739

Infectivity and clinical significance of defective hepatitis C virus clones in chronic hepatitis C patients

Shigeru Ohtsuru[1], Yoshihide Ueda[2], Tsutomu Chiba[2], Hiroyuki Marusawa[2]

Kyoto University Gastroenterology and Hepatology, Primary Care and Emergency Medicine Kyoto-Japan[1], Kyoto University Gastroenterology and Hepatology Kyoto-Japan[2]

Aims: Hepatitis C virus (HCV) with a defective genome has been found in liver and serum specimens of some HCV patients. However its infectivity is ambiguous. The aim of this study is to clarify its infectivity and to evaluate its clinical significance in chronic hepatitis C patients.
Methods: A total of 17 transplant recipients with genotype 1b HCV infection were enrolled in this study. We analyzed the existence of the defective HCV clones and the association with the response to the antiviral therapy in 12 patients. Using a massive-parallel ultra-deep sequencing technique, we determined full-genome HCV sequences in the liver and serum of 5 patients, and evaluated the changes in defective HCV clones in the serum of these cases before and after liver transplantation.
Results: We found the several defective HCV in 4 of 12 recipients' sera. All defective HCV clones had deletions in the envelope region. Interestingly, no patients with defective clones showed a prompt decrease in HCV RNA after the start of antiviral therapy. Defective HCV clones did not increase and full-genome HCV clones selectively increased immediately after liver transplantation. Re-increase of the same defective clone existing before transplantation was detected 22 months after transplantation in 1 patient.
Conclusions: The circulating defective HCV clones are present and might be associated with the response to the antiviral therapy. Dynamic changes in defective HCV clones after liver transplantation indicate that these clones have important roles in the HCV life cycle.

Topic 12: Hepatitis C

No: 2043

Monoclonal antibodies targeting novel epitopes of hepatitis C virus envelope glycoprotein precludes virus infection in vitro

Kai Deng[1], Ruyu Liu[2], Lai Wei[3]

Peking University Hepatology Institute Hepatology Beijing-China[1], Ditan Hospital Hepatolody Beijing-China[2], Peking University Hepatology Institute Hepatolody Beijing-China[3]

Background: Neutralizing antibody is one of the early key determinants for the prognosis of Hepatitis C virus (HCV) infection and a potential prophylactic/therapy vaccine. Many neutralizing antibodies against HCV envelop proteins have been reported recently. Now we report two monoclonal antibodies recognizing novel and relatively conserve epitopes of HCV glycoproteins with effective neutralizing activity in vitro.
Methodology: 42 overlapping peptides encompassing full-length HCV E1E2 glycoproteins were synthesized as immunogen to inoculate Balb/c mice, the corresponding polyclonal serum were screened in HCV pseudoparticles (HCVpp) assays of various genotypes (genotype 1-6) to determine their neutralizing activity. The peptides generating polyclonal antibodies with potent neutralizing activities were used to inoculate Balb/c mice, and the monoclonal antibodies clones were isolated and screened in HCVpp assays. The selected monoclonal antibodies were further tested in HCV cell culture (HCVcc, JFH and J6, genotype 2a) assay.
Results: 2 polyclonal antibodies recognizing conserved linear epitopes aa444-463, 604-618 potently neutralized a broad range of pseudoviruses from various genotypes. Monoclonal antibodies 2O18 and 2C21 (recognized epitopes 454-463 and 604-618, respectively) efficiently neutralized pseudoviruses from different genotypes and strains (IC50 ranged from 10 to 30 μg/ml). These two monoclonal antibodies completely neutralized HCVcc at concentrations as low as about 0.5–1 μg/ml.
Conclusions: Two monoclonal neutralizing antibodies against novel epitopes of HCV E2 protein were identified and could be prophylactic/therapy candidates.

Topic 12: Hepatitis C

No: 1904

Effect of the reversion of ns5a s2204i cell culture adaptive mutation on the replication of hepatitis C virus

Bora Jin[1], Aeri Chung[1], Kwang-hyub Han[1], Sang Hoon Ahn[1], Seungtaek Kim[2]

Brain Korea 21 Plus Project For Medical Science Yonsei University College of Medicine Seoul-Korea, South[1], Institute of Gastroenterology, Department of Internal Medicine Yonsei University College of Medicine Seoul-Korea, South[2]

Background and aims: Most of HCV RNAs require cell culture-adaptive mutations for efficient replication in Huh-7 hepatoma cells and a number of such mutations have been reported including a well-known S2204I in NS5A protein. In contrast, replication of JFH1 does not require any cell culture-adaptive mutation. In this study, we tested whether reversions/substitutions of cell culture-adaptive mutations of NS5A have any effect on virus replication in different genotypic backgrounds.

Methods: We generated various JFH1- or H77S-based NS5A chimeras including cell culture-adaptive mutations. Huh-7.5 cells were transfected with in vitro transcribed viral RNAs and virus replication was assessed by Gaussia luciferase reporter assay, focus-forming assay, and immunoblot.
Results: Replication of viral RNA was severely impaired in cells transfected with JFH1/H5A RNA, which contains H77S NS5A in the JFH1 background and includes both K2040R and S2204I cell culture-adaptive mutations of NS5A. However, the reversion of S2204I to the wild-type sequence (JFH1/H5A/IS) restored virus replication. A similar level of replication efficiency was also observed for the construct bearing both R2040 K and I2204S reversion mutations (JFH1/H5A/RKIS). But R2040 K substitution alone (JFH1/H5A/RK) did not restore viral replication. Interestingly, the substitution of serine with threonine at 2204 restored virus replication (JFH1/H5A/RKIT).
Conclusions: S2204I cell culture-adaptive mutation, which confers a robust viral replication in many genotypes of HCV, had negative effect in the context of JFH1. The results in this study suggest that phosphorylation of serine residue at 2204 in NS5A protein is important for the efficient replication of JFH1 RNA.

Topic 12: Hepatitis C

No: 1924

Long term entecavir monotherapy in treatment naïve chronic hepatitis B patients from a real world clinical practice in Korea

Chang Wook Kim[1], Hee Yeon Kim[1], Chung-hwa Park[1], Jong Young Choi[1], Seung Kew Yoon[1], Si Hyun Bae[1], Chang Don Lee[2]

The Catholic University of Korea Internal Medicine Uijeongbu-si-Korea, South[1], Incheon International St. Mary Internal Medicine Incheon-Korea, South[2]

Background: We aimed to evaluate the long-term efficacy of entecavir monotherapy in nucleos(t)ide-naïve chronic hepatitis B(CHB) patients with/without cirrhosis in real life.
Methods: We retrospectively analyzed data from 473 nucleos(t)ide-naïve CHB patients (n = 161; cirrhosis, n = 312; without cirrhosis) treated with entecavir at Uijeongbu St. Mary's Hospital. The primary endpoint was cumulative probability of achieving a virological response (serum HBV DNA < 112 copies/ml).
Results: The mean duration of treatment was 35.3 ± 19.4 months. HBeAg seropositivity was 61.3 %. Rates of virological response were 63, 84, 89, and 92 % at 1 year, 2 years, 3 years, and 5 years in HBeAg-positive CHB, and 96, 98, 100, and 100 % in HBeAg-negative CHB, respectively. The cumulative rate of HBeAg seroconversion was 17 % at 5 years of treatment. The rates of ALT normalization at 3 years were 98 %. of 428 patients who had been followed up for more than 12 months, 82 patients (19.2 %) had detectable HBV DNA at year 1 (partial virological response, PVR). of PVR patients, three switched to tenofovir at 16, 17, and 29 months of follow-up, and 6 patients developed entecavir resistance with continuous entecavir therapy(median treatment duration: 40 months). With continuous entecavir therapy, cumulative virological response rates in patients with PVR were 48 %, 66 %, 76 % at 2 years, 3 years, 5 years of treatment. Cumulative resistance rate at 5 years was 4 %. No serious adverse events were noted.
Conclusions: Long-term entecavir treatment was effective and safe in CHB patients in real-life. Patients with PVR achieved additional virological response with continuous entecavir therapy.

Topic 12: Hepatitis C

No: 1630

The bioinformatics detection of the potential recombination sites in the genomic structure of strains of genotype 2 hepatitis C virus

Nadia Zelinskaia[1], Alexei Paramonov[2], Igor Malov[1], Sergei Malov[1], Lilia Stepanenko[1], Olga Kolbaseeva[1], Vladimir Zlodin[1], Yuri Dzhioev[1], Zelinskaia N.E.[1], Paramonov A.I.[2], Malov I.V.[1], Malov S.I.[1], Stepanenko L.A.[1], Kolbaseeva O.V.[1], Zlobin V.I.[1], Dzhioev J.P.[1,2]

Irkutsk State Medical University Ministry of Health Irkutsk-Russia[1], Scientific Center of Family Health Problems and Human Reproduction Russian Academy of Sciences Irkutsk-Russia[2], 1Irkutsk State Medical University, Russia; 2 Scientific center of family health problems and human reproduction, Russia

Purpose: The goal of this research was the detection of potential recombination sites structure in genome sequences of the genotype 2 hepatitis C (HC) strain by the specifically adapted bioinformatics program methods
Methods: The potential recombination sites localization was detected by 7 program methods, realized in the software package RDP v 4.14: RDP, Geneconw, BootScan, Chimaera, 3Seq, SiScan, Maxchi. The recombination presence phylogenetic hypothesis was obtained by using the Neighbor-net method from the Splits Tree v 4.1. The statistical test was carried out by the Conduct Phi Test for Recombinations method from Splits Tree 4 software systems. The Phi-testing method was used for additional statistic backup.
Conclusion: In the sample of 26 complete genomes of genotype 2 HC strains (from GenBank) the recombination sites were detected in 14 strains. Phi-test confirmed the presence of recombination within those strains with a very high degree of confidence ($P = 0{,}00000$). On the split-tree phylogenetic model the biggest split was detected on four strain branches: AB690460, AB690461, JX227967, JX227968. By the quantitative variation degree of the recombination sites in one strain the below strains were dominate: AB690460 и AF169003 (11 and 5 sites respectively). For each recombinant the probabilistic parent strains were obtained.

Topic 12: Hepatitis C

No: 1017

The effectiveness of antiviral therapy in the patients with chronic hepatitis C in caucasians and Asians considering polymorphism of interleukin 28b gene of population

Sergei Malov[1], Nyamdavaa Pagvajav[2], Dulguun Badrakh[2], Larisa Orlova[1], Igor Malov[1]

Irkutsk State Medical University Infectious Diseases Irkutsk-Russia[1], National Centre Communicable Diseases Ulaanbaatar-Mongolia[2]

Background and aims: to assess the effectiveness of antiviral therapy in the patients with chronic hepatitis C in Caucasians and Asians, considering polymorphism of interleukin-28b gene of population.
Methods: 947 healthy people were examined in the Irkutsk region, the Republic of Buryatia and Mongolia (typing the locus rs 12979860 and rs8099917 of gene IL-28b). Also 97 people with 1 genotype of HCV-infection were observed. 33 % of them were Asians and 67 % - Caucasians. The patients with fibrosis > F3 on Metavir scale were not included in the research. The effectiveness of antiviral therapy

(combination of pegylated α2-interferon with ribavirin) was assessed on frequency of SVR.
Results: The prevalence of CC-genotype rs12979860 and TT-genotype rs8099917 in the population of Irkutsk region, the Republic of Buryatia and Mongolia were 40,0 % and 54,5 %; 64,6 % and 86,2 %; 82,2 % and 84,9 % accordingly. Evidently CC-genotype and TT-genotype are more characteristic for Asians. According census data (Russia 2010, Mongolia 2010) the portion of Asians was in the Irkutsk region—3,75 %; the Republic of Buryatia—30,2 %, Mongolia—96 %. The correlation ratio among Asians in population of each region and prevalence of CC-genotype was 0,9 ($P < 0,05$), indicating on strong straight connection. The rate of SVR in Caucasians was 53,8 ± 6.2 %, in Asians- 78,1 ± 7,3 % ($P < 0,05$).
Conclusions: The prevalence of CC-genotype locus rs 12979860 and TT-genotype rs8099917 of gene IL-28b is increased with increasing of Asians in the population of region. The effectiveness of antiviral therapy in the patients with chronic hepatitis C was more in Asians than in Caucasians.

Topic 12: Hepatitis C

No: 2165

CHADS2 scores in the prediction of ischemic stroke in patients with chronic hepatitis C infection

Chih-ming Lin[1], Kuan-fu Liao[1]

Taichung Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Taiwan Gastroenterology Taichung-Taiwan[1]

Objectives: Previous studies had demonstrated acute or chronic infectious disease in relation to ischemic stroke, including chronic hepatitis C infection. The aim of this study was to investigate whether CHADS2 score, which is composed with congestive heart failure (C), hypertension (H), age (A), diabetes (D), and stroke (S), helps to predict ischemic stroke in hepatitis C virus carrier in Taiwan.
Methods: This cohort study enrolled 7381 patients from the National Health Research Institute Database (NHIRD) of Taiwan between 2002 and 2009, with diagnosis of hepatitis C virus antibody seropositivity. The CHADS2 score and the incidence of ischemic stroke in hepatitis C virus carrier were measured.
Results: The incidence rate of ischemic stroke in different CHADS2 score, 0-2, 3 and over 4 was 0.1, 18.6 and 35.5 % respectively. There is significantly excellent correlation between CHADS2 score and stroke in patients with chronic hepatitis C infection (AUC = 0.97). The adjusted hazard ratios are 80.52 and 170.41 in CHADS2 score 3 and over 4 as comparison to CHADS2 score 0-2.
Conclusions: Ischemic stroke occurred in patients with chronic hepatitis C infection is a major health event as well as advanced liver disease. The CHADS2 score can be applied to evaluate the risk of ischemic stroke in hepatitis C carrier.

Topic 12: Hepatitis C

No: 1885

Our triple therapy results in treatment experienced chronic hepatitis C patients

Huseyin Alkim[1], Mehmet Bayram[1], Ali Rıza Koksal[1], Salih Boga[1], Meltem Ergun[1], Canan Alkim[1]

Sisli Hamidiye Etfal Education and Research Hospital Gastroenterology Clinic Istanbul-Turkey[1]

Aim: We aimed to evaluate the efficacy and tolerability of triple therapy with boceprevir or telaprevir in treatment-experienced chronic hepatitis C patients.
Method: We retrospectively analysed the results of patients treated with boceprevir or telaprevir together with pegylated interferon and ribavirin between February 2013 and March 2014.
Results: Total 16 patients aged between 50 and 68 years old, who 10 were female, were enrolled into the study. 12 was treated with telaprevir and 4 with boceprevir. In 9 of the patients treated with telaprevir, HCVRNA negativity was achieved at the 4th week, and a 24 week triple therapy were prescribed. All 9 patients were achieved sustained virological response (SVR). One of the patients was stopped treatment at the 3rd week. The second patient treatment was terminated at the 8th and the third patient at the 28th weeks because of severe side effects. This third patient was lost her life 1 month after ending the treatment. Severe side-effects were: 8 % hemorrhoidal disease, 17 % nausea/vomiting, 25 % skin rash and pruritis and 91 % anemia. Also 59 % of the patients required multiple red blood cell (RBC) replacement. Only 2 of the 4 patients treated with boceprevir were achieved SVR. Severe side-effects were 25 % nausea/vomiting, 50 % dysgeusia and 100 % anemia who 75 % required RBC replacement.
Conclusion: While 100 % of the patients that used recommended telaprevir triple therapy were achieved SVR, only 75 % of the patients can succeeded this. We experienced severe side-effects in all of the patients. Triple therapy with protease inhibitors

Topic 12: Hepatitis C

No: 1943

The changes of HCV genotype distribution in greece during the last 12 years

Dimitrios Dimitroulopoulos[1], Eleftheria Petroulaki[2], Sofia Gjovasho[3], Dimitrios Kypreos[1], Klisthenis Tsamakidis[1], Dimitrios Xinopoulos[1]

Agios Savvas Hospital Gastroenterology Athens-Greece[1], Okana Internal Medicine Athens-Greece[2], Onasion Hospital Cardiology Athens-Greece[3]

Information regarding the changing pattern of hepatitis C virus (HCV) genotypes in Greece during the last decade is not yet well known.
Aim: The aim of our study was to evaluate the frequency distribution of HCV genotypes and his changing pattern during the last 12 years among chronic HCV infected Greek patients.
Patients and method: The data of 598 consecutive, only Greeks in origin, naive patients (476 M, 122 F) that underwent treatment in our center for chronic HCV infection during the last 12 years (2002-2013), were reviewed retrospectively.
Results: The vast majority (63.5 %) of our patients were between 25 and 44 years old at the time of diagnosis. Intravenous drug use was the main route of HCV transmission (81.4 %). 149 (24.9 %) patients were infected with genotype 1, 6 (1 %) with genotype 2, 350 (58.5 %) with genotype 3 and 93 (15.5 %) with genotype 4. A changing pattern of HCV genotype prevalence was observed, with an increase in the relative proportion of genotype 1 and a decrease of genotypes 3 and 4 (figure 1 for all patients, figure 2 for females, and figure 3 for males). During the first 9 studied years (2002-2010), 3 was the predominant genotype with a percentage > 50 % yearly. The last 2 years (2012 and 2013) the percentage of genotype 1 was increased to 55.3 % and 53 % respectively.
Conclusion: This changed HCV genotype pattern might have direct impact on the disease outcome, the future therapeutic approaches and the health economics of the country.

Topic 12: Hepatitis C

No: 1736

Exposure safety analysis for asunaprevir and daclatasvir in dual combination in Japanese and non japanese subjects with hepatitis C virus infection

Phyllis Chan[1], Li Zhu[1], Timothy Eley[1], Marc Bifano[1], Eric Hughes[1], Mayu Osawa[2], Takayo Ueno[1], Frank Lacreta[1], Brenda Cirincione[1], Tushar Garimella[1], Malaz Abutarif[1]

Bristol-myers Squibb Bristol-myers Squibb Research and Development Lawrenceville, Nj-United States[1], Bristol-myers K.k. Bristol-myers Squibb Research and Development Tokyo-Japan[2]

Aim: The combination of daclatasvir (DCV) and asunaprevir (ASV) is approved in Japan for treatment of chronic HCV infection. This analysis characterized relationships between exposures and ALT, AST and total-bilirubin (Tbili) elevations.
Methods: Relationship between probability of on-treatment maximum grades 1/2 and 3/4 ALT, AST or Tbili elevations and model-predicted ASV Cavgss was previously described using ordinal logistic regression (OLR) models in 1413 subjects. The model was updated with additional data (N = 141) incorporating covariates for race and patient type. Sensitivity analysis was conducted to compare Japanese to the overall population.
Results: The observed incidence of grade 3/4 ALT and AST (< 4.5 %) was low during treatment at the approved doses. The base model for all endpoints was linear OLR models with positive slopes for ASV Cavgss. In final models for ALT and AST, ASV Cavgss was not statistically significant. Baseline values of ALT, AST and Tbili were the most significant predictors of on-treatment transaminase elevations. For Tbili, ASV Cavgss was statistically significant; however, observed incidence of grade 3/4 events was very low ($\sim$0.6 %). A higher rate of ALT (5 %) elevations in Japanese compared to non-Japanese (1.6 %) was predicted.
Conclusions: No significant relationships were observed between DCV exposures and safety events. A shallow relationship was observed between ASV exposures and incidence of transaminase elevations in the base but not in the final model. Differences between Japanese and non-Japanese in ALT elevations cannot be explained solely by exposures. Sensitivity analysis suggested applicability to allow for evaluation of Japanese subjects.

Topic 12: Hepatitis C

No: 1725

Next generation sequencing analysis of minor variants in ns5a and their impact on sustained virologic responses to daclatasvir plus asunaprevir

Fiona Mcphee[1], Fei Yu[1], Dennis Hernandez[1], Xin Huang[2], Kemin Zhou[2], Stefan Kirov[2], Saumya Pant[2], Paul Kayne[2]

Bristol-myers Squibb Discovery Virology Wallingford-United States[1], Bristol-myers Squibb Translational Technologies Hopewell-United States[2]

Aim: The combination daclatasvir (DCV) plus asunaprevir (ASV) is approved in Japan for treatment of HCV genotype (GT-)1b. Sustained virologic response (SVR) with DCV + ASV therapy is reduced in HCV patients harboring baseline NS5A resistance-associated variants (RAVs) to DCV (e.g. NS5A-L31 M/V, -Y93H). Next-generation sequencing (NGS) was used to determine whether baseline RAVs when present as minor variants impact SVR rates.
Methods: Baseline plasma samples from 222 prior non-responders and interferon-ineligible/intolerant patients infected with GT-1b who were subsequently treated with DCV (60-mg daily) + ASV (200-mg tablet or 100-mg capsule, twice daily) for 24 weeks in the Phase 3 clinical study AI447026 were prepared for NGS (Ion Torrent sensitivity cut-off $\geq$ 1 %).
Results: SVR was achieved in 99/116 (85 %) patients with baseline NS5A sequences analyzed to date. NS5A-L31F/I/M/V was detected in 9/116 (8 %) sequences at $\geq$ 1 % of the virus population: 7/9 (78 %) patients achieved SVR while 2/9 (22 %) patients did not; L31 M represented $\geq$98 % of the virus population in the 2 non-SVR12 patients. NS5A-Y93H was detected in 23/116 (20 %) sequences at $\geq$ 1 %; 4/12 (33 %) patients with Y93H representing > 20 % of the virus population achieved SVR and 8/11 (73 %) patients with Y93H representing 1-20 % of the virus population achieved SVR. In patients without Y93H at $\geq$ 1 %, 87/93 (94 %) achieved SVR. A complete analysis of all baseline samples will be presented.
Conclusion: In this interim analysis, SVR is not impacted when NS5A-L31F/IM/V is present at < 98 % of the virus population. The majority of patients with NS5A-Y93H at $\geq$1–20 % of the virus population achieve SVR.

Topic 12: Hepatitis C

No: 1710

Triple therapy of HCV management of infection or management of side effects

Birol Baysal[1], Yusuf Kayar[1], Mukaddes Tozlu[1], Maged Elshobaky[1], Ahmet Danalıoğlu[1], Orhan Kocaman[1], Ali Ince Tüzün[1], Kürşat Türkdoğan[1], Hakan Şentürk[1]

Bezmialem Vakif University, Faculty of Medicine Department of Gastroenterology Istanbul-Turkey[1]

Introduction: Adding either telaprevir (TPV) or boceprevir (BOC) to the standard dual therapy of chronic hepatitis C with Peg-IFN + ribavirin resulted in 10-15 % increase in sustained virological response. However, side effects of triple therapy lead to significant difficulties for patients and physicians.
Aim: To evaluate the side effects of triple therapy containing TPV or BOC and to compare both groups.
Methods: Study included 31 patients in TPV group (61.3 % female, age 57 $\pm$ 7 years) and 21 in BOC group (71.4 % female, mean 57 $\pm$ 8 years). Side effects were collected from clinical and laboratory findings.
Results: Of the patients who were cirrhotic initially, 3 developed severe side effects as following: Liver failure and hepatic encephalopathy (on BOC), a death because of intracerebral haemorrhage following a trauma (on BOC), an attack of transient ischemic attack (on TPV). Severe rash occurred in 2 patients at week 11 of TPV treatment. The therapy discontinuation rate due to side effects was 28.5 % in the TPV group and 12.9 % in the BOC group ($P = 0.16$).
Conclusions: Triple therapy with TPV very often results in anal discomfort and dermatological side effects. Cirrhotic patients should be carefully monitored for serious side effects. Although regimens containing protease inhibitors provide a 10-15 % increase in sustained virological response, their side effects that are difficult to manage overshadow their positive contribution.

Topic 12: Hepatitis C

No: 1247

Clinical characteristics efficacy and safety of HCV patients aged 70 years or older treated with pegylated interferon αand ribavirin

Seo Young Yang[1], Wonhyeong Park[1], Soo Hyun Yang[1], Do Young Kim[1], Woong Sun Yoo[1], Tae Gyoon Kim[1], Sung Hoon Kim[1]

Veterans Health Service Medical Center Internal Medicine Seoul-Korea, South[1]

Introduction: Age is frequently discussed as negative host factor to achieve a sustained virological response (SVR) to antiviral therapy of chronic hepatitis C. However, the information about clinical presentation and outcome of elderly HCV patients is limited. We performed this study to assess the impact of age on potential differences in clinical characteristics, efficacy and safety in elderly HCV patients.
Materials and methods: Clinical data of 51 "elderly" (>70 years old) and 116 "younger" (<70 years old) HCV patients treated at a single center between 2006 and 2012 were collected and compared using various parameters.
Results: Compared with younger patients, the elderly patients had a higher proportion of cirrhosis (72.5 % vs, 57.7 %, $P < 0.001$), less HCV RNA level, More co-mobidity, less liver function and more HBV co-infection. There was no significant difference between the two groups in gender and received a prior course of HCV therapy. Overall, SVR was 74.5 and 75 %, respectively, in elderly and young patients with HCV. SVR rates by genotype were similar [16/25 (64 %) vs 42/64 (65 %) Genotype 1 ($P = 0.56$), 22/26 (84 %) vs 45/52 (86 %) non-genotype 1 ($P = 0.63$)]. The adverse event was not significantly difference between the two groups but also leading to cessation of treatment were comparable [2/51 (4 %) vs 3/116 (3 %) $P = 0.66$].
Conclusions: Characteristics that distinguish elderly from younger HCV patients included more cirrhosis, less HCV RNA level, more extrahepatic manifestation, less liver function and more HBV co-infection. significant differences were observed in clinical characteristics, but the overall SVR and adverse events were not significantly different.

Topic 12: Hepatitis C

No: 1471

The first safety report of high aged patients over 76 years old administered daclatasvir and asnaprevir in single center experience in Japan

Masato Imai[1], Taro Nakamichi[2], Ryota Koyanagi[2], Yuto Hirashima[2], Kazuhiro Aoki[1], Hidetoshi Kumano[1], Masanobu Tanaka[1], Toshiaki Komori[1], Masanori Sawa[1], Masakatsu Sunagawa[1]

Utsunomiya Memorial Hospital Gi Surgery Utsunomiya-Japan[1], Utsunomiya Memorial Hospital Gastroenterology Utsunomiya-Japan[2]

Background: The first all-oral hepatitis C virus (HCV) treatment, combination daclatasvir (DCV: NS5A inhibitor) and asunaprevir (ASV: NS3 protease inhibitor), was going on the Japanese market in September 2nd, 2014 for the patients of genotype 1, interferon ineligible or intolerant, and non-responder to interferon-based therapy. Phase III trial in Japan (AI447-017) demonstrating the therapy is well-tolerated to elder patients. However the study only included under 75 years-old (y.o.) patients. Because half million of HCV patients are over 76 y.o. in Japan, we need safety profile of the combination therapy in over aged patients.
Methods: Resistance-associated variants (RAVs) on NS5A and NS3 of 20 HCV patients (over 76 y.o.) were verified using deep sequencing method. The patients with no RAVs received DCV/ASV. Treatment-emergent adverse events (AE) were confirmed.
Results: Pre-existing RAVs were detected in 25 % of over aged patients (all had Y93H variant). 2 patients (no RAVs) dropped out because existing HCC and cerebral haemorrhage. 13 patients received DCV/ASV. The age range of the treated patients was 75 to 86 (average 81). 9 patients showed rapid viral response and remaining were under 4 weeks medication. 3 patients had AE (one had fatigue grade1 and alanine aminotransferase (ALT) increased grade1, one had gastritis grade1 and blood bilirubin increased grade1, another had ALT increased grade2). There was no severe AE.
Conclusion: Combination DCV and ASV might be well tolerated and have no significant side effect regardless of high aged patients over 76 y.o. in Japan.

Topic 12: Hepatitis C

No: 1735

Exposure efficacy analysis for daclatasvir and asunaprevir in dual combination in non Japanese and Japanese subjects with genotype 1b hepatitis C virus infection

Li Zhu[1], Phyllis Chan[1], Timothy Eley[1], Marc Bifano[1], Mayu Osawa[1], Takayo Ueno[2], Eric Hughes[1], Malaz Abutarif[1], Brenda Cirincione[1], Frank Lacreta[1], Tushar Garimella[1]

Bristol-myers Squibb Research and Development Research and Development Lawrenceville, Nj-United States[1], Bristol-myers K. K. Research and Development Tokyo-Japan[2]

Aim: The combination of daclatasvir (DCV) and asunaprevir (ASV) is approved in Japan for the treatment of chronic HCV infection. The current analysis characterized the relationship between exposures of DCV and ASV and sustained virological response (SVR12) as well as treatment-naive status and Japanese race as predictors of response
Methods: The relationship between the probability of achieving SVR12 and model predicted Cavgss for ASV and DCV (E-R) was previously described using a logistic regression (LR) model with data from 4 studies in GT-1b subjects (N = 947). The existing model was updated with additional data (N = 141) and the covariates for race and patient type were incorporated. Sensitivity analysis was conducted with data from Japanese subjects only to compare the E-R relationship with overall data.
Results: The base E-R model was a linear LR model with intercept, slopes for DCV and ASV Cavgss, and interaction between DCV and ASV. In the final model only baseline resistance mutations (BRMs) Y93H and L31 M/V were the significant predictors of lower SVR12. Unlike the slope for DCV Cavgss, the slope for ASV Cavgss was not statistically significant. The additional covariates of treatment naive subjects and Japanese race predicted slightly higher SVR12 rates (approximately 93 %) compared to reference non-Japanese non-responder subjects (88 %).
Conclusions: The E-R model demonstrated a shallow relationship between DCV exposure and SVR12 and no or flat relationship between ASV exposure and SVR12. Presence of the NS5A BRMs were significant predictors of lower SVR12. Sensitivity analysis suggested applicability to allow for evaluation of Japanese subjects.

Topic 12: Hepatitis C

No: 1296

The disease profiles and outcome of hepatitis C infection a single centre experience

Nooraliza Mutalib[1], Soek Siam Tan[1], Haniza Omar[1], Hamiza Shahar[1]

Selayang Hospital Hepatology Batu Caves-Malaysia[1]

Aim: To describe the clinical profiles and outcome of our hepatitis C (HCV) patients.
Method: A cross-sectional study of consecutive HCV patients attending out/in-patient facilities from 1st January until 31st March 2012 and followed up until December 2013 was done retrospectively.
Results: A total of 272 HCV patients were studied, 74.6 % male and mean age of 47.7 + 11.8 years. The top two risk factors were intravenous drugs use (34.9 %) and blood products transfusion (30.5 %). At baseline, cirrhosis was diagnosed in 37.5 % with mean Child-Turcotte-Pugh Score (CTPS) 6.8 + 2.3 and MELD 12.7 + 5.8. The two commonest cirrhotic complications were ascites (30.3 %) and hepatocellular carcinoma (24.5 %). HCV genotypes (GT) distribution (n = 162) were GT3 (57.4 %), GT1 (41.3 %), GT2 (0.6 %) and GT4 (0.6 %). Liver biopsies were performed in 86 patients and the Histology Activity Index fibrosis scores were F0-F2 (51.2 %), F3-F4 (39.5 %) and F5-F6 (9.3 %). Elastrography were performed in 123 patients, the mean score was 14.96 + 12.8 kPa. During the 2 years follow-up, 206 remained under our care. of these, 13.1 % died and 9.7 % developed new complications from cirrhosis. Age > 50 years, cirrhosis, history of hospital admission were significantly associated with increased mortality ($P = 0.001$). Pegylated interferon and ribavirin were initiated in 126 patients and sustained virological response (SVR) rates were 72.9 % for GT3 and 35.1 % for GT1. The reasons for non-treatment (n = 146) were: patient refusal (n = 12), platelet < 80,000 (n = 21), decompensated cirrhosis or CTPS score > 8 (n = 36), psychiatric co-morbidities (n = 8), medical co-morbidities and others (n = 45).
Conclusion: Our HCV patients have severe liver disease with 2 years mortality of 13.3 %. The SVR for GT1 patients are poor and many were ineligible for interferon therapy.

Topic 12: Hepatitis C

No: 1848

Population pharmacokinetic analysis of ledipasvir sofosbuvir fixed dose combination tablet in Japanese subjects with chronic genotype 1 HCV infection

Kimberly Garrison[1], Bing Gao[2], Phil Pang[3], Steven Knox[3], Anita Mathias[1]

Gilead Sciences, Inc. Clinical Pharmacology Foster City-United States[1], Gilead Sciences, Inc. Biostatistics Foster City-United States[2], Gilead Sciences, Inc. Clinical Research Foster City-United States[3]

Background: Administration of ledipasvir (LDV)/sofosbuvir (SOF) fixed-dose combination tablet once-daily for 12 weeks achieved 100 percent SVR12 rates in treatment-naïve and treatment-experienced Japanese patients with chronic genotype 1 HCV infection (Phase 3: GS-US-337-0113). Pharmacokinetic (PK) data were collected in the study to examine the relationship between demographic variables and exposure–response and to compare results to studies conducted across various regions
Methods: Treatment-naïve (166) and treatment-experienced (175) subjects were enrolled and received LDV/SOF 90 mg/400 mg FDC either with or without ribavirin for 12 weeks. Intensive and sparse samples were collected to evaluate the pharmacokinetics of LDV and SOF (including metabolites) in Japanese subjects. Individual PK parameters were estimated using Population PK models for LDV, SOF, and GS-331007. The effect of demographic variables on LDV, SOF, and GS-331007 exposure was evaluated.
Results: Table 1 presents steady-state exposure for LDV, SOF, and GS-331007. Compared to historical data (overseas Phase 2/3 LDV/SOF population), LDV exposure was modestly higher in Japanese subjects; this increase was not considered clinically relevant. Sofosbuvir and GS-331007 exposures were similar between the two populations. Within the Japanese study population, no clinically relevant differences in the PK of LDV, SOF, or GS-331007 based on CLcr, age, sex, BMI, cirrhosis, prior treatments, or RBV were identified.
Conclusion: SOF and GS-331007 exposure was similar and LDV exposure was modestly higher in Japanese subjects compared to historical data. Based on safety, efficacy, and PK, these data support the use of LDV/SOF 90 mg/400 mg FDC for the treatment of GT1 HCV infection in Japanese patients.

Topic 12: Hepatitis C

No: 1840

Incidence rate of hepatocellular carcinoma in chronic hepatitis C patients who achieved sustained virological response

Keol Lee[1], Dong Hyun Sinn[1], Geum-youn Gwak[1], Young-han Paik[1], Moon Seok Choi[1], Joon Hyeok Lee[1], Kwang Cheol Koh[1], Seung Woon Paik[1], Byung Chul Yoo[1]

Samsung Medical Center Medicine Seoul-Korea, South[1]

Background: For chronic hepatitis C (CHC) patients who achieved sustained virological response (SVR), controversy exists whether patients need regular hepatocellular carcinoma (HCC).
Methods: A total of 598 CHC patients who achieved SVR between Jan 1999 to Dec. 2010 were followed up for a median of 5.1 years (range: 0.1 ~ 14.3 years). Annual incidence rate of HCC was analyzed.
Results: HCC was diagnosed in 8 patients and the median time to development of HCC was 3.8 years after achieving SVR (range: 2.0 ~ 8.9 years). The cumulative incidence of HCC was 0.2, 1.3 and 4.7 % at 3-years, 5-years and 10-years, respectively. Five factors were associated with the development of HCC; platelet levels at SVR ($P < 0.001$), α-fetoprotein levels at SVR ($P < 0.001$), aspartate aminotransferase to platelet ratio index ($P < 0.001$) at SVR, diabetes mellitus ($P = 0.003$), and cirrhotic configuration on ultrasonography ($P < 0.001$). The 5-years cumulative incidence rate of HCC was 5.2, 4.5, 14.1, 5.3 and 19.6 % for patients with thrombocytopenia, AFP ≥ 5 ng/ml, APRI ≥ 0.8, diabetes mellitus, and cirrhotic configuration on ultrasonography, respectively, and was 0, 1.4 and 11.6 % for patients without any risk factor, 1 – 2 risk factors, and ≥3 risk factors, respectively ($P < 0.001$).
Conclusion: The risk of HCC in CHC patients who achieved SVR was not low in patients with risk factors, indicating HCC surveillance is required even after achieving SVR.

Topic 12: Hepatitis C

No: 1248

Association of hepatitis C virus infection with diabetes mellitus focus on whether exposed to agent orange

Soo Hyun Yang[1], Wonhyeong Park[1], Seo Young Yang[1], Do Young Kim[1], Woong Sun Yoo[1], Tae Gyoon Kim[1], Sung Hoon Kim[1]

Veterans Health Service Medical Center Internal Medicine Seoul-Korea, South[1]

Introduction: Several studies from different parts of the world have found that 13 to 33 % of patients with HCV have associated diabetes mellitus (DM). Agent Orange (AO) is also reported to cause DM. However, a correlation between DM and AO in HCV infection is not yet proven. The aim of this study was to evaluate the association between DM and AO who were diagnosed with HCV infection. Additionally, we investigate the prevalence of DM and other metabolic manifestation among these patients.
Materials and methods: The study included newly diagnosed case of HCV infection recruited between 2005 and 2012. A retrospective, case–control study was performed.
Results: Among 402 patients with HCV infection, 274 patients had been exposed to AO. During observed period, diabetes was detected in 56 (43.7 %) who had been exposed to AO cases and in 72 (26.2 %) who had not been exposed to AO control subjects (odds ratio [OR], 2.18; 95 % confidence interval [CI]: 1.53-4.15). The diabetic patients in the HCV who had been exposed AO group (n = 56) presented with significantly more advanced liver disease, abnormal liver function and high HCV RNA level than those who had not been exposed AO group (n = 72). Ischemic heart disease also significantly increased in HCV who had been exposed AO group. But survival and HCC occurrence did not show difference whether exposed to AO.
Conclusions: Agent Orange may have a significant correlation with diabetes in HCV infection. Cirrhosis, abnormal liver function and high HCV RNA level are more common in the HCV infected diabetic patients who had been exposed AO.

Topic 12: Hepatitis C

No: 1785

Levels of micro RNA 122 micro RNA 199a micro rna 196 micro rna 491 and micro rna 16 and antiviral therapy in chronic HCV infection

Olga Tarasova[1], Pavel Ogurtsov[1], Natalia Mazurchik[1], Arslan Niyazov[1], Aleksandr Kochetov[1]

People's Friendship University of Russia Hospital Therapy Moscow-Russia[1]

Aim: To evaluate the levels of miRNA-122, miRNA-16, miRNA-199a, miRNA-196 and miRNA-491 in non-cirrhotic hepatitis C-positive patients and patients after antiviral therapy.
Materials and methods: A single quantitative testing of miRNA-122, miRNA-16, miRNA-199a, miRNA-196 and miRNA-491 was performed by use of real-time PCR in 40 patients.
Results: In 10 patients with sustained virological response (SVR) after antiviral therapy the levels of miRNA-122 was $1.6 \pm 0.5 \times 105$ copies/ml (median 1.0×10^5, copies/ml), miRNA-16-$2.6 \pm 2.0 \times 10^6$, copies/ml (median 6.7×10^5copies/ml), miRNA 199a $-1.9 \pm 1.5 \times 10^5$copies/ml (median 2.1×10^4, copies/ml), miRNA 491–$2.8 \pm 1.2 \times 10^3$, copies/ml (median 1.4×10^3, copies/ml). In 10 healthy volunteers the levels of miRNA-122 was $8.1 \pm 1.5 \times 10^4$copies/ml (median 6,9x104 copies/ml), miRNA-16 $-7.7 \pm 1.5 \times 10^5$copies/ml (median 5,8x105copies/ml), miRNA 199a $-1.5 \pm 0.4 \times 10^4$copies/ml (median 1.4×10^4copies/ml), miRNA 491 $-2.0 \pm 0.8 \times 10^3$copies/ml (median 1.6×10^3copies/ml). In SVR- group (10 patients): miRNA-122 $-7.4 \pm 3.3 \times 10^5$copies/ml (median $3,5 \times 105$copies/ml), miRNA-16 - $1,7 \pm 0,4 \times 106$copies/ml (median $1,3 \times 106$copies/ml), miRNA 199a $-2,3 \pm 0,7 \times 104$copies/ml (median $1,7 \times 104$copies/ml), miRNA 491 $-4,2 \pm 1,7 \times 103$ copies/ml (median $2,3 \times 103$copies/ml). In 10 patients with chronic hepatitis C miRNA-122 was $5,4 \pm 1,7 \times 105$copies/ml (median $4,4 \times 105$ copies/ml), miRNA-16 - $2,9 \pm 1,8 \times 106$ copies/ml (median $1,1 \times 106$ copies/ml), miRNA 199a $-2,7 \pm 0,8 \times 10^4$, copies/ml (median 2.1×10^4, copies/ml), miRNA 491 $-2,1 \pm 0,5 \times 10^3$, copies/ml (median 1.5×10^3, copies/ml). The level of miRNA-196 was below the detection level in all groups. In comparison of SVR + patients and SVR- patients there was reviled a significant difference in the levels of miRNA-122 ($P = 0.0039$) and miRNA-16 ($P = 0.043$). In concurrent groups SVR- and healthy control there was a difference between quantitative miRNA-122 ($P = 0.0001$) and miRNA-16 ($P = 0.0052$).
Conclusion: Low level of miRNA-122 and miRNA-16 can be a predictor of response to antiviral therapy in chronic HCV-infection.

Topic 12: Hepatitis C

No: 1071

Combined (imaging and seric) noninvasive score for predicting significant liver fibrosis in chronic hepatitis C

George Sebastian Gherlan[1], Cristian Szabo[2], Cristina Voinea[2], Petre Iacob Calistru[1]

"dr. Victor Babes" Center For Diagnostics and Treatment Infectious Diseases Bucharest-Romania[1], "dr. Victor Babes" Center For Diagnostics and Treatment Laboratory Bucharest-Romania[2]

Background: In order to make correct therapeutic and monitoring options in chronic hepatitis C, detection of significant fibrosis ($F \geq 2$) and cirrhosis are the most important landmarks. For cirrhosis most of the validated noninvasive methods are proved to be reliable. We aimed to combine two types of noninvasive methods (serologic and imaging) in one score to obtain a better performance in detecting/excluding significant fibrosis.
Methods: We prospectively collected and then analyzed the data of 147 patients with chronic hepatitis C who underwent liver biopsy, Fibromax, Fibroscan and hematology panel in the same week. We analyzed separately each component of Fibromax, age, sex, BMI, elastography and hematology panel components for direct correlations with the result of liver biopsy for fibrosis. Then we analyzed each of the correlated factors by their AUROC for $F \geq 2$. We obtained a score by binary logistic regression.
Results: We found ALT, AST, GGT, alfa2macroglobulin, haptoglobin, total bilirubin, glycaemia, total cholesterol, platelets, age and elastography to have the best and statistically significant AUROCs for $F \geq 2$ (0.664, 0.753, 0.707, 0.764, 0.650, 0.643, 0.664, 0.662, 0.687, 0.657, 0.880 respectively). After regression an algorithm for predicting significant fibrosis based on liver stiffness, ALT, AST, Bilirubin, cholesterol and apolipoprotein A1 was obtained. This formula had an AUROC for determining $F \geq 2$ in our group of 0.956, CI 95 % = 0.920 – 0.992, $p < 0.001$.
This score has to be verified in future trials in independent groups.
Conclusion: We found a combined score that performs better in our group than Fibroscan or Fibrotest (AUROCs of 0.880 respectively 0.799) in identifying significant fibrosis.

Topic 12: Hepatitis C

No: 1132

Factors influencing response of chronic hepatitis C to peginterferon and ribavirin therapy in Indian patients

Gautam Ray[1]

B.r.singh Hospital Medicine Kolkata-India[1]

Background: Though peginterferon and ribavirin remains the SOC in patients of chronic hepatitis C in India, the scenario might change with introduction of oral drugs. So better delineation of factors influencing outcome of such treatment is needed for optimal drug use.
Methods: 50 eligible patients of chronic hepatitis C (antiHCV and HCV RNA positive > 6 months) attending the liver clinic from June 2007–June 2013 underwent therapy with peginterferon & ribavirin for standard duration in standard dosage according to genotype and body weight. All patients were CTP class A, 13 had compensated cirrhosis based on biochemical, radiological, endoscopic and/or histological investigations. Patient with decompensation were excluded. Factors (affecting SVR) studied were age, sex, BMI, presence of diabetes mellitus (DM), alcohol use, viral load and genotype, presence of cirrhosis or risk factors for acquiring HCV and IL28B.
Results: Mean age 48.5 + 14.64 (range 7–78) years, 27 males, median viral load 84,500 (range 3000–4 × 109) copies/ml, DM 17, risk factors 21, alcohol intake 7 patients. Overall EVR 46 (92 %), EOTR 43 (86 %), SVR 32 (64 %). Genotypes (SVR %): G1 = 9 (6, 66.7 %) G2 = 1(1, 100) G3 = 37 (24, 64.9 %) G4 = 2 (1, 50 %) G6 = 1 (0), IL28B CC 17/20, TT 3/20. Significant predictors of SVR on univariate analysis were age, cirrhosis, absence of DM, EVR and EOTR but on multivariate analysis they were (with odds ratio and confidence interval) age 1.13 (1.02–1.25), cirrhosis -0.09(0.01-0.7), absence of DM 11.5 (1.09-121.44).
Conclusions: SOC for hepatitis C showed moderate overall response with definite predictors.

Topic 12: Hepatitis C

No: 1968

Hematologic parameters in therapy with peginterferone alfa 2b of hepatitis C subjects during buprenorphine substitution for heroin addiction (one year results of a single center in Turkey)

Memduh Sahin[1], Ilker Sen[2]

Mersin City Hospital Gastroenterology Mersin-Turkey[1], Mersin Toros Hospital Gastroenterology Mersin-Turkey[2]

Aim and methods: 34 male patients from south region of Turkey with a diagnosis of Hepatitis C was accepted to the study. 33 of them treated with Pegylated interferon alfa -2b (1.5 mg/kg) and ribavirin. They also take opioid substitution treatment during this time interval. The diagnostic Hepatits C RNA, genotype, hemoglobin, midplatelet volume (MPV) and red cell distribution width (RDW) was recorded at acceptance. 20 patients parameters can be evaluated at the third month of the treatment period.
Results: During the patient acceptance there was no woman subjects with a history of opioid injection (%100 male). The patients diagnosed with Hepatitis C was respectively in a younger age group. (min: 17, max: 42; mean: 26.1). Genotype 1a was the most prevalent hepatitis C variant among patients with opioid abuse (15 patients % 44.1). 13 patiens had genotype 3 (%38,2). There was 1 patients from each genotype 2(%2.9) and 1b(%2.9). 3 patients had a variant of genotype 2 (%8,8). Because of the low hepatitis C concentration one patients genotype couldn't be detected. Mean hemoglobin value for the pretreatment and the third month of the therapy was in order 14 mg/dl and 12.9 mg/dl. There was no statistically difference of pretreatment and third month values according to MPV ($P = 0.580$) and RDW ($P = 0.460$) recordings. When we compare the diagnostic HCV RNA value of genotype 1.4 (bad prognosis) and genotype 2.3 (good prognosis) groups there was statistically significant different between two genotype groups ($P = 0.027$).

Topic 12: Hepatitis C

No: 1519

Hepatitis C virus core protein up regulates the pluripotency homeobox gene nanog expression by PI3 K AKT signaling in HepG2 cells

Jiajia Zhou[1], Zhe Meng[1], Xiaogeng Deng[1], Rufu Chen[1]

Sun Yat-sen Memorial Hospital Department of Surgery Guangzhou-China[1]

Hepatitis C virus (HCV) Core protein plays an important role in the development of hepatocellular carcinoma (HCC), the molecular mechanism is still controversial. NANOG is a homeodomain-containing transcription factor that functions to maintain the pluripotency and self-renewal of embryonic stem cells. Aberrant expression of NANOG has been observed to be frequently altered in human solid tumors including HCC implicated as an oncogene. However, the relationship between Core and NANOG has not been clearly clarified. In this study, we found that HCV Core induces the up-regulation of NANOG expression in human hepatoma HepG2 cell line. The effect of Core-induced NANOG expression was abolished by RNA interference-mediated silencing of Core. Furthermore, Core-induced NANOG expression was accompanied by enforced expression of phosphorylated Akt protein and was attenuated by inhibition of Akt phosphorylation via the treatment of Phosphotidylinsitol-3-Kinase (PI3 K) inhibitor LY294002. However, ChIP experiment showed that phosphorylated Akt protein cannot bind to the promoter of NANOG, indicating Akt might regulate NANOG expression not in a direct pathway. In addition, Core-induced NANOG expression resulted in enhanced cell growth and cell cycle progression. Knockdown of NANOG blocked the cell cycle at the G0/G1 phases and inhibited the expression of cyclin D1 in Core-expressing cells. Taken together, our findings proposed a new mechanism by which HCV Core regulates NANOG expression via PI3 K/Akt signaling pathway, and also provided a new insight into the mechanism of hepatocarcinogenesis by HCV infection.

Topic 12: Hepatitis C

No: 1169

Correlation between serum hyaluronic acid and steatosis non alcoholic steatohepatitis and fibrosis in patients with chronic HCV infection

Mohamad Helal[1], Hasan Mahmoud[1], Ghada Osman[2], Ali Gweil[3], Hamdy Moustafa[4]

Lecturer Tropical Medicine and Gastroenterology Qena-Egypt[1], Lecturer Pathology Qena-Egypt[2], Ass. Prof. Tropical Medicine and Gastroenterology Qena-Egypt[3], Professor Tropical Medicine and Gastroenterology Al-azhar-Assiut-Egypt[4]

Background: Hyaluronic acid (HA) is an attractive alternative marker for noninvasive diagnosis of liver fibrosis instead of liver biopsy for both patients and physicians. We aimed to assess the role of HA not only for diagnosis of liver fibrosis but also for diagnosing the progression of steatosis to steatohepatitis (SH) in Chronic HCV patients.
Patients and methods: Ninety patients with chronic HCV infection; 77 (85.6 %) males and 13 (14.4 %) females, were included. Blood samples were collected for routine laboratory investigations, liver function tests and serum HA measurement. Liver biopsy was taken for histopathological examination.
Results: Steatosis only was found in 37 patients (41 %), fibrosis in 29 patients (32.2 %) and SH in 51 patients (56.6 %). Mean serum HA for all patients was 86.4 ± 48.2 ng/L. HA was significantly higher in patients with fibrosis (95.6 ± 53 vs 54.5 ± 3.5) and SH (88.7 ± 52 vs 49.9 ± 12) than those without (P value = 0.001 and 0.001 respectively). HA was significantly higher in patients with advanced fibrosis, SH and steatosis than those with mild degrees (P value = 0.000, 0.001 and 0.01 respectively). Positive correlations were found between serum HA and the degree of fibrosis, SH and steatosis (P value = 0.000) and r = + 0.758, 0.701 and 0.727 respectively). Mean HA Cut off value for diagnosis of fibrosis and SH was 70 and 60 ng/L respectively; with significant Sensitivity, Specificity, PPV, NPV and Accuracy.
Conclusions: Serum HA is a good noninvasive marker for diagnosis of fibrosis and steatohepatitis in patients with chronic HCV infection.

Topic 12: Hepatitis C

No: 1457

Cost effectiveness of pegylated inteferon and ribavirin combination in treating genotype 1 hepatitis C patients in Singapore

Victoria Sze Min Ekstrom[1], Mee Ling Yee[2], Wan Cheng Chow[1], Rajneesh Kumar[1]

Singapore General Hospital Gastroenterology & Hepatology Singapore-Singapore[1], Singapore General Hospital Pharmacy Singapore-Singapore[2]

Introduction: Genotype 1 (GT1) Hepatitis C (HCV) has poor response to treatment with Interferon and Ribavirin. In Singapore, response to treatment is unknown. The cost effectiveness of newer medications has not been assessed.
Aims: To determine response to treatment in GT1 with Pegylated interferon and Ribavirin (PR), cost evaluation of PR including the use of erythropoietin.
Methods: Retrospective analysis of HCV GT1 patients was done.
Results: Data of 61 patients treated with PR from January 2003 to December 2014 was available. Mean age of patients was 43.15 ± 12 years 83.6 % were males. Cirrhosis was seen in 4.9 %. 8.2 % had HCV RNA > 4,00,000 IU. Fatty liver was seen in 60.0 % on ultrasound. Overall sustained viral response (SVR) was 73.8 % and in patients with HCV RNA > 4,00,000 IU, it was 60 %. 3 patients had early discontinuation due to side effects. 16.4 % required erythropoietin and one patient required hospitalization for blood transfusion. The estimated cost of medication was S$2,583,169.23 for 100 patients treated with a success rate of 73 %, compared to an interferon-free regimen which is S$14,000,000 with a success rate of 95 %. The IL28B polymorphism of these patients is being studied.
Conclusion: The Singaporean population with GT1 has a better response to treatment compared to the western population and the use of newer medications can be reserved for patients predicted to have a poor response. IL28B polymorphism analysis can further predict response and limit the use of expensive medication. However, the side effects of PR is still significant.

Topic 12: Hepatitis C

No: 1318

Diabetes mellitus is more commonly associated with il28b non c c genotype than in c c genotype in patients with HCV

Varun Gupta[1], Ashish Kumar[1], Praveen Sharma[1], Vikas Singla[1], Anil Arora[1]

Sir Ganga Ram Hospital Gastroenterology and Hepatology New Delhi-India[1]

Objective: IL28b polymorphism is an important predictor for HCV response to antiviral therapy. However, whether IL28b genotypes also influence other non-treatment related clinical parameters is not clear.
Methods: In this retrospective analysis, patients with HCV related chronic liver disease attending Sir Ganga Ram Hospital, New Delhi, from 2012 to 2014 were analyzed. The SNPs rs12979860 (IL28B) was investigated by RT-PCR and IL28b genotypes were correlated with various clinical parameters.
Results: A total of 115 patients were included in the study (median age 48, range 15-76 years; 70 % males). The most common IL28b genotype was C/C 53 % (61/115), while rest 47 % were non-C/C [C/T 42 % (48/115) and T/T 5 % (6/115)]. Overall, 43/115 (37 %) patients had chronic hepatitis, while rest 72/115 (63 %) were cirrhotic. The IL28b genotype distribution was similar in chronic hepatitis and cirrhotic groups. Clinical and laboratory parameters like Hb, WBC, platelets, bilirubin, AST, ALT, and albumin were similar in C/C and non-C/C genotypes. Diabetes mellitus was found in 22 % (25/115) of patients. Patients with non-C/C genotype had significantly higher prevalence of diabetes mellitus than patients with C/C genotype (31 % [17/54] versus 13 % [8/61]; $P = 0.023$).
Conclusion: Diabetes Mellitus was found to be more commonly associated with IL28b non-C/C genotype than in C/C genotype in patients with HCV. Since insulin resistance is more common in carriers of the T allele of SNP rs12979860 than in CC homozygotes, this may explain higher prevalence of diabetes in non-C/C genotypes. We recommend doing IL28b in HCV patients to determine their likelihood of developing diabetes mellitus.

Topic 12: Hepatitis C

No: 2078

The effect of insulin resistance on eRVR in chronic hepatitis C patients under treatment with teleprevir treatment

Firdevs Topal[1], Elif Saritaş Yüksel[1], Belkis Ünsal[1]

Gastro Gastro Izmir-Turkey[1]

Extended rapid virologic response (eRVR), defined as an undetectable serum hepatitis C virus (HCV) RNA level at the 4th and 12th weeks of the treatment, predicts sustained virologic response (SVR). Reasons dependent to the host such as insulin resistance, advanced fibrosis, IL28B CT, IL28B TT polymorphisms and obesity cause lower sustained virologic response (SVR) rates in the combination HCV treatment with interferon and ribavirin. We have investigated if insulin resistance has a negative impact on eRVR and consequently SVR in HCV patients under triple treatment with Telaprevir 28

patients, who were treated with triple treatment consisting telaprevir, pegylated interferon alpha and ribavirin, were enrolled in the study. Three patients were excluded because they had diabetes mellitus. Mean age was 55, female/male ratio was 15/10, mean HCVRNA level was 106. All the patients were infected with genotype 1 HCV. Insulin resistance was calculated as HOMA-IR = fasting blood glucose(mmol/l) × fasting insulin(mU/l)/22,5. eRVR was achieved in 18 patients out of 25 patients. Eleven patients with eRVR did not have insulin resistance while 7 of the eRVR(+) patients had insulin resistance. On the contrary, 4 out of 7 patients without eRVR had insulin resistance. There is not a statistical difference between insulin resistance ratios in the eRVR(+) and eRVR (-) groups ($P = 0.9$).

In conclusion, eventhough insulin resistance seems to have a negative impact on SVR in interferon-ribavirin combination treatment, it is not effective on eRVR in triple treatment with Telaprevir.

Topic 12: Hepatitis C

No: 1123

Hepatitis C virus infection and risk of lymphoma whether exposed to agent orange

Wonhyeong Park[1], Soo Hyun Yang[1], Seo Young Yang[1], Tae Gyoon Kim[1], Woong Sun Yoo[1], Do Young Kim[1], Tae Kyu Lim[1]

Veterans Heath Service Medical Center Internal Medicine Seoul-Korea, South[1]

Introduction: Increasing evidence emerge a role of Hepatitis C virus (HCV) infection in the etiology of malignant lymphoma. Agent Orange is also reported to cause malignant lymphoma. However, a correlation between HCV and Agent Orange in lymphoma is not yet proven. The aim of this study was to investigate the association between HCV infection and Agent Orange who were diagnosed with lymphoma.
Materials and methods: The study included newly diagnosed case of any lymphoid malignancy recruited between 2005 to 2012. A retrospective, case–control study was performed.
Results: Among 546 patients with lymphoma, 202 patients had been exposed to Agent Orange. HCV infection was detected in 13 (6.5 %) who had been exposed to Agent Orange cases and in 8 (3.4 %) who had not been exposed to Agent Orange control subjects (odds ratio [OR], 2.32; 95 % confidence interval [CI]: 1.53-4.15). In subtype analyses, HCV prevalence was associated with diffuse large B-cell lymphoma (OR, 3.56; 95 % CI: 2.13-5.94) but not with T-cell lymphoma, chronic lymphocytic leukemia follicular, or Hodgkin's lymphoma. HCV infected person who had been exposed Agent Orange group (n = 13) presented with significantly more advanced liver disease and high HCV RNA level than those who had not been exposed Agent Orange group (n = 8).
Conclusions: Agent Orange may have a significant correlation with HCV infection in malignant lymphoma and establish a specific role in the diffuse large B-cell lymphoma. Advanced liver disease and high HCV RNA level are more common in lymphoma who had been exposed Agent Orange.

Topic 12: Hepatitis C

No: 1804

Prognostic value of serum leptin/adiponectin ratio in patients with chronic hepatitis C virus infection

Fathy Elghamry[1], Yusuf Nassar[1], Mostafa Sabrah[1], Mohamed Alboraie[1], Ahmad Fathy[2]

Al-azhar University Department Internal Medicine Cairo-Egypt[1], Al-azhar University Department of Clinical Pathology Cairo-Egypt[2]

Background/aim: There is an increasing interest in the role of Leptin and adiponectin in development of hepatic steatosis and fibrosis in patients with non-alcoholic fatty liver disease and chronic hepatitis C virus (HCV) infection. We aimed at evaluating the utility of serum leptin/adiponectin ratio in predicting disease progression in chronic HCV patients.
Methods: Thirty chronic HCV patients and 10 healthy controls were enrolled. They were subjected to: Complete blood count, blood glucose, AST, ALT, prothrombin activity, serum proteins, albumin, total bilirubin, direct bilirubin, alkaline phosphatase, serum urea, creatinine, HCV-Ab; HBV-sAg, thyroid functions tests, serum leptin, serum adiponectin, leptin/adiponectin ratio, abdominal ultrasound and liver biopsy for HCV patients. Patients were classified according to Child Turcotte Pugh (CTP) classification into three groups A, B and C.
Results: Univariate analysis showed that leptin, Adeponectin and leptin/adeponectin ratio were correlating to CTP class and fibrosis stage in HCV patients. Also there were significant correlations between: albumin, ALT/AST ratio, body mass index, platelet count, prothrombin time and total bilirubin with CPT class in HCV patients. Multivariate analysis was used to formulate a collective score "Factor Score" to predict CTP class. Factor Score was able to differentiate different CTP classes A, B and C. Mean values of Factor Score were 0.682, −0.315, −1.291 and 0.925 for CTP class A, B, C and control group respectively.
Conclusions: Leptin/adeponectin ratio is a good predictor of disease progression in HCV patients. Factor Score is a useful new score for prediction of CPT class in HCV patients.

Topic 12: Hepatitis C

No: 1828

A chronic hepatitis C patient presenting atrioventricular bloc while receiving pegylated interferon and clinical approach

Selma Ilkay Sahin[1], Yusuf Onlen[1], Tayibe Bal[1], Rasit Tanircan[2], Sabahattin Ocak[1], Omer Faruk Kokoglu[1]

Mustafa Kemal University School of Medicine Infectous Diseases and Clinical Microbiology Hatay-Turkey[1], Mustafa Kemal University School of Medicine Cardiology Hatay-Turkey[2]

Aim: A chronic hepatitis C patient who resulted with atrioventricular (AV) bloc while taking pegylated interferon therapy is presented. By this case, it is aimed to point out this rare complication.
Case: A 50 years old female patient was administered boceprevir +ribavirin +pegylated interferon alfa-2b 100 mcg therapy at December 2013. The preliminary laboratory tests were at normal ranges. Physical examination was normal and the anamnesis revealed no previous cardiac pathology. By the 31st week of therapy the patient was appealed with palpitation. In electrocardiography of the patient; PR elongation and a first degree AV bloc was determined. Due to 1st degree AV bloc the pegylated interferon therapy dose reduced to 80 mcg. The echocardiography of the patient was normal. After the dose reduction, the patient was hemodinamically stabilized although the persistence of the AV bloc, the therapy was completed to 48 week.
Conclusion: The pegylated interferon rarely has some life threatening cardiac side effects such as acute coronary syndrome, ventricular

arrhythmia, and sudden cardiac arrest. Therefore, all the patients should be detected for cardiac pathology before therapy and any cardiac complaint or symptom should be cautiously determined during the therapy. We aimed to state that the pegylated interferon therapy could be completed by modifying the dose if any cardiac side effect is encountered. The patient had neither individual nor familial cardiac risk history and the physical examination revealed no cardiac risk, so the AV bloc was considered as to be a side effect of the pegylated interferon therapy.

Topic 12: Hepatitis C

No: 1557

Efficacy and safety of daclatasvir plus asunaprevir in japanese patients with hepatitis C virus genotype 1b infection who are interferon ineligible naive or intolerant of interferon based treatment

Koichi Takaguchi[1], Yoshiyuki Suzuki[2], Kenji Ikeda[2], Joji Toyota[3], Yoshiyasu Karino[3], Kazuaki Chayama[4], Yoshiiku Kawakami[4], Akio Ido[5], Kazuhide Yamamoto[6], Tomoko Ueki[7], Hiroki Ishikawa[7], Michelle Treitel[8], Eric Hughes[8], Hiromitsu Kumada[2]

Kagawa Prefectural Central Hospital Department of Hepatology Kagawa-Japan[1], Toranomon Hospital Tokyo-Japan[2], Sapporo-Kosei General Hospital Sapporo-Japan[3], Hiroshima University Hiroshima-Japan[4], Kagoshima University Kagoshima-Japan[5], Okayama University Okayama-Japan[6], Bristol-myers Kk Tokyo-Japan[7], Bristol-myers Squibb Research & Development Princeton-United States[8]

Aim: All-oral dual therapy with daclatasvir (DCV; potent, pangenotypic NS5A inhibitor) plus asunaprevir (ASV; NS3 protease inhibitor) has demonstrated high sustained virologic response (SVR) rates in a phase 3 study in Japanese patients with genotype 1b infection. This analysis evaluated the efficacy and safety of DCV + ASV in interferon-ineligible and interferon-intolerant patients.
Methods: Interferon-ineligible patients were treatment-naive but ineligible for interferon-based therapy due to anemia/neutropenia/thrombocytopenia, advanced age (≥65 years), medical conditions requiring concomitant medication, or depression. Interferon-intolerant patients previously discontinued interferon-based therapy after < 12 weeks due to treatment-related toxicities. Patients received DCV 60 mg once daily plus ASV 100 mg twice daily for 24 weeks.
Results: Across subgroups, a majority of patients were female and had baseline HCV RNA levels ≥ 800 K IU/mL and IL28B CC genotype. High SVR rates (up to 94 %) were observed in intolerant patients and ineligible patients with anemia/neutropenia/thrombocytopenia, advanced age, or other complications. The response rate was lower in the ineligible subgroup with depression, which included few patients (Table). Incidences of serious adverse events (AEs) and AEs leading to discontinuation were generally low across subgroups. Grade 3/4 hemoglobin abnormalities were more common in the anemia/neutropenia/thrombocytopenia subgroup.
Conclusion: DCV + ASV achieved high SVR rates in subgroups of interferon-ineligible or interferon-intolerant patients with genotype 1b infection. DCV + ASV was generally well tolerated in subgroups of patients based on reason for interferon ineligibility. These findings support all-oral DCV + ASV as a treatment option for genotype 1b-infected Japanese patients who are unable to receive interferon-based therapies.

Topic 12: Hepatitis C

No: 1743

Anti HCV seropositivity rates remain under 0.1 % among voluntary non remunerated first time blood donors of Turkish red crescent and the patients admitted to the hospitals across Turkey

Akif Altınbas[1], Ahmet Yozgat[1], Abdulkadir Burkan[2], Armagan Aksoy[3], Dervis Ulger[3], Emre Ertugay[2], Tankut Koseoglu[1], Onur Baser[4], Gulsum Ozet[5]

Ankara Numune Education and Research Hospital Gastroenterology Ankara-Turkey[1], Social Security Institution Ankara-Turkey[2], Turkish Red Crescent Blood Services Ankara-Turkey[3], The University of Michigan, Dep. of Internal Medicine, Mi Internal Medicine Michigan-United States[4], Ankara Numune Education and Research Hospital Haematology Ankara-Turkey[5]

Introduction: Chronic hepatitis C virus (HCV) infection is still a major health problem. The real world data of HCV in our country is still lack. So, we aimed to determine the trends of the seropositivity rates of HCV in the first time blood donors from 2008 to date and the rates of HCV diagnosis in the years of 2010 and 2011 in the hospitals of Turkey.
Material method: To determine the rates of the patients took the diagnosis of HCV, we obtained the data of National database system of Turkey from Social Security Institute, retrospectively. From beginning of 2008, 6.359.731 voluntary healthy blood donors were screened for anti-HCV positivity via automatic EIA with microparticle enzyme immunoassay Confirmatory test was done by using third generation Line immune assay at the Red Crescent Center whole over Turkey.
Results: Almost 0.021 % and 0.022 % of the patients enrolled in the years of 2010 and 2011 were taken the diagnosis of chronic HCV infection. HCV rates increased with increasing of age till 70 years old. Screening test results revealed that anti-HCV positivity in blood donors declined from 0.55 % to 0.18 % between the years of 2008 and 2013. LİA test revealed that HCV positivity decreased from 0.08 % to 0.03 % in the same period.
Discussion: The previous studies showed that expected HCV positivity in our country is almost 0.85 %, the rates of HCV positive patients evaluated in health care system remain only 0.022 % of Turkish population. Finally, there is a dramatic decline in anti-HCV sero-positivity rates in the last decade.

Topic 12: Hepatitis C

No: 1652

Clinical usefulness of mean platelet volume as a fibrosis marker in chronic HCV patients

Asim Ulcay[1], Ergenekon Karagoz[1], Alpaslan Tanoglu[2], Muammer Kara[2], Vedat Turhan[2], Hakan Erdem[1], Yusuf Yazgan[2]

Gata Haydarpasa Training Hospital Infectious Diseases and Clinical Microbiology Istanbul-Turkey[1], Gata Haydarpasa Training Hospital Gastroenterology Istanbul-Turkey[2]

Introduction and aim: Hepatitis C virus is one of the main leading causes of liver failure all over the world. Liver biopsy is the gold standard method in detecting severity of liver fibrosis. However, the invasive nature of this method sometimes limits its use in disease follow-up. Mean platelet volume (MPV), which is largely overlooked, is one of the routine tests being part of complete blood count. The present study was designed to investigate the role of MPV as a fibrosis marker in HCV-infected patients.
Materials and methods: This is a retrospective case–control study evaluating chronic HCV-infected cases. The study included 98 naïve chronic hepatitis C cases followed-up due to diagnosis and treatment in GATA Haydarpasa Training Hospital. Patients were divided into two groups with fibrosis scores of 0–2 (Group 1) and 3–6 (Group 2) according to ISHAC score and compared whether MPV was an independent variable while determining the severity of liver fibrosis score.
Results: Of the 98 cases, 80 (81,6 %) were male, 18 (18,4 %) were female. The mean age of the patients was 40,6 ± 16,44 (min: 19, max: 73). Fibrosis scores of 29 cases (29,6 %) were ≥ 3 and the remaining 69 cases (70,4 %) had fibrosis scores < 3. There was a significant difference between these two groups for MPV (Group 1 = 8,19, Group 2 = 8,62; $P < 0.05$). Additionally, PDW to MPV ratio was significantly higher in the group 1 ($P < 0.05$).
Conclusion: MPV values are significantly increased in HCV infected patients associated with its severity and may be utilized as an independent predicting factor in hepatic fibrosis.

Topic 12: Hepatitis C

No: 2093

Efficacy and safety of simeprevir plus reduced dosage of pegylated interferonα2b and ribavirin in elderly patients with treatment experienced HCV genotype 1B

Kenich Kitada[1], Makoto Kuboki[1], Osamu Arai[1], Norikuni Shibata[1], Kenji Ohmoto[1]

Kurashiki Medical Center Gastroenterology and Hepatology Kurashiki-Japan[1]

Background: With an aging HCV genotype1b-infected population, the effect of peginterferon-α and ribavirin (RBV) is limited. We investigated the efficacy and safety of simeprevir plus PegIFNα2b and ribavirin treatment in elderly patients with chronic HCV genotype1b patients who did not respond (null response), had a partial response, or relapsed after treatment with PegIFNα and RBV.
Methods: We analyzed data from the patients who did not respond (null response), had a partial response, or relapsed after treatment with PegIFNα and RBV, treated simeprevir (100 mg, once daily) for 12 weeks plus PegIFNα2b (1.0–1.2 μg/Kg) and RBV (8.2–10.0 mg/Kg) for 24 weeks for the consecutive elderly patients (age > 65) from Dec.2013 to Feb.2014.
Results: Twenty-three patients were enrolled from Dec.2013 to Feb.2014. Mean age is 71 years old ranging from 65 to 81 years old with 8 male and 15 Female. The rate of SVR at 24 weeks is 78.3 % (18/23). There were no patients who have experienced treatment-related serious adverse events and treatment withdrawal.
Conclusions: Administration of simeprevir plus reduced dosage of PegIFNα2b and ribavirin for the elderly treatment-experienced patients is well tolerated and achieved higher SVR.

Topic 12: Hepatitis C

No: 1556

The perception of patients from hepatitis C a phenomenological study

Mohammad Hossein Somi[1], Morteza Ghojazadeh[2], Sevil Hakimi[3], Mehran Rahimi[4], Ahmad Reza Badali[4]

Liver and Gastrointestinal Research Center Internal Medicine Tabriz-Iran[1], Liver and Gastrointestinal Research Center Physiology Tabriz-Iran[2], Liver and Gastrointestinal Research Center Midwifery Tabriz-Iran[3], Liver and Gastrointestinal Research Center Medical Faculty Tabriz-Iran[4]

Aim: One of the valid methods in medical diagnosis is pay attention to subjective signs and realized experiences. Addressing to live experiences of patients and their real feelings guarantee the effectiveness of each type of caring and educational program.
Methods: This study has been conducted using of phenomenological approach and in-depth, without structure interviews. Besides of in-depth interview we use of another approaches of qualitative research such as behavior observation, non-verbal gesture and felid note taking. Samples were 16 patients suffering Hepatitis C which selected use of purposeful sampling and data were analyzed with content analysis.
Results: In this study 4 theme were extracted. The patients indicated to 4 factors as important causes in disease process. Social and moral behaviors, respect of hygienic principle, consider of some of limitation and hope to living, are most important factors in affection.
Conclusion: Experience of living with Hepatitis, unfamiliarity with hygienic principles and finally give of hope to the patients are prominent experiences of the patients which should be indicated in management of chronic disease.

Topic 12: Hepatitis C

No: 1723

The comparison of hematologic parameters between peginterferon alpha 2a and peginterferon alpha 2b treatment in patients with genotype 1 chronic hepatitis C

Bugra Tolga Konduk[1], Abdullah Emre Yildirim[1], Samet Alkan[2], Ramazan Erdem Er[1], Sezgin Barutcu[1], Ayhan Balkan[1], Murat Taner Gulsen[1]

Gaziantep University, Faculty of Medicine Gastroenterology Gaziantep-Turkey[1], Gaziantep University, Faculty of Medicine Internal Medicine Gaziantep-Turkey[2]

Aim: Although effects of Pegylated interferon (PEG-IFN) alpha-2a and PEG-IFN alpha-2b on blood cell profile are known, there are few study results available in which the two PEG-IFN types are compared head-to-head. We aimed to compare the hematologic effects of the two products.
Methods: We recruited 43 chronic hepatitis C patients with genotype 1b who received PEG-IFN alpha-2a/ribavirin or PEG-IFN alpha-2b/ribavirin combination therapy. Leukocyte, hemoglobin, neutrophil, lymphocyte and platelet counts were recorded initially and thereafter on the treatment months of 1, 3, 6, 9, and 12. Blood cell counts (BCC) were compared between the two groups, as well as comparing each group in itself with their initial values.

Results: Initial and the time-course change in BCC did not differ significantly between the two groups. Significant greater reduction in blood leukocyte counts in the third month of treatment was observed with PEG-IFN alpha-2b compared to initial values ($P = 0{,}009$). Lymphocyte levels declined significantly when compared to the initial values in the 3[SUP]rd[/SUP] month for PEG-IFN alpha-2a, however in the 9[SUP]th[/SUP] month for PEG-IFN alpha-2b ($P = 0{,}019$ $P = 0{,}016$, respectively). In both groups, hemoglobin values showed significant decline in the 3[SUP]rd[/SUP] month of the treatment ($P = 0{,}006$, $P = 0{,}002$, respectively), whereas no difference was found in repeated neutrophil and platelet counts according to their initial values.
Conclusion: Two types of PEG-IFN alpha products influenced the blood cell profile in different manners. Compared to PEG-IFN alpha-2b, monitoring of lymphocyte should be more taken into account for PEG-INF alpha-2a because of early decline of lymphocyte levels. [/SUP].

Topic 12: Hepatitis C

No: 2051

The effectivity and safety of triple therapy (telaprevir pegile interferon alfa and ribavirin) in patients with chronic hepatitis C a single center experience from Turkey

Murat Pekgöz[1], Selim Gürel[1], Murat Kıyıcı[1], Macit Gülten[1], Enver Dolar[1], Selim Giray Nak[1]

Uludağ University Gastroenterology Bursa-Turkey[1]

Background and aims: Patients with genotype 1 hepatitis C virus (HCV) who do not have a sustained response to therapy with peginterferon alfa and ribavirin have a low likelihood of success with retreatment.
Methods: Voluntary patients aged 18 and older with genotype-1 chronic HCV and without any contraindication were included. Treatment was organised as following: telaprevir was administered at a dose of 750 mg every 8 h; Peg-IFN α-2a was administered at a dose of 180 mcg per week and ribavirin was administered at a dose of 1000-1200 mg per day. HCV-RNA levels were measured before treatment, at 4, 12, 24 weeks of treatment, after treatment and after 24 week of treatment. Sustained virologic response was defined as undetectable HCV-RNA after 24 weeks of treatment.
Results: Sustained virologic response was obtained in 37 patients (%74). Breakthrough or early relapse was seen in 6 patients (%12) in total. Treatment had to be discontinued because of treatment related adverse events in 7 patients (%14).
Conclusions: Triple combination therapy included telaprevir is significantly better than classical Peg-IFN α-2a and ribavirin therapy in patients with chronic hepatitis-C infection.

Topic 12: Hepatitis C

No: 1906

Predictive value of non invasive serum markers on hepatic fibrosis in chronic hepatitis C patients

Hale Gokcan[1], Erkin Oztas[1], Ufuk Baris Kuzu[2], Fatih Saygili[1], Nuretdin Suna[2], Meral Akdogan Kayhan[1], Sabite Kacar[1], Zeki Mesut Yalın Kilic[1], Ertugrul Kayacetin[1]

Ankara Yuksek Ihtisas Research and Training Hospital Gastroenterology Ankara-Turkey[1], Ankara Yuksek Ihtisas Research and Training Hospital Internal Medicine Ankara-Turkey[2]

Purpose: This study aims to show the predictive value of non-invasive serum markers (NISM) on the hepatic fibrosis level.
Materials and methods: This cross sectional study involves 123 patients with chronic hepatitis C. Non-invasive markers were as follows: AST/ALT ratio (AAR), Cirrhosis discrimination score (CDS), FIB4, AST/thrombocyte index (APRI), age thrombocyte (AP) index, Göteborg University Cirrhosis Index (GUCI), King's score, FibroQ. Concurrent liver biopsies were evaluated with modified Ishac and Knodel scoring systems and scores of F3 or over were accepted as severe hepatic fibrosis. ROC analyses were carried out to compare the NISM with hepatic fibrosis level.
Results: Mean age of the patients was 51.9 ± 11.5. There were 10 patients (8.1 %) with Knodel scoring system and 27 patients (22 %) with Ishac scoring system that were evaluated to have F3 or higher hepatic fibrosis level. ROC analyses of NISM with Ishac score were as follows: CDS index = 0.5 ($P = 0.4$), AP index = 0.5 ($P = 0.2$), AAR index = 0.5 ($P = 0.8$), FIB4 index = 0.68 ($P = 0.007$), APRI index = 0.72 ($P = 0.01$), GUCI = 0.72($P = 0.001$), FibroQ = 0.54($P = 0.5$), King's score = 0.73 ($P = 0.001$), platelet count = 0.55 ($P = 0.45$). ROC analyses of NISM with Knodel score were as follows: CDS index = 0.66 ($P = 0.1$), AP index = 0.6 ($P = 0.2$), AAR index = 0.6 ($P = 0.3$), FIB4 index = 0.7 ($P = 0.03$), APRI index = 0.6 ($P = 0.06$), GUCI = 0.6 ($P = 0.09$), FibroQ = 0.6 ($P = 0.1$), King's score = 0.6 ($P = 0.06$), platelet count = 0.6 ($P = 0.2$).
Conclusion: We found that FIB4 index, APRI index, GUCI and King's score were useful to show severe liver fibrosis when compared to Ishac score and FIB4 was useful according to Knodel score.

Topic 12: Hepatitis C

No: 1235

Safety and tolerability of different antiviral regimens for chronic hepatitis C virus infection in cancer patients

Andreas Kyvernitakis[1], Parag Mahale[1], Harrys Torres[1]

The University of Texas Md anderson Cancer Center Infectious Diseases, Infection Control and Employee Health Houston-United States[1]

Background/aim: Adverse Events (AEs) are common in the treatment of chronic hepatitis C virus (HCV) infection, especially when interferon (IFN) and ribavirin are used. The AEs are often exacerbated in cancer patients due to baseline cytopenias or drug-drug interactions. We aimed to evaluate the safety and tolerability of different combinations of antiviral therapy (AVT) in cancer patients with chronic HCV infection.
Methods: Records of patients with any type of cancer treated for HCV infection at MD anderson Cancer Center between 8/2009 and 10/2014 were reviewed. Patients received pegylated-IFN plus ribavirin (PR), telaprevir or boceprevir plus PR (TB-PR), and sofosbuvir (SOF) plus either PR (SOF-PR), simeprevir (SOF-SIM) or ribavirin (SOF-R). We used the DAIDS table for grading AEs (version 1).
Results: Seventy-eight patient received 82 courses of treatment (Table 1). Almost one-half (48 %) of patients developed grade 3 or 4 AEs. AVT had to be discontinued in 18 % of the cases due to AEs. Common AEs were hematologic (78 %), psychiatric (33 %), sleep disturbances (29 %), gastrointestinal (28 %), and dermatologic (28 %). When compared to patients who received an IFN-containing,

those who received IFN-free regimens developed less grade 3 or 4 AEs (74 % vs. 14 %, $P < .001$) and required less AVT discontinuations (33 vs. 0 %, $P < .001$) (Figure 1). No grade 3 or 4 AEs were observed in the SOF-SIM regimen (Figure 2).
Conclusions: In HCV-infected cancer patients, safety and tolerability of IFN-containing regimens are inferior to the IFN-free combinations SOF-SIM and SOF-R. The combination of SOF-SIM offers the best safety profile in this patient population.

Topic 12: Hepatitis C

No: 1217

Reliability of a sustained virological response in chronic hepatitis C patients treated with peginterferon α2b and ribavirin seven year follow up in China

Jihua Lu[1], Zhenlong Liu[2], Yun Ling[1], Weizhong Gong[3], Tao Gao[1]

Shanghai Public Health Clinic Center, Affiliated To Fudan University Department of Gastroenterology Shanghai-China[1], Shanghai Haiyuan Hospital Shanghai-China[2], Haimeng Second Hospital Jiangsu-China[3]

Objective: To evaluate the reliability of sustained virological response (SVR) and long-term response (LTR) in chronic hepatitis C (CHC) patients accepted combination therapy with peginterferon-α2b/ribavirin (Peg-IFN/RBV), including the dose–effect of Peg-IFN and RBV.
Methods: In 2013, 147 CHC patients were followed to obtaining their virological response at the end of treatment with normal ALT, who accepted Peg-IFN/RBV combination treatment for 44 to 52 weeks from January 1 to December 31, 2006. Complete follow-up datas were obtained from 86 Patients, who were divided into non-SVR, non-LTR and LTR groups.
Results: Finally, the follow-up rate was 57.72 %. The relapse rate was 8.16 % and 3.79 % in non-SVR and SVR patients (the 3 relapsed patients within 3 years were assigned to the non-LTR group), respectively. 76 (96.21 %) patients achieved 7 years of LTR, whose long-term cumulative response rate was 88.4 % after withdrawal. The patients older than 50 years had lower LTR ($P = 0.02$). The significantly higher SVR were observed in patients accepted high RBV doses (> 13 mg/kg.d) than low doses (< 10 mg/kg.d), $P = 0.001$.
Conclusion: The definition of SVR currently used was reliability. LTR had been achieved in more than 95 % patients after SVR. At least 3 years of follow-up were required, and 7 years were better. Treatment also requires awareness and attention to weight-based dose of RBV.

Topic 12: Hepatitis C

No: 1771

An assessment of the treatment and side effects in copd and asthma patients with chronic viral hepatitis C

Ugur Kostakoglu[1], Arif Mansur Cosar[2], Gurdal Yilmaz[3]

Department of Infection Disease and Clinic microbiology Kanuni Training and Research Hospital Trabzon-Turkey[1], Departmant of Gastroenterology Faculty of Medicine, Karadeniz Technical University Trabzon-Turkey[2], Department of Infectious Diseases and Clinical Microbiology Faculty of Medicine, Karadeniz Technical University and Kanuni Training and Research Hospital Trabzon-Turkey[3]

Introduction: Chronic hepatitis C virus (HCV) infection is one of the leading causes of cirrhosis, liver failure and liver cancer and is an important public health problem. Mainly hematological side effects are observed during treatment. Pulmonary side effects are rare.
Materials and methods: In this study, patients with chronic HCV infection treated at Karadeniz Technical University and Kanuni Training and Research Hospital between the years 2010-2014 were analyzed retrospectively. 21 patients with COPD and asthma were studied as study group and 42 patients without COPD and asthma were studied as control group.
Findings: All patients included in the study were genotype 1b, and there was no difference between the two groups in terms of age and gender. Sustained virological response rate in patients with COPD or asthma was 47.6 % and 54.8 % in the control group. One patient was discontinued due to adverse effects of a treatment in both groups. Pegylated interferon or ribavirin dose was reduced due to any adverse impacts in 71.4 % of patients with COPD and asthma, and in 54.8 % of patients in the control group. Cough developed in 42.9 % of patients with COPD and asthma and shortness of breath developed in 23.8 %, but shortness of breath did not develop in patients in the control group, only cough developed in 4.8 % ($P < 0.05$)(Table 1).
Results: Cough and shortness of breath may occur in patients with COPD and Asthma during the treatment of chronic HCV infection. In the case of shortness of breath and persistent cough, patients should be examined for interstitial lung disease.

Topic 12: Hepatitis C

No: 1269

Esophageal varices due to hepatitis C virus the most frequent endoscopic finding in upper gastrointestinal bleed in Pakistani population

Salman Shakeel[1], Asif Mehmood[2], Asif Gul[2], Asim Hameed[2], Ghias Un Nabi Tayyab[2]

Postgraduate Medical Institute, Ameer Ud Din Medical College, Lahore General Hospital Medicine Lahore-Pakistan[1], Postgraduate Medical Institute, Ameer Ud Din Medical College, Lahore General Hospital Gastroenterology Lahore-Pakistan[2]

Objective: To see the Upper GI Endoscopy findings in patients with UGIB and its relationship with age, gender, symptoms and etiology.
Materials and methods: It is single centered, retrospective analysis of 4910 patients who presented to GI Department from January 2010 to October 2014 for endoscopic evaluation of UGIB. The data was analyzed on SPSS19, descriptive statistics were recorded and results were analyzed as in given table.
Results: The pattern of pathologies on EGD is as shown as: -
No Endoscopic Finding No. %age Mean Age (yrs) Male: Female ratio.

1 Esophageal varices (EV) 3392 69.1 % 46 1.95: 1
2 Peptic ulcer disease (PUD) 1011 20.6 % 40 1: 1
3 Normal EGD 206 4.2 % 35 1: 1.4
4 NSAIDs induced gastritis 103 2.1 % 39 1: 1.3
5 Gastric Neoplasm 64 1.3 % 45 1.4: 1
6 Esophageal Neoplasm 59 1.2 % 49 1.8: 1
7 Fundal Varices 29 0.6 % 42 1.3: 1
8 Portal Gastropathy 25 0.5 % 34 1: 1
9 Mallory Weiss 21 0.4 % 32 1: 1.3

The majority of the patients with UGIB presented with hematemesis alone (n = 2803, 57.1 %) followed by combined hemetemesis & malena (n = 991, 20.2 %), malena alone (n = 1061,

21.6 %) and hematochezia (n = 55, 1.1 %). EV were the most frequent finding of UGI Bleed (n = 2702, 69.1 %) followed by PUD (n = 806, 20.6 %) and then a Normal upper GI endoscopy (n = 165, 4.2 %). (n = 2408, 71 %) were HCV+ , (N = 203, 6 %) were HBV+ and (n = 271, 8 %) were both HCV+ and HBV+ .

Conclusions: Hemetemesis due to EV is the commonest cause of UGIB in our region as compared to the western world in which it is mainly due to PUD. It reflects the increasing proportion of people suffering from UGIB secondary to EV is indicative of increasing prevalence of liver cirrhosis due to HCV in our population.

Topic 12: Hepatitis C

No: 2004

Good viral response in Chinese chronic hepatitis C patients treated with pegylated interferon α 2a plus ribavirin upon relapse

Huiying Rao[1], Xinyue Chen[2], Lai Wei[3], Jia Shang[4], Zhiliang Gao[5], Qing Xie[6], Xiaoguang Dou[7], Xiaoyuan Xu[8], Guozhong Gong[9], Guofeng Chen[10], Jun Li[11], Dazhi Zhang[12], Junqi Niu[13], Hong Chen[14], Yinong Feng[15], Jinlin Hou[16], Hong You[17], Yun Wu[18], Peili Zhao[19]

Peking University Hepatology Institute Hepatology Department Beijing-China[1], Beijing Youan Hospital, Capital Medical University Hepatology Department Beijing-China[2], Peking University Hepatology Institute Hepatology Department Beijing-China[3], Henan Province People's Hospital Hepatology Department Henan-China[4], Sun Yatsen University Hepatology Department Guangzhou-China[5], Shanghai Jiao Tong University Ruijin Hospital Hepatology Department Shanghai-China[6], China Medical University Hepatology Department Shenyang-China[7], Peking University First Hospital Hepatology Department Beijing-China[8], The Second Xiangya Hospital of Central South University Hepatology Department Changsha-China[9], Military Hospital of China Hepatology Department Beijing-China[10] Nanjing Medical University Hepatology Department Nanjing-China[11] The Second Affiliated Hospital Chongqing Medical University Hepatology Department Chongqing-China[12] Jilin University Hepatology Department Changchun-China[13] Lanzhou University Hepatology Department Lanzhou-China[14] Shanxi Medical University Hepatology Department Taiyuan-China[15] Nanfang University Hepatology Department Guangzhou-China[16] Beijing Friendship Hospital Hepatology Department Beijing-China[17] The Affiliated Hospital of Inner Mongolia Medical Hospital Hepatology Department Huhehaote-China[18] The Third Hospital of Qinhuangdao Hepatology Department Qinhuangdao-China[19]

Aim: Direct-acting antiviral agents are not yet widely used in the Asia–Pacific region, and dual therapy remains the standard of care for chronic hepatitis C (CHC). This study compared the efficacy and safety profiles of treatment with pegylated interferon α-2a (Peg-IFN) plus ribavirin for 48 versus 72 weeks in patients experiencing relapse.

Methods: Patients who had relapsed with conventional IFN-α or Peg-IFN-based therapy were included. Patients were randomized into two groups treated with 180 μg/wk Peg-IFN plus 1000–1200 mg/d ribavirin for 48 or 72 weeks and followed up for 24 weeks after treatment completion. Single nucleotide polymorphisms at loci rs12979860 were determined.

Results: The study population included 124 patients [67 (54.0 %) males] treated at 18 Chinese hospitals. Baseline patient characteristics were similar between the groups (Table 1). For re-treated relapse patients, the overall SVR and ETVR rates were 80.0 % and 92.2 %, respectively, with no significant differences between the two groups (Table 1). The SVR rate was higher in patients with the IL28B CC genotype than in those with the IL28B CT/TT genotype (86.4 % vs. 64.7 %, $P < 0.05$). Patients who had a RVR or cEVR achieved good SVR rates of 92.3 % and 86.4 %, respectively. However, HCV genotype had no predictive value for SVR. Adverse events were reported by 77 patients.

Conclusion: Good viral response was observed, likely because the IL28B CC genotype is dominant in the Chinese population. RVR, cEVR, and IL28B genotype, but not HCV genotype, had good predictive value for identifying Chinese CHC patients who may achieve good SVR.

Topic 12: Hepatitis C

No: 2142

Research of the association between paraoxonase 1 gene polymorphism and response for the medical treatment of the patients with chronic hepatitis C infection

Kazım Kıratlı[1], Hanefi Cem Gul[1], Cumhur Artuk[1], Salih Kozan[2], Ali Oztuna[2], Yusuf Tunca[2], Can Polat Eyigun[1]

Gmma Infectious Diseases Ankara-Turkey[1], Gmma Medical Genetics Ankara-Turkey[2]

This study was aimed to determine if there is an affect of PON1 polymorphism on the response for chronic hepatitis C treatment or not.

The examination was planned as a study for the determination of manner for the treatment of chronic hepatitis C. DNA was isolated from patient blood samples via "spin column" method at the department of Medical Genetics. Analysis of PON1 enzyme at gene position of 55 and 192, "Tetra Primer Amplification Refractory Mutation System" method, developed by Hashemi et al., was used. When primer set was used just the same, some minor modifications were made at the polimerase chain reaction conditions and the master mix component ratios. As a result of the analysis of PON1 polymorphism; the medical treatment responders, LL genotype is %44,1, LM genotype is %44,1, MM genotype is %11,8 at the position of 55, QQ genotype is %55,9, QR genotype is %41,2 and RR genotype is %2,9 was found at the position of 192. When we examined the combined genotype analysis; there was only one LL/RR genotype and was responder. There were 8 LL/QQ genotypes, and 7 of them (%87,5) were responders. The association of polymorphism and the response for treatment was not unsignificant statistically ($p > 0,05$) by using Chi square test, and we think that the results are significant according to our clinic experience.

Future studies should address to the explanation of genetic mechanisms involved in PON1. Enlightenment of the association for polymorphism and treatment will be very precious for the drugs used in the chronic hepatitis C infection.

Topic 12: Hepatitis C

No: 2141

A case report about ribavirin induced excess iron accumulation in chronic hepatitis C

Yu-yong Jiang[1], Mei-li Han[2], Peng Wang[3], Yun-liang Xu[4], Xian-bo Wang[1]

Beijing Ditan Hospital, Capital Medical University Department of Integrated Traditional and Western Medicine Beijing-China[1], General

Hospital of Yanzhou Mining Group Department of Gastroenterology Zoucheng-China[2], Beijing Ditan Hospital, Capital Medical University Department of Pathology Beijing-China[3], Beijing Ditan Hospital, Capital Medical University Department of Radiology Beijing-China[4]

The standard treatment of chronic hepatitis C (CHC) in China is a combination of interferon and ribavirin. For better results, doctors and patients want to use sufficient dosages and durations of the two drugs. In case of hemolytic anemia caused by ribavirin, erythropoietin and food rich in iron can be used to overcome anemia. Massive hemolysis caused by ribavirin might result in excess iron accumulation in the liver. The authors report a novel case of a patient with CHC who received pegylated interferon alfa 2a (PEG IFN α 2a) and ribavirin antiviral treatment for 6 months. His hemoglobin level decreased from a baseline of 159 to 55.2 g/L, accompanied by abdominal pain, fever, and epistaxis. Magnetic resonance imaging scan indicated deposits of hemosiderin in the liver. Histological analysis of liver biopsy by staining with hematoxylin and eosin confirmed depositions of brown particles in the hepatic cells, which stained positively with Prussian blue. Serum ferritin levels were also found to be increased. The accumulation of iron in the liver was associated with hemolysis caused by ribavirin. PEG IFN α 2a and ribavirin combination therapy was terminated, following which the symptoms of anemia resolved. In conclusion, these findings demonstrate that anemia in this patient was associated with hemolysis caused by ribavirin, rather than a recurrence of his aplastic anemia. It should be noted that severe hemolytic anemia can cause serious iron deposition, which then leads to liver damage and fibrosis.

Topic 12: Hepatitis C

No: 1571

Effect of daclatasvir in combination with asunaprevir on the pharmacokinetics of a combined oral contraceptive containing ethinyl estradiol and norethindrone acetate in healthy women

Robert Adamczyk[1], Tushar Garimella[2], Michael Hesney[2], Jignasa Rana[1], Hamza Kandoussi[2], Elizabeth Colston[2], Richard Bertz[1], Timothy Eley[2], Marc Bifano[2]

Bristol-myers Squibb Research and Development Exploratory Clinical & Translational Research Hopewell-United States[1], Bristol-myers Squibb Research & Development Lawrenceville-United States[2]

Aim: This open-label, 3-cycle study in healthy women of childbearing potential (WOCBP) assessed effects of daclatasvir (DCV; potent, pangenotypic NS5A inhibitor) + asunaprevir (ASV; NS3 protease inhibitor) on the pharmacokinetics of norethindrone (NE) and ethinyl estradiol (EE) after dosing of a combined oral contraceptive (OC) containing NE acetate/EE at low (1000/20 μg) and high (1500/30 μg) doses.
Methods: WOCBP (age 18–40 years; BMI 18–32 kg/m2; N = 40) received OC 1000/20 μg during Cycle 1 (days 1–21) and OC 1500/30 μg during Cycles 2 (days 29–49) and 3 (days 57–77); DCV 60 mg QD + ASV 100 mg BID were also administered on days 67–77. Serial pharmacokinetic samples were collected in all 3 cycles. The impact of DCV + ASV coadministration with OC 1500/30 μg on the pharmacokinetics of NE and EE was assessed by comparison with OC 1500/30 μg alone (Cycle 3 vs 2) and OC 1000/20 μg alone (Cycle 3 vs 1).
Results: Following OC 1500/30 μg and DCV + ASV coadministration, NE exposure was unaffected and EE exposure was slightly reduced versus OC 1500/30 μg alone (Table). OC 1500/30 μg and DCV + ASV coadministration provided higher NE and EE exposures versus OC 1000/20 μg alone. OC 1500/30 μg and DCV + ASV coadministration was generally well tolerated; only 1 subject discontinued due to an adverse event (serious adverse event of appendicitis deemed unrelated to study drug).
Conclusion: Steady-state DCV + ASV, when coadministered with high-dose OC (1500/30 μg), provides NE/EE exposure that is not lower than with OC 1000/20 μg alone, and is within the range where safety/efficacy of the OC have been established.

Topic 12: Hepatitis C

No: 1475

Frequency of depression in patients with chronic hepatitis C during the treatment pegylated interferon alpha ribavirin

Ahmet Dogru[1], Fuat Ekiz[2]

Hatay Antakya State Hospital Psychiatry Hatay-Turkey[1], Hatay Antakya State Hospital Gastroenterology Hatay-Turkey[2]

HCV is a worldwide health problem and especially affected are the developing world countries. Pegylated-Interferon-α & ribavirin (PR) treatment has still been used for obtaining sustained virological response because of Turkish Health Communication Application. However, treatment can often cause intolerable physical and psychiatric side effects. In this study, we aimed to research depression rate in patients with HCV treated Pegylated-Interferon-α & ribavirin. In our study of 20 patients 7 male and 13 females were included to our study. Mean age was 49,55. Depression an affective disorder was found in only four patients (20 %) during the Pegylated-Interferon-α & ribavirin treatment. In two patients (50 %) had mild and two patients (50 %) had severe depression. In severe depression, drugs were stopped in an elderly patient, antidepressant drug was started interruption PR for other patient. In mild depression patients, they continued the drugs without using antidepressant. As a result, in this study, higher depression rate was found patients with interferon & ribavirin. Physicians should be kept in mind psychiatric complications during interferon & ribavirin treatment.

Topic 12: Hepatitis C

No: 1578

Telaprevir induced dress syndrome with salmonella infection

Tarık Akar[1], Selim Aydemir[2]

Bulent Ecevit University School of Medicine Gastroenterology Zonguldak-Turkey[1], Bulent Ecevit University School of Medicine Gastroenterolog Zonguldak-Turkey[2]

The addition of direct-acting antiviral agents, Telaprevir and Boceprevir, to standard peginterferon/ribavirin has dramatically changed the sustained virological response(SVR) in treatment of hepatitis C virus(HCV) infection, but the new spectrum severe adverse events have emerged in daily clinical practise. Dress syndrome(DS) is one of them and characterized by systemic symptoms with predominantly severe skin rash, fever and eosinophilia. DS is very rare in treatment of HCV with telaprevir(TVR), but can be life-threatening if unrecognized exactly. Even though the incidence of infection has increased in telaprevir based triple therapy, Salmonella infection has not been reported before now. Salmonella infection can cause typhoid fever,

rash, hepatitis and can cause clinical challenge with dress syndrome. Herein we present a case of telaprevir induced dress syndrome associated with Salmonella infection causing clinical challenge.

Topic 12: Hepatitis C

No: 1879

Hepatitis C genotypes in Syrian refugee patient in Turkey

Ahmet Metin Karadağ[1]

Dr. Ersin Arslan State Hospital Dr.ersin Arslan State Hospital Gaziantep-Turkey[1]

Backgrouns/aims: The prevalence hepatitis C is about 1 % in Syria. Hepatitis C prevalence resemble to Turkey. But hepatitis C genotypes range differ from Turkey. Hepatitis C genotypes divided into six distinct genotypes throughout the world with multiple subtypes. In Turkey genotypes 1a the most prevalent type, nearly 80 %. Gazinatep is southeast of Turkey. In Gazaintep also genotypes 1a the most prevalent type, like Turkey. Gaziantep is near the Syrian border. I investigated that any similarity between two region.
Methods: I investigated hepatitis C genotypes in ten Syrian refugee patients that given hepatitis C treatment. Patients were refugees coming from north path of the Syria. Average age was 48. 2 patient were male, 8 female.

Genotype 4a 6 patient 60 %
Genotype 5a 3 patient 30 %
Genotype 1a 1 patient 10 %

Results: Hepatis c genotypes differ between Turkey's Syrian border province Gaziantep and Syrian refugees. Genotypes 4 the most prevalent type in syrian refugees, genotype 5 very rare in Turkey but abundant in North Syria refugees But in Turkey genotype 1a most prevalent.
Conclusion: Gaziantep and North Syria is near places. Borders play an important role variation of hepatitis C genotypes and virus spreading.

Topic 12: Hepatitis C

No: 1617

Impact of support with erythropoietin and granulocyte colony stimulating factor on outcome of antiviral therapy in treatment naïve chronic hepatitis C patients from northern India

Vivek Saraswat[1], Nakul Morakhia[1], Gaurav Pandey[1], Sreejith Venugopal[1], Samir Mohindra[1]

Sanjay Gandhi Postgraduate Institute of Medical Sciences Gastroenterology Lucknow-India[1]

Background: Cytopenias during therapy with pegylated interferon (Peg-IFN) and ribavirin (RBV) in patients with chronic hepatitis C (CHC) are managed with dose reduction or withdrawal of therapy, which reduces sustained virologic response (SVR) rates. Support with erythropoietin (EPO) and granulocyte colony stimulating factor (GCSF) may allow completion of therapy without dose modification.
Methods: We have compared SVR at 12 weeks after end-of therapy in patients developing cytopenias (Hb < 8 gm/dl, TLC < 2000/mm3, platelets $< 30{,}000$/mm3) on Peg-IFN α-2a (180 μg/week) or α-2b (1.5 μg/kg/week)and RBV (800–1200 mg/day), managed by dose modification before 2012 (Group 1), with patients supported with EPO (4000-20,000 iu/week) and/or G-CSF (30-60 iu/week) after 2012 (Group 2).
Results: Groups 1 and 2 comprised of 246 (217 genotype 3, 29 genotype 1) and 51 (43 genotype 3, 8 genotype 1) patients respectively. Cirrhosis was more frequent in group 2 (35 % vs 24 %, $P = 0.04$). Genotype distribution was similar (genotype 1, 12 % vs 16 %, $P =$ ns). SVR rate in group 2 was higher (73 % vs 55 %, $P = 0.01$), inspite of a higher proportion of cirrhotics. It was also higher in group 2 among all genotype 3 patients (74 % vs 58 %, $P = 0.01$), and among genotype 3 patients with cirrhosis (69 % vs 35 %, $P < 0.01$), but not among genotype 3 patients without cirrhosis (76 % vs 63 %, $P = 0.07$).
Conclusions: Using hemopoeitic factors in cytopenic patients on treatment with Peg-IFN + RBV avoided dose reduction and increased SVR rates. This benefit was noted mainly in genotype 3 patients, particularly in those with cirrhosis. Larger studies are required.

Topic 12: Hepatitis C

No: 1987

Development of hepatocellular carcinoma despite successful antiviral treatment in hepatitis C related liver cirrhosis case report

Sule Poturoglu[1], Ali Erkan Duman[2], Asli Ciftcibasi Ormeci[2]

Haseki Training and Research Hospital Gastroenteroloy Istanbul-Turkey[1], Haseki Training and Research Hospital Gastroenterology Istanbul-Turkey[2]

Untreated chronic hepatitis C, can lead to serious complications such as cirrhosis, hepatocellular carcinoma (HCC). We present a HCC case which developed in a patient who was under HCV treatment and had rapid viral response.
Case:
Sixty-one year old male patient was admitted to our clinic with chronic hepatitis C recurrence (genotype 1). In the liver biopsy, HAI score was 5/18 and fibrosis score was 5/6. Alpha-fetoprotein (AFP) level was 20 ng/mL. Magnetic resonance imaging (MRI) was performed, imaging of the liver was unremarkable except mild lobulation. Triple therapy was started with pegylated interferon alfa-2a 180mcg once a week, ribavirin 200 mg 2x3 and telaprevir 375 mg 3x2. On the 4th and 12th weeks of treatment, HCV-RNA was negative. Telaprevir was stopped after 12 weeks of treatment. At week 24 the patient suddenly developed abdominal distension and jaundice. Paracentesis showed hemorrhagic ascites. AFP level was 3000 ng/mL. With the suspicion of HCC abdominal MRI was ordered, which confirmed the diagnosis. All the antiviral therapy was stopped. Unfortunately, the patient died in a few weeks' time.

The patient's decompensation considered to be caused by the HCC. HCC developed although HCV RNA was rapidly negative. Did the natural history of the disease continue after a process, even if the disease agent was removed or did HCC spread from a focus that could not be undetected on pretreatment imaging? This issue has not become clear.

We concluded that cirrhotic patients should be more frequently monitored than routine imaging while they are on antiviral treatment.

Topic 12: Hepatitis C

No: 1722

Six year distribution pattern of hepatitis C virus in Turkey a multicenter study

Mustafa Altindis[1], Tuba Dal[2], Isin Akyar[3], Onur Karatuna[3], Selma Gokahmetoglu[4], Seda Tezcan Ulger[5], Canan Kulah[6], Berrin Uzun[7], Mehmet Ozdemir[8], Sibel Aydogan[9], Huseyin Guducuoglu[10]

Sakarya Uni School of Medicine Medical Microbiology Sakarya-Turkey[1], Yb Uni School of Medicine Medical Microbiology Ankara-Turkey[2], Acibadem Uni School of Medicine Medical Microbiology Istanbul-Turkey[3], Erciyes Uni School of Medicine Medical Microbiology Kayseri-Turkey[4], Mersin Uni School of Medicine Medical Microbiology Mersin-Turkey[5], Be Uni School of Medicine Medical Microbiology Zonguldak-Turkey[6], Ikc Uni Atatürk Tr Hospital Medical Microbiology Izmir-Turkey[7], Ne Uni School of Medicine Medical Microbiology Konya-Turkey[8], Atatürk Training and Research Hospital Medical Microbiology Ankara-Turkey[9], Yy Uni School of Medicine Medical Microbiology Van-Turkey[10]

Hepatitis C virus (HCV) genotypes have different clinical outcome, and response to antivirals. The changing pattern of HCV infection could have a significant impact on future medical prevention practices and therapies. The aim of this study was to find out the frequency distribution and changing pattern of HCV genotypes overtime in Turkey.

During the 2009–2014 period, 5478 serum samples from HCV RNA positive patients were collected from eight hospitals located in different provinces of Turkey. of the samples 2250 were collected from Acibadem University Hospital, Istanbul; 1550 were EU Hospital, Kayseri; 480 were MU Hospital, Mersin; 359 were BU University Hospital, Zonguldak; 308 were IKC University Hospital, Izmir; 291 were NE University Hospital, Konya; 192 were Atatürk TR Hospital, Ankara, and 48 were YY University Hospital, Van. Detection of HCV RNA and genotyping were performed by different commercial molecular kits and systems.

During six year period Genotype 1 was the most common genotype(62 %) followed by nontypeable genotype 1 (9.7 %), genotype 4 (8.9 %), genotype 3 (6.8 %). The rates of genotype 1 were 65.9 %, 66.6 %, 64.1 %, 63.3 %, 60.6 %, 57.8 % in 2009, 2010, 2011, 2012, 2013, 2014, respectively. The second most prevalent genotype was nontypeable genotype 1 in 2009-2011, and 2013. In 2012 genotype 3 was the second most common genotype (9.3 %) whereas in 2014 genotype 4 (11.3 %).

In conclusion, in recent year genotype 3 and genotype 4 have gained importance. The modification of the HCV genotype pattern may require new therapeutic strategies and survey studies in the future.

Topic 12: Hepatitis C

No: 2150

Splenic embolization may be an option to overcome thrombocytopenia interfering with triple therapy in HCV (+) cirrhotic patients a case report

Murat Biyik[1], Mehmet Asil[1], Sami Cifci[1], Serhat Sayin[2], Ramazan Ucar[2], Orhan Ozbek[3], Huseyin Ataseven[1], Hakki Polat[2], Ali Demir[1]

Necmettin Erbakan University Gastroenterology Konya-Turkey[1], Necmettin Erbakan University Internal Medicine Konya-Turkey[2], Necmettin Erbakan University Radiology Konya-Turkey[3]

Treatment of hepatitis C sometimes may be challenging due to thrombocytopenia. Here we present a case of HCV (+) cirrhotic patient whom splenic embolization was successfully performed in order to overcome thrombocytopenia associated with triple therapy.

47 years of women was being followed in our clinic due to HCV cirrhosis for 6 years. She was given PEG-IFN+ ribavirin treatment for 48 weeks 6 years ago and relapsed. After the registration of protease inhibitor based triple therapy regimens in genotype 1b HCV patients, such treatment was planned. Laboratory investigations were consistent with Child Stage A cirrhosis. Abdominal ultrasound showed the presence of cirrhosis and splenomegaly. HCV RNA was 756000 copy/ml. Pretreatment hematologic parameters were as follows; Hb: 11,8 g/dL, WBC: 4600/μL, Platelet count: 64000/μL. Treatment was started with Peg IFN α-2a 135 mcg/week, ribavirin 800 mg/day and telaprevir 3x750 mg/day. Platelet count dropped to 42000/μL and than 14000/μL in two weeks. PEG-IFN dose was progressively reduced to 67,5 mcg/week. To overcome thrombocytopenia, splenic embolization was performed. Platelet count increased to 45000/μL in 1 week, PEG-IFN dose was increased to 135 mcg/week and platelet count remained around 60.000/μL throughout the rest of the treatment. She is on the 46th week of the treatment and HCV RNA was still negative in the 36th week.

Thrombocytopenia complicating HCV treatment frequently necessitates PEG-IFN dose reduction interfering with SVR rates. Treatment of severe thrombocytopenia with splenic embolisation may be an effective minimally invasive option in HCV (+) cirrhotic patients to whom PEG-IFN based treatment regimens are given.

Topic 12: Hepatitis C

No: 2125

The relationship between tumor necrosis factor alfa level and hepatic activity index in patients with chronic hepatitis C

Fatma Kesmez Can[1], Emine Parlak[2], Abdullah Can[3], Mehmet Parlak[2], Ahmet Özbek[4]

Palandöken State Hospital Department of Infectious Diseases and Clinical Microbiology Erzurum-Turkey[1], Ataturk University Department of Infectious Diseases and Clinical Microbiology Erzurum-Turkey[2], Horasan State Hospital Department of Anesthesiology and Reanimation Erzurum-Turkey[3], Sakarya University Department of Microbiology and Clinical Microbiology Sakarya-Turkey[4]

Objective: Hepatitis C virus (HCV) infection is a health problem all over the world. It is a major reason of cirrhosis and hepatocellular carcinoma. HCV is not a direct cytopathic virus, and liver damage is associated with immune-mediated mechanisms. TNF alpha released from macrophages and hepatocytes that stimulate inflammatory response is important in the first response defense to hepatitis C. In this study, we aimed to examine the relationship between liver Hepatic Activity Index (HAI) and Tumor Necrosis Factor Alfa (TNF alfa) levels in patients with chronic hepatitis C, and to determine whether there is a significant correlation.

Materials and methods: Thirty five chronic HCV patients, who were monitored by Infection Diseases and Clinic Microbiology Clinic, were taken into the study. Liver Biopsy samples were examined by the same pathologist and necroinflammatory activity was evaluated according to Knodell's classification. As the control group, 35 healthy volunteers without HCV infections were selected. TNF alfa was measured by ELISA method, for the serums acquired from bloods of patients and controls.

Findings: TNF Alfa and HAI levels was found to correlate in a positive, medium level, ($r = 0.379$, $P = 0.02$). TNF alpha, ALT and AST values were significantly higher in the cases with chronic hepatitis C compared to the control group ($p > 0.05$).
Results: In our study, we found a statistically significant relationship between HAI and TNF Alfa levels in patients with chronic hepatitis C. We presume that serum TNF Alfa level can be used to estimate the inflammation in the liver during HCV infection.

Topic 12: Hepatitis C

No: 2108

Assessment of pathological response in non virulogical responders to ifn rebavirin therapy

Mohamed Elateek[1], Eman Eissa[2], Hussein Khalaf[1]

Tanta Fever Hospital Hepatology Research Center Tanta-Egypt[1], Banha Teaching Hospital Clinical Pathology Banha-Egypt[2]

Introduction: As era of DAA start we begin to reevaluate the non responders to IFN for start of Sovaldi treatment
Aim of the work: Evaluation of pathological response in non responders to IFN
Patients and method: We select 150 patients previously treated with IFN/RIBAvirin not respond to treatment with other 50 patient as control group
All patients perform fibroscan before treatment and one year at least after stop of treatment with other usual investigations
We divided them into 4 group:

50 patients relapsers
50 patients not respond after 24 week
50 patients not respond after 12 week
50 patients naïve

Results:
Group 1:
A-36 patients (72 %) was F3-F4 (from 15-22 KP)
26 patients improved (76 %) improved 3 KP -10 patients (16 %) no change
B-14 patients (28 %) were F2-F3 (from 9.5–14.5 KP)
8 Patients (57 %) improved 3.5 KP)-5 patients (35 %): no change -1 patients (7 %) deteriorate
Group 2:
A-27 patients (54 %) were F3-F4 (from 15–22 KP)
15 patient (55 %) improved 2 kp (1–3 KP)-9 patients (33 %) show no change-3 patients (11 %) show deterioration average 4 KP
B- 23 patients were F2-F3 (from 9.5–14.5 KP)
14 patient (61 %) improved average 3 KP 9 patients (39 %) show no change
Group 3:
A-42 patients (84 %) were F3-F4 (from 15–22 KP)
34 patients (80 %) show no change-6 patients (14 %) show deterioration)-2 patients (6 %) show improvement 2 KP)
B-8 patients (16 %) were F2-F3 (from 9.5–14.5 KP)
No change
Group 4: control
All patient show no change except 2 improved and 6 deteriorate
Conclusion: Interferon significantly improve relatively the pathological condition of the liver in non responders after 24 weak treatment although not return no normal.

Topic 12: Hepatitis C

No: 1767

Baseline vitamin d level is not associated with sustained virologic response to interferon based antiviral therapy in chronic hepatitis C results of single center experience

Goktug Sirin[1], Omer Senturk[1], Altay Celebi[1], Hasan Yılmaz[1], Sadettin Hulagu[1]

Kocaeli University Gastroenterology Kocaeli-Turkey[1]

Aims: Although most of studies to date have yielded contraversial results, baseline 25-hydroxyvitamin D [25(OH) D] level has recently been reported to be an independent predictor of sustained virologic response (SVR) that obtained with traditional dual antiviral therapy in patients with chronic hepatitis C (HCV). We aimed that to clarify whether any association between baseline 25(OH)D level and SVR obtained with antiviral therapy.
Methods: Chronic hepatitis C patients treated with pegylated interferon (PEG-IFN) plus ribavirin (RBV) where baseline 25(OH)D level was tested last in 5 years enrolled this study. Patients with HBV or HIV co-infection, those receiving vitamin D supplementation were excluded. Mean baseline 25(OH)D level was compared between those who achieved and failed to achieve SVR. Pooled standard difference in mean 25(OH)D level, odds ratios (OR) and 95 % confidence intervals (CI) were calculated for each group.
Results: Total of 285 patients (genotypes 1: 270, genotypes 2/3 = 15) were included in the analysis. 198 patients had received antiviral therapy PEG-IFN and RBV. There was no significant association between mean baseline 25(OH)D level and SVR (OR 1.51, 95 % CI 0.78-1.86; $P = 0.21$), either in patients infected with genotypes 1 (OR 1.48, 95 % CI 0.76-1.94; $P = 0.082$) or genotypes 2/3 (OR 1.51, 95 % CI 0.45-9.95; $P = 0.76$). Statistically significant heterogeneity was present in all patients, and in the subgroup analysis of genotypes.
Conclusions: Baseline 25(OH)D level is not associated with SVR that obtained with traditional dual antiviral therapy including PEG-IFN plus RBV in chronic HCV infection. Any effect of vitamin D supplementation on SVR which needs further investigation.

Topic 12: Hepatitis C

No: 1485

Safety and tolerability of daclatasvir (DCV) in patients with chronic HCV infection

Ira Jacobson[1], Hiromitsu Kumada[2], Kazuaki Chayama[3], Greg Dore[4], Stanislas Pol[5], Stefan Zeuzem[6], Claire Jurkowski[7], Kim Tran[7], Misti J Linaberry[7], Michelle A Treitel[7], Eric Hughes[7]

Cornell Weill School of Medicine, Division of Gastroenterology and Hepatology, New York-United States[1], Toranomon Hospital, Tokyo-Japan[2], Hiroshima University Hiroshima-Japan[3], Unsw Australia, Sydney-Australia[4], Hôpital Cochin, Paris-France[5], Johann Wolfgang Goethe Universitaet, Frankfurt-Germany[6], Bristol-myers Squibb, Princeton-United States[7]

Background: HCV regimens containing DCV, a pan-genotypic HCV NS5A inhibitor, have been well tolerated in clinical studies. This analysis evaluated the combined safety profile of DCV 60 mg QD in 9 phase-2 and 3 phase-3 studies of DCV-based regimens.

Methods: Overall, 2052 patients received DCV: DCV + asunaprevir (ASV), n = 918; DCV + sofosbuvir (SOF) ± ribavirin (RBV), n = 211; DCV + ASV + peginterferon/RBV (P/R), n = 418; DCV + P/R, n = 505. Pooled safety data for each regimen were analyzed for adverse events (AEs) on-treatment, serious AEs, AE-related discontinuations, and Grade 3/4 AEs and laboratory abnormalities.
Results: Treatment-naive and -experienced patients with HCV genotypes 1–4 were included; 18.3 % had cirrhosis. Serious AEs and AE-related discontinuations were infrequent with all DCV-based regimens (Table). In regimens without P/R, the most common AEs were mild/moderate fatigue, diarrhea, headache, and nausea. Reversible grade 3/4 aminotransferase elevations were seen in < 4 % of patients with DCV + ASV and not considered attributable to DCV. In the HALLMARK-DUAL study, no clinically relevant differences in safety were seen with DCV + ASV versus placebo in treatment-naive patients through 12 weeks; the DCV + ASV safety profile was similar in cirrhotic and non-cirrhotic patients. Adding RBV to DCV + SOF increased incidences of anemia and other RBV-associated AEs. P/R-containing regimens were associated with AE spectra and incidences of grade 3/4 hematologic abnormalities consistent with the known safety profile of P/R alone.
Conclusion: Overall, DCV 60 mg QD combination regimens were safe and well tolerated, with no unique toxicities attributable to DCV. DCV + ASV and DCV + SOF showed improved safety and tolerability versus P/R-containing regimens, which had safety profiles consistent with that for P/R alone.

Topic 12: Hepatitis C

No: 1253

Triple combination therapy experience in relapsing chronic hepatitis C patients

Tansu Yamazhan[1], Hüsnü Pullukçu[1], Meltem Taşbakan[1], Raika Durusoy[2], Oğuz Reşat Sipahi[1], Hüseyin Aytaç Erdem[1], Sercan Ulusoy[1]

Ege University Infectious Diseases Izmir-Turkey[1], Ege University Public Healt Izmir-Turkey[2]

Introduction and aim: In this study we evaluated the response of our relapsing HCV patients to triple therapy and the side effects encountered during treatment.
Methods: Clinical and side effect data of all relapsed chronic HCV cases treated with triple therapy in our department were evaluated retrospectively. Friedman test was used to compare patients' baseline, 2nd, 4th, 6th and 8th week parameters.
Results: Seven patients received PEGIFN + RBV + TVR and two receiveds PEGIFN + RBV + BOC (median age 48 (min.26–max.58), baseline viral load 856.714 IU/ml(20.400-4.250.000)).None of the cases had clinical or laboratory evidence of cirrhosis. In the TVR treatment group, three patients were HCV-RNA positive on the 4th week (12, 20 and 24 IU/ml), their double treatment was continued until 48th week. Two other patients were HCV-RNA negative on the 4th week and their double treatment was continued until the 24th week. A patient having HCV-RNA 203.012 IU on 4th week was considered as unresponded and treatment stopped. Treatment of the last telepravir case was stopped due to hepatocellular carcinoma and transferred to the transplantation unit. Since HCV-RNA of boceprevir group was positive with 20 and 50 IU/ml on the 4th week, they received 32 weeks triple and 12 weeks double, thus 48 weeks therapy and both achieved SVR. The haemoglobin, leukocyte and thrombocyte counts decreased significantly (table). None of the patients encountered any serious side effect.
Conclusion: In our patients, 7/9 patients achieved SVR with triple therapy. This is probably due to the facts that none of our treatment group had advanced liver disease and their baseline hemogram values were good.
Table 1. Baseline and follow-up median (min–max) hematologic parameters of patients receiving triple combination.

Topic 12: Hepatitis C

No: 1016

Statins as add on therapy for chronic hepatitis C a meta analysis

Aq Taguba[1], Mt Panlilio[1], Mj Villamayor[1], Jp Ong[1], Mo Daez[1]

University of The Philippines-Philippine General Hospital Section of Gastroenterology Manila-Philippines[1]

Significance: The current standard therapy for chronic hepatitis C, the combination of pegylated interferon (PEG IFN) and ribavirin (RBV), has a 50 % failure rate in achieving sustained virologic response (SVR). The use of add-on protease inhibitors, such as boceprevir or telaprevir, results in SVR of as much as 70 %; however, marked anemia, anorexia, and neutropenia have been reported in the use of the triple regimen. This meta-analysis aims to determine the efficacy and safety of statins as add-on therapy with PEG IFN and RBV for chronic hepatitis C.
Methodology: A thorough search was done using the key terms "statin" and "hepatitis C." Six RCTs were included with a total of 704 patients. The proportion of patients achieving SVR was treated as dichotomous variables. Statistical analysis was done using the Peto Method with fixed-effect analysis model, and Peto odds ratio as effect measure. Weighted averages were reported as relative risks with associated 95 % confidence interval. Abstracted data were then analyzed using Review Manager 5 program.
Results: Results showed that triple therapy with PEG IFN, RBV, and statin was superior to standard therapy of PEG IFN and RBV in achieving SVR [RR 0.42 CI 95 % (0.31, 0.57)] and RVR [RR 0.25 CI 95 % (0.11, 0.58)]. No heterogeneity was found between studies for SVR($I2 = 0$; $P = 0.80$) and RVR ($I2 = 0$; $P = 0.51$). Conclusion. Statins are effective and safe as add-on therapy for chronic hepatitis C.

Topic 12: Hepatitis C

No: 1685

Distribution of hepatitis C virus genotype in Thailand

Rujipat Wasitthankasem[1], Nipaporn Siripon[1], Chutima Suya[2], Phrutsada Chulothok[2], Kasemporn Chaiear[3], Pairaya Rujirojindakul[4], Pisit Tangkijvanich[5], Yong Poovorawan[1]

Center of Excellence In Clinical Virology, Faculty of Medicine, Chulalongkorn University Pediatrics Bangkok-Thailand[1], Chiangrai Prachanukroh Hospital - Chiang Rai-Thailand[2], Udon Thani Hospital - Udon Thani-Thailand[3], Faculty of Medicine, Prince of Songkla University Pathology Songkhla-Thailand[4], Faculty of Medicine, Chulalongkorn University Biochemistry Bangkok-Thailand[5]

Although the genotypic distribution of hepatitis C virus (HCV) is diverse, some genotypes are more prevalent in certain geographical area. We aim to determine the viral genotypes and distribution in

Thailand where prevalence of HCV is high. The anti-HCV positive serum samples collected from the North (Chiang Rai province), the Northeast (Udon Thani and Khon Kaen provinces), the South (Songkhla province) and the Central (Bangkok) regions were analyzed for viral RNA. Sequences of the viral core and NS5B genes were obtained from samples positive for HCV RNA. We then performed phylogenetic analysis based on the nucleotide sequences of these two genes to determine the viral genotypes and their association to the 4 major geographical regions of Thailand (North, Northeast, Central, and South). From the total of 588 HCV-positive individuals, most were male (72.6 %, $P < 0.0001$), reside in Central Thailand (n = 256, 43.5 %), and have the mean age of 41.5 ± 10.6. The mean age of the infected individuals from the South (37.8 ± 9.3) was significantly lower than the Central (43.6 ± 11.4) and the Northeast (41.5 ± 9.4) area ($P < 0.0001$ and $P = 0.04$, respectively). HCV-3a was most predominant in all regions (36.7 %), followed by genotype 6 (20.9 %), genotype 1a (19.9 %), genotype 1b (12.7 %), genotype 3b (9.4 %), and genotype 2 (0.48 %). Furthermore, the distribution of HCV-6 was significantly higher in the North (28 %) than in the South (15.3 %) ($P = 0.04$). Our study showed that HCV-3a was the most common genotype found in all regions of Thailand. HCV-6 was detected throughout Thailand but higher prevalence was found in the North than the South.

Topic 12: Hepatitis C

No: 1181

A polymorphism in ifnl3 is an independent risk factor development of hepatocellular carcinoma after treatment of HCV infection

Kuo-chin Chang[1], Po-lin Tseng[5], Hung-chao Hung[5], Ming-tsung Lin[5], Tsung-hui Hu[1]

Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan Division of Hepato-gastroenterology, Department of Internal Medicine Kaohsiung-Taiwan[1]

Background and aims: Polymorphism of the IL28B gene may predict the therapeutic response and outcome of chronic hepatitis C virus (HCV) infection. However, the impact of IL28B polymorphism on the development of hepatocellular carcinoma (HCC) after antiviral treatment remains controversial.

Methods: We retrospectively analyzed tissues from 1118 histologically proven HCV patients after peg-IFN/RBV therapies from 2000 to 2009 for IL28B polymorphism (rs12979860).

Results: The frequency of the IL28B rs12979860 CC, CT, and TT genotypes in chronic HCV patients was 86.4, 13.2, and 0.3 %, respectively. The duration of follow-up ranged from 12 to 159 months, with a median of 60 months. At the end of follow-up, 108/1118 (9.66 %) patients developed HCC. The IL28B CT/TT genotype was positively correlated with high baseline AFP levels (≥ 20 ng/mL), advanced fibrosis stage, diabetes (DM), and failure to attain sustained virologic response (SVR; all $P < 0.05$). Multivariate Cox regression analysis showed that age ≥ 60 y, low platelet count (< 15 × 109 cells/L), AFP ≥ 20 ng/mL, advanced fibrosis stage, DM, non-SVR and the IL28B CT/TT genotype were significant risk factors for HCC development ($P < 0.05$). Subset analysis revealed that age, platelet count, AFP levels, and fibrosis stage were risk factors for patients with SVR. The impact of IL28B was not significant although HCC occurred in SVR patients with the CT/TT genotype. In contrast, for patients without SVR, only fibrosis stage and the IL28B CT/TT genotype (HR: 1.80, 95 % CI: 1.06-3.07, $P = 0.030$) were independent risk factors for HCC development.

Conclusions: The CT/TT IL28B polymorphism was associated with HCV-related HCC development, especially for patients without SVR after antiviral therapy.

Topic 12: Hepatitis C

No: 2245

Baseline characteristics of hepatitis C virus patients in Turkey the results of peg base cohort

Mehmet Demir[1], Iftihar Köksal[2], Reşat Özaras[3], Orhan Sezgin[4], Şebnem Gürsoy[5], Fehmi Tabak[6], Özgür Günal[7], Yusuf Önlen[8], Hayat Kumbasar[9], Meral Akdoğan[10], Hasan Özkan[11], Ulus Salih Akarca[12], Fatih Özdener[13], Seda Erdoğan[13], Abdülkadir Dökmeci[11]

Mustafa Kemal University School of Medicine Gastroenterology Hatay-Turkey[1], Karadeniz Technical University School of Medicine Infectious Diseases Trabzon-Turkey[2], Istanbul University Cerrahpaşa School of Medicine Infectious Diseases Istanbul-Turkey[3], Mersin University School of Medicine Gastroenterology Mersin-Turkey[4], Erciyes University School of Medicine Gastroenterology Kayseri-Turkey[5], Istanbul University Cerrahpaşa School of Medicine Infectious Diseases Istanbul-Turkey[6], Tokat Gaziosmanpasa University School of Medicine Infectious Diseases Tokat-Turkey[7], Mustafa Kemal University School of Medicine Infectious Diseases Hatay-Turkey[8], Haseki Training and Research Hospital Infectious Diseases Istanbul-Turkey[9], Ankara Yüksek Ihtisas Training and Research Hospital Gastroenterology Ankara-Turkey[10] Ankara University School of Medicine Gastroenterology Ankara-Turkey[11] Ege University School of Medicine Gastroenterology Izmir-Turkey[12] Roche Pharmaceuticals Clinical Research Istanbul-Turkey[13]

Introductions and aim: Baseline characteristics determine the outcome of Chronic Hepatitis C (CHC) treatments in a great extend. Varying combinations of favorable or unfavorable viral and host factors predict the sustained virologic response (SVR).

Patients and methods: Peg-Base is a global multicenter observational study which was designed to evaluate in routine clinical practice the efficacy of peginterferon alfa (Peg-IFN) plus ribavirin combination therapy and treatment regimens containing direct-acting anti-virals (DAA) in patients with CHC receiving such therapies according to local label and to document the predictive value of baseline characteristics on treatment outcome The present is a subanalysis of patients included in Turkey, aiming to determine the main baseline characteristics of the patients with CHC. Baseline characteristics, treatment options, the response to therapy, adherence, safety, and response outcomes of on-treatment, end of treatment (EOT) and SVR were recorded.

Results: A total of 148 CHC patients with genotype 1 were given treatment and included into this interim analysis. The vast majority of the patients were older than 45 years, with BMI > 25 kg/m2 and viral load > 400,000 IU/mL. 65 naïve patients received PR therapy (Group PR); 15 naïve patients with advanced fibrosis were given PR plus telaprevir (PR + T) (Group Naïve PRT) and 68 treatment experienced patients were given PR + T (Experienced PRT). SVR rates 12 weeks post-treatment were 52, 67, and 60 %, respectively.. In the 3 groups the percentage of patients with cirrhosis/transition to cirrhosis were 20, 93, and 43 %. Favorable IL28B polymorphism (rs12979860) CC rates were 23, 0, 18 % in PR, naïve PRT and experienced PRT groups respectively. IL28B polymorphism (rs8099917) TT, rates were as follows: 48, 13, 41 % in PR, naïve PRT and experienced PRT groups, respectively.

Conclusions: A considerable proportion of patients included in this cohort had unfavorable baseline characteristics for SVR, which might

explain the slightly lower rates in the PRT groups compared with phase III clinical trials. Nevertheless, SVR rates achieved are considered clinically meaningful.

Topic 12: Hepatitis C

No: 2207

Sustained virological response with short term telaprevir treatment a case report

Aysun Yalci[1], Ozge Leyla Sengezer[1], Ismail Balik[1]

Ankara University Faculty of Medicine Infectious Diseases and Clinical Microbiology Ankara-Turkey[1]

A 63 years old female patient with chronic hepatitis C admitted to our hospital at2012. Hermedical history revealed hypertension, atrial fibrosis, and chronic obstructive pulmonary disease. She was treated with pegylated ınterferon (PEG-IFN) and ribavirin 7 years ago. She relapsed 5 years ago and a liver biopsy was performed to the patient. Histopathologic examination revealed Ishak stage 9 grade 3. PEG-IFN, ribavirin and telaprevir treatment was started. During the treatment period the patient complained about nausea and vomitting. Due to these adverse events the patient couldn't eat anything and lost weight. At the 10th week of the treatment the patient wanted to stop the telaprevir treatment because of the side effects. But she continued the treatment with PEG-IFN and ribavirin for another 14 weeks. Nausea and vomitting reduced with the cessation of telaprevir. At the end of the treatment HCV-RNA was negative. Sustained virological response was obtained and the patient did not relapsed in two years after treatment. HCV-RNA is still negative.

Direct acting antivirals improved the sustained virological response (SVR) rate significantly in chronic hepatitis C. Normal treatment duration with telaprevir is 12 weeks. In our patient we stopped the treatment at week 10 because of adverse events.the sustained virological response was achieved with short term treatment.

Topic 12: Hepatitis C

No: 1037

Epidemiological and clinico biological aspects of the population co infected with human immunodeficiency virus and hepatitis C virus review of 22 cases in an infectious diseases unit

Nassima Belabas[1], Achour Amrane[1], Mohamed Zeroual[1], Fatma Zohra Aissat[1], Kamel Aknouche[1], Abdelouhab Dif[1]

Laadi Flici (el-kettar) Hospital Infectious Diseases Department Algiers-Algeria[1]

Background: Knowledge of epidemiological, clinical and biological profile of Human Immunodeficiency Virus (HIV) - Hepatitis C Virus (HCV) co-infected patients is an integral part of their care.
Objective: To describe the epidemiological, clinical and biological characteristics and outcomes of HC treatment in HIV-HCV co-infection.
Materials and methods: This is a retrospective study (January 2004 - May 2014). The variables studied were: epidemiological and Clinical aspects, immuno-virological parameters, efficacy of antiretroviral therapy (ART) and Peginterferon-α2a + Ribavrin (PR).
Results: 477 men were followed for HIV infection, including (22) showed HCV co-infection (04.6 %). The average age was 48 years, (36 %) were single, (91 %) are of Algerian nationality and (09 %) are sub-Saharan Africans. There was HIV- hepatitis B viral (HBV)-HCV co-infection in (09 %). The most common mode of transmission was injection drug use (IDU) (68 %). The average CD4 was 228 cells/mm3. (64 %) had HIV RNA ≥ 100,000 copies/ml. (54 %) had a HCV RNA ≥ 800,000 IU/ml. HCV genotype was entered in 07 cases: genotype 1 (05 cases), genotype 3 and genotype 4 in (01) case each. The average of liver stiffness was 12.7 kPa. Six patients received PR. There was a sustained virologic response in (67 %), HIV RNA was undetectable in all patients receiving ART.
Conclusion: The IDU appears to be the most common mode of transmission HIV and HCV. People are diagnosed at late-stage disease with severe advanced liver fibrosis. HIV-HCV co-infection poses difficulties combined support of these two infections.

Topic 12: Hepatitis C

No: 1561

Hepatitis C infection in high risk population in Iran a meta analysis

Mohammad Hossein Somi[1], Morteza Ghojazadeh[2], Haniyeh Ajdari[3], Nastaran Amous[3], Mehran Rahimi[3]

Liver and Gastrointestinal Research Center Internal Medicine Tabriz-Iran[1], Liver and Gastrointestinal Research Center Physiology Tabriz-Iran[2], Liver and Gastrointestinal Research Center Faculty Medicine Tabriz-Iran[3]

Aim: There is no overall estimation of hepatitis C infection (HCV) in Iran. We reviewed all of the published and unpublished evidences related to HCV infection in Iran in order to accurately estimate the prevalence of HCV infection in the Iranian high risk population to inform future health system programs.
Methods: In this meta-analysis, all papers, medical congresses, HCV-related reports, projects of Iranian research centers and medical universities, reports from the Deputy for Health Affairs (published or unpublished), and online theses about HCV in Iran were included. We selected descriptive and analytical cross-sectional studies and surveys related to the prevalence of HCV infection in the Iranian high risk population between 1996 and 2014 that have sufficiently declared objectives, proper sampling methods with identical and valid measurement instruments for all study subjects and proper analysis methods regarding sampling design and demographic adjustments. We used a survey data analysis method to estimate the national prevalence rate.
Results: From the 3350 studies we investigated 40 eligible studies reported a prevalence of HCV infection in the high risk population. They were from 12 (out of 32) provinces. We calculated that the HCV infection prevalence rate in Iran is 12 % (7-18 %) (95 % confidence interval).
Conclusions: In comparison with similar studies, the prevalence of HCV infection in Iran is low. This might be a result of having prevention programs for high-risk groups and strict blood screening programs.

Topic 12: Hepatitis C

No: 1311

Comparison strategems of post screening management of anti HCV positive community residents simple notification active referral or accessible medical care

Yuan-hung Kuo[1], Shen-nan Lu[1]

Kaohsiung Chang Gung Memorial Hospital Internal Medicine Kaohsiung City-Taiwan[1]

Aims: To elucidate the results of post-screening care stratagems for anti-hepatitis C virus (HCV)-positive subjects in the community.
Methods: Part I The intervention program A total of 151790 subjects underwent a large-scale health screening. We called back those who had anti-HCV-positive, alanine aminotransferase (ALT) more than 80 IU/L and age less than 65 years to answer a questionnaire. Those responders who met the reimbursement criteria for anti-HCV treatment of National Health Insurance in Taiwan were referred for treatment.
Part II The accessible medical care program Yujing, a mountain township, and 271 HCV residents were screened before. They were invited to a hepatitis clinic in Yujing health center biweekly.
Results: Part-I A total of 907 eligible anti-HCV-positive subjects responded and 197 (21.7 %) have been suggested to treat, but only 83 (9.2 %) did. Finally, 47 achieved sustained virological response (SVR). After this intervention program, 96 (10.6 %) additional patients were encouraged to refer and 33 (3.6 %) received treatment. Finally, 20 obtained SVR.
Part II A total of 140 (51.7 %) residents responded and 112 were anti-HCV-positive including 31 (27.7 %) HCV RNA-negative, 49 (43.8 %) HCV RNA-positive plus ALT less than 40 IU/L and 32 (28.5 %) HCV RNA-positive plus ALT more than 40 IU/L. During the follow-up, 14 of 49 patients had ALT more than 40 IU/L. Among 46 eligible HCV patients, 15 (32.6 %) received treatment and 10 achieved SVR.
Conclusions: Simple notification only made 9.2 % of screened HCV patients to treat. Active referral could encourage additional 3.6 % to be treated. Additionally, accessible medical care program could result 32.6 % of elder HCV candidates to treat.

Topic 12: Hepatitis C

No: 1154

Successful treatment of post renal transplant hepatitis C with sofusbuvir and simepravir only

Rajneesh Kumar[1], Ennaliza Salazar[1], Terence Kee[2], Wan Cheng Chow[1]

Singapore General Hospital Gastroenterology and Hepatology Singapore-Singapore[1], Gastroenterology and Hepatology Renal Medicine Singapore-Singapore[2]

Hepatitis C is a less common liver disease in general population in Singapore but is significantly higher in patients on hemodialysis. Treatment of hepatitis C is essential before undergoing renal transplant as the outcomes are significantly lower after renal transplant. Post renal transplant acquisition of hepatitis C is rare but being increasingly reported. Post renal transplant hepatitis C leads to poor outcome and significantly limits the use of immunosuppressant. Treatment with interferon carries a very high risk of transplant rejection. Use of new drugs for Hepatitis C has been limited for the data available. In this case we report the first case of treatment of hepatitis C genotype 1 with use of sofusbuvir and simepravir.

Topic 12: Hepatitis C

No: 1667

Standard treatment of chronic hepatitis C with pegylated interferon and ribavirin therapy can we continue to use

Birol Baysal[1], Yusuf Kayar[1], Ahmet Danalıoğlu[1], Mukaddes Tozlu[1], Maged Elshobaky[1], Orhan Kocaman[1], Ali Ince Tüzün[1], Zuhal Gücin[2], Hakan Şentürk[1]

Bezmialem Vakif University, Faculty of Medicine Department of Gastroenterology Istanbul-Turkey[1], Bezmialem Vakif University, Faculty of Medicine Department of Pathology Istanbul-Turkey[2]

Introduction: Until recently, the standard treatment for chronic hepatitis C was Peg-IFN + ribavirin. SVR rates of this therapy were insufficient. Then first generation protease inhibitors were added to standard therapy. Unfortunately these drugs had serious side effects, cost was not low and SVR was not as high as desired.
Aim: To evaluate the efficacy of standard dual therapy and to compare the efficacies of both regimens of Peg-IFN α2a + ribavirin and Peg-IFN α2b + ribavirin in chronic hepatitis C patients infected with genotype 1 virus.
Materials and methods: 173 patients were evaluated. 32 patients; 11 with genotype 3, 3 with chronic kidney disease, 2 with HBsAg positivity and 16 with insufficient data were excluded. Finally, 141 patients were included and divided into 2 groups. Group A was given Peg-INF α2a + ribavirin and group B Peg-INF α2b + ribavirin, both for 48 weeks.
Results: There were 79 patients in group A and 62 patients in group B. of the patients, 79.1 % were genotype 1b. Age, sex, BMI, duration of disease, initial fibrosis stage, ALT levels and viral load were similar in both groups ($p > 0.05$). SVR rate of group B was higher than that of group A (56.5 % vs 50.6 %; $P = 0.49$).
Conclusion: With the regimens of Peg IFN α2a or 2b, SVR can be achieved in approximately one out of every two patients. In countries like Turkey that new drugs can not be obtained due to the high cost, standard of care can continue to be used in patients with advanced fibrosis to prevent cirrhosis and decompensation.

Topic 12: Hepatitis C

No: 2010

A prospective randomized open label multicenter study on re treatment for non responsive Chinese chronic hepatitis C patients treated with pegylated interferon α2a plus ribavirin

Xinyue Chen[1], Huiying Rao[2], Lai Wei[3], Jia Shang[4], Zhiliang Gao[5], Qing Xie[6], Xiaoguang Dou[7], Xiaoyuan Xu[8], Guozhong Gong[9], Guofeng Chen[10], Jun Li[11], Dazhi Zhang[12], Junqi Niu[13], Hong Chen[14], Yinong Feng[15], Jinlin Hou[16], Hong You[17], Yun Wu[18], Peili Zhao[19]

Beijing Youan Hospital, Capital Medical University Hepatology Department Beijing-China[1], Peking University People's Hospital Hepatology Department Beijing-China[2], Peking University Hepatology Institute Hepatology Department Beijing-China[3], Henan Province People's Hospital Hepatology Department Zhengzhou-China[4], Sun Yatsen University Hepatology Department Guangzhou-China[5], Shanghai Jiao Tong University Ruijin Hospital Hepatology Department Shanghai-China[6], China Medical University Hepatology Department Shenyang-China[7], Peking University First Hospital Hepatology Department Beijing-China[8], The Second Xiangya Hospital of Central South University Hepatology Department Changsha-China[9], Military Hospital of China Hepatology Department Beijing-China[10] Nanjing Medical University Hepatology Department Nanjing-China[11] The Second Affiliated Hospital Chongqing Medical University Hepatology Department Chongqing-China[12] Jilin University Hepatology Department Changchun-China[13] Lanzhou University Hepatology Department Lanzhou-China[14] Shanxi Medical

University Hepatology Department Taiyuan-China[15] Nanfang University Hepatology Department Guangzhou-China[16] Beijing Friendship Hospital Hepatology Department Beijing-China[17] The Affiliated Hospital of Inner Mongolia Medical Hospital Hepatology Department Huhehaote-China[18] The Third Hospital of Qinhuangdao Hepatology Department Qinhuangdao-China[19]

Aim: To evaluate the efficacy and safety profiles of retreatment with Peg-IFN α-2a (Peg-IFN) plus ribavirin for an extended treatment duration in non-responsive chronic hepatitis C (CHC) patients.
Methods: CHC patients previously non-responsive to conventional IFN-α (C-IFN) or Peg-IFN-based therapy were randomized into two groups treated with 180 μg/wk Peg-IFN plus 1000–1200 mg/d ribavirin for 72 or 96 weeks and followed-up for 24 weeks after treatment completion. Single nucleotide polymorphisms at loci rs12979860 were determined.
Results: The study population included 81 patients [50 (61.7 %) males] treated at 18 Chinese hospitals. Baseline patient characteristics were similar between the groups (Table 1). Although virological responses did not differ significantly between the groups, the overall sustained virological response (SVR) rate was 65.4 % for re-treated non-responders (Table 1). Patients non-responsive to previous Peg-IFN treatment had a lower SVR rate than those non-responsive to C-IFN (58.3 % vs. 78.1 %, $P < 0.05$). The positive predictive values of rapid virological response (RVR) and complete early virological response (cEVR) for SVR were 100 % (17/17) and 91.2 % (31/34), respectively. Patients with the IL2B CC genotype achieved a higher SVR rate than those with the CT/TT genotype (82.9 % vs. 23.1 %, $P < 0.001$). Adverse events were reported by 38 patients, of whom 16 were given a lower dose and 1 stopped therapy.
Conclusion: For patients previously non-responsive to C-IFN-based treatment, PEG-IFN plus ribavirin treatment was highly efficacious. RVR, cEVR, and IL28B genotype had good predictive value for identifying Chinese CHC patients who may achieve good SVR.

Topic 12: Hepatitis C

No: 2182

The impact of the affective state on the satisfaction regarding treatment outcomes in patients with chronic viral hepatitis

Inna Vengher[1], Iulianna Lupasco[1], Vlada-tatiana Dumbrava[1], Natalia Taran[1], Gheorghe Harea[1], Elena Chirvas[1]

State University of Medicine and Pharmacy "Nicolae Testemitanu" Gastroenterology Chisinau-Moldova[1]

Introduction:. Depression is a frequent comorbidity in chronic viral hepatitis (CVH) and can affect clinical presentation, quality of life and patient satisfaction regarding the treatment outcomes.
Aim: To study the prevalence of symptoms and the patients' subjective attitude regarding the treatment outcomes in relation with affective state in CVH.
Materials and methods: 147 patients with CVH (B, C) have been investigated. We have measured the depressive scores using the Hamilton Rating Scale for Depression (HDRS-21). All patients were asked about their satisfaction regarding previous treatments.
Results: In 147 patients with CVH we found a large prevalence of depression 85 %. A third of patients have been detected incidentally, before diagnostics they were asymptomatic. After the disclosure of CVH, especially in depressive participants, the hearburn, eructation, epigastric pain and postprandial dyspeptic symptoms were found more often in comparison with anamnestic data before the diagnosis confirmation. 61.2 % of patients received treatments in the past, of whom 60 % mentions subjective improvement, 38.9 % consider lack of efficacy, 1.1 % believe that after treatment his condition worsened. All patients who denied the effect of prior treatments had depression.
Conclusion: CVH disclosure is a stressful event which may lead to the depression. In depressive patients we found a larger prevalence of clinical symptoms than in the nondepressive ones. Patients with comorbid depression tend to negate the effects of prior therapies.

Topic 13: Hepatitis D

No: 1115

Salmonella typhi testing in patients with delta hepatitis at an rural medical center in eastern part of Turkey

Ahmet Cumhur Dülger[1], Burak Suvak[1], Aysun Özel[1], Enver Aytemiz[2], Levent Demirtaş[3]

Yuzuncuyil University Hepatology Van-Turkey[1], Nizip State Hospital Internal Medicine Gaziantep-Turkey[2], Erzincan University Internal Medicine Erzincan-Turkey[3]

Background: Hepatitis D virus (HDV) is usually associated with chronic hepatitis, liver cirrhosis and hepatocellular carcinoma. Salmonella typhi infection may cause typhoid fever and enteritis. Despite evidence that bacterial infections are associated with end-stage liver disease, salmonellosis in patients with delta hepatitis related to liver disease has not been well characterized.
Materials and methods: We analyzed data from 96 delta hepatitis patients (mean age 52.5 ± 12.8 years; 50 male) with HDV of whom 52 (54 %) had biopsy-proven cirrhosis.117 control subjects (mean age 50.4 ± 7 years; 60 male) were selected from patients with splenomegaly.

Results of the samples that have HBsAg reactive anti-HDV antibodies micro-ELISA kits were determined. Gruber-Widal test was performed for all the subjects and patients. MELD scores of the cirrhotic delta hepatitis patients were compared according to salmonella status. The data obtained from the hospital records were entered into SAS software for data analyses.
Results: There was a positive correlation between MELD scores and Salmonella Gruber Widal H titers ($P = 0.012$). In addition, presence of H titers was correlated with rural origin of the delta hepatitis patients ($P = 0.028$). Most remarkably, delta hepatitis patients were more likely to have higher OH titers compared to controls ($P = 0.017$).
Conclusion: This preliminary analysis revealed that *Salmonella typhi* antibodies were prevalent in patients with delta hepatitis. Higher MELD scores were also associated with past salmonella infection. Patients who resident in rural areas of Asia have a high risk for both of delta hepatitis and salmonellosis. Future studies on the impact of salmonellosis on delta hepatitis are needed.

Topic 13: Hepatitis D

No: 1576

The effect of interleukin 28b gene polymorphisms on disease severity and treatment response of patients with chronic delta hepatitis

Murat Ispiroglu[1], Ibrahim H. Bahcecioglu[2], Mehmet Yalniz[2], Ulvi Demirel[2]

Firat University Faculty of Medicine Gastroenterology Elazig-Turkey[1], Faculty of Medicine Gastroenterology Elazig-Turkey[2]

Background/aim: We aimed to investigate the relationship between response of pegylated-interferon treatment, clinical prognosis and IL28B polymorphisms.
Method: Between 2007 and 2012, 47 patients with chronic HDV were examined which have followed up Firat University Medical Faculty Department of Gastroenterology. They have received at least one year pegylated-interferon treatment. Patients were grouped according to treatment response.
Results: Sustained viral response (SVR) 15 (%32), non-response 25 (%53) and relapse 7 (%15) group. Age, sex, biochemistry (albumin, total bilirubin, LDH, ALT, AST, ALP, GGT), hemogram, HBeAg, HBsAg, HBVDNA, HDVRNA and IL28B genotypes (CC, CT, TT), liver biopsy results were compared between groups. At he beginning of treatment AST, ALT, ALP, GGT, total bilirubin, serum albumin levels were significantly higher in non-responsed group but age and other laboratory levels was not different between groups. IL28B genotype comparison between three groups CC, CT, TT genotypes frequencies were not different. 8 (%53) CC, 7 (%47) CT, 0 (%0) TT in SVR group, 13 (%52) CC, 8 (%32) CT, 4 (%16) TT in non responsed group, 3 (%43) CC, 4 (%57) CT, 0 (%0) TT in relaps group, were determined. If frequency of patients with polymorphism (CC, CT) compared between the groups there is no different. Number of the patients without polymorphism (TT) is small (only 4 patients) so frequency could not be calculated statistically.
Conclusion: There is no relationship between IL28B rs12979860 polymorphism and response of chronic HDV treatment.

Topic 13: Hepatitis D

No: 1752

Virological histological and biochemical differences among delta hepatitis with active and inactive chronic hepatitis B patients

Mustafa Kemal Celen[1], Salih Hosoglu[1], Berivan Tunca[2], Celal Ayaz[1], Emel Aslan[1], Saim Dayan[1]

Dicle University Hosptial Infectious Diseases Diyarbakir-Turkey[1], Kiziltepe State Hospital Infectious Diseases Mardin-Turkey[2]

Aim: In this study, we aimed to evaluate the virological, histological and biochemical parameters of active and inactive chronic hepatitis B patients with delta hepatitis.
Method: Fifteen healthy hepatitis B carriers with "HBsAg positive, Anti-Delta positive, HDV-RNA positive, HBV-DNA negative, ALT > ULN" laboratory results and 18 chronic active hepatitis B patients with "HBsAg positive, Anti-Delta positive, HDV-RNA positive, HBV-DNA > 20.000 IU/ml, ALT > 2xULN" laboratory results that were followed in Dicle University Hospital between 2004 and 2014 were evaluated retrospectively. Ishak scoring system was used to commentate liver biopsies. Two groups were compared according to gender, age, numbers of platelets, ALT levels, HBV-DNA copies and fibrosis.
Results: This study included 15 patients in an inactive HBV group. Fibrosis stage 0 was observed in 4 (26.7 %), patients, 9 (60 %) patietnts were stage 1 and 2 (13.3 %) were stage 2. Among the 18 patients with active disease, fibrosis stage 0 was present in 4 (22.2 %) patients, stage 1 in 5 (27.8 %) patients, stage 2 in 5 (27.8 %) patients, stage 3 in 2 (11.1 %) patients and stage 4 in 2 (11.1 %) patients. In univariate analyses, ALT ($P = \leq 0.001$) and HBV-DNA copies ($P = \leq 0.001$) were found associated factors for active disease. In the multivariate analysis, only ALT levels (Odds Ratio = 1.06, Confidence Interval = 1.02-1.11, $P = 0.007$) was continued as independent associated factor for active disease.
Conclusion: Delta hepatitis is still maintains its importance as a serious problem in Southeastern Anatolia Region. The prognosis of hepatitis delta with chronic active hepatitis B is more severe histologically and serologically.

Topic 13: Hepatitis D

No: 1971

IL28B polymorphisms and hepatitis D virus infection in Uzbekistan

Erkin Musabaev[1], Muazzam Abdukadirova[2], Aziza Khikmatullaeva[2], Renat Latipov[3], Adkhamjon Mamatkulov[4]

Sriv Director Tashkent-uzbekistan[1], Sriv Hepatology Tashkent-uzbekistan[2], Sriv Deputy Director Tashkent-uzbekistan[3], Sriv National Reference Laboratory Tashkent-uzbekistan[4]

Background and aim: An IL28B genotype strongly predicts the outcomes of hepatitis C virus (HCV) infection. However, the applicability of the IL28B polymorphism marking the haplotype (rs8099917) to determine the outcomes of hepatitis B virus (HBV) and hepatitis D virus (HDV) infections is unclear. The study was aimed to determine association between frequency of HDV infection and IL28B genotype (rs8099917).
Methods: Totally 61 patients admitted to a clinic of the Research Institute of Virology (Tashkent, Uzbekistan) and diagnosed with HBV (9) and HBV + D (52) infection were enrolled in the study. DNA specimens were extracted from peripheral blood mononuclear cells and the IFNL3 SNP (rs8099917) and genotyped by the TaqMan assay.
Results: IL28B genotype was determined for 61 patients with median age of 36 years (range, 12-57). Cirrhosis distribution by Child-Pugh score was Class A—38 %, Class B 53 %, class C and transient consisted 4 % and 5 % respectively. The frequencies of the rs8099917 TT (MA) and GT(HE) + GG (MI) genotypes between HBV and HBV + D patients were 22.2, 77.8 and 63.5 %, 36 % respectively. When comparing with TT and GG + GT genotypes between HBV + D and HBV patients, the chance of HDV infection to be detected significantly higher in patients with MA genotype (OR 6.07 95 % CI 1.14-32.2; $P = 0.03$) then in patients with HE/MI genotype.
Conclusions: Due to low number of observations there is no sufficient evidence for statement of cause-and-effect relation between IL-28B rs8099917 SNP and HDV infection, but the data suggests a new direction in investigation of pathogenesis of HDV infection.

Topic 13: Hepatitis D

No: 1129

Familial spreading of the delta hepatitis in rural areas of Turkey. "Lone wolf" attack is not possible for all victims

Ahmet Cumhur Dülger[1], Kürşat Türkdoğan[2], Burak Suvak[1], Mahmut Ülger[3], Ümit Yakan[4]

Yuzuncuyil University School of Medicine Hepatology Van-Turkey[1], Bezmi Alem University Hepatology Istanbul-Turkey[2], Yuzuncuyil University School of Medicine Family Medicine Van-Turkey[3], Yuzuncuyil University School of Medicine Infectious Diseases Van-Turkey[4]

Aim: Hepatitis D virus (HDV) infection is a serious health problem worldwide as well as rural areas of the middle east. Familial aspects of HDV infection has not been reported in population-based studies. We examined this relationship using recent population-based data from the hospital data as well as patient interviews.
Materials and methods: We reviewed charts of 145 adult outpatients (80 female; aged 18–80 years) with chronic delta hepatitis (CDH) between July, 2013 and October, 2014. To obtain correct data, patients were also questioned. Anti HDV IgG and HBsAG levels were studied with Enzyme Linked Immunosorbent Assay (ELISA) by Cobas 601 device (Roche, Germany).
Results: The prevalence of HDV did not differ by gender. Among the 145 patients, 25 (17.2 %) of them was reported an intrafamilial exitus case due to liver cirrhosis-related complications. 63 (43.4 %) of study patients were also reported as having a close family member with hepatitis B infection. Half of them had also delta hepatitis infection.
Conclusion: Familial clustering of delta hepatitis patients was a striking finding, despite our enhanced surveillance system. Future studies on the impact of intra-familial behaviours and house-hold contacts on CDH infection and its impact on the natural history of HDV are needed particularly in rural areas of eastern Turkey where the disease is still endemic. On the other hand, increasing the awareness for familial HDV screening by healthcare providers should be needed.

Topic 13: Hepatitis D

No: 2126

Evaluation of delta hepatitis cases

Emine Parlak[1], Mehmet Parlak[1], Zülal Özkurt[1], Ayşe Albayrak[1], Kemalettin Özden[1]

Ataturk University Department of Infectious Diseases and Clinical Microbiology Erzurum-Turkey[1]

Objective: Hepatitis D virus (HDV) was first shown in 1977 by Rizzetto et al. It is especially common in Eastern and Southeastern Anatolia regions in our country. So far, there is no agent approved for the HDV treatment other than interferon-alpha. The purpose of this study was to evaluate 103 patients who are diagnosed with HDV.
Method: Patients HDV diagnoses were made by positive Anti-HDV results and quantitative measurement of HDV-RNA. Detection and measurement of HBV-DNA and HDV RNA were performed with real-time PCR methods. Liver Biopsy samples were evaluated according to Knodell scoring system.
Results: 2540 Hepatitis B patients were examined in the same period. 1555 (61.2 %) of them were male, and 985 (38.8 %) of them were female. The average age of them was 43.95 ± 13.22 (min 14-max 85); and the median was 43. 103 HDV infections were followed-up in the same period. Proportion of the patients with delta infection in the Hepatitis B patient group was found to be 4.05 %. 68 (66 %) of the patients were male. 10 (9.7 %) of the patients had developed liver cirrhosis.
Conclusion: Chronic delta hepatitis is the least common, but the most severe type of the chronic viral hepatitis with high pathogenic potential. It must be considered in activated chronic hepatitis B cases and when cirrhosis is developed in a short-period in hepatitis B cases. Since there is no effective treatment, hepatitis B vaccinations must be performed for the protection of healthy people and relatives of HBV patients.

Topic 13: Hepatitis D

No: 1118

Outcome of delta hepatitis near the Iranian border of Turkey

Ahmet Cumhur Dülger[1], Burak Suvak[1], Ali Irfan Baran[2], Kürşat Türkdogan[3], Bilge Gültepe[4]

Yuzuncuyil University Hepatology Van-Turkey[1], Yuzuncuyil University Infectious Disease Van-Turkey[2], Bezmi Alem University Gastroenterology Istanbul-Turkey[3], Bezmi Alem University Microbiology Istanbul-Turkey[4]

Objective: Hepatitis D virus (HDV) infection is a serious health problem leading to cirrhosis and hepatocellular carcinoma. On the other hand, eastern part of the country is still home to one of the world largest delta hepatitis populations. We therefore conducted the current study to determine the key points of HDV infection.
Materials and methods: We analyzed data from 96 consecutive delta hepatitis patients (mean age 52.5 ± 12.8 years; 50 male; 52 cirrhotics). Anti HDV IgG and HBsAg levels were studied with ELISA. Demographic features, laboratory data, results of ultrasonographic examination, MELD and CTP scores were also examined.
Results: There were 11 (11.4 %) (4 female) HCC patients in the study group. Among non-cirrhotic delta hepatitis patients (44 patients), 35 (79.5 %) of them were taking peg-interferon theraphy. Five of the non-cirrhotic patients were taking oral antiviral agents mostly tenofovir disoproxil. According to Child-Turcot-Pugh (CTP) classification; 33 cirrhotic patients were in CTP A; 15 in CTP B and 4 in CTP C groups. HBV-DNA positivity was detected in 20 (60 %) cirrhotic patients. Mean MELD score was 9.5 ± 3.2 among patients with delta hepatitis-related cirrhosis. Liver transplantation has been performed for 4 patients.
Conclusion: Delta hepatitis patients have a higher prevalence of cirrhosis and its related complications. Treatment rates have been relatively high in HDV patients in Turkey. The prevalence of cirrhosis was extraordinary high among those patients with HDV. Rate of livertransplantation was very low mostly due to lack of organ donation.Further steps are needed in eastern part of Turkey.

Topic 13: Hepatitis D

No: 1928

Is interferon alpha treatment make difference on chronic delta hepatitis versus natural course

Özgen Ahmet Yildirim[1], Sami Evirgen[2], Bilger Çavuş[2], Raim Iliaz[2], Filiz Akyuz[2], Kadir Demir[2], Fatih Beşişik[2], Sabahattin Kaymakoğlu[2], Mine Güllüoğlu[3], Mustafa Önel[4], Çetin Karaca[2]

Istanbul Medical Faculty Internal Medicine Istanbul-Turkey[1], Istanbul Medical Faculty Gastroenterohepatology Istanbul-Turkey[2], Istanbul Medical Faculty Pathology Istanbul-Turkey[3], Istanbul Medical Faculty Microbiology Istanbul-Turkey[4]

Introduction: Today the only treatment of CDH is interpheron alpha (IFNα). This study aims to asses long term histological, virological and biochemical outcomes with IFNα.
Material-methods: Data of 48 CDH patients who had been treated with IFNα for at least 1 year and who were non cirrhotic at the beginning were assessed retrospectively. Patients with any other chronic liver disease and who were still on IFNα therapy were excluded. Cirrhosis diagnosis was supported with objective findings

of portal hypertension. Pre-post treatment liver biopsy Ishak fibrosis staging scale scores were compared. Patients were grouped according to fibrosis score change as increasing, decreasing and steady groups. **Findings:** 48 patients were followed for mean 7 years. 24 of 48 patients were became cirrhotic during follow up. Virological response rate of classical IFNα was 37 %, pegylated IFNα was 41 %. Sustained virological response rate among patients was %37. There was statistical correlation in between histological, virological and biochemical responses. Pre-post treatment fibrosis scores of 24 patients who were non cirrhotic at the end of follow up; were compared, the result was statistically non-significant ($P = 0{,}979$). Decreasing or steady fibrosis scores are accepted as histological response. 6 patients (%13) were in decreasing, 10 patients (%21) were in steady while 8 patients (%16) were in increasing score group of total 24 patients with pre and post treatment liver biopsies.
Conclusion: This study revealed long term natural course of patients treated with IFNα at least for 1 year. IFNα therapy hasn't changed the natural course, however 2 of 3 patients have progressed.

Topic 13: Hepatitis D

No: 2232

Seroepidemiology of hepatitis delta among hbsag carriers

Kamuran Türker[1], Fatma Ekşi Polat[1], Elçin Balcı[2], Medine Hasçuhadar[3], Betül Taş[4], Münire Korkmaz Fidan[5]

Istanbul Bağcılar Training and Research Hospital Infectious Diseases Istanbul-Turkey[1], Erciyes University Faculty of Medicine Public Health Kayseri-Turkey[2], Ankara Atatürk Training and Research Hospital Infectious Diseases Ankara-Turkey[3], Istanbul Bağcılar Training and Research Hospital Dermatology Istanbul-Turkey[4], Istanbul Training and Research Hospital Infectious Diseases Istanbul-Turkey[5]

Background: Hepatitis B is a significant health problem and more than 350-450 million individuals are infected with hepatitis B virus (HBV) globally. About 5 % of these individuals are coinfected with hepatitis D virus (HDV). HDV is considered to be a subviral satellite because it can propagate only in the presence of the hepatitis B virus (HBV). Transmission of HDV can occur either via simultaneous infection with HBV (coinfection) or superimposed on chronic hepatitis B or hepatitis B carrier state (superinfection). HBV-HDV coinfection increases the rate of fulminant hepatitis, chronic hepatitis and cirrhosis. Infection is largely restricted to persons at high risk of hepatitis B infection, particularly injecting drug users and persons receiving clotting factor concentrates. Worldwide more than 15 million people are co-infected. HDV is rare in most developed countries, and is mostly associated with intravenous drug use. However, HDV is much more common in the immediate Mediterranean region, sub-Saharan Africa, the Middle East, and the northern part of South America. We aimed to evaluate the epidemiology of HDV in individuals positive for hepatitis B surface antigen (HBsAg) patients.
Materials and methods: We enrolled about 1000 patients with chronic viral hepatitis B that were consecutively admitted to our outpatient infectious disease clinic from July 2011 to November 2014. HBsAg-positive individuals were tested for anti-HDAg antibodies (anti-HDAbs). The samples positive for anti-HDAbs were also tested for detection of HDV RNA by reverse transcription-polymerase chain reaction (RT-PCR).
Results: 14 patients were HDV-seropositive (8 males and 6 females, 57.1 % and 42.9 %) with mean age of 40.7 years (range 18 -77).In HDV-seropositive patients, 6 were positive for HDV RNA. AST degree high were in 5 patients. Only one patient was HBsAg negative.
Conclusion: The seroprevalence of HDV in HBsAg-positive individuals in this study was about 1.4 % which seems to be lower than the global prevalence of HDV.

Topic 13: Hepatitis D

No: 2176

High prevalence of past hepatitis A virus infection in turkish delta hepatitis patients results of hospital based primary care screening

Ahmet Cumhur Dülger[1], Mesut Aydın[1], Ömer Candar[1], Ali Irfan Baran[2], Burak Suvak[1], Muhammed Aslanboga[3]

Yuzuncuyil University Hepatology Van-Turkey[1], Yuzuncuyil University Infectious Disease Van-Turkey[2], Yuzuncuyil University Internal Medicine Van-Turkey[3]

Objective: Hepatitis D virus (HDV) infection is a serious health problem leading to cirrhosis and hepatocellular carcinoma. In patients with delta hepatitis, acute infection with hepatitis A virus (HAV) may cause fulminant liver failure. So, guidelines recommend that all patients with hepatitis B or D should be vaccinated against HAV, if they have negative test result for anti-HAV IgG. However, prevalence of past HAV infection in patients with delta hepatitis never studied. Our goal was to examine the past HAV infection prevalence in Turkish delta hepatitis patients seeking tertiary care at a university hospital clinic in eastern Turkey.
Materials and methods: We analyzed data from 47 delta hepatitis patients (mean age 52.5 ± 12.8 years; 20 male. 200 control subjects with hepatitis B (mean age 50.4 ± 7 years; 120 male) were also selected. of the delta hepatitis patients, 35 (75 %) was living in the villages of the city.
Results: All the delta hepatitis patients tested positive for anti-HAV IgG. On the other hand, 190 (95 %) patients with hepatitis B had positive result for anti-HAV IgG. The prevalence of HAV markers did not differ between hepatitis B and delta hepatitis group.
Conclusion: Patients with delta hepatitis were not at risk of developing acute HAV infection that require hospitalizations Delta hepatitis patients from endemic areas of Turkey are not at higher risk of acute HAV infection and should not be screened for past HAV infection. Furthermore, they should not vaccinated against HAV infection.

Topic 13: Hepatitis D

No: 1116

Delta hepatitis patients should be screened for brucellosis in rural areas of Turkey

Ahmet Cumhur Dülger[1], Burak Suvak[1], Enver Aytemiz[2], Bilge Gültepe[3], Kürşat Türkdogan[4]

Yuzuncuyil University Hepatology Van-Turkey[1], Nizip State Hospital Internal Medicine Gaziantep-Turkey[2], Bezmi Alem University Microbiology Istanbul-Turkey[3], Bezmi Alem University Gastroenterology Istanbul-Turkey[4]

Introduction: Hepatitis D virus (HDV) infection is a serious health problem worldwide. Zoonotic infections including Brucellosis

represents a major limitation to the efficacy of interferon treatment targeting chronic HDV infection in endemic areas. Despite this, the characteristic features of the Brucellosis in chronic HDV patients never examined.

Patients and methods: We analysed 65 adult treatment-naïve non-cirrhotic patients with chronic delta hepatitis (CDH) between July, 2013 and July, 2014. Anti HDV IgG and HBsAG levels were studied with ELISA device by Cobas 601 device (Roche, Germany). Serum agglutination (Wright) test for Brucellosis, liver transaminases and other routine laboratory tests were examined during the study period. Pearson correlation test was used between parameters.

Results: 65 CDH patients (female 49 %, mean age 51.2 years) were enrolled. Six patients had also Brucellosis. Low hemoglobin levels ($P < 0.001$) and higher levels of ALP ($P < 0.001$) and GGT($P < 0.005$) were positively correlated with Brucellosis.

Conclusion: Both of CDH and human Brucellosis are still endemic in eastern part of Turkey. Elevated levels of cholestasis enzymes and low hemoglobin levels are the keys for diagnosing Brucellosis in patients with CDH. In endemic areas for Brucellosis, clinicians should also be vigilant for zoonotic diseases before initiating peg-interferon. But further studies are needed.

Topic 13: Hepatitis D

No: 1759

Lichen planus induced pegylated interferon alpha 2a treatment in a patient with delta hepatitis

Safak Kaya[1], Eyup Arslan[2], Sule Baykara[3]

Gazi Yasargil Training and Research Hospital Infectious Diseases Diyarbakir-Turkey[1], Selahaddin Eyyübi State Hospital Infectious Diseases Diyarbakir-Turkey[2], Selahaddin Eyyübi State Hospital Dermatology Diyarbakir-Turkey[3]

Lichen planus (LP), is an inflammatory disease characterized by chronic keratosis seen skin and/or mucous membranes. In literature, there are many publications related with lichen planus developing in patients treated with pegylated interferon alfa-2a because chronic hepatitis C. In this study, as we know that we reported the first lichen planus case induced by pegylated interferon alpha-2a therapy in a patient receiving pegylated interferon alpha-2a because of chronic delta hepatitis D.

Case

Thirty-year-old man was admitted to our clinic because of HBsAg positivity. There was fatique, weakness complaints of patient. He had no underlying disease. There were no abnormal findings on physical examination. Laboratory results showed HBV DNA negative, the total anti-delta positive, alanine aminotransferase (ALT) 72 U/L (upper limit of 41 U/L), platelet 119 000/mm^3, respectively. In accordance with these findings, a diagnosis chronic hepatitis D was made and pegylated interferon alpha-2a subcutaneously once a week was started. In 4th month of treatment, the common lace-looking lesions on the oral mucosa, white patches on his lips, papular lesions on the hands and feet of patient developed. Thereupon, topical treatment (mometasone furoate) was started with diagnosis of lichen planus by dermatology. In 5th month of treatment, oral mucosal biopsi was taken due to the persistence of lesions and dose of interferon was reduced to 135 mcg. The pathology report of patient was consistent with lichen planus. In 6th month of treatment interferon was stopped because there was no decline in the lesions.

Topic 14: Hepatitis E

No: 1283

Changing epidemiology of acute sporadic hepatitis in Nepal; increasing incidence of HAV

Ananta Shrestha[1], Thupten Lama[1], Sneha Karki[2], Smf Akbar[3]

Liver Foundation Nepal Hepatology Kathmandu-Nepal[1], Civil Service Hospital Medicine Kathmandu-Nepal[2], Toshiba General Hospital Medicine Tokyo-Japan[3]

Background/aim: Acute HEV hepatitis is thought to be endemic in Nepal. HAV contributed only 3-6 % of cases of acute hepatitis in adults in studies from 1987-1997. No etiology was found in one-third of patients during sporadic cases. In recent years, increase in acute HAV cases is noted in adults whereas HEV appears to be declining.

Patients and methods: Patients with acute hepatitis attending two hospitals (during April 2013-October 2013) of Kathmandu were checked for clinical parameters and serology for hepatitis viruses. Nucleic acids were isolated from all patients and checked for HAV, HBV, HCV and HEV. This Study was conducted with collaboration with Japan.

Results: A total of 45 cases of acute hepatitis were seen. All the cases had prodrome, jaundice and ALT levels at least 5 times upper limit of normal. HAV RNA and anti HAV IgM was detected in 17 patients. HEV RNA was isolated in only 1 out of 6 patients with Anti HEV IgM. HBV DNA and HCV RNA were found in one patient each. No etiology was found in 15 patients. Genotypes of HAV and HEV were IIIa and I respectively.

Conclusion: Contrary to previous findings, HAV was the commonest cause of acute hepatitis in adults in Kathmandu. Immunity against HEV due to past four epidemics of HEV (1973-2006) may have protected against HEV. Improving food and water hygiene during childhood may have made peoples susceptible during adulthood. Absence of any hepatitis virus in substantial proportion of acute hepatitis (Non A-E) should be addressed immediately. Continuous surveillance of acute hepatitis is needed to prevent further epidemics.

Topic 14: Hepatitis E

No: 1575

Hepatitis E virus infection in the general population of Iran a meta analysis

Mohammad Hossein Somi[1], Morteza Ghojazadeh[2], Ahmad Reza Badali[3], Mehran Rahimi[3], Haniyeh Ajdari[3], Nastaran Amous[3]

Liver and Gastrointestina Disease Research Center Interna Medicine Tabriz-Iran[1], Liver and Gastrointestina Disease Research Center Physiology Tabriz-Iran[2], Liver and Gastrointestina Disease Research Center Medical Faculty Tabriz-Iran[3]

Aim: Hepatitis E is a serious liver disease caused by the Hepatitis E virus (HEV) that usually results in an acute infection. It does not lead to a chronic infection. Hepatitis E is common in many parts of the world. We conducted a systematic review to put all evidence on HEV infection in I.R. Iran and to make an accurate estimate of HEV infection prevalence in Iran for further planning to control the infection.

A systematic review was constructed based on the computerized literature database. We selected descriptive and analytic cross-sectional studies and surveys related to the prevalence of HEV infection in the Iranian general population that have sufficiently declared objectives, proper sampling methods with identical and valid measurement

instruments for all study subjects and proper analysis methods regarding sampling design and demographic adjustments. We used a survey data analysis method to estimate the national prevalence rate.
Results: From the 25 studies we investigated, 14 eligible studies reported a prevalence of HEV infection in the general population. They were from 14 (out of 30) provinces, in which more than 50 percent of the country's population lives. We calculated that the HEV infection prevalence rate in Iran is 2 % (95 % confidence interval [CI]: 1 %-3 %). The prevalence of antibodies to HEV was greater among men than women and increased with age ($P < 0.001$).
Conclusion: In comparison with similar studies, the prevalence of HEV infection in Iran is low. This might be a result of having prevention programs for high-risk groups and strict blood screening programs.

Topic 14: Hepatitis E

No: 2096

Hepatitis E virus seropositivity in patients with chronic hepatitis C virus infection who have chronic liver disease and hepatocellular carcinoma (HCC)

Göktug Sirin[1], Omer Senturk[1], Altay Celebi[1], Hasan Yılmaz[1], Sadettin Hulagu[1]

Kocaeli University Gastroenterology Kocaeli-Turkey[1]

Background: Some studies show that the prevalence of hepatitis E virus antibodies (+HEV-IgG) increasing in patients with viral-induced chronic hepatitis. There are insufficient data about the impact of +HEV-IgG in patients with HCC who has chronic hepatitis C virus (HCV) infection so far.
Methods: Chronic hepatitis C patients data card investigated retrospectively and who has tested for HEV antibodies in Kocaeli University last in 5 years enrolled this study. Diagnosis of cirrhosis was made by radiology or liver biopsy. Categorical variables were compared using $\chi 2$ test or Fisher's exact test. Continuous variables were compared using Wilcoxon rank-sum test.
Results: Total of 85 patients (genotypes 1: 81, genotypes $2/3 = 4$) were included in the analysis. Five of 18 HCV-infected HCC patients and 1 of 67 HCV-infected non-HCC patients had +HEV-IgG. When compared to -HEV-IgG, +HEV-IgG was significantly associated with advanced age (median, 54 vs 65) birth in east and south-east of Turkey (0 % vs 100), hepatitis A virus antibodies (69.4 % vs 100). Overall, 45 (52.9 %) patients had cirrhosis. When compared to non-cirrhotics, more cirrhotic patients were male, had liver steatosis and all of them +HEV-IgG. There were no differences between cirrhotic and non-cirrhotic groups regarding years of HCV infection, history of alcohol consumption.
Conclusions: HEV seropositivity seems to be not so little in HCV-infected patients who have HCC and may be associated with cirrhosis in this population. The role of HEV infection in liver disease progression of chronically infected patients with HCV should be investigated by further research.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1431

Comparison of various staging systems in patients with hepatocellular carcinoma

Seong Hee Kang[1], Ji Hye Je[1], Ji Hoon Kim[1], Yang Jae Yoo[1], Hae Rim Kim[1], Sang Jun Suh[1], Young Kul Jung[1], Yeon Seok Seo[1], Hyung Joon Yim[1], Jong Eun Yeon[1], Kwan Soo Byun[1]

Korea University College of Medicine Internal Medicine Seoul-Korea, South[1]

Background: There has been still controversy which staging system is optimal. We compared various staging systems for predicting outcome in Korea.
Methods: Between January 2004 and December 2009, total of 875 patients with HCC who were diagnosed and treated at the Korea University Guro hospital were enrolled. They were followed up till April 2014. All patients were classified by modified UICC, BCLC, CLIP, CUPI, JIS, Tokyo score. The discriminatory ability of staging system was quantified using C-index. The homogeneity and monotonicity of staging system was assessed using likelihood ratio $\chi 2$ test correlated with a Cox's regression model neutralized by Akaike information criterion (AIC).
Results: 654 (74.7 %) patients died and the median survival time was 25 ± 1.5 months. Performance state, Child-Pugh class, serum alpha-fetoprotein level ≥ 400, tumor number and size, portal vein thrombosis, ascites, initial treatment modalities were related to the prognosis in multivariate analysis. CLIP stage had high discrimination ability (C-index 0.76) and the best monotonicity of gradient and homogeneity ability (LR $\chi 2$ test: 308.659, $P < 0.008$, AIC: 7789.566). JIS system had high discrimination ability (C-index 0.75) and good monotonicity of gradient and homogeneity ability (LR $\chi 2$ test: 320.3659, $P < .0001$, AIC: 7792.751). BCLC system had high discrimination ability (C-index 0.76) and relatively good monotonicity of gradient and homogeneity ability (LR $\chi 2$ test: 295.324, $P < .0001$, AIC: 7817.783).
Conclusions: CLIP, JIS and BCLC stage systems showed comparable prognostic stratification in HCC patients in Korea. Therefore, these staging systems are complementary to each other.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1289

VF MAP scores (virtual touch quantification fasting plasma glucose male age platelets) for prediction of hepato carcinogenesis

Tomoko Aoki[1], Chikage Nakano[2], Tomoyuki Takashima[3], Kenji Hashimoto[2], Hirayuki Enomoto[3], Nobihiro Aizawa[3], Naoto Ikeda[3], Hironori Tanaka[3], Yoshinori Iwata[3], Masaki Saito[3], Shuhei Nishiguchi[3], Hiroko Iijima[2]

Hyogo College of Medicine Hyogo College of Medicine Nishinomiya City-Japan[1], Hyogo College of Medicine Ultrasound Imaging Center Nishinomiya City-Japan[2], Hyogo College of Medicine Division of Hepatobiliary and Pancreatic Medicine, Department of Internal Medicine Nishinomiya City-Japan[3]

Background and aims: Shear wave elastography is an easily measureable test in daily clinical practice, since it is non-invasive and a good indicator of liver fibrosis. The aim for this study is to reveal the risk of liver carcinogenesis using Virtual Touch Quantification (VTQ).
Methods: Our research model was a retrospective cohort study. We continued to follow up 1847 patients for 40.5 ± 16.4 months: 73 patients developed hepatocellular carcinoma (HCC), the other 1774 patients did never develop HCC. We examined carcinogenesis factors by cox regression analysis.
Result: The univariate analysis between two groups: there were significant difference in age, sex, HCV infection, platelets, FIB4 index, VTQ, serum albumin and fasting plasma glucose (FPG)

($P < 0.05$). Cox regression analysis: there were significant differences in age, sex, platelets, FPG and VTQ ($P < 0.05$). Hazard ratio (HR) was 4.2 times in VTQ $\geqq$ 1.35 m/s, HR 2.2 times in FPG > 100 mg/dl, HR 2.1 times in male sex, HR 3.5 times in older than 61 y.o., HR 2.3 times in platelets $\leqq 15.3 \times 10000/\mu l$. We suggest the scoring system which named "VF map" scores (0-7 scores) according to this hazard ratio, in which we score 2 points for VTQ and Age, one point for FPG, Male and Platelets. 0-1 point patients never developed HCC. The carcinogenic rate of patients with 3-4 points of VF map score was around 5 %, and with above 5 points of the score, liver carcinogenesis rate was more than 10-23 %.
Conclusion: The VF map scores, which combines VTQ, FPG, Male, Age and Platelet counts, were very useful for predicting the HCC high-risk group.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1066

A case of extrahepatic metastasis of hepatocellular carcinoma to the pronator quadratus muscle of Rt. wrist

Young Wook Song[1], Byung Seok Lee[1], Seok Hyun Kim[1], Eaum Seok Lee[1], Heon Young Lee[1]

School of Medicine, Chungnam National University Internal Medicine Daejeon-Korea, South[1]

Hepatocellular carcinoma(HCC) is usually associated with chronic liver disease such as liver cirrhosis. 1 HCC can cause intrahepatic multiple occurrence and extrahepatic metastasis. Extrahepatic metastasis occurs in up to about 60 % of patients of HCC, and it usually depends on HCC stages. A majority of patients with extrahepatic HCC had intrahepatic stage IV or III tumor. 3,4 The most frequent site of extrahepatic metastasis of HCC was the lung. 3,4,5 HCC metastasized to soft tissues was unusually reported. 5,7 Extrahepatic metastasis of HCC, especially to unusual site, should not be overlooked and must be able to be controlled. We experienced a case that HCC was metastasized to skeletal muscle of wrist: the pronator quadratus muscle. Rt. and should be removed surgically.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1346

In situ analysis of Htert mRNA expression in human hepatitis B virus related hepatocellular carcinomas

Haeryoung Kim[1], Hyejung Lee[1], Young Nyun Park[2]

Seoul National University Bundang Hospital Department of Pathology Seongam-Republic of Korea[1], Yonsei University College of Medicine Department of Pathology Seoul-Republic of Korea[2]

Aim: We aimed to evaluate the expression of human telomerase reverse transcriptase (hTERT) mRNA in formalin-fixed paraffin-embedded hepatocellular carcinoma tissues using an in situ hybridization approach.
Methods: TERT mRNA expression was analyzed by in situ hybridization (RNAscope, Advanced Cell Diagnostics) on 156 surgically resected HCCs and corresponding non-neoplastic liver tissues. TERT-high cases showed TERT mRNA signals visible at 200x magnification, while TERT-low cases demonstrated barely visible signals at 400x magnification. Immunohistochemistry for K19, EpCAM and markers related to epithelial-mesenchymal transition (EMT) (vimentin, uPAR, S100A4, E-cadherin) was performed for the same cases.
Results: of 132 HBV-related HCCs, 37 (28.0 %) cases were TERT-high. These cases were associated with larger tumor size ($P = 0.086$), portal vein invasion ($P = 0.006$), higher pathologic T stages ($P = 0.019$), more frequent K19 ($P = 0.006$) and EMT-related marker expression (vimentin, uPAR, S100A4, E-cadherin loss; $P < 0.05$, all). hTERT-high HCCs were more frequently associated with cirrhotic background livers ($P = 0.005$). None of the 16 HCV-related and 8 alcohol-related HCCs were hTERT-high. In non-neoplastic livers, hepatocytes were negative for hTERT mRNA, while occasional hTERT mRNA signals were noted in ductular reactions and lymphocytes.
Conclusion: The evaluation of hTERT expression in tissue sections is difficult, due to the lack of good commercially available hTERT antibodies. By using the RNAscope assay, we were able to analyze the expression status of hTERT mRNA in situ at a single cell level in HCCs, non-neoplastic hepatocytes, ductular reactions and lymphocytes. High hTERT mRNA expression was more frequently seen in HBV-related HCCs, and associated with clinicopathologic features of aggressiveness and "stemness"- and EMT-related marker expression.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1946

Demographic epidemiological and clinical characteristics of patients with hepatocellular carcinoma (HCC) in southeastern Europe

Dimitrios Dimitroulopoulos[1], Dimitrios Kypreos[2], Nikolaos Saribeyoglou[2], Loukas Theodoropoulos[2], Matina Hatzinikolaou[2], Apostolos Malahias[2], Maria Nikaki[2], Stavros Stavrinidis[2], Klisthenis Tsamakidis[2], Dimitrios Xinopoulos[2]

Agios Savvas Hospital Gastroenterology Athens-Greece[1], Agios Savvas Hospital Gatroenterology Athens-Greece[2]

Demographic, epidemiological and clinical characteristics of HCC patients in Southeastern Europe are not yet well investigated.
Aim: Determination of demographic, epidemiological and clinical characteristics as well as the risk factors for HCC in Southeastern Europe.
Patients/methods: Data of 212 HCC patients (years 2007-013) were analyzed retrospectively.
Results: The median age of patients was 66 years (range 45-88). 158 (74.5 %) were males. 120 (56.6 %) were infected from HBV, 73 (34.45 %) were infected from HCV, 4 (1.9 %) were co-infected from the viruses reported above, 9 (4.2 %) reported chronic alcohol abuse and for 6 the cause of HCC was NASH/NAFLD. of these that were infected from HBV and HCV, 23 (11.6 %) reported also chronic alcohol abuse. 141 (66.5 %) were diagnosed in advanced stage of HCC, 52 (24.5 %) in intermediate and 19 (8.9 %) in early stage. 93 (43.8 %) presented elevated values of AFP, and 35 (16.5 %) of these AFP > 400 ng/ml. 66 (31.1 %) were diagnosed with multinodular HCC, 12 (5.6 %) with diffuse disease, 17 (8 %) with local lymph node metastases and 9 (4.2 %) with distant metastatic disease. With cirrhosis stage A were presented 122 (57.5 %) patients, with stage B 38 (17.9 %) and with stage C 23 (10.8 %). Hepatectomy, RFA, chemoembolization and sorafenib administration were the main therapeutic approaches.
Conclusion: In Southeastern Europe HCC is threefold more common in males than in females. HBV and HCV infections and chronic alcohol abuse are the main etiological factors. Elevated AFP levels can be useful for early diagnosis in high risk patients.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1326

The role of TNF α dependent angiogenesis in the development and progression of hepatocellular carcinoma

Olfat Hammam[1], Ola Mahmoud[2], Manal Zahran[2], Azza Sayed[2], Karim Hosny[3], Ahmed Farghly[3]

Theodor Bilharz Research Institute Pathology Giza-Egypt[1], Theodor Bilharz Research Institute Hematology Giza-Egypt[2], Kasr El Aini Hospital Surgery Cairo-Egypt[3]

To measure levels of messenger (m)RNA transcripts and protein for TNF-α and VEGF, to assess the implication that TNF-α induced angiogenesis provides a molecular link between inflammation and the development of hepatocellular carcinoma HCC in patients with chronic hepatitis C (CHC).
Methods: Ninety patients were enrolled: 30 cases of CHC without cirrhosis, 28 cases of CHC with liver cirrhosis, and 32 cases of HCC and hepatitis C virus infection. Ten wedge liver biopsies, taken during laparoscopic cholecystectomy, served as normal controls. Serum TNF-α levels were measured using the ELISA technique; in situ hybridization and immunohistochemical studies were used to detect hepatic levels of mRNA transcripts and protein, respectively, for both TNF-α and VEGF.
Results: The highest hepatic expression of TNF-α was noticed in liver cirrhosis specimens compared to noncirrhotic CHC and HCC. Hepatic expression of VEGF and serum level of TNF-α revealed significant increases in the progression of the disease. Moreover, cases with higher grades of inflammation or stages of fibrosis showed significant increases in serum TNF- α and expression of TNF-α and VEGF. Expression of mRNA of both TNF-α and VEGF shows increasing expression with positive correlation to progression of viral hepatitis to cirrhosis with more positivity in cases developed HCC.
Conclusion: VEGF signaling could be one of the molecular signaling pathways involved in TNF-α induced angiogenesis which might pose an important link between inflammation and fibrosis in CHC and HCC development and progression.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1796

Are inflammatory markers more useful than noninvasive fibrosis panels for prediction of hepatocellular carcinoma recurrence

Goktug Sirin[1], Omer Senturk[1], Hasan Yılmaz[1], Altay Celebi[1], Sadettin Hulagu[1]

Kocaeli University Gastroenterology Kocaeli-Turkey[1]

Background: Hepatocellular carcinoma (HCC) has a high risk of tumor recurrence after curative therapy. We aimed to compare fibrosis markers and inflammatory markers which methods can predict HCC recurrence after segmental resection or radiofrequency ablation (RFA) for cure.
Methods: We retrospectively reviewed the medical records of patient with HCC registered in outpatient hepatitis clinic of Kocaeli University gastroenterology department whom treated with segmental resection and/or RFA at several center from year 2007 to mid-2012. The median months of follow up were 34 month (12-64). NTLR: neutrophil to lymphocyte ration as ınflammatory parameter and fibrosis markers (APRI: AST platelet ratio index, FIB-4: Fibrosis-4 score) were calculated.
Result: Total 49 patients were included for analysis. There were 15 cases of recurrence (30.6 %). Thirty two patients (65.3 %) were male and the most common etiology was hepatitis B and C. Child-Pugh score (5.8 ± 0.7 vs 6.9 ± 1.1, $P = 0.011$), APRI (AST platelet ratio index) (1.2 ± 1.2 vs. 2.3 ± 1.8, $P = 0.005$), FIB-4 score (2.8 ± 2.2 vs. 4.0 ± 2.80, $P = 0.005$) were higher in recurrence group. At the cut off value of 3.95, the sensitivity and specificity of FIB4 were 65.6 % and 81.0 %. In multivariate analysis, notwithstanding that NTLR failed to significantly affect the time-to-recurrence, FIB4 (HR 1.4, CI 1.05-1.68, $P = 0.011$) and APRI (HR 1.2, CI 1.07-1.25, $P = 0.004$) were independent risk factor for tumor recurrence.
Conclusion: These findings show that noninvasive fibrosis markers could play an important role in predicting recurrence of HCC more than inflammatory indices after segmental resection or RFA.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1991

Usefulness of contrast enhanced ultrasound with perfluorobutane microbubble in the diagnosis of recurrent hepatocellular carcinoma after radical treatment

Buyanjargal Shagdarsuren[1], Hideyuki Tamai[1], Naoki Shingaki[1], Yoshiyuki Mori[1], Shuya Maeshima[1], Junya Nuta[1], Yoshimasa Maeda[1], Kosaku Moribata[1], Yosuke Muraki[1], Hisanobu Deguchi[1], Izumi Inoue[1], Takao Maekita[1], Mikitaka Iguchi[1], Jun Kato[1], Masao Ichinose[1]

Wakayama Medical University Second Department of Internal Medicine Wakayama-Japan[1]

Background/aim: Contrast-enhanced computed tomography (CECT) is generally used for follow-up after radical treatment for hepatocellular carcinoma (HCC). The aim of the present study was to evaluate the diagnostic ability of contrast-enhanced ultrasound (CEUS) with perfluorobutane microbubble (SonazoidTM) in recurrent HCC.
Method: A total of 514 consecutive patients, who were suspected to have recurrent HCCs on CECT after radical treatment, underwent CEUS. The largest lesion was examined in each patient. A recurrent HCC was diagnosed on the basis of the typical hallmarks of HCC by any of the contrast imaging modalities, such as CECT, dynamic magnetic resonance imaging, CEUS, or by resected tissue or tumor enlargement during follow-up.
Results: Of 514 suspicious lesions, 484 were diagnosed as recurrent HCCs. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of CECT were 68.3, 93.3, 99.3, 84.5, and 69.8 %, respectively. Seventy-two suspected lesions on CECT could not be assessed by CEUS. Excluding these lesions, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of CEUS were 90.8, 100, 100, 31.0, and 91.1 %, respectively. The HCC diagnostic rate of CEUS among lesions with atypical enhancement patterns on CECT was 70.7 %. On multivariate analysis of factors contributing to unassessable CEUS, tumor size, location, and abdominal wall thickness were independent factors.
Conclusions: Although the assessability of CEUS depends on tumor size, location, and abdominal wall thickness, the diagnostic accuracy of CEUS for recurrent HCCs is higher than that of CECT. Therefore, CEUS should be performed for lesions with atypical enhancement patterns on CECT.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1319

Comparison between computed tomography and magnetic resonance imaging in the diagnosis of small hepatocellular carcinoma

Korn Lertpipopmetha[1], Naichaya Chamroonkul[1], Teeravut Tubtawee[2], Teerha Piratvisuth[1]

Prince of Songkla University Department of Internal Medicine, Faculty of Medicine Songkhla-Thailand[1], Prince of Songkla University Department of Radiology, Faculty of Medicine Songkhla-Thailand[2]

Background: Hepatocellular carcinoma (HCC) less than 2 cm in size has the best outcome after curative therapy. However, diagnosis of small HCC can be problematic and require one or more dynamic imaging modalities.
Aim: To compare sensitivity and agreement between CT and MRI for diagnosis of small HCC.
Methods: CT and/or MRI of a diagnosed 1-2 cm HCC by histopathology or typical vascular pattern according to the AASLD 2010 criteria, was blindly reviewed by an abdominal radiologist. The reports were defined as conclusive/typical when arterial enhancement and washout during portal/delayed phases were seen and suspicious when typical vascular patterns were not seen. The sensitivity and Cohen's kappa (k) for the agreement were calculated.
Results: Of the 58 patients, 65 nodules of 1-2 cm HCC were included. The diagnostic sensitivity of a single imaging method (CT or MRI) was 81 % versus 48 % of both studies ($P = 0.002$). The CT-sensitivity was significantly higher than that of the MRI (84 % versus 62 %, $P = 0.02$). Among 27 nodules that underwent both CT and MRI, a discordance between CT and MRI in typical enhancement patterns was found ($k = 0.319$, $P = 0.05$). In case of inconclusive CT result, proceed to perform the MRI gave only an additional 3.7 % for reaching a diagnosis. In contrast, regarding inconclusive MRI result, a further CT gave an additional 29.6 %.
Conclusions: Single typical imaging modality is sufficient to diagnose a small HCC. Compared to MRI, the multiphasic CT has a higher sensitivity. Requirement of patient's co-operation and radiologist's expertise could explain limitations of the MRI.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1231

Serum tumor markers for detection of hepatocellular carcinoma

Ali Ghweil[1]

South Valley University Tropical Medicine and Gastroenterology Qena-Egypt[1]

Hepatocellular carcinoma (HCC) is one of the most frequent malignant tumors and is the second most common cause of cancer death in China. Therefore, it is very important to detect this disease and the recurrence at its earlier period. Serum tumor markers, as the effective method for detecting hepatocellular carcinoma for a long time, could be divided into 4 categories: oncofetal antigens and glycoprotein antigens; enzymes and isoenzymes; genes; and cytokines. Serum alpha fetoprotein (AFP) is the most widely used tumor marker in detecting patients with hepatocellular carcinoma, and has been proven to have capability of prefiguring the prognosis. However, it has been indicated that AFP-L3 and DCP excel AFP in differentiating hepatocellular carcinoma from nonmalignant hepatopathy and detecting small hepatocellular carcinoma. Some tumor markers, such as human cervical cancer oncogene and human telomerase reverse transcriptase mRNA, have also been indicated to have higher accuracies than AFP.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1841

Intrahepatic splenosis mimicking hepatocellular carcinoma a case report

Joji Yamamoto[1]

Kamagaya General Hospital Surgery Kamagaya-Japan[1]

Intrahepatic splenosisis is the autotransplantation of splenic tissue in the liver. Most of the cases develop after abdominal injury and splenectomy.

Many cases were misdiagnosed as hepatocellular carcinoma (HCC) because they showed similarities in the radiological findings.

A 63 year-old female was referred to our hospital with complaint of anterior chest discomfort. The patient has a history of splenectomy after splenic trauma 29 years ago.

To evaluate coronary artery, coronary computed tomography (CT scan) was performed. At this time a single space occupying lesion in the liver segment 6 was observed incidentally. Serous examination for hepatitis C was negative, HBs antigen was also negative, however HBc antibody was positive, which suggested a past history of hepatitis B viral infection. Alfa-fetoprotein (AFP) and Protein induced by vitamin K absence or antagonist- 2 (PIVKA-2) were within normal limits.

Enhanced CT scan showed a 30x20 mm tumor with strong enhancement in early phase and washing out in late phase. Magnet residensual imaging (MRI) showed low intensity in T1 weight phase and strong intensity in T2 weight phase. Both radiological findings indicated the lesion as HCC.

Partial resection of the liver was performed. Pathological examination of the resected specimen revealed hepatic splenosis without tumor cell.

As our case and previous cases are showing, it may be difficult to make differential diagnosis between hepatic splenosis and hepatocellular carcinoma only by imaging modalities. The most important point to diagnose hepatic splenosis is to consider this disease when we see a patient with a history of splenic trauma or splenectomy.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1798

Is FIB 4 index and gender useful for predicting the incidence of hepatocellular carcinoma in patients with chronic hepatitis C single center experience

Goktug Sirin[1], Sadettin Hulagu[1], Altay Celebi[1], Hasan Yılmaz[1], Omer Senturk[1]

Kocaeli University Gastroenterology Kocaeli-Turkey[1]

Background: Hepatitis C Virus (HCV) infected patients are at high risk for developing hepatocellular carcinoma (HCC). We aimed to investigate the use of FIB-4 index which calculated from ALT and

AST, age, and platelet count in predicting the incidence of (HCC) in patients with HCV.
Methods: HCV infected persons were followed from their first FIB-4 index metage in 2004 or later to the first HCC diagnosis, death or August, 2013 in Kocaeli University gastroenterology department. Individual patient's FIB-4 index was calculated 6 month intervals in a time-dependent manner. FIB-4 index categories were determined by JoinPoint method. HCC incidence was calculated for each FIB-4 index category.
Results: Of 457 patients (37-72 yrs), 28 (6.12 %) developed HCC over mean follow up of 5 yrs. Two HCC case reported in persons <40 yrs. The mean age at first HCC diagnosis was 49 yrs in men and 54 yrs in women. HCC incidence varied significantly by FIB-4 index, age and sex. Incidence was lower in women than in men according to similar age and FIB-4 index. In men aged 50-59 yrs, HCC risk was elevated when FIB-4 score was greater than 4.0, as was FIB4 score >3.0 for men ≥70 yrs. The patients with FIB-4 index >4.0 was at a highest risk for HCC development ($P < 0.001$).
Conclusions: FIB-4 index is closely associated with increase of HCC incidence among all age groups, particularly among those FIB-4 scores greater than 4.0.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 2058

The patatin like phospholipase domain containing protein 3 (PNPLA3) polymorphism in hepatocellular carcinoma relation with the etiology of liver disease

Apichaya Khlaiphuengsin[1], Sunchai Payungporn[1], Nutcha Pinjaroen[2], Pisit Tangkijvanich[1]

Faculty of Medicine, Chulalongkorn University Biochemistry Bangkok-Thailand[1], Faculty of Medicine, Chulalongkorn University Radiology Bangkok-Thailand[2]

Background: A single nucleotide polymorphism (SNP) of patatin-like phospholipase domain containing protein 3 (PNPLA3) (rs738409) has been associated with disease progression in nonalcoholic fatty liver disease. However, the role of the SNP in patients with hepatocellular carcinoma (HCC) is less clear.
Methods: A total of 388 consecutive patients with HCC were included in the study. Based on the etiologic factors, 309 were viral-related HCC (211 were HBsAg positive and 98 were anti-HCV positive) (group I), and the remaining 79 cases were non-viral related HCC (group II). The SNP rs738409 was detected by allelic discrimination using real-time PCR with TaqMan probes.
Results: The mean age of patients in group II was significantly higher than that of patients in group I (66.5 vs. 58.6 years, $P < 0.001$). However, there was no significant difference between groups in terms of gender distribution, Child-Pugh score, tumor size and tumor stage based on the BCLC classification. In group I, the frequencies of CC, CG and GG genotypes of rs738409 were 129 (41.8 %), 145 (46.9 %) and 35 (11.3 %), respectively. In group II, the corresponding genotypes were 29 (36.7 %), 33 (41.8 %) and 17 (21.5 %). The frequency of GG genotype was significantly higher in group II than in group I (21.5 % vs. 11.3 %, $P = 0.018$). There was no difference in survival between patients with GG and non-GG genotypes ($P = 0.182$).
Conclusion: In this study, a significantly higher frequency of GG genotype was found in non-viral related HCC in comparison with viral-related HCC. However, the genotype was not associated with the survival of Thai patients with HCC.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1852

Current status of hepatocellular carcinoma in Taiwan a national wide analysis

Sheng-nan Lu[1], Tsang-en Wang[2], Chun-ju Chiang[3]

Kaohsiung Chang-gung Memorial Hospital Internal Medicine Kaohsiung City-Taiwan[1], Mackay Memorial Hospital Internal Medicine Taiper City-Taiwan[2], Taiwan Cancer Registry Taipei City-Taiwan[3]

Aim: To realize the current status of hepatocellular carcinoma (HCC) in Taiwan, we analyzed the National Cancer Registration (NCR) database of 2012.
Methods: All newly diagnosed HCC cases should be reported to NCR system. There are two reported forms. One is a general form for all caner sites and the other is HCC-specific factors. We analyzed the decoded database of 2012.
Results: A total 8247 cases, 5879 men and 2368 female with a sex ratio of 2.48, of newly diagnosed HCC were enrolled in 2012. The mean age was 63.9 (standard deviation (SD) 12.8) years. Almost (98.2 %) all of them met consensus diagnostic criteria, including pathology (47.5 %), cytology (3.4 %), AFP > 200 ng/ml (15.8 %) and typical image (31.6 %). Limited to 6572 (79.7 %) cases with results of blood tests, the distributions of viral etiology were HBsAg 2696 (41.0 %), anti-HCV 2171(33.0 %), both 363 (5.5 %) and neither 1342 (20.4 %). For Child-Pugh classification, 5719 (69.3 %) were Class A, 1370 (16.6 %) were Class B, 511 (6.2 %) were Class C and 647 (7.8 %) were no available information. HCV related-HCC has significantly higher proportions of cirrhosis than HBV-related HCC (pathology 50.8 % vs. 42.0 %, image 78.6 % vs. 74.7 %). Staging by BCLC, they were 6.8 % for stage 0, 35.1 % for A, 22.9 % for B, 26.7 % for C and 8.4 for D. While staging by TNM (7th edition), 35.5 % for stage I, 26.4 % for II, 26.5 % for III and 11.6 % for IV.
Conclusions: This report provides current, representative and detail status of HCC in Taiwan. It is epidemiology and clinical information not only for domestic use but also for international comparison.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1838

Prediction of the development of hepatocellular carcinoma in patients with chronic hepatitis B

Jem Ma Ahn[1], Yeonseok Seo[1], Chang Ho Jung[1], Tae Hyung Kim[1], Sun Young Yim[1], Hyuk Soon Choi[1], Hyunggin An[2], Bora Keum[1], Young Kul Jung[1], Jihoon Kim[1], Hyungjoon Yim[1], Dong Sik Kim[3], Yoon Tae Jeen[1], Jong Eun Yeon[1], Hong Sik Lee[1], Hoon Jai Chun[1], Kwan Soo Byun[1], Soon Ho Um[1], Chang Duck Kim[1], Ho Sang Ryu[1]

Korea University, College of Medicine, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Seoul-Korea, South[1], Korea University, College of Medicine, Department of Biostatistics, Seoul-Korea, South[2], Korea University, College of Medicine, Department of Surgery, Seoul-Korea, South[3]

Backgound/aims: Most of hepatocellular carcinoma (HCC) prediction models were developed in treatment-naïve patients with chronic hepatitis B (CHB). Our study aimed to determine independent risk factors for HCC development in CHB patients mostly receiving anti-

viral treatment during follow-up period, and derive a new HCC prediction model based on histological findings.
Methods: A total of 517 patients with CHB were followed for the mean duration of 61.6 ± 44.2 months. Area under the receiver operating curve (AUROC) was calculated for assessing prediction accuracy of model.
Results: During follow-up, cumulative incidences of HCC at 5- and 10- years were 4.1 %, and 6.9 %, respectively. Independent risk factors for HCC development were heavy alcohol consumption (hazards ratio [HR], 8.20; $P = 0.003$], absence of anti-viral treatment history during follow up period (HR, 3.75; $P = 0.044$), HBeAg negative (HR, 2.84; $P = 0.029$), and API (HR, 1.91; $P < 0.001$). A HCC risk prediction model was developed with these four independent risk factors. AUROCs for predicting 5- and 10-year risk of HCC were 0.920, and 0.923, respectively. Risk scores of our model were significantly categorized as low, intermediate, and high HCC risk groups.
Conclusion: Our new model, adjusted by histological characteristics and effect of anti-viral treatment, excellently predicts HCC development. In the era with widespread anti-viral treatment, our model might be more suitable to predict HCC development in CHB patients with HBV DNA ≥ 2000 IU/ml.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1398

Improvement in survival of patients with hepatocellular carcinoma in a hepatitis B virus endemic area a nationwide cohort study

Bo Hyun Kim[1], Young-suk Lim[2], Eun-yang Kim[3], Hyun-joo Kong[3], Young-joo Won[3], Kyung-suk Suh[4], The Korean Liver Cancer Study Group[5], The Korea Central Cancer Registry[6]

National Cancer Center Center For Liver Cancer Goyang-Korea, South[1], Asan Medical Center, University of Ulsan College of Medicine Department of Gastroenterology, Liver Center, Seoul-Korea, South[2], National Cancer Center The Korea Central Cancer Registry, Division of Cancer Registration and Surveillance Goyang-Korea, South[3], Seoul National University College of Medicine Department of Surgery Seoul-Korea, South[4], The Korean Liver Cancer Study Group Seoul-Korea, South[5], The Korea Central Cancer Registry Goyang-Korea, South[6]

Backgrounds: Hepatocellular carcinoma (HCC) mortality remains largely variable across the world. Hepatic functional reserve is an independent predictor of survival in patients with HCC, which may be improved by cause-specific treatments. We aimed to investigate whether the mortality rate of patients with HCC in a hepatitis B virus (HBV) endemic area has changed over the last decade.
Methods: Out of 31521 and 38167 HCC registrants to the nationwide statutory Korea Central Cancer Registry (KCCR) in the period of 2003-2005 and 2008-2010, 4520 (Cohort 2003-2005) and 4596 (Cohort 2008-2010) patients, respectively, were randomly selected, and were investigated for clinical characteristics and outcomes through reabstracting audit.
Results: Patients in Cohort 2008-2010 was significantly older (59 vs. 57 years; $P < 0.001$), had better liver function (Child-Pugh class A, 71 vs. 64 %; $P < 0.001$), and had more advanced tumor stage (BCLC stage B-D, 51 vs. 46 %, $P < 0.001$), compared with those in Cohort 2003-2005. HBV was the predominant cause for HCC in both cohorts (61 % vs. 72 %; $P < 0.001$). The median overall survival of patients in Cohort 2008-2010 was significantly longer compared with those in Cohort 2003-2005 (28.4 vs. 17.5 months; $P < 0.001$). The significant difference in median survival between the two cohorts was exclusively observed in patients with HBV-associated HCC (30.7 vs. 16.3 months; $P < 0.001$).
Discussion: The overall survival of patients with HBV-associated HCC has significantly improved in Korea, a HBV endemic area, over the last decade. These results might be attributable to the widespread use of potent antiviral agents for HBV.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1718

Hepatocellular carcinoma leads to an increase in platelet count that contributes to tumor growth and metastasis

Chhagan Bihari[1], Archana Rastogi[1], Ajeet Singh Bhadoria[2], Anupam Kumar[3], Shiv K. Sarin[4]

Ilbs Pathology Delhi-India[1], Ilbs Clinical Research Delhi-India[2], Ilbs Research Delhi-India[3], Ilbs Hepatology Delhi-India[4]

Aim: To determine whether Hepatocellular carcinoma (HCC) encourages a rise in platelet number and increase in platelet count contributes to tumor growth and metastasis.
Materials and methods: Retrospective analysis of 423 HCC cases with cirrhosis and 1008 cirrhosis cases as control group was done. Follow up information of: platelet profile were recorded and analyzed. Cytokine profiling in HCC and cirrhosis (n = 10 each) was done. HCC was divided into six subgroups. Fine needle aspiration smears of HCC were assessed for platelet clustering around tumor cells. In vitro matrigel invasion assay was performed by HCC cell lines and activated platelets in graded concentrations.
Results: Mean age of HCC cases was higher than the cirrhotics ($P < 0.001$). Baseline median platelet numbers and platelet: lymphocyte ratios (PLR) were higher ($P < 0.001$) in HCC than cirrhosis. IL-6 ($P = 0.0275$) and thrombopoietin ($P = 0.007$) were significantly higher in HCC than cirrhosis. Median platelet counts and PLR were: higher after HCC conversion ($P < 0.001$) and significantly decreased ($P < 0.001$) after 2 months post-therapy. Platelets and PLR in recurrences were higher at the time of outcome than in the cases with ablated tumor. Upon multivariate logistic regression and ROC curve analysis platelets, PLR and AFP showed significant associations with distant metastasis. Prominent platelet clustering in cytosmears noted in HCC cases with distant metastasis ($P < 0.001$). Higher platelet counts were associated with number of invaded cells in the in vitro metrigel assay.
Conclusion: We conclude that HCC leads to production of additional platelets and that contribute to further development, growth, invasion, and metastasis of HCC.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1916

Comparison of HIV HBV and HIV HCV coinfected patients with hepatocellular carcinoma (HCC)

Maaz M. Badshah[1], Caitlin Citti[2], Meritxell Ventura[3], Ting-yi Chen[4], Heather Platt[5], Sonja Marcus[6], Emma Page[7], Luciana Kikuchi[8], Nicolas Merchante[9], Mark Nelson[7], Beatriz Minguez[3], Ayse Aytaman[10], Juan Pineda[9], Norbert Bräu[11]

Indiana University School of Medicine Medicine Indianapolis, In-United States[1], Icahn School of Medicine At Mount Sinai New York, NY-United States[2], Hospital Universitario Vall D'hebron Barcelona-Spain[3], University of Texas Southwestern Medical Center Dallas, Tx-United States[4], Columbia University Medical Center New York, NY-United States[5], James J Peters Va Medical Center Bronx, NY-United States[6], Chelsea and Westminster Hospital London-United Kingdom[7], Universidade De São Paulo São Paulo-sp-Brazi[8], Hospital Universitario De Valme Sevilla-Spain[9], Va New York Harborhcs & Suny Downstate Medical Center New York, NY-United States[10] James J Peters Va Medical Center & Icahn School of Medicine At Mount Sinai Bronx, NY-United States[11]

Background: Cases of HCC in HIV-infected patients have been reported with increasing frequency. The natural history of HIV/HBV- versus HIV/HCV-coinfected patients is unknown.
Methods: HIV-infected patients with HCC were retrospectively identified from 1992-2014 in 38 centers in 8 countries in North and South America, Europe, and Australia.
Results: Among 367 HIV-infected patients with HCC, 74 (20 %) were HBV-coinfected and 288 (79 %) were HCV-coinfected. HIV/HBV patients were younger than HIV/HCV patients (mean, 50.0 vs. 54.2 years, $P < 0.001$) and more commonly male (99 % vs. 90 %, $P = 0.015$). They tended to have a lower mean Child-Turcotte-Pugh score (6.5 vs. 6.9, $P = 0.094$), but had a similar rate of excessive alcohol consumption (24 % vs. 29 %, $P = 0.34$) and of being diagnosed through screening (60 % vs. 64 %, $P = 0.51$). HIV parameters were similar with HIV RNA < 400 copies/ml in 70 % (HBV) vs. 74 % (HCV, $P = 0.51$) and median CD4 + cell count of 316 vs. 322 per mm3 ($P = 0.56$). However, HIV/HBV patients had a larger median tumor size than HIV/HCV patients (5.3 vs. 3.6 cm, $P = 0.010$), more frequent portal vein thrombosis (32 % vs. 17 %, $P = 0.004$) and a higher median alpha-fetoprotein level (298 vs. 96 ng/ml, $P = 0.029$). There was no difference in BCLC staging (stages A&B, 47 % vs 51 %, $P = 0.57$), frequency of effective therapy (58 % vs. 65 %, $P = 0.25$) and median survival (14.3 vs. 16.4 months, $P = 0.72$, log rank).
Conclusions: Patients with HIV/HBV coinfection and HCC are younger than HIV/HCV patients and more commonly male. They present with larger tumors, higher AFP levels, and more frequent vascular invasion. However, tumor staging and survival are similar.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1294

Osteopontin promoter polymorphism is associated with the risk of hepatocellular carcinoma

Natthaya Chuaypen[1]

Faculty of Medicine, Chulalongkorn University Biochemistry Bangkok-Thailand[1]

Objectives: Osteopontin (OPN) plays an important role in cancer progression and prognosis of hepatocellular carcinoma (HCC). The aim of this study was to evaluate the role of single nucleotide polymorphisms (SNPs) of OPN in disease susceptibility and progression of HCC.
Methods: We analyzed 149 patients with HCC and 61 healthy controls. DNA extracted from blood samples was analyzed for the SNPs in the OPN promoter (rs28357094, rs11439060 and rs11730582) by direct sequencing. Serum OPN levels were measured by enzyme-linked immunosorbent assay.
Results: The serum OPN levels were significantly higher in patients with HCC than in controls ($P < 0.01$). Genotypes CT and CT + CC of rs11730582 were associated with the risk of HCC (odds ratio, 4.01; 95 % confidence interval, 2.02-7.95; $P < 0.001$). In HCC patients, those with CC and CT + CC genotypes tended to have higher mean serum OPN levels than those with TT genotype, but did not reach significant difference (419.5 vs. 256.4 ng/ml, $P = 0.085$). There was no correlation between the SNP genotypes and HCC staging based on BCLC classification. The SNPs rs28357094 and rs11439060 were not associated with HCC risk.
Conclusion: Our results suggest that the SNP rs11730582 in the OPN promoter is associated with the development of HCC in Thai patients.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1877

Serum dickkopf 1 (DKK 1) as a biomarker for the diagnosis of hepatocellular carcinoma

Seung Up Kim Kim[1], Jeon Han Park[2], Hyon-suk Kim[3], Jae Myun Lee[2], Hyun Gyu Lee[4], Hyemi Kim[4], Sung Hoon Choi[5], Shinhwa Baek[6], Beom Kyung Kim[1], Jun Yong Park[1], Do Young Kim[1], Sang Hoon Ahn[1], Jong Doo Lee[7], Kwang-hyub Han[1]

Institute of Gastroenterology, Yonsei University College of Medicine Department of Internal Medicine Seoul-Korea, South[1], Institute For Immunology and Immunological Diseases, Yonsei University College of Medicine Department of Microbiology Seoul-Korea, South[2], Yonsei University College of Medicine Department of Laboratory Medicine Seoul-Korea, South[3], Yonsei University College of Medicine Department of Microbiology Seoul-Korea, South[4], Institute of Gastroenterology, Yonsei University College of Medicine Liver Cirrhosis Clinical Research Center Seoul-Korea, South[5], Institute of Gastroenterology, Yonsei University College of Medicine Liver Cirrhosis Clinical Research Center Seoul-Korea, South[6], Institute of Gastroenterology, Yonsei University College of Medicine Department of Nuclear Medicine Seoul-Korea, South[7]

Background: Dickkopf-1 (DKK-1) is a Wnt/β-catenin signaling pathway inhibitor. We investigated whether DKK-1 is related to progression in hepatocellular carcinoma (HCC) cells and HCC patients.
Patients and methods: In vitro reverse-transcription (RT)-PCR, wound healing assays, and invasion assays, and ELISAs of patient serum samples were employed. The diagnostic accuracy of the serum DKK-1 ELISA was assessed using receiver operating characteristic (ROC) curves and area under ROC (AUC) analyses.
Results: RT-PCR showed high DKK-1 expression in Hep3B and low in 293 cells. Similarly, the secreted DKK-1 concentration in the culture media was high in Hep3B and low in 293 cells. Wound healing and invasion assay using 293, Huh7, and Hep3B cells showed that DKK-1 overexpression promoted cell migration and invasion, whereas DKK-1 knock-down inhibited them. When serum DKK-1 levels were assessed in 370 participants (217 with HCC and 153 without), it was significantly higher in HCC patients than in control groups (median 1.48 vs. 0.90 ng/mL, $P < 0.001$). The optimum DKK-1 cutoff level was 1.01 ng/mL (AUC = 0.829; sensitivity 90.7 %; specificity 62.0 %). DKK-1 had a greater AUC in diagnosing HCC than alpha-fetoprotein (AFP) and des-gamma-carboxy prothrombin (DCP) (AUC = 0.829 vs. 0.794 and 0.815, respectively). When all three biomarkers were combined (DKK-1 + AFP + DCP), they showed remarkably increased accuracy (AUC = 0.952).
Conclusion: DKK-1 might be a key regulator in HCC progression and a potential therapeutic target in HCC. In addition, serum DKK-1 could complement the diagnostic accuracy of AFP and DCP.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1261

Clinical validation of a revised sub staging in Korean patient with intermediate hepatocellular carcinoma (BCLC B)

Hee Jae Jung[1], Yeon Seok Seo[2], Sang Gyune Kim[1], Ji Sung Lee[1], Sae Hwan Lee[1], Soung Won Jeong[1], Jae Young Jang[1], Hong Soo Kim[1], Boo Sung Kim[1], Young Kul Jung[2], Ji Hoon Kim[2], Young Seok Kim[1]

Soon Chun Hyang University School of Medicine Digestive Disease Center and Research Institute, Department of Internal Medicine Bucheon-Korea, South[1], Korea University Department of Internal Medicine Seoul-Korea, South[2]

Aims: We aimed to propose new revised Barcelona Clinic Liver Cancer (BCLC) B subclassification according to tumor number and tumor size correlated with prognosis after TACE by multicenter study of a real practice.
Methods: Between January 2004 and December 2010, 463 BCLC B patients who were treated with intermediate hepatocellular carcinoma (HCC) were screened. Among these, 289 patients were initially treated with TACE. We revised new subclassification according to tumor number, tumor size, AFP and combination of tumor number and size. Bolondiet al. (B1-4) and our new revised BCLC B (Ba-Bc) subclassification were tested and modified on the basis of correlation with survival outcomes.
Results: According to Bolondiet al. subclassification, there were initially treated by TACE 70 (24 %), 163 (56 %), 19 (7 %), 37 (13 %) patients in B1, B2, B3 and B4, respectively. There was a difference in median survival time between B1 and B2 (53 vs 34 months, $P < 0.001$), B2 and B3 (34 vs 18 months, $P = 0.210$), B3 and B4 (18 vs 31 months, $P = 0.287$). Subclass B4 was longer mean survival time than B3 in our study. In our new revised subclassification, we analyzed 3 substaging and there were initially treated by TACE 70 (24 %), 94 (32 %), 125 (44 %) patients in Ba, Bb and Bc, respectively. The median survival times differed between revised subclasses Ba and Bb (49 vs 44 months, $P = 0.070$) and differed significantly between Bb and Bc (44 vs 26 months, $P = 0.0049$).
Conclusion: Our new revised subclassification would be an effective tool for stratifying this heterogenous population and facilitating per-subclass-based treatment options.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1660

Clinicopathological study of scirrhous hepatocellular carcinoma

Anthony W.H. Chan[1], Joanna H.M. Tong[1], Paul B.S. Lai[2], K.F. To[1]

The Chinese University of Hong Kong Department of Anatomical and Cellular Pathology Hong Kong-Hong Kong[1], The Chinese University of Hong Kong Department of Surgery Hong Kong-Hong Kong[2]

Scirrhous hepatocellular carcinoma (HCC) is a histological variant of HCC featured by a dense fibrous stroma in which trabeculae of tumour cells are embedded. Its clinicopathological characteristics and clinical outcome are not well characterized due to its rarity. We studied a retrospective cohort of 469 patients with primary HCC undergoing curative surgery. Scirrhous HCC was identified in 40 patients (85.3 %). Compared to patients having classical HCC (n = 347), patients with scirrhous HCC had higher serum alpha-fetoprotein ($P = 0.023$). Scirrhous HCC had higher expression of stem cell markers (EpCAM [$P = 0.004$] and cytokeratin 19 [$P = 0.001$]) and Glypican-3 ($P = 0.008$). Scirrhous HCC was associated with poorer disease-free survival (median survival: 24.2 months vs. 73.0 months; 5-year survival: 30.9 % vs. 51.7 %; $P = 0.022$) than classical HCC. The multivariate analysis revealed that scirrhous HCC was an independent prognostic factor for disease-free survival and the adjusted hazard ratio of tumour relapse was 1.73 (95 % CI: 1.13-2.65; $P = 0.011$). In summary, scirrhous HCC was an uncommon variant of HCC associated with expression of stem cell markers and Glypican-3 and poorer clinical outcome.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1245

Risk factors for hepatocellular carcinoma a single center experience

Muharrem Coşkun[1], Sebati Özdemir[1], Birol Baysal[2], Ibrahim Hatemi[1], Emine Köroğlu[1], Nuray Kepil[3], Kadir Bal[1], Abdullah Sonsuz[1], Murat Tuncer[1], Hakan Şentürk[2]

Istanbul University, Cerrahpaşa Faculty of Medicine Department of Internal Medicine, Division of Gastroenterology Istanbul-Turkey[1], Bezmialem Vakif University, Faculty of Medicine Department of Internal Medicine, Division of Gastroenterology Istanbul-Turkey[2], Istanbul University, Cerrahpaşa Faculty of Medicine Department of Pathology Istanbul-Turkey[3]

Aim: Hepatocellular carcinoma (HCC) is one of the important health problems in Turkey. In this study we retrospectively investigated demographic, biochemical, serological and radiological characteristics of the patients with HCC.
Methods: Research data were obtained from the 97 patients hospitalized (74 males, 23 females) (mean age: 63.2 ± 9.4 yr, range: 34-80 yr). Demographic characteristics, hepatitis B (HBV), hepatitis C (HCV) and hepatitis delta virus markers, routine liver tests, serum alpha-fetoprotein (AFP) level, imaging methods and liver biopsy findings of the patients were reviewed retrospectively.
Results: Demographic analysis showed that HCC was more common in males and in the elderly population. HBsAg, HBsAg + anti-delta, and anti-HCV were found positive in the patients with the ratio of 61.6 % (n = 63), 4.8 % (n = 5), and 21.3 % (= 22), respectively. AFP levels were higher than upper normal limits in 91.7 % (n = 89) of the HCC patients. Cirrhosis was present in 93.8 % (n = 91) of the cases. The main imaging method for diagnosis of HCC was ultrasonography (USG).
Conclusion: HBV is the most common etiologic cause with the ratio 61.6 % of the 97 patients and HCV was also a significant etiologic factor with a 21.3 % ratio. HCC developed on cirrhosis basis in most patients. As a result, HBV and HCV infections, causing HCC, have constituted to be a major problem in this country.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1826

What is the right age to start screening for hepatocellular carcinoma in Thailand

Taya Kitiyakara[1], Apinya Leerapun[2], Chinnavat Suttivana[3]

Ramathibodi Hospital, Mahidol University Gastroenterology and Hepatology Bangkok-Thailand[1], Chiangmai University Gastroenterology and Hepatology, Internal Medicine Chiangmai-Thailand[2], Bhumibol Adulyadej Hospital Gastroenterology and Hepatology Bangkok-Thailand[3]

Aim: Hepatocellular carcinoma (HCC) screening has been recommended in the Thai national guidelines to improve treatment outcomes. The new guidelines changed the age to start screening in patients with hepatitis B (HBV) from 45 years for both sexes, to 40 years for men and 50 years for women, similar to western guidelines. We reviewed the age of HCC patients who were admitted into public hospitals to see if this change was appropriate.
Method: The 2010 admission reimbursement data from the three public healthcare funds covering 62,514,239 people in Thailand were analysed. HCC patients were identified by ICD10 code C22.0.
Results: In 2010, 15,290 HCC patients were identified and admitted into public hospitals. There were 11,591 male and 3,699 female patients. The mean ages (SD) for males was 58.0 (12.1) years and 62.7 (13.0) for females ($P < 0.001$). 834 (4.3 %) male HCC patients were aged < 41 years, whilst 686 (18.6 %) female HCC patients were aged < 51 years. The total number of HCC patients with reported HBV infection was 2,683, with the mean age (SD) 55.5 (11.3) years for men, and 57.2 (12.7) years for women. 206 (9.6 %) male HBV HCC patients were aged < 41 years at the time of admission, compared to 158 (30.1 %) females were < 51 years.
Conclusion: For screening to start at 40 years and 50 years in HBV male and female patients, (using available data from admissions) a lower proportion of female HCC patients compared to males would be detected. However, more male HCC patients would be detected than females in absolute numbers.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1910

Usefulness of angio ct for the diagnosis and treatment of early hepatocellular carcinoma

Akihiro Deguchi[1], Hiroaki Ngamatsu[2], Tsutomu Masaki[3]

Kagawa Rosai Hospital Gastroenterology Marugame-shi, Kagawa-Japan[1], Yame Republic General Hospital Hepatology Yame-shi, Fukuoka-Japan[2], Kagawa University School of Medicine Gastroenterology and Neurology Miki-cho, Kagawa-[3]

Aim: Early hepatocellular carcinoma (HCC) is defined as well-differentiated HCC with an obscure tumor margin in the classification of the Liver Cancer Study Group of Japan. In this study, the value of Angio CT for the diagnosis and treatment of early HCC was examined.
Material and method: The imaging features of Angio CT, dynamic CT, EOB-DTPA MRI and contrast enhancement ultrasonography (CEUS) of 52 early HCC nodules in 42 cases were investigated. The diagnosis of all the nodules was definite by histological examination.
Results: 50 of 52 early HCC nodules showed hypointensity on hepatobiliary-phase (HP) of EOB-MRI and 25 of 50 early HCC nodules with hypointensity on HP of EOB-MRI also revealed hypoechoic pattern in postvascular phase of CEUS. In remaining 25 nodules without hypoechoic pattern in postvascular phase of CEUS, 15 of 20 nodules less than 20 mm in tumor diameter showed low density areas in CT during angio portgraphy (CTAP). 12 of these 15 nodules were treated with radiofrequency ablation therapy. But untreated 3 nodules became hyper vascular nodules within 2 years and tumor rupture was observed in one case.
Conclusion: 75 % of early HCC nodules less than 20 mm in tumor diameter showed the reduction of portal flow and predicted to be hyper vascular nodules in the near future. It may be possible to select these nodules by performing Angio CT in the diagnosis of early HCC.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1372

Retrospective analysis of patients with hepatocellular carcinoma (HCC) in our region

Filiz Yıldırım[1], Hakan Dursun[1], Fatih Albayrak[1], Nihat Okçu[1]

Ataturk University, Medical Faculty Department of Gastroenterology Erzurum-Turkey[1]

HCC is a common form of cancer which is seen all over the world.

This study included 107 patients who were diagnosed as HCC in Atatürk University Faculty.

As a result of the parameters derived, it is confirmed that the occuring age 62 of hepatocellular cancer in our region is 4.5/1 rate ratio as male/female. Patients 55.1 % of them were carrying the HBV infection. 47.7 % of the sick people were carrying cirrhosis and the presence of cirrhosis among the female was significantly lower than the presence among the male ones with the rate of 16 % and only 2.8 % of them were carrying the infection of HCV. The level of AFP at the Okuda first phase was lower than second phase and third phase. Totally the size of lesion of 22 sick people were lower than 50 % of the liver and at the second phase totally, the size of lesion of 13 sick people's liver covered lower than 50 % and at the third phase 50 % of the liver of only 2 sick people's covered. 21.4 % of them were at the first phase, 42.9 % of them were at the second phase and 35.7 % of them were at the third phase. The average survivals determined as 16.9 months, at the second phase it was 5.4 months and at the third phase it was determined as 3.2 months.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 2059

Expression and significance of micro RNA 21 in hepatocellular carcinoma

Dipu Bharali[1], P.C. Ray[2], Premashis Kar[1]

Maulana Azad Medical College Medicine New Delhi-India[1], Maulana Azad Medical College Biochemistry New Delhi-India[2]

microRNAs (miRNAs) are deregulated in Hepatocellular carcinoma (HCC). To detect differential expression of micro RNA-21 in HCC and chronic liver diseases without HCC. A total of 45 HCC cases along with 45 controls of chronic hepatitis without HCC and 10 healthy individuals were enrolled. Total RNAs isolated from 400 µl serum samples of all cases and Controls were reverse-transcribed using miR-21 RT stem loop primer followed by real time amplification. Expression changes of miR-21 were examined using SPSS19.0 using the comparative Ct method. The mean ages (±SD) of HCC and controls without HCC were 56.55 (±10.53) years and 48.1 (±10.6) years, respectively. ALT and AST both the liver enzymes were higher in HCC than controls without HCC,

84.44 ± 35.04 IU/ml and 107.66 ± 35.99 IU/ml respectively. The gender and age groups are shown to be non significant and ALT, AST, Albumin, Total bilirubin and AFP are significant with respect to HCC. miR-21 expression level is lower in healthy controls in comparison to higher expression of miR-21 in HCC with CHB ($p < 0.05$). 2.1 time fold changes of miR-21 expression level in HCC. miR-21 expression was significantly higher in HCC with cirrhosis ($P = 0.025$) and TNM stage (III-IV) ($P = 0.042$). miR-21 expression level and other clinicopathological factors had no correlation ($p > 0.05$). Area under ROC curve (AUC) was 0.728 (CI: 0.711–0.942, $P = 0.000018$) with a sensitivity of 59.3 %, specificity of 86.7 %. miR-21 is suitable to detect overall liver damage in chronic liver diseases. It might be associated with HCC but not in the patients survival.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1473

A case of false positive elevation of pivka ii in patient who undergone heptectomy

Heon Young Lee[1], Sun Wook Park[1], Byung Seok Lee[1], Seok Hyun Kim[1], Eaum Seok Lee[1], Dae Hyun Tak[1], Young Wook Song[1]

Chungnam National University Internal Medicine Dae Jeon-Korea, South[1]

PIVKA-II is widely used as a specific marker for hepatocellular carcinoma. We report a case of false positive PIVKA-II elevation in patient who undergone hepatectomy for hepatocellular carcinoma.

5 months ago, a 50-year-old man undergone right hepatectomy due to hepatocellular carcinoma in S4 and S8 segment. He started warfarinization for benign thrombosis of portal and hepatic vein, since post operate day 10. When he first diagnosed hepatocellular carcinoma, AFP (Alfa feto-protein) was 970 ng/mL and PIVKA-II was 1,826 mAU/mL. 1 month after hepatectomy, AFP decreased to 55 ng/mL but PIVKA-II increased to 4,786 mAU/mL. 2 months after hepatectomy, AFP was decreased to 16 ng/dL but PIVKA-II was 2,440 mAU/mL. Abdominal computerized tomography showed no recurrence of hepatocellular carcinoma and partial decreased two focal thrombosis in mid portal and hepatic vein, so we maintained the warfarinization. 3 months after hepatectomy, AFP was 7 ng/mL but PIVKA-II markedly increased to 13,201 mAU/mL but there was no recurrence on abdominal computerized tomography. We stopped warfarin for exclusion of warfarin-induced PIVKA-II elevation. 1 month after stopping warfarin, PIVKA-II decreased to 158 mAU/mL and then we restarted warfarinization. But 1 month later, PIVKA-II re-increased to 9,583 mAU/mL. Liver magnetic resonance imaging revealed no recurrence of Hepatocellular carcinoma and PET scan showed no recurrence, too. We could consider that the elevation of PIVKA II was not originated from recurred hepatocellular carcinoma but from wafarinization it is required caution for check PIVKA-II level in whom taken warfarin or Vitamin K antagonists.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1114

The prothrombin induced by vitamin K absence or antagonist li is a good diagnostic factor in the HBV related BCLC 0 B stage hepatocellular carcinoma

Youde Liu[1], Yanni Sun[1], Jiguang Yu[1], Zhiqiang Zou[1], Xiumei Wang[2]

Yantai Infectious Disease Hospital Hepatology Yantai-China[1], Yantai Yuhuangding Hospital Oncology Yantai-China[2]

Objective: To assess the diagnostic value of the prothrombin induced by vitamin K absence or antagonist-II (PIVKA-II) in Chinese patients with HBV related HCC.
Methods: The study group consisted of 82 HCC patients (group A, including 80 BCLC 0-B stage and 2 BCLC C stage), 169 patients with chronic hepatitis B or HBV-related liver cirrhosis (group B), 68 HBV or HBsAg carrier patients (group C) and 138 healthy controls (group D). All patients and controls were examined for serum levels of PIVKA-II and AFP.
Results: The median serum levels of PIVKA-II in group A, B, C and D were 209.5 (2,75000) mAU/ml, 16 (4,30174) mAU/ml, 17 (5, 73) mAU/ml and 15 (3, 48) mAU/ml, respectively. The median serum levels of AFP in group A, B, C and D were 71.9 (1.3,41065.2) ng/ml, 5.3 (1.0,1528.0) ng/ml, 3.8 (1.3,23.8) ng/ml and 2.4 (1.2,35.7) ng/ml, respectively. PIVKA-II had better area under the receiver operating characteristic curve [0.857(95% CI 0.804-0.913)] than AFP [0.729 (95% CI 0.654-0.801)], $P < 0.001$. The optimal PIVKA-II and AFP cutoff value were 26.5 mAU/ml and 20.0 ng/ml, respectively. A combination detection of serum levels of PIVKA-II and AFP could increase the sensitivity, speciality, NPV and PPV in diagnosis of HCC.
Conclusions: PIVKA-II is better than AFP in diagnosis of HBV related BCLC 0-B stage HCC and PIVKA-II can serve as a marker for screening of HBV related HCC.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1930

Diagnostic role of dickkopf proteins in hepatocellular carcinoma

Harun Erdal[1], Ibrahim Doğan[1], Özlem Gül Utku[1], Eylem Karatay[1], Selahattin Ünal[1]

Gazi University Gastroenterology Ankara-Turkey[1]

Background-aim: Wnt/ß-catenin pathway plays crucial role in hepatocellular carcinogenesis. Dickkopf (DKK) protein family which consists of four members (DKK1 to 4) is one class of the Wnt antagonist. Overexpression of DKK1 in HCC tissues was demonstrated. Also, DKK3 methylation is increased in HCC tissues and associated with poor prognosis in HCC.
We aimed to evaluate the diagnostic role of the serum DKK proteins levels in HCC and to compare with serum AFP levels.
Method: We included 40 HCC patients, 54 cirrhosis and 39 healthy controls in our study. HCC patients were divided into two groups as early HCC (BCLC stage A) ($n = 21$) and very early HCC (BCLC stage 0) ($n = 6$). Serum DKK1 and DKK3 levels were measured by enzyme-linked immunosorbent assay (ELISA) method. Serum AFP levels were measured by chemiluminescence method.
AFP, DKK1 and DKK3 levels cut-off value and AUC are calculated with ROC curve.
Results: Comparing HCC patients with cirrhosis, sensitivity, specificity, positive predictive value and negative predictive values of AFP were 77.5, 79.6, 73.8 and 82.9 % respectively. Sensitivity, specificity, positive predictive value and negative predictive values of DKK1 were 72.5, 66.7, 61.7 and 76.6 % respectively. Sensitivity, specificity, positive predictive value and negative predictive values of DKK3 were 63, 74.4, 77.3 and 59.2 % respectively.
Conclusion: DKK1 and DKK3 are not superior to AFP in diagnostic role of HCC. Although the combination of DKK1 and AFP

is superior than AFP alone, statistically significant difference is not found.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1496

Expression and significance of insulin receptor substrate 1 (IRS 1) in human hepatocellular carcinoma

Long Fang[1], Chun Gao[1], Shukun Yao[1]

China-Japan Friendship Hospital Gastroenterology Beijing-China[1]

Aim: Our study was designed to determine the expression and significance of insulin receptor substrate-1 (IRS-1) in human hepatocellular carcinoma (HCC) samples, compared with surrounding no-tumor tissues, liver cirrhosis and chronic hepatitis tissues.
Methods: A total of 133 samples, from the patients who were treated at our hospital in the period January 2003 to March 2010, were examined by immunohistochemistry (IHC), including 63 cases from HCC, 48 cases from paracancerous tissues, 13 cases from liver cirrhosis, and 9 cases from chronic hepatitis tissues. The multivariate logistic regression model was used to determine the independent factors associated with the positive-expression of IRS-1.
Results: The expression of IRS-1 protein was observed in 28 cases of HCC (28/63, 44.4 %), 8 cases of paracancerous tissues (8/48, 16.7 %), 5 cases of liver cirrhosis (5/13, 38.5 %), and 8 cases of chronic hepatitis (8/9, 88.9 %). After exclusion of the 19 samples from liver biopsy, adjustment for age, gender, HBV and HCV, hepatocellular carcinoma was the independent associated factor for the expression of IRS-1 (OR 2.846, 95 % CI 1.104-7.332, $P = 0.030$). Moreover, its expression was not related to the tumor grade of differentiation and presence of tumor thrombus. In addition, we found that the method of sampling was associated with the expression of IRS-1.
Conclusions: The expression of IRS-1 was higher in HCC than in surrounding no-tumor tissues, which may involve in the onset and development of human hepatocllular carcinoma.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1492

Assessment of the malignant potential of hepatocellular carcinoma using kupffer phase images of contrast enhanced sonography with sonazoid

Junya Nuta[1], Hideyuki Tamai[1], Yoshiyuki Mori[1], Naoki Shingaki[1], Syuya Maeshima[1], Yoshimasa Maeda[1], Kosaku Moribata[1], Yosuke Muraki[1], Hisanobu Deguchi[1], Izumi Inoue[1], Takao Maekita[1], Mikitaka Iguchi[1], Jun Kato[1], Masao Ichinose[1]

Wakayama Medical University Second Department of Internal Medicine Wakayama-Japan[1]

Background/aim: The gross type of hepatocellular carcinoma (HCC) is associated with malignant potential, and the single nodular with extranodular growth (SNEG) type and the confluent multinodular (CMN) type have poorer prognoses than the single nodular (SN) type. The aim of the present study was to clarify the correlation between gross type and the Kupffer-phase images of contrast-enhanced sonography with Sonazoid.
Methods: A total of 73 patients with HCCs under 5 cm in diameter who underwent Sonazoid ultrasound before hepatic resection were analyzed. The HCCs was classified into two groups according to tumor margin. The irregular type included HCC with an irregular or unclear margin on conventional B-mode or with an irregular margin on the Kupffer-phase images of Sonazoid ultrasound. Malignant potential was also classified based on gross types. SN type was considered low-grade malignancy, and SNEG and CMN types were considered high-grade malignancy.
Results: Thirteen SN type, 32 SNEG type and 28 CMN type were evaluated. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of prediction of high-grade malignancy using irregular type on conventional B-mode were 72 % (43/60), 85 % (11/13), 96 % (43/45), 39 % (11/28), and 74 % (54/73), respectively. In comparison with conventional B-mode, the corresponding values for prediction of high-grade malignancy using irregular type on the Kupffer-phase images were 93 % (56/60), 85 % (11/13), 97 % (56/58), 73 % (11/15), and 92 % (67/73), respectively.
Conclusions: The Kupffer-phase images more accurately predict the malignant potential of HCC than conventional B-mode images and can provide essential information to determine the optimal treatment strategy.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1845

Relation of insulin resistance and hepatocellular carcinoma in non obese non diabetic hepatitis C positive patients

Ehab Abdel-atty[1], Mohamed Korani[2], Basam Masoud[3]

Faculty of Medicine, Menoufia University Hepatology Menoufia-Egypt[1], Faculty of Medicine, Menoufia University Internal Medicine Menoufia-Egypt[2], Faculty of Medicene Menoufia University Tropical Medicine Menoufia-Egypt[3]

The aim is to assess the relationship between insulin resistance and HCC in non-obese non-diabetic HCV +ve Egyptian patients.
Patients and methods: The study included 60 chronic HCV +ve patients divided into two groups: HCC group consist of 30 HCV +ve patients with HCC and HCV group consists of 30 HCV +ve patients without HCC. Ten healthy individuals are selected as a control group. A blood sample was withdrawn for CBC, albumin, bilirubin, prothrombin activity (PT %), insulin and AFP. HOMA-IR was calculated. HCC is further confirmed by triphasic CT.
Results: There was a significant difference among studied groups with regard, platelet count, serum albumin, PT %, total bilirubin, serum insulin, HOMA-IR and AFP levels ($P < 0.05$). Platelets count and serum albumin level of HCC group were significantly lower than HCV group ($P = 0.009$ & 0.001). Platelets count, serum albumin level and PT % of HCC group were significantly lower than controls ($P = 0.01$). Total bilirubin level of HCC group was significantly higher than HCV group and controls ($P = 0.001$). Serum insulin and HOMA-IR levels of HCC group were significantly higher than HCV group and controls ($P = 0.001$). Serum insulin and HOMA-IR levels of HCV group were significantly higher than controls ($P = 0.03$). Multivariate logistic regression analysis showed that HOMA-IR and insulin level were independent predictors for the risk of HCC development ($P = 0.03$).
Conclusion: This study showed a significantly higher degree of insulin resistance in patients with HCV infection and HCC compared with HCV infection alone or healthy controls. We hypothesize that

the presence of a vicious cycle triggered by HCV infection leads to increased insulin resistance with subsequent increased risk of HCC.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1310

Alpha fetoprotein is still a useful test for screening hepatocellular carcinoma in hepatitis B endemic areas

Taya Kitiyakara[1], Waraporn Panjawong[1], Pongphob Intaraprasong[1], Abhasanee Sobhonslidsuk[1], Chomsri Kositchaiwat[1]

Ramathibodi Hospital, Mahidol University Gastroenterology and Hepatology Bangkok-Thailand[1]

Aim: Hepatocellular carcinoma (HCC) is a common cause for cancer related death worldwide. Screening detects earlier stage disease and is recommended for at-risk populations. However there is still controversy as to whether alpha-fetoprotein (AFP) should be part of the screening test or not, as suggested by AASLD guidelines. We reviewed data from HCC patients to see how useful AFP was in screening.
Method: Patients whose HCC's were detected by screening in our hospital were identified from our prospectively-collected HCC registry and their clinical and radiological data were reviewed. AFP was deemed additionally useful in detecting HCC only when ultrasonography done around the time of the AFP test did not detect any suspicious lesion in the liver requiring further investigation with CT or MRI.
Results: From 405 patients in the registry, 44 patients were identified as having their HCC detected by screening. Of these 44, 72.8 % were male and 56.8 % had underlying hepatitis B (HBV) infection. Cirrhosis was present in 86 % (the Child-Pugh class were A/B/C in 32/5/1 patients, respectively). 10/44 HCC's (22.7 %) were detected by AFP alone. of these, 7 patients had HBV and 3 had hepatitis C. The level of AFP at detection in these patients ranged from 12.0 to 9029 ng/dl (Normal < 7.2 ng/dl). All but one patient detected by AFP were within Milan criteria at diagnosis. 8/10 patients are currently alive.
Conclusion: AFP adds approximately another 20 % to HCC detection on top of ultrasonography during screening. It remains a useful test in HBV endemic areas.

Topic 15: Hepatocellular Carcinoma Diagnosis

No: 1211

The importance of circulating mir 122 for hepatocellular carcinoma

Engin Onan[1], Hikmet Akkiz[2], Macit Ümran Sandikçi[2], Haluk Demiryürek[3], A.bahadır Öztürk[4]

Adana Numune Training and Research Hospital Internal Medicine Adana-Turkey[1], Cukurova University Gastroenterology Adana-Turkey[2], Cukurova University General Surgery Adana-Turkey[3], Adana Numune Training and Research Hospital Family Medicine Adana-Turkey[4]

Background & aims: MicroRNAs are thought to be novel serum biomarkers in cancer diagnosis, prognosis and follow-up. For the reason of primary liver cancer is the 5th most common cancer worldwide and the third one in cancer mortality, it is very important to determine hepatocellular carcinoma at an early stage for prognosis and patient management. Hepatocellular carcinoma constitutes 85-90 % of primary liver cancer. There is still no ideal marker to detect hepatocellular carcinoma at early stage. Circulating microRNA-122 may be a novel biomarker for hepatocellular carcinoma.
Methods: This study was performed in 2011-2012 at Cukurova University, Faculty of Medicine, Balcalı Hospital. There were 43 patients and 43 controls in total group. We showed amounts of circulating miR-122 in different clinical stages of hepatocellular carcinoma in patients' serum with real time-PCR method.
Results: In our study serum miR-122 amount in hepatocellular carcinoma group was significantly higher than the level found in the control group. ($0.030173 \pm 0.053 > 0.00493 \pm 0.015$, $P < 0.0001$). According to the area under the ROC curve (0.724) the patient group were identified for the cut-off value of miR-122. In addition, patients' other diagnostic, clinical and prognostic data were compared with circulating miR-122 levels.
Conclusion: Our results indicate that serum miR-122 alone may not be a good biomarker to show diagnosis, prognosis and surveillance of hepatocellular carcinoma. To use other diagnostic, clinical, prognostic indicators in conjunction with serum miR-122 may be more meaningful.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1126

Repeated stereotactic body radiotherapy for hepatocellular carcinoma

Won Il Jang[1], Mi-sook Kim[1], Hyung Jun Yoo[1], Young Seok Seo[1], Kyubo Kim[2], Chul Ju Han[3], Su Cheol Park[3], Sang Bum Kim[4], Eung-ho Cho[4]

Korea Institute of Radiological and Medical Sciences Radiation Oncology Seoul-Korea, South[1], Seoul National University College of Medicine Radiation Oncology Seoul-Korea, South[2], Korea Institute of Radiological and Medical Sciences Internal Medicine Seoul-Korea, South[3], Korea Institute of Radiological and Medical Sciences Surgery Seoul-Korea, South[4]

Purpose: To determine the feasibility and efficacy of repeated stereotactic body radiotherapy (SBRT) for inoperable hepatocellular carcinoma (HCC).
Patients and methods: We retrospectively reviewed 28 HCC patients who were treated with the repeated SBRT at Korea Cancer Center Hospital between January 2004 and May 2014. All patients were unsuitable for surgery or local ablation and had incomplete response to transarterial chemoembolization. Twenty-seven patients (96 %) underwent the repeated SBRT for intrahepatic recurrence other than the lesion with the 1st SBRT, and only one patient underwent re-irradiation for the same lesion with the 1st SBRT. Twenty-seven patients (96 %) had Child-Turcotte-Pugh (CTP) class A (A5 in 23 and A6 in 4, respectively). The median dose was 51 Gy (range, 30-60 Gy in 3–5 fractions) and 44 Gy (range, 30–60 Gy in 3-4 fractions) in the 1st and the repeated SBRT, respectively.
Results: The median follow-up duration was 11 months (range, 2–56 months). The median interval between the first and the repeated SBRT was 11 months (range, 2–48 months). The 2-year local failure-free and overall survival rates were 77 % and 42 %, respectively. Three patients (11 %) experienced deteriorating of CTP score by greater than or equal to 2 within 3 months of SBRT without disease progression.
Conclusions: This study showed that the repeated SBRT can be safely and effectively administered to the patients with inoperable

HCC, and these results suggest that this technique might be considered a salvage treatment. A further well-controlled large-scale study and longer follow-up are needed to determine the optimal dose-volume constraints and characterize late complications.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1135

The meaning of the gross type in the aspects of cytokeratin 19 positivity and resection margin in patients with hepatocellular carcinoma who underwent liver resection

Sung Chang Gong[1], Mee-yon Cho[2], Sung Hoon Kim[1], Moon Young Kim[3], Soon Koo Baik[3]

Yonsei University Wonju College of Medicine Surgery Wonju-Korea, South[1], Yonsei University Wonju College of Medicine Pathology Wonju-Korea, South[2], Yonsei University Wonju College of Medicine Internal Medicine Wonju-Korea, South[3]

Backgrounds: There is no consensus about the safe resection margin in patients with hepatocellular carcinoma who underwent surgical resection. Surgeons decide the extent of resection according to the residual liver function and tumor location. We investigated the impact of resection margin in the aspects of the tumor gross type and cytokeratin 19 (CK 19) positivity.
Methods: We retrospectively reviewed the medical records of patients who underwent liver resection at Wonju Severance Christian hospital. We divided the patients into two groups as follows; group 1 included expanding and vaguely nodular types and group 2 included nodular with perinodular extension, multinodular confluent and infiltrative types. We divided the resection margin into narrow (0.1-1 cm) and wide (more than 1.1 cm). We compared the clinicopathological features and CK19 positivity.
Results: Clinical and operative characteristics did not show a difference between group 1 and group 2. However, group 2 had a higher prevalence of gross portal vein invasion (PVI), microscopic PVI, microvessel invasion, satellite nodule, intrahepatic metastasis, multicentric occurrence and positivity of CK 19. Group 1 showed no difference of recurrence according to the resection margin. However, Group 2 showed a higher recurrence rate in patients with narrow resection margins than that in patients with wide resection margins ($P = 0.043$). Patients with CK 19 positivity in group 2 showed higher prevalence of PVI ($P = 0.012$) and microvessel invasion ($P = 0.009$).
Conclusions: Although our study has the limitation of small case number, patients with hepatocellular carcinoma showing expanding and vaguely nodular gross types may safely undergo surgical resection with a narrow resection margin.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1364

Impact of liver damage and influence of liver function reserve by sorafenib treatment for hepatocellular carcinoma patients with chronic liver disease

Yoshiyuki Wada[1], Yuko Takami[1], Masaki Tateishi[1], Tomoki Ryu[1], Kazuhiro Mikagi[1], Hideki Saitsu[1]

National Hospital Organization Kyushu Medical Center Department of Hepato-biliary Pancreatic Surgery, Clinical Research Institute Fukuoka-Japan[1]

Background: Chemotherapy for hepatocellular carcinoma (HCC) patients with chronic liver disease may induce liver damage and impair liver function reserve. We investigated early and long-term effects of sorafenib treatment on liver damage and function reserve, respectively.
Patients and methods: From July 2010 to August 2013, 120 consecutive advanced HCC patients receiving sorafenib in our institution were enrolled. Correlation between liver function at baseline and early-stage liver damage was analyzed. Liver damage was evaluated by the Common Terminology Criteria for Adverse Events v3.0. To investigate sorafenib treatment impact on liver function, liver function tests at baseline and after 3 months were compared.
Results: Seventeen (14.2 %) and seven (5.8 %) patients showed grade 3 and 4 liver damage, respectively. Total bilirubin (1.49 ± 0.16 mg/dL), lactate dehydrogenase (LDH) (405 ± 48.6 IU/L), aspartate aminotransferase (AST) (108 ± 12.4 IU/L), alanine aminotransferase (ALT) (69.9 ± 7.9 IU/L), and prothrombin-time (80.9 ± 2.73 %) significantly correlated with grade 3 and 4 liver damage. Furthermore, LDH (738 ± 82.4 IU/L), AST (158 ± 22.7 IU/L), ALT (84.3 ± 14.9 IU/L), γ-glutamyl transpeptidase (222 ± 46.6 IU/L), alkaline phosphatase (741 ± 73.4 IU/l), and C-reactive protein (2.57 ± 0.74 mg/dL) were significantly correlated with grade 4 liver damage. LDH, AST, and ALT showed significant variation, but liver function reserve-related factors did not.
Conclusion: Sorafenib treatment for HCC patients with inflammatory reactions and high levels of transaminase may lead to severe liver damage development in the early stage. Long-term sorafenib treatment may not influence liver function reserve.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1649

Result of studying in vitro effect of *Scutellaria baicalensis* georgi which is in the cell of liver cancer

Tserentsoo Byambaa[1], Boldbaatar J[2], Tserendagva Dalkh[1], Zorig Tumur[3], Dagvatseren Begz[4], Oyunsuren Ts[2]

Mongolian National University of Medical Sciences Theory of Traditional Medicine Ulaanbaatar-Mongolia[1], Institute of Biology Mongolian Academy of Sciences Ulaanbaatar-Mongolia[2], Institute of Public Health Reference Laboratory For Medicines Ulaanbaatar-[3], Traditional Medical Science Technology and Production Corporation of Mongolia Ulaanbaatar-[4]

Introduction: *Scutellaria baicalensis* in medicinal trietises described its efficacy as: "…it has power to dry blood, clear upsetted heat and organ's heat". Based on this we choose to study liver disorders as its prevalent in Mongolia. According to statistics of World cancer research fund international, Mongolia has highest rates of liver cancer, 97.8 among men, 61.1 among women per 100 000 population. The goal of this study was to study effectiveness of *Scutellaria baicalensis* extract on the liver cancer cells via in vitro.
Methods: Extracts of *Scutellaria baicalensis* were prepared from its rhizomes and herbs. Primary cancer cells were grown RPMI-1640 containing 10 % fetel bovine serum, MDCK cells in DMEM.
Results: We observed that the number of MDCK and PCC cells in each area differs from each other and it depended on the concentration

of preparation. Cell growth were inhibited by 91 %, when concentration of *Scutellaria baicalensis* Georgi extract was increased to 500 μg/ml.
Conclusion: Extract, derived from the upper part of *Scutellaria baicalensis* suppress on PCC and MDCK cell line's cell division, migration and their adhesion. The plant extract of *Scutellaria baicalensis* and Skullcap preparation did not any difference on DNA fragmentation of the cancer cell genom and control cells. The extract of *Scutellaria baicalensis* derived from upper part of the plant does not induce apoptosis, but trans membrane proteins can block cancer cell division by inhibiting their gene expression.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1834

Short term virologic efficacies of telbivudine versus entecavir against hepatitis B related hepatocellular carcinoma

Young Woon Kim[1], Jung Hyun Kwon[2], Jeong Won Jang[3], Soon Woo Nam[1]

Medical College of The Catholic University of Korea Hepatobiliary Unit, Division of Gastroenterology, Department of Internal Medicine Incheon-Korea, South[1], Edical College of The Catholic University of Korea Hepatobiliary Unit, Division of Gastroenterology, Department of Internal Medicine Incheon-Korea, South[2], Edical College of The Catholic University of Korea Department of Internal Medicine Seoul-Korea, South[3]

Telbivudine has been reported to be more effective than lamivudine. However, because of the resistance rate to telbivudine, the current guidelines recommend entecavir or tenofovir as the first line therapy for Chronic hepatitis B. We investigated the short term viologic efficacy of telbivudine in comparison with entecavir as the first-line agent of HBV suppression in HBV related advanced HCC patients. A total of 86 consecutive patients with HBV-related HCC for whom antiviral treatment was initiated in Incheon St. Mary's Hospital between 2010 and 2013 were analyzed. Virologic responses were investigated on the 4 th, 12th and 24th weeks of the antiviral therapies. In patients with advanced TNM stage cancer (stage 3 or 4) and poor liver function (Child-Pugh class B or C), the virologic response rates at weeks 12 and 24 were 25 % (1/4) and 42.8 % (3/7) in the TLV group and 33.3 % (1/3) and 33.3 % (1/3) in the ECV group, respectively ($P = 0.424$, $P = 0.800$). The short term efficacy of telbivudine was similar to that of entecavir. Since telbivudine is highly cost-effective, it should be considered as a first line antiviral agent in patients with advanced HCC, poor liver function, and short life expectancies.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1159

Which is the suitable treatment for advanced hepatocellular carcinoma with major portal vein tumor thrombosis; sorafenib or transcatheter arterial chemo infusion

Tomonari Okudaira[1], Atsushi Hiraoka[1], Toshihiko Aibiki[1], Akiko Shiraishi[1], Tomoe Kawamura[1], Hiroka Yamago[1], Nobuaki Azemoto[1], Tomoyuki Ninomiya[1], Tadashi Murakami[2], Yoshihiro Ishimaru[2], Hideki Kawasaki[3], Koji Joko[4], Masashi Hirooka[5], Yoichi Hiasa[5], Kojiro Michitaka[1]

Ehime Prefectural Central Hospital Gastroenterology Center, Department of Internal Medicine Ehime -Japan[1], Ehime Prefectural Central Hospital Radiology Ehime -Japan[2], Ehime Prefectural Central Hospital Gastroenterology Center, Department of Surgery Ehime -Japan[3], Matsuyama Red Cross Hospital Hepatology Center Ehime -Japan[4], Ehime University Graduate School of Medicine Department of Gastroenterology and Metabology Ehime-Japan[5]

Aim/background: Sorafenib (SOR) has been recommended for advanced hepatocellular carcinoma (HCC). However, there have been few effective therapeutic modalities against HCC with major portal vein tumor thrombosis (PVTT). The prognosis of PVTT is poor. To elucidate the effective therapy against PVTT, we compared the prognosis of PVTT treated with SOR and those with transcatheter arterial chemo-infusion (TAI), retrospectively.
Material/method: From 2005 to 2013, Clinical findings for 42 PVTT without extra-hepatic metastasis were enrolled (male: female = 35:7, HCV:HBV: others = 27:4:11). The cases which were treated with both or switched each other were excluded. TAI was repeated every 6 weeks. Prognosis and therapeutic response evaluated by modified RECIST by CT 2 months after starting therapy were analyzed.
Result: In TAI-group (n = 31, Average age: 68.1 ± 9.3y.o., cisplatin: others = 26:5), TAI was repeated as long as hepatic reserve function was maintained. Response rate was 19.4 %. Obvious severe side effect over grade 3 was not observed. In SOR-group (n = 11, Average age: 70.4 ± 13.7y.o., 800:400 mg = 5:6), response rate was 27.3 %. Side effect over grade 3 was observed in 1 case (gastrointestinal bleeding from gastric varices). Hepatic reserve function at the starting therapy was better in SOR-group than TAI-group (Child-Pugh A:B:C = 10:1:0 vs. 15:12: 4, $P = 0.03$), whereas the 6-month and 1-year survival rates and MST of TAI-group were better than those of SOR-group (52.2 and 38.0 % vs. 34.1 and 0 %, 283 vs. 72 days, respectively) ($P = 0.01$).
Conclusion: Prognosis of TAI was better than SOR in HCC with major PVTT, though establishment of an effective regimen and additional evidence of the efficacy of transcatheter chemo-infusion therapy are needed.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1050

Combination therapy with sorafenib and transarterial chemoembolization (tace) significantly prolongs overall survival compared to tace alone

Takamasa Ohki[1], Koki Sato[1], Tomoharu Yamada[1], Mari Yamagami[1], Daisaku Ito[1], Kentaro Kojima[1], Toshihiko Arizumi[1], Michiharu Seki[1], Nobuo Toda[1], Kazumi Tagawa[1]

Mitsui Memorial Hospital Gastroenterology Tokyo-Japan[1]

Objectives: To evaluate the efficacy and safety of the combination therapy with sorafenib and transarterial chemoembolization (TACE) as a treatment for advanced hepatocellular carcinoma (HCC).
Patients and methods: In this retrospective study we enrolled 95 advanced HCC patients treated with TACE between June 2009 and December 2012 in our institution. of the 95 patients, 24 patients were treated with TACE followed by sorafenib (S-TACE group) and the 71 patients were treated with TACE alone (TACE alone group). Sorafenib was administered within 14 days after TACE. We compared the progression free survival (PFS) between the two groups and analyzed the predictive factors which affected on PFS.

Results: The median age was 72.2 years and 74 patients were male (77.9 %). Although the median tumor size was similar between the two groups, the mean numbers of tumors was significantly higher in S-TACE group: 16 vs. 8 ($P = 0.04$). The history of prior treatments was also significantly higher in S-TACE group. Other data was not significantly different between the two groups. There were no severe side effects between S-TACE group and TACE alone group. The mean PFS was significantly longer in S-TACE group: 176 days vs. 107 days ($P = 0.02$). Adjusting for significant factors in univariate analysis, multivariate analysis indicated that administration of sorafenib (OR: 0.38, $P < 0.01$), tumor size (OR: 1.12, $P < 0.01$) and ALT (HR: 1.04, $P < 0.01$) as independent factors which affected on PFS.
Conclusion: The combination therapy of sorafenib and TACE significantly improved PFS in patients with advanced HCC.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1690

Infectious complications related to radiofrequency ablation for liver tumors a role of antibiotics

Ryo Nakagomi[1], Ryosuke Tateishi[1], Shuichiro Shiina[2], Shintaro Mikami[3], Mayuko Kondo[1], Naoto Fujiwara[1], Masaya Sato[1], Tatsuya Minami[1], Koji Uchino[1], Kenichiro Enooku[1], Hayato Nakagawa[1], Yoshinari Asaoka[1], Yuji Kondo[1], Kazuhiko Koike[1]

Graduate School of Medicine, The University of Tokyo Gastroenterology Tokyo-Japan[1], Juntendo University Hospital Gastroenterology Tokyo-Japan[2], National Center For Health and Medicine Gastroenterology Tokyo-Japan[3]

Background/aims: Infectious complications related to radiofrequency ablation (RFA) for malignant liver tumors potentially lead to fatal outcome. To compare the effectiveness of single vs. continuous prophylactic antibiotic use prior to RFA, we conducted a prospective cohort study.
Methods: We switched from continuous to single antibiotic administration in December 2010. In January 2012 we performed interim analysis. Then we confirmed the non-inferiority of single administration by comparing with historical cohort in June 2014.
Results: The historical cohort with continuous administration consists of 6771 patients (mean age, 69.3; M/F = 4501/2270; hepatocellular carcinoma [HCC]/metastatic liver tumor [MLT] = 6163/608). In this cohort we administered twice a day of flomoxef sodium until the body temperature of patients declined below 37.5 degree. The single administration cohort consists of 1984 patients (mean age, 71.2; M/F = 1295/689; HCC/MLT = 1806/178). In this trial cohort we administered 3 g of ampicillin/sulbactam once just before RFA. Written informed consent was obtained in all subjects. Infectious complications occurred in 15 (0.22 %) and 7 patients (0.35 %) in the continuous and single administration cohort, respectively. The breakdown was as follows: liver abscess in 14, cholecystitis in 1, liver abscess in 5, cholecystitis in 1, and cholangitis in 1. Patients were diagnosed median of 14 (range, 1-154) days after RFA. The non-inferiority of single administration over continuous administration was confirmed with a statistical significance ($P = 0.04$).
Conclusion: The rate of infectious complications related to RFA was acceptably low. Single prophylactic antibiotic use did not significantly increase the rate of infectious complication related to RFA compared to more intensive protocol.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1521

A comparative study for survival benefits and safety of hepatic arterial infusion chemotherapy for advanced hepatocellular carcinoma in alcoholics versus non alcoholics

Myung Jin Oh[1]

Cha University School of Medicine Department of Internal Medicine Gumi-Korea, South[1]

Background: Hepatic arterial infusion chemotherapy (HAIC) can be an alternative option for intractable advanced HCC. In Korea, excessive alcohol intake is one of major causes of HCC. Thus, the aim of this study was to compare survival benefits and safety of HAIC for advanced HCC between the alcoholic patients and the non-alcoholic patients.
Methods: From January 2009 to December 2011, a total of 51 patients who received only HAIC with 5-fluorouracil (750 mg/m[SUP]2[/SUP] on days 1-4) and cisplatin (25 mg/m[SUP]2[/SUP] on days 1-4) for advanced HCC over one cycle, and divided into the alcoholics group (n = 21) and the non-alcoholics group (n = 30) were enrolled. Alcoholics was defined as a regular average consumption of > 20 g/day for women, > 40 g/day for men. After HAIC for advanced HCC, the overall survival (OS), progression-free survival (PFS), and adverse events in the alcoholics group and the non-alcoholics group were investigated retrospectively.
Results: No significant difference was observed in baseline characteristics between the alcoholics group and the non-alcoholics group. Median OS and PFS in the two groups were 5.1 months (95 % CI: 2.0-8.2) vs. 5.4 months (95 % CI: 2.0-8.7) and 4.4 months (95 % CI: 3.7-5.2) vs. 4.6 months (95 % CI: 2.5-6.7), respectively. Median OS and PFS were not statistically significant between the two groups ($P = 0.310$, $P = 0.375$). In addition, the serious adverse events ≥ -grade 3 arose from 21 patients (100 %) in the alcoholics group and 26 patients (83.9 %) in the non-alcoholics, respectively ($P = 0.143$).
Conclusions: Our study demonstrated that survival benefits and safety of HAIC for advanced HCC of alcoholic patients were comparable to those of non-alcoholic patients.

Topic 16: Hepatocellular Carcinoma Treatment

No: 2021

Long term survival analysis of patients with single hepatocellular carcinoma

Chia-yen Dai[1], Ming-lun Yeh[1], Shinn-cherng Chen[1], Yi-hung Lin[1], Po-cheng Liang[1], Chung-feng Huang[1], Jee-fu Huang[1], Zu-yau Lin[1], Ming-lung Yu[1], Wan-long Chuang[1]

Kaohsiung Medical University Hospital, Kaohsiung, Medical University Internal Medicine Kaohsiung-Taiwan[1]

Introduction: Curative therapies are the recommended treatments for single nodular type hepatocellular carcinoma (HCC). Surgery and local ablations including radiofrequency ablation (RFA), percutaneous ethanol injection (PEI) are safe and effective options. Herein, we aimed to investigate the long term survival in patients with single HCC receiving Curative therapies.
Methods: This cohort study is conducted as a retrospective analysis of HCC registered in the cancer registration database of a medical center in southern Taiwan. A total of 400 patients with the diagnosis of single HCC and of them, 190 patients received curative therapies

between 2005 and 2010 were studied. The clinical outcomes and associated factors were analyzed.
Results: Of the 400 patients, 258 (64.5 %) patients were male and the median age of diagnosis was 63 years old. The median follow up period was 26.6 months. In 190 (47.5 %) patients receiving curative therapy, including surgery in 125 and RFA/PEI in 65 patients, the 1-yr, 3-yr and 5-yr OS were 92.4, 72.5 and 58.8 %, respectively. Child-Pugh A, AFP level < 200 ng/mL, tumor < 5 cm and curative treatment were significant independent factors associated with better OS. Compared with RFA/PEI, surgery also had significant better OS ($P = 0.035$). The 1-yr, 3-yr and 5-yr DFS were 75.7, 53.5 and 37.5 %, respectively. Only Child-Pugh A and curative treatment were significant independent factors associated with better DFS. There was no difference of DFS between surgery and RFA/PEI.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1935

The relationship between the neutrophil to lymphocyte ratio and the uicc staging system for hepatocellular carcinoma after curative surgery

Yukiyasu Okamura[1], Teiichi Sugiura[1], Takaaki Ito[1], Yusuke Yamamoto[1], Katsuhiko Uesaka[1]

Shizuoka Cancer Center Hospital Hepato-Biliary-Pancreatic Surgery Sunto-Nagaizumi-Japan[1]

Background and aims: The neutrophil to lymphocyte ratio (NLR) is regarded as a predictor of survival for various types of cancer including hepatocellular carcinoma (HCC). The aims of this study were to elucidate the relationship between the NLR and the UICC staging system, and the role of NLR as a prognostic predictor after curative resection for HCC.
Methods: A total of 368 patients were finally included and evaluated in the present study. The cut-off value of the NLR was defined as 2.81 in accordance with the published literature.
Results: There were 225, 99 and 44 patients in UICC stage I, II and III or more, respectively. There were 42 (18.7 %), 22 (22.2 %) and 11 (25.0 %) patients with a NLR larger than 2.81 in the UICC stage I, II and III or more groups, respectively. There was no correlation between the NLR and the UICC staging system ($P = 0.216$). When the analysis was limited to patients in UICC stage I, the patients with a NLR > 2.81 had a significantly poorer prognosis than those with a NLR ≤ 2.81 (median survival time [years]: 5.0 vs. 8.2). On the contrary, there were no significant differences between the patients with a high and low NLR with a UICC stage of II or III or more ($P = 0.150$, $P = 0.197$, respectively).
Conclusions: The preoperative NLR is a valuable prognostic indicator for patients with UICC stage I HCC, which means those with a solitary tumor without vascular invasion.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1097

A prospective controlled trial of radiofrequency ablation for hepatocellular carcinoma performed by two hepatogastroenterologists with different training backgrounds (4)

Hitoshi Mochizuki[1], Shota Harai[1], Natsuhiko Kuratomi[1], Yoshimitsu Fukasawa[1], Yoji Suzuki[1], Kenji Hosoda[1], Yuichirou Kojima[1], Masao Omata[2]

Yamanashi Central Hospital Gastroenterology Yamanash-Japan[1], Tokyo University Gastroenterology Tokyo-Japan[2]

Background/aims: Although RFA procedure has been employed so widely as treatment option for therapy of HCC, training system for the beginner has not been established.
Methods: Ninety-two consecutive HCC patients were randomly assigned to two board-certified hepatogastroenterologists. One (KH) has performed more than 600 cases of RFA in the past 12 years, but principally self-trained. He is called, here, as the [I]Experienced[/I]. The other (HM) is also a board-certified gastroenterologist, never experienced ablation procedure for HCC in the past 30 years. Here, HM is called the [I]Beginner[/I]. However, the [I]Beginner[/I] had 6 months training session of RFA at high-throughput center before he stared to perform the ablation procedure.
Results: The [I]Beginner[/I] (HM) and the [I]Expert[/I] (KH) performed 43 and 49 ablations, respectively. There was no difference of background demographic and clinical feature of two patients cohort. The length of time required for ablation was longer (75 min) by the [I]Beginner[/I] than by the [I]Experienced[/I] (49 min). However, complication rate during and after the procedure and outcome of the treatment, namely HCC recurrence rate and survival rate within 4 years, were no different between the two operators. Differences noted were frequencies of employment of pleural effusion techniques, peritoneal effusion techniques by the [I]Beginner[/I] and the [I]Experienced[/I], respectively.
Conclusions: This prospective study concluded that the proper training, including the experience of ultrasound guided needling with the help of pleural or peritoneal effusion methods helped to start safe and effective ablation treatment procedure by the [I]Beginner[/I].

Topic 16: Hepatocellular Carcinoma Treatment

No: 2228

Hepatocellular carcinoma molecular subclass as a potential predictive biomarker of drug response

Shalini Bansal*[1], Anu Venkatesh*[1], Xiaochen Sun[1], Poh Seng Tan[1], Alexis Karlin[1], Anna Koh[1], Myron Schwartz[1], Yujin Hoshida[1]

Icahn School of Medicine At Mount Sinai Medicine NY-United States[1]

The lack of predictive biomarker of drug response has been recognized as a major challenge in development of effective medical therapies for hepatocellular carcinoma (HCC). We sought to examine whether HCC transcriptome subclasses are correlated with response to molecular targeted agents by combining organotypic ex vivo tissue culture system and a gene-expression-based HCC molecular classification assay. HCC tumor slices were obtained from surgical resections, and tissue viability was evaluated after culture with two agents (drug A and B). Gene-expression profiling was performed to subclassify the tumors into 3 different previously identified subclasses (S1, S2, and S3 subclasses), and correlation between therapeutic response and subclasses was tested. Drug A showed higher efficacy in S3 tumors compared to non-S3 tumors ($P = 0.048$), whereas drug B did not show such association. The results suggest that presence of S3 subclass is predictive of response to drug A, and may indicate that determination of the molecular subclasses could guide personalized administration of the drug upon further validation.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1447

The clinical outcomes and biliary complications after hypofractionated radiation therapy in hepatocellular carcinoma

Jeong Il Yu[1], Hee Chul Park[1], Do Hoon Lim[1], Seung Woon Paik[2]

Samsung Medical Center Radiation Oncology Seoul-Korea, South[1], Samsung Medical Center Medicine Seoul-Korea, South[2]

Purpose: To evaluate the efficacy of hypofractionated radiation therapy (RT) in unresectable, trans-arterial chemoembolization (TACE) failed or refractory hepatocellular carcinoma (HCC) and investigate the incidence of biliary complication after hypofractionated RT.
Methods: This retrospective study was conducted with the unresectable, TACE failed or refractory HCC patients who were treated with hypofractionated RT from July 2006 to December 2012. Perihilar region was defined as the area within 1 cm of right, left, common bile duct including gallbladder and cystic duct. The significant elevation of total bilirubin was defined as the elevation of total bilirubin more than 3.0 mg/dl, and two times of previous level after RT completion.
Results: During the study period, 50 patients received hypofractionated RT, and median follow-up was 24.7 months (range, 4.3 to 95.5 months). No classic radiation induced liver disease was developed, but four patients (8 %) experienced significant elevation of total bilirubin within one year after RT. During the follow-up, radiologic biliary abnormalities developed in 12 patients (24 %), but the toxicities requiring intervention was only two of them.
Local progression-free survival, progression-free survival and overall survival of all patients after hypofractionated RT were 89.7, 11.2, and 57.4 % at 3-years, respectively.
Conclusions: Biliary complication associated with higher dose exposure by hypofractionated RT was minimal, even in perihilar region. Hypofractionated RT showed excellent local control and it might be one of valuable options in unresectable and TACE failed or refractory HCC.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1769

Outcome of incidental hepatocellular carcinoma after liver transplantation

Walid El Moghazy[1], Samy Kashkoush[2], Glenda Meelberg[2], Norman Kneteman[2]

Sohag University Surgery Sohag-Canada[1], Hpb Surgery and Transplantation-Egypt[2]

With recent improvements in imaging, the frequency of incidental HCC (iHCC) appears to be declining.

As such, we aimed in this study to assess iHCC over different time periods, and to compare impact on outcome to pre-operatively diagnosed HCC (pdHCC) and non-HCC liver transplants.
Patients and methods: We analyzed the outcome of adult patients who were transplanted in our institution and had at least one year of follow-up. Patients were divided into three groups according to diagnosis of HCC.

Between 1990 and 2010, 887 adults (> 18 year old) were transplanted. Among them, 121 patients (13.6 %) had pdHCC and 32 patients (3.6 %) had iHCC; frequency of iHCC decreased markedly over years, in parallel with significant increase in pdHCC. Dividing patients into 5-year intervals, between 1990 and 1995, 120 patients had liver transplants, 4 (3.3 %) of them had iHCC and only 3 (2.5 %) had pdHCC while in the last 5 years, 263 patients were transplanted, 7 (0.03 %) of them had iHCC and 66 (25.1 %) had pdHCC ($P < 0.001$). There was no significant difference between groups regarding patient survival, with 1- and 5-year survivals in iHCC patients were 87.5 %, and 74 %, respectively and in pdHCC patients were 86.8 %, and 75.5 %, respectively and in patients transplanted for non-HCC indications were 88.5 % and 77.3 % and ($P = 0.702$).

Patients with iHCC had no recurrences after transplant while pdHCC patients experienced 17 recurrences (15.3 %) ($P = 0.016$).
Conclusions: Incidental HCC has significantly decreased despite steady increase in number of transplants for HCC. Patients with iHCC had excellent outcomes with no tumor recurrence, and survival comparable to pdHCC.

Topic 16: Hepatocellular Carcinoma Treatment

No: 2015

The role of 18f fdg pet ct in prediction of progression free survival after yttrium 90 radioembolization in patients with hepatocellular carcinoma

Wonseok Kang[1], Mijin Yun[2], Jin-young Choi[3], Jong Yun Won[3], Seung Up Kim[1], Kwang Hyub Han[1], Do Young Kim[1]

Yonsei University Internal Medicine Seoul-Korea, South[1], Yonsei University Nuclear Medicine Seoul-Korea, South[2], Yonsei University Radiology Seoul-Korea, South[3]

Background/aim: To investigate the prognostic value of 18[SUP][/SUP]F-FDG PET-CT in predicting progression-free survival (PFS) after Yttrium-90 radioembolization (Y-90 RE) in patients with hepatocellular carcinoma (HCC).
Method: Between 2009 and 2013, a total of 40 patients with HCC were treated with Y-90 RE. 18[SUP][/SUP]F-FDG PET-CT was performed before treatment and maximum standardized uptake value (SUVmax) was obtained in each patient. Tumor response was evaluated in accordance with modified RECIST criteria every 3 months after Y-90 RE. Chi square tests, Kaplan–Meier method and Cox proportional hazards model were used for statistical analysis.
Result: The median age was 56.5 years, and 29 (72.5 %) were males; 36 (90.0 %) patients were in Child-Pugh class A. Patients with low SUVmax (< 6.1) had a higher disease control rate than those with high SUVmax (> 6.1) (55.6 % vs. 23.1 %, respectively; $P = 0.05$). Median PFS was significantly longer in patients with low SUVmax than those with high SUVmax (22.1 vs. 6.5 months, respectively; $P = 0.03$). In addition, a longer PFS was observed in patients with BCLC stage A or B than those with BCLC stage C ($P = 0.01$). In multivariate analyses, low SUVmax was found to be a significant prognostic factor for a lower risk of disease progression (adjusted HR 2.51, 95 % CI 1.05 - 5.96; $P = 0.04$), along with BCLC stage A or B (adjusted HR 3.71, 95 % CI 1.32 - 10.47; $P = 0.01$).
Conclusion: High SUVmax based on 18F-FDG PET-CT performed before treatment and BCLC stage were independent prognostic factors for PFS after Y-90 RE in HCC patients.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1674

Applicability of various prognostic systems for hepatocellular carcinoma patients receiving transarterial chemoembolization

Yang Jae Yoo[1], Ji Hoon Kim[1], Seong Hee Kang[1], Ji Hye Je[1], Hae Rim Kim[1], Sang Jun Suh[1], Young Kul Jung[1], Yeon Seok Seo[1], Hyung Joon Yim[1], Jong Eun Yeon[1], Kwan Soo Byun[1]

Korea University College of Medicine Internal Medicine Seoul-Korea, South[1]

Aims: We aimed to compare the current prognostic systems for patients receiving 1st (HAP stage)and 2nd TACE (ART, ABCR).
Methods: Between January 2004 and December 2009, 622 HCC patients (group 1) received TACE as primary therapy. Among them, 363 patients (group 2) received second TACE session within 90 days. Additionally, 292 patients (group 3) who meet the original inclusion criteria of ART and ABCR score were selected.
Results: The OS was well differentiated according to HAP stage (47, 28, 13, 6 months in A, B, C, D, $P < 0.001$) as well as BCLC stage (52, 44, 30, 8 months in 0, A, B, C, $P < 0.001$) after 1st TACE. AUROC of survival according to HAP stage and BCLC stage were similar ($P = 0.6858$).

ART score did not dichotomize the survival of HCC patients after 2nd TACE (median OS; 25 versus 26 months in 0-1.5 versus ≥ 2.5, $P = 0.688$). However, ABCR score well differentiated the survival after 2nd TACE. (34, 18, 5 months in ABCR ≤ 0, 1-3, ≥ 4; 5, $P < 0.001$). Moreover, AUROC of survival for ABCR score were significantly wider than that for ART score. (0.717 versus 0.572, $P < 0.001$ in 1 year, 0.687 versus 0.51 in 2 year, $P < 0.001$). Furthermore, in group 3, ART was not valuable but ABCR score also well differentiated the survival after 2nd TACE.
Conclusions: The prognostic value of HAP score and BCLC were similar for first TACE session and ABCR was more useful than ART to predict prognosis after second TACE session.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1174

Fifty two lesions of advanced or terminal stage hepatocellular carcinoma classified by the barcelona clinic liver cancer classification and treated with the cyberknife

Hiroyuki Kato[1], Hideo Yoshida[1], Hiroyoshi Taniguchi[1], Ryutaro Nomura[2], Kengo Sato[2], Ichiro Suzuki[2], Ryo Nakata[1]

Japanese Red Cross Medical Center Gastroenterology Tokyo-Japan[1], Japanese Red Cross Medical Center Cyberknife Center Tokyo-Japan[2]

Aim: The Cyberknife® system delivers stereotactic body radiation therapy and has recently emerged as a treatment option for patients with hepatocellular carcinoma (HCC) unsuitable for other therapies. We aimed to report treatment outcomes of the Cyberknife for patients with HCC to clarify its safety and efficacy.
Methods: Patients with HCC and extrahepatic metastasis, vascular, or bile duct invasion were enrolled between May 2011 and February 2014. The Cyberknife was used to treat each lesion. Treatment response scores were based on Response Evaluation Criteria in Solid Tumors v1.1.
Results: Thirty-five patients with 52 lesions were enrolled. Based on the Barcelona Clinic Liver Cancer classification, all patients were either in advanced or terminal stage. The target lesions were as follows: 28 were bone metastasis; 5, lung metastasis; 5, brain metastasis; 5, portal vein invasion; 3, hepatic vein invasion; 2, bile duct invasion; and 4 were others. Tumors invading the hepatic vessels or bile duct had a median size of 29 (range: 12–59) mm. The median prescribed dose was 31 (range: 28-42) Gy. Extrahepatic lesions had a median tumor size of 23 (range: 10-53) mm and the median prescribed radiation dose was 24 (range: 8-48) Gy.
Response rate and disease control rate were 46 % and 63 %, respectively. Median survival time for advanced stage patients, terminal stage patients were 13.9 months and 1.7 months respectively. One patient had cerebral bleeding and another patient had esophageal ulcer.
Conclusions: The Cyberknife might be less invasive and useful for local tumor control and palliative care.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1402

Role of microwave ablation as an effective treatment for hepatocellular carcinoma

Enas Alkareemy[1], Hussein Elamin[1], Ossama Hetta[2], Ahmed Ashmawy[1]

Assiut University Internal Medicine Assiut-Egypt[1], Ain Shams University Radiology Cairo-Egypt[2]

The aim of this study: To evaluate immediate therapeutic efficacy and safety of thermal ablation for treatment of hepatocellular carcinoma (HCC) using microwave ablation energy; upper Egypt Experience.
Patients and methods: 30 patients with HCC were enrolled in the study. All the study patients had MW ablation of the hepatic lesion. Thereafter, follow up was done 30 days later to assess the efficacy and detect the complications of MW ablation.
Results: After 30 days, complete tumor necrosis was achieved in 27 patients (90 %). Both increased lesion size and advanced Child class were found to be associated with worse outcome and recurrence.
Conclusions: Microwave ablation is safe and effective technique and has a promising potential in the treatment of hepatocellular carcinoma.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1426

Prophylactic therapy for esophageal varices can improve the qol of both patients and medical staffs in patients with portal vein tumor thrombosis

Takafumi Sugimoto[1], Masatsugu Ishii[1], Toshihiro Kawai[1], Yoko Yashima[1], Shinpei Sato[1], Shuntaro Obi[1]

Kyoundo Hospital Gastroenterology and Hepatology Tokyo-Japan[1]

Objective: The aim of this study was to evaluate the effect of the prophylactic therapy for esophageal varices (EV) in advanced HCC with portal vein tumor thrombosis (PVTT).
Methods: A total of 118 consecutive patients were diagnosed as advanced HCC with PVTT in our hospital from April 2010 to March 2012. For one year before March 2011, hemostasis was

achieved endoscopically in the event of variceal rupture (Group A). For one year after April 2011, we performed the prophylactic band ligation to EVs with over F2 and red color sign (Group B). The cumulative bleeding rate and overall survival were compared between 2 Groups.

Results: A total of the 118 patients (male: female, 94: 24; mean age 67.2 yrs) were assigned to Group A (N = 63) and Group B (N = 55). 109 patients died and 13 patients vomited blood. The median survival time in each groups were 8.2 and 8.4 months, respectively ($P = 0.95$). Hematemesis was occurred: 10 (15.8 %) of Group A and 3 (5.5 %) of Group B ($P = 0.071$). The number of death related to hematemesis was significantly different: 6 (9.5 %) of Group A and 0 (0 %) of Group B ($P = 0.0052$). The number of the patients who needed the emergency endoscopy in the night was in 5 of Group A and 1 of Group B, respectively.

Conclusion: This study suggested that prophylactic treatment for EVs in patients with PVTT doesn't prolong the prognosis but can prevent the death of hematemesis. Prophylactic therapy may reduce the emergency endoscopy in the night and improve the QOL of both patients and medical staffs.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1706

The outcome of laparoscopic liver dissection for hepatocellular carcinoma

Noriyuki Oba[1], Hideyuki Kanemoto[1], Yusuke Kyoden[1], Michiro Takahashi[1], Masakazu Takagi[2]

Shizuoka General Hospital Hepato-billiary-pancreatic Surgery Shizuoka-Japan[1], Shizuoka General Hospital Surgery Shizuoka-Japan[2]

In this paper we will report the outcome of laparoscopic liver dissection (LSLD) for Hepatocellular carcinoma (HCC).

Patients and methods: From Aug. 2009 to Nov. 2013, we performed 24 cases of LSLD for HCC. Pure LSLD was done in 12 cases and hybrid operation in other 12cases. The mean age of the patients was 69.7(44 ~ 83) and the ratio of males to females was 16 to 8. Nineteen partial resections, one segmentectomy and one lobectomy were done.

Results: The mean operative duration was 272 (105 ~ 573) minutes and the operative blood loss was 387 ml. The postoperative complication occured in 3 cases (12 %), but those were not critical and we had no operative and hospital death. The mean duration of postoperative stay was 11 (5 ~ 26) days. The characters of tumors were shown in Tab.1. All cases except one who died of heart disease were survived for 21.4 (4 ~ 52) month. The cumulative survival rates in 1 and 3 years were respectively 100 and 95.8 %. The disease free survival rates in 1 and 3 years were 95.8 and 45.8 %.

Discussion: The postoperative course of the LSLD was same as the one of open abdominal liver dissection (OALD). The postoperative hospital stay of LSLD was about shorter than OALD. In high risk patients with old age, decreased respiratory function or poor liver workings, LSLD was done safely and redounded to favorable course.

Conclusion: LSLD rather than OPLD is recommended for the surgical treatment for HCC if the procedure.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1026

Adjuvant therapy for resected hepatocellular carcinoma a systematic review and network meta analysis

Ming-hua Zheng[1], Gui-qi Zhu[1], Ke-qing Shi[1], Hua-jian Yu[1], Sun-yue He[1], Han-yang Che[2], Martin Braddock[3], Yong-ping Chen[1]

The First Affiliated Hospital of Wenzhou Medical University Department of Infection and Liver Diseases, Liver Research Center Wenzhou-China[1], The Second Affiliated Hospital of Wenzhou Medical University Department of Hepatobiliary Surgery Wenzhou-China[2], Astrazeneca R&d Global Medicines Development Loughborough-United Kingdom[3]

Aim: Major adjuvant therapies for resected hepatocellular carcinoma include chemotherapy (CT), internal radiation therapy (IRT), interferon therapy (IFNT) and immunotherapy (IMT). Since the optimum treatment regimen remains inconclusive, we aimed to compare these therapies in terms of patient survival and recurrence rates after resection with a random-effects Bayesian network meta-analysis.

Method: We searched PubMed for randomized controlled trials comparing the above four therapies until 31 March 2014. We estimated the hazard ratios (HRs) for death and odds ratios (ORs) for overall recurrence among different therapies. Toxic effects were also evaluated.

Result: Fourteen eligible articles were included. IFNT improved 5-year survival greatly (HR 1.81, 95 % CI 1.01-3.81,$P = 0.034$), whereas CT (HR 0.33, 95 % CI 0.03-2.02), IRT (HR 3.27, 95 % CI 0.30-62.91) and IMT (HR 0.73, 95 % CI 0.05-9.12) all provided a poorer survival outcome after 1-year. Similarly, for 5-year survival rates, although differing, IRT did not provide a significant improvement in survival (HR 1.38, 95 % CI 0.34-5.19) compared with IFNT. CT (HR 0.49, 95 % CI 0.18-1.14) and IMT (HR 0.56, 95 % CI 0.17-1.59) did not appear to provide benefit over IFNT. CT was ranked highest in overall recurrence (OR 0.99 95 % CI 0.18-5.38) and most likely to cause toxic effects.

Conclusion: IFNT is the optimum adjuvant treatment regimen with a balanced benefit-toxicity ratio for resected HCC. CT was the most likely therapy to cause toxic effects.

Topic 16: Hepatocellular Carcinoma Treatment

No: 2007

Metronomic chemotherapy compared with conventional transcatheter arterial chemoembolization in patients with advanced hepatocellular carcinoma with poor liver function

Hyun Yang[1], Hee Chul Nam[1], Hae Lim Lee[1], Seung Won Lee[1], Do Seon Song[1], Si Hyun Bae[1], Jong Young Choi[1], Seung Kew Yoon[1]

The Catholic University of Korea Internal Medicine Seoul-Korea, South[1]

Background: Metronomic chemotherapy (MET) is a treatment modality by frequent administration of comparatively low doses of chemotherapeutic agent without extended break.This study is to evaluate the efficacy and safety of MET compared with conventional TACE in patients with advanced HCC and poor liver function.

Methods: Major inclusion criteria were BCLC stage C and Child class B or C. Minor criteria were the presence of PVTT, largest tumor diameter (> 8 cm) and infiltrative type HCC. We analyzed patients who fulfilled all major criteria and at least one minor criteria. Total of 45 patients who had undergone MET and 30 patients who had received conventional TACE between 2007 and 2013 were retrospectively analyzed. Epirubicin 35 mg/BSA was administrated every 4 weeks, and cisplatin 15 mg/BSA and 5-fluorouracil 50 mg/BSA were administrated weekly for 3 weeks with one week break between each cycle. In the MET group, the chemotherapeutic agents were administered through hepatic arterial chemoport.
Results: Median follow up period was 97 days (4-663). The patients in the MET group received median 2 cycles (range 1-6) of chemotherapy and the patients in the TACE group, 1 cycle (range 1-4) respectively. Overall survival time of the MET group and the TACE group were 130 days (4-663) and 89 days (7-367), respectively ($P > 0.05$).

Multivariate analysis revealed extrahepatic metastasis (hazard ratio (HR) = 1.832, $P = 0.043$), larger tumor size (HR = 1.066, $P = 0.022$), and TACE (HR = 1.891, $P = 0.029$) as independent predictive factors of poorer survival.
Conclusions: MET showed relatively a favorable outcome in terms of overall survival than conventional TACE in advanced HCC with poor liver function.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1933

The clinical experience of sorafenib in middle old and oldest old patients with hepatocellular carcinoma in a medical center of Taiwan

Tsang En Wang[1], Chien Yuan Hung[1], Ching Chung Lin[1], Tai Cherng Liou[1], Shu Jung Tsai[1], Cheng Hsin Chu[1]

Mackay Memorial Hospital Division of Gastroenterology, Department of Internal Medicine Taipei-Taiwan[1]

Background: The patients with BCLC class C hepatocellular carcinoma (HCC) are treated with sorafenib. The elderly have many comorbidity diseases and were more complex for treatment. Taiwan National Health Insurance Administration (NHIA) has criteria for sorafenib payment: Child-Pugh's A, with extra-hepatic metastasis or major/1st branch of portal vein cancer invasion. The patients were re-evaluated every 2 months.
Aim: We discussed clinical experience of sorafenib use under NHIA criteria in patients older than 75-year-old.
Methods: Retrospectively, the elderly with HCC (age > 75 years) were enrolled at our institution from Oct 1, 2011 to Jun 31, 2014. Their clinical data were analyzed.
Results: 145 Patients used sorafenib under NIHA criteria. 28 patients (age > 75 years) were enrolled: 20 men and 8 female. The common co-morbidity disorders were diabetes mellitus (7), hypertension (14) and cardiac disorders (7). Twenty-two had cirrhosis, 12 with HCV, 9 with HBV and 7 with NBNC. Extra-hepatic metastasis and portal vein tumor invasion were 50 and 50 %. 70 % patients had reduction dosage. The major complication was hand foot syndrome. 11/28(39 %) patients could apply 2nd course therapy, and five patients applied more than three courses. 23/28 received other treatment before sorafenib. Five patients received combination local therapy. The median survival time after sorafenib treatment was 9.8 ± 6.7.0 months.
Conclusion: Although, the patient's number and adverse event record were limits. The elderly HCC patients, who have good liver function, should be treated with sorafenib as general population. They might have survival times as findings of the SHARP and the Asia–Pacific trials.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1284

Can curative treatment confer survival benefit in elderly patients with hepatocellular carcinoma

Js Lee[1], Sd Kang[1], Jw Kim[1], Wk Bae[1], Nh Kim[1], K-a Kim[1]

Inje University, Ilsan Paik Hospital Internal Medicine Goyang-Korea, South[1]

Backgrounds/aims: The aim of this study was to compare the survival in elderly hepatocellular carcinoma (HCC) patients treated with curative modalities (radiofrequency ablation (RFA), percutaneous ethanol injection (PEIT) and surgery) to those treated with transcatheter arterial chemoembolization (TACE) and supportive care.
Methodology: Medical records of patients with HCC older than 75 years who had visited a single tertiary medical center from January 2000 to December 2011 were reviewed (n = 58). Multivariable-adjusted hazard ratios (HR) for mortality with 95 % confidence intervals (CI) were estimated using Cox proportional hazard models.
Results: Twenty-nine patients were treated by TACE, 19 patients by supportive care, and 10 patients by curative treatment (four by PEIT, three by surgery and three by RFA).Variables associated with increased survival were better Child-Pugh class and lower TNM stage. Treatment with curative intent showed significant survival benefit compared to TACE (HR for mortality, 0.10; 95 % CI, 0.01-0.95). In a subgroup analysis among patients with resectable HCC, supportive care showed significantly worse survival over TACE (HR for mortality, 6.47; 95 % CI, 2.14-19.56) and curative intent (HR for mortality, 16.23; 95 % CI, 1.92-136.83).
Conclusions: Curative treatment seems to have a better survival benefit in comparison with other treatment modalities in elderly HCC patients.

Topic 16: Hepatocellular Carcinoma Treatment

No: 2104

Risk factors for recurrence of hepatocellular carcinoma after radiofrequency ablation in a cohort of Egyptian patients with hepatitis C virus induced cirrhosis a double center analysis

Eslam Habba[1], Mohamed Sharaf-eldin[1], Sahar El-yamany[1], Mohamed Ghazy[2]

Faculty of Medicine Tropical Medicine & Gastroenterology Tanta-Egypt[1], Faculty of Medicine Radiology Ain-shams-Egypt[2]

Purpose/background: HCC is one of the major complications of liver cirrhosis. Radiofrequency ablation is the treatment of choice for patients with an early-stage HCC who are not candidates for surgical management; however, it is associated with recurrence rate 15–30 % after 1 year. The aim of this study was to analyze the risk factors for HCC recurrence in Egyptian patients after RFA.
Patients and methods: This study was conducted on a cohort of HCC patients presented to two large centers from November 2009 to January 2011. Only patients with an early-stage HCC, eligible for RFA, were included in the analysis and followed up for a period of 1 year.

Patient and tumor related risk factors associated with recurrence were studied.Forty-five patients were included in this study and classified into two groups: group I: patients who developed recurrence during follow-up (n = 30, 66.6 %) and group II: patients who did not show any recurrence during follow-up (n = 15, 33.3 %).
Results: The risk factors associated with recurrence included smoking (70 % group I vs. 40 % group II, $P = 0.015$), hepatomegaly (50 % group I vs. 40 % group II, $P = 0.001$), splenomegaly (90 % group I vs. 53.3 % group II, $P = 0.001$), heterogeneous liver (30 % group I vs. 6.66 % group II, $P = 0.001$), bilobar involvement (20 % group I vs. 6.66 % group II, $P = 0.001$), and tumors in contact with hepatic capsule (20 % group I vs. 6.66 % group II,$P = 0.017$).
Conclusion: Hepatomegaly, liver heterogeneity, and splenomegaly together with the tumor factors such as large size, bilobar involvement, and proximity to liver capsule were the factors that showed a significant association with tumor recurrence in this study.

Topic 16: Hepatocellular Carcinoma Treatment

No: 2098

Clinicopathologic feature of hepatocellular carcinoma surviving for more than ten years

Rikako Kinoshita[1], Seigo Abiru[1], Ayako Mine[1], Yuki Kugiyama[1], Shigemune Bekki[1], Ryu Sasaki[1], Shinjiro Uchida[1], Satoru Hashimoto[1], Akira Saeki[1], Shinya Nagaoka[1], Kazumi Yamasaki[1], Atsumasa Komori[1], Hiroshi Yatsuhashi[1]

Nho Nagasaki Medical Center Clinical Research Center Omura-Japan[1]

Background/aims: The characteristics in patients with hepatocellular carcinoma who survive for more than 10 years after initial diagnosis and treatment such as hepatectomy, radio-frequency ablation (RFA), and transcatherter chemoembolizain (TACE) remain unclear. The aim of this study was to assess the clinicopathologic factors for more than 10-year survival after treatment.
Method: We retrospectively reviewed the medical records of 163 HCC patients diagnosed between January 2003 and Jun 2004. We identified as short and medium term survivors (SM-group: < 10 years, n = 143) and long-term survivors (L-group: > or = 10 years, n = 20). Statistical analyses were performed using × 2 test and Mann–Whitney U-test.
Results: Number of patients with TNM stage 1, 2, 3, 4a and 4b were 42, 53, 34, 4 and 12, respectively. The survival rate of 5 year and 10 year were 56.0 % and 38.7 %, respectively. The patients in the L group were younger and lower AST level and higher Albumin level than those in the SM-group. The rate of Child A and B, the rate of HBs-Ag positivity, the rate of HCV-Antibody positive, stage I and II in TNM stage, history of RFA and history of hepatectomy in L group were significantly higher than in SM-group.
Conclusions: The present study suggests that good liver function, HBs-Ag positivity, early HCC stage, history of RFA and hepatectomy are associated with survival for more than 10 years after treatment.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1920

Balloon occluded transcatehter arterial chemoembolization (tace) as a procedure to improve therapeutic efficacy of miriplatin for patients with hepatocellular carcinoma (HCC)

Hiroshi Uchiya[1], Yukinori Imai[1], Masashi Takano[1], Yohei Fujii[1], Kazuki Hirahara[1], Taku Chikayama[1], Manabu Nakazawa[1], Satuki ando[1], Kayoko Sugawara[1], Mie Inao[1], Nobuaki Nakayama[1], Satoshi Mochida[1]

Saitama Medical University Gastroenterology and Hepatology Saitama-Japan[1]

Aim: TACE using miriplatin produces a favorable short-term outcome in patients with HCC, while local recurrence after the procedure developed in frequent (J Gastroenterol 2012). Insufficient distribution of miriplatin in HCC tissues due to high velocity of the agent may contribute to the unfavorable long-term outcome. To overcome such inferior characters of miriplatin, balloon-occluded TACE (B-TACE) using microballoon catheter was innovated.
Methods: 226 patients with unresectable HCC received TACE with miriplatin. The conventional TACE (C-TACE) was done in 190 patients seen between February 2010 and August 2013, while B-TACE in 36 patients seen then later. All patients had no previous TACE for HCC. BCLC stages were 0, A, B, C and D in 44, 114, 59, 8 and 1 patient(s), respectively. Doses of miriplatin were determined according to tumor sizes up to 120 mg. The feeding arteries of HCC were embolized with porous gelatin particles. For B-TACE, both miriplatin and embolic materials were injected under occlusion of blood flow with a microballoon catheter. Therapeutic efficacies were evaluated by contrast-enhanced CT 1 month later.
Results: The percentage of patients showing complete response (CR: 100 % necrosis) was 67 % in patients receiving B-TACE; the value was higher than that in those receiving C-TACE (52 %) ($P = 0.096$). CR was obtained in 85 % of patients with HCC of stage 0 or A.
Conclusions: B-TACE procedure improved therapeutic efficacy of miriplatin for patients with HCC in a short-term period, while the long-term efficacy of the procedure is required to be investigated in future.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1872

Long term follow up results of patients with advanced hepatocellular carcinoma who achieved complete remission after sorafenib therapy

Jung Gil Park[1], Soo Young Park[2], Su Hyun Lee[2], Se Young Jang[2], Yu Rim Lee[2], Won Young Tak[2], Young Oh Kweon[2], Won Im[3], Hyun Young Woo[3], Jung Heo[3]

Cha University, Gumi Cha Medical Center Internal Medicine Gumi-Korea, South[1], School of Medicine, Kyungpook National University Internal Medicine Daegu-Korea, South[2], School of Medicine, Pusan National University Internal Medicine Pusan-Korea, South[3]

Background: Sorafenib is currently the sole systemic chemotherapeutic agent that improves overall survival of advanced hepatocellular carcinoma (HCC). Despite the efficacy of sorafenib, response rate was varied in patient with advanced HCC. We analyzed retrospective series of complete response after sorafenib therapy in patients with advanced HCC in Korea.
Methods: 523 patients with advanced HCC were treated with sorefenib from 3 large tertiary referral hospitals in Korea. Sorafenib was given initially at a dose of 400 mg orally, twice daily. Tumor response and recurrence rates were assessed by radiologic study and tumor marker.
Results: Six patients with advanced HCC experienced complete response after sorafenib therapy. Median period of tumor-disappearance and observed disease-free was 4 months and 23 months, respectively. Four patients continued sorafenib after complete

response. From the entire cohort, recurrence of HCC was identified in three cases. of these, one patient early discontinued sorafenib. The patients recurred at the time of 3, 10 and 42 months after complete response. Two patients needed dose reduction for toxicity and adverse events.

Conclusion: Though complete response after sorafenib therapy was achieved in patients with advanced HCC, recurrence rate was relatively high. Subsequent treatments after sorafenib therapy are required to offer the chance for a cure. Further studies should be needed to identify the molecular features of these tumors.

Topic 16: Hepatocellular Carcinoma Treatment

No: 2095

Prognostic factors affecting treatment outcomes of acute variceal bleeding in patients with hepatocellular carcinoma a single center prospective study

Yu Rim Lee[1], Soo Young Park[1], Won Young Tak[1], Young Oh Kweon[1], Se Young Jang[1], Su Hyun Lee[1], Jeong Heo[2], Hyun Young Woo[2]

Kyungpook National University Hospital Internal Medicine Daegu-Korea, South[1], Pusan National University Hospital Internal Medicine Pusan-Korea, South[2]

Background and aims: We evaluated the treatment outcomes of acute variceal bleeding in patients with hepatocellular carcinoma(HCC) and determined the factors for treatment failure to control bleeding.

Patients and method: We prospectively enrolled 295 patients with variceal bleeding from 2009 to 2012. We analyzed 119 patients with HCC and 176 cirrhosis patients. We analyzed the outcomes of variceal bleeding and determined prognostic factors for treatment failure by Baveno criteria V.

Results: There were no significant baseline characteristics between two patients groups except age and Child score. The rate of treatment failure by Baveno V was 37.0 % in HCC patients and 19.4 % in non-HCC patients ($P = 0.001$). The 6-week rebleeding rate was 16.0 % in HCC patients and 9.1 % in non-HCC patients ($P = 0.098$). The mortality rate within 6 weeks was significantly higher in HCC patients than non-HCC patients (18.5 % in HCC patients vs 8.5 %, $P = 0.019$). The factors which significantly affects treatment failure were Child Pugh Classification, MELD score, shock at initial presentation, antibiotics prophylaxis, failure to control bleeding by endoscopy, HCC with PVT. In multivariate analysis, HCC with PVT ($P = 0.005$, HR = 5.612 and 95 % CI 1.686-16.355), failure to control bleeding by endoscopy ($P = 0.004$, HR = 17.571, and 95 % CI 2.488-123.114), antibiotics prophylaxis ($P = 0.020$, HR 0.258, and 95 % CI 0.080-0.854) were factors which affected the treatment outcome in these patients.

Conclusion: Factors that adversely affect the treatment outcomes of acute variceal bleeding in these patients include presence of PVT, failure to control bleeding by endoscopy and antibiotics prophylaxis.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1801

Endoscopic ultrasound guided fine needle aspiration helps to staging and treatment decision of hepatocellular carcinoma

Nevin Oruc[1], Ahmet Aydin[1], Ulus Salih Akarca[1], Deniz Nart[2], Ali Veral[2]

Ege University Gastroenterology Izmir-Turkey[1], Ege University Pathology Izmir-Turkey[2]

Hepatocellular Carcinoma (HCC) is worldwide common problem. Patients with HCC and liver cirrhosis are usually candidate for liver transplantation if Milan criteria is applicable. However HCC rarely accompanies lymph node metastasis. Presence of metastatic lymph nodes effects the treatment decision of HCC especially transplantation decision. Endoscopic ultrasound guided fine needle aspiration (EUS-FNA) is safe and effective method to obtain biopsy from these lymph nodes. Here we presented two case with HCC and distant lymphadenopaties that were suspicious for HCC metastasis.

Cases: Sixty five years old male patients have been followed with diagnosis of cryptogenic liver cirrhosis for 7 years. He was diabetic and viral serology was negative. Latest follow up computerized tomography showed lesions typical for HCC and liver transplantation was suggested. However CT also detected suspicious lymphadenopathies up to 25 mm in diameter in the mediastinum. There was also esophageal varices but, with help of EUS, FNA was performed safely. Cytopathologic exam reveled those as benign lymph nodes and patient referred for liver transplantation.Second case was 57 years old male patient with liver cirrhosis, HCC and suspicious lymph node in perigastric area. EUS-FNA showed benign lymph node.

We presented two cases with HCC and accompaniying lymphadenopaties in mediastinum or perigastric area that were suspicious for metastasis. They were otherwise in limits of Milan criteria and were good candidate for liver transplantation. The EUS FNA sampling of those suspicious lymph nodes proven that they were not metastatic and patients were referred for liver transplantation.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1867

Twelve year treatment outcomes of radiofrequency ablation as first line treatment for hepatocellular carcinoma in Milan criteria analysis of 804 patients in a single center

Se Young Jang[1], Won Young Tak[1], Soo Young Park[1], Young Oh Kweon[1], Suhyun Lee[1], Yu Rim Lee[1], Seong Jae Yeo[1], Myung Hi Kim[1]

Kyungpook National University School of Medicine Internal Medicine Daegu-Korea, South[1]

Background & aim: Radiofrequency ablation (RFA) has been widely performed for treatment of early hepatocellular carcinoma (eHCC) as a curative treatment. The aim of this study is to evaluate 12-year outcomes of RFA as an initial therapy for eHCC in a single center.

Method: From Nov 2001 to Dec 2013, 804 patients who diagnosed as eHCC (total 804, mean size: 2.1 cm) were treated with percutaneous RFA as an initial option. The mean follow up time was 38.1 months (range: 0–151 months). RFA was performed with ultrasound-guidance to single nodular HCC, less than 5 cm in maximum diameter or multiple (up to 3) nodular HCCs, each diameter should be under 3 cm in maximum.

Results: The study population showed male dominance (male: n = 608, female: n = 196) and mean age was 60.3, ranging from 24 to 86 years old. Patients had better child-Pugh class (A: n = 710, B: n = 94, C: n = 1) and AFP was elevated. (mean: 295.1, range: 0.7 - 42,690 ng/mL). Cumulative overall survival rates at 1-, 3-, 5-, 10-, 12-year were 92.9, 83.4, 59.4, 42.8, and 37.5 % respectively.

Cumulative disease free survival rates at 1-, 3-, 5-, 10-, 12-year were 75.7, 39.0, 23.1, 9.8, and 4.9 % respectively. Risk factors for tumor recurrence were age (HR = 1.334; 95 % CI = 1.102-1.613), tumor number (HR = 1.392; 95 % CI = 1.149-1.687) and size (HR = 1.260; 95 % CI = 1.103-1.440), AFP level (> 200 ng/mL, HR = 1.324; 95 % CI = 1.026-1.708), and Child-Pugh score (HR = 2.132; 95 % CI = 1.656-2.745).
Conclusions: We analyzed the treatment outcome of RFA as first line treatment for eHCC, which showed good results of overall survival and disease free survival.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1111

Outcomes of yttrium 90 radioembolization for hepatocellular carcinoma from early to advanced tumor stages

Hyun Young Woo[1], Do Young Kim[2], Jeong Heo[1], Chang Won Kim[3], Ki Tae Yoon[1], Young Mi Hong[1], Mong Cho[1], Won Lim[1]

Pusan National University Hospital Internal Medicine Busan-Korea, South[1], Yonsei University College of Medicine Internal Medicine Seoul-Korea, South[2], Pusan National University Hospital Radiology Busan-Korea, South[3]

Background & aims: A recent study showed that radioembolization is both safer and more effective than conventional treatments for hepatocellular carcinoma. This present study investigated the safety and efficacy of yttrium-90 radioembolization in hepatocellular carcinoma in a clinical setting.
Methods: Sixty-two patients were screened for treatment between September 2009 and June 2013. The response was evaluated using modified Response Evaluation Criteria in Solid Tumors criteria, and the overall survival rate was estimated using the Kaplan–Meier method.
Results: The eligibility rate for radioembolization was 80.6 % (n = 50). The median age was 66 years (range = 33–91 years). The etiology was hepatitis B virus in 66 % (33/50), hepatitis C virus in 20 % (10/50) and unknown in 14 % (7/50). The Barcelona Clinic Liver Cancer stage was A in 18 %, B in 46 % and C in 36 %. The median radiation dose per treatment was 1.8 GBq (range = 0.17–3.93 GBq). After a median of 3 months (range = 0.9–9 months), complete responses occurred in 20 % (10/50), partial responses in 38 % (19/50), stable disease in 28 % (14/50) and primary progression in 8 % (4/50). The tumor response was significantly associated with the Barcelona Clinic Liver Cancer stage ($P = 0.001$). The median overall survival time was 40.9 months (95 % CI = 10.2–71.6 months). The survival time was significantly associated with the baseline Barcelona Clinic Liver Cancer stage ($P = 0.007$). After radioembolization, one patient experienced radiation pneumonitis and two showed liver function aggravation.
Conclusions: Yttrium-90 radioembolization appears to have a tolerable safety profile and a favourable efficacy in HCC control from early to advanced stages.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1404

Hepatic arterial infusion chemotherapy versus transcatheter arterial embolization for patients with huge unresectable hepatocellular carcinoma

Wei-lun Tsai[1], Jin-shiung Cheng[2], Kwok-hung Lai[2], Hoi-hung Chan[2], Ping-i Shu[2]

Kaohsiung Veterans General Hospital Department of Gastroenterology, N Kaohsiung-Taiwan[1], Kaohsiung Veterans General Hospital Department of Gastroenterology Kaohsiung-Taiwan[2]

Background: The optimal treatment for huge unresectable hepatocellular carcinoma (HCC) remains controversial. Our previous study found that HAIC is a safe procedure and provides better survival than symptomatic treatment for the patients with huge unresectable HCC. But the therapeutic outcome of HAIC and transcatheter arterial embolization (TAE) remained unclear.
Aim: To compare the effect of HAIC versus TAE in patients with huge unresectable HCC.
Methods: Since 2000 to 2005, patients with huge (size > 8 cm) unresectable HCC were enrolled. Twenty-six patients received HAIC and 25 patients received TAE. Each patient in the HAIC group received 2.5 + 1.4 (range: 1-6) courses of HAIC and in the TAE group received 1.8 + 1.2 (range: 1-5) courses of TAE. Baseline characteristics and survival were compared between the HAIC and TAE group.
Results: The HAIC group and the TAE group were similar in baseline characteristics and tumor stages. The overall survival rates at one and two years were 42 % and 31 % in the HAIC group and 28 % and 24 % in the TAE group. The patients in the HAIC group had higher overall survival than the TAE group but did not reach statistical significance ($P = 0.077$). No patients died of the complications of HAIC but three patients (12 %) died of the complications of TAE.
Conclusion: In conclusion, HAIC is a safe procedure and provided similar survival as TAE for patients with huge unresectable HCC.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1631

Recurrence and survival analysis after curative resection of hepatocellular carcinoma patients in hepatitis B virus endemic area

Suk Bin Jang[1], Kyoung Hwang Shin[1], Suk Bae Kim[1], Il Han Song[1]

Dankook University College of Medicine Division of Hepatology, Department of Internal Medicine Cheonan-Korea, South[1]

Background/aim: Surgical resection is recognized as the best option for the cure of hepatocellular carcinoma (HCC). However, after radical liver resection of HCC, the recurrence rate is still high and the survival rate is also low. The present study was aimed to analyze the recurrence and survival after curative resection of HCC and to identify the associated factors affecting clinical outcomes.
Methods: We retrospectively enrolled 92 HCC patients who underwent curative resection at Dankook University Hospital from July 2004 to June 2013. Kaplan–Meier method with a log-rank test was used for recurrence and survival analysis, and Cox's proportional hazards model with logistic regression analysis was used for integrative analysis of associated clinical, biochemical, and tumor characteristics relevant to recurrence and survival.
Results: Among the 92 patients, 47 (51.1 %) developed recurrence. Median period of recurrence was 28.7 months, and the cumulative 1-, 3-, and 5-year recurrence rates were 26, 67, and 71 %, respectively. Tumor size ($P = 0.001$) was the only factor affecting tumor recurrence. Median overall survival was 104 months, and the cumulative 1-, 3-, and 5-year overall survival rates were 86, 76, and 65 %,

respectively. Disease-free survival rates of 1, 3, and 5 year were 68, 31, and 26 %, respectively. Child-Pugh classification ($P = 0.016$), HBsAg serostatus ($P = 0.029$), serum level of albumin ($P = 0.004$), aspartate aminotransferase ($P = 0.001$), alpha-fetoprotein ($P = 0.001$), and PIVKA II ($P = 0.003$) were significantly associated with overall survival.
Conclusions: Liver function, tumor markers, and tumor characteristics affected tumor recurrence and overall survival after curative resection of HCC patients in hepatitis B virus-endemic region.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1860

Predicting factors hepatocellular carcinoma progression after transarterial chemoembolization

Ga Won Song[1], Sun Young Shin[1], Kyu-hyun Han[1], Suk Pyo Shin[1], Seong Gyu Hwang[1], Kyu Sung Rim[1], Hana Park[1]

Cha Bundang Medical Center, Cha University Internal Medicine Seongnam-si-Korea, South[1]

Background/aims: Transarterial chemoembolization(TACE) is one of the locolesional treatment modalities for hepatocellular carcinoma(HCC). The aim of our study was to determine the predictors of progression after TACE in patients with HCC.
Methods: We retrospectively reviewed a total of 374 patients who had diagnosed as HCC and performed the first TACE in our institution from 2004 January to 2013 September. Tumor response was estimated as CR(complete response), PR(partial response), SD(stable disease) and PD(progressive disease) based on the results of computed tomography 4 weeks after TACE with modified RECIST criteria.
Results: Male gender predominated($n = 290$, 77.5 %), and the mean age was 59 years. Among a total 374 patients, 13 patients(3.5 %) had experienced previous TACE, and 361 patients(96.5 %) were TACE naïve. After 4 weeks after TACE, tumor response was as follows: CR 146(39.0 %), PR 124(3.2 %), SD 16(4.3 %) and PD 88(23.5 %). In patients with PD, there was a significantly greater portion of TACE experienced patients compared to those with CR, PR, and SD(8.0 vs. 2.1 %, $P = 0.016$). The mean size of largest tumor and total sum of tumor sizes were significantly greater in patients with PD(6.4 vs. 3.6 cm of largest tumor size, $P < 0.001$; 7.0 vs 4.1 cm of total sum of tumor sizes, $P = 0.001$, respectively). In multivariate analysis, previous TACE experience[Odds ratio (OR) 8.746, $P = 0.002$] and a total sum of tumor sizes($\geq$ 3 cm; OR 4.022, $P = 0.016$, $\geq$ 10 cm; OR 9.153, $P = 0.008$) were predictors of progression after TACE.
Conclusions: Progression of HCC after TACE is associated with history of previous TACE experience and the total sum of tumor sizes.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1399

Acute necrotizing pancreatitis after transarterial chemoembolization for hepatocellular carcinoma

Nuri Okkabaz[1], Ilter Ozer[1], Fahrettin Kucukay[2], E. Birol Bostanci[1]

Turkiye Yuksek Ihtisas Education and Research Hospital Gastrointestinal Surgery Ankara-Turkey[1], Turkiye Yuksek Ihtisas Education and Research Hospital Interventional Radiology Ankara-Turkey[2]

Background: Transarterial chemoembolization (TACE), as a palliative treatment modality for unresectable hepatocellular carcinoma (HCC), has been shown to offer survival benefit. However this procedure may cause some complications. Besides others, a rare but severe complication is acute necrotizing pancreatitis. Herein we presented a case with acute necrotizing pancreatitis complicating the first attempt of TACE in a patient with HCC.
Case report: A 47 × 45 mm lesion which was consistent with HCC was observed on the 6th segment of the liver on computerized tomography (CT) of a 68 year-old male with history of chronic hepatitis. The MELD score was 24. After discussed in multidisciplinary HCC meeting, TACE was decided. Then selective chemoembolization was performed by an experienced interventional radiologist. Patient suffered abdominal pain, nausea and vomiting on the first post-procedural day. There were abdominal tenderness and fever of 38.3oC. Laboratory results showed elevated blood amylase 1568 and leucocyte count 18.500/uL. On dynamic CT, signs of radiological mild pancreatitis were seen. Because clinical situation didn't improve despite of aggressive supportive care, a new CT scan was taken at day 12th. Necrosis up to 30 % of parenchyma and peripancreatic fluid collection was seen. Then total parenteral nutrition was administered for 7 days. In subsequent days, his symptoms have relieved and he tolerated oral intake. Then, he was discharged at postprocedural day 33. He has followed weekly with ultrasonography and no intervention is needed.
Conclusion: After chemoembolization, measurement of serum pancreatic enzymes should be routinely performed in cases of persistent abdominal pain to confirm pancreatitis, which can clinically mimick postembolization syndrome.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1483

The validation of Hong Kong liver cancer staging system and comparision with barcelona clinic liver cancer for prediction of survival and treatment in hepatocellular carcinoma patients

Hae Rim Kim[1], Ji Hoon Kim[1], Yang Jae Yoo[1], Seong Hee Kang[1], Sang Jun Suh[1], Young Kul Jung[1], Yeon Seok Seo[1], Hyung Joon Yim[1], Jong Eun Yeon[1], Kwan Soo Byun[1]

Korea University College of Medicine Internal Medicine Seoul-Korea, South[1]

Aim: We validated the Hong Kong Liver Cancer (HKLC) and compared it with BCLC in hepatocellular carcinoma (HCC) patients.
Method: The medical records of 875 HCC patients from 2004 to 2009 were retrospectively reviewed. The data including performance status, Child-Pugh score, tumor characteristics and survival were collected.
Result: Seventy-five percent of patients died during study period and median overall survival (OS) was 22.6 months. Both HKLC and BCLC well differentiated the survival ($P < 0.001$). However, HKLC significantly well predicted 1 and 2 year of survival than BCLC (AUROC; 0.824 versus 0.801 in 1 year, $P = 0.018$, 0.817 versus 0.797 in 2 year, $P = 0.05$). Furthermore, the survival of patients following recommended therapy by HKLC was better than BCLC ($P < 0.001$). In the patients in BCLC B and HKLC II, the curative therapy group recommended by HKLC showed better survival compared to TACE which recommended by BCLC ($P = 0.003$). In the patients in BCLC C and HKLC II, the curative therapy group recommended by HKLC showed better survival compared to systemic therapy which recommended by BCLC ($P = 0.003$). In the patients in

BCLC C and HKLC III, the TACE group recommended by HKLC showed better survival compared to systemic therapy which recommended by BCLC ($P < 0.001$). We compared survival according to HKLC and BCLC subclass in BCLC B patients and there was no significant difference ($p > 0.05$).
Conclusion: The HKLC system showed better survival compared to BCLC system in our population. The more individualized therapy could be considered by HKLC for management of HCC patients to improve prognosis.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1453

Quantitative analysis of correlation between dose to normal liver parenchyma and radiological change on follow UP GD EOB DTPA enhanced hepatobiliary phase magnetic resonance imaging after stereotactic ablative radiotherapy for hepatocellular carcinoma

Sang Hoon Jung[1], Jeongil Yu[1], Jin Sung Kim[1], Youngyih Han[1], Hee Chul Park[1], Do Hoon Lim[1]

Samsung Medical Center, Sungkyukwan University School of Medicine Department of Radiation Oncology Seoul-Korea, South[1]

In order to evaluate quantitatively radiological response of normal liver parenchyma after stereotactic ablative radiotherapy (SABR) for hepatocellular carcinoma, we investigated quantitative correlation between dose delivered to liver parenchyma and radiological change on follow-up Gd-EOB-DTPA-enhanced hepatobiliary phase magnetic resonance imaging (MRI). A total of 12 diagnostic and follow-up MR images for six patients treated with SABR were investigated. All the MR images were acquired in the hepatobiliary phase, 20 min after injection. Six pre-treatment MR images acquired on median days of 48 days before SABR were used as the baseline images. Follow-up MR images were acquired on the median days of 105 days after. All the MR images were registered to the planning CT images. Using a in-house software, it was calculated that dose to normal liver parenchyma was correlated to radiological change between the pre-treatment and follow-up MR images. Relationship of the dose to the normal liver parenchyma to the radiological change was well correlated to the Boltzmann equation. Median center of the curve fitting was evaluated to be 23.5 Gy (18.3 Gy $\sim$ 39.4 Gy) and slope at the center was evaluated to be 7.2 %/Gy (3.3 %/Gy $\sim$ 9.1 %/Gy). For all the patients, median R2 was evaluated to be 0.935 (0.748 $\sim$ 0.985). For the four patients whose R2 s were over 0.9, median R2 was 0.971 (0.906 $\sim$ 0.985). The R2 s for the others were 0.780 and 0.748. It was evaluated that dose delivered to liver parenchyma could be correlated to radiological change on follow-up Gd-EOB-DTPA-enhanced hepatobiliary phase MRI quantitatively.

Topic 16: Hepatocellular Carcinoma Treatment

No: 1601

Resectable hepatocellular carcinoma (hcc) in non alcoholic steatohepatitis (nash)—a poorer prognosis compared to hepatitis B

En Xian Sarah Low[1], Jianyi Calvin Koh[1], Alfred Kow[2], Krishnakumar Madhavan[2], Maureen Da Costa[2], Seng Gee Lim[1], Yock Young Dan[1]

National University Health System Department of Medicine, Gastroenterology & Hepatology Singapore-Singapore[1], National University Health System Department of Surgery, Hepatobiliary & Pancreatic Surgery Singapore-Singapore[2]

Background: The incidence of Non-alcoholic Steatohepatitis (NASH) is on the rise relative to viral hepatitis. Yet the difference in Hepatocellular Carcinoma (HCC) behavior is not well characterized. Given its rise in prevalence and importance, it is imperative to understand its complications.
Aim: To determine survival rates of resectable HCC in NASH versus Hepatitis B.
Methods: Patients with HCC treated with resection of primary tumour were studied over a 20-year period. The decision for resection was based on hepatic function, size and number of liver lesions. Key outcome measures were then evaluated.
Results: 157 patients underwent HCC resection in our center, of which Hepatitis B was the underlying etiology in 100 of these, with 43 patients having presumptive NASH cirrhosis (Non-Hepatitis B/C/Ethanol use)Patients with HCC from NASH had significantly worse survival (median 21 months range 0 - 165 months) compared to patients with Hepatitis B (median 46 months range 0 – 249 months).Recurrence occurred in approximately half of Hepatitis B and NASH patients equally. There was no significant difference in tumour grade at resection, with 75.3 % in Hepatitis B and 82.1 % in NASH patients comprising of well to moderately differentiated tumors.
Conclusion: Amongst patients who underwent resection for HCC, survival rates for patients with NASH were worse than those in the Hepatitis B group. This difference is independent of cirrhosis stage and tumour grade. This could be due to the availability of anti-viral agents for control of Hepatitis B as compared to NASH, where there is currently limited effective treatment.

Topic 17: Hepatology Research

No: 1522

Significance of homeobox gene nanog expression in the liver cancer stem like cells

Jiajia Zhou[1], Zhe Meng[1], Xiaogeng Deng[1], Rufu Chen[1]

Sun Yat-sen Memorial Hospital Department of Surgery Guangzhou-China[1]

Cancer stem cells (CSCs) are regarded as the cause of tumor initiation and recurrence. Emerging evidence revealed the existence of CSCs in various solid cancers including liver cancer. NANOG plays a key role in regulation of stem cell self-renewal and pluripotency. Abnormal expression of NANOG was observed in several types of solid tumors. However, the role of NANOG in liver cancer remains uncertain. In this study, liver cancer stem like cells was isolated by side population (SP) cell sorting method. We found that (2.3 ± 0.8) % and (5.49 ± 1.0) % SP cells were sorted from liver cancer cell line Huh7 and Hep3B. NANOG mRNA and protein were highly expressed in SP cells than in NSP cells. In-vitro experiment showed that cell proliferation ability and invasion capacity of SP cells was higher than that of NSP cells, and stronger drug resistance to 5-fluorouracil and doxorubicin than NSP cells. Knockdown of NANOG inhibits the proliferation and invasiveness of SP cells, and sensitive SP cells toward 5-fluorouracil and doxorubicin. Together, these results suggest that Homeobox Gene NANOG is highly expressed in liver cancer

stem like cells and NANOG could be used as a novel potential therapeutic target toward liver CSCs.

Topic 17: Hepatology Research

No: 1603

Polymorphisms in type i tgf β receptor gene and the risk for liver disease in ethnic Indonesians

Ivet Suriapranata[1], Gladys Langi[1], Rino Gani[2], andri Sanityoso[2], Irsan Hasan[2], Unggul Budihusodo[2], Laurentius Lesmana[2], Ali Sulaiman[3], George Mathew[4]

Mochtar Riady Institute For Nanotechnology-universitas Pelita Harapan Snp Division Tangerang-Indonesia[1], Cipto Mangunkusumo Hospital Hepatology Division Jakarta-Indonesia[2], Klinik Hati Prof. Ali Sulaiman Jakarta-Indonesia[3], Mochtar Riady Institute For Nanotechnology-universitas Pelita Harapan Tangerang-Indonesia[4]

Objective: The transforming growth factor beta (TGF-β) signaling pathway has been reported to be altered in hepatocellular carcinoma (HCC). In particular, HCC tissues are shown to have increased type I TGF-β receptor (TGFBR1) protein expression compared to normal tissues. This study aims to investigate the association between single nucleotide polymorphisms (SNPs) in the TGFBR1 gene and liver disease susceptibility.
Materials and methods: A total of 20 SNPs was analyzed in the promoter and exon 1 region of TGFBR1 gene. A total of 656 subjects comprising of 102 healthy controls, 210 chronic, 200 cirrhosis, and 144 HCC patients were enrolled in the study. Genotyping was conducted using Polymerase Chain Reaction (PCR)-based DNA direct sequencing. Logistic regression was used to estimate the odds ratios (OR) and 95 % confidence intervals (CI) with adjustment to gender and age.
Results: Variants of rs10819636 in TGFBR1 gene are significantly associated with liver diseases. GT genotype of rs10819636 significantly increases the risk of chronic HBV ($P = 0.025$, OR (95 % CI) = 1.947) and HBV-related HCC ($P = 0.008$, OR(95 % CI) = 2.669). TT genotype of rs10819636 is significantly associated with the presence of HBV-related HCC in control ($P = 0.015$, OR (95 % CI) = 1.701) and cirrhosis (HBV) subjects ($P = 0.004$, OR (95 % CI) = 1.804).
Conclusions: The polymorphisms of rs10819636 are associated with susceptibility to chronic HBV and HBV-related HCC. No significant association was detected between SNPs in TGFBR1 gene and HCV-related liver disease. The G to T substitution in rs10819636 may create an additional binding site for FOXP3 and this might explain the increased risk of chronic HBV and HBV-related HCC.

Topic 17: Hepatology Research

No: 1749

Cold storage of porcine hepatocyte spheroids

Ji Bao[1], Hong Bu[1]

West China Hospital, Sichuan University Laboratory of Pathology Chengdu-China[1]

Bioartificial liver treatment rely on a high-quality supply of hepatocytes and a means for storage during transportation from site of isolation to site of usage. Unfortunately, frozen cryopreservation is associated with unacceptable loss of hepatocyte viability after thawing. The purpose of this study was to optimize conditions for cold storage of pig hepatocyte spheroids without freezing.

Pig hepatocytes were isolated by a novel three-step perfusion method; hepatocyte spheroids were formed during 24 h of rocked culture in serum-free medium (SFM). 20 gram spheroids were then maintained in rocked culture at 37 °C (control condition) or cold stored at 4 °C for 24 or 48 h in four different cold storage solutions in 50 mL CryoMACS Freezing Bags: SFM alone; SFM + 1 mM deferoxamine (Def); University of Wisconsin (UW) solution alone, UW + 1 mM Def. Performance metrics after cold storage included viability, gene expression, albumin production, and functional activity of cytochrome P450 enzymes and urea cycle proteins.

We observed that cold-induced injury was reduced significantly by the addition of the iron chelator (Def) to both SFM and UW solution. Performance metrics (ammonia detoxification, albumin production) of pig hepatocyte spheroids stored in SFM + Def for 24 h were significantly increased from SFM alone and approached those in control conditions, while performance metrics after cold storage in SFM alone or cold storage for 48 h were both significantly reduced.

A SFM supplemented with Def allowed hepatocyte spheroids to tolerate 24 h of cold storage with less than 10 % loss in viability and functionality.

Topic 17: Hepatology Research

No: 1850

In vivo immunogenic cell death in syngeneic hcc through hcc specific adenoviral gene therapy via mtert targeting trans splicing ribozyme

Mi Ha Ju[1], Yang Hyun Paik[2], Sung Wook Lee[2], Sang Young Han[2], Jin Sook Jeong[3]

Dong-a University College of Medicine Pathology Busan-Korea, South[1], Dong-a University College of Medicine Internal Medicine and Liver Center Busan-Korea, South[2], Dong-a University College of Medicine Pathology and Liver Center Busan-Korea, South[3]

Background: HCC-specific adenoviral gene therapy inserted with cancer-specific human telomerase reverse transcriptase(hTERT) RNA-targeting trans-splicing ribozyme, liver specific phosphoenolpyruvate carboxykinase(PEPCK) promoter and HSV thymidine kinase(TK) suicidal gene has been developed, proving excellent efficacy followed by ganciclovir treatment. Next construct designed with insertion of mTERT and antisense target sequence of liver-specific microRNA(miR122a), which will provide null expression in normal hepatocytes (Ad-PEPCK-mTERT.Ribo-TK-mir122aT[PRT-mir122aT], enabling immunocompentent animal study. We studied the possible operation of immunogenic cell death in HCC-specific antitumor efficacy of PRT-mir122aT in vivo.
Methods: Vectors(PRT-mir122aT, PRT, Ad-PEPCK-TK[PT]) were prepared. mTERT(+), miR122a(-) Hepa1-6 mouse HCC cell was used. Multifocal HCC models in C57BL mice and nude mice were made by splenic subcapsular cell injection, and for re-challenge test in C57BL mice, subcutaneous cell injection was done after last injection of ganciclovir. Vectors administered, systemically.
Results: In multifocal HCC model of immunocompetent C57BL mouse, all mice treated with PT died. PRT-mir122aT showed efficient antitumor efficacy, compared with PRT and PBS (n = 6, each, 1 × 1011vp, $P < 0.0001$). In multifocal HCC model of immunodeficient nude mouse, PRT-mir122aT showed suboptimal antitumor response, compared with PBS (n = 5, each, 1 × 1011vp, $P = 0.059$). In re-challenge test, subcutaneous tumor growth did not appear in PRT-

mir122aT treated HCC-bearing mice, but appeared in HCC-bearing mice without treatment (n = 4, each).
Conclusions: The HCC- specific adenoviral gene therapy by mTERT targeting TSR, TK suicidal gene, and liver specific promoter and microRNA regulation shows in vivo operational evidence of immunogenic cell death.

Topic 17: Hepatology Research

No: 2068

The real prevalance and test of adrenal insufficiency in cirrhotic and non cirrhotic portal hypertension

Erkan Ozcan[1], Cetin Karaca[2], Filiz Akyuz[2], Kadir Demir[2], Sabahattin Kaymakoglu[2], Fatih Besisik[2]

Istanbul Faculty of Medicine Internal Medicine Istanbul-Turkey[1], Istanbul Faculty of Medicine Gastroenterology Istanbul-Turkey[2]

Introduction: Measurements of serum levels of total cortisol can overestimate the prevalence of adrenal insufficiency (AI) in patients with cirrhosis because of low concentrations of corticosteroid-binding globulin and albumin in cirrhotics. The aim of this study was determined real prevalance of the AI in cirrhotics and non-cirrhotic portal hypertension (PHT) patients.
Materials and methods: Sixty-one cirrhotic patients (Child A-B–C; 22, 20, 19 respectively), 21 non-cirrhotic PHT and 21 healthy people as control were enrolled. Stimulation test with 1 μg synthetic corticotrophin was performed. 24 h-urine cortisol level was determined. To assess AI, measurement of serum total cortisol (STC) and urine free cortisol (UFC) were used. Whom STC < 18 μg/ml and UFC < 36 μg/24-hour.
Results: STC < 18 μg/ml(n) UFC < 36 μg/24-hr(n) AI according to STC and UFC(n).
Cirrhotics 12 13 3
Non-cirrhotic PHT 0 4 0
Control 2 0 0
p value 0.075 0.16
Conclusion: AI was established in only cirrhotics. In order to investigate the real prevalance of AI, STC and UFC should be evaluated together.

Topic 17: Hepatology Research

No: 2074

Hbeag negative chronic hepatitis B adolescents have relatively benign disease

Md. Fazal Karim[1], Salimur Rahman[2], Mamun Al-mahtab[2]

Sir Salimullah Medical College Mitford Hospital Department of Hepatology Dhaka-Bangladesh[1], Bangabandhu Sheikh Mujib Medical University Department of Hepatology Dhaka-Bangladesh[2]

Introduction: Hepatitis B is endemic in Bangladesh. The magnitude of HBV infection among Bangladeshi adolescents is less known. Chronic hepatitis B (CHB) in teenagers commonly present with Immune tolerant phase. Subsets of these patients present in Immune clearance, Inactive carrier or Reactivation phase.
Methodology: Teenagers between 13 and 19 year presenting with diagnosis of HBsAg positivity with either HBeAg positive or negative chronic hepatitis B were included in this study. This was a prospective randomized study. CHB patients were divided into two groups, Group A was HBeAg positive and Group B was HBeAg negative.
Result: All 21 patients were asymptomatic. 11 patients with HBeAg positivity (M: F = 10: 1), 10 patients with HBeAg negativity (M: F = 7: 1). ALT range in HBeAg positive population was 15-77 U/L (Mean 45.8 U/L), in HBeAg negative population was 16-46 U/L (Mean 30.6 U/L). HBV DNA level in HBeAg positive patients was 10[SUP]5[/SUP]-10[SUP]12[/SUP], mean 10[SUP]10[/SUP], in HBeAg negative patients was 10[SUP]3[/SUP] -10[SUP]7[/SUP], mean 10[SUP]6[/SUP], However HBV DNA was mostly low in HBeAg negative variety. Histologic activity index and fibrosis scores were similar in both groups.
Conclusion: Teenagers with chronic Hepatitis B are potential treatment candidates. So demographic studies with histologic scoring is needed as a guide to start treatment. Present study reveals presence of Group B (HBeAg negative) variant in teenagers. As compared to adult population Group B in teenagers presents with relatively benign disease in those having normal or minimally raised alanine aminotransferase levels.

Topic 17: Hepatology Research

No: 2084

Sonographic assessment of fatty liver intraobserver and interobserver variability

Mustafa Cengiz[1], Senem Şentürk[2], Bülent Çetin[3], Aylin Bayrak[4], Senem Bilek[4]

Dr.a.y. Ankara Oncology Training and Research Hospital Gastroenterology Ankara-Turkey[1], Göztepe Training and Resarch Hospital Radiology Istanbul-Turkey[2], Van Training and Research Hospital Oncology Van-Turkey[3], Dicle School of Medicine Radiology Diyarbakır-Turkey[4]

Non-alcoholic fatty liver disease (NAFLD) is a common liver disease worldwide and ultrasonography is widely used in the diagnosis and the follow-up We purposed to assess intraobserver and interobserver variability in the sonographic evaluation of the existence and steatosis grades of NAFLD. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels and AST to ALT (AST/ALT) ratio were compared between the grades of hepatosteatosis. Hepatic ultrasonography (US) examinations consisted of 5-10 static images of 113 successive adult patients, whose records were in the picture archiving and communication system (PACS) of our hospital were retrospectively evaluated by two experienced radiologists.. Hepatic images were graded into 4 groups; as normal, mild, moderate or severe hepatic steatosis. Evaluation of hepatic steatosis of the same set of images was repeated after 1 month under the same conditions. Interobserver and intraobserver agreement was assessed by using kappa (κ) statistics. In each group, the percentage of individuals with high ALT and/or AST, or AST/ALT ratio over 1 was calculated. The intraobserver agreement was 51 %, fair kappa (κ = 0.356) for observer 1; and 68 %, moderate (κ = 0.591) for observer 2. The interobserver agreements in the initial and second readings were 39 and 40 %, fair (κ = 0,208) and (κ = 0,225), respectively. Elevations of ALT and/or AST levels were similar between groups depending on the degree of hepatosteatosis among the patients. Visual assessment of NAFLD by ultrasonography has substantial interobserver variability, and reproducibility of results is limited. More objective imaging modalities are needed to evaluate the degree of hepatosteatosis.

Topic 17: Hepatology Research

No: 1795

Early blockade of pge2 pgd2 receptors confer protection against schistosoma mansoni infection in mice

Rasha Abdel-ghany[1], Ibrahim Rabie[2], Eman El-ahwany[3], Sameh Saber[1], Rasha Gamal[1], Ola Mahmoud[4], Faten Nagy[3], Walid Barakat[1]

Faculty of Pharmacy, Zagazig University Pharmacology and Toxicology Zagazig-Egypt[1], Theodor Bilharz Research Institute Parasitology Giza-Egypt[2], Theodor Bilharz Research Institute Immunology Giza-Egypt[3], Theodor Bilharz Research Institue Hematology Giza-Egypt[4]

Schistosomiasis is a chronic disease with considerable social impact. Despite the availability of affordable chemotherapy, drug treatment has not significantly reduced the overall number of disease cases.

Among other mechanisms, the parasite produces PGE2 and PGD2 to evade host immune defenses. To investigate the role of PGE2 and PGD2 in schistosomiasis, we evaluated the effect of L-161,982, Ah6809 (selective EP4 and EP2 antagonists respectively alone or combined with each other) and MK-0524 (a selective DP1 antagonist) during early phase of Schistosoma mansoni infection. Drugs were administered intra-peritoneally one hour before and 24 h after infection of C57BL/6 mice with 100 Schistosoma mansoni cercariae.

L-161,982, Ah6809, their combination and MK-0524 decreased the infection intensity by activating cell mediated immune reactions through biasing immune response towards Th1 phenotype which affect parasite killing directly by IFN-γ activated immune cells and indirectly by blocking parasite migration.

These results suggest that selective blockage of EP2, EP4, DP1 receptors confers protection against Schistosoma mansoni infection in mice and that they may be useful as adjunctive therapy to current anti-schistosomal drugs or vaccines.

Topic 17: Hepatology Research

No: 1653

Genipin crosslinking prepared immunogen reduced decellularized porcine liver for bioengineered hepatic tissue

X. Wu[1], Y. Wang[2], J. Bao[3], Q. Wu[2], Y. Li[2], Y. Zhou[2], H. Bu[3], M. Xie[1]

Luzhou Medical College Epartment of Clinical Medicine Luzhou-China[1], West China Hospital, Sichuan University Laboratory of Pathology Chengdu-China[2], West China Hospital, Sichuan University Aboratory of Pathology Chengdu-China[3]

Decellularized biologic matrices are plausible biomedical materials for the bioengineering in liver transplantation. However, one of the concerns for safe medical application is the lack of objective assessment of the immunogen within the materials and the in vivo immune responses to the matrices. The purpose of this study was the production of immunogen-reduced and biocompatible matrices from porcine liver.

Whole porcine liver were perfusion-decellularized and cross-linked with glutaraldehyde (GA) or genipin (GP). Proteins were extracted and the migratory response of human leukocytes toward protein extracts was examined using an in vitro migration chamber. In addition, biopsy specimens of decellularized scaffolds were implanted subcutaneous into rodents to investigate scaffold immunogenicity.

Histological staining confirmed cellular clearance from pig livers, with removal of nuclei and cytoskeletal components and widespread preservation of structural extracellular molecules. Scanning electron microscopy confirmed preservation of an intact liver capsule, a porous acellular lattice structure with intact vessels and striated basement membrane. The PCR analysis showed that galactose-a-1,3 galactose b-1,4-N-acetylglucosamine (1,3 gal), swine leukocyte antigen (SLA), and porcine endogenous retrovirus (PERV) were completely removed in the matrices. Decellularization significantly reduced the migration of monocytes compared to native porcine tissue. Although the proportion of transmigrating lymphocytes was much lower, cross-linked again reduced the migratory response. After implanted 4 weeks, the decellularized and native samples were degraded, and the glutaraldehyde-treated group occurred severe inflammatory reaction, however, minimal inflammatory cells infiltration was seen in the genipin-treated group during 8-week investigation periods.

In conclusion, our study provided evidences that GP crosslinking could significantly reduce the immunogenicity of decellularized liver biomaterials.

Topic 17: Hepatology Research

No: 1491

Reduced human immune responses to genipin cross linked decellularized porcine whole liver matrices as scaffolds for hepatic bioengineering

Wang Y. Wang[1], Bao J. Bao[1], Wu X. Wu[2], Wu Q. Wu[1], Li Y. Li[1], Zhou Y. Zhou[1], Bu H Bu[3]

West China Hospital, Sichuan University Laboratory of Pathology Chengdu-China[1], Luzhou Medical College Department of Clinical Medicine Luzhou-China[2], West China Hospital, Sichuan University Department of Pathology Chengdu-China[3]

Background: In the field of liver tissue engineering, xenogeneic extracellular matrix (ECM) have potential to mimic the micro-environment of original liver, and thus support the survival of hepatocytes. Nevertheless, there are risks caused by the exogenous antigens of ECM which may result in severe inflammation and degradation of the engineered tissue. Crosslinking is a clinical strategy for organ transplantation to lower the immunogenicity of implanted grafts. Therefore, we aimed to reduce the immunogenicity of porcine decellularized liver matrix through crosslinkage with the chemical agent glutaraldehyde or a new natural agent genipin.

Methods: Whole porcine liver were decellularized and crosslinked with glutaraldehyde or genipin. The abilities to induce human immune responses of materials (native, decellularized-only, glutaraldehyde-treated and genipin-treated) were investigated in vitro through CFSE-labled human peripheral blood mononuclear cell (PBMC) proliferation assays. Proliferation patterns of PBMCs treated with liver materials were analyzed by FACS, and the cytokine release profiles of PBMCs were determined by Luminex assay.

Results: Glutaraldehyde or genipin treatment showed no alterations in liver ECM morphology, as assessed by light microscopy and SEM. We observed strong immune responses of PBMC co-cultured with native or decellularized liver. On the other hand, glutaraldehyde and genipin can alleviate the host responses by means of reducing lymphocytes and their subsets proliferation. The strong immune responses we observed for native and decellularized tissue are relevant with the intense induction of some of Th1 and Th2 cytokines, such as IL-6 and IFN-γ.

Conclusion: Natural crosslinking agent genipin showed outstanding modification effects on the liver decellularized ECM to reduce the immunogenicity as glutaraldehyde.

Topic 17: Hepatology Research

No: 1436

Prediabetes diabetes and the risk of hepatocellular carcinoma in residents without chronic hepatitis B and C infection a prospective study in Taiwan

Ming-jeng Kuo[1], Amy Ming-fang Yen[2], Wei-shiung Yang[3], Hsiu-hsi Chen[4], Chi-ling Chen[3]

Tainan Municipal Hospital Department of Hepatogastroenterology Tainan-Taiwan[1], College of Oral Medicine, Taipei Medical University School of Oral Hygiene Taipei-Taiwan[2], College of Medicine, National Taiwan University Graduate Institute of Clinical Medicine Taipei-Taiwan[3], College of Public Health, National Taiwan University Graduate Institute of Epidemiology and Preventive Medicine Taipei-Taiwan[4]

Aim: We aimed to elucidate the relationship between prediabetes, diabetes and risk of hepatocellualr carcinoma (HCC) in HBsAg and anti-HCV seronegative residents and further explore whether there is a threshold or non-linear dose–response relationship between fasting glucose and HCC.
Methods: A cohort of 79,940 HBsAg-negative, anti-HCV negative residents participated in the Keelung Community-Based Integrated Screening program were followed between 1999 and 2007. Prediabetes was defined as fasting glucose between 100 and 125 mg/dL, and diabetes as $>$ 126 mg/dL or with a medical history. Cox-proportion hazards regression models were used to assess the influence of prediabetes/diabetes on the incidence of HCC. Polynomial regression with restricted cubic splines were conducted to evaluate the departure from linear trend between fasting glucose and HCC among residents without diabetes at enrollment.
Results: After 394,079 person-years follow-up, 114 individuals had developed HCC. The adjusted hazard ratios were 1.59 (95 % CI, 0.84-3.01) and 3.21 (95 % CI, 1.88-5.47) for prediabetes and diabetes, respectively (p for trend $<$ 0.001). These associations were mainly contributed by males, with a significantly increased risk for prediabetes (HR = 2.25, 95 % CI = 1.09–4.66) and a fourfold increased risk for diabetes (HR = 4.02, 95 % CI = 2.10–7.71). Prediabetes was also a significant predictor in those with lower total cholesterol ($<$240 mg/dl), lower low-density-lipoprotein-cholesterol ($<$ 130 mg/dl) and never smokers. In males, there appeared a non-linear trend with HCC risk started to increase rapidly at fasting glucose level of 85 mg/dL.

Early intervention for prediabetic males, even in those with high normal levels of fasting glucose sheds some light in the reduction of HCC risk.

Topic 17: Hepatology Research

No: 1330

Expression and significance of insulin receptor substrate 2 in human hepatocellular carcinoma

Chun Gao[1], Hui Zhang[1], Long Fang[1], Shu-kun Yao[1]

China-Japan Friendship Hospital, Ministry of Health Department of Gastroenterology Beijing-China[1]

Background: Diabetes mellitus had been regarded as a risk factor for hepatocellular carcinoma (HCC) and the insulin signaling pathway may contribute to human HCC. Insulin receptor substrate-2 (IRS2) is the main effector of insulin signaling in the liver; however, the role of IRS2 in HCC is unknown. Our recurrent study was performed to explore the expression and significance of IRS2 in human HCC.
Methods: A total of 115 samples were derived from patients who were treated at the China-Japan Friendship Hospital during the period from January 2003 to March 2010, including 60 HCC tissues, 39 tumor adjacent tissues and 16 cirrhosis tissues. Immunohistochemistry (IHC) was used to examine the expression of IRS2 in these tissues. Univariate analysis and multivariable logistic regression analysis were used to determine the associations between clinical and pathological factors and IRS2.
Results: The main expression of IRS2 was in the cytoplasm. The positive expression of IRS2 was detected in 9 of 60 HCC tissues (15.0 %), 31 of 39 tumor adjacent tissues (79.5 %) and 6 of 16 cirrhotic tissues (37.5 %). Compared with HCC and cirrhotic tissues, the expression of IRS2 was higher in tumor adjacent tissues ($P < 0.001$ and $P = 0.003$). Multivariable logistic regression analysis also showed that the expression of IRS2 was associated with tumor adjacent tissue (OR: 4.829, 95 % CI 1.043-22.358, $P = 0.044$). We also found that its expression was associated with presence of ascites.
Conclusions: Expression of IRS2 was higher in human HCC adjacent tissues and it may play some roles in malignant transformation of human HCC. Future studies are needed to clarify the mechanisms.

Topic 17: Hepatology Research

No: 2120

Evaluation of quality of life with sf 36 in patients with chronic hepatitis B and C at various stages of disease

Güray Can[1], Hatice Can[2], Bülent Yılmaz[3], Uğur Korkmaz[3], Hasan Ümit[4], Emrah Poşul[1], Mevlüt Kurt[1]

Abant Izzet Baysal University, Faculty of Medicine Department of Gastroenterology Bolu-Turkey[1], Abant Izzet Baysal University, Faculty of Medicine Department of Internal Medicine Bolu-Turkey[2], Bolu Izzet Baysal State Hospital Department of Gastroenterology Bolu-Turkey[3], Trakya University, Faculty of Medicine Department of Gastroenterology Edirne-Turkey[4]

Aim: In chronic diseases, the majority of patients with the disease have limitations in social life, difficulties in performing physical activity. While patients with chronic hepatitis (CH) have no symptoms in the early stages of disease, the quality of life can be deteriorated significantly by complications of cirrhosis in advanced stages. In our study, comparison of the quality of life is aimed among various stages of the disease in CHB and CHC.
Material-methods: Totally 175 chronic hepatitis patients with different stages of disease were enrolled (129 with CHB, 46 with CHC). SF-36 quality of life questionnaire was administered.
Results: The internal consistency of SF-36 questionnaire was high for both diseases (Cronbach α: 0.95 for CHB and CHC). More restriction in physical and social functioning, more reduction in vitality and energy, and believing of more worsening of their health are seen while increasing the stages of disease in CHB. Generally, physical and mental health, and overall quality of life worsen significantly in advanced stages. In CHC, limitation in work and daily activities happens due to only worsening the physical health while increasing the stages of disease. (Table-1). In univariate regression analysis, environment, education, diagnosis and disease stage were established as factors affecting quality of life.
Conclusion: Longer disease duration, complications and psychological morbidity in patients with cirrhosis, and side effects of the treatment significantly reduce the quality of life in patients with CHB and CHC.

To improve the quality of life, the disease must be treated appropriately and risk factors affecting quality of life must be decreased.

Topic 17: Hepatology Research

No: 1565

The effects of dexpanthenol on acetic acid induced colitis in rats

Yasir Furkan Cagin[1], Hakan Parlakpinar[2], Alaadin Polat[3], Nigar Vardi[4], Yahya Atayan[1], Mehmet Ali Erdogan[1], Yılmaz Bilgic[1], Hulya Aladag[5], Murat Aladag[1]

Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[1], Inonu University Faculty of Medicine Farmacology Malatya-Turkey[2], Karabuk University Faculty of Medicine Physiology Karabük-Turkey[3], Inonu University Faculty of Medicine Histology Malatya-Turkey[4], Inonu University Faculty of Medicine Obstetric&gynecology Malatya-Turkey[5]

Background and aims: While the pathogenesis of IBD is unclear, reactive oxygen species (ROS) are considered to have a significant effect. This, in turn, can result in tissue injury, dysfunction, and eventually apoptosis. The aim of this study was to investigate the efficacy of dexpanthenol (Dxp), which has anti-oxidant, anti-inflammatory and epithelization-stimulating effects on colitis models in rats.
Materials and methods: Animals were randomly divided into four equal groups (n = 8/group). Group I (control group); Group II (Group AA): animals received 4 % AA (acetic acid) (1 ml/day, into the colon via rectum) as a single dose for three consecutive days; Group III (Group AA + Dxp): animals received 4 % AA (as group II) Starting from day 4, a single dose of Dxp (500 mg/kg) was administered intraperitoneally; Group IV (Group Dxp): Dxp was administered similar to Group III.
Results: AA treatment led to an increase in MDA, TOS and OSI levels; however, it led to a decrease in SOD, CAT, GPX,GSH and TAC levels and caused oxidative stress. The histopathological examination showed that AA treatment caused tissue injury. At the same time, AA treatment increased caspase-3 activity in the distal colon and triggered apoptosis. Dxp treatment caused biochemical and histopathological improvements in these parameters.
Conclusions: In the present study, biochemical and histopathological examinations showed that oxidative stress and apoptosis increase in the IBD pathogenesis. Furthermore, our results show that Dxp has positive effects of tissue lipid peroxidation, anti-oxidant system, and apoptosis, and can be a treatment option to stop the spread of IBD.

Topic 17: Hepatology Research

No: 2116

Social stigmatization in patients with chronic hepatitis B and C

Güray Can[1], Hatice Can[2], Bülent Yılmaz[3], Uğur Korkmaz[3], Emrah Poşul[1], Mevlüt Kurt[1]

Abant Izzet Baysal University, Faculty of Medicine Department of Gastroenterology Bolu-Turkey[1], Abant Izzet Baysal University, Faculty of Medicine Department of Internal Medicine Bolu-Turkey[2], Bolu Izzet Baysal State Hospital Department of Gastroenterology Bolu-Turkey[3]

Introduction: Turkey has around 4 million adults living with chronic hepatitis B and C who face several difficulties in their social environment as a stigma and discrimination. Any study about the stigmatism in the patients with chronic hepatitis was not conducted in Turkish population having a different socio-cultural background. The objective of our study was to investigate and compare the level of stigma in the people living with chronic hepatitis B and C in Turkey.
Methods: Forty five patients with chronic hepatitis C and 114 patients with chronic hepatitis were enrolled in the study. Berger's scale was used for stigmatization composed of four point-likert type 40 items. It has four subscales named as personalized stigma, disclosure, negative self-image and public attitude.
Results: In the internal consistency analysis of Berger stigma scale, Cronbach's alpha values were 0.95 and 0.96 for chronic hepatitis C and B respectively. Overall mean stigma scores were 1.97 ± 0.58 and 2.14 ± 0.57 for chronic hepatitis B and C respectively ($P = 0.10$). There were stigma in %47.4 of the patients with chronic hepatitis B, %60 of the patients with chronic hepatitis C ($P = 0.15$).
Conclusion: Most of the patients with chronic hepatitis C and half of the patients with chronic hepatitis B have stigma in Turkish population. These rates are higher than that of western population. The reason for this is that Turkish people are more conservative. The fear of discrimination in the patients prevents early diagnosis, effort of seeking care and adherence of medical therapy. A multidisciplinary approach increases the success of medical treatment and prevents discrimination of patients.

Topic 17: Hepatology Research

No: 1365

Activated hepatic stellate cells with senescence associated secretory phenotype signature in steatohepatitic hepatocellular carcinoma

Jee San Lee[1], Yoo Jeong Eun[1], Young Nyun Park[1]

Yonsei University College of Medicine Department of Pathology, Bk21 Plus Project For Medical Science Seoul-Korea, South[1]

Aim: Steatohepatitis hepatocellular carcinoma (SH-HCC), a new histologic variant of HCC has been reported to be associated with the metabolic syndrome, however, its pathologenesis remains unclear.
Methods: The diagnosis of SH-HCC was made if the tumour fulfilled four of the following five criteria: steatosis (> 5 % tumour cells), ballooning or Mallory–Denk body formation, interstitial fibrosis and inflammatory infiltrates. SH-HCC (n = 21) and comparable set of HCC, termed conventional HCC (C-HCC) (n = 34) were selected and analyzed their difference in clinical, pathological, and molecular aspects. The hepatic stellated cell activation and senescence-associated secretory phenotype (SASP) were also evaluated with their markers, α-smooth muscle actin (α-SMA), and p21Waf1/Cif1, γ-H2AX and IL-6, respectively, by immunohistochemistry.
Results: SH-HCC showed a significant association with metabolic syndrome and older aged patients.

SH-HCC showed significantly more activated hepatic stellate cells expressing p21Waf1/Cif1 and DNA damage signal, γ-H2AX than C-HCC. In addition, inflammatory cytokine IL-6 expression that was detected along with the activated stellate cells was also higher in SH-HCC compared to C-HCC. For non-tumor pathology, non-alcoholic fatty liver disease (NAFLD) was major one in SH-HCC, but this was relatively rare in C-HCC. This higher SASP expression in SH-HCC were found in both tumor and non-tumor regions.
Conclusion: SASP expression in activated hepatic stellate cells, including DNA damage signal and inflammatory cytokine is suggested to be the important molecular event in SH-HCC.

Topic 17: Hepatology Research

No: 1813

Liver fibrosis protective effect of hovenia dulcis fruit

Jae Dong Lee[1], Min Dong Song[2]

Konkuk University Hospital Gastroenterology Chungju-Korea, South[1], Konkuk University Biotechnology Chungj-Korea, South[2]

This study was conducted to investigate the effects of the fruit extract from Hovenia dulcis (HD) on liver fibrosis in rats. In these experiments, liver fibrosis was induced by carbon tetrachloride(CCl4) treatment. Forty rats were randomly divided into four groups: Normal group (corn oil subcutaneous injection), CCl4y group(CCl4y-induced liver fibrosis group; 50 % CCl4y1.0 mL/kg), Normal group + HD group(20 % HD, 4.0 mL/kg), CCl4y +HD group(20 % HD, 4.0 mL/kg). To study the effect of extracts from HD fruit on the liver fibrosis in rats, which was induced CCl4, enzyme activities such as Alanine aminotranferase(AST) and Aspartate aminotransferase(AST) were measured in the serum. Bilirubin concentration in the serum and expression of collagen I and III in the liver tissue were also analysed. In addition, the pathology of the liver tissue was evaluated. Tetrazolium-based colorimetriic(MTT) and Sulforbodamin B (SRB) were used to analyze the effect of treatment on hepatic stellate cell (HSC) proliferation. In the present study, the ALT, AST and Bilirubin levels and expression volume of collagen I and III in the CCL4 + HD group were found to be lower than in the CCl4group. In addition, HD treatment reduced the accumulation of collagen in the liver tissue and inhibited HSC proliferation. These results indicated the extracts from HD fruit may inhibit liver fibrosis and thus could be used as a therapeutic agents to prevent liver fibrosis.

Topic 17: Hepatology Research

No: 1359

Insights into glycan biosynthesis of chemically induced hepatocellular carcinoma in rats a glycomic analysis approach

Amr Amin[1], Asma Bashir[1], Diane Mccarthy[2], Nazar Zaki[3], Sanjida Ahmed[4], Mohamed Lotfy[1]

Uae University Biology Al-ain-United Arab Emirates[1], Ezose Sciences Inc. - Nj-United States[2], Uae University College of It Al-ain-United Arab Emirates[3], Eastern Biotech and Life Sciences - Dubai-United Arab Emirates[4]

Hepatocellular carcinoma (HCC) is one of the most common types of cancer worldwide. Adequate markers are not currently available for the diagnosis of hepatocellular carcinoma. Glycans are emerging as sensitive and simple biomarkers for various malignant diseases. The aim of the present study was set to evaluate, the qualitative and quantitative changes in N-linked glycosylation of proteins that occur in association with HCC in rodent model. Liver tissue samples of 2 groups of rats- 1) normal (non-tumor-bearing) rats; 2) tumor-bearing rats; were collected and the liver lysates were used for biochemical and GlycanMap® analyses. Briefly, GlycanMap® analysis is high-throughput assay that provides a structural and quantitative readout of protein-associated glycans using a unique, automated 96-well assay technology coupled to matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) and custom bioinformatics. Histopathological studies were also done to ensure the development of HCC in rat models. The N-glycomic analysis revealed 5 glycans that showed statistically significant differences between the normal and tumor-bearing rats. There was increase in high-mannose structures in HCC rats compared to normal. Importantly, HCC rats showed increase both in tumor-associated carbohydrates and in the branched glycan. The changes in glycans correlated well with the glycan flow changes reported in glycan biosynthetic pathway that implicates the importance of enzyme activities involved in glycan synthesis at different subcellular localizations.

Topic 17: Hepatology Research

No: 1567

Usefulness of synapse vincent(r) with pre check imaging of tumor location

Masako Izuta[1], Chikara Ogawa[1], Soichi Arasawa[1], Mitsushige Shibatoge[2], Masatoshi Kudo[3]

Takamatsu Red Cross Hospital Gastroenterology and Hepatology Takamatsu-Japan[1], Takamatsu Red Cross. Hospital Gastroenterology and Hepatology Takamatsu-Japan[2], Kinki University Gastroenterology and Hepatology Osakasayama-Japan[3]

Purpose: To evaluate the usefulness of a virtual ultrasound (US)imaging device as atool to assist novice sonographers.
Materials and method: A prospective blinded pilot study was conducted involving patients with liver lesions.One medical doctor with less 5 years of experience performed US examinations. The time needed to scan liver and to detect liver lesions on US,with and without using the virtual US imaging device SYNAPSE VINCENT (R) (Fujifilm Medical Co., Tokyo, Japan)before US examination, were evaluated.
Results: Fifteen patients with the following liver lesions were included: liver cyst (n = 32), hemangioma (n = 2),liver calcification (n = 1), liver abscess (n = 1), and liver metastasis (n =). The maximal diameter of these lesions ranged from 0.3 to 1.5 cm (mean ± SD,0.8 ±). The average time for examining liver on US was s (range,-) with vINCENT and s (range,-) without VINCENT before US examination. There were significant differences in the duration of US examination with and without VINCENT (P = Student's test). The rates for accurately detecting liver lesions were and % (/) in US beginners with and without VINCENT, respectively. Significantly higher detection rates were found in the US beginners who used VINCENT compared to those who did not use VINCENT (P = Fisher's exact test).
Conclusion: Before US examination,a reference with VINCENT could controbute to the successful detection of liver lesions and could be time-saving for US beginners.

Topic 17: Hepatology Research

No: 1467

Hyperinsulinemia rather than hyperglycemia can accelerate the progression of hepatocellular carcinoma

Hayato Baba[1], Koichi Tsuneyama[1]

University of Toyama Department of Diagnostic Pathology Toyama-Japan[1]

Purpose: We have recently reported that neonatal streptozotocin (STZ) treatment causes type 1 diabetes mellitus (DM) and subsequent

hepatocellular carcinoma (HCC) in DIAR mice. In the present study, to examine the relation between DM and HCC, we evaluated the effect of blood glucose control on the incidence and/or severity of HCC in this model.
Methods: Newborn male ddY, Institute for Animal Reproduction (DIAR) mice were divided into three groups; STZ-treated group (N = 13), STZ/Insulin-treated group (N = 20), and control group (N = 8). All mice were sacrificed and examined at 12 weeks of age.
Results: STZ-treated mice had significantly lower body weight and higher blood glucose level than controls. At 12 weeks of age, higher level of total cholesterol, triglyceride, free fatty acid, and ALT were recognized in STZ-treated mice compared to controls. In contrast, there was no difference between STZ/Insulin-treated mice and controls on all of those points. In histopathological analysis, HCC was observed more frequently in the livers of STZ/Insulin-treated mice than those of STZ-treated mice (39 % versus 15 %, $P = 0.011$), although there was no difference in the incidence of neoplastic lesions. Moreover, the average size of tumors was significantly larger in STZ/Insulin-treated mice than in STZ-treated mice. In immunohistochemical analysis, the expression of ERK1/2, a downstream substrate of insulin signal activating cell proliferation, were significantly higher in STZ/INS-treated mice than in STZ-treated mice.
Conclusions: Insulin treatment improved disorder of glycolipid metabolism, but accelerates the progression of HCC. Hyperinsulinemia rather than hyperglycemia can accelerate the progression of HCC via insulin signaling.

Topic 17: Hepatology Research

No: 1861

Scrub typhus associated hepatic dysfunction and abdominal ct findings

Hyoun Soo Lee[1], Sang Goon Shim[1], Man Je Park[1]

Samsung Changwon Hospital, Sungkyunkwan University School of Medicine 1department of Internal Medicine Changwon-si -Korea, South[1]

Backgroud/aims: This retrospective study investigated abnormal hepatic dysfunction and abdominal computed tomography (CT) findings in scrub typhus, and severity of hepatic dysfunction according to the number of CT findings.
Methods: 349 adult patients were diagnosed with scrub typhus. 94 underwent abdominal CT. The CT images were reviewed by the attending radiologist. Patient data of history, symptoms, signs, and results of laboratory tests were collected from the electronic medical records.
Results: In 349 patients with scrub typhus, elevation of AST (78.5 %) and ALT (63.0 %) were dominant compared to ALP (27.2 %) and total bilirubin (16.1 %) (Table 1). Abdominal CT findings of 94 patients were, in descending order of frequency, enlarged lymphnode (53.2 %), inhomogenous enhancement of liver (47.9 %), splenomegaly (46.8 %), ascites (28.7 %), low attenuation of periportal areas (27.7 %), gallbladder wall thickening (17.0 %), and splenic infarct (6.4 %) (Table 2) (Figure 1). Also, the level of aspartate transaminase tended to be elevated according to the number of CT findings ($P = 0.028$).
Conclusions: When scrub typhus is suspected in an endemic area, the hepatocellular pattern of hepatic dysfunction and the aforementioned findings of abdominal CT may be helpful to the accurate diagnosis and improvement the patient prognosis, such as by the appropriate selection of antibiotics.

Topic 17: Hepatology Research

No: 1887

Identification and characterization of metastasis related genes via a mouse model in liver cancer

Chia-jung Liao[1], Kwang-huei Lin[1]

Chang-gung University Biochemistry Taoyuan-Taiwan[1]

Despite numerous investigations on metastasis, the determinants of metastatic processes remain unclear. We aimed to identify the metastasis-associated genes in hepatocellular carcinoma (HCC). Potent metastatic SK-hep-1 (SK) cells, designated 'SKM', were generated using Transwell assay followed by selection in a mouse model. Genes expressed differentially in SKM and SK cells were identified via microarray analyses. A small form of Neural precursor cell-expressed developmentally downregulated 4 (sNEDD4) was identified to be overexpressed in SKM cells, which was confirmed as a novel transcript using liquid chromatography-mass spectrometry (LC–MS/MS). In clinical specimens, sNEDD4 was significantly overexpressed in tumors and serves as a poor prognostic factor for male patients with HCC ($P = 0.035$). Upon subcutaneous introduction of sNEDD4-overexpressing SK cells into flanks of nude mice, tumors grew faster than those of the control group. Furthermore, sNEDD4-mediated promotion of tumor metastasis was demonstrated in the orthotopic mouse model. Overexpression of sNEDD4 increased the invasive ability of SK cells through upregulation of matrix metalloproteinase 9 and inhibited serum deprivation-induced apoptosis via upregulation of myeloid cell leukemia 1 (Mcl-1). In conclusion, sNEDD4 is a novel metastasis-associated gene, which prevents apoptosis under nutrient restriction conditions. The present findings clearly support the prognostic potential of sNEDD4 for HCC.

Topic 17: Hepatology Research

No: 2190

Evaluation of chronic hepatitis and liver cirrhosis patients with bioelectrical impedance method

Hasim Nar[1], Necati Yenice[1], Cemil Sert[2], Ahmet Uyanikoglu[1], Timuçin Aydoğan[1], Betül Nar[3], Hüseyin Taşkin[4], Selahattin Biçak[5]

Harran University Gastroenterology Sanlıurfa-Turkey[1], Harran University Biophysics Sanlıurfa-Turkey[2], Harran University General Surgery Sanlıurfa-Turkey[3], Viranşehir State Hospital Internal Medicine Sanlıurfa-Turkey[4], Şehit Kamil State Hospita Internal Medicine Gaziantep-Turkey[5]

Objective: The aim of this study was the investigate to whether difference between chronic hepatitis, cirrhosis patients and healthy individuals with bioelectrical impedance analysis method.
Method: Thirty one chronic hepatitis B and C, 35 liver cirrhosis patients who had been followed up in Gastroenterology outpatient clinic were included into the study. Thirty-eight individuals were selected as the control group. Cases were divided into three groups as chronic hepatitis, liver cirrhosis and healthy controls.
Results: Cirrhosis group's hematocrit and blood sodium level is significantly lower ($P < 0.05$). Body capacitance value in chronic hepatitis and cirrhosis group is higher than the control group ($P < 0.05$). Resistance in chronic hepatitis B group is lower than the

control group ($P < 0.05$). Body cell mass value in chronic hepatitis group is higher than the control group ($P < 0.05$). Chronic hepatitis group's basal metabolic rate value is higher than the control group ($P < 0.05$). Chronic hepatitis group's lean body mass value is higher than the control group ($P < 0.05$). Chronic hepatitis group's intracellular water and total body water values is higher than the control group ($P < 0.05$). Phase angle is higher in chronic hepatitis group compared to other groups is high, though absent statistically significant ($p > 0.05$).

Conclusion: Although was not determine significantly changed between cirrhotic patients, chronic hepatitis patients and control groups with BIA, determined changes in patients with chronic hepatitis are promising for the future in terms of BIA. However, liver biopsy seems to be the most effective method for the diagnosis and follow up of these patients with these findings.

Topic 17: Hepatology Research

No: 1323

Efficacy of Wharton's jelly derived mesenchymal stem cells combined with praziquantel in schistosoma mansoni induced liver fibrosis in mice

Olfat Hammam[1], Nagwa Elkhafif[2], Yasmeen Attia[3], Tarek Mansour[4], Mohamed Elmazar[3], Rania Mohsen[5], Sanaa Kenawy[5], Aiman El-khatib[5]

Theodor Bilharz Research Institute Pathology Giza-Egypt[1], Theodor Bilharz Research Institute Electron Microscope Giza-Egypt[2], Faculty of Pharmacy, The British University Pharmacology and Biochemistry El Sherouk,cairo-Egypt[3], National Cancer Institute Virology and Immunology Unit, Cancer Biology Cairo-Egypt[4], Faculty of Pharmacy, Cairo University Pharmacology and Toxicology Cairo-Egypt[5]

Aim: To investigate feasibility of liver damage repair using Wharton's jelly derived mesenchymal stem cells (WJMSCs) combined with praziquantel (PZQ) to treat Schistosoma (S.) mansoni induced liver fibrosis.

Methods: Mice received early (8th week post infection) and late (16th week post infection) intra-hepatic injection of WJMSCs, alone or combined with oral PZQ, to investigate treatment efficacy on both acute and chronic stages of liver fibrosis. Histopathological, morphometric, and immunohistochemical analysis for alpha fetoprotein, alpha smooth muscle actin, Hep par-1, cytokeratin-18, vimentin, and β2-globulin, were performed. Relative mRNA expression of albumin, alpha fetoprotein, alpha smooth muscle actin, collagen I, and interleukin 13 was measured by real time reverse transcription polymerase chain reaction (RT-PCR). Gelatin zymographic for matrix metalloproteinase (MMP)-2 and 9 was performed.

Results: Histopathological and morphometric findings showed a regression in fibrosis in WJMSCs-treated groups and better results were obtained when PZQ was combined to stem cell therapy. Immunohistochemical and RT-PCR findings showed positive expression for hepatocyte specific markers in transplanted groups and an amelioration of fibrosis related markers. Gelatin zymography results showed an elevation of enzymatic activity of MMP-2 and -9 in WJMSCs treated groups. PZQ caused a reduction in the activity of both enzymes. Combined treatment, however, caused no or little change.

Conclusion: The differentiation of transplanted WJMSCs into functioning hepatocyte like cells in the livers of S. mansoni infected mice may have contributed to partial repair of liver fibrosis, especially when PZQ is administered concomitantly.

Topic 17: Hepatology Research

No: 2137

Preliminary examination of the relations between disease stage illness perceptions coping strategies and psychological morbidity in chronic hepatitis B and C guided by the common sense model of illness

Güray Can[1], Hatice Can[2], Bülent Yılmaz[3], Uğur Korkmaz[3], Vesile Uyanık[4], Emrah Poşul[1], Mevlüt Kurt[1], Hasan Ümit[5]

Abant Izzet Baysal University, Faculty of Medicine Department of Gastroenterology Bolu-Turkey[1], Abant Izzet Baysal University, Faculty of Medicine Department of Internal Medicine Bolu-Turkey[2], Bolu Izzet Baysal State Hospital Department of Gastroenterology Bolu-Turkey[3], Edirne State Hospital Department of Psychiatryh Edirne-Turkey[4], Trakya University, Faculty of Medicine Edirne-Turkey[5]

Aims: Chronic hepatitis (CH) has a spectrum from asymptomatic disease to cirrhosis and hepatocellular carcinoma (HCC). Psychological consequences of the disease may vary depending on patients' perception of illness and coping strategies. In our study, we aimed to establish the relations between disease stage, illness perception, coping strategies and psychological morbidity in CH.

Methods: Totally 182 CH patients were enrolled. B-IPQ, Brief COPE and HADS questionnaires were applied to the patients. Correlations were measured with Pearson's test. Relations were evaluated by structural equation modeling (SEM).

Results: In CHB, combining the questionnaire data using SEM resulted in a final model with an excellent fit ($\chi2\ (2) = 0.00$, $P = 1.000$, $\chi2/N = 0.00$, $RMSEA < 0.001$, $CFI = 1.000$, $GFI = 1.000$). Disease stage had a significant direct influence on illness perceptions ($\beta = 0.23$, $P = 0.006$). Illness perceptions had a significant direct influence on emotional coping strategy, depression and anxiety ($\beta = 0.20$, $P = 0.019$, $\beta = 0.33$, $P < 0.001$, $\beta = 0.59$, $P < 0.001$, respectively). While use of emotional coping strategies was associated significantly ($P = 0.01$) with the presence of anxiety, problem-focused coping strategy was associated with depression ($P = 0.004$). In CHC, SEM resulted in a final model with an excellent fit ($\chi2\ (2) = 0.078$, $P = 0.962$, $\chi2/N = 0.039$, $RMSEA < 0.001$, $CFI = 1.000$, $GFI = 0.999$). Disease stage did not have a significant direct influence on illness perceptions. Illness perceptions had a significant direct influence on depression and anxiety ($\beta = 0.27$, $P = 0.023$, $\beta = 0.44$, $P < 0.001$, respectively).

Conclusion: The psychological consequences of the disease vary depending on the person's perception of illness and coping strategies. Because each patient's perception and coping strategies related to illness will be different, psychological support applied to each patient must be different.

Topic 17: Hepatology Research

No: 1623

Promotion of hepatic differentiation of human umbilical cord mesenchymal stem cells with aggregate culture on decellularized liver extracellular matrix

Y. Li[1], J. Bao[2], Q. Wu[1], Y. Wang[1], X. Wu[3], Y. Zhou[1], H. Bu[2]

West China Hospital Laboratory of Pathology,key Laboratory of Transplant Engineering and Immunology Chengdu-China[1], West China Hospital Laboratory of Pathology, key Laboratory of

Transplant Engineering and Immunology,department of Pathology Chengdu-China[2], Luzhou Medical College Department of Clinical Medicine Luzhou-China[3]

End-stage liver failure is a high mortality disease with metabolism and detoxication dysfunction. Conventional hepatocyte-like-cell-related treatment offers a promising prospect. However, monolayer hepatocyte-like-cell culture cannot undergo complex microenvironment contacts and interactions of stem cells with the extracellular matrix (ECM), which have been reported, could improve and maintain the phenotype and function of hepatocyte-like cells. The combination of three-dimensional (3D) culture and decellularized liver scaffolds in our hepatocyte-like-cell culture is a novel method, which human umbilical cord MSCs (hUC-MSCs) self-aggregated into spheroids in 3D culture plate and were planted into the decellularized liver scaffolds.

Significantly higher expression of liver-specific proteins, including Albumin (ALB), Cytokeratin18 (CK18), CK 19 and α-fetoprotein (AFP) was observed. Also, it was significantly higher expressed liver-specific transcripts such as CYP1A2, CYP2A6 and lower expressed stem-cell-specific transcripts such as OCT-4, SOX-2. Moreover, the function of ALB excretion and ammonia metabolism were more effective. Hepatocyte-like cells in combination culture did not express HLA-class II markers, or cause human lymphocyte proliferation response.

This combination culture system may provide a promising strategy for generating hepatocyte-like cells for portable liver micro-organ, to meet the demands of clinical transplantation, bioartificial liver (BAL) device and drug research.

Topic 17: Hepatology Research

No: 1645

Anti viral action mechanism of mixed herb extracts SG-001 on mouse hepatitis virus (mhv) induced chronic hepatitis in balb c mice

Kyoung Min Sohn[1], Chung-seop Kim[2], Seon-gil Do[2], Hajin Nam[2], Jun-gyo Suh[2], Yeon Ju Jeon[1]

We Want Healthcare Internal Medicine Seoul-Korea, South[1], Hallym University Medical Genetics Chuncheon-Korea, South[2]

To elucidate immunological mechanism of therapeutic effect of SG-001, the mixed herbal extracts, in the MHV-2 cc-induced chronic hepatitis model of BALB/c mice, we examined, the peripheral blood leukocytes populations by FACS analysis, the liver-infiltrated lymphocytes by immunohistochemical staining of macrophage and CD4 + and CD8 + helper T cells, and the Th1 or Th2 cytokines expression in the liver-infiltrated lymphocytes and splenocytes by immunohistochemistry. and finally, viral clearance was confirmed by the titration of MHV in the liver extracts. In the FACS analysis of peripheral blood leukocytes, the population of NK cell of the SG-001 treated chronic hepatitis mice was recovered to normal range, whereas that of SG-001 untreated mice showed decreased level. In the liver of the SG-001 untreated mice, macrophage and CD4 and CD8-positive cells were increased as well as IL-4,-10,-12, IFN-γ-positive cells compared with normal mice. However, SG-001-treated chronic hepatitis mice did not show any difference from normal mice. When compared with normal mice, the splenocytes positive for IL-2, IFN-γ, IL-4 and IL-10 were increased in both group of chronic hepatitis induced mice regardless of SG-001 treatment, however, the SG-001 treated chronic hepatitis mice showed more increased number of IL-2-positive cells than untreated mice. The acceleration of the viral clearance from liver was detected in the SG-001 treated mice by the MHV titration of the liver extracts. In this study, we could suggest plausible mechanism of therapeutic effects of SG-001: SG-001 stimulates IL-2 secreting Th1 T-cell, and IL-2 activates NK cells, the activated NK cell may accelerate the clearance of MHV from liver.

Topic 17: Hepatology Research

No: 1035

Enhanced hepatic expression of nuclear factor e2 related factor and small maf in patients with chronic liver diseases

Kazuhito Kawata[1], Yoshimasa Kobayashi[1], Yurimi Takahashi[1], Yukimasa Oba[1], Kazuyoshi Ota[1], Shin Shimoyama[1], Satoru Yamazaki[1], Takeshi Chida[1], Hidenao Noritake[1]

Hamamatsu University School of Medicine Hepatology Division, Internal Medicine Ii Hamamatsu-Japan[1]

Background: The imbalance of hepatic oxidant and antioxidant status is an important pathophysiological mechanism in chronic liver disease. With oxidative stress, nuclear factor-E2-related factor (Nrf2) is activated to translocate into the nucleus, form heterodimers with small Maf proteins (sMaf) and bind antioxidant response element (ARE) to activate ARE-dependent genes. However, it remains unknown how hepatic Nrf2 and sMaf contribute to antioxidant defense in chronic liver disease.
Aim: The aim of the current study was to examine hepatic expression of Nrf2 and sMaf with 8-OHdG in patients with chronic liver disease.
Methods: Liver biopsies were obtained from chronic hepatitis B (HBV), chronic hepatitis C (HCV), autoimmune hepatitis (AIH), and non-alcoholic steatohepatitis (NASH). Normal liver tissue (control) was obtained from surgical resection specimens. Hepatocellular nuclear Nrf2, sMaf and 8-OHdG expressions were determined by immunohistochemistry.
Results: The percentages of Nrf2-, sMaf-, or 8-OHdG-positive hepatocellular nuclei were significantly higher in HBV, HCV, AIH or NASH livers than in normal livers. The degree of Nrf2 expression was positively correlated with that of 8-OHdG expression in HBV, HCV and NASH livers, but not AIH livers. The degree of sMaf was positively correlated with that of 8-OHdG expression in HCV livers not in any other groups.
Conclusions: Enhanced expression of hepatocellular nuclear Nrf2 and sMaf exists in patients with chronic liver disease. Hepatocellular oxidative stress-dependent Nrf2 activation may contribute to the antioxidant defense in HBV, HCV and NASH livers. In HCV, hepatocellular oxidative stress-dependent up-regulation of sMaf may influence the transcriptional regulation of Nrf2/ARE-dependent genes.

Topic 17: Hepatology Research

No: 1456

The characteristic changes in hepatitis B virus x region for hepatocellular carcinoma a comprehensive analysis based on global data

Wenwen Li[1], Kaku Goto[1], Yasuo Matsubara[1], Sayaka Ito[1], Ryosuke Murayama[1], Qiang Li[2], Naoya Kato[1]

Advanced Clinical Research Center, The Institute of Medical Science, The University of Tokyo, Tokyo-Japan[1], Affiliated Infectious Disease Hospital, Shandong University, Jinan-China[2]

Aim: Mutations in hepatitis B virus (HBV) X region (HBx) play important roles in hepatocarcinogenesis while the results remain

controversial. We sought to clarify potential hepatocellular carcinoma (HCC) characteristic mutations in HBx from HBV genotype C infected patients and the distribution of those mutations in different disease phases and genotypes.
Methods: HBx sequences downloaded from a global HBV database were screened and then classified into Non-HCC or HCC group. Logistic regression was performed for evaluating the relative risks of HCC characteristic mutations.
Results: 1) 1115 HBx sequences (HCC, 161; Non-HCC, 954) across 29 countries/areas were extracted from downloaded 5956 HBx sequences. Genotype C occupied 40.6 % of Non-HCC (387/954) and 89.4 % of HCC (144/161). 2) 16 nucleotide positions showed significantly different distributions between genotype C HCC and Non-HCC groups. 3) Logistic regression showed that mutations A1383C [OR: 2.32 (95 % CI: 1.34-4.01)], R1479C/T [1.96 (1.05-3.64)/5.15 (2.53-10.48)], C1485T [2.40 (1.41-4.08)], C1631T [4.09 (1.41-11.85)], C1653T [2.58 (1.59-4.19)], G1719T [2.11 (1.19-3.73)], and T1800C [23.59 (2.25-247.65)] were independent risk factors for genotype C HCC, presenting different trends among individual disease phases. 4) Several genotype C HCC risk mutations pre-existed, even as major types, in early disease phases with other genotypes.
Conclusions: Mutations associated with HCC risk were mainly located in HBx transactivation domain, viral promoter, protein/miRNA binding sites, and the area for immune epitopes. Furthermore, the signatures of these mutations were unique to disease phases leading to HCC, suggesting molecular counteractions between the virus and host during hepatocarcinogenesis.

Topic 17: Hepatology Research

No: 1634

Promotion of hepatic differentiation of bone marrow mesenchymal stem cells with aggregate culture on decellularized liver extracellular matrix

Q. Wu[1], J. Bao[1], Y. Li[1], Yj. Wang[1], Yj. Zhou[1], Xj. Wu[2], H. Bu[1]

West China Hospital Laboratory of Pathology Chengdu-China[1], Luzhou Medical College Department of Clinical Medicine Chengdu-China[2]

Hepatocyte-like cells derived from stem cells hold great potential for clinical and pharmaceutical applications. Interactions between stem cells and extracellular matrix (ECM) are requisite for inducing lineage-specific differentiation and maintaining biological functions of mesenchymal stem cells by providing a composite set of chemical and structural signals. Spherical aggregates (spheroids) of stem cells, non-adherent multi-cell aggregates, provide a 3-dimensional (3D) tissue construct. Here we investigated if cell-deposited ECM and spheroid tissue constructs mimicked in vivo liver's stem cell microenvironment and facilitated hepatogenic maturation.

The combination of aggregate culture and decellularized liver scaffolds in our hepatocyte-like-cell culture is a novel method, which rat bone marrow mesenchymal stem cells (BM-MSCs) self-aggregated into spheroids in 3D culture plate and were planted into the decellularized liver scaffolds.

Decellularization process preserved the fibrillar microstructure and a mix of matrix proteins in porcine liver ECM, such as type I collagen, type IV collagen, fibronectin, and laminin that were identical to those found in native liver. Compared with the cells on tissue culture polystyrene (TCPS), BM-MSCs spheroids cultured on liver ECM showed a spindle-like shape, a robust proliferative capacity, and a suppressed level of intracellular reactive oxygen species. Hepatocyte-like cells differentiated from BM-MSCs spheroids on ECM were determined with a more intensive staining of glycogen storage, an elevated level of urea biosynthesis, albumin secretion and higher expressions of hepatocyte-specific genes in contrast to those on TCPS.

These results demonstrate that liver ECM with aggregate culture can be an effective method to facilitate hepatic maturation of BM-MSCs and promote stem-cell-based liver regenerative medicine.

Topic 17: Hepatology Research

No: 1829

The value of doppler parameters in predicting chronic hepatitis or cirrhosis are there cut off values to estimate end stage liver disease

Gökhan Söker[1], Bahadır Öztürk[2], Bozkurt Gülek[1], Ferit Kuşçu[3], Ayşe Bolat[1], Muhammed Arslan[1], Ümit Doğan[4], Cengiz Yılmaz[1]

Numune Teaching and Research Hospital Radiology Adana-Turkey[1], Adiyaman University Faculty of Medicine Family Medicine Adıyaman-Turkey[2], Numune Teaching and Research Hospital Infectious Disease and Microbiology Adana-Turkey[3], Mustafa Kemal University Faculty of Medicine Gastroenterology Antakya-Turkey[4]

Objective: The aim of this study was to define cut-off values between compensated cirrhosis and chronic hepatitis, in terms of the criterions of Doppler parameters of liver vascularity.
Methods: 70 chronic hepatitis and 30 cirrhosis patients were included in this prospective study. The diagnostic decisiveness properties of the Doppler values in the pre-determination of liver cirrhosis were evaluated by the Receiver Operating Characteristics curve analysis.
Results: Taking the cut-off value for hepatic vein waveform index as 0.605, a sensitivity rate of 80 % and a specificity rate of 77.1 %, were obtained. The sensitivity rate was 80 %, and the specificity rate was 68.6 %, for a peak portal flow velocity cut-off value of 18.25 cm/s. When the hepatic artery resistivity index cut-off value was taken as 0.705 for the diagnosis of cirrhosis, the sensitivity was found to be 82.5 %, and the specificity 72.1 %, concerning the chronic hepatitis and cirrhosis groups. For a hepatic artery pulsatility index cut-off value of 1.295, a sensitivity rate of 82.5 % and a specificity rate of 72.1 %, were found.
Conclusion: The hepatic vasculature must be evaluated by color Doppler ultrasonography during the routine controls of chronic hepatitis patients. The obtaining of Doppler cut-off values may be of serious help in the selection of patients to undergo the procedure of liver biopsy.

Topic 17: Hepatology Research

No: 2118

Can soluble ST2 levels be use as a fibrosis marker in chronic hepatitis B infection

Erkin Öztaş[1], Ufuk Barış Kuzu[1], Nesliah Inci Zengin[2], Ismail Hakkı Kalkan[1], Fatih Oğuz Önder[1], Hüseyin Tuğrul Çelik[3], Mesut Yalın Kılıç[1], Aydın Şeref Köksal[1], Sabite Kaçar[1], Meral Akdoğan[1], Nurgül Şaşmaz[1], Ertuğrul Kayaçetin[1]

Turkiye Yuksek Ihtisas Training and Research Hospital Gastroenterology Çankaya-Turkey[1], Turkiye Yuksek Ihtisas Training and Research Hospital Pathology Ankara-Turkey[2], Turgut Ozal University School of Medicine Medical Biochemistry Ankara-Turkey[3]

Aim: Interleukin-33 (IL-33) is a member of the IL-1 family, induces synthesis of T Helper 2 (Th2)-type cytokines via its ST2 receptor. Soluble ST2 binds IL-33 and function as a decoy receptor that blocks the ability of IL-33 to signal through transmembrane ST2. Th2-type cytokines play an important role in fibrosis thus we here aimed to answer to the Can soluble ST2 levels be surrogate marker of fibrosis in CHB infection ?" question.
Method: Study contained 19 healthy controls, 54 patients chronic hepatitis B (CHB) and 14 cirrhosis consequence of CHB. Serum ST2 levels were measured in sera of 87 patients using "Human ST2/IL-1 R4 Quantikine ELISA Kit".
Results: sST2 levels were significantly higher in CHB patients (median: 1133 pg/ml) compared to controls (median: 762.5 pg/ml) (p: 0.035). In CHB patients; APRI-score and FIB-4 index showed weak correlation with liver fibrosis (correlation coefficent (cc): 0.239, p: 0.082 and cc: 0.342, p: 0.01 respectively) while sST2 levels showed moderate correlation (cc: 0.424 p: 0.001). The AUC of the sST2 levels was 0.71; > 1174 pg/ml predicted fibrosis (Ishak-score > 2) with a sensitivity of 61.3 %, a specificity of 74.5 %, a PPV of 71.43 % and a NPV of 57.7 % p: 0.003. The AUC's of the APRI-score and FIB-4 index for differentiating between fibrosis and non-fibrosis were 0.62 and 0.68 respectively. The AUC of the sST2 levels for differentiating cirrhosis and non-cirrhosis was 0.51.
Discussion: sST2 levels can be use to distinguish hepatitis B patients with and without significant fibrosis. This marker need to be validated in larger cohorts.

Topic 18: Liver Cirrhosis and Complications

No: 1595

Event related potential P300 using auditory "oddball" paradigm in patients with minimal hepatic encephalopathy

Sehyun Cho[1], Joonyeol Han[1], Jinmo Yang[2], Soonwoo Nam[2], Youngsok Lee[2]

Yoido St. Mary Hepatology Seoul-Korea, South[1], St. Mary Hepatology Seoul-Korea, South[2]

P300 is an event-related potential (ERP) elicited by relevant stimuli employed in the so called "oddball" paradigm. The P300 component (amplitude and latency) is consistently reduced in patients with cognitive dysfunction during stimulus discriminate task. This study was designed to evaluate the clinical availability of P300 in patients with minimal hepatic encephalopathy who were also known to show cognitive dysfunction.

To elicit P300, the 2-stimulus auditory oddball paradigm was employed for patients with minimal hepatic encephalopathy (N = 17) and normal controls (N = 17). The 2-stimulus auditory oddball paradigm was composed of standard tone (1000 Hz, 75 dB, 80 %) and target tone (2000 Hz, 75 dB, 20 %) with 10 ms rise/fall time 50 ms duration.

P300 amplitude was low in patients with minimal hepatic encephalopathy across midline electrodes ($F = 26.9$, $P < 0.001$). There was no interaction between groups and electrodes ($F = 2$, $P > 0.2$). The P300 latency was shown to be delayed in patients with minimal hepatic encephalopathy across midline electrodes ($F = 11.1$, $P < 0.01$) and there was no interaction between group and midline electrodes ($F = 1.4$, $P > 0.2$).

This suggests that P300 could be useful for detecting and exploring cognitive dysfunction in the patients with hepatic encephalopathy.

Topic 18: Liver Cirrhosis and Complications

No: 1870

Sexual dysfunction in cirrhosis

Falak Naz[1], Adnan Bawany[1]

Aims Gastroenterology Hyderabad-Pakistan[1]

Objectives: To find out the frequency of sexual dysfunction in the patients with chronic liver disease at Asian institute of medical sciences.
Methodology: This observational study was conducted at Asian institute of medical sciences Hyderabad with the duration of _1__ year from 2012 to 2013, in this study one hundred and fifty cases of chronic liver disease with both gender on the basis of history and signs/symptoms of sexual dysfunction were selected.
Results: Out of 150 patients, 69.8 % were male and 30.2 % were females, from 100 % of the cases 51.1 % were noted with sexual dysfunction and 48.9 % were without sexual dysfunction. On the comparison of both sexes females were 52.8 % with sexual dysfunction and male were 51.54 % with sexual dysfunction. From all of the cases HCV was positive in 75.5 %, HBV positive 11.8 %, both HBV + HCV positive was in 2.9 %, HBV + HDV positive 1.5 %. Patients and alcoholic sexual dysfunction were only 0.7 %.
Conclusion: In the conclusion of this study the sexual dysfunction is the common complication in chronic liver disease patients.

Topic 18: Liver Cirrhosis and Complications

No: 1433

Outcomes of emergent and elective intervention in cirrhotic patients with gastric old blood clots

Sook Kyoung Oh[1], Dae Hwan Kang[1], Hyung Wook Kim[1], Cheol Woong Choi[1], Su Bum Park[1], Yu Yi Choi[1], Ji Ha Kim[1], Wan Chul Kim[1]

Pusan National University Yangsan Hospital Internal Medicine Yangsan-si-Korea, South[1]

Background/aim: In cirrhotic patients, endoscopic intervention is widely used for prevention of variceal rebleeding. When there is no evidence of recent bleeding on endoscopy, information or data about timing of endoscopic intervention after initial endoscopy is lacking. The aim of our study is to determine the effects and complication between emergent endoscopic varix ligation (EVL) and elective intervention in cirrhotic patients with gastric old blood clot on initial endoscopy.
Methods: We retrospectively analysed data about patients performed emergent prophylactic EVL in 26 cases (Emergent group) and elective intervention (EVL or EVO [endoscopic variceal obturation] or BRTO [balloon-occluded retrograde transvenous obliteration]) in 38 cases (Elective group)from Jan 2009 to June 2014. Patients were identified blood clots in the stomach without active bleeding or the stigmata. We evaluated clinical outcomes of each group including rebleeding rate, mortality.
Results: There was no significant difference in the 6-week rebleeding rates between the emergent and elective groups (3/26 [11.5 %] and 2/38 [5.3 %], respectively). But the 5-day rebleeding rates was significant difference between two groups (emergent group4/26 [15.4 %], elective group 0/38 [0 %], $P = 0.024$). In elective group, 6 gastric varices (21.1 %) identified during second-look endoscopy

were treated by EVO or BRTO. Mortality for the variceal bleeding was similar between to groups. But the death due to bleeding was only in emergent group (3/26[10.7 %] and 0 %, $P = 0.062$).
Conclusion: Elective EVL after initial endoscopy may be more effective than emergent EVL for prevention of rebleeding in cirrhotic patients with gastric old clots without active bleeding or stigmata.

Topic 18: Liver Cirrhosis and Complications

No: 1958

Preliminary study of factors about the effect of tolvaptan to liver cirrhosis

Shigemune Bekki[1], Ayako Mine[1], Rikako Kinoshita[1], Ryu Sasaki[1], Yuki Kugiyama[1], Satoru Hashimoto[1], Akira Saeki[1], Shinya Nagaoka[1], Seigo Abiru[1], Kazumi Yamasaki[1], Atsumasa Komori[1], Hiroshi Yatsuhashi[1]

Nho Nagasaki Medical Center Clinical Research Center Omura-Japan[1]

Background & aims: Tolvaptan is a nonpeptide antagonist that selectively blocks the binding of arginine vasopressin to V2 receptors, inhibits water reabsorption and induces the excretion of electrolyte-free water. It was reported that tolvaptan decreased body weight and improved intractable ascites in patients with decompensated liver cirrhosis, but factors that influence the efficacy of tolvaptan are not known. Aim of this study was to clarify the factors responsible for the effect of tolvaptan to liver cirrhosis.
Patients & methods: There were 650 patients with liver cirrhosis admitted to NHO Nagasaki Medical Center between November 2010 and July 2014. The rate of Child-Pugh grade A, B, and C was 78.7 %, 17.2 %, 4.1 %, respectively. Among them, 38 patients with intractable ascites were included in this study. We defined patients who achieved over 1 kg decrease of their body weight by 1 week from the start of tolvaptan as Effective, and the others as Not Effective. Then we compared characteristics of these two groups.
Results: All patients already received other diuretics. Out of 38 patients, 16 patients (42.1 %) were Child-Pugh grade C. Body weight decreased 1.79 kg by 1 week from the start of tolvaptan. Comparing 'Effective' group and 'Not Effective' group, pretreatment serum potassium concentration was significantly lower in Effective group (3.8 mEq/L vs 4.2 mEq/L, $P < 0.01$).
Considerations & conclusions: Tolvaptan was effective in patients with ascites refractory to conventional diuretics. The relation of tolvaptan and serum potassium concentration may be influenced by serum renin or aldosterone, and by renal tubular function.

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No: 1589

Urinary excretion of aquaporin 2 (AQP2) correlated with urinary osmolality in patients with refractory ascites due to cirrhosis

Takanori Hosokawa[1], Masayuki Kurosaki[1], Namiki Izumi[1], Jun Itakura[1], Kaoru Tsuchiya[1], Hiroyuki Nakanishi[1], Shoko Suzuki[1], Yutaka Yasui[1], Nobuharu Tamaki[1], Shuya Matsuda[1], Natsuko Nakakuki[1], Hitomi Takada[1], Mayu Higuchi[1], Yu Asano[1], Koichi Gondo[1]

Musashino Red Cross Hospital Gastroenterology and Hepatology Tokyo-Japan[1]

The non-peptide vasopressin type 2 (V2) receptor antagonist, tolvaptan, is used for the treatment of refractory ascites and/or hyponatremia in cirrhotic patients. Tolvaptan selectively blocks the binding of vasopressin to V2 receptors in renal collecting ducts, leading to the dislocation of aquaporin-2 (AQP2) from the apical plasma membrane to the cytoplasm of collecting duct cells, thus inhibiting water reabsorption and promoting the excretion of urine. Tolvaptan was administered to 37 patients with massive ascites due to cirrhosis. Bodyweight and urinary volumes were measured every day, whereas urinary excretion of AQP2 and osmolality were measured every 4 h. The mean decrease in bodyweight from baseline was 2.75 % after the administration of tolvaptan for 7 days. Reductions in bodyweight were ≥ 2 % and ≥ 1 % in 55.3 % and 68.4 % of patients, respectively. Urinary AQP2 levels decreased by 22.5 % at 4 h and 19.5 % at 8 h and returned to baseline after 24 h. Similar to urinary AQP2 levels, urinary osmolality levels decreased by 59.7 % at 4 h and 58.5 % at 8 h and returned to baseline after 24 h. Urinary levels of AQP2 were significantly correlated with urinary osmolality ($r = 0.778$, $P < 0.001$) and negatively correlated with serum sodium levels ($r = -0.426$, $P = 0.010$).Correlation between urinary excretion of AQP2 and urinary osmolality indicates that the vasopressin/AQP2 system plays a major role in fluid retention and hyponatremia in patients with hepatic cirrhosis. Monitoring the urinary excretion of AQP2 can be used as an indicator of the action and efficacy of tolvaptan in renal collecting ducts.

Topic 18: Liver Cirrhosis and Complications

No: 1053

Impact of bisphosphonate supplementation in patients with osteoporosis secondary to non choleastatic liver cirrhosis

Rinkesh Bansal[1], Piyush Ranjan[1], Vinit Shah[2], Mandhir Kumar[1], Munish Sachdeva[1]

Sir Ganga Ram Hospital Gastroenterology and Hepatology New Delhi-India[1], Sir Ganga Ram Hospital Gastroenterology and Hepatology New Delhi-India[2]

Background & Objectives: Patients with liver cirrhosis are more prone to develop bone disease i.e. Hepatic osteodystrophy (HOD). Treatment of HOD has not been standardized; calcium and vitamin D supplementation alone are not helpful. Aim of this study was to determine impact of bisphosphonates in patients with osteoporosis in non- choelastatic liver cirrhosis.
Methods: Consecutive patients with liver cirrhosis admitted at Sir Gangaram Hospital, Delhi between 2012-2013 were enrolled. Bone mineral density was measured by DEXA at the lumbar spine. Oral bisphosphonate i.e. Ibandronate 150 mg once a month was given in patients with osteoporosis and DEXA scan along with baseline investigations were repeated after 6 months.
Results: Total 215 patients with liver cirrhosis were enrolled. HOD were found in 142 (66 %), out of which 47 had osteoporosis. Out of 47 osteoporotic individuals, 34 % (n-16) died and 26 % (n-12) were lost to follow-up. 40 % (n-19) completed the treatment and were followed up after 6 months and assigned as Treatment group.
19 patients (Male-18) with mean age 50.9 ± 11 years were analyzed. Serum calcium and vitamin D significantly improved in treatment group in comparison to baseline. BMD and t-score also improved significantly. No significant adverse events related to drugs were noted.
Conclusions: This is the only Indian study on role of oral bisphosphonate in osteoporosis in patients with liver disease. Being oral, once a month and very less adverse effects, Ibandronic acid is a very good drug in osteoporosis in patients with liver disease.

Topic 18: Liver Cirrhosis and Complications

No: 1193

Daily single dose rifaximin for prevention of hepatic encephalopathy in patients with chronic liver disease

Muhammad Omar Qureshi[1], Farzana Shafqat[1], Muhammad Salih[1], Nasir Khokhar[1]

Shifa International Hospital Gastroenterology Islamabad-Pakistan[1]

Objective: To determine the efficacy of Rifaximin once a day dose in prevention of hepatic encephalopathy in patients with liver cirrhosis as compared twice daily dose of Rifaximin.
Design: Randomized control trial.
Place and Duration of Study: Shifa International Hospital, Islamabad, Pakistan from November 2012 to February 2014.
Methods: Patients with known chronic liver disease with at least one episode of hepatic encephalopathy (HE) in the past were randomized to Group A (Given Rifaximin 550 mg OD) and Group B (Given Rifaximin 550 mg BD) after fulfilling the inclusion criteria. Each patient was followed for 6 months for any episode of HE. Patients in each group for any breakthrough episode of encephalopathy during this period were identified. Data was analyzed using Statistical Package for Social Sciences (SPSS) version 16. Chi square test and t-test were applied where required to determine the significant difference between the two groups.
Results: There were total 306 patients. 128 patients in Group A while 178 in group B. Majority of patients (75.81 %) had hepatitis C virus with mean age of 52.30 + 9.92, MELD score 13.58 + 8.3 and (55.22 %) were in Child Pugh B. Total 81 patients had episode of hepatic encephalopathy during the study period. There were 27 patients in group A, while 54 patients in group B with breakthrough episode of HE (P value = 0.088).
Conclusion: This study suggests that there is no significant difference in Rifaximin once a day or twice daily dose in preventing hepatic encephalopathy.

Topic 18: Liver Cirrhosis and Complications

No: 1544

Non invasive parameters of oesophageal varices diagnosis which sensitive and applicable

Zain Elabdeen Sayed[1], Elham Hassan[2], Abeer Abd El-rehim[2], Mustafa Hareedy[3]

Assiut University Hospital Internal Medicine; Gastroenterology and Hepatology Unit Assiut-Egypt[1], Assiut University Hospital Tropical Medicine and Gastroenterology Assiut-Egypt[2], Assiut University Hospital Internal Medicine; Gastroenterology and Hepatology Unit Assiut-Egypt[3]

Aim: Oesophageal varices (OV) have the greatest clinical impact and the most severe complications. Upper endoscopy is the gold standard for diagnosis of OV, despite its own limitations. So, noninvasive detection of OV promises to decrease the necessity of endoscopic screening.

Our aims were to assess non-invasive parameters; blood ammonia, spleen longitudinal (SLD), portal (PVD), splenic (SVD) vein diameters, platelet count and platelet/SLD ratio (PLT/SLD) to elaborate the reliable method to predict the presence of to predict portosystemic collaterals mostly OV and their correlation with the size of varices.

Patients and methods: Sixty cirrhotic patients were recruited to participate in upper gastrointestinal endoscopy screening (for the presence and size of OV and portal hypertensive gastropathy) and abdominal ultrasonography screening (for PVD, SVD, SLD, and large spontaneous shunts). Fasting blood ammonia, PLT/SLD ratio were measured.
Results: Apart from PLT/SLD ratio; blood ammonia, PVD, SVD and SLD were significantly higher in patients with OV than those without ($P < 0.001$ for all). Using area under receiver operating characteristic curve (AUC), these parameters were good predictors for the presence of OV where, PVD had the highest AUC (I.00) followed by ammonia (AUC 0.99). Blood ammonia positively correlated with the size of varices (rho = 0.442, $P = 0.002$).
Conclusion: Blood ammonia, PVD, SVD and SLD were good non-invasive predictors for OV with the superiority of PVD and ammonia. Blood ammonia could be clinically useful, as it correlated with size of OV so, pinpoint those patients requiring closer follow-up and endoscopic screening.

Topic 18: Liver Cirrhosis and Complications

No: 2171

Non invasive predictors of esophageal varices in patients with chronic viral hepatitis associated cirrhosis

Güray Can[1], Uğur Korkmaz[2], Hatice Can[3], Bülent Yılmaz[2], Emrah Çağlar[4], Emrah Poşul[1], Mevlüt Kurt[1]

Abant Izzet Baysal University, Faculty of Medicine Department of Gastroenterology Bolu-Turkey[1], Bolu Izzet Baysal State Hospital Department of Gastroenterology Bolu-Turkey[2], Abant Izzet Baysal University, Faculty of Medicine Department of Internal Medicine Bolu-Turkey[3], Bolu Izzet Baysal State Hospital Department of Radiology Bolu-Turkey[4]

Aims: It is known that there are some non-invasive parameters in the prediction of the presence of esophageal varices caused serious complications. In this study, non-invasive parameters in prediction of existence of varices are evaluated among the patients who have a chronic hepatitis B and C associated chronic liver disease.
Methods: Eighty-one cirrhotic patients with hepatitis B and C were included in the study. Determination of platelets number and ultrasonographic evaluation (spleen size, portal and splenic vein diameter, portal flow) was performed to patients on admission. The relationship between laboratory and radiological data and varices was analyzed. The sensitivity and specificity values were calculated by ROC analysis. We also assessed the significant data that can be predictors of the presence of varices by using regression analysis.
Results: Sixty-nine out of 81 patients were chronic hepatitis B related cirrhosis and 12 of them were chronic hepatitis C related cirrhosis. Twenty-eight of patients (35 %) were female and 53 of them (65 %) were male. The average age was 59 (± 10). Thirty-nine of patients (48 %) were Child-A, 25 (31 %) were Child-B and 17 (21 %) were Child-C. Observing the results of 69 patients with varices and 12 patients without varices, it was found that there were significant difference in Child score, platelet number, spleen size, portal vein diameter and rate of platelet number/spleen (mm). Among these data, it was found that only platelet number/spleen size rate can predict presence of varices. ($P = 0{,}001$).
Conclusion: Platelet number/spleen size rate is a significant non-invasive factor in predicting of existence of varices in cirrhotic patients.

Topic 18: Liver Cirrhosis and Complications

No: 1650

The diagnostic accuracy of red cell distribution width to platelet ratio in assessment of liver fibrosis in patients with chronic hepatitis B

Wonseok Kang[1], Beom Kyung Kim[1], Seung Up Kim[1], Jun Yong Park[1], Do Young Kim[1], Sang Hoon Ahn[1], Young Nyun Park[2], Kwang Hyub Han[1]

Yonsei University Internal Medicine Seoul-Korea, South[1], Yonsei University Pathology Seoul-Korea, South[2]

Background/aim: Precise assessment of liver fibrosis is necessary in patients with chronic liver diseases. We investigated the performance of red cell distribution width (RDW)-to-platelet ratio (RPR) for the assessment of liver fibrosis in patients with chronic hepatitis B (CHB).
Methods: In consecutive 482 patients with CHB who underwent liver biopsy between October 2005 and May 2011 were recruited. Liver stiffness (LS) using transient elastography (TE), FIB-4, RPR, and aspartate aminotransferase-to-plate ratio index (APRI) were assessed.
Results: Among the study population, 56.2 % (n = 271) were male and the median age was 44 years. F1, F2, F3 and F4 fibrosis stage were identified in 68 (14.1 %), 137 (28.4 %), 64 (13.3 %) and 213 (44.2 %) patients, respectively. The mean RPR increased with severity of liver fibrosis: F1, 0.065; F2, 0.077; F3, 0.097; and F4, 0.121 ($P < 0.01$). The area under the receiver operating characteristic curve (AUROC) of RPR for predicting $\geq$ F2 was 0.747, which was inferior to TE (0.866, $P = 0.004$), but comparable to FIB-4 (0.782, $P = 0.427$) and APRI (0.716, $P = 0.507$). The AUROC of RPR for predicting F4 was 0.811, which was inferior to LS (0.915, $P < 0.001$), but comparable to FIB-4 (0.804, $P = 0.805$) and superior to APRI (0.680, $P < 0.001$). Using the optimized cut-offs (0.10 and 0.16), RPR correctly predicted 95.5 % of cases with $\geq$ F2 and 80.5 % of cases with F4.
Conclusions: RPR showed acceptable accuracy in assessing $\geq$ F2 and F4 in patients with CHB. Thus, RPR can be used to reduce the need for liver biopsy in patients with CHB when TE is not available.

Topic 18: Liver Cirrhosis and Complications

No: 2205

Esophageal varices as an additional site for platelet sequestration effect of variceal eradication on platelet count

Ahmed Abdulghany[1], Taher Elzanaty[2], Mona Hegazy[2]

Faculty of Medicine, Cairo University Internal Medicine and Gastroenterology Cairo-Egypt[1], Faculty of Medicine, Cairo University Internal Medicine Cairo-Egypt[2]

Background: Abnormalities in hematological parameters are common in patients with cirrhosis due to portal hypertension-induced sequestration, alterations in bone marrow stimulating factors, viral- and toxin-induced bone marrow suppression and consumption or loss. The aim of this work was to study the effect of variceal eradication either by endoscopic band ligation or injection sclerotherapy on platelets count.
Methods: This study was conducted from Jan 2011 to Aug 2011 on 43 patients with liver cirrhosis, child group A and B, with esophageal varices. Presented by hematemesis or had endoscopic feature indicating either band ligation or injection sclerotherapy. Patients were divided into 2 groups. Group I (22 patients) undergone band ligation and, group II (21patients) undergone injection sclerotherapy. Ten liver cirrhosis patients Child group A, and B on 40 mg probranolol/day were the control group. All patients were followed for 3 month.
Results: Platelet count showed significant ($P = 0.024$) elevation in the Third compared to month 0 in Control group on B-blocker. Platelet count showed no changes all the 3 month in group I & II.
Conclusion: Medical portal decompression using 40 mg probranolol/day effectively increased platelet count, while eosophageal eradication either by injection sclerotherapy or band ligation had no short term effect on platelet count.

Topic 18: Liver Cirrhosis and Complications

No: 2027

The preliminary study of long term administration of tolvaptan for refractory ascites due to liver cirrhosis

Ayako Mine[1], Shigemune Bekki[1], Rikako Kinoshita[1], Yuki Kugiyama[1], Ryu Sasaki[1], Satoru Hashimoto[1], Akira Saeki[1], Shinya Nagaoka[1], Seigou Abiru[1], Kazumi Yamasaki[1], Atumasa Komori[1], Hiroshi Yatsuhashi[1]

Nagasaki Medical Center Clinical Research Center Nagasaki-Japan[1]

Background & aims: Tolvaptan is an orally effective, nonpeptide antagonist that selectively blocks the binding of arginine vasopressin to V2 receptors. It was reported that tolvaptan decreased body weight and improved intractable ascites and edema in patients with decompensated liver cirrhosis, but there were few reports of long term administration of tolvaptan. The aim of this study was to clarify the characteristics of patients with long term administration of tolvaptan.
Patients & methods: A total of 44 patients with liver cirrhosis having a refractory ascites received tolvaptan in National Hospital Organization Nagasaki Medical Center between November 2010 and July 2014. Among them, twelve patients (group A) had tolvaptan more than 90 days, and ten patients (group B) discontinued tolvaptan within 30 days from the administration because of side effects or reduced response. We compared clinical characteristics of these two groups.
Results: In comparison between group A and B, there were significantly different in weight change after one week from the administration (-2.60 and -0.68 kg, $P = 0.007$), pretreatment serum potassium concentration (3.9 and 4.5 mEq/L, $P = 0.025$), and prothrombin activity of pretreatment (55.9 and 45.2 %, $P = 0.005$).
Consideration & Conclusions: Our study shows that patients with good response to tolvaptan and preserved liver function had tolvatpan for a long time.

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No: 1157

Elevated TGF β1 IL-23 pathway is associated with the disease severity of hepatitis B virus related liver cirrhosis

Xueping Yu[1], Ruyi Guo[1], Milong Su[2], Chengzu Lin[1], Julan Li[1], Zhijun Su[1]

The First Hospital of Quanzhou Affiliated To Fujian Medical University Infectious Diseases Quanzhoku-China[1], The First Hospital of Quanzhou Affiliated To Fujian Medical University Clinical Laboratory Quanzhoku-China[2]

The TGF-β1/IL-23 pathway plays an important role in the process of cell injury and inflammation. Fibrosis arises from chronic liver injury

and ongoing hepatic inflammation. However, the involvement of the TGF-β1/IL-23 pathway in the fibrotic process of hepatitis B virus related-liver cirrhosis (HBV-LC) remains unclear. This study was aimed to investigate TGF-β1/IL-23 expression at different stages of chronic HBV infection. The quantitative serum levels of TGF-β1, IL-9, IL-10, IL-17, IL-22, IL-23, IL-31, IL-33 and IL-35 were analyzed among patients with chronic hepatitis B (CHB, n = 19) and HBV-LC (n = 20) and the normal control (NC, n = 18). Disease severity in patients with HBV-LC was assessed with the MELD scores. Serum TGF-β1 levels were strongly positively correlated with IL-31 in all subjects, and both of them were positively correlated with IL-22, IL-33 and IL-17. In CHB and HBV-LC patients, TGF-β1 and IL-31 levels were both increased significantly compared with NC and positively correlated with GLB, AFP, Cr, WBC and PLT levels. HBV-LC patients showed the highest serum levels of TGF-β1 and IL-31, which were positively correlated with MELD scores. Furthermore, levels of TGF-β1 and IL-31 were markedly up-regulated in HBV-LC patients who did not have esophageal varices, and IL-31 displayed the highest sensitivity and specificity (90.9 % and 66.7 %; respectively) if it were used for correlating no occurrence of esophageal varices in HBV-LC patients. In summary, the TGF-β1/IL-23 pathway was elevated along the progress from CHB to LC and was well correlated with the severity of HBV-LC suggesting possible roles of TGF-β1/IL-23 pathway in the pathogenesis of liver fibrosis.

Topic 18: Liver Cirrhosis and Complications

No: 1788

Etiological distribution and clinical features of cirrhotic patients single tertiary referral center experience

Ayhan Balkan[1], Samet Alkan[2], Sezgin Barutçu[1], Buğra Tolga Konduk[1], Abdullah Emre Yıldırım[1], Ramazan Erdem Er[1], Murat Taner Gülşen[1]

Gaziantep University Faculty of Medicine Gastroenterology Gaziantep-Turkey[1], Gaziantep University Faculty of Medicine Internal Medicine Gaziantep-Turkey[2]

Aim: Cirrhosis has various etiologies, and the etiologic distribution differs from center to center. Our aim is to reveal the etiological distribution and clinical features of cirrhotic patients.
Methods: We retrospectively recruited 1144 patients. of patients, 480 were cirrhotic, 664 were non-cirrhotic. Patients were diagnosed by means of clinical features, laboratory values, radiologic imaging and biopsy when required.
Results: Of the 480 cirrhotic patients, 250 were male (52 %), and the mean age was 57.6 years. Distribution of etiological causes is summarized in table 1. In cirrhotics, 239 (49.7 %) patients were decompensated. However, HBV-HCV coinfection and Budd-Chiari syndrome found to have highest tendency of decompensation (85.7 %, 84.6 % respectively). Child Pugh classification was evaluated: A, B, C: 243 (50.6 %), 164 (34.2 %), 73 (15.2 %) respectively. Ascites in 206 (42.9 %), hepatic encephalopathy in 55 (11.4 %), hepatocellular carcinoma in 23 (4.7 %), and spontaneous bacterial peritonitis in 17 (3.5 %) of the patients were determined. In the group of patients with viral etiology, while 160 (53.9 %) of 297 cirrhotic patients were HCV, 137 (46.1 %) were HBV, 503 (75.8 %) out of 664 non-cirrhotic were HBV, 161 (24.2 %) were HCV infected.
Conclusion: Although HBV was more common in chronic hepatitides, cirrhosis was mostly caused by HCV infection. The reason of this may be due to anti-viral use for HBV. We found that decompensation rate was higher for Budd-Chiari syndrome and HBV-HCV coinfected patients. Cryptogenic cirrhosis still continues to have high prevalence. The reason for this may be undiagnosed autoimmune liver disease, non-alcoholic steatohepatitis, occult HBV or gluten enteropathy.

Topic 18: Liver Cirrhosis and Complications

No: 1868

Epidemiology of liver cirrhosis in Ankara single centre study

Zeliha Asilturk[1], Sebahat Basyigit[2], Yasar Nazligul[3], Metin Uzman[4], Bora Aktas[2]

M.d. Internal Medicine Ankara-Turkey[1], M.d. Gastroenterology Ankara-Turkey[2], Prof. Gastroenterology Ankara-Turkey[3], Associate Prof. Gastroenterology Ankara-Turkey[4]

Background: Chronic liver disease (CLD) is one of the most common cause of mortality in the world. The causes of CLD differ between countries and regions in the same country. But, no reliable data exist about this. It is important to examine the epidemiology of CLD because of it is a reasonably preventable disease. Our study is aimed to determine the epidemiological characteristics and etiological causes of CLD.
Method: Data of patients with liver cirrhosis presenting to outpatient and inpatient clinics at a single medical centre in Turkey (Kecioren Training and Research Hospital) from 1 January 2011 to 31 September 2014 records were examined for liver cirrhosis.
Results: 135 patients included in the study (91 male patients (67 %) and 44 female patients (33 %),with a mean age of 63 ± 14,3 years (range: 15–87 years). The major causes of cirrhosis were: chronic hepatitis B (HBV), n = 52, 38.5 % and cryptogenic, n = 33, 24,4 %; HBV was the main etiology in males (49.5 %) and cryptogenic was the predominant etiology in females (40.9 %). Patients with alcoholic cirrhosis were absolutely male. Ratio of autoimmune hepatitis was higher in female (70 %). HBV was significantly higher (63 %) and HCV was significantly lower (3.7) in patients under 60 years of age compared to patients over 60 years of age (respectively 32.4 % and 27 %).
Conclusion: Because national vaccination programme has started in 1998 for HBV, it is the most common cause in adult population in our country.

Topic 18: Liver Cirrhosis and Complications

No: 1912

High dose oral furosemide with salt ingestion in the treatment of refractory ascites of liver cirrhosis

Ender Serin[1], Tolga Yakar[1], Özlem Doğan[2]

Baskent University School of Medicine Gastroenterology Adana-Turkey[1], Baskent University School of Medicine Internal Medicine Adana-Turkey[2]

Aim: Refractory ascites is a critical and difficult-to treat complication of advanced liver cirrhosis. Patients with this condition were evaluated fort the efficacy and safety of high dose furosemide (intravenously or orally) with hypertonic saline solution (HSS) intravenously (i.v.) or salt orally.
Methods: Patients (37 men and 19 women, age range 35-85 years) were assigned to receive i.v. furosemide (200-300 mg b.i.d.) and 3 % HSS (one or two times a day) (20 patients, group A) or furosemide tablets orally (360-520 mg b.i.d.) and salt orally (2.5 grams b.i.d.) (9 patients, group B) or total paracentesis with albumin infusion (27 patients, group C). Patients without hyperkalemia received 100 mg of spironolactone/day during treatment period.

Results: In group A and B patients remarkable increase in diuresis were observed after beginning to treatment (706 ± 116 mL vs 2425 ± 633 mL and 691 ± 111 mL vs 2405 ± 772 mL). Serum sodium levels were improved in both groups, as well. Hepatic encephalopathy and spontaneous bacterial peritonitis were significantly occured more in group C patients than the others ($P < 0.002$). Hospitalization for ascites decreased significantly in group B patients ($P < 0.001$). There was no significant difference in survival among groups.
Conclusion: This small sized study suggests high dose oral furosemide with salt ingestion can be an alternative, effective, safe and well tolerated method of therapy for refractory ascites as well as high dose i.v. diuretic plus HSS infusion.

Topic 18: Liver Cirrhosis and Complications

No: 2070

Correlation of ascitic fluid and venous blood electrolytes in cirrhotic patients

M. A. Rahim[1], Sheikh Mohammad Noor-e Alam[2], Mohammad Faiz Ahmad Khondaker[3], Ahmed Lutful Moben[4], Mamun Al-Mahtab[5], Salimur Rahman[5]

Mats Noakhali Mats Noakhali-Bangladesh[1], Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh Hepatology Dhaka-Bangladesh[2], Shaheed Suhrawardy Medical College Hospital, Hepatology Dhaka-Bangladesh[3], Shaheed Suhrawardy Medical College, Dhaka Medicine Dhaka-Bangladesh[4], Bsmmu Hepatology Dhaka-Bangladesh[5]

Aim: Serum electrolytes derangement is common in cirrhotic patient. Ascitic fluid electrolytes related to various complications during ascitic fluid management. This study is directed to find out any relationship between ascitic fluid and serum electrolytes.
Method: A cross sectional observational study was conducted between 2011-2012 in Hepatology department of BSMMU. Total 50 patients of different etiologies were included.Most of them 54 % related to HBV followed by 38 % non-B non-C. Mean age of the patient were 45.68 ± 13.8 years. Male: Female were 4: 1. Data was analyzed by SPSS 17.
Result: Sodium, potassium, chloride were analyzed.Positive statistically significant correlation were found all three sets of data.
Conclusion: From this study we may suggest that ascitic fluid electrolytes are a reflection of serum electrolytes. In cirrhotic patient ascitic fluid electrolytes directly correlated with serum electrolytes. So measurement of ascitic fluid electrolytes can be an alternative of serum electrolytes as a monitoring tool for cirrhotic patient, especially on diuretics therapy.

Topic 18: Liver Cirrhosis and Complications

No: 1067

Distinct effecacies on the reversal of TGF β1 and aberrant igg glycosylation in patients with liver cirrhosis between entevavir and telbivudine

Cheng-hsun Ho[1], Rong-nan Chien[2], Shu-hui Chen[3], Ting-tsung Chang[1]

National Cheng Kung University Hospital Department of Internal Medicine Tainan-Taiwan[1], Chang Gung Memorial Hospital Liver Research Unit Keelung-Taiwan[2], National Cheng Kung University Department of Chemistry, Tainan-Taiwan[3]

Background: The pharmaceutical effects of different antiviral therapies on the reversal of aberrant serum IgG N-glycome in patients with liver cirrhosis have never been assessed.
Methods: Thirty-nine entecavir-naive and 29 telbivudine-naive patients with HBV-related liver cirrhosis who had been treated for at least 48 weeks were enrolled.
Serum IgG N-glycome and cytokine profiles in patients before and after treatment were analyzed using liquid chromatography-mass spectrometry and enzyme-linked immunosorbent assay, respectively.
Results: The level of serum galactose-deficient (total G0) IgG in patients decreased after 48 weeks of entecavir treatment ($P < 0.001$) but increased after telbivudine treatment ($P < 0.05$). Moreover, the increase of IgG-Fc sialylation was only detected in patients with entecavir treatment. In regard to serum cytokine profiles, 48 weeks of entecavir treatment resulted in stronger declines in serum interleukin (IL)-8 ($P < 0.05$) and transforming growth factor (TGF)-β1 ($P < 0.05$) levels in patients than did telbivudine. From baseline to week 48, the change in TGF-β1 level (ΔTGF-β1) was correlated with the change in galactose-deficient (Δtotal G0, r = 0.456; $P < 0.001$), fully galactosylated (Δtotal G2, r = -0.324; $P < 0.01$), and sialylated (Δtotal S, r = -0.316; $P < 0.01$) IgG levels. Baseline levels of IgG-G0F and IgG-G2FS glycoforms were significantly correlated with the change in total serum IgG level after 48 weeks of treatment.
Conclusions: Forty-eight weeks of entecavir but not telbivudine treatment reversed aberrant serum IgG N-glycosylation in patients with HBV-related liver cirrhosis. TGF-β1 might determine the efficacies of different antiviral therapies on the restoration of serum IgG N-glycosylation.

Topic 18: Liver Cirrhosis and Complications

No: 1901

Development of a smartphone application to enable remote monitoring in the outpatient management of cirrhotic ascites

Phil Ha[1], Sherryne Warner[2], Paul O[2], Patricia anderson[2], Dilip Ratnam[2], Anouk Dev[2], Suong Le[2], William Sievert[2]

Monash University Faculty of Medicine Melbourne-Australia[1], Monash Health Department of Gastroenterology & Hepatology Melbourne-Australia[2]

Patients who develop hepatic decompensation with ascites have a poor prognosis and often experience other complications including spontaneous bacterial peritonitis, hepatic encephalopathy and variceal bleeding. We hypothesised that smartphone (SP)-enabled remote monitoring of patients with ascites may enable early detection of infection and acute decompensation, facilitate timely intervention and improve patient outcomes. This pilot study aimed to design, develop and implement a remote monitoring system (RMS) for outpatients with cirrhotic ascites. Surveys were undertaken with patients and hepatologists to quantify the demand for a RMS and identify issues regarding implementation. A native app for android SP and a web-based app for all other internet-enabled devices were developed. Patients used the RMS in a 6-week prospective non-randomised trial. 27 patients (mean age 56 years, 67 % male, 54 % Child-Pugh B, 74 % alcoholic liver disease) and 5 hepatologists were surveyed. 65 % of patients reported that they would use a RMS. The system schematic (Fig. 1) and apps (Fig. 2) were designed based on survey data. 9 patients used the RMS for a mean 40.3 days and entered 15 ± 14.5 updates. 13 automated alerts occurred, of which 30 % resulted in clinically significant changes to management (inpatient

admission n = 1, outpatient appointment n = 2, avoided admission n = 1). Isolated weight gain (3 kg) had the least predictive value for requiring intervention (12.5 %); presence of symptoms had the highest predictive value for changing management (60 %). We have successfully designed an internet-enabled RMS for outpatients with cirrhotic ascites that could be an adjunct to nurse-lead clinics. Future studies will optimise the alert thresholds, assess long-term patient adoption and quantify clinical impact.

Topic 18: Liver Cirrhosis and Complications

No: 2178

Potential effects of anemia in hepatorenal syndrome

Gokhan Gungor[1], Murat Akyildiz[2], Muharrem Keskin[1], Yalcin Solak[3], Abduzhappar Gaipov[4], Murat Biyik[5], Sami Cifci[6], Huseyin Ataseven[6], Hakki Polat[6], Ali Demir[6]

Konya Training and Research Hospital Gastroenterology and Hepatology Konya-Turkey[1], Bilim University, Florence Nightingale Hospital Liver Transplantation Center Gastroenterology and Hepatology Istanbul-Turkey[2], Sakarya Training and Research Hospital Nephrology Sakarya-Turkey[3], National Scientific Medical Research Center Nephrology Astana-Kazakhstan[4], Adiyaman Training and Research Hospital Gastroenterology Adiyaman-Turkey[5], Neu Meram School of Medicine Gastroenterology Konya-Turkey[6]

Introduction: Hepatorenal syndrome (HRS) is a severe complication of cirrhosis which is characterized by renal dysfunction and associated with poor survival. Anemia is a non-rare condition in advanced liver cirrhosis. Studies have demonstrated that anemia can cause renal tissue ischemia/hypoxia and it may play a potential role in the pathogenesis of kidney injury. We aimed to investigate clinical effects of anemia on renal functions in HRS.

Materials and methods: A total of 29 cirrhotic patients with HRS who fullfilled HRS diagnostic criteria (9 patients with type 1HRS, 20 with type 2 HRS) and 37 cirrhotic patients without HRS were included in the study. Correlation and regression analysis were performed among the anemia parameters and renal functions.

Results: Patients with type 1 and type 2 HRS had significantly lower hemoglobine concentrations and hematocrites compared with non-HRS cirrhosis (Table 1). There was a negative correlation between hematocrite and serum creatinine ($r = -0.583$, $P < 0.001$). The higher CTP and MELD scores, higher ascites grades, lower hemoglobine and hematocrite levels were associated with higher creatinine levels and lower creatinine clearance (Figure 1).

Discussion: Anemia may facilitate the HRS and deteriorate the renal functions in HRS. While variceal bleeding causes volume depletion, anemia causes chronic ischemia. Anemia can lead to microcirculary renal ischemia, tissue hypoxia and tubular damage in kidney and can increase sympathetic activity in pathogenesis of HRS. In our knowledge, there is no publication about the pathogenetic effect of anemia in HRS. Finally, inclusion of severe anemia as a precipating factor in HRS and also its role in pathogenesis of HRS can be discussed.

Topic 18: Liver Cirrhosis and Complications

No: 1470

The sensitivity and specificity of inhibitory control test in the diagnosis of minimal hepatic encephalopathy a Meta analysis

M.t. Panlilio[1], A. Taguba[1], M.e. Villamayor[1], J. Ong[1]

University of The Philippines-Philippine General Hospital Section of Gastroenterology Manila-Philippines[1]

Minimal hepatic encephalopathy (MHE) is a complication of liver cirrhosis that does not show symptoms of overt hepatic encephalopathy. MHE has a subtle but negative impact on a patient's life, which includes the ability to perform complex tasks such as driving.

Diagnosis of MHE is difficult, as the absence of clinical evidence of encephalopathy is key to its diagnosis. Psychometric Hepatic Encephalopathy Score (PHES) is accepted as a reference standard. Inhibitory Control Test (ICT), a simple computer-assisted outpatient test, may be a good tool for detecting MHE.

Search was done on COCHRANE and MEDLINE for articles from January 2003 to October 2013. Studies included were those that compared ICT with the accepted reference standard in cirrhotics. Three studies met the inclusion criteria. Data analyses were performed using Meta-Disc. Summary estimates of sensitivity, specificity, likelihood ratios, and diagnostic odds ratio were calculated.

The search identified 133 studies. Based on pre-stated criteria, three studies were included in the final review. There were 235 patients with liver cirrhosis and a matched control group that underwent both psychometric testing and ICT. Pooled data showed that the ICT had a sensitivity of 88 % ($I2 = 0$ %) and specificity of 72 % ($I2 = 69.2$ %). A symmetrical sROC depicted an area under the receiver operator curve (AUC) of 0.89.

ICT is a good tool to exclude cirrhotic patients without minimal hepatic encephalopathy. It is effective in discriminating patients with MHE from those without MHE. It has potential as a screening test. However, more high-quality studies are needed to establish test accuracy.

Topic 18: Liver Cirrhosis and Complications

No: 1094

Mortality related risk factors for culture positive spontaneous bacterial peritonitis

Elif Sahin Horasan[1], Fehmi Ates[2], Enver Ucbilek[2], Orhan Sezgin[2], Ali Kaya[1]

Mersin University Infectious Diseases Mersin-Turkey[1], Mersin University Gastroenterology Mersin-Turkey[2]

We aimed to evaluate mortality related risk factors in chirotic patients with culture positive-SBP.

All patients who had culture-positive SBP in patients with chirosis between January 2004 to January 2013 at the University of Mersin through searching records were identified retrospectively. Clinical data were recorded on standardized forms and analyzed for age, gender, clinical and laboratory, ascit culture results and antimicrobial susceptibility findings. Spontaneous bacterial peritonitis is defined as a positive bacterial finding in ascites, together with increased polymorphonuclear leukocytes in ascites (> 250 cells/mm3).

52 patients were retrospectively included into the study. The mean age of the patients was 62,5 years, 59 % of the patients were male, 48 % had hepatic cirrosis of viral etiology (HBV, HCV). Hospital mortality rate was 44 %. A total of 52 isolates were recovered from the cases of SBP. E.coli was the most common isolate overall (n = 17, 32.7 %) and Coagulase-negative Staphylococcus spp. (CoNS) (n = 14, 27 %) was the second common isolate. In statistical comparison, Hepatic encephalopathy ($P = 0.031$), fever ($P = 0.032$), Renal failure ($P = 0.005$)) were found to significantly associated with mortality. In laboratory tests,

lower thrombocyte count significantly associated with hospital mortality ($P = 0.02$). Other factors (age, gender, vital signs, during of cirrhosis, etiology of cirrhosis, complications, laboratory findings) were not found statistical associated.

Hepatic encephalopathy, fever, Renal failure and lower thrombocyte count were found to significantly associated with hospital mortality in patients with culture-positive SBP.

Topic 18: Liver Cirrhosis and Complications

No: 1922

Therapeutic strategy for patients with liver cirrhosis complicating bleeding gastric fundal varices

Yohei Fujii[1], Yukinori Imai[1], Masashi Takano[1], Keisuke Shiokawa[1], Hiroshi Uchiya[1], Taku Chikayama[1], Manabu Nakazawa[1], Satsuki ando[1], Mie Inao[1], Nobuaki Nakayama[1], Masashi Oka[1], Satoshi Mochida[1]

Saitama Medical University Gastroenterology and Hepatology Saitama-Japan[1]

Aim: Endoscopic injection sclerotherapy (EIS) with α-cyanoacrylate monomer (CA) is useful for initial hemostasis of bleeding gastric fundal varices, while bleeding from the lesions recurs in frequent. The usefulness of therapeutic strategy combined with endoscopic therapies and balloon-occluded retrograde transvenous obliteration (B-RTO) for such patients was evaluated.
Methods: 49 consecutive patients with liver cirrhosis showing bleeding from gastric fundal varices were enrolled. EIS with CA was done for initial hemostasis, and then either additional therapies were performed; B-RTO for patients with gastro-renal shunts (GRS) and EIS using ethanolamine oleate as well as CA for those without GRS. Additional therapies were not done in patients of Child-Pugh class C and/or those showing complete occlusion of GRS following initial hemostasis.
Results: EIS with CA were done in 42 patients, and initial hemostasis was achieved in all of these patients. Spontaneous hemostasis was obtained in the remaining 7 patients. 36 patients with GRS were subjected to B-RTO, and the procedures were successfully done in 34 patients (94 %). 3 patients without GRS received EIS again. Also, EIS was repeatedly done in 2 patients in whom B-RTO failed to occlude GRS. No patients showed rebleeding from gastric varices over a medium observation period of 19 months. The cumulative survival rates at 1, 3, 5 years were 91, 73 and 65 %, respectively, with the cumulative esophageal varices exacerbation of 9, 27 and 35 %, respectively.
Conclusions: Therapeutic strategy combined with endoscopic therapies and B-RTO was useful for patients with liver cirrhosis showing bleeding from gastric fundal varices.

Topic 18: Liver Cirrhosis and Complications

No: 2138

Etiology and natural course of end stage liver disease in the real world setting

Xheni Deda[1], Cagdas Kalkan[1], Onur Keskin[1], Ali Tuzun[1], Mustafa Yakut[1], Guner Kilic[1], Fatih Karakaya[1], Ramazan Idilman[1]

Ankara University Gastroenterology Ankara-Turkey[1]

Background and aim: The aims of this study were to describe etiology and natural course of end-stage liver disease of 757 cirrhotic patients in clinical practice.
Materials and methods: A total of 757 patients diagnosed with end-stage liver disease were included into this analysis. Cirrhosis was defined clinically and histologicaly when available. The median follow-up period was 33 months.
Results: Median age was 59.0 years, and 60 % were male. Hepatitis B virus (HBV) was the most common cause of end-stage liver disease (34 %), followed by hepatitis C virus (HCV) (17 %), cryptogenic (16 %), fatty liver diseases (10 %), autoimmune liver diseases (8 %), hepatitis delta virus (6 %) and others. During admission, 34 % of the patients had compensated disease, and 46 % were Child-Pugh class A, 46 % class B and 8 % class C. Median MELD score was 11. Ascites was the most common sign of the decompensation (56 %), followed by variceal haemorrhage (19 %) and hepatic encephalopathy (18 %). Forty-five had diagnosed with hepatocellular carcinoma (HCC).

During the follow-up period, 22 % of the compensated patients were progressed to decompensated stage, and 38 developed de novo HCC. HCC occurred more frequently in patients with HBV-induced cirrhosis (71 %) and followed by HCV-induced cirrhosis (18 %). Eight percent of the patients underwent liver transplantation. The overall mortality was 12.0 %.
Conclusion: Based on the result of the present study, HBV infection remains the leading cause of the end-stage liver disease and HCC in Turkish population. Hepatic decompensation and HCC may still develop, though at a lower rate in natural course of disease.

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No: 1109

Safety and efficacy of eltrombopag olamine in patients with thrombocytopenia on the background of hepatitis C virus related cirrhosis of liver initial experience from a tertiary centre in Bangladesh

Mamun Al Mahtab[1], Sheikh Mohammad Fazle Akbar[2], Salimur Rahman[1]

Bangabandhu Sheikh Mujib Medical University Hepatology Dhaka-Bangladesh[1], Toshiba General Hospital Medical Sciences Tokyo-Japan[2]

Aim: Eltrombopag olamine is a relatively new agent, indicated for correction of thrombocytopenia in HCV cirrhotics and ITP patients. Aim of this study was to assess safety and efficacy of this agent in Bangladeshi patients with HCV cirrhosis.
Methods: 15 patients, 38- 66 years, 5 females, 10 males were recruited. All had thrombocytopenia on background of HCV liver cirrhosis. Cause of thrombocytopenia was hyperspleenism in 6 and pegylated interferon induced in rest. Baseline platelet count was between 30,000-60,000/cmm. All received eltrombopag olamine 25 mg orally daily for 28 days. Platelet count was repeated after 28 days.
Results: At end of treatment, platelet count was >90,000/cmm in 13 patients. of these 13 in all but 2, count was >150,000.
Conclusion: This study demonstrates safety and efficacy of eltrombopag olamine in Bangladeshi HCV cirrhotics with thrombocytopenia and results are comparable with that experienced elsewhere.

Topic 18: Liver Cirrhosis and Complications

No: 1360

Clinical effect of apelin on portal hypertension and prognosis of liver cirrhosis

Yoo Li Lim[1], Youn Zoo Cho[1], Moon Young Kim[1], Soon Koo Baik[1], Ki Tae Suk[2], Gab Jin Cheon[3], Young Don Kim[3], Dae Hee Choi[4]

Wonju Severance Christan Hospital Internal Medicine Wonju-Korea, South[1], Chuncheon Sacred Heart Hospital Internal Medicine Chuncheon-Korea, South[2], Kangneung Asan Hospital Internal Medicine Kangneung-Korea, South[3], Kangwon University School of Medicine Internal Medicine Chuncheon-Korea, South[4]

Backgrounds and aim: Apelin is an endogenous ligand of angiotensin like-receptor regulating body fluid. Several preclinical studies have reported a close correlation between serum apelin level (s-apelin) and hepatic fibrosis or hemodynamic abnormality however; no clinical data is available. So we investigated the clinical significance of s-apelin as a noninvasive biomarker in cirrhosis.
Methods: From January 2006 to December 2012, 215 patients who were undertaken clinical data collection, hepatic venous pressure gradient (HVPG) measurement and liver biopsy were enrolled. All patients have been prospectively observed until December 31, 2014 for the development of clinical decompensation and mortality.
Results: The mean age was 50.78 years (29-73). The most frequent cause of liver cirrhosis was alcohol (155, 72.1 %). The median follow-up period was 22 months. of the 215 subjects, 44 (20.5 %) expired during the study period. s-apelin showed significant correlation with Child-Pugh's score (Pearson's correlation coefficient (R2) = 0.079, $P < 0.001$) and MELD score (R2 = 0.1, $P < 0.001$). It also showed significant correlation with liver stiffness measured by transient elastography (R2 = 0.263, $P < 0.001$) and collagen proportion area (R2 = 0.213, $P < 0.001$). A significant, linear association between s-apelin and HVPG was also observed (R2 = 0.356, $P < 0.001$). In a multivariate analysis using Cox regression hazard model, s-apelin was valuable in predicting mortality (hazard ratio = 1.003, $P < 0.001$) and in a Kaplan–Meier analysis with cut-off value of 700 pg/mL, patients with s-apelin more than 700 pg/mL showed shorter mean survival time ($P < 0.001$).
Conclusion: This study confirmed a clinically significant association between s-apelin, PHT and histological severity of cirrhosis. It also showed a possibility of s-apelin as a prognostic biomarker for cirrhosis.

Topic 18: Liver Cirrhosis and Complications

No: 1963

A long non coding RNA n334975 is up regulated in tgf βtreated human hepatic stellate cell

Long Chen[1], Feng Liu[1], Lai Wei[1]

Peking University Hepatology Institute Beijng-China[1]

Background/aims: The hepatic stellate cell(HSC) activation is the hallmark in the initiation of hepatic fibrosis. Long non-coding RNAs(lncRNAs) are a class of newly described non-coding RNA longer than 200nt. Recent studies have revealed that lncRNAs are associated with HCC and may predict disease progression. However, the role of specific lncRNAs involved in the pathogenesis of hepatic fibrosis is not well elucidated. In this study, we observed the up-regulation of a lncRNA in TGF-β activated human HSC.
Methods: LX-2 cells were divided into TGF-β treated group (n = 3) and untreated group (n = 3), cells were treated with recombinant human TGF-β1 or medium vehicle for 20 days. To validate HSC activation by TGF-β, we analyzed α-smooth muscle actin (α-SMA) expression by qRT-PCR. We performed microarray to detected deregulated mRNA and lncRNA in TGF-β activated LX-2 cell. We used qRT-PCR to validated candidate up/down-regulated lncRNAs.
Results: α-SMA expression was significantly higher in TGF-β treated group ($P < 0.01$). We observed 220 up-regulated and 342 down-regulated genes in TGF-β treated group. 7 genes were associated with TGF-β signaling pathway by KEGG pathway analysis. We observed 119 up-regulated and 235 down-regulated lncRNAs in TGF-β treated group. n334975, a lncRNA recorded in NONCODE v4.0 database, with relatively high fold-change (1.69) was further validated by qRT-PCR. Consistent with microarray data, n334975 was significantly higher in TGF-βtreated group (n = 6) than untreated control (n = 6) by qRT-PCR ($P < 0.001$).
Conclusions: lncRNA-n334975 is up-regulated in TGF-β treated human hepatic stellate cell.Future validation study and functional study is needed to fully understand the role of n334975 in pathogenesis of hepatic fibrosis.

Topic 18: Liver Cirrhosis and Complications

No: 1568

A rare microorganism causing peritonitis listeria monocytogenes

Çınar Yildirim[1], Talat Ayyildiz[2], Murat Pekgöz[1], Kader Irak[3], Murat Kiyici[1], Selim Gürel[1], Selim Giray Nak[1], Macit Gülten[1], Enver Dolar[1]

Uludağ University Faculty of Medicine Gastroenterology Bursa-Turkey[1], 19 Mayıs University Faculty of Medicine Gastroenterology Samsun-Turkey[2], Kanuni Sultan Suleyman Education and Research Hospital Gastroenterology Istanbul-Turkey[3]

Introduction: Listeria monocytogenes is a rare cause of peritonitis and less than only 50 cases were reported in medical literature until now and there is no case reported from Turkey according to our knowledge. In this case we aimed to discuss the clinical course and treatment of spontaneous bacterial peritonitis (SBP) caused by L. Monocytogenes.
Case presentation: A 62 year-old male patient, who was diagnosed as liver cirrhosis due to autoimmune hepatitis, admitted to our hospital with fever, abdominal distension and abdominal pain. Physical examination and laboratory findings (WBC: 1.31 K/μL (Neu: 72,7 %) in the ascites analysis) were consistent with SBP. Despite the treatment with iv Cefotaxime his fever persisted and in the analysis of ascites WBC count was 1.19 K/μL (Neu: 85 %) by 48 h after antibiotherapy started. Then the antibiotherapy was switched to imipenem. In the fourth day of hospitalization tonic–clonic convulsions were observed and hypoxemia and hypercapnia were determined in arterial blood. The patient was diagnosed as Acute Respiratory Distress Syndrome, intubated and mechanically ventilated. Vancomycin was added to antibiotherapy because of persistance of the high temperature. In the sixth day of hospitalization, ascites and blood cultures were positive for L. monocytogenes. Vancomycin was stopped and ampicillin 3 g q6 h IV was added to the treatment. By the time Multiple Organ Dysfunction Syndrome was observed. The patient died in the eleventh day of hospitilization.

Conclusions: By considering listerial peritonitis, early ampicillin treatment (alone or combined with gentamicin) may be life-saving in patients who are unresponsive to conventional SBP antibiotherapy.

Topic 18: Liver Cirrhosis and Complications

No: 1523

Does etiology affect performance of liver stiffness measure in Chinese in liver fibrosis diagnosis by transient elastography

Bing Li[1], Dong Ji[1], Qing Shao[1], Fan Li[1], Guofeng Chen[1]

Military Hospital Liver Fibrosis Diagnosis and Treatment Center Beijing-China[1]

Aim: To evaluate whether etiology affect performance in liver stiffness measure (LSM) for liver fibrosis diagnosis by Transient elastography (TE) in Chinese patients.
Methods: In the retrospective study group, altogether 438 Chinese patients who underwent both liver biopsy and successful LSM during 2010 to 2012, were assessed. Area under the receiver operating characteristics(AUROC) was used to evaluate performance of LSM for diagnosing liver fibrosis compared with biopsy and optimal cut-off point was respectively calculated considering the different etiology. In prospective study group, two hundred and forty patients whose background is the same as patients in retrospective study group were enrolled from 2013 to 2014. With Optimal cut-off point considering or not considering the different etiology in liver fibrosis diagnosis, accuracy of diagnosis and necessity of applying different cut-off point according to etiology were assessed.
Results: Multivariate analysis found that LSM of all patients in retrospective study group correlated with etiology, fibrosis stage, ALB and Bilirubin. AUROC for LSM was 0.958, 0.953, 0.975, 0.958, 0.952 for fibrosis stage(F) >/=2 respectively for CHB, CHC, ALD, DILD, AILD and NAFLD and there was significant difference between different etiologies ($P = 0.000$). Cut-off points of LSM for severe fibrosis and cirrhosis in ALD and AILD are much higher than that of viral liver diseases. In retrospective study group, there was no statistically significant difference.
Conclusions: This study confirms that TE is a useful tool in noninvasive assessment of chronic liver fibrosis related with six clinical common etiologies. Cut-off points of LSM in viral liver diseases might be similar, but might be higher in ALD and AILD.

Topic 18: Liver Cirrhosis and Complications

No: 1570

Assessment of liver fibrosis with acoustic radiation force imaging (arfi) versus liver histology in patients with chronic hepatitis C a pilot study

Mohamed Kohla[1], Osama El-abd[2], Sameera Ezzat[3], El-sayed Tharwa[1], Samah Kohla[4], Mohamed Abdel-rahman[5]

National Liver Institute Hepatology Shebin El-kom-Egypt[1], National Liver Institute Radiology Shebin El-kom-Egypt[2], National Liver Institute Epidemiology Shebin El-kom-Egypt[3], Hamad Medical Corporation Laboratory Medicine and Pathology Doha-Qatar[4], National Liver Institute Pathology Shebin El-kom-Egypt[5]

Background: ARFI imaging involves the mechanical excitation of tissue with use of short-duration acoustic pulses to generate localized displacements in tissue. The displacements results in shear-wave propagation, tracked by using U/S correlation-based methods and recorded in meters per seconds.
Aim: To compare acoustic radiation impulse imaging technology (ARFI), integrated into a conventional Ultrasonography (US) with the standard histological examination of liver biopsy specimens for assessment of liver fibrosis.
Materials and methods: Eighty patients with chronic hepatitis C underwent ARFI as well as well as standard liver biopsy, the maximum time interval between ARFI and liver biopsy was 3 months. Histological staging was done using Metavir scoring system. Results of ARFI were compared to histological findings.
Results: ARFI findings were identical to the biopsy findings in 61 (76.25 %) patients, among the 20 patients diagnosed as having advanced fibrosis (F3 and F4) by histology, 20 of them, showed advanced fibrosis by ARFI, showing a sensitivity for diagnosis of advanced fibrosis of 100 %. Among the 26 patients who were found to have advanced fibrosis by ARFI (F3 and F4), only 6 of them were not found to have advanced fibrosis on biopsy, accordingly, AFRI could exclude correctly the presence of advanced fibrosis in 54 out of 60 patients, with a specificity of 90 %. ARFI showed a positive predictive value of 76.9 % and a negative predictive value of 100 %.
Conclusions: ARFI imaging is a promising non-invasive US-based method for assessment of liver fibrosis in chronic hepatitis C virus infected patients with a diagnostic accuracy comparable to that of liver.

Topic 18: Liver Cirrhosis and Complications

No: 1351

Comparison of the accuracy between liver and spleen elastography using acoustic radiation force impulse and other noninvasive tests in predicting the presence of esophageal varices

Yang-hyon Baek[1], Sang-young Han[1], Sung-wook Lee[1], Jin-sook Jeong[2], Hee-jin Kwon[3]

Dong-a University College of Medicine Division of Gastroenterology and Hepatology, Department of Internal Medicine Busan-Korea, South[1], Dong-a University College of Medicine Department of Pathology Busan-Korea, South[2], Dong-a University College of Medicine Department of Radiology Busan-Korea, South[3]

Purpose: This study aimed to evaluate the accuracy of liver elastography, spleen elastography, and other noninvasive tests (aspartate aminotransferase (AST)-alanine aminotransferase (ALT) ratio [AAR], AST: Platelets Ratio Index (APRI, platelet count, and platelet/spleen ratio) in predicting the presence of esophageal varices in liver cirrhosis.
Materials & methods: We studied 244 consecutive patients with hepatitis B virus (HBV) (n = 126), hepatitis C virus (HCV) (n = 49), or alcohol-induced liver cirrhosis (n = 69) who underwent biochemical tests, gastrointestinal endoscopy, and liver and spleen elastography by acoustic radiation force impulse (ARFI). The median liver and spleen stiffness values from 5 successful measurements per participant were obtained.
Result: Among the 244 patients, spleen elastography was not reliable in 64 patients. Among the 180 patients with a valid measurement, 43 % had no esophageal varices, whereas the others had esophageal varices. On univariate analysis, the platelet count, platelet/spleen ratio, and spleen elastography were independently associated with esophageal varices. However, in cases of alcohol-induced liver cirrhosis, spleen stiffness was not reliable for prediction of esophageal varices.

Conclusion: The liver and spleen stiffness values measured by ARFI elastography are well correlated, and spleen stiffness measured by ARFI can potentially be used as a non-invasive method for determining the presence of esophageal varices. However, the evidence supporting a similar role for replacing endoscopy is lacking because spleen stiffness is less reproducible compared to liver stiffness and, further, it is not an appropriate predictor for esophageal varices in alcoholic cirrhosis.

Topic 18: Liver Cirrhosis and Complications

No: 1624

The efficacy of tolvaptan as a treatment for refractory ascites in advanced cirrhosis patients with chronic kidney disease

Tomoharu Yamada[1], Takamasa Ohki[1], Koki Sato[1], Nobuo Toda[1], Kazumi Tagawa[1]

Mitui Memorial Hospital Gastroenterology Tokyo-Japan[1]

Objective: Ascites or pleural effusion is one of the most common complications for patients with liver cirrhosis. The aim of this study was to evaluate the efficacy and safety of tolvaptan in Japanese cirrhosis patients with refractory ascites or pleural effusion.
Method: In this retrospective study, we enrolled 40 cirrhosis patients with refractory ascites or pleural effusion between October 2012 and November 2013. Patients were hospitalized and maintained tolvaptan on between 3.75 mg and 15 mg once daily until their symptom had been improved.
Result: Of the 40 patients, 32 (80.0 %) patients were male and the median age was 64.7 years. The main cause of liver cirrhosis was hepatitis C virus infection (N = 22, 55.0 %) and 13 (32.5 %) patients were Child-Pugh class C. The median estimated glomerular filtration rate (eGFR) was 38.1 ml/min/1.73m2 which indicated existence of chronic kidney injury (CKD) equal to stage 3. Finally, 25 (62.5 %) patients achieved improvement. Mean serum sodium concentration 24 h after administration was 135.2 mEq/l and reached a maximum of 138.3 mEq/l at day 4. Multivariate logistic regression analysis which were adjusted for significant factors in univariate analysis showed that only uncontrollable hepatocellular carcinoma as an independent factor for failure of improvement (hazard ratio = 0.19; 95 % CI, 0.04 to 0.98; $P = 0.048$).
Conclusion: Tolvaptan significantly improves ascites or pleural effusion in cirrhosis patients with CKD stage3.

Topic 18: Liver Cirrhosis and Complications

No: 2208

Vitamin D deficiency in patients of liver cirrhosis a nepalese study

Dilip Sharma[1], Sudhamshu K.c.[1]

Nams, Bir Hospital Liver Kathmandu-Nepal[1]

Background: Many studies done in recent years have demonstrated a very high prevalence of vitamin D deficiency and insufficiency in patients of liver cirrhosis. There is no study on prevalence of Vitamin D deficiency in patients of liver cirrhosis from Nepal.
Aim: We evaluate serum 25-hydoxy vitamin D (25 OHD) level in patients with liver cirrhosis of varying severity attending outpatient department of center for liver disease.
Methods: A Serum level of 25 OHD was estimated in consecutive liver cirrhosis patients attending outpatient department. A normal 25 OHD level was defined as a concentration greater than 30 ng/ml, Vitamin D insufficiency was defined as a 25 OHD level of 20-30 ng/ml, and vitamin D deficiency was defined as a 25 OHD level less than 20 ng/ml. Patients who were taking vitamin D supplement were excluded from the study.
Results: 90 patients (median age 55 years [range 20-76 years]) were enrolled. The etiology of liver cirrhosis was alcohol in 70 %, viral in 20 %, autoimmune in 2 %, cryptogenic in 8 %. Their CTP class was A in 15 %, B (35 %) and C (50 %).The median 25 OHD level was 10 (8-34) ng/ml. 4 patients (5 %) have normal 25 OHD while 4 patients (5 %) have vitamin D insufficiency. Most patients (82, 90 %) had vitamin D insufficiency. 25 OHD levels were significantly lower in CTP B and C than CTP A.
Conclusion: We found that most of the patients with liver cirrhosis in Nepal, irrespective of their etiology, have vitamin D deficiency. The vitamin D level further decreases as the disease progresses. Thus patients with liver cirrhosis are considered as a high risk group for osteoporosis and fractures.

Topic 18: Liver Cirrhosis and Complications

No: 1384

A novel glycobiomarker wisteria floribunda agglutinin + MAC 2 binding protein for predicting carcinogenesis and survival of liver cirrhosis patients

Etsuko Iio[1], Makoto Ocho[2], Akira Togayachi[2], Atsushi Kuno[2], Noboru Shinkai[3], Yuzuru Ikehara[2], Kei Fujiwara[3], Shunske Nojiri[3], Takashi Joh[3], Masashi Mizokami[4], Hisashi Narimatsu[2], Yasuhito Tanaka[1]

Nagoya City University Graduate School of Medical Sciences Virology and Liver Unit Nagoya-Japan[1], National Institute of Advanced Industrial Science and Technology Research Center For Medical Glycoscience Tsukuba-Japan[2], Nagoya City University Graduate School of Medical Sciences Gastroenterology and Metabolism Nagoya-Japan[3], International Medicalcenter The Research Center of Japan, Hepatitis and Immunology, Kohnodai Hospital Ichikawa[4]

Background/aims: The aim of this study was to assess the utility of measuring a novel liver fibrosis glycobiomarker Wisteria floribunda agglutinin (WFA) - Mac-2 binding protein (M2BP) for hepatocarcinogenesis and outcome in patients with HCV.
Methods: WFA[SUP] + [/SUP]-M2BP levels were measured by HISCL M2BPGi (Sysmex Co., Japan) in serum samples from 128 consecutive HCV-infected patients histopathologically diagnosed F3 or F4. The median age was 65 (29-85) and male was 74 (57.8 %). Among 128 patients, 79 patients without hepatocellular carcinoma (HCC) at baseline were analyzed for survival and carcinogenesis rates during a median of 51 months (0-195).[Results] Serum WFA[SUP] + [/SUP] -M2BP levels were significantly higher in patients with F4 than F3 [2.3 (0.5-14.0) vs. 7.0 (0.5-39.2)COI] ($P < 0.001$). In F3 and F4 patients without HCC (n = 79), five/eight years survival with high WFA[SUP] + [/SUP] -M2BP (≥ 4, n = 39), was 78 %/48 % respectively, whereas for patients with intermediate WFA[SUP] + [/SUP] -M2BP (1-4, n = 33), was 100 %/82 %, respectively. The patients with low WFA[SUP] + [/SUP] -M2BP (< 1, n = 7) were no one died. The survival rate differed significantly among the three groups ($P = 0.0041$, log-rank test). HCC incidence in patients with high WFA[SUP] + [/SUP] -M2BP was higher than in those with low WFA[SUP] + [/SUP] -M2BP ($P = 0.0019$).

Cumulative carcinogenesis rates in the high WFA[SUP] + [/SUP]-M2BP > 4 group were 48.7 % after 4 years, contrasted with 16.9 % in the WFA[SUP] + [/SUP]-M2BP 1-4 group, whereas for patients with low WFA[SUP] + [/SUP] -M2B$P < 1$ group, no one occurred HCC. The cumulative carcinogenesis rate differed significantly among the three groups ($P = 0.002$, log-rank test).
Conclusions: Assessing serum levels of WFA[SUP] + [/SUP]-M2BP has diagnostic utility for predicting carcinogenesis and survival of patients with advanced fibrosis.

Topic 18: Liver Cirrhosis and Complications

No: 2023

Partial spleen embolization in patients with thrombocytopenia accompanied by liver cirrhosis compared to control group

Dae Sung Lee[1], Byung Ik Kim[1], Yong Kyun Cho[1], Hong Joo Kim[1], Woo Kyu Jeon[1], Mi Sung Kim[2], Hyun Pyo Hong[2]

Kangbuk Samsung Hospital Internal Medicine Seoul-Korea, South[1], Kangbuk Samsung Hospital Radiology Seoul-Korea, South[2]

Background and aims: Partial splenic embolization (PSE) has been proposed in patients with thrombocytopenia caused by secondary hypersplenism combined with liver cirrhosis.. Many studies have identified the prolonged increase in platelet count in PSE patients. We retrospectively evaluated the effect and safety of PSE compared with non-PSE patients.
Methods: Thirty patients with cirrhosis with severe thrombocytopenia were treated with PSE (platelet count < 45 × 103/mm3). Fifty-five patients were enrolled in non-PSE group. Serial transverse images of the enhanced abdominal CT scan were obtained and the volume was calculated by multiplying height in PSE group.
Results: The mean infarction ratio was 71.9 ± 19.8 % in PSE group. The platelet value was more increased in PSE patients than control group ($P < 0.001$). The platelet was increased as 98.8 × 103/mm3, 75.8 × 103/mm3 and 61.8 × 103/mm3 at 1, 6 and 12 month after PSE, respectively. Child-Turcotte-Pugh (CTP) and model for end stage liver disease (MELD) score were similar between groups ($P = 0.481$ and $P = 0.878$). The platelet count before PSE ($P < 0.001$; r = -0.585) and infarct ratio ($P = 0.028$; r = 0.469) were related with prolong increasing platelet value.
Conclusion: PSE was effective and safe for thrombocytopenia in patients with liver cirrhosis compared to control group. Liver function as CTP and MELD score was stable after PSE at 1 year.

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No: 1604

Effects of uncleoside analog on long term outcomes of treatment naïve patients with hbv related decompensated cirrhosis a retrospective cohort study

Gangde Zhao[1], Pei Hu[1], Huijuan Zhou[1], Weiliang Tang[1], Qing Xie[1]

Ruijin Hospital, School of Medicine, Shanghai Jiao Tong University, Department of Infectious Diseases Shanghai-China[1]

Background: Data regarding the long term outcome of HBV-related decompensated cirrhosis is rare, especially following oral nucleos(t)ide analogues use in such patients.
Aims: A retrospective cohort study of the oral anti-viral agents in patients with HBV-related decompensated cirrhosis was performed to evaluate the long term outcome including survival, liver function improvement, clinical status and virologic response after treatment with nucleos(t)ide analogues.
Methods: Patients with Child-Turcotte-Pugh (CTP) score ≥ 7 treated with either lamivudine or other agents were enrolled between January 2005 and December 2009. Patients co-infection with other hepatitis virus and/or human immunodeficiency virus were excluded. Survival analysis is performed.
Results: One hundred and sixty-six patients(125 males, 89 e-negative), including 54 untreated patients as control, were analyzed. The median follow-up period was 39.2 months and 52 months in treated and untreated cohort, respectively. The cohort of patients receiving antiviral therapy had significantly better 5-year actuarial survival compared with untreated patients (74.1 vs 34.9 % respectively, $P < 0.01$). But for patients with MELD score > 18, actuarial survival was not significantly different between the two cohorts ($P = 0.073$).
Conclusions: Antiviral therapy significantly improves the long-term outcome and survival. Treatment of patients with HBV-related decompensated cirrhosis should focus on management of the complications of cirrhosis, and if applicable, preparation for orthotopic liver transplant.

Topic 18: Liver Cirrhosis and Complications

No: 1363

Non invasive prediction of clinically significant portal hypertension using transient elastography and spleen diameter platelet count ratio in b viral and alcohol cirrhosis external validation study

Yoo Li Lim[1], Youn Zoo Cho[1], Moon Young Kim[1], Yoon Ok Jang[2], Soon Koo Baik[1], Ki Tae Suk[3], Gab Jin Cheon[4], Young Don Kim[4], Dae Hee Choi[5]

Wonju Christian Hospital Internal Medicine Wonju-Korea, South[1], Wonju Christian Hospital Cell Therapy and Tissue Engineering Wonju-Korea, South[2], Chuncheon Sacred Heart Hospital Internal Medicine Chuncheon-[3], Kangneung Asan Hospital Internal Medicine Kangneung-[4], Kangwon University School of Medicine Internal Medicine Chuncheon-[5]

Backgrounds and aim: We externally validated LS and two proposed index; LSPS (LSM × spleen diameter/platelet count), PH risk score (-5.953 + 0.188 X LS + 1.583 X sex (1: male; 0: female) + 26.705 X spleen diameter/platelet count ratio) for cirrhosis related with HBV or alcohol.
Methods: For 81 HBV-related and 288 alcohol-related cirrhosis, LS and HVPG were performed and we analyzed the correlation between LS, LSPS, PH risk score and HVPG.
Results: In HBV cohort, the mean HVPG and LS were 14.0 ± 6.0 mmHg and 33.0 ± 20.8 kPa. LS (r2 = 0.466, $P < 0.001$), LSPS (r2 = 0.430, $P < 0.001$) and PH risk score (r2 = 0.490, $P < 0.001$) showed significant linear correlation with HVPG. The AUROC of each index for the prediction of CSPH were 0.857, 0.879 and 0.873. The sensitivity and specificity of LS were 83.6 % and 70.0 % with a cut-off value 16.7 kPa for CSPH. In alcohol cohort, the mean HVPG and LS were 13.4 ± 5.5 mmHg and 38.3 ± 22.2 kPa. LS (r2 = 0.374, $P < 0.001$), LSPS (r2 = 0.2350, $P < 0.001$) and PH risk score (r2 = 0.395, $P < 0.001$) showed significant linear correlation with HVPG. The AUROC of each index for the prediction of CSPH were 0.857, 0.859 and 0.867. The sensitivity and specificity of LS were 85.0 % and 70.9 % with a cut-off value 22.9 kPa for CSPH.

Conclusion: In CSPH in HBV related and alcohol related cirrhosis,LS, LSPS, PH risk score showed good predictive value and there was no significant difference among them in predictive power.

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No: 1192

Evaluation of the correlation and discrepancy in three different shear wave based ultrasound elastography devices

Chikage Nakano[1], Tomoko Aoki[2], Masahiro Yoshida[1], Norihiro Tanaka[1], Akio Ishii[2], Kenji Hashimoto[1], Tomoyuki Takashima[2], Nobuhiro Aizawa[2], Naoto Ikeda[2], Hirayuki Enomoto[2], Masaki Saito[2], Seiichi Hirota[3], Shuhei Nishiguchi[2], Hiroko Iijima[1]

Hyogo College of Medicine Ultrasound Imaging Center Nisinomiya - Japan[1], Hyogo College of Medicine Division of Hepatobiliary and Pancreatic Medicine, Department of Internal Medicine, Nishinomiya-Japan[2], Hyogo College of Medicine Department of Surgical Pathology Nishinomiya-Japan[3]

Aims: We have evaluated differences and similarities between three different shear-wave based ultrasound elastography devices, Virtual Touch Quantification (VTQ), Shear Wave Elastography (SWE), and Transient Elastography (TE) by comparing liver stiffness measured by these methods on the same day.
Patients and methods: From March 2012 to February 2014, 289 patients with chronic liver disease diagnosed by liver biopsy were included, and their liver stiffness were measured by these three methods on the same day of the liver biopsy. We used ACUSON S2000 for VTQ, Aixplorer for SWE, Fibroscan for TE. For TE measurement, we converted it into m/s to use as the TE value.
Results: VTQ values were lower than those of other two devices. In two devices comparison, the correlation coefficient R of VTQ vs SWE was 0.87, VTQ vs TE was 0.85, and SWE vs TE was 0.84 ($P < 0.001$), and VTQ showed the strongest correlation with other devices. The ability to diagnose liver cirrhosis by each device was determined by the area under the receiver operating characteristic curve (AUROC) analysis, and the AUROC of VTQ/SWE/TE was 0.96/0.94/0.93, and showed good ability in all devices.
Conclusion: Measurements of liver stiffness using three methods are equally useful for the diagnosis of liver cirrhosis. Understanding the performance and characteristics of each method will lead to precise and credible data.

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No: 1011

Validation of hepa index as a non invasive biomarkers panel for assessment of hepatic fibrosis in Egyptians with chronic hepatitis C

Kerstin Schütte[1], Mohamed Alboraie[2], Marwa Khairy[3], Marwa Elsharkawy[4], Noha Asem[5], Gamal Esmat[3], Peter Malfertheiner[1], Egyptian Liver Fibrosis Study Group[2]

Otto-von-guericke University Department of Gastroenterology, Hepatology and Infectious Diseases Magdeburg-Germany[1], Al-azhar University Department of Internal Medicine Cairo-Egypt[2], Cairo University Tropical Medicine and Hepatology Department Cairo-Egypt[3], Cairo University Department of Clinical and Chemical Pathology Cairo-Egypt[4], Cairo University Department of Public Health and Community Medicine Cairo-Egypt[5]

Background: Hepa-Index is a newly proposed serum surrogate biomarker panel for non-invasive assessment of hepatic fibrosis.
Aims & methods: We aimed at validating the diagnostic performance of Hepa-Index in detecting different stages of hepatic fibrosis in chronic hepatitis C Egyptian patients. Hundred treatment naïve chronic hepatitis C Egyptian patients were enrolled. They were subjected to: platelet count, alpha-2-macroglobulin (α2-MG), total bilirubin, gamma glutamyl transpeptidase (GGT), total cholesterol, liver biopsy and histolopathological staging of hepatic fibrosis according to METAVIR scoring system. Hepa-Index was calculated according to the formula: Hepa-Index = exp (-0.021 x Platelet +1.65 × α2-MG + 0.2 × Total bilirubin + 0.026 × GGT -1.215 × Total cholesterol)/(1 + exp(-0.021 × Platelet + 1.65 × α2-MG + 0.2 × Total bilirubin + 0.026 × GGT -1.215 × Total cholesterol).
Results: Chosen cut off values of Hepa-Index were: 0.2, 0.3 and 0.4 for significant hepatic fibrosis (≥ F2 METAVIR), severe hepatic fibrosis (≥ F3 METAVIR) and cirrhosis (F4 METAVIR) respectively. Hepa-Index was able to detect significant fibrosis with sensitivity, specificity and AUROC of: 69.4 %, 76.3 % and 0.803 respectively. Hepa-Index was also able to detect severe hepatic fibrosis with sensitivity, specificity and AUROC of: 79.2 %, 64.5 % and 0.783 respectively and cirrhosis with sensitivity, specificity and AUROC of 81.8 %, 68.5 % and 0.744 respectively.
Conclusion: Hepa-Index is a good non-invasive biomarkers panel that can be used for non-invasive assessment of hepatic fibrosis in chronic hepatitis C patients.

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No: 1664

Renal dysfunction in liver cirrhotic patients and its role to predict mortality

Lidwina Cahyadinata[1], Cosmas Rinaldi A. Lesmana[1], Levina S. Pakasi[1], Laurentius A. Lesmana[1]

Digestive Disease and Gi Oncology Centre Medistra Hospital Jakarta-Indonesia[1]

Background: Renal dysfunction, as assessed by the estimated glomerular filtration rate (eGFR), may often seen in patients with compensated cirrhosis.
Objective: This study was aimed to evaluate the presence of renal dysfunction and its ability to predict mortality of patients with liver cirrhosis.
Method: A retrospective cohort study was held in patients with liver cirrhosis between January 2009 and September 2014. Clinical data was obtained from the patients' medical records. Differences between patients with and without renal dysfunction were tested using Chi square test. Survival difference and mortality prediction was analyzed using the Kaplan–Meier survival curve and Cox proportional-hazards regression analyses. Estimated GFR calculated by the abbreviated MDRD equation: 186 x (Creat/88.4)-1.154 x (Age)-0.203 x (0.742 if female).
Results: A total of 158 cases were re-evaluated; 104 (65.8 %) were men. Patients' mean age was 61.7 + 13.27 years. Renal dysfunction was found in 77 (48.7 %) of cases. The etiology of cirrhosis was hepatitis B (38.6 %), hepatitis C (34.2 %) and others (27.2 %). Type 2 diabetes was found in 66 (41.8 %) cases. Diabetic patients tend to be more in patients with than without renal dysfunction (54.5 % vs. 45.5 %; $P = 0.216$). Patients with renal dysfunction had shorter median survival than patients without it (17 vs. 36 months; log-rank $P = 0.015$). Renal dysfunction was a significant prognostic factor of

mortality (hazard ratio 2.054; 95 % confidence interval: 1.114-3.790; $P = 0.021$).
Conclusion: Renal dysfunction is commonly found in cirrhotic patients in this study (48.7 %). Its presence is associated with shorter overall survival of liver cirrhotic patients.

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No: 1306

Hepatic ascites treatment with novel diuretics—vasopressin V2 receptor antagonist (TOLVAPTAN)

Hideo Yoshida[1], Hiroyoshi Taniguchi[1], Ryo Nakata[1]

Japanese Red Cross Medical Center Gastroenterology and Hepatology Tokyo-Japan[1]

Background: Medical treatment of hepatic ascites has been based on furosemide and spironolactone for long time. Recently, novel diuretics of Tolvaptan become available in Japan.
Methods: Tolvaptan was administered for 17 patients with refractory hepatic ascites between September 2013 and October 2014. Patients received 3.75 mg/day or 7.5 mg/day of Tolvaptan orally. Demographic data, body weight, daily urine volume, serum creatinine, serum sodium concentration, and liver numbers were collected.
Results: In 17 patients, 13 were male and 4 were female. Age of patients ranged between 46 and 81 (median 65yo). Etiology of liver disease was as follows: HCV 9, Alcoholic liver disease 5, NASH 2, and PBC 1. Child Pugh score ranged between 8 and 13 (median 10). Four were Child B and 9 were Child C. Urine volume increased +659 $\pm$ 824, +590 $\pm$ 668, and +534 $\pm$ 582 in day 1, 7, and 14 respectively. Sixty two percent of patients had BW loss more than 1 kg in 2 weeks. No severe adverse effect including elevation of serum sodium level was seen. Four patients stopped taking Tolvaptan because of no effect, general malaise, encephalopathy, and of recovery from ascites.
Conclusions: Tolvaptan was safely administered for the treatment of hepatic ascites. This novel diuretics provide one option for the treatment of end stage liver disease.

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No: 1831

Recurrent cellulitis and subcutan abscess in a patient with cirrhosis

Sebahat Basyigit[1], Yasar Nazligul[2], Metin Uzman[3], Zeliha Asilturk[4]

M.d. Gastroenterology Ankara-Turkey[1], Prof. Dr. Gastroenterology Ankara-Turkey[2], Associate Prof. Gastroenterology Ankara-Turkey[3], M.d. Internal Medicine Ankara-Turkey[4]

A 62-year-old woman with liver cirrhosis (Pudge-Child grade C) was presented to the hospital with disorientiation and redness over the right leg. She had been hospitalized several times for SBP and hepatic encephalopathy (HE). Her last two admission was due to cellulitis. Physical examination revealed stigmata of cirrhosis, ascites, umblical hernia and mild HE. Her temperature was 35.67 C; pulse rate, 120/min; and blood pressure, 89/40 mmHg. Laboratory findings were convenient with chirrosis and C-reactive protein was 9 gr/dl. Paracentesis on the admission was unsuccessful. Ultrasonography revealed no evidence of hepatobiliary infection. There was no evidence of infection except cellulitis over proximal part of her right leg.

She was given empirical treatment with daptomycin 1x 350 mg i.v for cellulitis. Two days later, localized fluctuant swelling with peripheral erythema has appeared over the right abdominal wall (Figure). Ultrasonography confirmed a 5 cm dimeter subcutan abscess formation and drainage was made. Cultures of blood, urine and ascites -obtained on day 6- were negative. Sore culture yielded Staphylococcus aureus that was susceptible to methicillin. Despite intensive therapy, she died 10 days later.

Bacterial infections are frequent and a common cause of morbidity and mortality in cirrhotic patients because of their defective defense mechanisms. The most common infections were spontaneous bacterial peritonitis (SBP). Cutaneous infections in cirrhotic patients has seldom been reported in the literature. As a result of frequent antibiotic use for prophylaxis and SBP, gram positive infections can become dominant.

Topic 18: Liver Cirrhosis and Complications

No: 1633

Cardiac cirrhosis caused by constrictive pericarditis a case report

Kyoung Hwang Shin[1], Hyun Don Joo[1], Suk Bae Kim[1], Il Han Song[1]

Dankook University College of Medicine Division of Hepatology, Department of Internal Medicine Cheonan-Korea, South[1]

Background: Cardiac cirrhosis, an uncommon disease entity of chronic liver injury, usually results from long-standing right-sided heart failure in which an elevated venous pressure was transmitted via inferior vena cava (IVC) and hepatic vein to sinusoids of the liver. Long-term hepatic congestion with relative ischemia can induce centrilobular necrosis, leading to pericentral fibrosis.
Case: A 67 year-old male with liver cirrhosis of unknown origin was admitted with pretibial pitting edema, ascites and progressive dyspnea on exertion for 1 month. At that time on admission, electrocardiography showed typical atrial flutter with 2: 1 or 3: 1 conduction and serum cardiac enzymes were within normal limit. A chest radiograph showed a remarkable cardiomegaly with bilateral pleural effusion, being ascertained as transudate. Chest computed tomography (CT) scan showed the anterior pericardial calcification with wall thickening. Dynamic liver CT scan showed a nodular hepatic contour with a small amount of ascites, especially, accompanying with the regurgitation of contrast materials to intrahepatic veins via IVC from right-sided heart chamber. Transthoracic echocardiography demonstrated moderate tricuspid regurgitation and left ventricular ejection fraction of 40 %. Liver histology by ultrasound-guided needle biopsy revealed macrovesicular steatosis and bridging fibrosis with a minimal hepatic necroinflammation. Cardiac cirrhosis was confirmed by histological and radiological findings. After symptomatic improvement following conservative managements including diuretics, the patient is being followed up regularly.
Conclusions: Based on the histological and radiological features, we report an uncommon case of cardiac cirrhosis caused by constrictive pericarditis accompanying with pericardial calcification.

Topic 18: Liver Cirrhosis and Complications

No: 1018

Collagen arrangement in space of disse correlates with fluid flow in normal and cirrhotic rat livers

Raksawan Poonkhum[1], Wisuit Pradidarcheep[1], Somneuk Nilbunga[1]

Faculty of Medicine Anatomy Bkk-Thailand[1]

Little is known about collagen arrangement in the space of Disse in relation to the fluid flow in normal and cirrhotic livers. We examined the changes in the arrangement of type-I collagen fibers in thioacetamide (TAA)-induced cirrhotic rat livers by light microscopy of Sirius-red stained tissues, type-I collagen immunohistochemistry and scanning electron microscopy (SEM) of vascular corrosion casts and alkali-water macerated tissues. Most of the sparse bundles of collagen fibers in the spaces of Disse were elongated fibers with a disorganized arrangement in each nodule of the cirrhotic liver. These bundles were connected with the broad fibrous septa. Based on the comparison of the architecture of the collagen fibers and the established flow of fluid in the space of Disse, we hypothesize that the fluid in the space of Disse streams along collagen fibers in all directions to broad fibrous septa. The appearance of the perinodular vascular plexus in cirrhotic rat livers probably helps to reduce portal hypertension.

Topic 18: Liver Cirrhosis and Complications

No: 1899

Emergency endoscopic variceal ligation following variceal rupture in patients with advanced hepatocellular carcinoma and portal vein tumor thrombosis

Toshihiro Kawai[1], Yoko Yashima[1], Takafumi Sugimoto[1], Takahisa Sato[1], Miho Kanda[1], Nobuyuki Enomoto[2], Shinpei Sato[1], Shuntaro Obi[1]

Kyoundo Hospital Department of Gastroenterology and Hepatology Chiyoda-ku-Japan[1], University of Yamanashi First Department of Internal Medicine Chuo-Japan[2]

Background and aim: The outcome of ruptured varical treatment in patients with hepatocellular carcinoma (Hcc) and portal vein tumor thrombus (PVTT) is unclear. We evaluated the long-term outcomes defined as rebleeding and death and short-term outcome defined as immediate death within 24 h of diagnosing variceal bleeding, of patients with PVTT who underwent emergency treatment of potentially fatal variceal bleeding.
Methods: A total of 62 consecutive patients with PVTT and endoscopically proven esophageal or gastric variceal bleeding, who were admitted in our hospital between 2007 and 2012, were included. Emergent endoscopy was performed within 24 h after haemorrhage. The bleeding varices were ligated using a pneumatic EVL device. (Results) Most of patients were decompensated cirrhosis with the liver function stages of the patients were Child-Pugh B (56 %) or C (36 %). 58 patients (94 %) had esophageal variceal bleeding and 4 (6 %) patient had gastric variceal bleeding. Except for one patient, the bleeding was managed using endoscopic variceal ligation (98 %). 24 patients experienced rebleeding, and a median overall survival time of 36 days. Absence of portal vein tumor thrombus in the main trunk was associated with rebleeding-free survival (hazard ratio 3.706, $P = .0223$), and α-fetoprotein-L3 level (hazard ratio 2.153, $P = .015$) and Child-Pugh Class C (hazard ratio 0.398, $P = .007$) were related to over-all survival.
Conclusions: EVL is a safe and effective treatment of variceal ruptures, even in patients with HCC and PVTT. After successful hemostasis, alleviation of the underlying liver function impairment and tumor control are equally important for better prognosis.

Topic 18: Liver Cirrhosis and Complications

No: 1500

Cases of portal vein thrombosis in hepatocellular carcinoma and liver cirrhosis treated with anticoagulation

Heon Young Lee[1], Byung Moo Ahn[1], Eaom Seok Lee[1], Seok Hyun Kim[1], Byung Seok Lee[1]

Chungnam National University Hospital Department of Gastroenterology Daejeon-Korea, South[1]

The prevalence of portal vein thrombosis (PVT) with cirrhosis has been reported more frequently in recent years. The reported prevalence of PVT is in the range of 0.6 ~ 15.8 % in patient with liver cirrhosis or portal hypertension. If the patient has hepatocellular carcinoma(HCC), thrombus is likely to be malignant thrombus. Malignancy, frequently of hepatic origin, are responsible for 21 ~ 24 % of overall cases. The overall mortality rate of PVT has been reported to be less than 10 %, but is increased to 26 % when associated with HCC and cirrhosis. Because actually it is not easy to distinguish between malignant thrombus and benign thrombus in clinical aspect, PVT in HCC are still debatable whether or not treatment when it diagnosed. Many studies have been made to distinguish malignant PVT and benign PVT. Fine needle biopsy of the thrombus has the potential of clarifying the nature of PVT. Tarantino et al. noted a sensitivity of only 76 % for portal vein sampling in determining malignancy. Clinically, benign PVT was imaging documentation of at least 12 months of stability, and rapid progressive thrombi (within 3 months) despite adequate anticoagulation therapy were considered malignant. In recent years, the possibility of using color Doppler sonography, contrast-enhanced color Doppler sonography, CT, MRI and 18FDG-PET scan to determine the benign or malignant nature of PVT has been reported. We experienced 3 cases of PVT(54 year-old male, 73 year-old female and 50 year-old male) with LC and HCC and treated with anticoagulation. After treatment, PVT has been improved and the patients receives a maintenance anticoagulation therapy without complication.

Topic 18: Liver Cirrhosis and Complications

No: 1449

Assessing the feasibility of existing clinical guidelines for the management of advanced liver disease for use in resource limited settings

Tatsuya Yamashita[1], Kuniaki Arai[1], Philippa Easterbrook[1], Stefan Wiktor[1]

World Health Organization Global Hepatitis Programme, Department of Hiv Geneva-Japan[1]

Aim: Advanced liver disease (ALD) is common in resource limited settings (RLS), but clinicians lack guidance on its clinical management. We assessed the applicability of existing ALD clinical practice guideline (CPG) recommendations for use in RLS.
Methods: We systematically searched for CPG for ALD from relevant medical societies and ministries of health web sites. We grouped recommendations by clinical manifestation of ALD and assessed their feasibility in RLS based on availability of recommended medicines in RLS and qualitative factors determined by discussion with specialists from the each region. Existing evidence were also preliminary

screened in MEDLINE. The recommendations were selected to consider feasibility, existing evidence and clinical importance in RLS.
Result: We found 34 CPG related to ALD: four for hepatic encephalopathy (HE), seven for ascites, nine for varices and 14 for hepatocellular carcinoma (HCC). Most (65 %) were from Europe or America regions, and none were from Africa. These CPGs recommended 27 different interventions, of which 11 (41 %) were assessed as being feasible in RLS; most (87 %), were supported with high level of evidence. We selected 12 recommendations as being most suitable for RLS: one for HE, six for ascites including spontaneous bacterial peritonitis, two for varices, and four for HCC.
Conclusion: A number of existing CPG recommendations developed in high-income countries and supported by high-quality evidence and are suitable for use in RLS. If implemented, they could reduce morbidity and mortality from ALD.

Topic 18: Liver Cirrhosis and Complications

No: 1956

Grade II III oesophageal varices in cirrhotic patients can be predicted by measuring liver stiffness with fibroscan

Ahmed Lutful Moben Moben[1], Farjana Majid Majid[2], Mamun Al Mahtab Mahtab[3], Salimur Rahman Rahman[3]

Shahed Suhrawardy Medical College Hospital, Dhaka, Bangladesh. Medicine Dhaka-Bangladesh[1], Taerunessa Medical College Virology Dhaka-Bangladesh[2], Bsmmu Hepatology Dhaka-Bangladesh[3]

Background/aim: Repeated and periodic endoscopy is recommended for follow up of esophageal varices (OV) in cirrhotic patients. A non-invasive test is always preferred over endoscopy. So, we have evaluate liver stiffness measurement (LSM) for the prediction of G-II-III OV.
Methods: A cross sectional observational study was conducted between July'2010 to July'2011. A total of 46 patients with cirrhosis were divided into two groups. Group-I patients had group-I had Grade-I OV (n = 23) and group-II had Grade-II/III OV (n = 23) at endoscopy. Liver stiffness was measured by fibroscan & data was analyzed by SPSS.
Results: Mean age were 35.20 ± 11.36 years with highest frequency 19 (38 %) in 21-30 years age group. Etiologies were different with leading causes includes HBV (76 %) followed by HCV (6 %), alcohol (2 %) and 14 % were unknown. Liver stiffness was significantly higher in group II than group-I.Liver stiffness at a cut off value 32.52 kPa with sensitivity, specificity, positive predictive value, negative predictive value, accuracy respectively 82.6 %, 77.8 %, 76 %, 84 %, 80 % can predict the Grade-II-III oesophageal varices (AUROC = 85.2 %).
Conclusion: Liver stiffness may be suitable for prediction of Grade-II-III oesophageal varices. Liver stiffness measurement can be used to follow up cirrhotic patient.

Topic 18: Liver Cirrhosis and Complications

No: 1191

Danaparoid sodium thrombolytic therapy followed by warfarin in cirrhotic patients with portal vein thrombosis

Etsushi Kawamura[1], Masaru Enomoto[1], Atsushi Jogo[2], Kohei Kotani[3], Hiroyuki Motoyama[1], Ritsuzo Kozuka[1], Atsushi Hagihara[1], Akira Yamamoto[2], Hideki Fujii[4], Sawako Uchida-kobayashi[1], Shuji Iwai[1], Norifumi Nishida[2], Hiroyasu Morikawa[1], Joji Kawabe[3], Yoshiki Murakami[1], Akihiro Tamori[1], Susumu Shiomi[3], Norifumi Kawada[1]

Osaka City University, Graduate School of Medicine Department of Hepatology Osaka-Japan[1], Osaka City University, Graduate School of Medicine Department of Radiology Osaka-[2], Osaka City University, Graduate School of Medicine Department of Nuclear Medicine Osaka-[3], Juso Municipal Hospital Department of Gastroenterology and Hepatology Osaka[4]

Background: Portal vein thrombosis (PVT) is a complication of cirrhosis that reduces the hepatic reserve and causes variceal bleeding. In Japan, the efficacy of danaparoid sodium (Orgaran®), a hepa-rinoid anti-coagulation factor Xa, therapy (DS) for PVT has been reported.
Methods: We retrospectively analyzed 41 hospitalized cirrhotic patients: 16 hepatitis C virus, 5 hepatitis B virus, 20 others; the model for end-stage liver disease (MELD) score 8.6 ± 4.7; platelets 80 ± 40 × 10[SUP]3[/SUP]/μL; 3 esophageal varices F0, 16 F1, 5 F2, 0 F3, and 17 unknown. DS 2500 units were administered daily (n = 41, mean duration: 9.5 days), followed by oral warfarin (prothrombin time-international normalized ratio: 1.5 ± 0.3) in outpatient clinic (n = 16, 25.8 weeks). The volume of PVT (PVTV) measured with a three-dimensional-image analyzer (SYNAPSE VINCENT®, n = 28), serum D-dimer (n = 29), and scinti-graphic portal shunt indices (normal, ≤ 10 %; n = 6) were monitored.
Results: Thrombi formed at one site in 25 patients (18 portal, 4 superior mesenteric, and 3 splenic veins) and at two or more sites in 16. At the end of DS, the PVTV decreased to 55.1 ± 40.2 % of baseline (8.6 ± 10.3 cm[SUP]3[/SUP], $P < 0.0001$), D-dimer decreased from 11.8 ± 12.6 μg/mL to 7.0 ± 7.4 μg/mL ($P = 0.007$), and the shunt indices decreased from 62.4 ± 10.5 % to 56.9 ± 7.1 % ($P = 0.250$). During DS, Grade 2 intraperitoneal bleeding occurred in one patient (2.4 %). During follow-up, PVTV increased in 33.3 % of the patients, MELD score in-creased in 37.5 %, platelets decreased in 50.0 %, and varices grade increased in 18.2 %.
Conclusions: PVT could be resolved with DS with relative safety. Warfarin did not always maintain the effects of DS.

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No: 1209

Pre endoscopic clinical characteristics of variceal and non variceal gastrointestinal bleeding in the patients with liver cirrhosis chronic liver disease

Byung Seok Kim[1], Hyun Hee Kim[1], Sun Mi Kang[1], Si Hye Kim[1], Joon Seok Park[1], Jang Seok Oh[1], Hyun Sik Hwang[1], Chang Hyeong Lee[1]

Catholic University of Daegu School of Medicine Department of Internal Medicine Daegu-Korea[1]

Background/aim: Variceal bleeding is a common type of gastrointestinal (GI) bleeding in patients with liver cirrhosis (LC)/chronic liver disease (CLD). But non-variceal GI bleeding also may develop in them. Differentiating variceal bleeding from non-variceal bleeding prior to emergent endoscopy may be useful for deciding on the use of vasoconstrictor and the timing of endoscopy.
Methods: We reviewed 296 LC/CLD patients who had evidence of upper GI bleeding and underwent endoscopy within 24 h of presentation. The medical records for demographics, accompanying symptoms, vital signs, laboratory findings, imaging studies, severity of underlying liver disease and endoscopic findings were investigated.
Results: The mean age was 58.38 ± 11.77 years, and 235 patients (79.4 %) were men. 220 patients (74.3 %) represented variceal bleeding.

The causes of non-variceal GI bleeding were gastric ulcer (44.7 %), Mallory-Weiss syndrome (42.1 %), duodenal ulcer (6.6 %) and others (6.6 %). Subjects with variceal bleeding showed lower platelet count (99.8 × 103 vs. 134.56 × 103/mm3, $P = 0.004$), higher alkaline phosphatase level (321.26 vs. 233.83 IU/L, $P = 0.001$), more prolonged prothrombin time (18.18 vs. 16.9 s, $P = 0.016$) and more frequent splenomegaly (97.26 vs. 52.63 %, $P = 0.000$) than those with non-variceal bleeding. In multivariate analysis, splenomegaly was the only predictive factor for variceal bleeding in LC/CLD patients ($P = 0.001$).
Conclusions: Splenomegaly was the only predictive factor for variceal bleeding in LC/CLD patients. But it is not enough to judge for variceal bleeding. and non-variceal GI bleeding in LC/CLD patients was in a minority. Therefore, use of vasoconstrictor and rapid access to endoscopy may be considered for LC/CLD patients with evidence of upper GI bleeding.

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No: 1260

Value of plasma neutrophil gelatinase associated lipocalin in cirrhotic patients and hepatocellular carcinoma patients

Jeong Han Kim[1], Soon Young Ko[1], Won Hyeok Choe[1], So Young Kwon[1]

Konkuk University Internal Medicine Seoul-Korea, South[1]

Background: Neutrophil gelatinase-associated lipocalin (NGAL) is a troponin like biomarker for human acute kidney injury. Data about clinical implication of NGAL in chronic liver disease such as liver cirrhosis (LC) and hepatocellular carcinoma (HCC) is limited. We aimed to investigate value of NGAL in such patients.
Methods: Medical records of LC and HCC patients admitted Konkuk University Medical Center between July 2013 and January 2014 were reviewed. The patients were divided into normal kidney function, chronic kidney disease (CKD) and acute kidney injury (AKI). Plasma NAGL level (ng/ml), cystatin C (mg/L) and estimated glomerular filtration rate (eGFR, mL/min/1.73m2) at admission were compared.
Results: Sixty-two LC patients and Seventy-six HCC patients with normal eGFR were included in this analysis. There were no significant differences between LC and HCC patients in median Child-Pugh score (7.5 vs. 7.0, $P = 0.278$), eGFR (90.0 vs. 90.0, $P = 0.212$), cystatin C (0.9 vs. 1.01, $P = 0.138$). Median plasma NGAL level was higher in HCC patients (77.5) than LC patients (58.0) significantly ($P = 0.021$). In LC group, CKD (n = 5) and AKI (n = 15) patients showed higher NAGL (131.0, $P = 0.009$ and 315.0, $P < 0.001$) than normal but no difference between CKD and AKI ($P = 0.315$). CKD (n = 2) and AKI (n = 5) patients in HCC group also showed higher NGAL (187.0, $P = 0.206$ and 388.0, $P < 0.001$) but no differences between CKD and AKI ($P = 0.245$).
Conclusions: There is a tendency of higher plasma NGAL level in HCC patients to LC patients even though patients have normal eGFR. The value of plasma NGAL in differentiation of AKI from CKD for LC of HCC patients needs further evaluation.

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No: 1034

Prospective validation of baveno v definitions and criteria for failure to control bleeding in portal hypertension

Sun Young Ahn[1], Won Young Tak[2], Young Oh Kweon[2], Soo Young Park[2]

Daegu Medical Center Internal Medicine Daegu-Korea, South[1], Kyungpook National University Hospital Internal Medicine-[2]

New definitions and criteria were released at the Baveno V consensus meeting. The purposes of this study were to verify Baveno V definitions and criteria for failure to control bleeding and to determine the usefulness of combined use of the Adjusted Blood Requirement Index [ABRI: (number of blood units)/(final hematocrit-initial hematocrit) + 0.01] with Baveno V criteria. Two hundred and forty-six consecutive liver cirrhosis patients with acute bleeding associated with portal hypertension were enrolled prospectively between January 2010 and October 2012. The treatment outcome on day 5 was assessed by endoscopy. For the ABRI calculation, two hematocrit levels were used as the initial hematocrit: the first level measured upon patient arrival (ABRI-A) and the lowest level measured before transfusion (ABRI-B). Treatment failures were identified in 53 patients, of whom 24 died. Based on repeated endoscopic findings, 29 patients were identified as treatment failures, while according to Baveno V criteria, 47 patients were regarded as treatment failures. The area under the receiver operating characteristic curve (AUROC) of Baveno V criteria was 0.906, and the sensitivity, specificity, positive predictive value, negative predictive value,positive likelihood ratio, and negative likelihood ratio were 83.0 %, 98.4 %, 93.6 %, 95.5 %, 53.41, and 0.17, respectively. The AUROC of Baveno V criteria was significantly greater than those of Baveno IV ($P = 0.0001$) and Baveno II/III ($P < 0.0001$) criteria. Adding ABRI-A or -B to Baveno V criteria resulted in a significant reduction of the AUROC ($P < 0.01$).

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Prevalence etiology and clinical characteristics of non cirrhotic portal hypertension in a south East Asian cohort

Pik-eu Chang[1], Ravishankar Asokkumar[1], Mithun Sharma[1], Chee-kiat Tan[1]

Singapore General Hospital Gastroenterology & Hepatology Singapore-Singapore[1]

Objective: Non-cirrhotic portal hypertension(NCPH) refers to a clinical entity characterized by features of increased portal pressure in the absence of liver cirrhosis. There is little data on NCPH in South-East Asia. This study aims to evaluate the prevalence, etiology and clinical characteristics of NCPH in Singapore.
Methods: Single-center retrospective review of patients in our Cirrhosis Registry who fulfilled diagnostic criteria of NCPH, i.e. clinical evidence of portal hypertension (splenomegaly, hypersplenism and varices) in the absence of clinical cirrhosis.
Results: Fifty-four cases of NCPH were identified from a cohort of 902 cirrhotics. Mean age was 42 ± 17 years with 54 % males. Main etiology of NCPH was extra-hepatic portal vein obstruction, EHPVO (46 %), myeloproliferative disorders, MPD(33 %), idiopathic portal hypertension,IPH(7 %) and miscellaneous(13 %). The most common presentation was GI bleeding(37 %). Prothrombotic disorders were identified in 20 %, mainly in the EHPVO group. EHPVO patients were younger compared to MPD patients (mean age 34.8 ± 13.5 vs. 54.6 ± 10.1 years, $P < 0.05$). Gastric varices were more common in the MPD group (67 % vs. 29 %, $P < 0.05$) whereas portal hypertensive gastropathy(PHG) was significantly more common in the EHPVO group. LSM and HVPG values tended to be higher in the

MPD group. Variceal bleeding was equally common in both groups (58 % vs. 50 %). Spleen size was a useful predictor of variceal bleeding in the MPD group (AUROC 0.82) but not in the EHPVO group(AUROC 0.52).
Conclusion: Prevalence of NCPH in Singapore is approximately 6 % and is most commonly due to EHPVO and MPD. Spleen size may be a clinically useful predictor of variceal bleeding in MPD patients but not in EHPVO.

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No: 1462

The benefit of cystatin c in evaluation of renal function and prediction of prognosis in patients with cirrhosis

Meguru Adachi[1], Atsushi Tanaka[1], Kotaro Miura[1], Ryo Miura[1], Mitsuhiko Aiso[1], Yoriyuki Takamori[1], Hajime Takikawa[1]

Teikyo University School of Medicine Medicine Tokyo-Japan[1]

Background and aims: The assessment of renal function is of vital importance for prediction of prognosis in patients with cirrhosis. While serum creatinine (Cr) is routinely used for this purpose, Cr-based estimated glomerular filtration rate (eGFR) does not reflect true renal function because of muscle wasting and impaired liver function. By contrast, cystatin C (CysC), another biomarker for renal function, is unrelated to muscle volume and liver function. In this study we examined whether CysC is beneficial in assessment of renal function in patients with cirrhosis.
Methods: First, we assessed the performance of GFR-estimating equations based on serum Cr and CysC (the Japanese Society of Nephrology, 2012) in 14 patients with cirrhosis, comparing inulin clearance as a gold standard of GFR (measured GFR; mGFR). Next, in 49 patients with cirrhosis, we examined Cr and CysC at baseline, and examined which eGFR, Cr-based or CysC-based, is beneficial for predicting the prognosis.
Results: In the first experiment, mGFR in 9 patients was 54.3 ± 23.0 (ml/min). Cr-based and CysC-based eGFR was 64.0 ± 13.7 and 53.2 ± 12.1, respectively, indicating Cr-based eGFR was significantly higher than mGFR ($P < 0.001$). In the next experiment, we followed up 49 patients for 30.7 ± 32.0 months in average, and 22 deaths were noted during the observation. Multivariate analysis demonstrated that decreased CysC-based eGFR at baseline (< 50 ml/min), not Cr-based eGFR, was independently associated with the mortality ($P = 0.008$, HR = 3.727 [1.361-10.205]).
Conclusion: These results suggest that CysC-based eGFR could predict mGFR and the prognosis more precisely compared to Cr-based eGFR in patients with cirrhosis.

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No: 1092

Clinical biochemical and morphological peculiarities of liver cirrhosis depending on etiological virus

Sayfullo Avezov[1], Giesiddin Mirojov[1], Saodat Azimova[1], Rohatillo Odinaev[1], Dilorom Ishankulova[1], Mirhoji Khuzhamurotov[1], Nazira Tukhtaeva[1], Muhriddin Giyosov[1], Nigora Orifjonova[1], Jalolidin Pulatov[1], Khayri Rahimova[1], Saidhomid Mahmadaleev[1]

Institute of Gastroenterology Hepatology Dushanbe-Tajikistan[1]

Aims: The study of clinical, biochemical and morphological signs of discrepancy of LC depending on etiological virus (HBV or HCV).
Methods: A total of 289 patients (183 men and 106 women, average age 44.7 ± 5.3 years) with LC were included in this study. The etiology of LC was HBV in 148, HCV in 141 patients. At 52 patients was done liver biopsy with morphological study. Survival was assessed according to the Kaplan–Meier method.
Results: LC of HBV-etiology is met more often at young people (72 % patients up to 40 years old), LC of HCV-etiology at people over 50 years old (68 %). The average age of patients with LC of HBV-etiology was 32.3 ± 2.5, patients with LC of HCV-etiology was 54.5 ± 4.6 years. The estimated term of HBV-related LC development made 9.5 ± 2.1; at HCV infection—25.2 ± 4.3 years. The dominating signs of portal hypertension were observed at 55 % patients with LC of HBV-etiology and at 32 % patients with LC of HCV-etiology. The 3-years survival rate of patients with LC of HBV-etiology was 38 % and of patients with LC of HCV-etiology was 52 %. LC of HBV-etiology more often (67 %) had the macro nodular type and LC of HCV-etiology—mixed (macro–micro nodular) type of cirrhosis.
Conclusion: Virus LC depending from etiology has different degree of formation rate, the severity of clinical, biochemical and morphological flow. The HBV-related LC develops earlier, faster and flows heavy.

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No: 1918

Usefulness of partial splenic embolization (pse) for patients with for portal hypertension due to liver cirrhosis

Kayoko Sugawara[1], Yukinori Imai[1], Masashi Takano[1], Yoshihito Uchida[1], Yohei Fujii[1], Hiroshi Uchiya[1], Kazuki Hirahara[1], Taku Chikayama[1], Manabu Nakazawa[1], Satsuki ando[1], Inao Mie[1], Nobuaki Nakayama[1], Satoshi Mochida[1]

Saitama Medical University Gastroenterology & Hepatology Saitama-Japan[1]

Aim: PSE is shown to be useful as a therapeutic procedure to attenuate thrombocytopenia in patients with liver cirrhosis, while the efficacies of the procedure for the other complications of portal hypertension are to be elucidated. Thus, therapeutic efficacies for esophageal varices as well as thrombocytopenia were evaluated in patients receiving PSE.
Methods: A total of 29 patients with liver cirrhosis (the mean age of 56.4 years old, Child-Pugh class of A, B and C in 14, 12 and 3, respectively) were given PSE between April 2007 and August 2014; 10 patients for thrombocytopenia (group-A), 6 patients for intractable esophageal varices (group-B) and 13 patients for prevention of esophageal varices development after B-RTO procedures (group-C). Branches of the splenic artery were embolized with gelatin sponges of 5-7 mm cubes and metalic coils to induce partial splenic infection.
Results: In group-A, peripheral platelet counts were increased significantly compared to the baseline levels (9.7 ± 1.4 vs 5.4 ± 1.8 × 104/μL) and all these patients received Interferon therapy. In group-B, total number of varices recurrence requiring endoscopic therapies among 6 patients were 2 times after PSE, while were 23 times before the procedures during mean observation period of 7.6 months. In group-C, the cumulative exacerbation rate of esophageal varices was 30.8 % at 1 year after the procedure and ascites were increased only in 2 patients (15 %).
Conclusions: PSE was useful as a therapeutic procedure for esophageal varies as well as thrombocytopenia in patients with liver cirrhosis.

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No: 1107

Growth differentiation factor 15 can predicts severity of chronic liver disease

Eaum Seok Lee[1], Seok Hyun Kim[1], Hee Seok Moon[1], Heon Young Lee[1], Byung Seok Lee[1], Kwan Woo Nam[2]

Chungnam National University Hospital Internal Medicine Daejeon-Korea, South[1], Sun Medical Center Internal Medicine Daejeon-Korea, South[2]

Background/aims: Growth differentiation factor 15 (GDF-15) belongs to the transforming growth factor-β superfamily. GDF-15 is emerging as a biomarker of several diseases. The aim of this study was to determine the clinical performances of GDF-15 for the prediction of liver fibrosis and severity in chronic liver disease.
Methods: Serum GDF-15 levels were examined by enzyme-linked immunosorbent assay in 145 patients with chronic liver disease and 101 healthy individuals. Patients with chronic liver disease consists 54 patients with chronic hepatitis, 44 patients with compensated liver cirrhosis, 47 patients with decompensated liver cirrhosis.
Results: Among patients with chronic liver diseases, decompensated liver cirrhosis patients had higher level of serum GDF-15 (3483 ng/L) than those with compensated liver cirrhosis (1861 ng/L) and chronic hepatitis (1232 ng/L). GDF-15 levels correlated positively with CDS ($r = 0.447$), child-pugh score ($r = 0.474$), MELD score (0.415). The overall diagnostic accuracies of GDF-15, as determined by the area under receiver operating characteristics curves, were chronic hepatitis = 0.656 (> 574 ng/L, sensitivity 53.7 %, specificity 79.2 %) compensated liver cirrhosis = 0.886 (> 760 ng/L, sensitivity 75.6 %, specificity 92.1 %), decompensated liver cirrhosis = 0.984 (> 869 ng/L, sensitivity 97.9 %, specificity 94.1 %).
Conclusion: This is the first study that demonstrates availability of GDF-15 in chronic liver disease. GDF-15 was very useful biomarker for the prediction of liver fibrosis and severity in chronic liver disease. In particular, a GDF-15 value 869 ng/L was proposed as a significant cut-off value for diagnosis of compensated liver cirrhosis.

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No: 1808

Adrenal dysfunction may play a role in the pathogenesis of hyponatremia in cirrhosis

Maryam Moini[1], Mitra Yazdani Sarvestani[2], Mesbah Shams[3]

Shiraz University of Medical Sciences Gastroenterohepatology Research Center Shiraz-Iran[1], Fasa University of Internal Medicine Shiraz-Iran[2], Shiraz University of Medical Sciences 3endocrinology and Metabolism Research Center Shiraz-Iran[3]

Introduction: Patients with cirrhosis especially in the advanced form suffer of multiple complications. Several studies have shown a high prevalence of adrenal insufficiency in cirrhotic patients with a possible role in the complications as hypotension and/or septic shock.
Aims & methods: In this study we evaluated the function of hypothalamic hypophyseal—adrenal axis in.
105 adult cirrhotic patients in subspecial liver clinics of Shiraz University of Medical sciences in 2013. Disease severity categorization was done according to model for end-stage liver disease (MELD) score. Adrenocorticotropic hormone (ACTH) stimulation testing was done using 250 μg of synthetic short acting ACTH for each patient and radio immunoassay method was used to measure plasma cortisol level.
Results: Of all 105 cirrhotic with the mean age of 40.3 ± 1.28 (mean ± SD) years and the mean MELD score of 18.28 ± 5.4, only 15 (14 %) had a low serum cortisol level at base or when stimulated. Patients with normal adrenal tests (group 1) and those with abnormal results (group 2) had no statistically significant difference in creatinine level, blood urea nitrogen level, systolic blood pressure and ascites. The mean of serum sodium was the only variable with a significant difference between the two groups (P value = 0.01).
Conclusion: In this study, the prevalence of adrenal dysfunction was not very high in high MELD cirrhotic patients. However, the result of this study suggests a possible role for adrenal dysfunction as a factor in the pathogenesis of hyponatremia in cirrhosis beside other known factors as neurohormonal activation secondary to systemic vasodilation.

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No: 1751

Usefulness of prokalsitonin in predicting the diagnosis and severity of cirrhotic patients diagnosed with spontaneus bacteriel peritonitis

Erdoğan Şeyran[1], Nihat Okçu[2], Hakan Dursun[2], Fatih Albayrak[2], Ömer Yılmaz[2]

Ataturk University, Medical Faculty Internal Medicine Erzurum-Turkey[1], Ataturk University, Medical Faculty Gastroenterology Erzurum-Turkey[2]

Spontaneus bacterial peritonitis(SBP) is a frequently encountered and imported complication of decompensated liver cirrhosis and delay is SBP diagnosis causes serious problem. Procalcitonin is a calcitonin precursor protein which is the produced by cells of thyroid gland in healthy individuals. A half-life of procalcitonin in serum in 20-24 h which makes it suitable for daily monitoring and enables to control a course of treatment and to distinguish bacterial infection from other types of inflamations.

A hundred individuals included in the study are divided into three groups;

Group 1 (n: 50): Decompensated cirrhotic patients with spontaneous bacterial peritonitis (polymorphonuclear cells > 250/mm3 in acidic fluid and/or positive acidic fluid culture).

Group 2 (n: 25): Decompensated cirrhotic patients with sterile acidic fluid(< 250/mm3) in asidic fluid and negative acidic fluid culture).

Group 3 (n: 25): Healthy individuals in the control group included some functionally is disorders such as functionally dyspepsia or irratable bowel syndrome.

İn conclusion whether there is no difference the level of serum procalcitonin in spoantan bacterial peritonitis group, sterile ascitic fluid group and in control group. Our study showed that the predictor value of peripheral blood PCT levels in the evaluation of prognosis of decompensated cirrhotic patients is not important role.

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No: 2175

Clinical characterization and prevalence of metabolic risk factors in patients with cryptogenic cirrhosis a case control study

Shivaram Prasad Singh[1], Ayaskanta Singh[1], Preetam Nath[1], Bijay Misra[1], Pallavi Bhuyan[2], Kaumudi Pattnaik[2], Niranjan Rout[3], Chudamani Meher[4], Omprakash Agrawal[4]

Scb Medical College Gastroenterology Cuttack-India[1], Scb Medical College Pathology Cuttack-India[2], Acharya Harihara Regional Cancer Institute Pathology Cuttack-India[3], Beam Diagnostic Center Radiodiagnosis Cuttack-India[4]

Aim: To study the clinical profile of Cryptogenic Cirrhosis (CC) and evaluate the prevalence of metabolic risk factors in patients with CC.
Methods: Consecutive patients of CC with at least one episode of decompensation admitted between April and November 2014 were included. Patients with cirrhosis due to known etiology served as disease controls.
Results: 46 CC patients were compared with 40 disease controls. Controls consisted of cirrhotic patients due to alcohol abuse (29), chronic hepatitis B (10) and autoimmune hepatitis (1). Males outnumbered the females in the ratio of 2: 1 in the CC group. Ascites (66.7 %) and jaundice (33.3 %) were common mode of presentation. 32.6 % of CC patients were Child A, 52.2 % Child B and 15.2 % Child C cirrhosis. The prevalence of T2DM (26.1 % vs 15 %; OR-2.0, 95 % CI 0.67-5.94), obesity (50.0 % vs 17.5 %; OR-4.71, 95 % CI 1.74-12.81) and hypertension (19.6 % vs 10 %; OR-2.19, 95 % CI 0.62-7.75) was higher in CC patients than in disease controls. CC group patients were older (54.74 ± 15.53 vs 45.80 ± 10.31, $P = 0.003$), had higher BMI (23.07 ± 4.1 vs 20.89 ± 4.14 $P = 0.017$), FBS (126.9 ± 64.8 vs 92.7 ± 28.0, $P = 0.005$) and triglyceride (122.7 ± 44.5 vs 96.6 ± 34.8, $P = 0.005$). The Child and MELD scores were higher in the control group. There were no differences in total platelet count, liver function tests and lipid profile (except TG) between the two groups. On multivariate analysis only FBS was significantly higher in the CC group.
Conclusion: The patients with CC are older, diabetic, obese and hypertensive.These findings support the hypothesis that non-alcoholic steatohepatitis (NASH) may play an under-recognized role in CC.

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No: 1727

Hepatogenous diabetes and complications of liver cirrhosis

Jonila Cela[1], Anila Kristo[2], Jovan Basho[2], Liri Cuko[2], Bashkim Resuli[3]

University "a. Xhuvani" Faculty of Medical Science Elbasan-Albania[1], Uhc "Mother Teresa" Service of Hepatology and Gastroenterology Tirana-Albania[2], Uhc "mother Teresa" Service of Hepatology and Gastrenerology Tirane-Albania[3]

Background: Alterations in carbohydrates metabolism are prevalent in liver cirrhosis but its clinical implication on cirrhosis needs to be evaluated.
Aim: To evaluate the association of hepatogenous diabetes with complications in liver cirrhosis.
Methods: From January 2010 to December 2011, 75gm oral glucose tolerance test were evaluated in 100 heterogeneous patients with liver cirrhosis (83 % males and 17 % females, mean age 54.3 ± 11.7 years old) who had no history of diabetes mellitus. The etiology of cirrhosis population was alcohol (64 %), viral hepatitis B (19 %), viral hepatitis C (6 %) and cryptogenic (11 %). Patients recently treated with corticosteroids or with family history of DM2 are excluded. Glucose intolerance was defined as IGT or HDM. Multiple regression analysis was used to investigate the association between plasma glucose concentration and gender, age and complications in liver cirrhosis with significant p values ≤ 5 %.
Results: IGT and HDM were found 31 % and 20 % of the patient, respectively.There were no significant correlation between plasma glucose concentration and gender ($P = 0.712$, CI: 0.55–1.99), age ($P = 0.312$, CI: 0.67–1.23). The presence of HDM showed significant correlation with variceal haemorrhage and high HVPG, development of ascites and bacterial infections ($P = 0.02$, $P = 0.03$, $P < 0.05$, $P = 0.01$) respectively. We realized that 45 % patients with HDM had hepatic encephalopathy vs 18 % in patients with normal blood glucose levels ($P = 0.02$).
Conclusion: Prevalence of IGT and DM is significantly high in patients with liver cirrhosis. HDM have significant relationship with severe portal hypertension and variceal bleeding, ascites, bacterial infections and hepatic encephalopathy. Hepatogenous diabetes is a precipitating factor for complications of cirrhosis.

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No: 1065

Serum ca 125 levels are significantly elevated in patients with liver cirrhosis with ascites

Sebati Özdemir[1], Ibrahim Hatemi[1], Nurhan Demir[1], Murat Özbalak[1], Nuray Kepil[2], Eren Imre[1], Dildar Konukoğlu[3], Kadir Bal[1], Abdullah Sonsuz[1]

Istanbul University, Cerrahpaşa Faculty of Medicine Department of Internal Medicine, Division of Gastroenterology Istanbul-Turkey[1], Istanbul University, Cerrahpaşa Faculty of Medicine Department of Pathology Istanbul-Turkey[2], Istanbul University, Cerrahpaşa Faculty of Medicine Department of Biochemistry Istanbul-Turkey[3]

Aim: Tumor markers have been used in the diagnosis and follow-up of malign tumors. However, elevated serum levels of tumor markers may be found in benign diseases. The aim of this study was to investigate serum CA 125 level in patients with liver cirrhosis.
Methods: A total of 87 (56 males, 31 females) cirrhotic patients were included in the study (mean age: 61.3 ± 7.5; range: 41-84 yr). The etiology was hepatitis B (n = 42), hepatitis C (n = 31), alcoholic liver disease (n = 9), and cryptogenic cirrhosis (n = 5). Patients were grouped as cirrhosis with ascites (n = 53) and without ascites (n = 34). The control group consisted of 31 patients with inactive HBsAg carriers.
Results: All patients were controlled at least three times with a six-month interval and there were no malignancies in the patients. Serum CA 125 levels were slightly increased in 35.3 % (12/34) of cirrhotic patients without ascites. There was no statistically significant difference between cirrhotic patients without ascites and control group ($P = 0.06$). Serum CA 125 levels were elevated in 88.7 % (47/53) of patients with ascites; elevations of CA 125 were more than 200 U/mL in 26.4 % (14/53) of this group. Serum CA 125 levels were significantly elevated in cirrhotic patients with ascites compared to cirrhotic patients without ascites ($P < 0.0001$) and to control group ($P < 0.0001$).
Conclusion: These significantly elevated serum levels of CA 125 in patients with liver cirrhosis with ascites may be due to the reaction of the peritoneal mesothelial cells against ascites and/or may be related to the deterioration of the antigen clearance by the liver.

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No: 1566

Clinical consequences of hyponatremia in liver cirrhosis

Anila Kristo[1], Jonila Cela[2], Jovan Basho[1]

Uhc "Mother Teresa" Service of Hepatology and Gastroenterology Tirana-Albania[1], University "a. Xhuvani Faculty of Medical Science Elbasan-Albania[2]

Background: Hyponatremia is a frequent complication of cirrhosis and is associated with increased morbidity and mortality.
Aim: To determine the prevalence of hyponatremia and its impact in complication of liver cirrhosis.
Methods: From January 2009 to December 2011, 170 patients with liver cirrhosis hospitalized in UHC "Mother Teresa" were evaluated for the prevalence of hyponatremia (Na $<$ 135) and its correlation with Child-Pugh score, complications of liver cirrhosis. Patients were divided in two groups based on the level of serum sodium concentration (Na $\leq$ 130 mmol/l and 130 mmol/l $<$ Na $<$ 135 mmol/l). T test were used and values of $P < 0.05$ were considered statistically significant.
Results: In our study the prevalence of hyponatremia defined by serum sodium concentration $\leq$ 130 mmol/l, is 21.6 %. If the cutoff level of 135 mmol/l is used, the prevalence increases up to 58.8 %. In 170 patients with cirrhosis, 61.8 % and 38.2 % had a serum sodium concentration $>$130 mmol/l and $\leq$130 mmol/l, respectively. In our study 25 % of patients with hyponatremia $\leq$130 mmol/l were classified in Child B vs 72 % of them with Child C ($P < 0.002$). Hepatorenal syndrome, spontaneous bacterial peritonitis and hepatic encephalopathy were evaluated in 82, 68 and 75 % of patients with hyponatremia $\leq$130 mmol/l vs 20, 30 and 32 % of them with serum sodium concentration $>$130 mmol/l, respectively ($P < 0.05$, $P < 0.05$ and $P < 0.04$).
Conclusion: In patients with cirrhosis, the existence of hyponatremia is a major risk factor for the development of complications, which appear with greater frequency in patients with more severe hyponatremia and advanced liver disease.

Topic 18: Liver Cirrhosis and Complications

No: 1104

Procalcitonin is a surrogate marker of infection in cirrhosis patients with hepatocellular carcinoma after transarterial chemoembolization or radiofrequency therapy

Soo Hyun Yang[1], Wonhyeong Park[1], Seo Young Yang[1], Tae Gyoon Kim[1], Woong Sun Yoo[1], Do Young Kim[1]

Veterans Health Service Medical Center Internal Medicine Seoul-Korea, South[1]

Background/aims: Bacterial infections are life-threatening complications in patients with cirrhosis. But it is rather difficult who patients with hepatocellular carcinoma after loco-regional therapy such as transarterial chemoembolization (TACE) or radiofrequency ablation (RFA). The goal of this study was to determine the ability of serum procalcitonin in the diagnosis of bacterial infection in cirrhosis patients with hepatocellular carcinoma after TACE or RFA.
Methods: 256 patients with HCC after TACE or RFA were analysed and stratified into three groups according bacteriological and cirrhotic finding; cirrohotic with (group A = 48) and without (group B = 114) infection, and non-cirrhotic and non-infected (group C = 94). This retrospective cohort study which was conducted from June 2011 to May 2013. Measurement of serum procalcitonin and CRP level was performed on during admission after TACE or RFA.
Results: Serum procalcitonin levels were significantly higher in cirrhotic patients with bacterial infection (Group A; 3.4 ng/ml [0.4-25.1]) rather than without infection (Group B; 0.6 ng/ml [0.1-7.8]) and non-cirrhotic and non-infected (Group C; 0.4 ng/ml [0.1-1.6]), respectively. Using a cut-off level of 0.8 ng/ml, provided the most accurate in identifying patients with infection (AUC: 0.91, Sensitivity: 94 %, Specificity: 75 %). In subgroup analysis by treatment modality, Serum procalcitonin level was also helpful in the TACE-treated group and RFA-treated group. However, serum CRP level was less sensitive and specific for the diagnosis of infection.
Conclusions: Serum procalcitonin is a useful marker to predict the clinically significant bacterial infection in patients with hepatocellular carcinoma after loco-regional treatment such as transarterial chemoembolization or radiofrequency ablation.

Topic 18: Liver Cirrhosis and Complications

No: 1984

Impact of portal vein thrombosis in the survival of cirrhosis patients

Hale Gokcan[1], Meral Akdogan Kayhan[1], Sabite Kacar[1], Erkin Oztas[1], Orhan Coskun[2], Nuretdin Suna[1], Zeki Mesut Yalin Kilic[1], Ertugrul Kayacetin[1]

Ankara Yuksek Ihtisas Research and Training Hospital Gastroenterology Ankara-Turkey[1], Ankara Yuksek Ihtisas Research and Training Hospital Internal Medicine Ankara-Turkey[2]

Background & aims: Portal vein thrombosis (PVT) may ensue in the natural course of cirrhosis. Despite being a frequent complication, impact of PVT itself, is not clear in the survival of cirrhosis patients. Therefore in this single center study, we did retrospective survival analysis on cirrhosis patients to reveal the effect of PVT.
Methods: We reviewed files of 240 cirrhosis patients that were diagnosed and followed up at our institution between 1988-2012. Survival analyses were done by Kaplan–Meier analyses.
Results: There were 150 (61.5 %) males in this study. Mean age was 48.6 $\pm$ 11.9. There were 150 (45.9 %) child A, 120 (49.2 %) child B, 7 (6.25 %) child C patients in this analysis. MELD score was between 12-25 (mean 12.6). Mean follow up was 78.2 months (between 24-312 months). PVT was diagnosed in 37.7 % (92 patients) in this group. 41 patients (16.8 %) died in the follow up. Survival rates were 97.8, 95.3 and 73.1 % in 3, 5 and 10 years in PVT group and 96, 87.3 and 66 % in 3, 5 and 10 years in the patients with patent portal vein. Cumulative survival was estimated as 240.4 $\pm$ 14.3 months in patients with PVT and 230.7 $\pm$ 15.4 months in patients with patent portal vein. No significant difference in survival was found between those two groups ($P = 0.25$).
Conclusions: We did not find a significant effect of PVT on survival in cirrhosis patients. Further multicenter prospective studies are needed to clarify this matter.

Topic 18: Liver Cirrhosis and Complications

No: 1185

Platelet count spleen diameter ratio non invasive marker for predicting bleeding from esophageal varices

Roxanne Mae Butal[1]

Chong Hua Hospital Internal Medicine Cebu City-Philippines[1]

Background and objectives: Esophageal varices are a common complication of portal hypertension. Fifty percent of cirrhotic patients per year will develop varices over their lifetime; of these, 5-15 % per year would bleed. Although bleeding may resolve spontaneously in 40 %, it has a mortality rate of at least 20 % at 6 weeks. However, the cost of endoscopy had been detrimental to compliance to management, increasing mortality associated with variceal bleeding. This study will determine the platelet count/spleen diameter (PCSD) ratio cut-off that can be a non-invasive marker for predicting bleeding from esophageal varices.
Methods: This is a cross sectional retrospective chart review study of patients with esophageal varices in a tertiary hospital from January 2010 to June 2014. Data were collected from medical records and from the computer generated data system of the hospital. PCSD ratio for each patient were calculated, tabulated and analyzed.
Results: A total of 47 patients were included. Results show that spleen diameter, varix grade and PCSD ratio are all significantly associated with bleeding esophageal varices. A PCSD ratio of < 1014 is independently associated with bleeding with a sensitivity of 78 % and specificity of 55 %. PPV and NPV were 70 % and 64.7 % respectively.
Conclusion: PCSD ratio of < 1014 with a sensitivity of 78 % and specificity of 55 %, PPV and NPV of 70 % and 64.7 % may allow timely detection and more aggressive management, including earlier access to endoscopy. However, to conduct large, prospective, multicenter studies regarding PCSD ratio as a non-invasive marker for predicting variceal bleeding is encouraged to further validate its usefulness.

Topic 18: Liver Cirrhosis and Complications

No: 1256

The correlation between 25 hydroxy vitamin d level and liver fibrosis by transient elastography in patient with compensated chronic liver disease

Bong Jin Ko[1], Young Seok Kim[1], Sang Gyune Kim[1], Sae Hwan Lee[1], Soung Won Jeong[1], Jae Young Jang[1], Hong Soo Kim[1], Boo Sung Kim[1], Sun Mi Kim[1], Young Don Kim[2], Gab Jin Cheon[2]

Soon Chun Hyang University School of Medicine Digestive Disease Center and Research Institute, Department of Internal Medicine Bucheon-Korea, South[1], Gangneung Asan Hospital, University of Ulsan College of Medicine Department of Internal Medicine Gangneung-Korea, South[2]

Backgrounds: Low 25-hydroxy Vitamin D [25(OH)D3] serum levels were correlated with severe liver fibrosis in chronic hepatitis C patients. The purpose of this study was to evaluate correlation between 25(OH)D3 level and liver fibrosis by TE in patient with compensated chronic liver disease (CLD).
Methods: Between January 21, 2013 and May 31, 2014, total 227 CLD patients were determined 25(OH)D3 serum levels and liver stiffness values using TE. Among 227 CLD patients, 179 compensated CLD patients were enrolled. We retrospectively reviewed the medical records and analyzed.
Results: The mean age of patients was 48 years and 131 (73.2 %) patients were male. Main etiology was chronic hepatitis B (n = 97, 54.2 %), other etiologies comprised chronic hepatitis C (n = 15 8.4 %), non-alcoholic fatty liver disease (n = 15 8.4 %), alcohol (n = 37, 20.7 %) and other causes (n = 15 8.4 %). The median liver stiffness value was 6.8 kPa and mean 25(OH)D3 level was 14.2 ng/ml. The number of patients with 25(OH)D3 deficiency (< 20 ng/ml), severe 25(OH)D3 deficiency (< 10 ng/ml) and advanced liver fibrosis by TE (> 12.5 kPa) were 80 (44.7 %) 66 (36.9 %) and 43 (24 %) respectively. There was a significantly correlation between 25(OH)D3 deficiency and liver stiffness ($r = 0.227$, $P < 0.002$). We evaluated factors associated with advanced liver fibrosis. On the multivariate analysis, AST [aOR1.02(95 % CI 1.00-1.04),$P = 0.017$], Severe 25(OH)D3 deficiency [OR 3.58(95 % CI 1.09-11.66),$P = 0.034$] and total bilirubin [OR 3.16(95 % CI 1.02.-9.71),$P < 0.045$] were significantly associated with advanced liver fibrosis.
Conclusions: Low 25(OH)D3 levels are associated with advanced liver fibrosis by TE in compensated CLD. Thus, large prospective study are needed to evaluate the prognosis of low 25(OH)D3 levels in compensated CLD patients.

Topic 18: Liver Cirrhosis and Complications

No: 1822

Left ventricular geometric remodelling and diastolic dysfunction proportion and correlation with stage of liver dysfunction severity

Prionggo Mondrowinduro[1], Irsan Hasan[2], Rasmijon Rasmijon[3], Idrus Alwi[3], Murdani Abdullah[2]

Faculty of Medicine University of Indonesia-Cipto Mangunkusumo General Hospital Internal Medicine Department Jakarta-Indonesia[1], Faculty of Medicine University of Indonesia-Cipto Mangunkusumo General Hospital Gastroenterohepatology Division of Internal Medicine Jakarta-Indonesia[2], Faculty of Medicine University of Indonesia-Cipto Mangunkusumo General Hospital Cardiology Division of Internal Medicine Jakarta-Indonesia[3]

Aim: To determine proportion of left ventricular diastolic dysfunction and left ventricular geometry remodelling among liver cirrhotic patients according to American Society of Echocardiography-European Association of Echocardiography 2009 (ASE-EAE),to determine any correlation between left ventricular diastolic dysfunction severity stage with severity stage of liver dysfunction in cirrhotic liver patients represented by numerical Child Turcotte Pugh score.
Method: This cross sectional study included 96 liver cirrhotic patients within age 18-60 year old due to any cause who were admitted to Cipto Mangunkusumo General Hospital. It started in November 2013 until sample size was obtained completely. Exclusion criterion were applied to eliminate any causes of diastolic dysfunction and myocard remodelling but diabetes, remedies of propranolol and spironolactone were included. An ASE-EAE standard calibrated echo unit of Esaote MyLabFive SN-05-01879.2010-03 was operated.Interobserver validity between 2 operators who had similar qualification in echocardiography training were corroborated with Kappa level and mean difference.Proportion, normality test and Spearman correlation were elaborated.
Result: Causes of liver cirrhosis were hepatitis B 57.3 %,C 2.6 %, NAFLD 9.4 %, biliary cirrhosis 2.1 %, unknown 5.2 %. Proportion of Child A is 50 %, B 34.3 %, C 15.7 %. Prevalence of portal hypertension was 76 %. Left ventricular geometry proportion includes concentric hypertrophy 64,58 %,eccentric hypertrophy 29.16 %, concentric remodelling 4.17 %, normal geometry 2.08 %. Diastolic dysfunction prevalence is 34.3 % and 21.9 % has normal diastolic function with left atrial enlargement. R value is 0.42 $P = 0{,}000$ with confidence interval 0.22–0.62. Subgroup analysis in 62 patients that excluding diabetes and spironolactone results in r 0.51 $P = 0.000$ with confidence interval 0.25–0.77.

Conclusion: There are high proportion of left ventricular and left atrium remodelling among liver cirrhotic patients with moderately positive correlation between severity of diastolic dysfunction with severity of liver dysfunction.

Topic 18: Liver Cirrhosis and Complications

No: 1268

Serum ca 125 levels are significantly elevated in patients with liver cirrhosis with ascites

Sebati Özdemir[1], Ibrahim Hatemi[1], Nurhan Demir[1], Murat Özbalak[1], Nuray Kepil[2], Eren Imre[1], Dildar Konukoğlu[3], Kadir Bal[1], Abdullah Sonsuz[1]

Istanbul University, Cerrahpaşa Faculty of Medicine Department of Internal Medicine, Division of Gastroenterology Istanbul-Turkey[1], Istanbul University, Cerrahpaşa Faculty of Medicine Department of Pathology Istanbul-Turkey[2], Istanbul University, Cerrahpaşa Faculty of Medicine Department of Biochemistry Istanbul-Turkey[3]

Aim: Tumor markers have been used in the diagnosis and follow-up of malign tumors. However, elevated serum levels of tumor markers may be found in benign diseases. The aim of this study was to investigate serum CA 125 level in patients with liver cirrhosis.
Methods: A total of 87 (56 males, 31 females) cirrhotic patients were included in the study (mean age: 61.3 ± 7.5; range: 41-84 yr). The etiology was hepatitis B (n = 42), hepatitis C (n = 31), alcoholic liver disease (n = 9), and cryptogenic cirrhosis (n = 5). Patients were grouped as cirrhosis with ascites (n = 53) and without ascites (n = 34). The control group consisted of 31 patients with inactive HBsAg carriers.
Results: All patients were controlled at least three times with a six-month interval and there were no malignancies in the patients. Serum CA 125 levels were slightly increased in 35.3 % (12/34) of cirrhotic patients without ascites. There was no statistically significant difference between cirrhotic patients without ascites and control group ($P = 0.06$). Serum CA 125 levels were elevated in 88.7 % (47/53) of patients with ascites; elevations of CA 125 were more than 200 U/mL in 26.4 % (14/53) of this group. Serum CA 125 levels were significantly elevated in cirrhotic patients with ascites compared to cirrhotic patients without ascites ($P < 0.0001$) and to control group ($P < 0.0001$).
Conclusion: These significantly elevated serum levels of CA 125 in patients with liver cirrhosis with ascites may be due to the reaction of the peritoneal mesothelial cells against ascites and/or may be related to the deterioration of the antigen clearance by the liver.

Topic 18: Liver Cirrhosis and Complications

No: 2039

Prediction of oesophageal varices by measuring blood ammonia level in cirrhotic patients

Mohammad Faiz Ahmad Khondaker[1], Sheikh Mohammad Noor-e Alam[2], M.a Rahim[3], Ahmed Lutful Moben[4], Sharmin Akter Sumi[5], Mamun Al- Mahtab[6], Salimur Rahman[6]

Shahed Suhrawardy Medical College Hospital, Dhaka, Bangladesh. Hepatology Dhaka-Bangladesh[1], Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh Hepatology Dhaka-Bangladesh[2], Mats, Noakhali Mats Noakhali-Bangladesh[3], Shaheed Suhrawardy Medical College, Dhaka Medicine Dhaka-Bangladesh[4], Dhaka Medical College, Dhaka Plastic Surgery Dhaka-Bangladesh[5], Bsmmu Hepatology Dhaka-Bangladesh[6]

Aim: Portal hypertension in cirrhosis leads to formation of varices as well as rise of ammonia level in systemic circulation. Realizing the need for non-invasive markers of oesophageal varices (OV) in order to reduce the number of endoscopy screening, this study was aimed to determine whether blood ammonia concentrations can predict the size of OV.
Method: This was a cross-sectional study conducted upon forty consecutive cirrhosis patients and forty age matched non cirrhotic control subjects. Fasting blood ammonia was measured in both groups and meticulous survey by upper gastrointestinal endoscopy was done in cirrhotic patients to note different sizes of OV.
Results: Cirrhosis patients group had mean ammonia level of 84.88 μmol/L compared to 28.47 μmol/L in control group. The mean (± SD) blood ammonia concentration in small OV group was 72.00 (± 39.13) μmol/L and in medium or large OV group was 97.75 (± 31.34) μmol/L. The difference was significant at P value < 0.05 level. Blood ammonia level 63 μmol/L had sensitivity of 95 % and specificity of 50 % in detecting medium and/or large OV in patients with cirrhosis. Its positive predictive value (PPV) was 65.5 and negative predictive value (NPV) was 90.9 with accuracy of 72.5.
Conclusion: There was a moderate but significant correlation between blood ammonia level and size of OV. It could be a good tool at identifying individuals with large OV who will need to undergo endoscopy more frequently.

Topic 18: Liver Cirrhosis and Complications

No: 1811

"Hyponatremia" is prognosis factor of refractory ascites in decompensated liver cirrhosis patients

Shuntaro Obi[1], Shinpei Sato[1], Toshihiro Kawai[1], Masatugu Ishii[1], Takafumi Sugimoto[1], Yoko Yashima[1], Takahisa Sato[1], Miho Kanda[1]

Kyoundo Hospital Gastroenterology Tokyo-Japan[1]

Aim: To evaluate the prognosis factor in decompensated liver cirrhosis patients with or without further complications, such as hepatorenal syndrome and/or hepatocellular carcinoma.
Methods: Twenty-six patients (median age 67 years, males: 20) with decompensated liver cirrhosis and refractory ascites were enrolled. All patients received diuretics (20-80 mg/day of furosemide and 50-100 mg/day of spironolactone). Furthermore we add tolvaptan (7.5-15 mg/day for 7 days). The etiology of cirrhosis included hepatitis B (19 %), hepatitis C (46 %) and non B non C hepatitis (35 %). For analysis of prognosis, we perform multivariate analysis by cox proportional hazard model. Changes in the body weight were assessed. The serum sodium levels were also measured, and adverse events were recorded. A follow-up assessment was conducted 7 days after treatment with tolvaptan.
Results: Median survival time (MST) was 65 days. In multivariate analysis, prognostic factor was hyponatremia ($P = 0.037$, O.R. 0.278, 95 % CI 0.086-0.906). MST was 50 days in hyponatremia group (n = 14), 268 days in normal group (n = 12). The incidence of hyponatremia was 54 %. In patients with hyponatremia, the serum sodium levels increase after tolvaptan.
Conclusion: "Hyponatremia" is prognosis factor of refractory ascites in decompensated liver cirrhosis patients. Tolvaptan is a promising

aquaretic for the treatment of hyponatremia in refractory ascites with decompensated liver cirrhosis patients.

Topic 18: Liver Cirrhosis and Complications

No: 1089

The accuracy of the fib 4 index for the diagnosis of significant fibrosis in children with chronic hepatitis B

Hong Shi[1], Jianyun Zhu[1], Haixiang Sun[1], Yutian Chong[1]

The Third Affiliated Hospital of Sun Yat-sen University Department of Infectious Diseases Guangzhou-China[1]

Objective: The aim of our study was to assess the accuracy of the FIB-4 index for the diagnosis of significant fibrosis in children with chronic hepatitis B by comparing their results with histological features.
Methods: 144 children with a mean age of 15 years were collected from Third Affiliated Hospital of SUN Yet-sen University. All of them underwent liver biopsy with a blood sample taken simultaneously. The serum level of ALT, AST, PLT were tested. These results together with age of these patients were put into the formula and final results of FIB-4 were computed. An endpoint were studied according to liver fibrosis stage, namely significant fibrosis (S2 to S4). With liver biopsy as the gold standard, ROC curve were delineated for the endpoint. The area under the ROC curves reflected its diagnostic values.
Results: The distribution of their grade of liver inflammation and stage of liver fibrosis using the Scheuer criteria was as follows: G1 45(31.2 %),G2 58(40.3 %),G3 51(28.5 %); S0 2(1.4%), S1 50(34.7%), S2 75(52.1%), S3 15(10.4%), S4 2(1.4%). About two-thirds patients had significant fibrosis (S2-S4). The AUC of FIB-4 for significant fibrosis was 0.752 (95 % CI 0.664–0.809, $P < 0.01$). When the cut-off value was set at 0. 23, the negative predictive value to exclude significant fibrosis was 89 % with a sensitivity of 68.1 % and a specificity of 72.1 %.
Conclusion: The FIB-4 index is a simple, accurate and inexpensive method to assess liver fibrosis in children with chronic hepatitis and may reduce the need for liver biopsy.
[Key words] hepatitis B, chronic, FIB-4 index, liver fibrosis, children

Topic 18: Liver Cirrhosis and Complications

No: 1952

Is prealbumin rather than albumin a more sensitive indicator of liver dysfunction in child a cirrhosis

Murat Kekilli[1], Dag Zuhal[2], Dogan Zeynal[1], Cakal Basak[1], Biyikoglu Ibrahim[1], Filik Levent[1], Babali Aysegul[1]

Ankara Education and Research Hospital Gastroenterology Ankara-Turkey[1], Ankara Education and Research Hospital Internal Medicine Ankara-Turkey[2]

Objective: Patients with chronic liver diseases are at an increased risk for having nutritional deficiency. Prealbumin is a hepatic protein, sensitive and cost-effective methods for assessing malnutrition in patients with chronic disease. In this study, we aim to evaluate the serum prealbumin concentration might be a more sensitive indicator than albumin in assessing liver dysfunction in Child A cirrhosis.
Methods: A total of 42 patients with cirrhosis including 27 (64.3 %) of Child A cirrhosis and 15 (35.7 %) of Child B cirrhosis were recruited in the study. Cirrhosis etiologies for patients were as follow: 18 of hepatitis B, 5 of hepatitis C, 16 of cryptogenic, 1 of alcohol, 1 of autoimmune, 1 of hepatosteatosis. Baseline characteristics of two groups of patients are seen in Table 1.
Results: Prealbumin levels were significantly lower in patients with Child B cirrhosis than those with Child A cirrhosis ($P < 0.001$). There were not significant difference for body mass index (BMI) between two groups ($p > 0.996$). There were no significant differences for prealbumin and BMI when patients divided into groups for cirrhosis etiologies ($p > 0.599$, $p > 0.385$ respectively). Albumin, INR and hemoglobin values were significantly lower in patients with Child B cirrhosis ($P < 0.001$, $P < 0.001$, $P < 0.031$ respectively) (Table 1). Prealbumin was significantly more sensitive than albumin to predict Child A cirrhosis rather than Child B cirrhosis ($P < 0.019$, $p > 0.068$ respectively).
Conclusion: Prealbumin monitoring in patients with chronic liver diseases may predict the progression to cirrhosis earlier independently from BMI, albumin and INR.

Topic 19: Liver Transplantation

No: 1554

Is there long term viral relapse in the cases that underwent liver transplantation for hbv and received Tenofovir

Murat Aladag[1], Salih Kilic[2], Yilmaz Bilgic[1], Murat Harputluoglu[1], Yasir Furkan Cagin[1], Mehmet Ali Erdogan[1], Yahya Atayan[1], Oğuzhan Yildirim[1], Yuksel Seckin[1], Melih Karincaoglu[1], Cuneyt Kayaalp[3], Sezai Yilmaz[3]

Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[1], Inonu University Faculty of Medicine Internal Medicine Malatya-Tunisia[2], Inonu University Faculty of Medicine General Surgery[3]

Introduction and aim: The present study aimed to retrospectively evaluate the patients, who underwent liver transplantation in Hepatology clinic between 2009 and 2014 due to HBV-related cirrhosis and received Tenofovir, in terms of viral suppression and HBV relapse.
Material and method: A total of 189 patients (143 males and 46 females) that fulfilled the criteria were enrolled in the study among 250 patients with a mean age of 46 years. Whilst the study comprised that patients that received tenofovir for at least 12 months after transplantation. Viral suppression and relapse rate at the end of 5 years were evaluated in the patients.
Results: Of the 189 patients, 104 have been receiving tenofovir, 82 have been receiving lamivudine, before transplantation. Considering postoperative 1st, 3rd, 6th and 12th-month and then yearly HBV-DNA values, it was observed that HBV-DNA value notably decreased as of the first month and became negative after the 12th month. In the present study, HBV DNA values on the 12th month after liver transplantation performed due to HBV-related cirrhosis revealed complete response in 180 patients (95.24 %), partial response in 8 (4.26 %) patients and inadequate response in 1 (0.5 %) patient. That is to say, satisfactory response was obtained in 99.5 % of the participants. Resistance against Tenofovir was not observed in any of the cases.
Conclusion: In conclusion, it was demonstrated that tenofovir is an effective and safe agent to be used after liver transplantation performed due to chronic hepatitis B-related cirrhosis and prevents HBV relapse, and no resistance developed against tenofovir therapy.

Topic 19: Liver Transplantation

No: 1543

Hepatic tuberculosis in explants of patients undergoing liver transplantation

Deeplaxmi Borle[1], Kishore Bharathy[1], Senthil Kumar[1], Archana Rastogi[2], Sachin Kumar[3], Viniyendra Pamecha[1]

Institute of Liver & Biliary Sciences (ilbs) Liver Transplantation and Hpb Surgery New Delhi-India[1], Institute of Liver & Biliary Sciences (ilbs) Pathology New Delhi-India[2], Institute of Liver & Biliary Sciences (ilbs) Pulmonary Medicine New Delhi-India[3]

Aims: To review the incidence of hepatic tuberculosis (TB) in patients undergoing liver transplantation, their clinical course and outcome.
Methods: Hepatic TB was defined by characteristic granulomas identified on explant pathology. Case records and explant histopathology slides of all 166 patients undergoing a liver transplantation from March 2010 to October 2014 in a predominantly living donor program at a referral, teaching hospital were scrutinised to identify patients with hepatic TB. Data pertaining to the diagnosis, perioperative course and management of TB was collected.
Results: Three men (1.8 %), aged 52-60 years, had multiple caseating epitheloid granulomas consistent with hepatic TB, diagnosed on the explant and periportal lymph nodes. Two were clinically silent. Two had a pre-operative diagnosis of extra-hepatic TB (TB pleural effusion diagnosed by polymerase chain reaction; mediastinal lymph node positive for acid fast bacilli [AFB] on endoscopic ultrasound guided biopsy); they received modified anti-tubercular treatment (ATT) pre-operatively. Only one of these had a positive tuberculin skin test. Two had an associated hepatocellular carcinoma. None of the granulomas showed AFB. All patients tolerated ATT post transplant. One succumbed to sepsis at 6 weeks. Two have completed 12 months of ATT and are recurrence free at 13 and 16 months respectively.
Conclusion: Hepatic TB can be silent in liver transplant candidates and hence should be diligently looked for in explants. Patients with caseating epitheloid granulomas in explants should be treated by a modified ATT regime.

Topic 19: Liver Transplantation

No: 1986

Liver transplantation for incurable alveolar echinococcosis an early report of 30 cases from an endemic region in Turkey

Bülent Aydinli[1], Gürkan Öztürk[1], Şükrü Arslan[1], Ercan Korkut[1], Abdullah Kisaoğlu[1], Ayşenur Dostbil[2], Önder Tan[3], Kemalettin Özden[4], Abdülmecit Kantarci[5]

Ataturk University Faculty of Medicine General Surgery Erzurum-Turkey[1], Ataturk University Faculty of Medicine Anesthesia and Reanimation Erzurum-Turkey[2], Ataturk University Faculty of Medicine Plastic Surgery Erzurum-Turkey[3], Ataturk University Faculty of Medicine Infectious Diseases Erzurum-Turkey[4], Ataturk University Faculty of Medicine Radiology Erzurum-Turkey[5]

Aim: Alveolar echinococcosis is a disease having tumor-like pathophysiology with a mortal prognosis, if left untreated; sometimes with the only treatment option left being liver transplantation. In this study, we aimed to share the early results of the patients who had undergone liver transplantation with the indication of alveolar echinococcosis.
Material-method: Patients who had undergone liver transplantation with the diagnosis of alveolar echinococcosis in our center between April 2011 and October 2014 were analyzed retrospectively. Patients who underwent liver transplantation in the last 3 months were excluded from the study. The demographic characteristics and clinical features of 30 patients who participated in the study were noted.
Results: Among transplanted patients, 22 underwent living-donor transplantation (73.3 %) while in 8 patients cadaveric (26.7 %) liver transplantation was performed. The most common indication for transplantation was hilar invasion (14 patients, 46.6 %). Prior to transplantation, drainage procedures were performed in 12 patients (40 %). Because of AE invasion, vena cava resection was made in 5 patients and vena porta resection in 2 patients. The mean follow-up period of the patients following transplantation was 17.9 months. Primary nonfunction developed in 2 patients after transplantation. A total of 6 patients died during follow-up, with the most common cause of death being sepsis (3 patients).
Conclusion: When compared to the conventional liver transplantation, surgical challenges are more frequently encountered in liver transplantation with the indication of hepatic alveolar echinococcosis. Therefore, the surgical team should be capable of using various reconstruction techniques for revision of hepatic artery, portal vein and vena cava.

Topic 19: Liver Transplantation

No: 2081

Development of malignancy after liver transplantation a case series

Sabite Kacar[1], Hale Gökcan[1], Murat Ulaş[2], Erol Aksoy[2], Meral Akdoğan[3], Birol Bostancı[2], Musa Akoğlu[2]

Tyih Gastroenterology Ankara-Turkey[1], Tyih Gastroenterology Surgery Ankara-Turkey[2], Tyih Gastroenterogy Ankara-Turkey[3]

1Kacar Sabite, 1Gökcan Hale, 2Ulaş Murat, 2Aksoy Erol, 1Akdoğan Meral, 2Bostancı Birol, 2Akoğlu Musa

Introduction: The cumulative incidence of de novo cancer is reported higher among LT recipients versus an age- and sex-matched non-transplant control population. It increases from 3 % at 1 to 20 % at 10 years after LTx. Cutaneous malignancies, lung cancer, oropharyngeal cancer, colon cancer, cervix cancer, lymphoproliferative malignancies are reported after LTx. We present 3 patients developed different malignancies after LTx.
Cases: There were 87 patients with LTx in our series. Liver disease etiologies are as follows: 39 HBV, 11 HCV, 3 HBV + HCV, 1 HDV, 16 HCC (11 HBV, 4 HCV, 1 HBV + HCV), 11 idiopathic, 6 ALF, 6 WD, 3 PBC, 3 alcohol, 1 AIH, 1 BCS, 1 hemangioendothelioma, 1 GSD. 3 patients developed non-HCC malignancy in follow up (Table).
Results: The development of postTx cancer could be a great problem. Skin cancer incidence is reported as 0.70 %, 2.31 % in 5 and 15 years. The SIR values of de novo malignancy after LTx are 0-212 for Kaposi's sarcoma. The incidence of post-transplant lymphoproliferative disorder varies from 1 to 20 % depending on the type of transplant. Not only is the risk of developing cancer higher, the diagnosis is likely to carry a worse prognosis after LTx. 2 patients were died in our series in a short time after diagnosis of malignancy.

Topic 19: Liver Transplantation

No: 2188

Mucormycosis in liver transplant recipients case report

Aysun Yalci[1], Menekse Ozcelik[2], Deniz Balci[3], Ramazan Idilman[4], Alpay Azap[1], Ismail Balik[1]

Ankara University Faculty of Medicine Infectious Diseases and Clinical Microbiology Ankara-Turkey[1], Ankara University Faculty of Medicine Anesthesiology and Reanimation Ankara-Turkey[2], Ankara University Faculty of Medicine General Surgery Ankara-Turkey[3], Ankara University Faculty of Medicine Internal Medicine, Gastroenterology Ankara-Turkey[4]

Case I:

A 50 year old woman with cryptogenic liver cirrhosis was candidate for liver transplantation. Since she had nasal congestion paranasal sinus computed tomography (CT) was performed. Tomography revealed left pansinusitis. Endoscopic examination a lesion was seen at posterior wall of the nasopharynx. Biopsy revealed mucormycosis. After 20 days of amphotericin B treatment the paranasal sinus CT showed no improvement so, posaconasol was added to the treatment. But due to hepatic encephalopathy she was transferred to intensive care unit and died due to other infectious complications before transplantation.

Case II:

A 60 year old man underwent liver transplantation due to chronic hepatitis B and hepatocellular carcinoma. After three months, he complained about toothache. His tooth was extracted and his nasal examination revealed necrosis in right lower concha. The necrotic material was debrided and pathology revealed mucormycosis. Mucorales grew in the tissue cultures. Amphotericin B and posaconasol was added to his treatment. His immunosuppressive treatment was adjusted. His treatment completed and he is doing well now.

Hepatic failure and liver transplantation may result with opportunistic infections. Zygomycosis are life-threatening infections. Factors influencing the outcome include early diagnosis and therapy, dissemination of the disease at the time of diagnosis, as well as the underlying immunosuppression. Reduction of the immunosuppression, control of hyperglycemia and antifungal therapy are treatment modalities. Posaconazol is used as a salvage therapy. High success and survival rates reported provide encouraging data regarding posaconazole as an alternative therapy for zygomycosis.

Topic 19: Liver Transplantation

No: 1792

First report of over 150 living donor liver transplants in a public sector hospital in India

Viniyendra Pamecha[1], Senthil Kumar[1], Kishore Gs Bharathy[1], Tk Chattopadhyay[1], Piyush Sinha[1], Chandrakant Pandey[2], Seema Alam[3], Amar Mukund[4], Shivkumar Sarin[5]

Institute of Liver and Biliary Sciences Hpb Surgery New Delhi-India[1], Institute of Liver and Biliary Sciences Anesthesia and Critical Care New Delhi-India[2], Institute of Liver and Biliary Sciences Pediatric Hepatology New Delhi-India[3], Institute of Liver and Biliary Sciences Radiology New Delhi-India[4], Institute of Liver and Biliary Sciences Hepatology New Delhi-India[5]

Introduction: Public sector hospitals are the mainstay of health care for the vast majority of the population in India. Living donor liver transplantation (LDLT), is the predominant modality of LT and there is no other successful LDLT program in a public sector hospital, currently in India. Methods: Analysis of prospectively collected data on 162 patients who had LT between March 2010 and October 2014, in a HPB Surgery and Liver Transplant Unit in a teaching hospital.
Results: Among 162 liver transplants (156 LDLT; 6DDLT), 144 were adult and 18 paediatric. Overall, 100 were elective for chronic liver disease (CLD), while 54 (33 %) were emergency (24 ACLF and 30ALF). of the 18 paediatric recipients (17 LDLT), 11 had ALF. Alcoholic ($n = 56$) and cryptogenic liver disease ($n = 29$) were the commonest etiologies for CLD; 8 patients had HCC (6 Milan;2 UCSF criteria). About 37 % of CLD patients had a MELD-Na > 25.About 15 % had biliary complications. Hepatic artery thrombosis occurred in 6 %. All but one were salvaged successfully (thrombolysis: 3;surgical: 7). For the entire cohort, the in-hospital mortality was 18 % and major morbidity rate was 35 %. An era effect was noticed with a tendency to better results with time, when comparing procedures done before 2013 to those done in 2013: In hospital mortality (27 % vs 6.5 %); HAT (9 % vs 6.5 %); biliary complications (14 % vs 8.6 %); donor morbidity (23 % vs 2 %). of the 156 live donors major complication rate ($\geq$ Clavien-DindoIIIB) was seen in 3.6 %.
Conclusion: With increasing experience, good results with LDLT can be achieved in a public sector setting in India.

Topic 19: Liver Transplantation

No: 2186

Liver transplant experience in republic of Moldova

Vladimir Hotineanu[1], Adrian Hotineanu[1], Natalia Taran[2], Iulianna Lupasco[2], Angela Peltec[3], Grigore Ivancov[4]

State University of Medicine and Pharmacy "n.testemitanu" Department of Surgery N2 Chisinau-Moldova[1], State University of Medicine and Pharmacy "n.testemitanu" Scientific Laboratory of Gastroenterology Chisinau-Moldova[2], State University of Medicine and Pharmacy "n.testemitanu" Clinics of Gastroenterology, Department of Internal Medicine Chisinau-Moldova[3], Central Republic Hospital Chisinau-Moldova[4]

Introduction: Republic of Moldova occupies a leading place in liver cirrhosis (LC) mortality rate, which in 2012 reached 81,6 cases per 100,000 population. LC has occupied the third pace in death causes in the population structure of RM.
Aim: assessment of liver transplantation (LT) as a life-preserving procedure for people with organ failure.
Materials and methods: The waiting list for LT consists of 70 patients, mean age 30,21 $\pm$ 2,04 years, of whom 18 patients died (25,7 %) during 1 year of transplant waiting. LC of HDV (46,15 %) and HCV (21,15 %) etiology predominate in the list.
The first succeeded LT was achieved in 2013. We present the preliminary experience of the first 12 cases of LT, conducted in 2013-2014, - 7 were performed from living donor and 5 whole liver LT from brain dead donor .
Results: The study included: 2 LT patients with LC HDV and hepatocellular carcinoma, 2 - LC HCV, 2- LC HBV, 4 - LC HDV and 1 patient with primary biliary cirrhosis. Postoperative morbidity was estimated in two cases: 1—brain haemorrhage and 2 - acute rejection. In one case developed postoperative hepatic artery thrombosis (day 3) with performance of liver re-transplant (day 5). Post transplant postoperative complications presented: renal - 2, respiratory - 4, postoperative bleeding - 1, acute rejection—2, convulsions-1. Mortality in 1 year—0.

Conclusion: The introduction of liver transplantation in RM became a crucial moment in the development of liver surgery in the country, improving survival rate of patients.

Topic 19: Liver Transplantation

No: 1891

Incidence and predictors of infections within 3 months post transplant in living donor liver transplant recipients

Harikumar Nair[1], Harshavardhan Rao[2], Sudheendran Surendran[3], Rama Venu[4], Balakrishnan Vallath[4]

Amrita Institute of Medical Sciences Digestive Diseases Institute Cochin-India[1], Amrita Institute of Medcal Sciences Digestive Diseases Institute Cochin-India[2], Amrita Institute of Medical Sciences Solid Organ Transplat Institute Cochin-India[3], Amrita Institute of Medical Sciences Digestive Diseases Institute Cochin-India[4]

Introduction: Infections are extremely common in the immediate post-operative period and is one of the leading causes of morbidity and mortality, especially in the Asian transplant centres which mostly perform Living donor Transplant.
Methods: Retrospectively collected data were analyzed from 104 consecutive living donor liver transplants done for End stage liver disease over 36 months from January 2009–April 2013. Baseline data on the incidence of infections as confirmed with culture positivity (Blood, sputum, urine & drain fluid) were collected.Univariate and multivariate analysis to assess risk factors to predict infections during the initial 3 months post transplant.Correlationof incidence of infections with duration of ICU stay and hospital stay.
Results: A total of 104 patients were included for the study. The mean age of the study population was 46.61 years with a male preponderance (85 %). Any-Culture positivity (Blood, urine, sputum or drain) was seen in 43 % of patients. of all the variables assessed, only Age and Trough Sodium were found to have statistically significant correlation with Any-culture positivity. Significant proportion of patients with infection (12.9 % v/s 1.7 %) had renal dysfunction requiring dialysis (p -0.04). the mean duration of ICU stay and hospital stay in patients with infections were 12.27 days and 24.69 days (p—0.45).
Conclusion: Infections were seen in a significant number of our patients (43 %). Age and Trough Sodium were found to be independent risk factors for the incidence of infections post-transplant. Culture positivity was found to have

Topic 19: Liver Transplantation

No: 1376

Expression of hbv antigens in hepatocyte for fibrosing cholestatic hepatitis B post liver transplantation

Xianli Chen[1], Dengming He[1], Guohua Yan[1], Jie Xia[1], Xuemei Kuang[1], Xingnan Pan[2], Yuming Wang[1]

Southwest Hospital, Third Military Medical University Institute of Infectious Disease Chongqing-China[1], The 180th Hospital of Chinese Pla Institute For Infectious Diseases Quanzhou-China[2]

Background and Aim: HBV reactivation in the condition of immune suppression may lead to liver dysfunction, even liver failure. Post liver transplantation, high HBV load enhances the progression of fibrosis and may result in fibrosing cholestatic hepatitis B (FCH-B). We aimed to further explore the role of HBV antigens in the mechanism of HBV reactivation and to analyze the role of related factors in the case of immune deficiency.
Methods: 27 liver failure patients were divided into FCH group, chronic HBV infection acute on chronic liver failure (ACLF group), and drug-induced liver failure. Liver samples were stained with H&E, Masson's trichrome, and immunohistochemistry. HBV antigen quantitation was detected by confocal immune fluorescence.
Results: HBV DNA levels of FCH group was significantly higher than ACLF group. All of the FCH patients were found to have evidence of biliary tract diseases (bile leaks, cholangiolithiasis, biomass or strictures). Widespread expression of both HBsAg and HBcAg in hepatocytes was observed in all FCH patients. The highest expression of HBsAg was seen in hepatocellular cytoplasm of FCH patient, but not in nucleus. The highest expression of HBcAg was seen in not only hepatocellular cytoplasm but nucleus of FCH patient. The significant correlation between HBV antigen quantitation and related factors was seen between HBsAg quantitation and HBV DNA ($r = 0.763$, $P = 3.78 \times 10\text{-}6$) or between HBcAg quantitation and HBV DNA ($r = 0.870$, $P = 3.88 \times 10\text{-}9$).
Conclusion: High expression of HBV antigen in hepatocyte was an important characteristic of FCH-B and associated with HBV DNA levels. The biliary tract complication may be a potential pathological base of FCH-B post liver transplantation.

Topic 19: Liver Transplantation

No: 2215

Changes in foxp3 + regulatory t cells and interleukin 17 producing t helper cells in de novo hepatitis B virus infection after orthotopic liver transplantation

Yinjie Gao[1], Min Zhang[1], Zhenwen Liu[1]

Beijing 302 Hospital Liver Transplantation Center Beijing-China[1]

Objective: To observe the expression of Foxp3 + Regulatory T cells (Treg) and interleukin-17-producing T helper cells (TH17) in De Novo Hepatitis B Virus infection after orthotopic Liver Transplantation, and analyze the possible correlation between the expression and clinical tests and prognosis of the disease.
Methods: We enrolled from the liver transplantation and research center at Beijing 302 Hospital 12 health controls (HC) and 24 patients, including 12 diagnosed with De Novo Hepatitis B Virus infected patients after orthotopic liver transplantation (DNHB-OLT) and 12 diagnosed with acute Hepatitis B Virus infection (AHB), into the study. Flow cytometry was used to detect the expression of Treg and TH17 and ELISA kit to detect the concentration of IL-6, IL-22, TGF-β and IL-2 in peripheral blood. We also measured the gene expression by real time-quantitative and protein expression using immunohistochemistry and western-blot. The differences were compared.
Results: The percentage of Treg cells in DNVH-B group was significantly higher than that of HBV and HC groups. The same also applied to gene and protein expression in the liver. The percentage of interleukin-17-producing Th17 cells in DNVH-B group was significantly lower than that in HBV group, but not in the HC group. The RORγt mRNA and protein expression was also consistent. When compared to HC and AHB groups, the ratios of Treg to TH17 DNVH-B were significantly higher. IL17 or Treg didn't closely correlate with serum ALT. However, the ratio of Treg to TH17 in DNHB-OLT positively significantly correlated with ALT. TH17, Treg and the ratio of Treg to TH17 didn't closely correlate with HBVDNA level in all groups. Interestingly in DNHB-OLT groups, TH17 and Treg did not

correlate with HBV clearance, but the non-clearance subgroup had significantly higher percentage of Treg to TH17 ratios compared with clearance subgroup. The ratio of Treg to TH17 decreased during the 24 weeks of follow-up in non-clearance DNHB-OLT patients.
Conclusion: In DNHB-OLT patients, Treg and Th17 cells showed changes in genes, protein levels. The increasing ratio of Treg to TH17 during the follow-up phase of DNHB-OLT was associated with ALT and prognosis, which suppressed immune inflammation reaction as well as inhibited ability of specific HBV clearance and led to immune escape and chronicity. These findings provide new information regarding the pathogenesis of DNHB-OLT, and the ratio of Treg to TH17 may represent a potential prognostic marker for the disease.

Topic 19: Liver Transplantation

No: 2020

Vitamin d deficiency among liver transplant patients prevalence predictive factors adverse outcomes and replacement doses required

Jonathan Lee[1], Kieron Lim[1], Priscilla Wee[1], Charlene Soon[1], Lee Guan Huei[1], Tan Poh Seng[1], Dan Yock Young[1], Lee Yin Mei[1], Thwin Maung Aye[1], Lim Seng Gee[1], Krishnakumar Madhavan[1], Low How Cheng[1]

National University Health System, Yong Yoo Lin School of Medicine, National University of Singapore National University Centre For Organ Transplantation (nucot) Singapore-Singapore[1]

Background: Majority of liver transplant candidates are reported to be vitamin D deficient, whereby deficiency is associated with acute cellular rejection (ACR).
Aim: To assess the prevalence and predictive factors of vitamin D deficiency amongst liver transplant patients. To identify optimal doses of vitamin D supplementation.
Method: We reviewed medical records of fifty-five adult patients who underwent liver transplantation between January/2011 and September/2014. 25-(OH)-vitamin D levels, age, gender, etiology of cirrhosis, glycosylated haemogloblin (HbA1c), presence of hepatocellular carcinoma, MELD score, body mass index, bone mineral density results and ACRs were recorded. Fourteen patients were excluded for incomplete laboratory data.
Results: 76.5 % (n = 13) of pre-transplant and 87.5 % (n = 21) of post-transplant patients were vitamin D insufficient (<30 ng/mL) or severely deficient (<10 ng/mL). Mean 25-(OH)-vitamin D levels of pre-transplant and post-transplant patients were 23.9 ± 13.1 ng/mL and 18.1 ± 9.74 ng/mL respectively.
HbA1c linearly correlated with 25-(OH)-vitamin D levels of pre-transplant patients (R[SUP]2[/SUP] = 0.616, Pearson correlation = -0.785, $P = 0.001$). Univariate analyses using student's t-test, Chi square and logistic regression did not find any other statistically significant predictor of 25-(OH)-vitamin D.

Seven (17.1 %) patients had ACR; all were vitamin D insufficient (n = 4) or severely deficient (n = 3).

6.7 % (n = 2) of patients achieved adequate 25-(OH)-vitamin D levels post replacement. Patients taking >3000 IU/day (n = 5) had higher 25-(OH)-vitamin D levels (Mean 30.3 ± 4.1,Δ19.2 ± 7.2) than those taking ≤ 3000 IU/day (n = 15; Mean 20.5 ± 12.4, Δ1.1 ± 6.8) ($P = 0.02$).
Conclusion: Majority of liver transplant patient are vitamin D deficient, whereby > 3000 IU/day of vitamin D are required for adequate supplementation. Poor glycemic control pre-transplant linearly predicts vitamin D deficiency. However further prospective studies into the immunological and metabolic mechanisms of vitamin D among liver patients are warranted.

Topic 19: Liver Transplantation

No: 1396

Long term results of post transplantation HCV treatment

Murat Aladag[1], Yilmaz Bilgic[1], Hulya Aladag[2], Murat Harputluoglu[1], Yasir Furkan Cagin[1], Mehmet Ali Erdoğan[3], Yahya Atayan[3], Oğuzhan Yıldırım[3], Yuksel Seckin[3], Melih Karincaoglu[3], Cüneyt Kayaalp[4], Sezai Yilmaz[4]

Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[1], Inonu University Faculty of Medicine Gynecology Malatya-Turkey[2], Inonu University Gastroenterology Malatya-Turkey[3], Inonu University General Surgery Malatya-Turkey[4]

Introduction and objective: In the present study, we aimed to evaluate our study results in HCV cases post-transplantation in the present study.
Materials and methods: Between years 2002 and 2004, etiologic agent was HCV in approximately 6.8 % of 1400 patients operated in our liver transplantation unit. Thirty patients with the mean age of 45 years satisfying this criterion were enrolled in the study. Baseline HCV-RNA level of patients was 1.4 million (400.000-8 million copy/ml). Patients received 180 microg PEF-IFN alpha-2a once a week and 1000-1200 mg/day ribavirin treatment. HCV-RNA values of patients were evaluated in the first month and then in every 3-month time. WBC, AST, ALT, and other parameters were regularly measured. Patients were followed up closely for side effects.
Results: HCV-RNA values were decreased nearly in all cases at the end of the first month, and more than 2 log decreases was encountered in 24 cases at Week 12. Since more decrease in HCV-RNA was not encountered in 6 cases (20 %) and they could not withstand side effects, treatment was discontinued at Week 24. HCV-RNA was negative in 80 % of cases (24/30) at Week 36, whereas it was negative in 73.3 % (22/30) of cases at Week 48. HCV-RNA was negative in 21 cases (/70) at postoperative Month 6. Only one patient responded treatment at Week 48 recurred in post-transplantation 6th month.
Conclusion: In experienced centers, high rates of HCV eradication can be achieved due to PEG-IFN + ribavirin combination treatment started according to postoperative protocol biopsy results, and HCV recurrence can be prevented.

Topic 19: Liver Transplantation

No: 1701

Telaprevir based treatment successfully prevents post transplant relapse in patients with cirrhotic HCV

Murat Aladag[1], Hulya Aladag[2], Yilmaz Bilgic[1], Murat Harputluoglu[1], Yasir Furkan Cagin[1], Mehmet Ali Erdogan[1], Yahya Atayan[1], Oguzhan Yildirim[1], Yuksel Seckin[1], Melih Karincaoglu[1], Cuneyt Kayaalp[3], Sezai Yilmaz[3]

Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[1], Inonu University Faculty of Medicine Gynecology Malatya-Turkey[2], Inonu University Faculty of Medicine General Surgery Malatya-Turkey[3]

Introduction and purpose: In this study, we aimed at assessing the postoperative HCV relapse in cirrhotic patients whom we prepared for transplantation with a telapravir-based triple therapy.
Materials and methods: A total of 24 patients, 15 female and 9 male, with a mean age of 56.4 (22-74) were involved. The patients were started a triple combination therapy with telaprevir. As the conditions of 4 of the patients were worse than those of the others, HCV-RNA negativity was ensured in them at Weeks 4 through 12 and they were taken to their operations without waiting for a long time. HCV RNA was monitored in the postoperative period regularly.
Results: All of the patients completed the 4-week follow-up period without any problems. HCV-RNA that was measured at the end of Weeks 4 and 12 turned out 100 % (24/24) negative in all patients. Four of the patients were taken to liver transplantation at Weeks 12, 13, 16 and 18 while their HCV RNAs were negative. The initial HCV RNA levels of these patients were 600.000 copy/ml on the average. In the postoperative period, HCV RNA was found negative in these 4 patients at the beginning and at Months 1, 3, 6 and 9. The liver function tests (AST and ALT) of the patients were found normal.
Conclusion: If therapies involving telaprevir are administered to cirrhotic patients with severe conditions in clinics experienced in this field in order to achieve HCV RNA negativity in a short time and conduct the transplantation, a postoperative relapse of HCV can be prevented successfully.

Topic 19: Liver Transplantation

No: 1536

Longterm effects of entecavir therapy and hbig prophylaxis on hbv relapse in liver transplant cases

Murat Aladag[1], Hulya Aladag[2], Yilmaz Bilgic[1], Murat Harputluoglu[1], Yasir Furkan Cagin[1], Mehmet Ali Erdogan[1], Yahya Atayan[1], Oguzhan Yildirim[1], Yuksel Seckin[1], Melih Karincaoglu[1], Cuneyt Kayaalp[3], Sezai Yilmaz[3]

Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[1], Inonu University Faculty of Medicine Gynecology Malatya-Turkey[2], Inonu University Faculty of Medicine General Surgery Malatya-Turkey[3]

Introduction and purpose: We aimed at retrospectively evaluating cases who had a liver transplant in our Hepatology clinic between the years 2005 and 2014 due to cirrhosis associated with HBV and who use hepatitis B hyperimmunoglobulin (HBIG) in combination with Entecavir in terms of viral suppression and HBV relapse.
Equipment and method: Between 2005-2014 in our clinic 130 patients who used Entecavir for at least 12 months following the transplant were included in the study. were included in our study. Therapy results of patients were monitored for 8 years. Viral suppression and long-term biochemical and virological parameters were evaluated.
Results: Evaluation of HBV DNA results in the 12th month following liver transplant secondary to HBV showed full response in 120 patients (92,3 %), partial response in 8 patients (6,1 %) and insufficient response in 2 patients (1,5 %). Subsequently, it was seen during evaluations made at 3-month intervals that the viral response rate gradually increased and that the negative HBV-DNA reached 100 % at the end of 8 years. In the evaluation made, Entecavir resistance was not detected in any cases. Side effects which require discontinuation of therapy was not seen in any cases.
Conclusion: It was seen in our study that viral suppression and biochemical response rates increased as the duration of treatment following liver transplant due to HBV is extended. Negative HBV-DNA value rates exceeded 99 % after 5 years.

In conclusion, it was demonstrated that concurrent use of HBIG with Entecavir following liver transplant due to chronic hepatitis B cirrhosis is fairly effective and safe, prevents HBV relapse, recurrence.

Topic 19: Liver Transplantation

No: 1766

Experience of liver transplantation in Uludag university preliminary results

Talat Ayyildiz[1], Murat Kiyici[2], Tanju Basarir Ozkan[3], Gurkan Turker[4], Naile Bolca Topal[5], Remzi Iscimen[4], Nalan Yildirim[5], Ekrem Kaya[6]

Ondokuz Mayis University, Medical Faculty Gastroenterology Samsun-Turkey[1], Uludag University, Medical Faculty Gastroenterology Bursa-Turkey[2], Uludag University, Medical Faculty Pediatric Gastroenterology Bursa-Turkey[3], Uludag University, Medical Faculty Anesthesiology Bursa-Turkey[4], Uludag University, Medical Faculty Radiology Bursa-Turkey[5], Uludag University, Medical Faculty General Surgery Bursa-Turkey[6]

Introduction: Liver transplantation is a viable treatment option for end-stage hepatic failure. Uludag University Liver Transplant Center (UULTC) has begun performing liver transplant operations in December 2007 and in this presentation, we will review outcomes of 34 cases of liver transplantation performed until August 2010 including 30 with cadaveric livers and 4 from living donors.
Methods: Data on the etiology, demographics, mortality and complications recorded for liver transplant surgeries which were performed at UULTC between the aforementioned dates for end-stage liver disease were reviewed retrospectively.
Results: Throughout the aforementioned period, 34 patients including 31 adults and 3 children had liver transplants. Mean age of the patients was 42. 6 years of whom 70 % were male and 30 % were female. ABO blood type of the donor and recipient was identical in 30 patients and compatible in 4 patients. Patients with liver cirrhosis (35 %) associated with chronic HBV infection and cryptogenic liver cirrhosis (17.6 %) represented most of the cases. Mean duration of cold ischemia was 8.8 $\pm$ 0.8 h. The MELD and PELD scores of patients were 20.5 $\pm$ 1 and 18.3 $\pm$ 3, respectively. Bile ducts were reconstructed using choledochocholedochostomy for 31 patients and Roux-en–Y hepaticojejunostomy for 3 patients. Perioperative mortality rate and overall mortality rate were 11.7 % and 14.7 % respectively. Survival rates at 24 months were 84.2 % (Confidence interval: 7.308 (4. 4- 9. 7)).
Conclusion: We achieved a 24-month survival rate of 84.2 % in our center and liver transplantation surgeries continue with an acceptable success rate.

Topic 19: Liver Transplantation

No: 2079

Development of malignancy after liver transplantation a case series

Sabite Kacar[1], Hale Gökcan[1], Murat Ulaş[2], Erol Aksoy[2], Meral Akdoğan[1], Birol Bostancı[2], Musa Akoğlu[2]

Tyih Gastroenterology Ankara-Turkey[1], Tyih Gastroenterology Surgery Ankara-Turkey[2]

Introduction: The cumulative incidence of de novo cancer is reported higher among LT recipients versus an age- and sex-matched non-transplant control population. It increases from 3 % at 1 to 20 % at 10 years after LTx. Cutaneous malignancies, lung cancer, oropharyngeal cancer, colon cancer, cervix cancer, lymphoproliferative malignancies are reported after LTx. We present 3 patients developed different malignancies after LTx.
Cases: There were 87 patients with LTx in our series. Liver disease etiologies are as follows: 39 HBV, 11 HCV, 3 HBV + HCV, 1 HDV, 16 HCC (11 HBV, 4 HCV, 1 HBV + HCV), 11 idiopathic, 6 ALF, 6 WD, 3 PBC, 3 alcohol, 1 AIH, 1 BCS, 1 hemangioendothelioma, 1 GSD. 3 patients developed non-HCC malignancy in follow up (Table).
Results: The development of postTx cancer could be a great problem. Skin cancer incidence is reported as 0.70 %, 2.31 % in 5and 15 years. The SIR values of de novo malignancy after LTx are 0-212 for Kaposi's sarcoma. The incidence of post-transplant lymphoproliferative disorder varies from 1 to 20 % depending on the type of transplant. Not only is the risk of developing cancer higher, the diagnosis is likely to carry a worse prognosis after LTx. 2 patients were died in our series in a short time after diagnosis of malignancy.

Topic 19: Liver Transplantation

No: 2056

Asian patients undergoing colonoscopy assessment for pre liver transplant work up were found to have a higher incidence of colonic polyps and advanced neoplasia than general population

Gloria Chan[1], Jonathan Lee[2], How Cheng Low[3]

National University Hospital Internal Medicine Singapore-Singapore[1], National University Hospital Gastroenterology and Hepatology Singapore-Singapore[2], National University Hospital Gastroenterology and Hepatology Singapore-Singapore[3]

Background: Colonoscopy is widely used as a screening tool for colorectal carcinoma. The local data in Singapore (2014 APDW abstract) demonstrated an incidence of colon polyps (25.2 % of which 6 % were advanced neoplasia and 1.4 % cancer) in asymptomatic patients. The incidence of colon polyps in patients requiring liver transplants is not widely known.
Aim: To evaluate the colonoscopy detection of colon polyps and characteristics in pre-transplant patients (more than 50 years old).
Method: A retrospective analysis of electronic medical records for patients who were referred for adult liver transplantation in the National University Hospital (NUH) between 2011 and 2013 were evaluated.
Results: There were 190 adult patients referred for liver transplant and 53.6 % (n = 102) underwent screening colonoscopy. 52.9 % (n = 54) of patients who underwent colonoscopy had abnormal findings on colonoscopy and of these, 42.5 % (23) of them had colon polyps. Majority of the 18 retrieved polypectomies demonstrated tubular adenoma low grade dysplasia 69.5 % (n = 16) while the remaining were serrated adenoma and benign polyp mucosa. 17.4 % (n = 4) of these polyps were > 10 mm. However, none of the histology of these polyps were high-grade dysplasia or malignant.
Conclusion: There was a higher incidence of colon polyps and advanced neoplasia polyps in patients undergoing pre-liver transplant assessment than the general Singapore population. Therefore, colonoscopy should remain the preferred tool for screening as it also has a therapeutic role.

Topic 19: Liver Transplantation

No: 2052

Retained foreign body in a transplanted liver

Cuneyt Kayaalp[1], Serdar Kirmizi[1], Ramazan Kutlu[2], Mehmet Ali Yagci[1], Burak Isik[1], Sezai Yilmaz[1]

Liver Transplantation Institute Surgery Malatya-Turkey[1], Liver Transplantation Institute Radiology Malatya-Turkey[2]

Liver transplantation is a technically complex and long surgical procedure. A large quantity of materials such as catheters, sutures, needles and clips are frequently used during the procedure. These materials may enter in the liver from the vascular or biliary orifices inadvertently. A 50-year-old patient who had hepatic failure due to HBV underwent a deceased donor liver transplantation. The deceased donor was a 75 year-old HbsAg (+) man. The recipient had subfebrile fever and leukocytosis postoperatively. A control computed tomography revealed a cuneiform ischemic area, and a foreign body inside the right anterior portal vein branch proximal to this ischemic area. A 10F Nelaton catheter of 5 cm was removed from the portal vein by surgery. Retrospectively, we understood that the portal vein was cut during the back-table procedure and the portal vein catheter was replaced with a larger one for better irrigation. Most probably, the original catheter was cut together with the portal vein, and the tip of the catheter was retained in the portal system and migrated into the liver. As far as we know, such a complication of liver transplantation has never been described previously.

Topic 19: Liver Transplantation

No: 2189

Survival analysis of sirolimus based immunosuppression in liver transplantation for patients with hepatocellular carcinoma beyond ucsf criteria

Shilei Xu[1], Jianrong Liu[1], He Huang[1], Kunpeng Hu[1], Zhicheng Yao[1]

Lingnan Hospital of Sun Yat-sen University General Surgery Guangzhou-China[1]

Objective: To analysis the influence of sirolimus-based immunosuppressive protocols on the survival in liver transplantation (LT) recipients with hepatocellular carcinoma (HCC) beyond UCSF criteria.
Methods: We retrospectively analyzed 32 patients who underwent LT for HCC in our hospital during Jan. 2006 to Jan. 2011, who were divided into SRL-treat group (16 cases) and control group (18 cases). The disease-free survival time were compared using the Kaplan–Meier method.
Results: In the control group, the median disease-free survival time was 7 months (2.5–53 months), and the 1-year disease-free survival rate were 48.6 %. In SRL group,the median disease-free survival time was 4 months (2–53 months),and the 1-year disease-free survival rate were 33.3 %. The comparison of disease-free survival ($P = 0.142$,) between the two groups shows.
Conclusions: Sirolimus cannot prolong the survival time of patients with HCC beyond UCSF criteria.

Topic 19: Liver Transplantation

No: 2055

Calcineurin inhibitor induced pain syndrome in liver transplant patient

Ozlem Tasoglu[1], Hale Gokcan[2], Sibel Demir Ozbudak[1], Didem Yenigun[1], Meral Akdogan Kayhan[2], Sabite Kacar[2]

Ankara Physical Medicine and Rehabilitation Training and Research Hospital Physical Medicine and Rehabilitation Ankara-Turkey[1], Ankara Yuksek Ihtisas Research and Training Hospital Gastroenterology Ankara-Turkey[2]

Introduction: Calcineurin inhibitors are used in a group of disorders and one of them is organ transplantation. Musculoskeletal pain due to calcineurin inhibitors is rare but severely disabling and worth emphasizing.
Case: 48 year old male patient was admitted to our clinic due to excruciating pain in his both feet continuing for the last 6 months. He described the pain as deeply aching, severe and sometimes extending to the knees. He had no known rheumatologic disorders, but detailed questioning revealed a liver transplantation 15 months ago due to alcoholic cirrhosis. He was on a treatment regimen including tacrolimus 2 × 2 mg and mycophenolate mofetil 2 × 1000 mg. The neuromuscular examination was normal. The magnetic resonance imaging of both feet and technetium 99 m bone scintigraphy of whole body were normal. The blood tacrolimus level was 5.1 ng/ml. The patient was diagnosed as calcineurin-inhibitor induced pain syndrome (CIPS). He was consulated with the gastroenterology department. As the blood level of tacrolimus was normal, medication was continued on given dose and pregabaline 2 × 150 mg was started according to the neuropathic pattern of the CIPS.
Discussion: CIPS is a rare but severe side effect of tacrolimus and cyclosporine treatment. The accurate diagnosis is based on typical pain pattern. Magnetic resonance imaging and bone scintigraphy can also be used, although normal results don't exclude the diagnosis. Raising awareness of this rare clinical presentation is important to avoid decline in quality of life.

Topic 19: Liver Transplantation

No: 1134

Living donor liver transplantation for glycogen storage disease type iv; a case report

Erdal Birol Bostancı[1], Volkan Öter[1], Ilter Özer[1], Nesrin Turhan[2], Musa Akoğlu[1]

Turkiye Yuksek Ihtisas Teaching and Research Hospital Department of Gastroenterological Surgery Ankara-Turkey[1], Turkiye Yuksek Ihtisas Teaching and Research Hospital Department of Pathology Ankara-Turkey[2]

Aim: Glycogen storage disease type IV (GSD-IV) is a rare autosomal recessive disorder caused by deficient glycogen branching enzyme activity. This deficiency leads to accumulation of amylopectin-like glycogen and results in variable clinical presentations. Our aim was to report a treatment of a patient with liver cirrhosis and hepatocellular carcinoma associated with GSD-IV.
Method: A 23-year-old woman with a history of GSD-IV for five years, was admitted with hepatomegaly. On physical examination, the liver was palpable below the rib and abdomen was distended with ascites. Hemoglobin level was 11.8 g/dL, platelet count was 63,000/mm3 and other laboratory values were normal. Patient's echocardiogram or cardiac catheterization was in normal limits before the transplantation. Computerized Tomography (CT) showed a hypervascular mass (2.5 × 2.3 × 1.9 cm) in the right hepatic lobe which looked like hepatocellular carcinoma (HCC). An ultrasound guided fine needle aspiration biopsy was done and histopathological diagnosis was reported as HCC. She underwent living donor liver transplantation from her sister. After transplantation, early postoperative period was uneventful. However after 18 months she experienced cardiac symptoms, and myocardial biopsy was obtained. 18 months after transplantation. Histopathological examination of heart biopsy demonstrated accumulation of amylopectin. She died because of cardiomyopathy and heart failure due to GSD-IV, two years after transplantation.
Conclusion: Liver transplantation did not changed the extrahepatic progression of the GDH-IV. Therefore, despite liver transplantation was successful long-term follow up is required for neuromuscular and cardiac complications.

Topic 19: Liver Transplantation

No: 1113

Potential of positron emission tomography with fluorine 18 fluorodeoxyglucose (fdg pet) in identifying recurrence in hepatocellular carcinoma post liver transplantation

Surbhi Pande[1], Vishal Agarwal[1], Dhanraj Jangid[1], Ashok Sen[1]

Medanta-the Medicity Nuclear Medicine Gurgaon-India[1]

Aim: The relationship between primary tumor and recurrence in HCC (hepatocellular carcinoma) after liver transplant remains unknown. Although FDG-PET is insufficiently sensitive for primary diagnosis of HCC, the metabolic information could provide insights into tumor behaviour. Our aim was to assess it's usefulness in optimizing patient selection by correlating FDG uptake with outcome after transplant.
Methods: FDG PET scans of 82 patients on the transplant service were retrospectively reviewed. FDG positivity was defined as tumor/non tumor background ratio > 1.5 (group A, n = 40), while non-avid tumors were categorized into group B (n = 42). Results were correlated after transplant with clinical, biochemical and radiological follow up (mean 1- 3 years).
Results: Of the 40 patients with FDG positivity, 29 (75 %) presented with recurrence (intra and extra hepatic). In 59 %, the primary tumor was less than 5 cm. There was significant association between recurrence and FDG avidity ($P = 0.0001$).None of the patients with tumour to background ratio > 3 had tumour free survival exceeding 8 months. Whereas in group B (n = 42), there were only 3 (7 %) recurrences, tumour free survival being 100 % at 20 months.
Conclusion: FDG positivity in HCC correlates with adverse outcome, the information being independent of tumor size. Although FDG avidity as a contraindication for liver transplant remains to be conclusively established, for now it merits inclusion with other criteria for assessing suitability for transplant in HCC.

Topic 19: Liver Transplantation

No: 1291

Reactivation primary disease after ldlt in Mongolia

Tuul Nyamdavaa[1], Enkhjargal Batmunkh[1]

First Central Hospital of Mongolia Center of Gastroenterology and Hepatology Ulaanbaatar -Mongolia[1]

Introduction: Liver cirrhosis (LC) and hepatocellular carcinoma (HCC) are considered as leading causes of death in the Mongolia. Mongolia is the country which estimated with high prevalence of HBV and HCV as well as among the population HCV $\geq$ 10, HBV $\geq$ 7-8 is the ultimate cause of liver disease.
Methods: 169 patients have been involved in our study after liver transplantation. The endpoint was the comparison of recurrent HBV and HCV after LDLT.
Result: We are following up 169 patients who have been performed the LDLT in India, Korea, Mongolia and China. 143 (84.6 %) of them performed LT between 2012 and 2014. By diagnose, were as followings: 101 patients with HBV-LC, 40 patients with HCV-LC, 2 patients with Cryptogenic LC, 1 patient with Alcoholic-LC, 3 patients with Biliary atresia, 54 patients with HCC.
HBV reactivated in 5 cases of 101 patients and successfully treated with high and double dose of nucleoside analoges. HCV reactivated in 33 (82.5 %) of 40 cases. 8 patients underwent antiviral treatment, SVR was in 1 case and relapse occurred in 3 patients, as well as another 3 patients had EVR. 13 of 54 patients with HCC was over Milan criteria, 2 of them developed recurrent HCC and 2 patients with De novo malignancy.
Conclusion: Reactivation of HBV in 5/4.9 %/and HCV in 33/86.5 %/ occurred after LDLT. 2 of 54 patients with recurrent HCC were over Milan criteria.

Topic 19: Liver Transplantation

No: 1361

Liver transplantation in a patient with liver cirrhosis secondary to portal hypertensive biliopathy a case report

Ekrem Kaya[1], Talat Ayyildiz[2], Murat Kiyici[3], Cuneyt Erdoğan[4], Macit Gulten[3]

Uludag University General Surgery Bursa-Turkey[1], Ondokuz Mayis University Gastroenterology Samsun-Turkey[2], Uludag University Gastroenterology Bursa-Turkey[3], Uludag University Radiology Bursa-Turkey[4]

Introduction: Portal Hypertensive Biliopathy (PHB) is a rare clinical condition. With this case report, we aimed to share our experience with liver transplantation in a patient with liver cirrhosis secondary to PHB.
Case: A 22-year-old female patient, blood type A, presented with complaints of progressive jaundice and weakness. Laboratory results were as follows: total/direct bilirubin 12/9 mg/dl, AST 183 UI/L, ALT 251 UI/L, ALP 440 UI/L, GGT 205 UI/L, HBsAg (-), Anti-HCV (-). ERCP showed stenosis at the 2 cm segment of the common bile duct and dilation of intrahepatic bile ducts beyond the narrowing. Abdominal CT detected aneurysmatic dilatation (4.5 x 4 cm) in the portal vein at the portal hilus level. TIPS procedure was performed. Grade II esophageal and fundal varices were identified using upper gastrointestinal endoscopy. TIPS was obstructed 6 months later. About two years after the onset of symptoms, a cadaveric liver was found and transplanted using piggy-back technique. Donor was 8 years old with blood type O and cold ischemia time was 25 h. Bile leakage developed after transplantation and was treated with percutaneous external biliary drainage. The patient continues to be well 5 years after the surgery clinically and with respect to laboratory measures.
Conclusion: Extrahepatic Portal Venous Obstruction is the most common cause of portal hypertension. Liver transplantation may be performed for patients with advanced disease. The most distinctive feature of our case is that this is one of the few cases reported in English literature with successful liver transplantation in the setting of portal biliopathy.

Topic 19: Liver Transplantation

No: 2185

The influence of sirolimus based immunosuppression in liver transplantation for patients with hepatocellular carcinoma in the milan criteria

Shilei Xu[1], Kunpeng Hu[1], Jianrong Liu[1], Zhicheng Yao[1], He Huang[1]

Lingnan Hospital of Sun Yat-sen University, General Surgery Guangzhou-China[1]

Objective: To investigate the influence of sirolimus-based immunosuppressive protocols on the survival in liver transplantation (LT) recipients with hepatocellular carcinoma (HCC) meeting the Milan criteria.
Methods: We retrospectively analyzed 72 patients who underwent LT for HCC in our hospital during Jan. 2006 to Jan. 2011, who were divided into SRL-treat group (32 cases) and control group (40 cases). The disease-free and tumor bearing survival time were compared using the Kaplan–Meier method.
Results: No significant difference was observed between these two groups with the disease-free survival time (DFS). In the control group, the median disease-free survival time was 30 months (7 - 53 months), and the 1- and 2-year disease-free survival rate were 90 %, 78.3 %.In SRL group,the median disease-free survival time was 25 months (6 - 55 months), and the 1- and 2-year disease-free survival rate were 87.8 %, 78 %. The comparison of disease-free survival ($P = 0.991$) between the two groups shows no statistical significance.
Conclusions: Sirolimus cannot prolong the survival time of patients with HCC meet the Milan criteria.

Topic 19: Liver Transplantation

No: 1400

Healthy pregnancy and birth after liver transplantation 6 cases 9 births

Hulya Aladag[1], Murat Aladag[2], Yilmaz Bilgic[2], Murat Harputluoglu[2], Yasir Furkan Cagin[2], Yahya Atayan[3], Mehmet Ali Erdogan[3], Oğuzhan Yıldırım[3], Yuksel Seckin[3], Melih Karincaoglu[3], Cüneyt Kayaalp[4], Sezai Yilmaz[4]

Inonu University Faculty of Medicine Gynecology Malatya-Turkey[1], Inonu University Faculty of Medicine Gastroenterology Malatya-Turkey[2], Inonu University Gastroenterology Malatya-Turkey[3], Inonu University General Surgery Malatya-Turkey[4]

Objective: In the present study, we aimed to evaluate six cases, which gave birth to healthy babies in our clinic after liver transplantation.
Material and method: In our clinic, six cases with a mean age of 26 years, which underwent liver transplantation at childbearing age

and became pregnant and gave birth to nine babies after transplantation between 2006 and 2013.

Whilst four cases had developed end-stage liver insufficiency secondary to chronic hepatitis B and/or D infection, end-stage liver insufficiency was secondary to Budd-Chiary Syndrome in one case and no etiology could be defined in the other case (cryptogenic).

Results: After operation Immunosuppressive therapies of the patients were arranged and tenofovir therapy was commenced as antiviral therapy because they were pregnant. One of the cases became pregnant in the 7th month of surgery and gave birth to twin babies after 8 months; the same case gave birth to another baby 2 years after the first pregnancy.

The pregnant women that underwent Tx due to HBV received Tenofovir over the course of pregnancy period, and prophylaxis was performed with HBIG + hepatitis B vaccine during surgery and thereafter immunization program continued regularly. AntiHBs antibody titer, which was analyzed in all babies in the 12th month of birth, was over 100 IU/ml providing adequate prevention.

Conclusion: Transplant patients can become pregnant under the supervision of experienced clinicians and give birth to healthy babies with appropriate follow-up and treatment.

Topic 20: Metabolic and Genetic Liver Diseases

No: 1267

Wilson's disease a retrospective analysis

Sebati Özdemir[1], Ibrahim Hatemi[1], Kadri Atay[1], Eren Imre[1], Nuray Kepil[2], Murat Özbalak[1], Sibel Ertan[3], Kadir Bal[1], Abdullah Sonsuz[1]

Istanbul University, Cerrahpaşa Faculty of Medicine Department of Internal Medicine, Division of Gastroenterology Istanbul-Turkey[1], Istanbul University, Cerrahpaşa Faculty of Medicine Department of Pathology Istanbul-Turkey[2], Istanbul University, Cerrahpaşa Faculty of Medicine Department of Neurology Istanbul-Turkey[3]

Aim: Wilson's disease (WD) is an inherited autosomal recessive disorder of copper metabolism. The aim of this study was to identify the demographic, clinical, and laboratory features of patients with WD.

Methods: A total of 31 patients with WD were included in this retrospective study. The diagnosis of WD was made according to the consistent clinical and laboratory parameters with WD and/or determining of a high liver copper concentration.

Results: Of the 31 patients with WD, 13 were male and 18 (58 %) were female. The age of the patients at the diagnosis of WD ranged from 7 to 50 years (mean: 20.9 ± 10.85). Most of the patients (24/31 [77.4 %]) had clinical symptoms and signs at the time of diagnosis; their presentations were with neurologic disturbances in 14 patients (45.2 %) and hepatic disease in 10 patients (32.2 %). Two patients (6.5 %) had nonspecific symptoms at the time of diagnosis. Five patients (16.1 %) were diagnosed with a family history. Three of patients with neurologic presentation also had hepatic manifestations. Liver cirrhosis was present in six patients. Kayser-Fleischer rings were present in 20 (%64.5). 24-hour urinary copper excretion was elevated in all but one of the patients. Serum ceruloplasmin levels were low in 29 (93.5 %). WD was confirmed by the liver copper content determination in six patients.

Conclusion: The majority of our patients with WD were diagnosed in the symptomatic period. The prognosis of WD depends substantially on early diagnosis and treatment. Thus, early diagnosis of WD is important in terms of both prognosis and quality of life of patients.

Topic 20: Metabolic and Genetic Liver Diseases

No: 1150

Pyogenic liver abscess in the elderly clinical characteristics outcomes in Korean patients older than 65 years

Chunghwan Jun[1], Sungkyu Choi[1], Eunae Cho[1]

Chonnam National University Medical School Department of Internal Medicine Gwangju-Korea, South[1]

Background and aim: Pyogenic liver abscess (PLA) in elderly has an increasing incidence in the world. However, PLA remains poorly characterized in elderly patients, and comprehensive data are limited. This study was conducted to compare the differences in clinical features and outcomes of PLA according to age.

Methods: A total of 602 patients who were diagnosed with PLA were analyzed retrospectively from January 2004 to July 2013. The patients were divided into two age groups: $\geq$ 65 yr (n = 296) and $<$ 65 yr (n = 306).

Results: Older PLA patients, compared to younger patients, had significantly higher prevalence rates of females, hypertension, hepatobiliary disease, hepatobiliary procedure, associated gastrointestinal malignancy, sepsis at admission, culture positivity of antibiotic resistant organism, occurrence of complication and higher WBC, but lower prevalence rates of chronic alcoholics, right lobe abscess, fever and higher CRP. There were no significant differences in underlying diabetes mellitus, chronic kidney disease, other symptoms, causative organism, treatment modalities, length of hospital stay, and mortality. Regarding complication, elderly patients had higher prevalence of septic shock, and cardiovascular disease during hospital stay.

Conclusion: Older age is not associated with a longer hospital stay and a higher mortality rate. However, older PLA patients tend to have more atypical presentations and complications than younger patients. Thus, clinicians should be on high alert for these findings.

Topic 20: Metabolic and Genetic Liver Diseases

No: 1397

Rapid and dramatic recovery of a very long benign recurrent intrahepatic cholestasis attack with short term steroid treatment

Huseyin Alkim[1], Canan Alkim[1], Meltem Ergun[1], Ali Riza Koksal[1], Salih Boga[1], Mehmet Bayram[1], Muveddet Banu Yilmaz[2]

Sisli Hamidiye Etfal Education and Research Hospital Gastroenterology Clinic Istanbul-Turkey[1], Sisli Hamidiye Etfal Education and Research Hospital Pathology Clinic Istanbul-Turkey[2]

Aim: Benign recurrent intrahepatic cholestasis (BRIC) is an autosomal recessive, non-progressive liver disease presenting with spontaneously resolving intermittent cholestasis attacks. Here we present a BRIC which recovered with steroid treatment.

Case: A 35 year-old female patient, who diagnosed as having BRIC at 16 year-old, was admitted with jaundice. Her total/direct bilirubin was 2.24/1.78 mg/dl, AST: 41 U/L, ALT: 69 U/L, GGT: 66 U/L and ALP: 243 U/L. Ursodeoxycholic acid was prescribed. One month later she readmitted with intense pruritis and worsening jaundice. Total/direct bilirubin was 34/30 mg/dl. During the following 6 months her bilirubin remained above 30 mg/dl despite multiple treatment efforts. First we try rifampicin and cholestyramine with no effects. Then we placed a nasobiliary drainage catheter. Nothing changed. When bilirubin levels reached to 40 mg/dl

bilirubinophoresis was done. Her bilirubin level fell down to 15 mg/dl after 7 bilirubinophoresis sessions, but return over 30 after 1 week. Then we performed liver biopsy. Severe hepatocellular and canalicular cholestasis, medium grade portal-periportal and lobular inflammation and medium grade biliary fibrosis was seen. When compared with the liver biopsy done 10 years ago, progression in the inflammation and fibrosis levels was detected. Methylprednisolone 40 mg/day was started. Bilirubin level decrease to 23 mg/dl at the seventh day and turn to normal after 30 day. Then steroid stopped. Her bilirubin level remained normal for the following 6 months.
Conclusion: According to the literature steroids has no place in the treatment of BRIC. Because of the inflammation seen at the liver biopsy we try steroids and our patient fully recovered.

Topic 20: Metabolic and Genetic Liver Diseases

No: 1300

Laennec® (hepcidin containing biological drug derived from human placenta) can replace the phlebotomy on congenital iron and copper metabolism disorder

Yuki Hamada[1]

Hamada Clinic Hepatology Sapporo-Japan[1]

Aims: Recent studies indicate that hepcidin deficiency underlies most known forms of hereditary hemochromatosis(H.H.). The high affinity of hepcidin for copper also suggests that hepcidin could bind copper in vivo. Thus Laennec® which contains hepcidin may be effective not only for H.H. but for Wilson disease by regulating iron and copper through the action of hepcidin. Case1 H.H.: 46 years-old male patient that developed type2 diabetes mellitus had elevated serum ferritin level(10,191 ng/ml). Liver biopsy revealed remarkable iron deposition. Chromosomal analysis revealed the presence of TfR2mutations. As the substitute for the repeated phlebotomy, the infusion with Laennec® (672 mg/d,3times/w) has been done for 36 months. At the end of the treatment the serum ferritin level was decreased to 652 ng/ml. HbA1c also improved with the same dose of insulin(8.8◇7.2 %). Case2 Wilson's disease: 39 years-old male patient with compensated liver cirrhosis presented neuropsychiatric signs. Liver biopsy revealed the presence of the deposition of copper and iron. The infusion with Laennec® (672 mg/3times/W) has been done for 27 months. Pleural liver biopsies revealed the remarkable improvement of both in fibrosis and iron deposition in the liver. **Conclusion:** The discovery of hepcidin and its role in heavy metal metabolism could lead to the development of novel therapies for H.H. and Wilson disease. The placenta-derived Laennec® which contains hepcidin actually improved iron overload of H.H. patient without repeated phlebotomy, and the impaired copper metabolism through chelating excessive copper in Wilson disease. The results suggest that Laennec® can take the place of venesection for H.H. and other hepcidin-deficient diseases.

Topic 20: Metabolic and Genetic Liver Diseases

No: 1226

Haemochromatosis in liver a case report

Ayşe Nur Değer[1], Filiz Özyiğit[2], Berciş Imge Uçar[3], Özlem Altundaş Aydin[4], Hayat Kumbasar Karaosmanoğlu[5]

Dumlupinar University Medicine Faculty Department of Pathology Kutahya-Turkey[1], Dumlupinar University Medicine Faculty Department of Pharmacology Kutahya-Turkey[2], Dumlupinar University Medicine Faculty Department of General Surgery Kutahya-Turkey[3], Haseki Eğitim Ve Arş Hastanesi Department of Microbiology Istanbul-Turkey[4], Haseki Eğitim Ve Arş Hastanesi Department of Microbiology Istanbul-Turkey[5]

Primary haemochromatosis is an autosomal recessive condition due to abnormal HFE gene; the protein product of which regulates iron absorption from the gastrointestinal tract. Secondary haemochromatosis is rare, and is usually seen in association with diseases that mainly cause haemosiderosis (effective erythropoiesis, parenteral iron overload, liver disease, transfusion,etc.). It leads to bronze pigmentation of skin, diabetes mellitus (because of the pancreatic involvement), cardiac arrhythmias (because of the myocardial involvement), liver diseases, arthritis, amenorrhea, impotence, hypogonadism, osteopenia and osteoporosis. Laboratory studies including genetic tests, transferrin saturation level, serum ferritin level and hepatic iron concentration are used to evaluate suspected hemochromatosis.

We present here a 64-year-old male patient admitted to hospital with right upper quadrant tenderness. Haemochromatosis was detected in tru-cutt biopsy specimen. Histologic examination showed mononuclear infiltration around periportal areas, focal hepatocellular necrosis and mild fibrosis. Prussian blue iron staining demonstrated hepatocellular granular iron deposits in periportal area nearly reached to centrilobular region. Reactive atypia was detected in hepatocytes. Histomorphological appearance was considered as haemochromatosis. More detailed clinical and laboratory investigations are needed to clarify the etiology of the disease.

Topic 20: Metabolic and Genetic Liver Diseases

No: 1434

Colitis during trientine therapy for wilson disease a case report

Salih Boga[1], Dhanpat Jain[2], Michael Schilsky[1]

Yale University School of Medicine, Yale New Haven Hospital Department of Digestive Diseases, Department of Liver Transplantation New Haven-United States[1], Yale University School of Medicine, Yale New Haven Hospital Department of Pathology New Haven-United States[2]

Case: A 40 year old female patient with recent diagnosis of Wilson disease (WD) with predominant neuropsychiatric symptoms was started on triethylene tetramine dihydrochloride (trientine) 250 mg three times daily and developed bloody diarrhea. Trientine was discontinued, and a colonoscopy showed active ileitis and severe colitis of indeterminate nature. She was started on prednisone, and had acute worsening of her neuropsychiatric symptoms and was referred to us with the pre-diagnosis of steroid psychosis. Zinc therapy was initiated for her WD and the prednisone was stopped. Clinical symptoms of colitis improved and sigmoidoscopy showed resolution of her colitis. Due to persistent neuropsychiatric symptoms, trientine was restarted. She again developed multiple bloody bowel movements so trientine was discontinued. Evaluation for other causes of colitis was negative for infection and markers for IBD. A repeat colonoscopy at this time showed active colitis and proctitis. Histology showed extensive inflammation with cryptitis, crypt abscess formation and ulcerations, suggestive of a medication-induced colitis. The patient was restarted on zinc therapy for her WD and had resolution of symptoms of colitis without recurrence. All of her neurological symptoms improved and

resolved over a longer period of time. She had stable liver function while on zinc maintenance therapy.
Conclusion: Chelation therapy is an integral part of the initial therapy of symptomatic patients with WD, however patients must be monitored appropriately for side effects. Colitis is a rare side effect of trientine and zinc is an alternative therapy for patients with WD with side effects due to chelation therapy.

Topic 20: Metabolic and Genetic Liver Diseases

No: 1196

Loss of FGF21 in diabetic mouse during hepatocellular carcinogenetic transformation

Quan Zhang[1], Yan Li[2], Tingting Liang[1], Lu Cai[3], Mingliang Cheng[1]

Guiyang Medical College Infectious Department Guiyang-China[1], School of Medicine, University of Louisville Surgery Department Louisville-United States[2], 5. kosair Children's Hospital Research Institute, University of Louisville Pediatrics Department Louisville-United States[3]

Diabetes associated metabolic syndrome was shown as an independent risk factor for the development of hepatocellular carcinoma (HCC). Cirrhosis, in fact, was not always a prerequisite of HCC development and this might particularly apply to the metabolic abnormality associated HCC. This study was to investigate the diabetes associated HCC and the potential role of FGF21 during the carcinogenetic transformation of HCC. Diethynitrosamine (DEN) was used to induce HCC in the diabetic OVE26 mice. Pronounced liver damages characterized by steatohepatitis were found in the liver of diabetic mice. Steatohepatitis accompanied by constant cell proliferation and tumor cell growth were also found in the hepatic tissues of diabetic OVE26 mice when DEN being administrated. FGF21 protein level increased in the live tissues at early stage with steatohepatitis in diabetic OVE26 mice, but decreased in live tissues at later stage when HCC was developed. In addition, the decreased FGF21 protein level was associated with the cancerous hyper-proliferation and aberrant p53 and TGF-β/Smad signaling during the development of HCC. In conclusion, loss of FGF21 might play an important role in HCC carcinogenetic transformation during the metabolic liver injury in the diabetic animals. The present finding called attention to control the metabolic disorders in diabetes, and might further develop a protective strategy against HCC.

Topic 20: Metabolic and Genetic Liver Diseases

No: 1068

Wilson's disease a retrospective analysis

Sebati Özdemir[1], Ibrahim Hatemi[1], Kadri Atay[1], Eren Imre[1], Nuray Kepil[2], Murat Özbalak[1], Sibel Ertan[3], Kadir Bal[1], Abdullah Sonsuz[1]

Istanbul University, Cerrahpaşa Faculty of Medicine Department of Internal Medicine, Division of Gastroenterology Istanbul-Turkey[1], Istanbul University, Cerrahpaşa Faculty of Medicine Department of Pathology Istanbul-Turkey[2], Istanbul University, Cerrahpaşa Faculty of Medicine Department of Neurology Istanbul-Turkey[3]

Aim: Wilson's disease (WD) is an inherited autosomal recessive disorder of copper metabolism. The aim of this study was to identify the demographic, clinical, and laboratory features of patients with WD.
Methods: A total of 31 patients with WD were included in this retrospective study. The diagnosis of WD was made according to the consistent clinical and laboratory parameters with WD and/or determining of a high liver copper concentration.
Results: Of the 31 patients with WD, 13 were male and 18 (58 %) were female. The age of the patients at the diagnosis of WD ranged from 7 to 50 years (mean: 20.9 ± 10.85). Most of the patients (24/31 [77.4 %]) had clinical symptoms and signs at the time of diagnosis; their presentations were with neurologic disturbances in 14 patients (45.2 %) and hepatic disease in 10 patients (32.2 %). Two patients (6.5 %) had nonspecific symptoms at the time of diagnosis. Five patients (16.1 %) were diagnosed with a family history. Three of patients with neurologic presentation also had hepatic manifestations. Liver cirrhosis was present in six patients. Kayser-Fleischer rings were present in 20 (%64.5). 24-hour urinary copper excretion was elevated in all but one of the patients. Serum ceruloplasmin levels were low in 29 (93.5 %). WD was confirmed by the liver copper content determination in six patients.
Conclusion: The majority of our patients with WD were diagnosed in the symptomatic period. The prognosis of WD depends substantially on early diagnosis and treatment. Thus, early diagnosis of WD is important in terms of both prognosis and quality of life of patients.

Topic 20: Metabolic and Genetic Liver Diseases

No: 1616

Molecular genetic diagnosis of PFIC 3 overlapping presentation with Wilson disease and response to treatment

Salih Boga[1], Dhanpat Jain[2], Michael Schilsky[1]

Yale University School of Medicine, Yale New Haven Hospital Department of Digestive Diseases, Department of Liver Transplantation New Haven-United States[1], Yale University School of Medicine, Yale New Haven Hospital Department of Pathology New Haven-United States[2]

Case: The patient presented age 15 years with fatigue and findings of splenomegaly and mild thrombocytopenia. Further testing included 24 h urine copper [> 100 mcg], no Kayser–Fleischer rings, normal ceruloplasmin level and no mutations of ATP7B. Liver biopsy showed chronic hepatitis, focal bridging fibrosis, moderate bile duct proliferation and a markedly elevated hepatic copper content (1471 μg/g), suggesting WD. She was started on zinc therapy, but was switched to trientine due to gastrointestinal side effects. Though treated with trientine for > 12 months, her transaminase levels didn'timprove and urine copper remained elevated. Further evaluation for another possible etiology revealed increased bile acids. A trial of ursodeoxycholic acid (UDCA) was initiated for PFIC3. ABCB4 gene sequencing showed heterozygous c.984T > G (p.Y328*) mutation consistent with a diagnosis of PFIC3. Trientine was discontinued and she was continued on UDCA. With UDCA treatment, transaminases decreased but didn't normalize (Table). Liver biopsy was repeated after 4 months of therapy and showed hepatic copper content dramatically decreased to 135 μg/g dry weight liver. After 10 months liver indices remained mildly abnormal but synthetic function was stable.
Conclusions: Hepatic copper accumulation can be seen in cholestatic disorders such as PFIC3 at levels above the diagnostic threshold for WD, and therefore the diagnosis of PFIC3 should be considered in patients with elevated hepatic copper without clear features of WD and who fail to adequately respond to treatment. UDCA ameliorates

cholestasis in PFIC3 and we show for the first time a reduction in hepatic copper in response to treatment.

Topic 20: Metabolic and Genetic Liver Diseases

No: 1347

Profile and outcome of metabolic liver disease in under fives with liver related pediatric emergencies in a tertiary care pediatric hepatology centre

Seema Alam[1], Vikrant Sood[1], Bikrant Bihari Lal[1], Rajeev Khanna[1], Dinesh Rawat[1]

Institute of Liver and Biliary Sciences Pediatric Hepatology New Delhi-India[1]

Objective: (i) To study clinical profile and outcome of metabolic liver disease (MLD) in infants and young children < 5 yrs of age presenting as liver related pediatric emergencies.
Methods: All infants and young children less than 5 years of age, admitted between January 2011 and October 2014 with liver related pediatric emergencies were included in the protocol based approach that we follow for MLD at ILBS. Poor outcome was defined as death or liver transplantation within 12 weeks of presentation. The etiological spectrum was studied and the factors affecting outcome were analyzed.
Results: There were 3 children with encephalopathy & liver dysfunction and all of them were diagnosed with gluconeogenetic defect (Fructose 1,6 biphosphatase deficiency, Fbpase). Fructose was removed from the diet and cornstarch was added. With dietary elimination of fructose, all the three children are thriving well with no further encephalopathy and normalized liver functions. of the 5 children admitted with cyclical vomiting, none turned out to be MLD. In 50 children less than 5 years with acute liver failure (ALF), 11 had etiology of MLD: Galactosemia (4), Fructosemia (2), Tyrosinemia (1), Mitochondrial disorders (2), Urea cycle disorder (1) and one of the children with Fbpase also had ALF. Two of the 4 Galactosemia and child with urea cycle defect survived.. Poor outcome was seen in 8 out of 11 acute liver failure. None could be transplanted due to non availability of organ and logistics constraints.
Conclusions: MLD is a common cause of liver related pediatric emergencies and the outcome is poor.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1662

Non alcoholic fatty liver and non alcoholic fatty pancreas diseases partner in crime

Levina S. Pakasi[1], Cosmas Rinaldi A. Lesmana[1], Sri Inggriani[2], Laurentius A. Lesmana[1]

Digestive Disease and Gi Oncology Centre Medistra Hospital Jakarta-Indonesia[1], Department of Radiology Medistra Hospital Jakarta-Indonesia[2]

Background: Unlike the non-alcoholic fatty liver disease (NAFLD), the clinical significance of non-alcoholic fatty pancreatic disease (NAFPD) is largely unknown. It is often an incidental finding on abdominal ultrasound, which is not explored further and left untreated.
Objective: The aim of this study was to evaluate the presence of NAFPD and its association with NAFLD risk factors.
Method: A cross-sectional study was done among adult medical check-up patients underwent abdominal ultrasound between January and December 2013 in Medistra Hospital, Jakarta. Clinical was obtained from medical records. The presence of NAFLD and NAFPD was diagnosed by ultrasound.
Results: A total of 901 eligible cases were included in this study. Fatty pancreas was present in 315 (35 %) patients. Coexistence of NAFL and NAFP was present in 232 (25.8 %) of patients. Fatty pancreas was found in 53.1 % of patients with fatty liver whereas fatty liver can be found in 73.7 % of patients with fatty pancreas. There was a significant association between fatty pancreas and fatty liver (OR: 5.195; 95 % CI 3.838-7.032; $P < 0.001$). The presence of fatty pancreas were significantly associated with male gender, age > 35 years, higher systolic and diastolic blood pressures, fasting blood glucose > 100 mg/dL, triglycerides, total and LDL-cholesterol, and lower HDL cholesterol levels. Independent risk factors for fatty pancreas were age > 35 years, BMI > 25 kg/m2, FBG > 100 mg/dL and total cholesterol levels > 200 mg/dL.
Conclusion: NAFLD is significantly associated with NAFPD. Independent risk factors of NAFPD include body mass index, fasting blood glucose, and total cholesterol levels, which are also risk factors of.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1737

Nonalcoholic steatohepatitis and metabolic disorder of different organs in young and aged diet induced obesity model with c57bl 6 mice

Ching-wei Chang[1], Hung-chang Lee[2], Tung-hu Tsai[3], Chia-yuan Liu[3], Jen-shiu Chiang Chiau[4], Mei-lien Cheng[4], Tsang-en Wang[1], Chien-yuan Hung[5], Shou-chuan Shih[1]

Mackay Memorial Hospital Division of Gastroenterology Taipei-Taiwan[1], Mackay Memorial Hospital Pediatrics Taipei-Taiwan[2], National Yang-ming University Institute of Traditional Medicine Taipei-Taiwan[3], Mackay Memorial Hospital Medical Research Taipei-Taiwan[4], Mackay Medical College Medicine New Taipei City-Taiwan[5]

Background: In aged individuals, obesity is increasing at alarming rates and it is suggested that aged individuals are more vulnerable to the deleterious metabolic injury of obesity than younger individuals. For elucidate the issue, optimized animal model to evaluate the phenotype of aging and obesity is necessary.
Aim: We aimed to examination metabolic damage from different organs in mice with diet-induced obesity in different age.
Methods: Male C57BL/6 J mice aged 6 (young group) and 44 weeks (aged group) were fed 12 weeks of a standard chow (SC) or high fed diet (HFD). For liver damage, histology and alanine transaminase were analyzed. For pancreatic injury, blood sugar, insulin and HOMA-IR were used. For adipose tissue damage, triglyceride, total cholesterol and fat composition by computer tomography (CT) scan were included.
Results: After 12-weeks HFD feeding, weight gain, increased level of ALT, insulin, cholesterol, triglyceride, insulin, and HOMA-IR, fat accumulation, hepatic steatosis and gut microbiota change occurred in both young and aged group ($P < 0.05$). Compared with young HFD group, AST and ALT, but not hepatic steatosis, were significant increased in aged HFD group ($P < 0.05$). In addition, cholesterol,

triglyceride and insulin, HOMA-IR, fat accumulation, and gut microbiota change were also significant increased in aged HFD group compared with young HFD group ($P < 0.05$).
Conclusion: Age in obese mouse model play an important role for steatohepatitis, dyslipidemia, insulin insensitivity, fat accumulation and fecal gut microbiota change. This aged obese model could help to elucidate multiple organ alterations associated with metabolic disorder and age.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1569

The relationship between serum fetuin a and liver fibrosis in patients with non alcoholic fatty liver disease (NAFLD)

Alpaslan Tanoglu[1], Taner Akyol[1], Ergenekon Karagoz[2], Yusuf Yazgan[1]

Gata Haydarpasa Training Hospital Gastroenterology Istanbul-Turkey[1], Gata Haydarpasa Training Hospital Infectious Diseases and Clinical Microbiology Istanbul-Turkey[2]

Aim: Fetuin-A, represents an attractive biological candidate to link NAFLD. It has been demonstrated that the serum levels of Fetuin-A were elevated in obesity, diabetes mellitus, metabolic syndrome and NAFLD, whereas this level was found to be decreased in end-stage liver diseases. We aimed to investigate the potential role of Fetuin-A in determining liver fibrosis in patients with NAFLD.
Material and method: 42 biopsy proven NAFLD patients and 30 healthy subjects were included in the study. NALFD patients were divided into two groups according to presence of fibrosis. Serum fetuin-A levels of all subjects included in the study were determined by a commercially available ELISA kit.
Result: There was a significant difference between NAFLD group and healthy subjects in terms of Fetuin-A. The mean serum Fetuin-A level was 504,51 ± 293,51 in NAFLD group and 382,75 ± 184,25 in healthy subjects(Independent Sample T test, $P = 0{,}049$).On the other hand, Fetuin-A levels were found to be lower in the patient group who have hepatic fibrosis(Fetuin-A in NAFLD patients with hepatic fibrosis: 398,33 ± 308,74, Fetuin-A in NAFLD patients without hepatic fibrosis: 601,05 ± 247,90.ROC AUC: 0,691, $P = 0{,}034$).Fetuin-A was found to be negatively correlated with liver fibrosis according to Pearson correlation($P = 0{,}023$, $r = -0{,}349$).
Conclusion: Fetuin-A levels were found to be statistically significantly higher in NALFD patients.However, NAFLD patients having hepatic fibrosis had lower serum Fetuin-A levels than NALFD patients who have no hepatic fibrosis. These results demonstrate us that Fetuin-A levels may be used to predict NAFLD as a non-invasive method. These results may provide novel insights into pathogenesis of NAFLD and may also help clinical hepatologists.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2063

Changings in nash predicting non invasive tests after bariatric surgery

Ahmet Yozgat[1], Baris Yildiz[2], Basak Cakir[3], Akif Altınbas[1], Selim Demirci[1], Faruk Coskun[2], Emin Altiparmak[1]

Numune Education and Research Hospital Gastroenterology Ankara-Turkey[1], Numune Education and Research Hospital General Surgery Ankara-Turkey[2], Numune Education and Research Hospital Internal Medicine Ankara-Turkey[3]

Introduction: Non alcoholic steatohepatitis (NASH) is a common feature of morbid obese patients and may lead to liver fibrosis, cirrhosis and hepatocellular carcinoma. Bariatric surgery is the only curative treatment for morbid obesity. Investigators determined some non-invasive tests to predict the severity of underlying fibrosis related with steatosis before. However, the changings in the tests, predicting the fibrosis, after successful weights lose have not been investigated yet. Thus, we aimed to compare these non-invasive parameters before and 6 months after the bariatric surgery.
Subject and material: Totally 84 patients undergoing bariatric surgery, between April 2011- September 2013 in our hospital, included in the study retrospectively.
Results: Mean age of the patients were 38,3 ± 7,8 years old and %83,3 of them were woman. Sleeve gastrectomy were performed in %66,7 of the patients and the remained were Roux-N-Y gastric bypass surgery. Basic demographic data, MPV values, APRI indexes, HOMA scores and BMI values of the patients were similar in both type of surgery groups.
BMI and triglycerid values significantly decreased in both group, whereas APRI and HOMA index did not change. Moreover, MPV values were found to increase at the follow up period.
Discussion: In the recent studies, MPV values were determined as an independent risk factor for prediction of underlying NASH and it significantly increased in patients with NASH. In contrast, in our study, MPV values still increased after bariatric surgery. In addition, there were no significant changes in HOMA and APRI indexes, even though BMI values decreased significantly during the follow up period.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2226

Toll like receptor 7 promotes non alcoholic steatohepatitis by induction of tumor necrosis factor α in mice

Bumseok Kim[1], Yoon Seok Noh[1], Surim Park[1], Jong Won Kim[1], Chae Woong Lim[1]

1biosafety Research Institute and Laboratory of Pathology, College of Veterinary Medicine (bk21 Plus Program) Chonbuk National University Jeonju-Korea, South[1]

Aim: Non-alcoholic steatohepatitis (NASH) is a major form of chronic liver disease and characterized by steatosis, inflammation and progressive fibrosis, and can ultimately lead to cirrhosis. Recent evidences suggest that increased bacterial translocation to the liver are implicated in the development of NASH. Toll-like receptor 7 (TLR7) is a pattern recognition receptor that recognizes bacteria and host-derived RNA and activates innate immunity. Kupffer cells act as major innate immune cells in the progression of NASH. In the present study, we have focused on the role of TLR7 signaling in Kupffer cell in NASH.
Methods Wild-type (WT) and TLR7-deficient BALB/C mice (8-10 weeks of age, 25-30 g body weight) were fed on a methionine–choline-deficient (MCD) diet for 17 days or 6 weeks and then assessed the severity of steatohepatitis.
Result: The MCD diet induced NASH in WT mice, characterizing steatosis, inflammation and fibrosis. TLR7-deficient mice showed less steatohepatitis and liver fibrosis than WT mice. In the acute NASH model, serum and hepatic TNF-α expression levels were suppressed in TLR7-deficient mice compared to WT mice. Kupffer cells

produced TNF-α in response to R848, TLR7 ligand. TNF-α acts synergistically with H2O2 to induce cell death in cultured hepatocytes. Furthermore, treatment of IRS661, an antagonist of TLR7, efficiently ameliorated the NASH in vivo.
Conclusion: This study demonstrated a novel role of TLR7 in mediating experimental NASH. TLR7 signaling mediates TNF-α production in Kupffer cells, which subsequently induces hepatocyte apoptosis and may also increase the T cell activation leading to the progression of NASH. Therefore, ODN-based TLR7 antagonist proves a successful therapeutic strategy to regulate NASH.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1162

Relationship between hepatic steatosis assessed by ultrasound and controlled attenuation parameter in patients with alcoholic liver disease and those with non alcoholic fatty liver disease

Jem Ma Ahn[1], Yong-han Paik[1], Ju Yeon Cho[1], Won Sohn[1], Dong Hyun Sinn[1], Geum-youn Gwak[1], Moon Seok Choi[1], Joon Hyeok Lee[1], Kwang Cheol Koh[1], Seung Woon Paik[1], Byung Chul Yoo[1]

Samsung Medical Center, Sungkyunkwan University School of Medicine Division of Gastroenterology, Department of Medicine Seoul-Korea, South[1]

Background/aim: The aim of this study was to evaluate relationship of controlled attenuation parameter (CAP) with hepatic steatosis assessed by ultrasound (US) in patients with alcoholic liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD).
Methods: Patients with either ALD or NAFLD, who were diagnosed as fatty liver with US and measured CAP with transient elastography, were enrolled in this study. The hepatic steatosis assessed by US was categorized into mild (S1), moderate (S2), and severe (S3) degree.
Results: A total of 186 patients were included: 106 with NAFLD, 80 with ALD.
According to hepatic steatosis, CAP was correlated well with US in both NAFLD and ALD ($\rho = 0.569$, $P < 0.001$; $\rho = 0.519$, $P < 0.001$) and there was no significant difference between etiologies ($P = 0.635$). Using CAP, AUROCs in patients with NAFLD were 0.79 for $\geq$ S2 steatosis and 0.82 for $\geq$ S3 steatosis: in those with ALD, 0.78 for $\geq$ S2 steatosis and 0.87 for $\geq$ S3 steatosis, respectively. For the sensitivity $\geq$ 90 %, cut-offs of CAP for the detection of $\geq$ S2 steastosis were 255.5 dB/m (sensitivity 90.8 % and specificity 60.0 %) in NAFLD and 245.0 dB/m (sensitivity 91.4 % and specificity 62.2 %) in ALD: the cut-offs of CAP for the detection of $\geq$ S3 steatosis were 290.5 dB/m (sensitivity 92.6 % and specificity 59.5 %) in NAFLD, and 279.5 dB/m (sensitivity 100 % and specificity 68.1 %) in ALD, respectively.
Conclusion: Regarding hepatic steatosis, CAP significantly correlated with US in both NAFLD and ALD groups with similar level.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2028

Comparative study of old versus young NAFLD patients in coastal eastern India

Shivaram Prasad Singh[1], Girish Kumar Pati[1], Ayaskanta Singh[1], Bijay Misra[1], Debasis Misra[1], Manas Kumar Panigrahi[2], Sanjib Kumar Kar[3], Kaumudee Patnaik[4], Pallavi Bhuyan[4], Niranjan Rout[5], Chudamani Meher[6], Omprakash Agrawal[6]

S.c.b.medical College Dept. of Gastroenterology Cuttack-India[1], Ims & Sum Hospital Department of Gastroenterology & Hepato-biliary Sciences Bhubaneswar-India[2], Gastro & Liver Care Dept. of Gastroenterology Cuttack-India[3], S.c.b.medical College Dept. of Pathology Cuttack-India[4], Ahrcc Dept. of Oncopathology Cuttack-India[5], Beam Diagnostics Department of Radiodiagnosis Cuttack-India[6]

Background and aims: Non-alcoholic fatty liver disease (NAFLD), is associated with insulin resistance (IR) and metabolic syndrome (MS), which are common in the aged (> 40 years). There are reports that older patients have more severe disease compared to young. The present study was aimed at comparing the older (> 40 years) versus younger NAFLD patients.
Materials and methods: The anthropometric, biochemical and histological parameters of 270 old and 243 young NAFLD patients were compared
Results: The old NAFLD cases (mean age: 50.09 ± 7.26 years) compared to younger patients (mean age: 33.48 ± 4.8 years) had higher anthropometric indices (Waist circumference: 97.64 ± 10.79 vs. 94.4 ± 7.87; $P = 0.0007$, Waist-Hip ratio: 0.98 ± 0.07 vs. 0.95 ± 0.05; $P < 0.0001$, Waist-Height ratio: 0.6 ± 0.07 vs. 0.57 ± 0.05; $P < 0.0001$), higher fasting blood glucose (103.85 ± 33.5 vs. 94.39 ± 24.46; $P = 0.001$), Homeostasis model assessment IR (HOMA-IR) (3.18 ± 3.22 vs. 2.44 ± 1.3; $P = 0.01$), higher prevalence of hypertension (49.66 % vs. 39.25 %; $P = 0.02$) and fasting hyperglycemia (38.34 % vs. 18.28 %; $P < 0.0001$) but paradoxically lower transaminitis (ALT: 44.73 ± 15.29 vs. 59.84 ± 37; $P = 0.0001$). The mean BMI (27.6 ± 3.52 vs. 27 ± 2.89; $p > 0.05$), fasting insulin (11.31 ± 6.29 vs. 10.7 ± 5.46; $P = 0.41$), triglyceride (204.33 ± 143.17 vs. 201 ± 110.53; $P = 0.8$), HDL Cholesterol (42.94 ± 17 vs. 44.16 ± 15.93; $P = 0.47$), and prevalence of MS (50.44 % vs. 41.3 %; $P = 0.19$) were not statistically different between the old and young. Although, there was a trend towards greater prevalence of definite NASH [47 % vs. 41 %; $P = 0.41$] and fibrosis [36.47 % vs. 25.26 %; $P = 0.1$] in older NAFLD, the differences were not statistically significant.
Conclusion: Older NAFLD patients did not have more severe histological disease, despite higher anthropometric indices and metabolic risk factors compared to younger patients.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1055

Effects of glutamine on intercellular junction protein expression of intestinal epithelium in rats with nonalcoholic fatty liver disease

Wenjin Ding[1], Jianjun Qin[2]

Xinhua Hospital, Shanghai Jiao Tong University Department of Gastroenterology Shanghai-China[1], Tongji University Shanghai Institute of Disaster Prevention and Relief Shanghai-China[2]

Objective: To investigate the effects of glutamine on intestinal epithelial tight junction protein of NAFLD rat and confirm its protective effect on the intestinal mucosal barrier. Methods: NAFLD rat model was established. 36 SD rats were divided into normal group, model group and glutamine group. Liver index, hepatic pathology, serum endotoxin and TNF-α were recorded at the 8th and 12th week. Intestinal occludin protein was detected by Western blot. Its orientation and distribution was detected by immunohistochemistry.

Results: Establish NAFLD rat model successfully by high fatty diet. At the point of 8th week, liver index, endotoxin and TNF-α content of model and glutamine group were higher than those in normal group with no significant difference; So does in glutamine group, compared with model group. At the week of 12th, indexes as above increased significantly in model group and glutamine group, compared with normal one (3.75 ± 0.56, 3.47 ± 0.73 vs 2.75 ± 0.91; 0.279 ± 0.033, 0.203 ± 0.012 vs 0.114 ± 0.021; 29.73 ± 5.34, 28.77 ± 3.61 vs 6.84 ± 1.87, $P < 0.05$). Serum endotoxin decreased with statistical significant by glutamine treatment (0.203 ± 0.012 vs 0.279 ± 0.033, glutamine group vs model group, $P < 0.05$). Intestinal occludin protein expressed weaker in NAFLD rats than the other two group. Glutamine can upregulate its expression. No significant differences of occludin localization among three groups, but the intensity and range of brown staining was stronger in normal and glutamine group.
Conclusion: Glutamine could repair intestinal mucosa barrier in rats with NAFLD. Its mechanism involves reducing serum TNF-α, up-expressing intestinal epithelial tight junction protein named occludin, and then improving endotoxemia.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1572

Non invasive measurement of liver steatosis and fibrosis by controlled attenuation parameter (CAP) and fibroscan® is useful to access clinicopathololgic conditions of nonalcoholic fatty liver disease (NAFLD)

Kenichiro Enooku[1], Kazuya Okushin[1], Hidetaka Fujinaga[2], Takeya Tsutsumi[1], Kyoji Moriya[3], Hiroshi Yotsuyanagi[4], Kazuhiko Koike[1]

The University of Tokyo Gastroenterology Tokyo-Japan[1], The University of Toko Gastroenterology Tokyo-Japan[2], The University of Tokyo Infection Control and Prevention Tokyo-Japan[3], The University of Tokyo Infectious Disease Tokyo-Japan[4]

Background/aim: The aim of this study was to evaluate the performance of controlled attenuation parameter (CAP) and Fibroscan® for the assessment of nonalcoholic fatty liver disease (NAFLD).
Methods: We enrolled patients with chronic liver injury who met the following criteria: (1) those who visited the authors' hospital from March 2012 to September 2013, (2) diagnosed as having NAFLD or cryptogenic cirrhosis by liver biopsy with a history of alcohol consumption <20 g/day, (3) underwent 10 valid liver stiffness measurements by Fibroscan. NAFLD was classified according to the Matteoni types. Patients with advanced fibrosis and no steatosis were classified as cryptogenic cirrhosis. We evaluated CAP and Fibroscan values according to each Matteoni types.
Results: A total of 161 patients fulfilled the inclusion criteria (70.8 % male), and the median age was 56.6 years (IQR 42.4–67.0). The number of patients with Matteoni type I, type II, type III-IV and cryptogenic cirrhosis were 14, 36, 99 and 12, respectively. The median Fibroscan values of patients with Matteoni type I, type II, type III-IV and cryptogenic cirrhosis were 6.1 (IQR 5.0–8.9), 6.3 (5.5–7.8), 10.3 (7.4–15.2), and 19.7 (12.9–24.2) kPa, respectively. The median CAP values were 292.5 (IQR 255.2–321.2), 285 (267–317), 312 (284.5–332.5), and 218.5 (180–243.5) dB/m, respectively. In patients with Fibroscan values higher than 7.0 kPa, sensitivity and specificity of CA$P < 247$ dB/m for detecting cryptogenic cirrhosis were 83.3 % and 88.7 %.
Conclusions: CAP and Fibroscan are useful tools to assess progression of NAFLD non-invasively.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2224

Chronic administration of nicotine exacerbates nonalcoholic steatohepatitis via increased hepatic fat loss and fibrosis

Jong Won Kim[1], Surim Park[1], Chae Woong Lim[1], Bumseok Kim[1]

Biosafety of Institute and Laboratory of Pathology (bk21 Plus Program), College of Veterinary Medicine Chonbuk National University Jeonju-Korea, South[1]

Aim: Cigarette smoking is a major risk factor for cardiovascular disease, chronic kidney disease and nonalcoholic fatty liver disease. Nicotine, a major tobacco alkaloid, has various biological effects and a binding ability to the nicotinic acetylcholine receptors. The objective of this study was to evaluate the effects of nicotine on nonalcoholic steatohepatitis (NASH) in mice.
Methods: C57BL/6 male mice were randomized to receive either vehicle (2 % saccharin) or nicotine (100 μg/ml in 2 % saccharin) in the drinking water ad libitum. After 1 week, animals in the vehicle or nicotine-treated group were re-randomized to feed a normal chow diet or methionine-choline-deficient (MCD) diet for 6 weeks. Histopathologic changes, hepatic gene and protein expression were assessed for evaluation of liver damage and lipid metabolism.
Results: Hepatic expression of genes related to liver fibrosis revealed that the mRNA levels of α-SMA, COL1A1 and TIMP-1 were significantly increased in mice on MCD plus nicotine, compared with mice on MCD alone. Although increased liver damage was confirmed by high levels of ALT and AST in mice on MCD plus nicotine, compared with mice on MCD alone, the expression levels of pro-inflammatory gene such as TNF-α, IL-6 and IL-1β in liver were not different in both groups. Interestingly, light microscopic image analysis and the level of hepatic triglycerides showed markedly lower lipid accumulation in livers of mice on MCD plus nicotine, compared with mice on MCD alone. Immunoblot analysis revealed that hepatic fat loss in chronic nicotine administered mice was associated with significantly increased phosphorylation of AMP-activated protein kinase (AMPK) compared to vehicle treated mice. Furthermore, decreased expression of hepatic sterol regulatory element-binding protein (SREBP)-1c and its downstream genes fatty acid synthase (FAS), acetyl-coenzyme A carboxylase 1 (ACC1) was closely related to the hepatic fat loss. In accordance with these results, high serum adiponectin levels are exhibited in mice on MCD plus nicotine.
Conclusion: These findings support a prominent role of nicotine in NASH-related fibrosis and hepatic fat loss, so-called "burnt-out" NASH, which in part is mediated via increased serum adiponectin and up-regulation of AMPK phosphorylation in liver.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2209

Rifaximin protects against the development of fructose induced steatohepatitis in rats

Nese Cabuk Celik[1], Ibrahim Halil Bahcecioglu[2], Murat Ispiroglu[2], Mehmet Tuzcu[3], Necip Ilhan[4], Ibrahim Hanifi Ozercan[5], Kazim Sahin[6]

Firat University, Faculty of Medicine Internal Medicine Elazig-Turkey[1], Firat University, Faculty of Medicine Gastroenterology Elazig-Turkey[2], Firat University, Faculty of Science Biology Elazig-Turkey[3], Firat University, Faculty of Medicine Biochemistry Elazig-

Turkey[4], Firat University, Faculty of Medicine Pathology Elazig-Turkey[5], Firat University, Faculty of Medicine Animal Nutrition Elazi-Turkey[6]

Background/aim: Non alcoholic fatty liver disease is the most frequent liver disease in the worldwide. In addition it is commonly interested with the metabolic syndrome. There is possibility that the disease may be associated with the increase fructose consumption. In this study, which will be inducing by high fructose in an experimental model of fatty liver, we aimed to investigate the protective effects of rifaximin.
Method: There are 42 male Sprague–Dawley rats in the study. They were divided into 6 equal groups according to following feed types: Control group; given the 50 % fructose solution; given one time rifaximin per week with fructose solution; given three times rifaximin per week with fructose solution; normal diet with given one time rifaxmine per week; normal diet with given three times rifaximin per week. After eight weeks, the tissue samples, getting from rat liver, were taken for histopathological examination and tissue levels of MDA, TNF-α, NF-kB, Nrf-2. Blood samples were taken for biochemical examination and TNF-α level.
Results: It was seen in histopathological examination that the development of ballooning degeneration, inflammation and macrovesicular steatosis in the group of feeding with 50 % fructose solution. On the other hand, the significant decreasing in the findings of steatohepatitis was observed in group of taking % 50 fructose solution with rifaximin.

The level of TNF-α of plasma and tissue, tissue NF-kB, MDA, Nrf-2 were observed as low in the group taken rifaximin placed with pathogenesis of steatohepatitis. There was not significant difference between one and three dose rifaximin in a week.
Conclusion: Rifaximin protects against steatosis, ballooning degeneration and inflammation induced by high fructose diet in rats. It was thought that rifaximin may be prevent the steatohepatitis inhibiting NF-kB, TNF-α, with decreasing intestinal translocation of endotoxin. New studies on this subject are needed.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1592

Limited utility of plasma m30 in discriminating non alcoholic steatohepatitis from steatosis—a comparison with routine biochemical markers

Wah Kheong Chan[1], Pavai Sthaneshwar[2], Nik Raihan Nik Mustapha[3], Sanjiv Mahadeva[1]

University of Malaya Department of Medicine Kuala Lumpur-Malaysia[1], University of Malaya Department of Pathology Kuala Lumpur-Malaysia[2], Hospital Alor Setar Department of Pathology Alor Setar-Malaysia[3]

Background: The utility of Cytokeratin-18 fragment, namely CK18Asp396 (M30), for the diagnosis of non-alcoholic steatohepatitis (NASH) is currently uncertain.
Methods: The accuracy of M30 for detecting NASH was compared with serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and gamma glutamyl transpeptidase (GGT) levels in consecutive adult subjects with biopsy-proven non-alcoholic fatty liver disease (NAFLD).
Results: Data for 93 NAFLD subjects (mean age 51.0 ± 11.1 years old and 51.6 % males) and 20 healthy controls (mean age 50.2 ± 16.4 years old and 33.3 % males) were analyzed. There were 39 NASH subjects (41.9 %) and 54 non-NASH subjects (58.1 %) among the NAFLD subjects. Plasma M30, and serum ALT, AST and GGT were significantly higher in NAFLD subjects than in healthy controls (349 U/L vs. 162 U/L, 70 IU/L vs. 26 IU/L, 41 IU/L vs. 20 IU/L, and 75 IU/L vs. 33 IU/L, respectively). Serum ALT, AST and GGT were significantly higher in NASH subjects compared to non-NASH subjects (86 IU/L vs. 61 IU/L, 58 IU/L vs. 34 IU/L, and 97 IU/L vs. 56 IU/L, respectively), but no significant difference was observed with plasma M30 (435 U/L vs. 331 U/L). The accuracy of plasma M30, and serum ALT, AST and GGT was good for predicting NAFLD (AUROC 0.91, 0.95, 0.87 and 0.85, respectively) but less so for NASH (AUROC 0.59, 0.64, 0.75 and 0.68, respectively).
Conclusion: The utility of M30 in the detection of NASH in clinical practice appears limited, in comparison to routine biochemical markers.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1765

Value of controlled attenuation parameter (cap) liver ultrasound and metabolic parameters in the evaluation of steatosis in asymptomatic adults

Eser Vardareli[1], Seyhmus Getiren[1], Nurdan Tözün[1]

Acibadem University Gastroenterology Istanbul-Turkey[1]

Aim: Controlled attenuation parameter (CAP) is a recent method for noninvoice assessment of steatosis. Its usefulness in clinical practice is unknown. The aim of this study is to investigate the relationship between CAP, liver ultrasound (US), transient elastography (TE) scores and metabolic markers in asymptomatic subjects.
Method: 103 subjects (58 males, mean age: 46,4 ± 13,2 years) were selected from 250 individuals who had applied for an annual check up to our unit after secondary causes of liver steatosis (drugs, viral hepatitis, metabolic diseases) were excluded. Serum biochemistry tests, homeostatic model assessment (HOMA) and body mass index(BMI) were obtained. US was performed by 2 experienced radiologists. CAP and elastography scores were obtained by Fibroscan M probe (3.5 MHz).
Results: A total of 103 subjects were included: Mean CAP value was 246 ± 64,2 dB/m. 55,3 % of subjects had steatosis (CAP value > 238 dB/m). While CAP values correlate moderately with elastography results, triglycerides, uric acid, gamma-glutamyl transferase (but not aminotransferases) levels, significant correlation exists with HOMA and BMI ($r > 0,5$, $P < 0,05$). Elastography is correlated well with liver enzymes and HOMA levels ($r > 0,5$, $P < 0,05$). Although there was moderate correlation between CAP values and US scores ($r = 0,47$, $P = 0,000$), if cut-off value for steatosis is defined at 238 dB/m measured with CAP, only grade 2 and 3 US scores are related to existence of steatosis($z = 2,8$, $P = 0,005$).
Conclusion: CAP appears to be a reliable diagnostic tool for noninvasive assessment and quantification of steatosis. It maybe of special clinical importance in long term follow up of asymptomatic patients with marked steatosis.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1375

Controlled attenuation parameter(CAP) assessment may be clinically useful for liver transplant purposes

Young Mi Hong[1], Ki Tae Yoon[1], Mong Cho[1], Dae Hwan Kang[1], Hyung Wook Kim[1], Cheol Woong Choi[1], Su Bum Park[1], Jeong Heo[2], Hyun Young Woo[2], Won Lim[2]

Pusan National University Yangsan Hospital Internal Medicine Yangsan-si-Korea, South[1], Pusan National University Hospital Internal Medicine Busan-Korea, South[2]

Background & aims: The controlled attenuation parameter (CAP) using transient elastogarphy is an noninvasive method of assessing hepatic steatosis. The presence of hepatic steatosis is associated with an increased risk of graft loss. Therefore, we assessed the accuracy and the efficacy of CAP for the detection of hepatic steatosis in potential liver donors.
Methods: We enrolled potential liver donors and all patients underwent CAP assessment, MRI (Dixon in phase/out of phase (Dixon IP/OP) with/without fat saturation images) and ultrasonography-guided liver biopsy.
Results: A total of 10 potential liver donors were included: 9 were male and median age was 29 years. Clinical and laboratory variables were analyzed according to CAP values. The median CAP value was 269.5 dB/m (range, 181-371) and CAP value was only positively correlated with BMI ($r = 0.784$, $P < 0.01$), waist circumference ($r = 0.742$, $P < 0.01$). On liver biopsy, 1 (10.0 %) patients had S0, 6 (60.0 %) had S1, 3 (30.0 %) had S2. A close relationship was observed between the percentage of steatosis estimated by MRI ($r = 0.675$, $P < 0.05$), CAP values and histologic steatosis scores ($r = 0.825$, $P < 0.01$). The CAP values increased significantly ($P < 0.001$) for each steatosis stage on liver biopsy: S0, 190 dB/m; S1, 260 dB/m; S2, 310 dB/m.
Conclusions: CAP can screen and identify potential liver donors at high risk of fatty liver disease.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1524

Relation between smoking and non alcoholic fatty liver disease

Nasrin Taghizadieh[1], Parisa Ramazanilar[1], Sara Ebrahimi[1]

Tabriz University of Medical Sciences Liver and Gastrointestinal Research Center Tabriz-Iran[1]

Background and aim: Metabolic syndrome, which includes obesity, hyperglycemia, dyslipidemia, and hypertension, is an important risk factor for the incidence of nonalcoholic fatty liver disease (NAFLD). Cigarette smoking is a risk factor for metabolic syndrome, but the effect of active smoking on development of nonalcoholic fatty liver disease (NAFLD) is controversial.

Smoking increases insulin resistance. Given the pathophysiological role of insulin resistance in NAFLD, characterization of the influence of smoking in NAFLD is warranted. The aim of this paper is to give a narrative review of the association between cigarette smoking and NAFLD.
Method & results: We did a narrative study and gathered data from different articles. We searched pub med and Google scholar and… for finding articles. One of the studies was done in Chinese people and the conclusion was that Active smoking has a synergistic effect on prevalent NAFLD. another 10 year study which was done between years 1998 and 2008 showed that out of 1,560 subjects without NAFLD in 1998, 266 (17.1 %) were newly diagnosed with NAFLD in 2008.

Also the study which was done on the obese rats (which are susceptible for NAFLD) showed that smoking increases the severity of NAFLD.
Conclusion: Few studies have been done in this category and there aren't a lot of data but according to the researches that have done, it can be estimated that there is a relation between smoking and fatty liver disease and smoking can be considered as a risk factor for fatty liver disease.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1608

Impact of hypothyroidism on development non alcoholic fatty liver disease; 4 year retrospective cohort study

Kil Woo Lee[1], Yong Kyun Cho[1], Byung Ik Kim[1], Eun Jung Lee[2], Heon Ju Kwon[3]

Sungkyunkwan University School of Medicine Department of Gastroenterology, Kangbuk Samsung Hospital Seoul-Korea, South[1], Sungkyunkwan University School of Medicine Department of Endocrinology, Kangbuk Samsung Hospital Seoul-Korea, South[2], Sungkyunkwan University School of Medicine Department of Radiology, Kangbuk Samsung Hospital Seoul-Korea, South[3]

Aims: Hypothyroidism is reported to contribute to the development of Non-alcoholic fatty liver disease (NAFLD). We aimed to compare the risk for development of NAFLD among three groups according to thyroid hormonal status (Control, Subclinical hypothyroidism, Overt hypothyroidism) in 4 year retrospective cohort of Korean subjects.
Methods: From health check-up in 2008, 18,544 Koreans aged 20-65 years were apparently healthy without NAFLD included. These subjects were conducted annual health check-up for 4 consecutive years until December 2012 for the cohort study. Based on initial serum free thyroxine(fT4) and thyroid-stimulating hormone (TSH), they were classified into Control, Subclinical hypothyroidism [TSH > 4.2mIU/L, normal fT4] and overt hypothyroidism[TSH > 4.2mIU/L, fT4 < 0.97 ng/dl] groups. NAFLD was diagnosed on the basis of ultrasono graphic findings.
Results: Of 18,544 participants, NAFLD were developed in 2,348 subjects. The overall incidence of NAFLD was 12.7 %. In detail, it was 12.8 %, 11.0 %, 12.7 % in Control, Subclinical hypothyroidism, Overt hypothyroidism group, respectively. The incidence of NAFLD was not statistically significantly different according to baseline thyroid hormonal status, even after multivariate adjustment. (Subclinical hypothyroidism: Harzard ratio (HR) 0.965, 95 % confidence interval (CI) [0.814-1.143], $P = 0.67$) (Overt hypothyroidism group: HR 1.255, 95 % CI [0.830-1.899], $P = 0.28$).
Conclusions: Our study suggests that subclinical and overt hypothyroidism is not related to an increased incidence of NAFLD.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2032

Determine effect of weight loss on serum level of inflammatory cytokines IL 1 IL 6 CRP and TNF α in obese patients with fatty liver disease

Mohammad Hosein Somi[1], Behrooz Ziad Alizadeh[2], Kamal Boostani[1], Mohammad Khaneshi[3]

Liver and Gastrointestinal Diseases Research Center Medical Faculty Tabriz-Iran[1], Universiteit Van Amsterdam, Nederland Department Gastroenterologie En Hepatologie Amesterdam-Netherlands Antilles[2], Liver and Gastrointestinal Diseases Research Center Medical Education Tabriz-Iran[3]

Introduction: Obesity which is connected to a wide range of functional and hormonal disorders, results is a mild and chronic inflammatory state leading to long term adverse effects. The aim of this study is to evaluate effect of low calorie diet and weight loss on serum level of inflammatory markers in patients with fatty liver disease in Iranian population.
Methods: In a clinical trial, 40 patients with fatty liver disease in Gastro-hepatology clinic of Tabriz Imam Reza hospital, who fulfilled the inclusion criteria, were introduced to receive a low calorie diet in nutrition clinic. Serum level of proinflammatory factors (IL-1, IL-6, TNF-α and Hs-CRP) were measured and compared before and after a 8 week trial of diet.
Results: The mean value of weight and body mass index of participants decreased significantly (a mean decrease of 6.47 ± 3.40 percent in weight) after 8 weeks. Weight loss in men was significantly more than women.
The mean level of IL-1, IL-6, TNF-α and Hs-CRP was significantly decreased after weight loss in both men and women. There was no correlation between amount of weight loss (or decrease in BMI or percentage of weight loss) with decrease of IL-1, IL-6, TNF-α or Hs-CRP. Decrease of TNF-α was more in younger patients.
Conclusion: Weight loss with low calorie diet can decrease the level of IL-1, IL-6, TNF-α and Hs-CRP of patients with fatty liver during 8 weeks independent from gender and degree of weight loss.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1688

Association between nonalcoholic fatty liver disease and metabolic syndrome in apparently healthy Korean adults

Kyoung Min Sohn[1], Yeon Ju Jeon[1], Jiwoo Sohn[1], Hajin Nam[2]

We Want Healthcare Internal Medicine Seoul-Korea, South[1], Hallym University Institute of Natural Medicine Chuncheon-Korea, South[2]

The prevalence of non-alcoholic fatty liver disease (NAFLD) has increased and several studies have shown that there is an association between NAFLD and metabolic syndrome(MetS). The aim of this study was to determine how much impact the risk factors of metabolic syndrome has on ultrasonographic fatty liver, especially NAFLD. A total of 41,258 adults who underwent routine comprehensive health evaluations, including abdominal ultrasonography, were selected. We calculated the adjusted prevalence ratios (PRs) for components of MetS (high blood pressure (BP), impaired fasting glucose, low high-density lipoprotein cholesterol (HDL-C), and high triglycerides (TG)) according to NAFLD. NAFLD was found in 13.8 % of non-obese subjects and 52.3 % of obese subjects. NAFLD was associated with most components of MetS in both obese and non-obese subjects. However, non-obese NAFLD patients had significantly higher PRs for certain components of MetS than did obese patients, especially among women. Body mass index, waist circumference, fasting blood glucose, triglyceride, HDL-C and aspartate aminotransferase, alanine aminotransferase, γ-glutamyl transpeptidase levels all affected NAFLD independently. The prevalence of metabolic syndrome was increased in mild (40.8 %) and moderate (57.8 %) NAFLD groups. When odd ratio (95 % CI) for NAFLD group was compared to the contrast group, there was an increased risk of metabolic syndrome with odd ratio of 12.8 (95 % CI, 9.1 ~ 17.0). NAFLD and its severity has a close connection with MetS and also with each risk factors of MetS. Therefore, assessment for concurrent MetS among NAFLD patients is considered to be necessary.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1172

The evaluation of non alcoholic fatty liver disease (nafld) and its associate factors in psoriasis patients using ultrasonography and the controlled attenuation parameter (cap) measured with transient elastography

Abhasnee Sobhonslidsuk[1], Jamrus Pongpit[1], Saneerat Porntharukchareon[1], Natta Rajatanavin[1], Ammarin Thakkinstian[2], Piyaporn Kaewdoung[1], Kwannapa Promson[1], Wasana Stitchantrakul[3], Duangporn Saengwimol[3], Supanna Petraksa[1], Chomsri Kositchaiwat[1]

Ramathibodi Hospital Medicine Bangkok-Thailand[1], Ramathibodi Hospital Section For Clinical Epidemiology and Biostatistic Bangkok-Thailand[2], Ramathibodi Hospital Research Center Bangkok-Thailand[3]

Background: Psoriasis is linked to metabolic syndrome and non-alcoholic fatty liver disease (NAFLD). NAFLD can be diagnosed by ultrasonography (US) but sensitivity is reduced when steatosis <30 %. Controlled attenuation parameter (CAP) measures liver fat using US signal acquired by transient elastography (TE, Fibroscan®).
Aims: To estimate the prevalence of NAFLD, to identify factors associated with NAFLD and to assess the performance of CAP.
Methods: Subjects underwent US and CAP using TE. Grading of NAFLD was classified as mild, moderate or severe. Factors with p-value of univariate analysis <0.20 were entered logistic regression model. Cutoffs of CAP were determined.
Results: 168 psoriasis patients were enrolled. TE failure occurred in 3 patients. NAFLD was detected in 105 (63.6 %) patients. Fifty-six (33.9 %), 38 (23.0 %) and 11 (6.7 %) patients had mild, moderate and severe fatty liver. Mean CAP and liver stiffness measurement in normal, mild, moderate and severe fatty liver were 182.93 (41.8), 247.96 (43.0), 307.86 (39.1), 329.27 (32.5) dB/m, and 4.28 (1.7), 5.02 (3.4), 6.05 (2.1), 9.16 (4.3) kPa. CAP was associated with NAFLD with OR 1.05 (95 % CI 1.03-1.07, $P < 0.001$). The optimal cutoffs of CAP for mild and severe fatty liver were 238 and 315 dB/m yielding the AUROC, sensitivity and specificity of 0.92, 79.05 %, 95.00 % and 0.90, 81.82 %, 88.31 %. Hypertension (OR 7.94, 95 % CI: 1.05-60.00; $P = 0.045$), BMI 23-25 kg/m2 (OR 71.02, 95 % CI: 6.51-774.43; $P = 0.000$) and BMI > 25 kg/m2 (OR 35.32, 95 % CI 3.64-343.14; $P = 0.002$) were associated with NAFLD.
Conclusions: 64 % of psoriasis patients have NAFLD. CAP using TE can be used to evaluate NAFLD in psoriasis.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1720

The effect of probiotics on nonalcoholic fatty liver disease and metabolic disorder of aged obese mice induced by high fat diet

Chia-yuan Liu[1], Shou-chuan Shih[2], Yu-jen Chen[3], Hung-chang Lee[4], Jen-shiu Chiang Chiau[5], Mei-lien Cheng[5], Ching-wei Chang[1], Tsang-en Wang[1]

Mackay Memorial Hospital Division of Gastroenterology Taipei-Taiwan[1], Mackay Medical College Department of Medicine Taipei-Taiwan[2], National Yang-ming University Institute of Traditional Medicine Taipei-Taiwan[3], Mackay Memorial Hospital Department of

Pediatrics Taipei-Taiwan[4], Mackay Memorial Hospital Medical Research Taipei-Taiwan[5]

Background: Obesity is associated with excessive amount of body fat, nonalcoholic fatty liver disease (NAFLD), and serious metabolic abnormalities include diabetes mellitus, dyslipidemia and heart disease. Aging makes organisms more vulnerable to metabolic diseases. Both obesity and aging are characterized by a low-grade inflammation. Probiotics has a potential pharmaceutical applications as an anti-inflammatory agent.
Aim: Evaluating the effect of probiotics on aged obese mice induced by high-fat diet.
Methods: The 44-week male C57BL/6 J mice (n = 12) were fed with high fat diet (HFD) or standard chow (SC). These aged mice are fed with probiotics, Infloran (*Bifidobacterium bifidum* and *Lactobacillus acidophilus*) or not for 12 weeks. Hepatic pathology, metabolic characteristics, and plasma composition were studied. Inflammation was determined by serum lipopolysaccharide (LPS) level. Gut microbiota composition was analyzed by sequencing 16S ribosomal RNA genes from stool samples.
Results: After 12 weeks, the HFD group gained more weight and had higher ALT, cholesterol, triglyceride, glucose, insulin and LPS levels than did SC group ($P < 0.05$). In addition, increased HOMA-IR, fat accumulation and hepatic steatosis occurred in response to HFD feeding ($P < 0.05$). Supplementation of HFD group with probiotics significantly reduced weight, triglyceride, insulin, HOMA-IR and LPS level ($P < 0.05$). Furthermore, ALT was significantly decreased and liver steatosis was ameliorated following probiotic treatment ($P < 0.05$). The Firmicutes/Bacteroidetes ratio was significantly increased in HFD group ($P < 0.05$), but significantly decreased following probiotic treatment ($P < 0.05$).
Conclusions: In aged mouse model, high-fat diet-induced obesity is associated with NAFLD and multiple metabolic disorder. Its associated chronic inflammation and gut microbiota change can also be treated by probiotics.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1117

Correlation between anthropometric measures lipid profile and serum adiponectin and steatosis in nondiabetic nonalcoholic fatty liver disease

Hasan Ali[1], Mohamad Helal[1], Mohammed Hassan[2], Mahmoud Sherif[3]

Lecturer Tropical Medicine and Gastroenterology Qena-Egypt[1], Lecturer Medical Biochemistry Qena-Egypt[2], Lecturer Pathology Assiut-Egypt[3]

Background: Non alcoholic fatty liver Disease (NAFLD) has been increasing mainly because of the increased prevalence of obesity and its management is mandatory. Aim of the study: to evaluate the relationship between the grade of steatosis and anthropometric measures, fasting lipid profile and serum adiponectin.
Patients and methods: Fifty patients with US evidence of fatty liver disease and normal fasting and post-prandial serum glucose were included. No history of alcohol consumption. Liver function tests, fasting lipogram, complete blood count and serum adiponectin were measured. Both Body mass index (BMI) and waist circumference (WC) were measured. Liver biopsy was done to confirm the presence and detect the degree of steatosis.
Results: The mean age of patients were 40 ± 12 years. Patients with steatosis showed statistically significant higher value for BMI and WC than those without (P value = 0.000). Cholesterol, triglyceride, Low density lipoprotein-cholesterol (LDL-C) also were significantly higher in patients with steatosis (P value = 0.00). High density lipoprotein-cholesterol (HDL-C) and serum adiponectin were significantly lower in patients with steatosis (P value = 0.00). Patients with severe steatosis showed higher values for BMI and WC, cholesterol, triglyceride, LDL-C and lower values for adiponectin and HDL-C (P value < 0.05) than others. Significant positive correlations were detected between the grade of steatosis and the age, BMI and WC, cholesterol, triglyceride, LDL-C and negative correlations with adiponectin and HDL-C.
Conclusions: Anthropometric measures, fasting lipogram and serum adiponectin are associated with steatosis in Nondiabetic patients with NAFLD. So their detection is important for evaluation and management of those patients.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1774

Tumor necrosis factor like weak inducer of apoptosis (TWEAK)

Umit Cintosun[1], Teoman Dogru[2], Halil Genc[3], Cemal Nuri Ercin[2], Gurkan Celebi[2], Hasan Gurel[2], Erdim Sertoglu[4], Ali Fuat Cicek[5], Hüseyin Kayadibi[6], Serkan Tapan[4], Yıldırım Karslioglu[5], Ilker Tasci[7], Kenan Saglam[1], Sait Bagci[2]

Gulhane School of Medicine Department of Internal Medicine Ankara-Turkey[1], Gulhane School of Medicine Department of Gastroenterology Ankara-Turkey[2], Izmir Military Hospital Department of Gastroenterology Izmir-Turkey[3], Gulhane School of Medicine Medical Biochemistry Ankara-Turkey[4], Gulhane School of Medicine Department of Pathology Ankara-Turkey[5], Adana Military Hospital Medical Biochemistry Adana-Turkey[6], Gulhane School of Medicine Department of Geriatrics Ankara-Turkey[7]

Background: Tumor necrosis factor-like weak inducer of apoptosis (TWEAK), a member of the tumor necrosis factor (TNF) superfamily, plays an important role in immune and inflammatory diseases. Circulating TWEAK levels have been found associated with glucose and lipid parameters and also insulin resistance in several trials. However, there is no study regarding the relationship between non-alcoholic fatty liver disease (NAFLD) and TWEAK. We aimed to investigate the association of circulating levels of TWEAK with metabolic parameters, insulin resistance and histopathological findings in histologically proven NAFLD.
Methods: One hundred and two patients with NAFLD and 56 healthy subjects were enrolled. Plasma TWEAK, TNF-alpha and interleukin-6 levels were measured by enzyme-linked immunosorbent assay (ELISA). Serum high sensitive C reactive protein (hsCRP) levels were measured with immunoturbidimetric assay. HOMA-IR index was used to estimate insulin resistance.
Results: NAFLD group had significantly higher TNF-alpha, interleukin-6 and hsCRP levels as compared to healthy controls ($P < 0.001$, for all). No significant difference was found regarding to circulating TWEAK between two groups. In subgroup analysis, plasma TWEAK levels were significantly higher in NAFLD subjects with fibrosis than subjects without fibrosis ($P < 0.036$). Besides, a borderline association was observed between TWEAK and liver fibrosis ($P = 0.05$).
Conclusion: Our findings indicate that plasma TWEAK levels may be associated with liver fibrosis in human NAFLD. Further large prospective studies are needed to clarify the role of circulating TWEAK in the pathogenesis of liver fibrosis in this clinically relevant condition.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1014

The interaction between metabolic factors and disease progression in nonalcoholic steatohepatitis patients

Jee-fu Huang[1], Ming-lun Yeh[1], Chung-feng Huang[1], Chia-yen Dai Dai[1], Ming-lung Yu[1], Wan-long Chuang[1]

Hepatobiliary Division, Department of Internal Medicine Kaohsiung Medical University Hospital Kaohsiung-Taiwan[1]

Background & aims: Asians are more susceptible to non-alcoholic steatohepatitis (NASH) as well as metabolic disorder than other ethnicities. We aimed to assess the interaction between metabolic factors and fibrosis progression in Asians NASH patients.
Methods: A total of 130 biopsy-proven Taiwanese NASH patients (94 males, age = 43.0 ± 13.0 years) were consecutively enrolled. Their demographic data, metabolic profiles and histopathological manifestations were analyzed.
Results: There were 24 (18.5 %) non-obese patients. Eighty-one (76.4 %) of the 106 obese patients were males, which was significantly higher than that (54.2 %) of the non-obese patients ($P = 0.04$). The prevalence of metabolic syndrome and hypertension were 60.8 % and 44.6 %, respectively. The prevalence of diabetes rose from 23.8 % to 39.4 % after oral glucose tolerance test validation. Twenty-two (16.9 %) patients were of significant fibrosis (F2), whilst 12 (9.2 %) patients were of advanced fibrosis (F3-4). Fourteen (38.9 %) of the 36 female patients were of ≧F2, which was significantly higher than their 94 male counterparts (20.2 %) ($P = 0.04$). The gender disparity was also observed in patients of F3-4 (16.7 % of females vs 5.3 % of males, $P = 0.04$). There was a significant inverse correlation between uric acid level and fibrosis stages, ranging from 7.2 ± 1.3 mg/dL of F0, 6.5 ± 1.7 mg/dL of F1, 6.3 ± 1.6 mg/dL of F2, and 6.0 ± 0.8 mg/dL of F3-4, respectively ($P = 0.04$).
Conclusions: Asian NASH patients had a high proportion of metabolic disorders. Females were more susceptible to fibrosis progression than males. The gender disparity became indistinct in those non-obese patients.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1131

A study of metabolic parameters in non diabetic patients of fatty liver who do not consume alcohol

Gautam Ray[1]

B.r. Singh Hospital Medicine Kolkata-India[1]

Background: Fatty liver is common in patients with diabetes mellitus or ethanol consumers. Though its causative metabolic factors in such patients are well delineated, risk factors in non diabetic teetotaller persons who constitute a small but definite percentage of fatty liver patients in India are not defined.
Methods: In this case control study, the metabolic parameters of 50 non diabetic teetotaller patients (Gr1) were compared with those of 50 patients of IGT (impaired glucose tolerance) (Gr2) and 50 overt diabetics (Gr3). Fatty liver was diagnosed on USG/CT Scan abdomen and NAFLD fibrosis score was calculated to assess severity. The studied parameters were age, sex, BMI, FBS, fasting plasma insulin, complete lipid profile, HOMA-IR, HBA1c whose correlation with NAFLD fibrosis score was assessed by univariate and multivariate analysis with significance set at $P < 0.05$.. By the latter, factors affecting development of IGT and diabetes in comparison to the cases were also studied.
Results: Total cholesterol (R2 0.7, p 0.01) and triglyceride (R2 0.75, p 0.01)) were the only significant contributors of fatty liver in Gr1.When Gr1 and 2 were analysed together with IGT as outcome variable, high HBA1c (OR 6.88 CI 1.56–30.3) and triglyceride (OR 1.08 CI 1.02–1.15) was associated with development of IGT. When Gr1 + 2 was compared with Gr3 with diabetes mellitus as outcome variable, high HBA1c (OR 4.05 CI 1.82–9.02) and HOMA-IR (OR 1.21 CI 1.07–1.36) was associated with development of diabetes mellitus.
Conclusion: Dyslipidemia is associated with fatty liver in nondiabetic teetotallers.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2087

Histopathological metabolic features and ace gene polymorphism comparison of non alcoholic fatty liver disease

Demet Deniz Tekateş[1], Ibrahim Halil Bahcecioglu[2], Murat Ispiroglu[2], Necip Ilhan[3], Mehmet Yalniz[2], Ulvi Demirel[2]

Firat University, Faculty of Medicine Internal Medicine Elazig-Turkey[1], Firat University, Faculty of Medicine Gastroenterology Elazig-Turkey[2], Firat University, Faculty of Medicine Biochemistry Elazig-Turkey[3]

Background/aim: The aim of the present study is to investigate the effects of ACE and ACE gene polymorphism on histological and clinical characteristics and progression of the disease in patients with non- alcoholic fatty liver disease (NAFLD).
Method: Biopsy proven thirty-one patients with nonalcoholic fatty liver disease and 40 healthy controls, totally 71 individual were included to the study.
Results: ACE level was 11.69 ± 1.99 ng/ml in the NAFLD group, and 11.52 ± 1.72 ng/ml in the control group ($P = 0.70$). ACE level was compared with respect to AST/ALT, ALT, CRP, BMI, HOMA-IR and the difference was significant only for the HOMA-IR ($P = 0.008$). The study group was divided into four groups according to ACE gene polymorphism (D/D homozygot, I/I homozygot, D/I heterozygot, I/D heterozygot). No difference was found with respect to age and sex in the whole group. However, there was significant difference between the D/I and I/D subgroups in terms of age ($P = 0.39$). Fasting blood glucose was also significantly different among the D/D, I/D ile D/I, I/D subgroups ($P = 0.02$). ACE levels were comparable in various grade and stages (p was 0.68 for grade and stage). ACE gene polymorphism was also not different among the different grade and stages (p was 0.42 for grade and 0.92 for stage).
Conclusion: The effect of ACE and ACE gene polymorphism on NAFLD was investigated and no clinical, biochemical and histopathological difference was found among the gene polymorphisms.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1815

Serum macrophage migration inhibitory factor transforming growth factor β interleukin 17 and interleukin 23 concentrations are associated with the severity of liver disease in patients with nonalcoholic fatty liver disease

Jing You[1], Yuanzhi Yan[2], Lin Zhuang[3], Yanhua Che[4], Sijia Ma[5], Hongying Chen[1], Xia Feng[6], Hutcha Sriplung[7], Alan Geater[7], Virasakdi Chongsuvivatwong[7], Junhua Huang[8], Shaoming Yan[9], Ruyi Zhang[1], Shaofeng Rao[1], Ming Lou[1], Chen Tu[1], Zhi Jin[1], Jie Ding[1]

The First Affiliated Hospital of Kunming Medical University Department of Infectious Diseases Kunming-China[1], The First Affiliated Hospital of Kunming Medical University Department of Pharmacy Medicine Kunming-China[2], The Third People's Hospital of Kunming Department of Hepatology Kunming-China[3], The First People's Hospital of Kunming Department of Medicine Kunming-China[4], Kunming Medical University, Kunming-China[5], The First Affiliated Hospital of Kunming Medical University Department of Laboratory Medicine Kunming-China[6], Prince of Songkla University Epidemiology Unit, Faculty of Medicine Hat Yai-Thailand[7], The Yunnan General Hospital of The Chinese People's Armed Police Forces Department of Infectious Diseases Kunming-China[8], The Third People's Hospital of Yunnan Province Department of Internal Medicine Kunming-China[9]

Background/aims: Nonalcoholic fatty liver disease (NAFLD) is the most common form of chronic liver disease worldwide, ranging from simple steatosis to steatohepatitis which may progress to cirrhosis, and hepatocarcinoma. However, the molecular mechanisms underlying NAFLD development have not been completely characterized. The aims of present study were to investigate the levels of macrophage migration inhibitory factor(MIF), transforming growth factor-β (TGF-β), interleukin-17 (IL-17), interleukin-23 (IL-23) and interleukin-10(IL-10) and their correlation with liver disease in NAFLD.
Patients and methods: Clinical and biochemical characteristics were collected from 128 NAFLD patients [including nonalcoholic simple fatty liver (NASFL), nonalcoholic steatohepatitis (NASH), nonalcoholic-related liver cirrhosis (NALC)]. Thirty normal individuals were as control group. Serum levels of MIF, TGF-β, IL-17, IL-23 and IL-10 were measured using an enzyme-linked immunosorbent assay.
Results: NAFLD patients had significantly increased serum levels of MIF, TGF-β, IL-17, IL-23 and decreased IL-10 compared with normal individuals ($P < 0.001$,0.01,0.001,0.01; respectively). Both NASH and NALC patients had significantly increased serum levels of MIF, TGF-β, IL-17, IL-23, ALT, AST, TG, TC, LDL and BMI, but decreased IL-10 and HDL compared with normal individuals and NASFL patients ($P < 0.001$,0.01,0.05, respectively). Univariate analysis showed a similar pattern of the parameters MIF, TGF-β, IL-17 and IL-23 were significantly associated with levels of high TG, TC, LDL, BMI, and severity of liver disease, all with $P < 0.05$. Multivariate analysis showed that the levels of increment of MIF, TGF-β, IL-17 and IL-23 were associated with the increment of severity of liver disease.
Conclusion: Increased serum levels of MIF, TGF-β, IL-17 and IL-23 correlate positively with the severity of liver disease in NAFLD.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1387

Hepatic expression of endocannabinoid receptors in nonalcoholic steatohepatitis and metabolic syndrome

Ayca Eroglu[1], Enver Dolar[2], Talat Ayyildiz[3], Fatma Oz Atalay[4], Saduman Balaban Adim[4], Omer Yerci[4]

Uludag University Internal Medicine Bursa-Turkey[1], Uludag University Gastroenterology Bursa-Turkey[2], Ondokuz Mayis University Gastroenterology Samsun-Turkey[3], Uludag University Pathology Bursa-Turkey[4]

Objectives: In this study, we examined whether metabolic syndrome and non-alcoholic fatty liver disease (NAFLD) are associated with expression of cannabinoid receptors.
Methods: Fifty-four individuals with nonalcoholic steatohepatitis (NASH) and 17 with steatosis based on pathology reports of liver biopsies were included in the patient group. Forty individuals were normal in pathology reports were selected as the control group. The association between cannabinoid receptor-1 (CB1-R) and -2 (CB2 R) expression, determined immunohistochemically, and metabolic syndrome criteria and NASH activity score were determined.
Results: A comparison of control (n = 40), steatosis (n = 17) and NASH groups (n = 54) revealed a significant difference in CB2-R expression between patients with steatosis and patients with NASH ($P = 0.017$), but showed no significant difference in CB2-R expression between NAFLD and control groups ($P = 0.924$).
Conclusion: CB2-Rs were expressed in liver cells of all patients as well as those of controls, and this expression was associated with several parameters, including blood pressure, obesity, hyperlipidemia, and lobular inflammation.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2213

Hepatic steatosis a novel coronary risk factor for aviators

Mustafa Aparcı[1], Gokcen Aktas[2], Alpaslan Tanoglu[3], Mehmet Karaduman[4], Mustafa Kaplan[3], Cengiz Ozturk[1], Sercan Okutucu[1]

Etimesgut Military Hospital Cardiology Ankara-Turkey[1], Etimesgut Military Hospital Radiology Ankara-Turkey[2], Gata Haydarpasa Training Hospital Gastroenterology Istanbul-Turkey[3], Etimesgut Military Hospital Internal Medicine Ankara-Turkey[4]

Background: Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease all over the world. Patients with NAFLD, especially those with obesity and metabolic syndrome, have higher cardiovascular mortality compared with the general health population. We aimed to research the frequency of ultrasound-diagnosed NAFLD and other metabolic disorders among aviators.
Methods: 32 aviators with ultrasound-diagnosed NAFLD and 32 healthy aviators were included in the study. Age, height, weight, body mass index, systolic and diastolic blood pressure, serum levels of fasting blood glucose, total cholesterol, low density lipoprotein and high density lipoprotein cholesterol, triglyceride, alanine aminotransferase, aspartate amino transferase, γ-glutamyltransferase were obtained from the medical history, physical examination and laboratory result chart of medical recordings.
Results: The frequency of ultrasound-diagnosed hepatic steatosis (HS) was %16.9 (n = 32). Aviators with HS were older than aviators without HS. Mean weight (74.6 ± 7.0 vs 81.2 ± 7.8, $P = 0.001$), BMI (24.0 ± 1.9 vs 26.1 ± 1.9, $P < 0.001$), systolic blood pressure (110.7 ± 7.5 vs 119.1 ± 11.2, $P = 0.001$) and diastolic blood pressure (70.1 ± 6.9 vs 76.6 ± 7.6, $P = 0.001$) of the aviators with HS were significantly higher than healthy aviators. Fasting blood glucose levels (90.1 ± 12.8 vs 97.7 ± 9.1, $P < 0.05$), total cholesterol (191.2 ± 30.1 vs 219.9 ± 42.3, $P < 0.05$), LDL (117.9 ± 22.2 vs 140.2 ± 34.3, $P < 0.05$), VLDL cholesterol (23.9 ± 12.5 vs 32.1 ± 14.5, $P < 0.05$) were again significantly higher among aviators with HS.
Conclusion: Although being known to having lower risk factors in view of obesity, hyperlipidemia, diabetes, NAFLD and other metabolic disorders, all aviators should be closely screened for these cardiovascular risk factors. Sedentary lifestyle, overweightness,

hyperlipidemia, diabetes and eating disorders play crucial role development and progression of NAFLD. In order to screen NAFLD, USG can be used as a reliable, noninvasive diagnostic tool among aviators.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2122

Is there a relationship between severities of fatty infiltrations of the liver with silent myocardial ischemia in obese patients

Yavuz Furuncuoglu[1], F. Fusun Bolukbas[2], Cengiz Bolukbas[2], Munire Gundogan[3]

Medicalpark Goztepe Hospital Internal Medicine Istanbul-Turkey[1], Bahcesehir University School of Medicine Gastroenterology Istanbul-Turkey[2], Dalhousie University Department of Diagnostic Imaging Iwk Health Centre Radiology Halifax-Canada[3]

Background: Fatty infiltration of the liver is the best predictor of metabolic syndromes including obesity; type 2 diabetes mellitus, dyslipidemia and hypertension.
Aim: To determine if there is a relationship between severities non-alcoholic fatty liver diseases (NAFLD) with increased risk of cardiovascular disease.
Method: We consecutively selected 226 patients (group I); 115 male and 111 female for this study among the patients who came to our hospital for an annual checkup examination and a total 44 subjects (group II); 25 male and 19 female, with mild fatty liver on ultrasound in our study who were followed-up patients with metabolic syndrome. The mean age was 42y ± 8y (ranges 27y-66y) in whole group. Smoking, alcohol usage and a family history of ischemic heart disease at young age were exclusion criteria.
Results: Ultrasonographic assessment of the patients with BMI over 27 revealed Grade 1 to 3 fatty infiltration of the liver. All of these patients demonstrated a normal ECG findings and with no evidence of ischemia or arrhythmia.. However, 38 patients with initially normal ECG findings demonstrated ischemia findings on effort testing in group I and only 2 patients in group II (16.8 % vs. 4.5 % respectively and $P = 0.04$). There was no significant difference in terms of frequency of hypertension and hyperlipidemia in both groups.
Conclusion: Non-alcoholic medium or severe fatty infiltration of the liver has significant association with subclinical atherosclerosis.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1620

The relationship between simple serum natural anti oxidant levels in nonalcoholic fatty liver disease

Abdullah Emre Yildirim[1], Bugra Tolga Konduk[1], Nuh Atas[2], Reskan Altun[3], Murat Taner Gulsen[1]

Gaziantep University, Faculty of Medicine Gastroenterology Gaziantep-Turkey[1], Sehitkamil Hospital Internal Medicine Gaziantep-Turkey[2], Medicana International Hospital Gastroenterology Ankara-Turkey[3]

Aims: Nonalcoholic fatty liver disease (NAFLD), is the most common of the chronic liver diseases worldwide. Imbalance between pro-oxidant and antioxidant defense mechanisms may play an important role in the progression of NAFLD. Natural anti-oxidants such as uric acid, bilirubin, and albumin have strong anti-oxidant activities. The aim of this study is to evaluate the relationship between simple serum natural anti-oxidant levels and NAFLD.
Methods: 130 check up patients in 2014 were analyzed. Fatty liver was determined by the findings of ultrasonography. NAFLD was defined by the presence of fatty liver, after exclusion of secondary causes that leads to liver fat accumulation. Simple serum natural anti-oxidants known as uric acid, indirect bilirubin and albumin levels were measured.
Results: 80 patients with NAFLD, 50 healthy control subjects were included in this cross-sectional study. In the NAFLD group 55 % (n = 44)were female with the mean age of 46,06 ± 11,9 years, while in the control group 84 % (n = 42) of patients were female and the mean age was 44 ± 14,3 years. Serum albumin, uric acid and indirect bilirubin levels were statistically significantly higher in the NAFLD group ($P = 0{,}002$, $P < 0{,}001$, $P = 0{,}004$, respectively).
Conclusion: It may be speculated that the natural anti-oxidants known as uric acid, bilirubin, and albumin may form a natural occurring mechanism which may prevent the progression of NAFLD by correcting the imbalance between oxidant and anti-oxidant defense mechanisms in favor of antioxidants.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2082

Increased serum soluble lectin like oxidized low density lipoprotein receptor 1 levels in patients with biopsy proven nonalcoholic fatty liver disease

Oguzhan Ozturk[1], Yasar Colak[1], Ebubekir Senates[1], Yusuf Yilmaz[2], Celal Ulasoglu[1], Levent Doganay[1], Seyma Ozkanli[3], Yasemin Musteri Oltulu[4], Ender Coskunpinar[4], Ilyas Tuncer[1]

Goztepe Teaching and Research Hospital, Istanbul Medeniyet University Gastroenterology Istanbul-Turkey[1], Marmara University School of Medicine and Institute of Gastroenterology, Marmara University Gastroenterology Istanbul-Turkey[2], Goztepe Teaching and Research Hospital, Istanbul Medeniyet University Pathology Istanbul-Turkey[3], Institute of Experimental Medicine Research, Istanbul University Molecular Medicine Istanbul-Turkey[4]

Aim: Nonalcoholic fatty liver disease (NAFLD) is the most frequent chronic liver diseases. The inflammation degree and the grade of fibrosis should be determined to make a NAFLD diagnosis. In this study, we evaluated the relationship between serum lectin-like oxidized low-density lipoprotein receptor-1 (LOX-1) levels and the clinical and histopathological features of biopsy-confirmed NAFLD patients.
Methods: Fifty-three consecutive biopsy proven NAFLD patients and 26 age and gender matched healthy controls were included. The mean age was 39 ± 10.7 and 42.5 ± 9.6, mean BMI was 28.7 ± 5.1 and 31.6 ± 5.3 for controls and patients, consecutively. Serum LOX-1 levels were measured by ELISA in both patients and healthy controls.
Results: The mean serum LOX-1 level in biopsy proven NAFLD patients was 8.49 ± 6.43 ng/ml compared to 4.08 ± 4.32 ng/ml in healthy controls ($P = 0.001$). When the cut-off value for serum LOX-1 level was set at 5.35 ng/ml, and a ROC curve analysis was performed to distinguish steatohepatitis patients from controls, the sensitivity and specificity of the serum LOX-1 level were 69.8 and 69.2 %, respectively.
Conclusions: Serum LOX-1 levels were significantly higher in NAFLD patients than in healthy controls. Additionally, serum LOX-1 levels could differentiate steatohepatitis patients from healthy controls.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1936

Daily moderate coffee intake inhibits pancreatic beta cell damage and nonalcoholic steatohepatitis without improving obesity in a mouse model of spontaneous metabolic syndrome

Koichi Tsuneyama[1], Hayato Baba[1], Takeshi Nishida[1], Hideki Hatta[1], Johji Imura[1]

University of Toyama Diagnostic Pathology Toyama-Japan[1]

Metabolic syndrome is one of the most important health issues worldwide. Obesity causes insulin resistance, hyperlipidemia, diabetes, and various diseases in whole body. Its liver phenotype is called nonalcoholic steatohepatitis (NASH), which frequently progresses to hepatocellular carcinoma. We recently established a new animal model, TSOD mice, that spontaneously exhibits obesity, diabetes, hyperlipidemia, and NASH with liver nodules. We examined the effects of coffee intake on various conditions of metabolic syndrome using TSOD mice. For translation to human habits, the volume of coffee administered as daily intake was limited to appropriate quantities. To clarify the effects of specific components, we divided animals into two coffee-intake groups, with and without caffeine. Coffee intake did not significantly affect obesity and hyperlipidemia in TSOD mice. In contrast, coffee intake improved pancreatic beta-cell damage and steatohepatitis with liver carcinogenesis in various degrees. Most of the effects were considered to be caused by a synergistic effect of caffeine and other components such as polyphenols; however, the antifibrotic effects of coffee seemed to be emphasized by polyphenols, and not by caffeine. A daily habit of drinking coffee may represent a consistent prevention of metabolic syndrome.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1770

Insulin resistance but not visceral adiposity index is associated with liver fibrosis in nondiabetic subjects with nonalcoholic fatty liver disease

Cemal Nuri Ercin[1], Teoman Dogru[1], Halil Genc[2], Gurkan Celebi[1], Fatih Aslan[3], Hasan Gurel[1], Muammer Kara[4], Erdim Sertoglu[5], Serkan Tapan[5], Sait Bagci[6], Manfredi Rizzo[7], Alper Sonmez[8]

Gulhane School of Medicine Department of Gastroenterology Ankara-Turkey[1], Izmir Military Hospital Department of Gastroenterology Izmir-Turkey[2], 3katip Celebi University Department of Gastroenterology Izmir-Turkey[3], Haydarpasa Training Hospital Department of Gastroenterology Istanbul-Turkey[4], Gulhane School of Medicine Medical Biochemistry Ankara-Turkey[5], Gulhane School of Medicine Gastroenterology Ankara-Turkey[6], Palermo University Department of Clinical Medicine and Emerging Diseases Palermo-Italy[7], Gulhane School of Medicine Department of Endocrinology Ankara-[8]

Aims: Nonalcoholic fatty liver disease (NAFLD) is associated with obesity, type 2 diabetes and dyslipidemia. It is well known that the presence of visceral fat increases the risk for metabolic complications of obesity, especially NAFLD. Visceral Adiposity Index (VAI), a novel marker of visceral fat dysfunction, showed a strong association with insulin resistance and also cardiovascular and cerebrovascular events. However, there is conflicting data regarding the association between VAI and NAFLD. Our aim was to assess the relationship between VAI, insulin resistance, adipocytokines and liver histology, in nondiabetic subjects with NAFLD.
Methods: Two hundred and four patients with biopsy-proven NAFLD were included. Among this group, 101 patients whose blood samples were available, and comparable to the entire population, serum levels of adiponectin, tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6) and high-sensitive c-reactive protein (hsCRP) were measured.
Results: Higher levels of γ-glutamyltransferase, total cholesterol, triglyceride, insulin and low high-density lipoprotein cholesterol were associated with higher VAI. On the other hand, no significant association was found between VAI and adiponectin, TNF-α, IL-6 and hsCRP levels. When we compare the patients with ($n = 116$) and without ($n = 88$) fibrosis, HOMA-IR index and insulin values were significantly higher in patients with fibrosis.
Conclusions: Our findings suggest that VAI is not related to the severity of hepatic inflammation or fibrosis in nondiabetic patients with NAFLD. The lack of association between the adipocytokines and VAI also implies that the VAI may not be a significant indictor of the adipocyte functions.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1716

Obstructive sleep apnea as a risk factor of nonalcoholic fatty liver disease in non obese patients

Chan Ran You[1], Jung Whan Oh[1], Sang Haak Lee[1], Si Hyun Bae[1], Jong Young Choi[1], Seung Kew Yoon[1], Sang Wook Choi[1]

College of Medicine, The Catholic University of Korea Department of Internal Medicine Seoul-Korea, South[1]

Background: In several studies using animal models, chronic intermittent hypoxia was associated with severe liver damage in diet-induced fatty liver. The aim of this study was to investigate the relationship between OSA and NAFLD in non-obese patients.
Methods: We assessed the OSA risk using Berlin questionnaire (BQ) in 996 patients who visited health promotion center in our hospital. We excluded subjects with any other liver disease, a history of malignancy, alcohol intake $\geq$ 20 g/day and missing baseline data. We also excluded subjects with BMI $\geq$ 28 kg/m2. The total number of eligible subjects for this study was 103. NAFLD was defined as fatty liver in ultrasonographic findings and ALT $\geq$ 30 IU/L.
Results: Of all 103 subjects, 35 patients (34.0 %) were classified as high risk of OSA through the BQ. Serum ALT level was significantly higher in subjects with high risk of OSA compared to low risk of OSA (mean ALT $\pm$ SD, 30.31 $\pm$ 17.82 IU/L vs. 22.37 $\pm$ 14.48 IU/L, $P = 0.017$). The rate of fatty liver was not different between low risk of OSA and high risk of OSA (35.3 % vs. 42.9 %, $P = 0.309$). However, the rate of NAFLD was significantly higher in subjects with high risk of OSA than in subjects with low risk of OSA (31.4 % vs. 5.9 %, $P = 0.001$). BMI was at higher level in subjects with NAFLD than subjects without NAFLD (24.73 $\pm$ 2.48 kg/m2 vs. 23.41 $\pm$ 2.19 kg/m2, $P = 0.036$). High risk of OSA remained correlated with NAFLD (OR 5.9; 95 % CI, 1.615 to 21.552; $P = 0.007$) after adjusting for BMI.
Conclusions: NAFLD is associated with high risk of OSA regardless of BMI in non-obese patients.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1257

Carbohydrate and simple sugar consumption is related with non alcoholic fatty liver disease

Sang Bong Ahn[1], Byung Kwan Son[1], Yong Kyun Cho[2], Dae Won Jun[3], Eun Chul Jang[4], Se Whan Lee[5], Ki Tae Suk[6], Seung Min Lee[7]

Eulji University College of Medicine Gastroenterology Seoul-Korea, South[1], Sungkyunkwan University School of Medicine Gastroenterology Seoul-Korea, South[2], Hanyang University College of Medicine Gastroenterology Seoul-Korea, South[3], Soonchunhyang University Preventive Medicine and The Institute of Industrial Medicine Chonan-Korea, South[4], Soonchunhyang University College of Medicine Gastroenterology Chonan-Korea, South[5], Hallym University College of Medicine Gastroenterology Chuncheon-Korea, South[6], Sungshin Women's University Food and Nutrition Seoul-Korea, South[7]

Background: Fruit, vegetables, high fiber foods and reduced intakes of saturated fats may be universally recommended to NAFLD patients. But, the effect of carbohydrate and simple sugar that is main diet in Korean for the treatment of NAFLD has not been carefully evaluated. We examined the relation of carbohydrate, simple sugar and steatohepatitis by food frequency questionnaire (FFQ), laboratory findings and ultrosonography.
Methods: Five hundred and thirteen patient who take a medical examination enrolled this study. All patients do the FFQ for measuring the amount of carbohydrate and simple sugar in diet. We measured the BMI (height and weight), abdomen ultrasonography, laboratory findings. We categorize the patient according to ultrasonography findings, ALT, and amount of carbohydrate and simple sugar intake.
Results: In comparison with the lower one third carbohydrate group (<257 g/day), upper one third carbohydrate group (>307 g/day) shows increased number of elevated serum ALT patients (25.4 % to 41.9 %, $P = 0.09$). Similarly, upper one third simple sugar consumption group (> 60 g/day) have more elevated serum ALT patients compared with lower one third group (< 25 g/day) (21.4 % to 40.5 %, $P = 0.04$). A significant increase of elevated ALT group was observed in upper one third carbohydrate (OR = 0.48, $P = 0.04$) and simple sugar consumption group (OR = 0.38, $P = 0.04$). NAFLD was established by presence of ultrasonographic findings is significantly increased in upper one third carbohydrate and upper one third simple sugar group in women (OR = 0.26, $P = 0.008$).
Conclusions: NAFLD and elevated serum ALT patients is increased as more consumption of carbohydrate and simple sugar. Low carbohydrate and low simple sugar diet could improve the NAFLD.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2037

Biochemical scoring system for diagnosing non alcoholic steatohepatitis

Sheikh Mohammad Noor-e Alam[1], Ahmed Lutful Moben[2], M.a Rahim[3], Faiz Ahmad Khondaker[4], Bilkish Chowdhury[5], Mamun Al- Mahtab[6], Salimur Rahman[6]

Shahed Suhrawardy Medical College Hospital, Dhaka, Bangladesh. Hepatology Dhaka-Bangladesh[1], Shaheed Suhrawardy Medical College Hospital, Dhaka, Bangladesh Medicine Dhaka-Bangladesh[2], Mats, Noakhali Mats Noakhali-Bangladesh[3], Shaheed Suhrawardy Medical College, Dhaka Hepatology Dhaka-Bangladesh[4], Sir Salimullah Medical College & Mitford Hospital, Dhaka. Paediatrics Dhaka-Bangladesh[5], Bsmmu Hepatology Dhaka-Bangladesh[6]

Background: Nonalcoholic fatty liver disease (NAFLD) is a clinicopathological syndrome that encompasses a spectrum of conditions ranging from simple steatosis to nonalcoholic steatohepatitis (NASH), fibrosis, and end stage liver disease
Objective: To evaluate a biochemical score for diagnosing non-alcoholic steatohepatitis.
Methods: An observational, cross sectional study was carried out for a period of two years (2010–2012) in the Department of Hepatology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. Patients of Non-alcoholic fatty liver disease (NAFLD) attending at outpatient and inpatient department of Hepatology were selected as case. Biochemical parameters of 43 patients were analyzed.
Results: In our study we evaluated a biochemical score (TAAG score) assigned 1 point for each parameter (fasting serum triglyceride > ULN, alanine aminotransferase > ULN, AST/ALT ratio (AAR) ≤ 1 and gamma-glutamyl transferase > ULN). TAAG score ≥ 3 was present in 32.5 % of study population and 40 % of NASH patients. It had a sensitivity of 40 %, specificity 26 % and AUROC 0.54.
Conclusion: Biochemical scoring system comprising traditional biomarkers did not significantly predict NASH. Biopsy is the only way to estimate steatohepatitis and/or fibrosis.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1613

Age dependant counter impact of fat reducing agents on renal function test of diet induced non alcoholic fatty liver disease in *Rattus norvegicus*

Afshan Syed[1], Nadeem Sheikh[1]

University of The Punjab Zoology Lahore-Pakistan[1]

The aim behind the current study was to scrutinize the impact of fat reducing agents on Fat rich diet (FRD) induced non alcoholic fatty liver disease (NAFLD) linked renal function test of different age groups. Two groups of *Rattus norvegicus*, Adult (200 g) and Weaning (30 g) were subdivided into four groups (n = 10) depending upon the different diet compositions, designated as 0 (negative control), I (positive control), II and III (experimental). Group 0 was fed on diet "A" (100 % rat chow), group I received fat rich diet (FRD) "B" (34 % Rat chow + 33 % Sucrose + 20 % commercially available tea whitener + 13 % water), and group II received diet "C" (1000 g diet "B" + 50 g N. sativa seeds and group III was fed on diet "D" (1000 g diet "B" + 50 g P. ovata husks. After 16 weeks the blood samples were analyzed on biochemical basis. The assessment of renal function test (RFT) demonstrated significant elevation in serum creatinine ($P = 0.0001$), urea ($P = 0.0014$) and uric acid ($P = 0.0276$) in adult groups fed on FRD only. P. ovata husk and N. sativa seeds lowered the serum creatinine and urea below normal levels. However changes were found not to be significant in the groups of weaning rats. Conclusively, it can be said that NAFLD, and fat reducing agents have variant impact on the serum levels of creatinine, urea and uric acids of the adult rats only.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1003

MK 0626 a selective dpp 4 inhibior ameliolates hepatic steatosis in OB OB mice

Tatsuya Ohyama[1], Ken Sato[1], Yuichi Yamazaki[1], Norio Horiguchi[1], Satoru Kakizaki[1], Masanobu Yamada[1]

Gunma University Graduate School of Medicine and Molecular Science Maebashi-Japan[1]

Background: Previous studies showed that inhibition of DPP-4 prevents hepatic steatosis in animal models. However, the mechanisms of the DPP-4 inhibitor on hepatic steatosis have not been fully elucidated. MK-0626 is a potent, orally active DPP-4 inhibitor with excellent selectivity, oral bioavailability in preclinical species and in vivo efficacy in animal models. Our study goal was to investigate the in vivo effects and its mechanisms of a DPP-4 inhibitor, MK-0626 on hepatic steatosis using ob/ob mice.
Methods: Obese male (ob/ob) 6-week-old mice and their lean littermates were randomly divided into four groups including lean mice group, MK-0626-untreated ob/ob mice group, and two MK-0626-treated ob/ob mice groups at 1.5 mg/kg and 3 mg/kg respectively. We fed an experimental diet to all mice ($n = 16$ per treatment group) for either four or eight weeks. Then, their sera and livers were collected.
Results: Administration of dietary MK-0626 at the level of 1.5 mg/kg and 3 mg/kg ameliorated the hepatic lipid accumulation in ob/ob mice. MK-0626 treatment reduced serum ALT and glucose, insulin levels and calculated HOMA scores in ob/ob mice in a dose-dependent manner. MK-0626 treatment significantly increased the expressions of PPAR-α and MTP mRNA but significantly reduced SREBP-1c, FAS and SCD in ob/ob mice. MK-0626 treatment significantly increased the activity of AMPK in ob/ob mice(both treatment groups).
Conclusions: Our results suggested that DPP4 inhibition could attenuate hepatic steatosis because of the enhancement of AMPK activity and inhibition of hepatic lipogenic gene expression, and the enhancement of triglyceride secretion fatty liver increasing serum adiponectin levels.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1076

Relationship between insulin resistance non alcoholic fatty liver disease and colorectal carcinoma

Sebahat Basyigit[1], Ayse Kefeli[2], Bora Aktas[1], Abdullah Ozgur Yeniova[3], Metin Uzman[1], Gulcin Simsek[4], Yasar Nazligul[1]

Kecioren Research and Training Hospital Gastroenterology Ankara-Turkey[1], Siirt State Hospital Gastroenterology Siirt-Turkey[2], Samsun State Hospital Gastroenterology Samsun-Turkey[3], Kecioren Research and Training Hospital Pathology Ankara-Turkey[4]

Aim: Colorectal carcinoma (CRC) and non-alcoholic liver disease (NAFLD) share common risk factors. Insulin resistance has an important role in both disease. High prevalence of CRC and adenoma have been shown in patients with NAFLD. It is unclear whether NAFLD is a risk factor for colorectal neoplastic lesions or this association was an only a coexistence because of the same risk factors. We aimed to assess the risk for CRC in patients with NAFLD in relation to IR.
Method: This study was performed cross-sectionally. Asymptomatic individuals without history of chronic liver disease who underwent screening colonoscopy were included. We determined NAFLD by ultrasonography and measured IR by the homeostatic model of assessment-insulin resistance model. Participants were analysed for risk and prevalence of CRC and adenoma according to NAFLD and IR presence.
Results: The prevalences of CRC and adenoma were showed that significantly higher in individuals in patients with IR (respectively; p: 0.005, p: 0.008). But prevalence of CRC was found significantly lower in subjects with NAFLD negative (p: 0.001). In multivariate logistic regression analysis, the risks of colorectal adenoma and carcinoma were significantly associated with IR positivity (respectively; OR: 4,238, p: 0.003 and OR: 6,523, p: 0.001The risk of CRC was significantly associated with NAFLD negativity (OR: 7,280, p: 0.010). IR positivity with NAFLD negativity was associated with significantly high risk for carcinoma (OR: 7,218, p: 0,017).
Conclusion: The risk of CRC increase IR positive but NAFLD negative subjects.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2201

The roles of interleukin 6 and interleukin 8 gene polymorphisms in the non alcoholic steatohepatitis

Mustafa Cengiz[1], Demet Yaşar[2], Mehmet Ali Ergün[3], Gülen Akyol[4], Seren Özenirler[5]

Dr. A.Y. Ankara Oncology Training and Research Hospital Gastroenterology Ankara-Turkey[1], Gazi University Faculty of Medicine Internal Medicine Ankara-Turkey[2], Gazi University Faculty of Medicine Genetics Ankara-Turkey[3], Gazi University Faculty of Medicine Pathology Ankara-Turkey[4], Gazi University Faculty of Medicine Gastroenterology Ankara-Turkey[5]

Background and aim: Genetic polymorphisms may play role in the pathophysiology of non-alcoholic steatohepatitis (NASH). We purposed to assess the roles of interleukin 6 (IL 6) and interleukin 8 (IL 8) gene polymorphisms in the pathogenesis of NASH.
Patients and methods: Consecutive patients with biopsy proven NASH and age- and sex matched healthy individuals with normal liver function tests and normal ultrasonography were enrolled in the study. Histopathological findings were recorded according to non-alcoholic fatty liver disease activity score (NAS). Patients were classified according to fibrosis scores as fibrosis score < 2 (mild fibrosis group) and fibrosis score ≥ 2 (significant fibrosis group). Blood samples were collected and genomic DNA isolation kit was used to evaluate genetic polymorphisms.
Results: Consecutive thirty eight patients 27/38 (71 %) in mild fibrosis group and 11/38 (29 %) in significant fibrosis grup and 38 age- and sex matched healthy controls were enrolled in the study. The frequencies of the genotypes G/C and G/G of IL 6 among the NASH group and healthy controls were 39.5 % and G/G 60.5 % vs. 53.6 % and 46.4 %, respectively and ($P = 0.32$). The frequencies of the genotypes of IL 8 among the NASH group were 47.2, 44.6, and 8.2 % for T/T, A/T, and A/A, and in healthy controls, they were 50, 28.6 and 21.4 %, respectively, ($P = 0.568$). IL 8 gene T/A and T/T genotypes were not significant statistically ($P > 0.05$). However, the frequency of A/A genotype in significant fibrosis group was higher than in the mild fibrosis group ($P = 0.0016$). The differences of -251 A/T polymorphism in the IL 8 and -174 C/G polymorphism in the IL 6 were not statistically significant between fibrosis groups ($P > 0.05$).

Conclusion: IL 6 and IL 8 gene polymorphisms have no role in NASH pathogenesis and liver fibrosis process, but the presence of the A/A genotype in the IL 8 gene is associated with disease progression.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1105

Short term low dose thiazolidinediones can be a useful bridging therapy in nash patients without side effects

Sang Hoon Park[1], Myung Seok Lee[1], In Ho Moh[1], Su Rin Shin[1]

Hallym University College of Medicine Department of Internal Medicine Seoul-Korea, South[1]

Background and aims: Thiazolidinediones (TZDs) improve insulin resistance and have shown effect in the treatment of NASH. However, only low-dose TZDs are available in non-diabetic patients in South Korea due to national health insurance reimbursement policy. Meanwhile, administration of low-dose TZDs can be used more safely while TZDs have adverse effects such as edema, fatigue, and weight gain. We assessed the effect of low-dose TZDs in non-diabetic NASH patients.
Methods: We conducted a prospective study of biopsy proven NASH patients without diabetes from 2003 through 2013. Patients were treated with low-dose TZDs (rosiglitazone 4 mg or pioglitazone 15 mg, once daily) for 12 weeks. AST, ALT, ALP, total protein, albumin, total cholesterol, triglyceride, fasting blood glucose (FBS), body mass index, and HOMA-IR were measured at baseline and after 12 weeks. Data were compared with Wilcoxon Signed Rank Test.
Results: Twenty-eight patients were enrolled. Ten cases were female with a mean age of 36.3 ± 13.7 years. After 12 weeks, a significant decrease in AST (71.1 ± 42.8 to 37.3 ± 16.9, $P < 0.01$), ALT (121.7 ± 60.1 to 59.8 ± 34.1, $P < 0.01$), FBS (104.2 ± 28.1 to 97.9 ± 15.3, $P = 0.013$) and HOMA-IR (2.3 ± 1.5 to 1.9 ± 1.1, $P = 0.039$) levels was observed without weight gain or other side effects. TZDs did not affect plasma ALP, total protein, albumin, total cholesterol, and triglyceride.
Conclusions: Twelve weeks administration of low-dose TZDs in non-diabetic NASH patients showed beneficial effects on liver function without side effects. Low-dose TZDs can be used as a useful bridging therapy while weight loss by dietary control and exercise takes time to be effective.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1354

Interaction between hepatocytes and hepatic stellate cells as a crucial factor during fibrogenesis in a nash in vitro model

Pablo J. Giraudi[1], Varenka J. Barbero Becerra[2], Veronica Marin[1], Norberto C. Chavez-tapia[3], Claudio Tiribelli[1], Natalia Rosso[1]

Fondazione Italiana Fegato Centro Studi Fegato Trieste-Italy[1], Medica Sur Clinic & Foundation Medica Sur Mexico-Mexico[2], Medica Sur Clinic & Foundation Obesity and Digestive Diseases Unit Mexico-Mexico[3]

Activation of hepatic stellate cells (HSC) and dysregulation of several mediators such as matrix metalloproteinases (MMPs) and their inhibitors (TIMPs) play a determinant role during fibrogenesis in the progression from NAFLD to NASH. This study was aimed to establish the interplay between hepatocytes and HSC in an in vitro cell model of NASH.

The effect of free fatty acids (FFA) (Oleic: Palmitic, 2: 1) was analyzed at short (24 h) and long (96 h) exposure in different experimental set-ups: 1) Monoculture of each cell type; 2) Transwell system (soluble mediators effects) and 3) simultaneous co-culture (SCC) by seeding both cell types together (cell-to-cell interaction). In each system was assessed the amount of steatosis; expression of HSC activation marker (α-SMA), extracellular matrix turnover regulators (MMP-2 and TIMP-2) as well as collagen biosynthesis and compared vs untreated cells (ctrl).

The amount of steatosis was comparable among all the experimental set-ups. However, HSC activation in terms of α-SMA was only increased in the SCC (2.20 ± 0.25-folds, 1.70 ± 0.20-folds, gene and protein expression respectively; $P < 0.01$) and was maximal after 24 h of FFA exposure. Similarly, the close contact of the two cell types induced an up-regulation of TIMP2 protein (1.42 ± 0.27-folds; $P < 0.05$) which was inversely correlated both with MMP-2 protein (0.58 ± 0.10-folds; $P < 0.01$) and gelatinolytic activity (0.70 ± 0.13-folds; $P < 0.05$). This dysregulation was accompanied by an increase of collagen biosynthesis at longer FFA exposure times (1.50 ± 0.10-folds, $P < 0.01$). Any of these effects was directly induced by FFA (monoculture) nor by the soluble mediators (transwell). Our data suggest that hepatocytes-to-HSC interaction is essential for fibrogenesis.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1591

A novel 2 step approach combining the nafld fibrosis score and liver stiffness measurement for predicting advanced fibrosis

Wah Kheong Chan[1], Nik Raihan Nik Mustapha[2], Sanjiv Mahadeva[1]

University of Malaya Department of Medicine Kuala Lumpur-Malaysia[1], Hospital Alor Setar Department of Pathology Alor Setar-Malaysia[2]

Background: The non-alcoholic fatty liver disease (NAFLD) fibrosis score (NFS) is indeterminate in a proportion of NAFLD patients. Combining the NFS with liver stiffness measurement (LSM) may improve the prediction of advanced fibrosis. We aim to evaluate the accuracy of NFS and LSM in predicting advanced fibrosis in NAFLD patients.
Methods: The NFS was calculated and LSM obtained for consecutive adult NAFLD patients scheduled for liver biopsy. The accuracy of predicting advanced fibrosis using either modality and in combination were assessed. An algorithm combining the NFS and LSM was developed from a training cohort and subsequently tested in a validation cohort (Figure 1).
Results: There were 101 and 46 patients in the training and validation cohort, respectively. In the training cohort, the percentages of misclassifications using the NFS alone, LSM alone, LSM alone (with grey zone), both tests for all patients and a 2-step approach using LSM only for patients with indeterminate and high NFS were 7.1, 30.7, 2.0, 2.0 and 4.0 %, respectively. The percentages of patients requiring liver biopsy were 30.7, 0, 36.6, 36.6 and 18.8 %, respectively. In the validation cohort, the percentages of misclassifications were 8.7, 28.3, 2.2, 2.2 and 8.7 %, respectively. The percentages of patients requiring liver biopsy were 28.3, 0, 41.3, 43.5 and 19.6 %, respectively.

Conclusions: The novel 2-step approach reduced the number of patients requiring liver biopsy whilst maintaining the accuracy to predict advanced fibrosis. The combination of NFS and LSM for all patients provided no advantage over using either of the tests alone.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1719

Association of cardiovascular disease risk and steatosis severity in non alcoholic fatty liver disease

Mehmet Celikbilek[1], Mustafa Kozan[2], Yurdanur Akyuz[3], Savas Sarıkaya[4]

Bozok University Gastroenterology Yozgat-Turkey[1], Bozok University Internal Medicine Yozgat-Turkey[2], Bozok University Radiology Yozgat-Turkey[3], Bozok University Cardiology Yozgat-Turkey[4]

Objective: Heart ectopic fat accumulation leads to increased cardiovascular disease risk. Carotid intima-media thickness (CIMT) is considered as an indicator of cardiovascular disease risk and atherosclerosis. In our study, we investigated the relation with the severity of steatosis, epicardial adipose tissue (EAT) thickness and CIMT in patients with non-alcoholic fatty liver disease (NAFLD).
Material and method: EAT thickness and CIMT was measured in sixty-three patients diagnosed as NAFLD by abdominal ultrasonography (USG). The demographic and laboratory data of all patients were evaluated. Patients were divided into 2 groups according to the severity of steatosis in USG. Patients with grade 1 steatosis detected on USG was classified as mild steatosis, Patients with grade 2-3 steatosis detected on USG was classified as severe steatosis.
Results: Characteristics of patients according to the severity of steatosis were given in Table 1. EAT thickness was found to be higher in patients with severe steatosis. ($p < 0,05$). CIMT was also significantly higher in the severe steatosis group ($p < 0,05$).
Conclusion: Our study showed that hepatic steatosis severity detected by USG is associated with EAT thickness and CIMT. Advanced stages of hepatic steatosis in patients with NAFLD should aware physicians in terms of cardiovascular disease risk.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1161

The role of genetic variability of pnpla3 (rs738409) on histological progression of non alcoholic fatty liver disease

Ramazan Idilman[1], Onur Keskin[1], Senem Karataylı[1], Gokhan Kabacam[1], Ali Tuzun[1], Berna Savaş[2], Atila Elhan[3], Mithat Bozdayı[1]

Ankara University Gastroenterology Ankara-Turkey[1], Ankara University Pathology Ankara-Turkey[2], Ankara University Biostatistics Ankara-Turkey[3]

Background and aims: The aims of the present study were to investigate the role of genetic variability of the patatin-like phospholipase domain-containing 3 (PNPLA3, rs738409) on predisposition to non-alcoholic fatty liver disease (NAFLD), disease severity, and the natural course of the disease through longitudinal liver biopsy assessments.
Methods: This cohort consisted of a total of 325 individuals, including 174 patients with biopsy-proven NAFLD and 151 healthy controls were genotyped for the PNPLA3. DNA was extracted from peripheral blood, and the rs738409 C > G single nucleotide polymorphism was assessed by PCR-DNA sequencing.
Results: The frequency distribution of the GG genotype of the PNPLA3 was significantly higher in NAFLD patients than in healthy controls ($P = 0.01$). In patients with NAFLD, the GG genotype was associated with lower platelet counts ($P = 0.001$) and the presence of steatohepatitis ($P = 0.048$) and hepatic fibrosis ($P = 0.016$). After adjustment for age, gender, obesity, and diabetes mellitus, the GG genotype was an independent predictor of advanced hepatic fibrosis (adjusted odds ratio = 3.031 $P = 0.012$).

Fifty-one patients had sequential liver biopsies. The median interval between the two biopsies was 44 months. From the baseline to sequential liver biopsies, the progression of NAS in NAFLD patients slightly higher in GG genotype than that of CC and GG genotypes ($P = 0.180$). However, progression of fibrosis in such patients did not differ in each genotype ($p > 0.05$).
Conclusion: The GG genotype of the PNPLA3 gene predisposes to steatosis in the NAFLD patient cohort. The GG genotype is a predictor of disease severity but a lack association with disease progression.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1717

Efficacy and safety of vildagliptin for the treatment of type 2 diabetes mellitus with nonalcoholic fatty liver disease

Mehmet Celikbilek[1], Ahmet Aktas[2], Elif Borekci[2], Tugba Ozdemir[2], Murat Suher[3]

Bozok University Gastroenterology Yozgat-Turkey[1], Bozok University Internal Medicine Yozgat-Turkey[2], Bozok University Endocrinology Yozgat-Turkey[3]

Aim: It is known that dipeptidyl peptidase-4 inhibitors were useful for the treatment of type 2 diabetes mellitus (DM). However, effects of these drugs on liver function and glucose metabolism in nonalcoholic fatty liver disease (NAFLD) have not been determined. The aim of this study was to evaluate the affect of vildagliptin on liver functions and hepatic steatosis and also to evaluate efficacy and safety of vildagliptin in NAFLD patients with type 2 DM.
Method: We included 19 patients with Type 2 DM whom were newly started vildagliptin treatment and diagnosed as NAFLD by ultrasonography. Patients AST, ALT, GGT, ALP, HbA1c, Fatty Liver Index (FLI), Hepatic Steatosis Index (HSI), Body Mass Index (BMI), APRI Score, waist circumference and demographic characteristics were recorded before treatment and the first month of the treatment. Vildaliptin treatment was given 100 mg per day.
Results: Characteristics of patients were given in Table 1. In our study 8 patients were male (42.1 %), 11 patients were female (57,9 %). There were no significant difference between patients AST, ALT, GGT, ALP, FLI, BMI, HSI, waist circumference, APRI score before treatment and the first month of the treatment ($p > 0.05$). We found a significant difference between HbA1c levels before treatment 9,1(8,2-12,1) and the first month of the treatment 8,3(7,8-9,6)($p < 0.05$).
Discussion: Our preliminary study results showed that vildagliptin treatment have favorable effect on blood sugar regulation in NAFLD patients with Type 2 DM. We could not found any effect on the liver functions and steatosis severity with one month vildagliptin treatment.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1297

Laennec® derived from human placenta improves type 2 diabetes complicating with Nash through normalizing iron metabolism by the action of hepcidin

Yuki Hamada[1]

Hamada Clinic Hepatology Sapporo-Japan[1]

Aims: The expression of hepcidin in pancreatic β-cells is regulated by iron, which means the pancreas may contribute to the regulation of glucose level in relation with the iron metabolism. In many NASH cases complicating with type 2 diabetes, remarkable declines of serum ferritin and HbA1c were observed after treating with Laennec® (derived from placenta). Then, we examined whether Laennec® could restore the pathological background of type2 diabetes through regulating iron metabolism in NASH cases.
Methods: We divided 56 NASHcases (all cases liver biopsied) into two groups retrospectively. Laennec®-treated 28cases were treated with the infusion of 2 ampules (224 mg) of Laennec® 1-2times/W, in addition to the ordinary liver supporting. Serum ferritin, ALT and HbA1c were measured, and liver re-biopsy was carried out to evaluate changes of iron deposition in 7 cases of each group respectively.
Results: By infusing Laennec®,serum ferritin level declined from 276.7 ± 321.5 ng/ml (before medication) to 56.2 ± 48.3(after)(Wilcoxon $P < 0.01$) in NASH patients. Serum ALT also declined from 53.2 ± 20.2U/L to 25.9 ± 16.1($P < 0.001$). HbA1c level improved from6.2 ± 1.1 % to5.6 ± 0.7 ($P < 0.01$). In Non-Laennec® -treated 28cases, all of these parameters also changed significantly. When compared these results in two groups, the changes observed in Laennec®-treated group were significantly larger than non-treated group(Mann–Whitney $P < 0.05$). In multiplex-logistic analysis, the improvement of iron deposition in the liver correlate significantly with the decline of serum ferritin ($P < 0.01$).
Conclusions: The improvement of type 2 diabetes complicating with NASH by the administration with Laennec® suggests the importance of iron regulation on refractory type 2 diabetes which shows the presence of hyperferritinemia.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2230

Serum levels and liver distribution of myeloperoxidase and calprotectin in Nash patients

Ercan Bicakci[1], Fatma Gerin[2], Ali Yaman[3], Goncagul Haklar[3], Cigdem Ataizi Celikel[2], Deniz Duman[1]

Marmara University Medical Faculty Gastroenterology Istanbul-Turkey[1], Marmara University Medical Faculty Pathology Istanbul-Turkey[2], Marmara University Medical Faculty Biochemistry Istanbul-Turkey[3]

Background: Inflammation and oxidative stress play crucial role in the pathogenesis of NAFLD.Hepatic neuthrophyl infiltration increases in NASH. Myeloperoxidase (MPO) and calprotectin are two of major neuthrophyl activation markers.
Aim: The study was designed to compare the serum level of MPO and calprotectin in NASH patients and healthy control. Furthermore,we also aimed to investigate if there is any correlation between the MPO and calprotectin staining cell distribution in the liver immunohistochemically and the histological activity.
Methods: Fourty eight biopsy-proven NASH patients and twenty five healthy controls were included in the study. The histological disease severity was classified according to NAFLD activity scoring system. Serum MPO and calprotectin levels measured by ELISA. MPO and calprotectin specific immunohistochemical staining was performed to the liver biopsies and those cells staining positive were counted.
Results: There was not significant difference between serum levels of MPO of NASH patients and healthy control (14,5 ± 7,5 and 16,2 ± 7,1 ng/ml, respectively, $P = 0,259$). The serum Calprotectin level of NASH patients was significantly lower than that of the control group (1044 ± 847 and 1626 ± 964 ng/ml respectively, $P = 0,005$). There was not significant difference between MPO and calprotectin staining positive cells distribution in NASH patients having definitive (NASH score ≥ 5) or borderline NASH (NASH score 3 or 4) groups ($P = 0,910$ and $P = 0,642$, respectively).
Conclusion: Our findings showed that MPO and caprotectin which are the markers of neutrophil activation have not increased in the serum of NASH patients compared to healthy controls despite the ongoing neutrophilic inflammation in liver. Furthermore, the histological severity of NASH has not correlated with the hepatic immunohistochemical staining of those markers in liver biopsies.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1324

Effect of rosuvastatin or and β carotene and dietary control on non alcoholic fatty liver (NAFLD) in rats

Olfat Hammam[1], Sayed Seif El-din[2], Naglaa El-lakkany[2], Abeer El-naggar[2], Hekma Abd El-latif[3], Afaf Ain-shoka[4], Fatma Ebeid[2]

Theodor Bilharz Research Institute Pathology Giza-Egypt[1], Theodor Bilharz Research Institute Pharmacology Giza-Egypt[2], Faculty of Pharmacy, Umm Al-qura University Pharmacology Meka-Saudi Arabia[3], Faculty of Pharmacy, Cairo University Pharmacology Cairo-Egypt[4]

This study investigates the effect of rosuvastatin (RSV) or/and β-carotene (βC) in NAFLD-induced rats.
Method: Rats were classified into 9 groups; normal (I), NAFLD-induced with high-fat diet (HFD; II), NAFLD switched to regular diet (RD; III), NAFLD-HFD or NAFLD-RD treated with RSV (IV, V), βC (VI, VII) or both RSV + βC (VIII, IX) respectively for 4 wk (weeks 13-16) and then killed to obtain serum samples and liver tissues.
Results: Liver histology, lipid profile, liver oxidative stress markers, and adipocytokines were measured. Liver sections of NAFLD-HFD rats revealed steatosis, loss of hepatic architecture, inflammation and hepatocyte vacuolation with high percentage of cell fibrosis. Serum levels of ALT, AST, ALP, GGT and lipid profile (triglycerides, cholesterol, LDL and VLDL) was significantly increased ($P < 0.05$) compared with normal group. Also, hepatic MDA level and serum NASH biomarkers; leptin, TNF-α and TGF-β1 were furthermore increased. Meanwhile, activity of hepatic SOD, content of GSH and serum HDL and adiponectin were decreased ($P < 0.05$) vs normal. These changes were to a less extent in NAFLD-RD group. Administration of RSV or βC improves almost of the previously mentioned parameters. Moreover, hepatic steatosis was decreased and inflammation markedly ameliorated with reduction of TNF-α and TGF-β1. These results were more pronounced in the groups VIII and IX vs each drug alone.

Conclusion: RSV and βC could be beneficial for the treatment and prevention of NAFLD. Combined administration of βC as supplement gave better results than using RSV alone.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1966

Nonalcoholic steatohepatitis (nash) in 2 siblings

Vedat Goral[1]

Izmir University School of Medicine Gastroenterology Izmir-Turkey[1]

Nonalcoholic steatohepatitis (NASH) is the most common chronic liver disease in the World and also in Turkey. The etiology is believed to be multifactorial with a substantial genetic component; however, the heritability of NASH is undetermined. We report two siblings (two women, 64 years old) with NASH. The female sibling was diagnosed with NASH in 1996. This two patients were initially diagnosed with cryptogenic cirrhosis and all had a long-standing history of obesity with insulin resistance. ANA, ASMA, ANTİ- LKM1, AMA, HBV, HCV, HCV markers were negative. There was no history of alcohol history, iron metabolism disease and cupper metabolism disease, chronic drug using (i.e. NSAID and others). They had chronic liver disease findings at ultrasonography and abdominal CT. Two patients had liver biopsy consistent with NASH. The following of this two patients is go on and they are clinically stable patients. In the future liver transplantation is planing for this patients. The coexistence of nonalcoholic steatohepatitis with and without cirrhosis within siblings suggests a common pathogenesis and possible genetic risk.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1091

Chronic pancreatitis linked to obesity in Tajikistan

Sayfullo Avezov[1], Giesiddin Mirojov[1], Saodat Azimova[7], Mirhoji Khuzhamurotov[7], Dilorom Ishankulova[7], Rohatillo Odinaev[7], Munira Amirkulova[7]

Institute of Gastroenterology Hepatology Dushanbe-Tajikistan[1]

Metabolic disorders arising from obesity are etiological factors of liver and pancreatic diseases. Infiltration of fat in the parenchymal organs, as well as the accumulation of inflammatory mediators in obesity, contributes to organ dysfunction.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1241

Efficacy of a Chinese herbal formula on blood lipid indicators in non alcoholic steatohepatitis rats

Yufeng Xing[1], Guangdong Tong[1], Daqiao Zhou[1], Jinsong He[1], Chunshan Wei[1]

Shenzhen Hospital of Traditional Chinese Medicine Hepatology Shenzhen-China[1]

Objective: The therapeutic effects of the traditional Chinese medicine has been confirmed in treating nonalcoholic steatohepatitis (NSAH). The study was designed to observe the effect of a Chinese herbal formula (shugan xiaozhi recipe, SGXZR) on blood lipid indicators of nonalcoholic steatohepatitis rats.
Methods: 60 rats were randomly divided into control group,hyperlipidemia model group, fenofibrate group (0.1 g kg-1 d-1), SGXZR high, medium, low doses (40 g kg-1·d-1, 20 g kg-1 d-1,10 g kg-1 d-1). Except for the control group,the other groups were given high fat diet to induce non-alcoholic steatohepatitis rats model. At the same time, the control group and hyper-lipidemia model group were given distilled water and other groups were given corresponding drug. After 8 weeks, blood lipid (cholesterol,triglyceride),free fatty acid,liver function (alanine transaminase, aspartate aminotransferase) and blood rheology were detected.
Results: Compared with the model group,the levels of indicators were obviously decreased in SGXZR high dose group,triglyceride [(1.51 ± 0.18), (2.08 ± 0.15) mmol·L-1, $P < 0.01$], cholesterol [(6.17 ± 0.23), (7.24 ± 0.45) mmol·L-1, $P < 0.01$], free fatty acid [(196.26 ± 40.24), (357.19 ± 87.65) μmol·L-1, $P < 0.01$], whole blood viscosity (low shear) [(17.7 ± 1.9), (35.2 ± 13.6) mPa·s, $P < 0.01$], plasma viscosity [(1.79 ± 0.06), (1.92 ± 0.04) mPa·s, $P < 0.01$], red blood cell aggregation index [(7.5 ± 0.7), (11.9 ± 2.4), $P < 0.01$], alanine transaminase [(54.21 ± 9.42), (78.32 ± 17.67)U·L-1, $P < 0.01$] and aspartate aminotransferase [(49.24 ± 8.51), (67.49 ± 10.23)U·L-1, $P < 0.01$].
Conclusion: SGXZR has the effect of lowering blood lipid levels,protecting liver and diminishing enzymes in non-alcoholic steatohepatitis rats. This finding can provide a basis for the evaluation of TCM treatment effect in NASH.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2045

Alleviation of early liver fibrosis in mcd diet induced non alcoholic steatohepatitis by jiang zhi granule

Yang Liu[1], Haiyan Song[1], Xiangbing Shu[1], Hanchen Xu[1], Guang Ji[1]

Institute of Digestive Diseases Longhua Hospital, Shanghai University of Traditional Chinese Medicine Shanghai-China[1]

Background: Non-alcoholic steatohepatitis (NASH), belonging to Non-alcoholic fatty liver disease (NAFLD), is characterized by steatosis, inflammation and ballooning with or without fibrosis in liver. Part of NASH patients progress from liver fibrosis to cirrhosis which are difficult to reverse. Jiang Zhi granule (JZ), is used for promoting symptom of NAFLD patient in China. Previous animal experiments confirmed JZ could reduce liver fat accumulation and serum transaminases in NAFLD. This study aims to study the effect of JZ on liver fibrosis in NASH mice.
Methods: C57BL/6 mice were randomly divided into control, MCD and JZ group. The control mice were fed with a standard diet, while the other with Methionine and Choline deficient (MCD) diet. Simultaneously JZ mice were intragastrically treated with JZ. After 6 weeks, the mice were sacrificed. Liver tissues were stained with Sirius red. The level of serum PAI-1 was assessed by ELISA. Hepatic levels of PAI-1, TGF-β1, α-SMA, COL1A1 were measured by quantitative RT-PCR and/or Western blot.
Results: Liver of MCD group showed increased sinusoidal deposition of collagen, which were improved by JZ. JZ also reversed serum PAI-1 level which was significantly increased in MCD group. In addition,

MCD group expressed higher level of PAI-1, α-SAM, TGF-β and COL1A1, which were reduced in JZ group.
Conclusion: JZ could prevent early onset of liver fibrosis in NASH. The underlying mechanism might partially lie in inhibiting the activation of hepatic stellate cells and collagen production, as well as promoting extracellular matrix degradation, through regulating the expression of liver fibrosis-related factors in NASH pathology.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1726

High plasma levels of pentraxin 3 is associated with endothelial dysfunction in non alcoholic fatty liver disease

Halil Genc[1], Teoman Dogru[2], Gurkan Celebi[2], Cemal Nuri Ercin[2], Hasan Gurel[2], Ali Fuat Cicek[3], Erdim Sertoglu[4], Huseyin Kayadibi[5], Yildirim Karslioglu[3], Serkan Tapan[4], Sait Bagci[2]

Izmir Military Hospital Gastroenterology Izmir-Turkey[1], Gulhane Medical School Gastroenterology Ankara-Turkey[2], Gulhane Medical School Pathology Ankara-Turkey[3], Gulhane Medical School Biochemistry Ankara-Turkey[4], Adana Military Hospital Biochemistry Adana-Turkey[5]

Background: Pentraxin-3 (PTX-3), an acute-phase protein belongs to the family of the PTXs. It has been reported that PTX-3 was significantly associated with obesity, metabolic syndrome and cardiovascular diseases (CVD). In this study, we aimed to investigate the relationship of PTX3 with circulating markers of endothelial dysfunction and atherosclerosis in subjects with in non-alcoholic fatty liver disease (NAFLD).
Methods: Seventy patients with biopsy proven NAFLD and seventy healthy controls were enrolled in the study. Plasma asymmetric dimethylarginine (ADMA), adiponectin and PTX-3 levels were determined by enzyme-linked immunosorbent assay (ELISA). Serum high sensitive C reactive protein (hsCRP) levels were measured with immunoturbidimetric assay. Insulin resistance was estimated by HOMA-IR index.
Results: PTX-3 and hsCRP levels were significantly higher in NAFLD group when compared to healthy controls ($P < 0.001$ for both). Adiponectin levels were significantly lower in NAFLD group ($P < 0.001$). In correlation analysis, a significant positive correlation was observed between ADMA and PTX-3 levels ($r = 0.960$, $P < 0.001$).
Conclusion: Our study demonstrated for the first time that circulating levels of PTX3 are increased in patients with NAFLD. Moreover, it is associated with endothelial dysfunction. Large prospective studies are needed to establish the independent predictive value of circulating PTX-3 for CVD endpoints.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 2042

Investigation of genomic instability in peripheral blood lymphocytes of patients with nonalcoholic steatohepatitis using chromosome breakage and micronucleus assays

S. Arikan[1], T. Gulten[1], T. Ayyildiz[2], M. Gulten[3], T. Yakut[1]

Uludağ University Faculty of Medicine Department of Medical Genetics Bursa-Turkey[1], Ondokuz Mayis University Faculty of Medicine Department of Gastroenterology Samsun-Turkey[2], Uludağ University Faculty of Medicine Department of Gastroenterology Bursa-Turkey[3]

Aim: In this study, by comparing spontaneously occurred micronuclei and chromosomal aberrations in peripheral blood lymphocytes of NASH patients with those of healthy individuals, we aimed to investigate whether genomic instability is associated with the presence of NASH and also with anthropometric measurements and laboratory findings of individuals.
Method: A total of 57 volunteers (32 NASH patients, 5 nonalcoholic fatty liver disease patients who do not meet criteria for NASH, and 20 healthy individuals) were included in the study. Whole blood lymphocyte cultures were prepared for each individual and assessed for chromosomal aberrations and micronuclei.

There was no difference between evaluated genomic instability parameters of NASH patients and healthy individuals. In NASH patients, some chromosomal aberration parameters were positively correlated with factors related to the disease such as waist circumference, glycosylated hemoglobin (HbA1c), and number of the components of metabolic syndrome. Assessments in all of the three groups (NASH patients, healthy individuals, and all of the volunteers) revealed that some chromosomal aberration parameters are more frequent in overweight or obese individuals, which indicates that genomic instability is associated with obesity. Serum alanine transaminase levels were positively correlated with chromosome type aberrations in the group of healthy individuals, and also with micronuclei in the group of all volunteers.
Conclusion: Our findings revealed that genomic instability is associated with obesity, waist circumference, number of the components of metabolic syndrome, HbA1c and alanine transaminase levels.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1195

Prevalence of hypothyroidism in nonalcoholic fatty liver disease patients in western India

Pathik Parikh[1], Prabha Sawant[1]

Lokmanya Tilak Municipal Medical College and General Hospital, Department of Gastroenterology, Mumbai-India[1]

Aim: The aim of this study was to confirm the correlation between hypothyroidism and non alcoholic fatty liver disease (NAFLD).
Methods: The patients visiting gastroenterology OPD were investigated for NAFLD. 300 controls were selected on the basis of negative ultrasound. All patients with alcohol intake greater than 20 g/d, HBsAg or Anti HCV positivity and history of liver disease were excluded. Full thyroid profile was carried out in all patients and they were classified as: Subclinical hypothyroidism (TSH > 5.5 IU/ml but < 10 IU/ml) and Overt hypothyroidism (TSH > 10 IU/ml).
Results: 800 (500 NAFLD and 300 controls) patients were studied. The mean age of NAFLD patients was 44.3 ± 3.2 and of controls was 41.6 ± 3.89 respectively ($p > 0.05$). Female to male ratio of NAFLD patients was 1.8: 1 and of controls was 1.94: 1 respectively ($p > 0.05$). Hypothyroidism was significantly more common in NAFLD patients as compared to controls. 84 patients were detected to have hypothyroidism in NAFLD group compared to only 4 patients in control group ($P < 0.001$). Mean ALT (55 vs 21 IU), AST (44 vs 18 IU) and BMI (29.17 vs 25.14 kg/m2) were significantly higher in NAFLD hypothyroid group compared to Non hypothyroid NAFLD. Multivariate regression analysis showed that NAFLD was statistically significantly associated with hypothyroidism [odds ratio (OR) 14.94,

95 % confidence interval (CI), 3.5 to 62.6]. Steatohepatitis was more common in hypothyroid as compared to non hypothyroid group. [OR 3.9, 1.2 to 11.1 (95 % CI)].
Conclusion: The prevalence of hypothyroidism in NAFLD is 16.8 %. Hypothyroidism is closely associated with NAFLD independently of known metabolic risk factors, confirming a significant clinical relationship between these two diseases.

Topic 21: Non Alcoholic Fatty Liver Disease

No: 1287

Expression of abc transporter bile salt export pump is inversely correlated with nafld activity score in the liver of patients with non alcoholic fatty liver disease

Kazuya Okushin[1], Takeya Tsutsumi[2], Kenichiro Enooku[1], Hidetaka Fujinaga[1], Kyoji Moriya[1], Hiroshi Yotsuyanagi[2], Kazuhiko Koike[1]

The University of Tokyo Gastroenterology Tokyo-Japan[1], The University of Tokyo Infectious Diseases Tokyo-Japan[2]

Background and aims: Non-alcoholic fatty liver disease (NAFLD) is increasing in the world including Asian countries. NAFLD includes a disease spectrum ranging from simple steatosis to nonalcoholic steatohepatitis (NASH). The latter is considered as a progressive disease and its pathogenesis remains largely unclear. Recently, bile acid (BA) metabolism is focused as a therapeutic target of NASH. The aim of this study was to identify changes of bile acid metabolism in NAFLD patients in terms of disease progression.
Methods: Thirty-five male patients histologically diagnosed as NAFLD by Matteoni classification were analyzed. Patients taking UDCA were excluded in this study. Disease progression was estimated by NAFLD activity score (NAS). Intrahepatic expression levels of genes related to BA metabolism were determined by quantitative PCR.
Results: FXR, the nuclear receptor for BA, and its downstream transcriptional repressor SHP mRNA levels were not significantly changed. Key enzymes of BA synthesis (CYP7A1 and CYP27A1) and transcripts of a BA uptake transporter, NTCP, were also similarly expressed. However, expressions of an export transporter, bile salt export pump (BSEP), and MRP2 were significantly down-regulated with the elevation of NAS ($P = 0.0018$ and $P = 0.007$). Furthermore, the BSEP expression had an inverse correlation with the severity of each component of NAS (steatosis, lobular inflammation and ballooning).
Conclusions: BSEP expression is significantly down-regulated in patients with high NAS. The down-regulation of BSEP may cause the excess of BA in hepatocyte and excessive BA may induce hepatocellular injuries. The mechanism of down-regulation of BSEP remains to be elucidated, but this finding might lead to a therapeutic option for NASH.

Topic 22: Other Liver Tumors

No: 1587

An unusual case with hepatic fasciolasis mimicking liver metastases

Burçak Evren Taşdoğan[1], Nevin Akçaer Öztürk[1], Banu Kara[1]

Numune Research and Training Hospital Gastroenterology Adana-Turkey[1]

Hepatobiliary fasciolasis is a frequent parasitic infection in undeveloped and developing countries. We would like to present a case referred to our hospital for the detection of primary site for liver metastases who was diagnosed as hepatic fasciolasis.

A sixty seven-year-old female patient attended to another hospital with abdominal pain localized at upper abdomen ongoing for 3 recent months. In the upper abdominal ultrasonography, widespread multiple liver lesions consistent with liver metastases were found and the patient was referred to our hospital for detailed examination. She had no past surgery and systemic disease history. At physical examination, abdominal tenderness was detected. Laboratory tests revealed leukocytosis with predominant eosinophilia (72 %) and CRP elevation (2.1 mg/dl, normal range: 0-0.5). Liver functioning tests were all in the normal limits. The dynamic liver tomography showed predominantly subcapsuler liver lesions localized widespread at both lobes of the liver with uncertain margins and tendency to link each other. With these results, the patient was diagnosed as hepatic fasciolasis both clinically and radiologically and triclabendasole treatment was started. In her follow-up examinations, abdominal pain and liver lesions regressed, eosinophilia decreased (17 %) and CRP level was normalised.

Especially in countries where parasitic infections are frequently seen, as in our region, hepatobiliary fasciolasis must recur to the mind for the diagnosis of the patients presenting with abdominal pain, eosinophilia and liver lesions.

Topic 22: Other Liver Tumors

No: 1234

Six cases of hepatic epithelioid hemangioendothelioma

Wanyu Li[1], Yanjun Cai[1], Yue Qi[1], Na Wu[1]

The First Hospital of Jilin University Hepatology Changchun-China[1]

Hepatic epithelioid hemangioendothelioma (HEHE) is an infrequent vascular tumor of endothelial origin that primarily occurs in women in the mid-fifth decade of life without underlying chronic liver disease or cirrhosis. It is usually defined as a low- to intermediate-grade malignancy with an overall unpredictable prognosis. The aim of the present study was to summarize the characteristics of HEHE in our hospital. In total, six patients diagnosed with HEHE at the first hospital of Jilin university between 2010 and 2014. Over the past 4 years, six patients with pathologically confirmed HEHE were identified. The demographic and clinical characteristics, including treatment and outcome of these patients, are summarized in Table. The biochemical parameters of the six patients included mildly elevated alkaline phosphatase (ALP;4/6), γ glutamyl transpeptidase (GGT; 6/6), alanine transaminase (ALT;3/6) and aspartate transaminase (AST; 2/6) levels.The viral markers for hepatitis B virus (HBV) was positive only in one patient. All patients had multiple lesions in two lobes (Fig. 1). Diagnosis of HEHE was established in all six Chinese patients by core liver biopsy, according to the presence of CD34/CD31 bearing epithelioid or dendritic endothelial cells (Fig. 2). One patient received liver resection and one patient received cytotherapy. A total of five out of the six patients survived, with the survival period ranging between 4 and 28 months,excluding one patient loss of follow-up. No identifiable underlying risk factors were identified. This preliminary result merits further study in HEHE.

Topic 22: Other Liver Tumors

No: 1133

Giant intrahepatic biliary cystadenoma mimicking hepatic hydatid cyst

Volkan Öter[1], Murat Ulaş[1], Ilter Özer[1], Erdal Birol Bostancı[1]

Turkiye Yuksek Ihtisas Teaching and Research Hospital Department of Gastroenterological Surgery Ankara-Turkey[1]

Aim: Biliary cystadenomas (BCA) are rare hepatobiliary cystic tumors arising from the biliary epithelium. They are more common in middle-aged women and their most being site is the right hepatic lobe. Our aim is to report a BCA case which was confused with hepatic hydatid cyst (HHC) of the liver.
Method: A 49-year-old woman presented with complaints of coughing and abdominal pain for the last three months. She had no other symptoms and a medical history of liver disease. Her physical examination, vital signs and laboratory values were normal. A multiloculated mixed echo cystic mass of 11.7 × 11 cm in the left lobe of liver was detected in abdominal ultrasonography (US). Abdominal Computer tomography (CT) revealed a multiloculated cystic mass containing daughter vesicles which was likely to be HHC. She underwent laparotomy and partial cyst excision was performed. The histopathological examination of the cyst wall yielded a final diagnosis of BCA. The transplantation and hepatology council discussed the patient and a decision of left lobectomy was taken. The patient underwent to surgery, left lobectomy was performed. The histopathological examination for the resected specimen revealed BCA. Resection margins were tumor free. The patient was discharged on postoperative 7th day. She is doing well during consecutive follow up.
Conclusion: BCA and HHC may have similar radiological characteristics such as multilocular cyst with internal septations. When the multilocular cystic mass was detected in the liver BCA should be kept in mind.

Topic 22: Other Liver Tumors

No: 1362

Strategy of surgical treatment using microwave coagulo necrotic therapy for unresectable multiple colorectal liver metastases

Yoshiyuki Wada[1], Yuko Takami[1], Masaki Tateishi[1], Tomoki Ryu[1], Kazuhiro Mikagi[1], Hideki Saitsu[1]

National Hospital Organization Kyushu Medical Center Department of Hepato-biliary Pancreatic Surgery, Clinical Research Institute Fukuoka-Japan[1]

Background/aim: Five or more colorectal liver metastases (CRLM) are considered marginally resectable. We investigated the efficacy of surgical treatment with intraoperative microwave coagulo-necrotic ablation (MCN) and/or hepatic resection (Hr) for marginally resectable or unresectable multiple CRLM.
Patients/methods: Eighty-two of 287 consecutive CRLM patients undergoing surgery from 1994 to 2012 had > 5 CRLM and were enrolled. Presuming all CRLM were resected curatively, a preoperative virtual remnant liver volume (VRLM) < 30 % was defined as unresectable. Patients were divided into marginally resectable (VRLM > 30 %; Group Y; 29 patients) and unresectable (VRLM < 30 %; Group N; 53 patients). Clinical outcome and recurrence pattern were analyzed retrospectively.
Results: The largest tumor diameter and tumor number were 3.1 cm and 6.0 and 3.3 cm and 11.3 in Groups Y and N, respectively. Surgical methods included MCN (16 patients), MCN + Hr (9 patients), and Hr (4 patients) in Group Y, and MCN (28 patients) and MCN + Hr (25 patients) in Group N. One- and 2-year disease-free survival rates were 38.0 % and 22.8 % and 18.9 % and 3.8 % in Groups Y and N, respectively. However, the 1-, 3-, and 5-year survival rates of Group N (86.8, 44.6, and 33.7 %, respectively) were similar to those of Group Y (82.8, 51.4, and 33.3 %, respectively). Recurrence mostly occurred in remnant liver tissue (Group Y, 80.7 %; Group N, 90.3 %), and repeated hepatic surgery was performed in 12 Group Y and 21 Group N patients.
Conclusion: MCN may improve survival in unresectable multiple CRLM patients, similar to that in marginally resectable multiple CRLM patients.

Topic 22: Other Liver Tumors

No: 2136

A rare benign case which imitates liver malignity hamartoma

Ercan Korkut[1], Şükrü Arslan[1], Erdem Karadeniz[1], Nurhak Aksungur[1]

Ataturk University General Surgery Erzurum-Turkey[1]

Introduction: The CA19-9 level generally does not exceed the 1000 kU/L level in benign diseases. In this article, a case which was considered as Cholangiocellular CA due to a bulk in the liver and the high level of CA 19-9; however, which was later reported as being benign upon the pathology findings, is presented because of its being a very rare case.
Case: A 25-year-old male patient applied to our clinic with stomachache complaints. It was learned from his history that he had choledoch resection and hepaticojejunostomy surgery in a pediatric surgery clinic due to choledoch cyst 12 years ago. In the physical examination, sensitivity was detected in the epigastric area and in the left hypochondrium. The laboratory parameters of the patient were as follows: AST: 20 ALT: 20 GGT: 113 T-Bilirubin: 0.8, D-bilirubin: 0.2, and the CA19-9 level was 1368U/mL. In the perfusion CT of the patient, it was reported that there was a lesion that stretched along the intrahepatic biliary tract. The lesion was in accordance with the Cholangiocellular carcinoma, approximately 10 cm in diameter and filling the 2-3segments of the left liver lobule. Left lateral segmentectomy was applied to the patient. The intraoperative frozen was reported as being benign. The postoperative CA19-9 levels were decreased quickly at the end of the first week. The pathology result of the patient was reported as hamartoma.
Result: Bulk in the liver and high CA19-9 levels might as well be observed in the benign diseases of the liver other than the malign diseases. Hamartoma is one of the rarest ones among these benign diseases.

Topic 22: Other Liver Tumors

No: 2100

Endoscopic ultrasound guided fine needle aspiration (eus fna) for diagnosis of liver lesions

Ahmet Aydin[1], Nevin Oruc[1], Deniz Nart[2], Ali Veral[2]

Ege University Gastroenterology Izmir-Turkey[1], Ege University Pathology Izmir-Turkey[2]

Endoscopic ultrasonography (EUS) is useful tool for diagnosis of gastrointestinal lesions. Hepatology is new area of EUS applications. EUS-FNA of liver lesions is safe and effective method. Here we presented our experiences of EUS-FNA for liver lesions.
Method: We analyzed EUS reports between 2010-2014 retrospectively and EUS-FNA applications for liver lesions were recorded. There were 7 EUS-FNA applications for liver lesions.
Results: The liver lesions detected during EUS were mainly on the left liver lobe. The largest diameter of lesion were 50 mm (range 14–50 mm) and all patients had multiple lesions in liver that were suspicious for metastasis. EUS-FNA's were performed with 22G needles. The mean number of passes were 2 (2–3). Cytopathological exam revealed that there were enough material for diagnosis of lesions. Cell blog and the immuno-histochemical stain were possible in all samples. Cytopathological exam confirmed final diagnosis of squamous cell carcinoma metastasis in one, adenocarcinoma metastasis in 6 patients.
Conclusions: EUS allows to reach liver lesions that were not suitable to biopsy with other techniques percutaneously. EUS-FNA is safe and effective method to diagnose liver lesions.

Topic 22: Other Liver Tumors

No: 2088

AFP producing hepatoid type adenocarcinoma metastasis of unkown origin

Erhan Ergin[1], Nevin Oruç[2], Fatma Dilek Kaymakçı[3], Çiğdem Çelikel[3]

Manisa State Hospital Gastroenterology Department Manisa-Turkey[1], Faculty of Medicine, Ege University Gastroenterology Department Izmir-Turkey[2], Pendik Training Hospital, Marmara University Pathology Department Istanbul-Turkey[3]

Aim: Hepatoid adenocarcinoma (HAC) is specific type of extrahepatic adenocarcinoma which is morphologically very similar to hepatocellular carcinoma (HCC). Highly aggressive clinical course and poor prognosis are characteristic of this type carcinoma.
Case: 32-year-old male patient was referred to our clinic with abdominal pain that started 15 days ago. He was a carrier of hepatitis B virus and laboratory analysis showed slightly elevated transaminase levels. Bilirubin, albumin, globulin, INR levels and complete blood count was normal. AFP level was studied two times and were 60.000 and 90.000 ng/ml. Viral serology showed HBsAg (+), anti-HBs (-) antiHBc (+) Anti-HCV (-), HBV DNA 2.612 IU/ml. Thorax and abdominal CT metastatic liver lesions as well as metastatic lesions in lung and metastatic lymph nodes in mediastinum, hepatopancreatic and peripancreatic areas. Percutaneous fine needle aspiration biopsy of liver lesions revealed neoplastic cells with mild cytoplasmic CK7 and CK20 immunohistochemical stain positivity and Heppar negativity. IHC for AFP and PCEA were strongly positive in cytoplasm of neoplastic cells. Histomorphological findings and IHC findings were suggestive for diagnosis of AFP-producing hepatoid type adenocarcinoma. Since CD30 and PLAP negative germ cell tumor metastasis is not considered in differential diagnosis. Gastroscopy and colonoscopy were normal. Patient referred for chemotherapy due to AFP-producing hepatoid type adenocarcinoma metastasis of unknown origin.
Results: Here we presents a rare case with high AFP levels, without liver cirrhosis and diagnosed as AFP-producing hepatoid type adenocarcinoma metastasis of unknown origin. This patients has poor prognosis and high metastatic capacity.

Topic 22: Other Liver Tumors

No: 2212

Giant focal nodular hyperplasia in right liver lobe of a young male

Alpaslan Tanoglu[1], Kemal Oncu[1], Muammer Kara[1], Yusuf Yazgan[1]

Gata Haydarpasa Training Hospital Gastroenterology Istanbul-Turkey[1]

Background: Focal nodular hyperplasia (FNH) is a benign tumour-like mass of the liver. FNH has characteristic radiographic features but multi-modality imaging should be performed in order to diagnose atypical cases. It is most commonly seen in young to middle aged female adults, and not frequently diagnosed among young males. Here a rare case of a giant focal nodular hyperplasia, which is almost completely covering the right lobe of a young male's liver, has been reported.
Case: 23-year-old male patient was referred to our clinic because of a huge liver right lobe covering mass which was diagnosed with ultrasonography in another hospital. The patient had no complaints, moreover his personal and family history was negative. In physical examination the liver was palpable 4-5 cm below the lower edge of the ribs, the remainder of the physical checking was normal. Aspartate aminotransferase, alanine aminotransferase gamma-glutamyl transferase, alkaline phosphatase and bilirubin levels were within normal range. Viral hepatitis markers were negative and alpha fetoprotein level was also normal. Upper abdominal magnetic resonance imaging revealed a huge, approximately 18x14x11 cm diameter mass in right lobe of the liver. The mass was hypointense on T1 weighted images and minimal to mild hyperintense on T2 weighted images. At the beginning, a giant focal nodular hyperplasia was suspected, however, a liver biopsy was recommended to exclude the diagnosis of fibrolamellar hepatocellular cancer. Finally, histopathological examination of liver biopsy sample was reported as FNH.
Results: FNH masses are either found incidentally on imaging or present due to mass effect with right upper quadrant pain in 20 %. Unlike hepatic adenomas, FNH are only rarely complicated by spontaneous rupture and haemorrhage. As FNH is usually managed conservatively, accurate imaging (ultrasound, CT, MRI or nuclear medicine) is essential in preventing unnecessary intervention. In case of high clinical suspect, histopathological evaluation with biopsy samples should be performed.

Topic 22: Other Liver Tumors

No: 1230

Neuroendocrine tumor metastatic to the liver a case report

Ayşe Nur Değer[1], Filiz Özyiğit[2], Hayat Kumbasar Karaosmanoğlu[3], Berciş Imge Çoşar[4], Özlem Altuntaş[3]

Dumlupinar University Medicine Faculty Department of Pathology Kutahya-Turkey[1], Dumlupinar University Medicine Faculty Department of Pharmacology Kutahya-Turkey[2], Haseki Eğitim Ve Arş Hastanesi Department of Microbiology Istanbul-Turkey[3],

Dumlupinar University Medicine Faculty Department of General Surgery Kutahya-Turkey[4]

Neuroendocrine tumors (NETs) are a heterogeneous group of neoplasms most commonly occur in gastrointestinal system. However, lung, kidney, adrenal glands and ovaries can be the primary site for NETs. Although primary NETs are characterized by slow growth, the metastatic spread to the liver with a significantly worse prognosis is common in NETs. Surgical resection, transplantation, ablation, transarterial chemoembolization, chemotheraphy and somatostatin analogs are generally used for the treatment of hepatic metastasis in NETs.

We present here a 58 years old male patient with NET metastatic to the liver. A tumoral lesion was diagnosed in Tru-cutt liver biopsy specimen obtained from the patient with multiple mass in his liver. The tumor cells having hyperchromatic oval nuclei and eosinophilic cytoplasm were observed to form trabecular structures and solid islands. Tumor cells showed positive immunoreactivity for CD56 and synaptophysin in the immunohistochemical examination whereas only focal and weak positive staining was observed for pankeratin. No significant pathology was detected besides multiple metastatic lesions in liver according to the thorax and abdominal CT scan. Case was evaluated as a NET with liver metastatic of unknown origin. Patient was treated with chemotheraphy. We aim to enhance the awareness about the liver metastatic of NETs with relatively good prognosis.

Topic 22: Other Liver Tumors

No: 2044

A case of hepatocellular adenoma treated with percutaneous radiofrequency ablation

Ryo Shimizu[1], Nobuhito Taniki[1], Hiroko Miura[1], Ryo Kanazawa[1], Tomoyasu Ito[1], Hiroaki Saito[1], Jin Kan Sai[1], Sumio Watanabe[1], Shuichiro Shiina[1]

Juntendo University School of Medicine Gastroenterology Bunkyo-ku-Japan[1]

A 32-year-old woman. She did not have any particular medical history or medicines. She was found to have a liver tumor of 3 cm in diameter in segment 4/8 when she underwent medical checkup in November, 2010. Because CT and MRI failed to give sufficient information for the diagnosis, she underwent liver tumor biopsy which confirmed the diagnosis of hepatocellular adenoma (HA) in April, 2011. Hypervascularity of the tumor had gradually become more evident while the tumor size had not increased. Surgical resection was recommended. However, she chose radiofrequency ablation (RFA). RFA was performed using cool-tip RF needle (COVIDIEN). CT scan after RFA showed entire tumor necrosis in January, 2013. No complications related to the procedure occurred. Follow-up EOB-MRI and blood test were performed every four months. MRI showed a reduction in tumor size with no abnormal enhancement or other evidence of recurrence. HA is a rare benign tumor occurring primarily in young women. HA is associated with use of oral contraceptives, anabolic androgens, and glycogen storage disease. In women using contraceptives in long term, the estimated annual incidence is 30-40 per 1,000,000 per year while in women not using contraceptives, the estimated annual incidence is 1 per 1,000,000 per year. HA has risk of rupture and malignant transformation. Although surgical resection is a generally recommended treatment for large or symptomatic HA, RFA may be a treatment of choice in selected patients.

Topic 22: Other Liver Tumors

No: 1817

Hepatic granulomas is associated with increased risk for pancreatitis in case of brucellosis

Ahmet Cumhur Dülger[1], Mehmet Coşkun Aykaç[2], Yasemin Bayram[3], Kürşat Türkdoğan[4], Enver Aytemiz[5]

Yuzuncuyil University Faculty of Medicine Hepatology Van-Turkey[1], Yuzuncuyil University Faculty of Medicine Emergency Medicine Van-Turkey[2], Yuzuncuyil University Faculty of Medicine Microbiology Van-Turkey[3], Bezmi Alem University Faculty of Medicine Gastroenterology Istanbul-Turkey[4], Nizip State Hospital Internal Medicine Gaziantep-Turkey[5]

Aim: Liver granulomas are circumscribed lesion that forms as a result of an inflammatory reaction in hepatic tissue. Granulomas can be present in the liver in a variety of conditions including human Brucellosis. Although the granulomas themselves rarely cause structural liver damage, it is important to identify the connection systemic diseases. Brucella may rarely cause acute pancreatitis. We therefore researched the connection between Brucellosis-related acute pancreatitis and Brucellar hepatic granulomas.
Methods: 95 patients (40 female; aged 18-80 years) with acute Brucellosis were enrolled for the study. of these, 15 patients (8 female) had Brucella-related acute pancreatitis. The diagnosis of brucellosis was considered in subjects with otherwise unexplained chronic fever and nonspecific complaints. Serum agglutinin titers of $\geq$ 1: 320 were considered diagnostic of Brucella infection. Diagnosis of acute pancreatitis was also done according to Atlanta criteria. Patients with biliary pancreatitis were excluded from the study.
Results: Among 80 patients who had no pancreatitis, 10 (11.1 %) of them had liver granulomas. On the other hand, there were 6 (40 %) patients with hepatic granulomas among 15 patients with Brucella-related pancreatitis. There was a statistically significant association between Brucellar hepatic granulomas and Brucella-related pancreatitis ($P = 0.009$).
Conclusions: Our results demonstrate a unique relationship between Brucellar hepatic granulomas and Brucella-related pancreatitis. These findings suggest that Brucella-related hepatic granuloma could be an important, economically feasible strategy for detecting pancreatitis in cases with Brucellosis.

Topic 22: Other Liver Tumors

No: 1495

Sonazoid enhanced sonographically guided real time needle biopsy for focal liver lesions

Shuya Maeshima[1], Hideyuki Tamai[1], Naoki Shingaki[1], Yoshiyuki Mori[1], Junya Nuta[1], Yoshimasa Maeda[1], Kosaku Moribata[1], Yosuke Muraki[1], Hisanobu Deguchi[1], Izumi Inoue[1], Takao Maekita[1], Mikitaka Iguchi[1], Jun Kato[1], Masao Ichinose[1]

Wakayama Medical University Second Department of Internal Medicine Wakayama-Japan[1]

Background and aims: Gaseous perfluorobutane (Sonazoid) is an ultrasound contrast agent that accumulates in Kupffer cells, thus enabling not only vascular imaging, but Kupffer imaging as well. The present study aimed to assess the usefulness of Sonazoid-enhanced sonographically guided real-time needle biopsy for liver lesions from

which adequate tissue for diagnosis is difficult to sample under conventional ultrasound guidance.
Methods: Between January 2007 and July 2013, 20 patients with liver lesions underwent needle biopsy under contrast-enhanced ultrasound (CEUS) with Sonazoid. Fourteen patients with small lesions who could not be identified under conventional B-mode but who could be identified on contrast computed tomography and/or magnetic resonance imaging underwent needle biopsy during the Kupffer phase, and 6 patients with large tumors showing necrotic areas underwent biopsy during the vascular phase. Median size of lesions invisible on B-mode and tumors with necrotic areas were 11 mm and 69 mm, respectively.
Results: All small lesions that could not be identified on B-mode were able to be visualized as enhancement defects during the Kupffer phase. In all large tumors with necrotic areas, vascular areas could be biopsied during the vascular phase. Diagnostic rates for invisible tumors by B-mode and large tumors with necrotic areas were 93 % (13/14) and 100 % (6/6), respectively. of 14 lesions invisible on B-mode, 7 were malignant, 6 were benign, and 1 was a sampling error.
Conclusion: Real-time needle biopsy under CEUS with Sonazoid appears useful in the diagnosis of liver lesions invisible under conventional B-mode and large tumors with necrotic areas.

Topic 22: Other Liver Tumors

No: 1781

Radiofrequency ablation in the treatment of liver recurrent pancreatic cancer underwent pancreticoduodenectomy

Masatsugu Ishii[1], Shinpei Sato[1], Toshihiro Kawai[1], Yoko Yashima[1], Takashi Sugimoto[1], Miho Kanda[1], Yukihiro Koike[2], Hideo Yoshida[3], Takamasa Ooki[4], Shuntaro Obi[1]

Kyoundo Hospital Hepatology Tokyo-Japan[1], Kanto Central Hospital Gastrointestinal Medicine Tokyo-Japan[2], Japanese Red Cross Medical Center Gastrointestinal Medicine Tokyo-Japan[3], Mitsui Memorial Hospital Gastrointestinal Medicine Tokyo-Japan[4]

Aim: To assess the feasibility and outcome of radiofrequency ablation (RFA) in the treatment of liver recurrent pancreatic cancer underwent pancreticoduodenectomy (PD).
Background: Percutaneous ablative therapies such as RFA are effective treatment for certain metastatic liver cancers and are associated with good local control and lower mortality. However, De Jong et al. showed RFA is danger for patients who underwent PD because of high risk complications.
Method: RFA was performed in 2000 cases for liver cancer in our hospital and associated institution by 2013. We intended for 19 patients (1 %) whom RFA was performed in for liver metastases for pancreatic cancer after PD. All cases cool-tip RFA electrode was used percutaneously. Mechanical and chemical preparation was performed before RFA and preventive antibiotics was performed after RFA. We paid attention to ablate only tumor and to extend ablation time.
Result: 19 cases were performed for liver metastases after PD in 4 institutions including our hospital, survival rate was 14 %. PS0, liver metastases in patients of 5 cm or less and were the tendency that OS had better than a case only for chemotherapy for cases ten or less for the same period. Cholangitis was two cases (10.5 %) and operation death was not found with complications. Complication cases were two cases (10.5 %). MST after RFA was 14.1 months.
Conclusion: These complications rate were low rates than the complications of the existing report. It was thought to be able to be in one of choices of the treatment of the liver metastases after the pancreatoduodenectomy.

Topic 22: Other Liver Tumors

No: 1140

A case of Cholangiocellular carcinoma with elevated serum alpha fetoprotein

K. Itamoto[1], A. Shimizu[1], S. Hata[1], M. Teruya[1], M. Kaminishi[1]

Showa General Hospital Department of Surgery Kodaira, Tokyo-Japan[1]

Aim: We report a case of mass-forming type Cholangiocellular carcinoma (CCC) with elevated serum alpha-fetoprotein (AFP).
Method: A case report
Introduction: CCC is known to be associated with elevation of serum carbohydrate antigen 19-9 or Carcinoembryonic antigen level. CCC with elevated serum AFP is infrequent. Relationship between progression or recurrence and serum AFP level is not well-known.
Case presentation: A 60-year-old man was admitted because of acute aortic dissection. Computed tomogram (CT) accidentally showed low density areas in the right anterior sector of the liver. The maximum diameter was 5.5 cm. It was multilobulated, enhanced in marginal region. These findings suggested a diagnosis of CCC, but laboratory findings showed elevated serum AFP (299.4 ng/ml).
We made a preoperative diagnosis of combined hepatocellular-cholangiocarcinoma. He underwent extended right paramedian sectoriectomy. Microscopic examination showed the mass-forming Cholangiocellular carcinoma, well to poorly differentiated adenocarcinoma, with intrahepatic metastasis and portal invasion, T2bN0M0, Stage II (The UICC seventh edition TNM classification). Immunohistochemical staining was negative for AFP. After surgery, serum AFP level decreased to normal range.

Gemcitabine was given for a year as postoperative adjuvant chemotherapy. A year and five months after surgery, serum AFP increased to 42.5 ng/ml. CT revealed multiple intrahepatic recurrence.
Discussion: Although immunohistochemical staining was negative, serum AFP level decreased after surgery and increased on disease recurrence. It suggests CCC produced AFP in this case. The mechanism of AFP elevation remains unexplained.
Conclusion: In the case of CCC with elevated serum AFP, measuring serum AFP level can be valuable for detecting progression or recurrence, although immunohistochemical staining is negative for AFP.

Topic 22: Other Liver Tumors

No: 2163

Challenges in diagnosing hepatocellular adenoma a case report

Juferdy Kurniawan[1], andri Sanityoso[1], Toar J.m. Lalisang[2], Maria Mayasari[2], Ening Krisnuhoni[3], Sahat Matondang[4], Abirianty P. Araminta[5], Lutfie Lutfie[5]

Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo Hospital Department of Internal Medicine, Hepatobiliary Division Jakarta-Indonesia[1], Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo Hospital Department of Surgery, Digestive Surgery Division Jakarta-Indonesia[2], Faculty of Medicine Universitas

Indonesia, Cipto Mangunkusumo Hospital Department of Anatomic Pathology Jakarta-Indonesia[3], Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo Hospital Department of Radiology Jakarta-Indonesia[4], National Hepatopancreatobiliary Center - Jakarta-Indonesia[5]

Hepatocellular adenoma is an extremely rare benign tumor of the liver which predominantly in young women. Its rare incidence with estimated 3-4 cases per 1.000.000 annually makes it a diagnostic challenge. Here we present a series of work up tools in diagnosing hepatocellular adenoma. A 30-years old female patient presented with right upper-quadrant abdominal pain since one year prior to admission. The patient had no symptoms related to the liver mass, no history of jaundice, blood transfusions, hepatitis or excessive alcohol consumption. She appeared healthy from physical and laboratory examination with no abnormal findings. Ultrasonography was performed and found liver nodule. Liver biopsy finding suggested hepatocellular adenoma with differential diagnosis of low-grade hepatocellular carcinoma. Immunohistochemical staining showed suggestive low-grade hepatocellular carcinoma. Computed tomography found a solitary hypodense oval-shaped nodule, 5 cm in diameter, in the right lobe of liver. Additional cytological examination of cystic mass was performed and found no malignant cells. The patient underwent a segmental resection of segment V. Pathological examination of resected specimen showed hepatocellular adenoma, confirmed by immunohistochemical staining. This case illustrates the superiority of excision biopsy as the preferred diagnostic tools of hepatocellular adenoma as well as therapeutic modality to prevent malignant transformation.

Topic 22: Other Liver Tumors

No: 1233

Six cases of hepatic epIthelioid hemangioendothelioma

Wanyu Li[1], Yanjun Cai[1], Yue Qi[1], Na Wu[1]

The First Hospital of Jilin University Hepatology Changchun-China[1]

Hepatic epithelioid hemangioendothelioma (HEHE) is an infrequent vascular tumor of endothelial origin that primarily occurs in women in the mid-fifth decade of life without underlying chronic liver disease or cirrhosis. It is usually defined as a low- to intermediate-grade malignancy with an overall unpredictable prognosis. The aim of the present study was to summarize the characteristics of HEHE in our hospital. In total, six patients diagnosed with HEHE at the first hospital of Jilin university between 2010 and 2014. Over the past 4 years, six patients with pathologically confirmed HEHE were identified. The demographic and clinical characteristics, including treatment and outcome of these patients, are summarized in Table. The biochemical parameters of the six patients included mildly elevated alkaline phosphatase (ALP; 4/6), γ glutamyl transpeptidase (GGT; 6/6), alanine transaminase (ALT;3/6) and aspartate transaminase (AST; 2/6) levels. The viral markers for hepatitis B virus (HBV) was positive only in one patient. All patients had multiple lesions in two lobes (Fig. 1). Diagnosis of HEHE was established in all six Chinese patients by core liver biopsy, according to the presence of CD34/CD31 bearing epithelioid or dendritic endothelial cells (Fig. 2). One patient received liver resection and one patient received cytotherapy. A total of five out of the six patients survived, with the survival period ranging between 4 and 28 months, excluding one patient loss of follow-up. No identifiable underlying risk factors were identified. This preliminary result merits further study in HEHE.

Topic 22: Other Liver Tumors

No: 1156

A rare case of hepatobiliary mucinous cystadenoma with ovarian like stroma

Masaru Aoki[1], Tadatoshi Takayama[1], Yutaka Midorikawa[1], Akira Kanamoto[1], Shintaro Yamazaki[1], Nao Yoshida[1], Masamichi Moriguchi[1], Tokio Higaki[1], Takao Okubo[1], Hisashi Nakayama[1], Haruna Nishimaki[2], Shinobu Masuda[2], Masahiko Sugitani[2]

Nihon University, School of Medicine Digestive Surgery Tokyo-Japan[1], Nihon University, School of Medicine Pathology Tokyo-Japan[2]

Aim (background): Hepatobiliary mucinous cystadenomas are rare tumors. We here present in case of mucinous cystadenoma with ovarian-like stroma of the liver.
Method (Case): A 55-year-old woman was admitted to our hospital for suspicious of biliary cyst adenoma or cystadenocarcinoma detected complete physical medical examination. The patient had no symptom. She had no past medical history except for endometriosis. The abdominal ultrasound demonstrated a 16 × 12 cm well-defined and multi separated liver cyst. Biochemical laboratory test was unremarkable. Contrast enhanced CT scan showed a large cystic mass that compressed the left lateral hepatic lobe and septum and a dense nodule (1.6 cm) could be distinguished in the superior region. Surgery was performed and discovered a large cystic mass 16 × 10 cm belonged to the hepatic segments II. A total of 515 ml of brown, mucinous fluid was evacuated by puncturing the cystic mass. Liver resection was performed including cyst. Postoperative course was uneventful. Histological report revealed benign mucinous hepatic cystadenoma with ovarian like stroma. Hepatobiliary cystadenoma and cystadenocarcinoma constitutes less than 5 % of intrahepatic cysts originating from the bile duct. Complete resection of the Hepatobiliary cystadenoma with intact hepatic resection margin is recommended for malignant potential.
Conclusion: We presented in rare case of Hepatobiliary mucinous cystadenoma with ovarian-like stroma.

Topic 22: Other Liver Tumors

No: 1357

Spontaneous rupture of hepatic metastases from neuroendocrine carcinoma of unknown primary site

Shojiro Hata[1], Daisuke Ito[1], Atsushi Shimizu[1], Masanori Teruya[1], Michio Kaminishi[1]

Showa General Hospital Department of Surgery Tokyo-Japan[1]

Aim: To report a patient with spontaneous rupture of hepatic metastases from neuroendocrine carcinoma (NEC) of unknown primary site, who underwent transcatheter arterial embolization (TAE) followed by hepatic resection.
Method: Case report
Introduction: NEC is aggressive malignant disease and has poor prognosis because of its high incidence of metastasis. However, spontaneous hepatic rupture induced by metastatic cancer, which presented as hemoperitoneum, is not common. For patients with no history of liver diseases, such an event is too rare to warrant consideration in the differential diagnosis of patients with acute abdomen.

Case Presentation: A 31-year-old man was admitted to hospital following a sudden attack of abdominal pain. A left adrenal tumor had been detected by his medical checkup a month before, and he had planned further examination. He was diagnosed with hemoperitoneum secondary to spontaneous rupture of liver metastases by ultrasound examination and computed tomography. He underwent emergent TAE to control the haemorrhage. A right hepatectomy was performed on the third day after TAE. Pathological examination of the specimen revealed to be metastases of neuroendocrine carcinoma to the liver. Further examination detected multiple pulmonary metastases but no other primary site was detected. He was diagnosed with hepatic, pulmonary and left adrenal metastases from neuroendocrine carcinoma of unknown primary site. Postoperative course was uneventful and chemotherapy was started one month after surgery.
Conclusion: It is necessary to consider the possibility of spontaneous rupture in cases of acute abdomen, even in patients with liver metastases. In such cases, TAE followed by hepatectomy may be beneficial.

Topic 23: Other viral Hepatitis

No: 1994

Researching the hav seroprevalence of health care providers

Selma Tosun[1], Alpay Ari[1], Fatma Bal[1], Betul Ersoz[1], Gulsum Altın[1]

Izmir Bozyaka Research and Education Hospital Infectious Diseases Izmir-Turkey[1]

Aim: In recent years, a change in the epidemiology of Hepatitis A Virus (HAV) infection has been observed around the world. Similarly in our country, the age of HAV exposure is shifting into adolescence and young adult period. As compared to the other individuals, health care providers are more likely to be exposed to HAV. Thus, it would be appropriate to know the HAV exposure of health care providers and to vaccinate the ones with seronegative.
Method: The recordings regarding the HAV exposure of health care providers working at İzmir Bozyaka Education and Research Hospital have been taken from the documents of Infection Control Committee.
Results: The recordings of 1320 health care providers aged between 18 and 63 were examined. The number of persons having no HAV examination is 756. Totally 455 (81 %) of 564 health care providers having HAV examination were defined to have HAV IgG positive and 109 (19 %) of them defined to have HAV IgG negative. The distribution according to age groups are demonstrated on Table 1 and it is considerable that the number of seronegative health care providers is higher during young adulthood.
Discussion: Acute HAV infection may be more complicated as the person gets older and our country is still endemic in terms of HAV infection and the virus circulation is continuing widely. In our study, it has been determined that seronegativity in young adults is distinctively high. For this reason, it would be appropriate to examine the health care providers and vaccinate the ones with seronegativity.

Topic 23: Other viral Hepatitis

No: 1837

Aetiology and outcome of sporadic acute viral hepatitis in Bangladesh

Mohammad Izazul Hoque[1], Md. Belalul Islam[2], Abdullah Al- Faruk[3], Md. Abdul Matin[4], Mohammad Selim[5]

Comilla Medical College Hepatology Comilla-Bangladesh[1], Comilla Medical College Medicine Comilla-Bangladesh[2], Comilla Medical College Pathology Comilla-Bangladesh[3], Comilla Medical College Hospital Hepatology Comilla-Bangladesh[4], Comilla Medical College Hospital Gastroenterology Comilla-Bangladesh[5]

Background: Sporadic acute viral hepatitis (AVH) is a public health problem in Bangladesh due to poor sanitation, lack of safe drinking water, health education and vaccination against hepatitis B virus. Aims of the study was to see the aetiology and outcome of sporadic AVH.
Methods: This prospective study was done in Hepatology department of Comilla Medical College, Bangladesh during the period January 2012 to December, 2013. 302 consecutive patients of AVH were studied for their aetiology and out come. Hepatitis due to other cause were excluded from the study. Viral markers (HBsAg, Anti HBc IgM, IgM Anti HEV, IgM Anti HAV, Anti HCV) were measured by ELISA using commercial kits. Liver function tests (bilirubin, transaminases, prothrombin time) were done in all cases. Patients were followed till clinical and biochemical recovery.
Result: Among 302 patients, 233(77 %) were male and 69(23 %) were female. Median age was 27.1 years. Causes of AVH were hepatitis E virus (HEV) in 109(36 %), hepatitis B virus (HBV) in 118(39 %), hepatitis A virus (HAV) in 9(3 %), acute HEV in chronic HBV carrier in 12(4 %) patients and hepatitis C virus (HCV) in none. 54(18 %) patient were negative for all viral markers. During follow-up one patient of AVH-B and one patient of acute HEV in chronic HBV carrier died of acute liver failure. Clinical and Biochemical recovery was earlier in AVH due to HEV than HBV which is significant ($P < 0.01$).
Conclusion: HBV is the commonest cause of AVH in adults, followed by HEV. Clinical and Biochemical recovery occurs early in HEV than HBV.

Topic 23: Other viral Hepatitis

No: 1254

Hepatic involvement in Epstein barr virus and cytomegalovirus a series of 20 patients

Hüseyin Aytaç Erdem[1], Tansu Yamazhan[1], Hüsnü Pullukçu[1], Meltem Taşbakan[1], Oğuz Reşat Sipahi[1], Sercan Ulusoy[1]

Ege University Infectious Diseases Izmir-Turkey[1]

Aim: Epstein-Barr virus (EBV)and Cytomegalovirus (CMV) are the main causes of infectious mononucleosis (IM) and IM-like sendrom in humans.In this study it was aimed to evaluate the clinical characteristics and liver enzymes changes in cases with EBV and CMV infections accompanying hepatic involvement in our department
Methods: The hospital records of immune competent cases with EBV and CMV infections accompanying hepatic involvement who were followed up in our department between 2008-2014 were evaluated in terms of demographic characteristics, underlying diseases, laboratory, clinical data and treatment results retrospectively.
Results: There were a total of 20 patients (14 men, 6 female) aged 24,6 ± 7.6 (16 patients with EBV, 4 with CMV). The most common clinical symptoms were fever (19 patients 95 %), fatigue (8 patients 40 %), sore throat (7 patients 35 %), vomiting (6 patients 30 %), and swelling in the neck (5 patients 25 %). Palpable servical lymph nodes (6 patients 30 %) and hepatosplenomegaly(3 patients 15 %) were the most common physical findings. Liver enzyme values on the 1st day and an average of 10 days after (10. ± 4,5) (Range 3-20, 19 patients' liver enyzmes follow up values are on table.

In the EBV group; EBV VCA IGM was positive in all cases and EBV VCA IGG was positive in 81 % (13 patients).In the CMV group;anti CMV IgM and anti CMV IgG was positive in all cases. All patients were hospitalized for an average of 6.6 days (± 2, min: 3-max: 12) and discharged as healthy. There was no icteric hepatitis.
Conclusion: We conclude that the EBV and CMV serologic markers should be monitored as well as other hepatitis virus markers in the evaluation of cases with increased liver enzymes.

Topic 23: Other viral Hepatitis

No: 1144

Comparison of immunogenicity between inactivated and live attenuated hepatitis A vaccines among young adults a three years follow up study

Xueen Liu[1], Haiying Chen[2], Zheng Liao[2], Yisheng Zhou[2], Hairong Wen[2], Shihui Peng[2], Yan Liu[3], Jie Li[1], Hui Zhuang[1]

Peking University Health Science Center Department of Microbiology and Center of Infectious Disease, School of Basic Medical Sciences Beijing-China[1], Nanchang Center For Disease Control and Prevention Nanchang-China[2], Sinovac Biotech Co. Ltd. Beijing-China[3]

Objectives: To compare immunogenicity between an inactivated hepatitis A vaccine (Healive®) and a live attenuated vaccine in young adults.
Methods: A single-blind, randomized clinical trial was conducted among healthy adults aged 16-21 years in colleges. Subjects were randomly assigned to three groups. Two groups were administered one-dose or two-dose inactivated vaccine and the remaining group was immunized with the attenuated vaccine, respectively. Serum samples were collected at 1.5- or 7-, 12-, 24- and 36-month follow-ups. Anti-HAV IgG was measured with a microparticle enzyme immunoassay.
Results: The significant differences were observed in seroprotection rates among the three groups at 12-, 24- and 36-month, respectively ($P < 0.05$). The geometric mean concentrations (GMCs) of anti-HAV IgG were significantly higher in the two-dose Healive® group than in the one-dose Healive® and the attenuated vaccine groups at 1.5- or 7-, 12-, 24- and 36-month, respectively ($P < 0.05$). In the one-dose Healive® group, the GMCs were significantly higher than that in the attenuated vaccine group at 1.5-, 12-, 24- and 36-month, respectively ($P < 0.05$). There were no significant differences in the adverse event rates among three groups through 3-day observation post-immunization, and no serious adverse events were observed.
Conclusions: The higher seroprotection rates and GMCs of anti-HAV IgG were induced in the two-dose Healive® group than in the one-dose Healive® and the live attenuated vaccine groups, and the one-dose Healive® presented more confident immunogenicity than the live attenuated vaccine during the three years follow-up. The inactivated vaccine Healive® and the live attenuated hepatitis A vaccine were all well tolerated by the young adults.

Topic 23: Other viral Hepatitis

No: 1733

Prevalence of hepatitis A in health professionals

Mahmut Sunnetcioglu[1], Ali Irfan Baran[1], Osman Mentes[2], Mustafa Kasım Karahocagil[1]

Yuzuncu Yil University Faculty of Medicine Infectious Diseases and Van-Turkey[1], Bingol State Hospital Infectious Diseases and Bingol-Turkey[2]

Objective: Our objective in conducting this study was to determine the levels of immunization against infectious diseases like hepatitis A which can be prevented through vaccines in health professionals working in Van, creating an awareness for immunization in those people.
Material and method: This study has been conducted within the context of sectional and identifiable epidemiology in order to determine HAV IgG antibody levels in health professionals working various medical institutions in Van.
Result: A total of 276 individuals-154 males (%55,8) and 122 females- (%44,2)who were working in Van as health professionals were included in the study. The mean age of those included in the study was 28.37 ± 7.15.The age and gender distributions of those individuals who were included in the study have been shown in Table 1. 36.2 % of these individuals were nurses, 21. 4 % of them were health officials, %19.2 of them were doctors, 8 %of them were administrative staff and 15.2 % of these individuals were composed of paramedics, laborants etc.The hepatitis A IgG seroprevalence of the health professionals being involved in the study was found to be % 87.3.
Conclusion: Individuals may experience more frequent symptoms and complications in case of being infected with the hepatitis A in later stages of their lives; therefore, it would have been more beneficial to know the immunization of the health professionals in order to have a more adequate understanding of the prophylactic measures.

Topic 23: Other viral Hepatitis

No: 1058

Acoustic radiation force impulse imaging the "normal" variability between two measurements

George Sebastian Gherlan[1], Madalina Neata[1], Alma Gabriela Kosa[1], Petre Iacob Calistru[1]

"Dr. Victor Babes" Center For Diagnostics and Treatment Infectious Diseases Bucharest-Romania[1]

Background: Acoustic Radiation Force Impulse Imaging (ARFI) is a new technique used for the assessment of liver fibrosis. We aimed to establish what difference between two measurements arises from the technique itself and what difference should be considered significant in terms of improvement or aggravation of a disease.
Methods and patients: We analyzed the data of 136 patients with different liver diseases or without any known disease who underwent two consecutive sets of 10 ARFI measurements each, performed by the same experienced operator. Only measurements considered valid, with interquartile range (IQR) less than 30 % of the median value of 10 measurements were included. The cut-offs were set at 1.34 m/s for F >=2 and 2 m/s for F4.
Results: The intraclass correlation coefficient (ICC) for the two measurements was 0.975 (CI95 % = 0.965–0.982, $P < 0.001$) showing an excellent intraoperator reproducibility. We found a mean variation between two consecutive complete sets of measurements of 9.59 % with standard deviation 9.29. The disagreement between two measurements was significantly influenced by BMI ($P = 0.01$, $r = 0.320$) and not by sex, etiology or age. Based on the mentioned cut-offs, 11 patients (8.08 %) were differently classified by the two

measurements as significant/non-significant fibrosis (F >=2/F <=2) while for F4, only one patient (0.73 %) was considered cirrhotic by one measurement and non-cirrhotic by the other.

Conclusions: We found a normal variability between two liver stiffness ARFI measurements performed by the same operator of 9.59 % ± 9.29 %. Therefore, only a variation of over 18.88 % should be considered significant as a proof of a liver disease improvement or worsening.

Topic 23: Other viral Hepatitis

No: 1239

Hepatitis virus screening in Japan and it's issues to be overcome

Terumu Kaishima[1], Kazuaki Sakamune[1], Masayuki Ohisa[1], Tomoyuki Akita[1], Keiko Katayama[1], Junko Tanaka[1]

Hiroshima University Department of Epidemiology, Infectious Disease Control and Prevention Hiroshima-Japan[1]

Aim: According to the national sampling survey in 2012 by MHLW in Japan, the percentage of people, who had awareness that they underwent screening tests of hepatitis B virus (HBV) or C virus (HCV), was as low as 17.6 % for both.

We conducted a second-order analysis based on the survey and another survey to determine the status of consultation following hepatitis screening and to show the issues in the current measures against hepatitis in Japan.

Method: 1) In 2012, national random sampling survey, which was mailed to 74,000 people. 2) In 2012-2013, the survey to investigate the actual utilization of consultation, which was mailed to 5,381 people who were found to be positive by hepatitis examination.

Results: 1) A total of 23,720 responses were obtained, representing a 32.1 % return rate. When including the people who had no awareness that they underwent hepatitis screening, the overall rate of undergoing the examination of HBV and HCV in Japan was 57.4 and 48.0 %. 2) A total of 2,177 responses were obtained, representing a 40.5 % return rate. The rate of visiting medical institutions after found to be positive at HBV and HCV screening was 61.6 and 68.9 %, respectively.

Conclusion: National screening of hepatitis viruses in Japan was introduced from 2002 for the first time in the world and screened rate in Japan is almost 50 %, but not satisfied still. The present most important issue in Japan is to improve the rate of consult doctor after the screening.

Topic 23: Other viral Hepatitis

No: 1929

Hepatosplenomegaly and liver function tests of 102 brucellosis cases a retrospective experience of eight year

Serhat Uysal[1], Fatih Dana[2], Meltem Işıkgöz Taşbakan[1], Erkan Kısmalı[2], Oğuz Reşat Sipahi[1], Hüsnü Pullukçu[1], Tansu Yamazhan[1], Sercan Ulusoy[1]

Ege University Department of Infectious Diseases and Clinical Microbiology Izmir-Turkey[1], Ege University Department of Radiodiagnostic Izmir-Turkey[2]

Aim: Brucellosis is a systemic infection involving many organs including hepatic involvement. In this study, it was aimed to review all cases with the diagnosis of brucellosis followed up in our clinic.

Method: All cases followed up in our clinic between July 2006 October 2014 with brucellosis were retrospectively reviewed. The diagnosis was established via microbiological culture confirmation and/or Standard Wright agglutination test (SWAT) positivity with a titer of 1/160 or higher.

Results: There were a total of 102 cases fulfilling the inclusion criteria (43 female, 59 male, aged 47.1 ± 16). Eighty-two(80.3 %) patients had a titer of 1/160 or more SWAT positivity. Three patients had negative SWAT but were diagnosed with anti-human globulin test. Seventeen (16.7 %) patients were diagnosed with only blood culture. Main symptoms of patients were represented in table 1. Hepatomegaly and splenomegaly were determined with ultrasonography in 16 (15.,8 %) and 19 (18.8 %) cases respectively. The mean levels of Laboratory findings are represented in table 2. About 23.8 %, 24.8 %, 26.8 %, 36.6 %, 12.9 % had elevated levels of AST, ALT, ALP, GGT and T.bilirubin, respectively. Forty-two (41.2 %) patients had no pathology in the liver. Treatment regimens used are presented in table 3. Liver function tests and hepatosplenomegaly completely healed in all cases by treatment. There were no adverse drug reaction during the treatment.

Conclusion: Brucellosis primarily affects the reticuloendothelial system.But it is also a zoonotic disease that can cause liver damage. Because of the long duration of the treatment and some hepatotoxic antibiotics (such as rifampicin) should be made with caution.

Topic 23: Other viral Hepatitis

No: 2072

Complicated hydatid cyst disease of the liver evaluation of eleven cases

Serhat Uysal[1], Ayşe Uyan[2], Meltem Işıkgöz Taşbakan[2], Hüsnü Pullukçu[2], Oğuz Reşat Sipahi[2], Tansu Yamazhan[2], Ekin Ertem[2]

Ege University Department of Infectious Diseases and Clinical Microbiologdepartment of Infectious Diseases and Clinical Microbiology Izmir-Turkey[1], Ege University Department of Infectious Diseases and Clinical Microbiology Izmir-Turkey[2]

Introduction: Hydatid disease is a zoonotic infection caused by the cestode Echinococcus spp. It is transmitted by ingestion of infectious cestode eggs, especially through to dog feces. The two organs most commonly affected are the liver and the lung, respectively. In this abstract, a series of eleven cases with symptomatic and complicated liver hydatid cyst are presented.

Material and method: Eleven patients with hepatic hydatid disease treated between 2008 and 2014 were evaluated retrospectively. Demographic characteristics, symptoms (fever, abdominal pain, pruritus, weakness, icterus, cough, sputum, nausea-vomiting), signs (hepatomegaly, splenomegaly, defense, rebound, auscultation findings), radiological-laboratory findings, hepatic involvement levels, complications, involvements in other tissues and treatment modalities of the patients were recorded.

Results: Nine (81.8 %) of the patients were female. The mean age of the patients was 52.4 ± 19.6 year. All patients had cystic lesions in the liver in ultrasonography. Five patients had leukocytosis and tree patient had eosinophilia. Renal involvement was only seen in one patient. All patients received treatment with albendazole PO 2x400 mg tablets. Mean duration of treatment was 28.7 ± 21.5 weeks. Four, tree, two, one and one case were complicated with lung cyst, splenic cyst, amoebic liver abscess, spondylodiscitis and intraabdominal dissemination, respectively. All patients are summarized in table 1.

Conclusion: Hydatid cyst is an infectious disease that may affect various organs. Patients with hydatid cyst in the liver should be checked carefully regarding other system involvement, including the lung and/or spleen region.

Topic 23: Other viral Hepatitis

No: 1530

Findings from a public opinion survey on viral hepatitis B and C in Japan

B. Ellsworth[1], J. Tanaka[2], James Smith-plenderleith[3]

Janssen Pharmaceutical Kk Janssen Pharmaceutical Kk Tokyo-Japan[1], Hiroshima University Department of Epidemiology Infectious Disease Control and Prevention Hiroshima-Japan[2], Janssen Asia Pacific Pharmaceuticals Mong Kok-Hong Kong[3]

Aim: To estimate viral hepatitis screening rates in Japan and understand factors affecting testing and treatment rates.
Method: A large web-based public opinion survey of the general population (aged > 20 years) from the Basic Resident Register (March 2013) was conducted in November 2013. Survey participants answered 16 questions on their opinions and awareness of viral hepatitis testing, treatment and government policy.
Results: 15,003 participants (48 % male; 39 % ≥ 60 years) representative of the population completed the survey. 53 % of respondents had not been tested for viral hepatitis, and the most common reasons were 'Do not think I'm infected' and 'Not included in health check'. The most frequently cited motivators for testing were 'Notice of free testing' and 'Inclusion in health check' and for treatment were 'Low costs' and 'Higher probability of cure'. Awareness of treatment advances and probability of cure was low (24 %). Overall, only 13 % and 10 % of respondents knew of government-sponsored free viral hepatitis screening (available since 2002) and subsidies for treatment costs (available since 2011), respectively. 85-87 % of participants considered it 'Important' or 'Very important and should be strengthened' for government bodies to plan to raise awareness of free screening, treatment advances, and treatment subsidies.

These findings complement those from large Japanese Ministry of Health surveys (2012-2013) that reported viral hepatitis screening rates of 48-57 % and showed that only 62-69 % of those screened positive sought treatment.
Conclusion: Despite free screening and treatment subsidies, public awareness is still low and national policy coordination is required to optimise viral hepatitis screening and treatment rates.

Topic 23: Other viral Hepatitis

No: 1583

Q fever as a cause of acute and chronic hepatitis

Chang Kn Park[1], Kyoung Suk Lee[2]

Daegu Fatima Hospital Departtment of Internal Medicine Daegu-Korea, South[1], Daegu Fatima Hospital Department of Internal Medicine Daegu-Korea, South[2]

Background/aim: Q fever is a relatively rare zoonosis caused by infection of Coxiella burnettii in Korea. Here, we present a total of 15cases of Q fever characterized by acute febrile illness with acute or chronic hepatitis.
Methods: Demographic features, clinical manifestations, histologic findings of liver, laboratory findings and therapeutic outcomes of all cases were evaluated. Q fever was diagnosed by an indirect micro-immunoflurorescence assay (MIFA) and polymerase chain reaction (PCR).
Results: A total of 15 patients with Q fever was diagnosed from January 2006 to July 2014. The mean age was 47 years old (range: 24-78) and 13patients were male. Seven patients had a history of animal contact. Fever(100 %) was the most common symtom, followed by myalgia (82.3 %), headache (67 %), anorexia (60 %), and chill (53 %). All patient showed mild to moderate elevation of liver enzymes. Three patients showed only transient febrile episodes followed by chronic elevation of liver enzymes. All cases were diagnosed by high titers of anti-phase II antibody (Ig M > 1: 50, Ig G > 1: 200) and positive nested PCR. In three cases, liver biopsies revealed the presence of compact fibrin-ring granuloma which was characteristic histologic finding in this disorder. All cased showed complete recovery after antibiotic treatment (doxycycline).
Conclusion: Although it is rare, Q fever is possible cause of acute or chronic hepatitis accompanied by febrile illness.

Topic 23: Other viral Hepatitis

No: 1961

Liver involvement in adult with five measles

Mahmut Sunnetcioglu[1], Mustafa Kasım Karahocagil[1], Ali Irfan Baran[1], Mehmet Çelik[2], Sevdagul Karadas[2]

Yuzuncu Yil University, Medical Faculty Department of Infectious Diseases and Clinical Microbiology Van City-Turkey[1], 1yuzuncu Yil University, Medical Faculty Department of Infectious Diseases and Clinical Microbiology Van City-Turkey[2]

Objective: Acute hepatitis liver enzyme was defined as five times the upper limit of normal. Acute hepatitis can usually be observed in A, B, C, D and E types on a common frequency. In this study, we aimed to present hepatitis cases linked to the measles virus.
Materials and methods: In Yuzuncu University, Faculty of Medicine Infectious Diseases and Clinical Microbiology Service, between 1 December 2012- June 1, 2013 the measles 5 Patients Diagnosed with measles were clinically, serologically and radiologically examined.
Results: 5 cases of measles coexistent with hepatitis were followed in our service and then presented. One of the patients was male and 4 were females and the average age was 27. All the patients had fever, skin rash, abdominal pain, weakness and fatigue various other complaints. Laboratory analyzes the most frequent cause of viral hepatitis, hepatitis A, B, C, D, E and related tests were negative. In all patients SGOT, SGPT was over five times superior of GGT and LDH were also normal. 2 sedimentation height in patients with elevated CRP levels were detected in 4 patients. Abdominal ultrasonography in 3 abdominal ultrasonography in a patient revealed hepatosplenomegaly; hepatomegaly patients were within normal values.
Conclusion: It can be stated that the other viral factors apart from those of hepatitis which can be frequently observed in the aetiology of the disease in the acute stage in adolescents may also be an underlying cause of hepatitis and therefore should be taken into consideration.

Topic 24: Pediatric Gastroenterology

No: 1343

Profile and outcome of metabolic liver disease in under fives with liver related pediatric emergencies in a tertiary care pediatric hepatology centre

Seema Alam[1], Vikrant Sood[1], Bikrant Bihari Lal[1], Rajeev Khanna[1], Dinesh Rawat[1]

Institute of Liver and Biliary Sciences Pediatric Hepatology New Delhi-India[1]

Introduction: Inborn errors of metabolism, where hepatomegaly and/or abnormal liver function form part of the clinical disease, are known as "Metabolic liver disease (MLD)". Dietary exclusions, antioxidants and chelation therapy with immunoglobulins can offer good outcome in some of the treatable MLD. Liver transplantation for MLD shows markedly improved outcome. The presentations of an MLD in an infant or child can be varied. Common liver related emergencies like encephalopathy with liver dysfunction (Reye's like syndrome), Cyclical vomiting and acute liver failure are often seen associated with MLD. Lack of awareness delays the identification and causes increased mortality.
Objective: (i) To study the clinical profile and outcome of MLD in infants and young children < 5 yrs of age presenting as liver related pediatric emergencies.
Methods: All infants and young children less than 5 years of age, admitted between January 2011 and October 2014 with liver related pediatric emergencies were included in the study. Based on presenting feature being encephalopathy and or acute liver failure, these patients were managed as per the 2 protocols developed by the department for the management of these cases. We follow protocol based approach for various presentation of MLD at ILBS. The diagnostic criteria for ALF in this age group was taken as evidence of synthetic liver dysfunction with uncorrectable coagulopathy (INR ≥ 2 irrespective of presence or absence of encephalopathy, 6 h after 2nd dose of parenteral vitamin K 10 mg each). Poor outcome was defined as death or liver transplantation within 12 weeks of presentation. The etiological.

Topic 24: Pediatric Gastroenterology

No: 1945

Endoscopic ultrasound with fine needle aspiration a feasible technique in a five year old child

Victoria Kok[1], Yusri Yusuf[2], Maylene Kok[1]

Sarawak General Hospital Medicine Kuching-Malaysia[1], Sarawak General Hospital Pathology Kuching-Malaysia[2]

Introduction: Endoscopic Ultrasound (EUS), with or without Fine Needle Aspiration (EUS-FNA), has been extensively used as a diagnostic and therapeutic tool in the adult population. This has been explored in the paediatric population recently, usually by adult gastroenterologists.
Aim: To report the outcome of a successful EUS-FNA performed in a five year old boy at the Sarawak General Hospital, Malaysia.
Result: A five year old boy presented with gastric outlet obstruction and anaemia. Physical examination revealed pallor, and a large, non-tender, epigastric mass.
His Haemoglobin was 5.1 g/dL and the Lactate Dehydrogenase was markedly raised at 1058 U/L. There was iron deficiency anaemia with thrombocytosis, but absence of immature cells on peripheral blood film.

Computed tomography scan (CT scan) showed a non-obstructing large tumour in the region of duodenum. Oesophagogastroduodenoscopy (OGDS) under general anaesthesia showed an extrinsic compression of the antrum and the first part of the duodenum, with normal mucosa. This was followed with EUS using the PentaxEG-3270UK slim linear echoendoscope. FNA was performed using a 22G Cook Medical ProCore FNA needle, with in-room cytology demonstrating abundant lymphocytes. The cytology was reported as malignant small round blue tumour, favouring lymphoblastic lymphoma. This was later confirmed to be Non Hodgkin's lymphoma, mature B phenotype from the cell block preparation. Chemotherapy was started and he responded well.
Conclusion: EUS or EUS FNA, although technically challenging, is feasibly safe in the paediatric population if performed by experienced gastroenterologists. The presence of rapid on-site examination (ROSE) during FNA ensures a rapid diagnosis and should be the current standard of care, where possible.

Topic 24: Pediatric Gastroenterology

No: 2127

A rare cause of upper gastrointestinal bleeding gastroduodenal artery pseudoaneurysm and haemorrhage linked to acute pancreatitis

Tanju Başarır Ozkan[1], H.ayşegül Otuzbir[1], N.ulkü Sahin[1], Figen Palabıyık[2], Omer Fatih Nas[2], Erdoğan Cüneyt[2]

Uludağ University Pediatric Gastroenterology, Hepatology and Nutrition Bursa-Turkey[1], Uludağ University Radiology Bursa-Turkey[2]

Introduction: The actual frequency of pseudoaneurysm which is a complication of pancreatitis is not known;however it has been reported to vary from 1.3 % to 10 % in case series of various age groups.We reported a rare case of gastroduodenal pseudoaneurysm in a child with acute pancreatitis.
Case: A 14-year-old male patient presented with abdominal pain and hematemesis. Except paleness and fatigue, physical examination and vital signs were normal. According to the laboratory examination results,he had high levels of amylase [801 IU/L (25-125)] and lipase [1154 IU/L (8-78)]. Abdominal ultrasonography showed a normal liver,gallbladder and biliary tract and a complicated fluid appearance of 58.5*48.5 mm with a heterogeneous and intense content and a thick walled septation which originated from the pancreatic site.Abdominal tomography showed a spherical,uniformly bounded mass appearance fluid appearance of 58.5*48.5 cm with a heterogeneous content localizing in the head and neck section of the pancreas.Celiac angiography that was performed by interventional radiology department showed a pseudoaneurysm in the gastroduodenal and gastroepiploic arteries linked to pancreatitis as well as a hematoma of 6.5 cm.Pseudoaneurysm which developed in the gastroduodenal and gastroepiploic arteries and the adjacent hematoma were embolized by coils in the same session.Postoperative imaging showed complete closure of the aneurysm as well as disappearance of the contrast of the contrast agent stagnation in the hematoma.
Discussion: In patients with upper gastrointestinal bleeding and abdominal pain,presence of normal hemodynamic parameters and clinical well-being,as in our case,may mislead the clinicians,causing missed diagnosis of the underlying pancreatitis and pseudoaneurysm,which is a complication of pancreatitis.Therefore,early diagnosis and intervention is crucially important for reduced mortality and morbidity.

Topic 24: Pediatric Gastroenterology

No: 1240

A case of hemophagocytic lymphohistiocytosis caused by ebv and parvovirus

Meltem Ugras[1], Tuba Giray[2], Oznur Kucuk[2], Suat Bicer[2], Ayca Vitrinel[2]

Yeditepe University Medical Faculty Pediatric Gastroenterology Hepatology Istanbul-Turkey[1], Yeditepe University Medical Faculty Pediatrics Istanbul-Turkey[2]

Hemophagocytic lymphohistiocytosis (HLH) is a rare clinical syndrome with manifestations include high fever, maculopapular rash, neurological symptoms, coagulopathy, and abnormal liver function tests. HLH can be either primary, that is, due to an underlying genetic defect, or secondary, associated with malignancies, autoimmune diseases, or infections. Infection associated HLH are mostly herpes group. We report a case diagnosed with HLH.
Case report: A previously healthy 11-years-old infant was admitted to our clinic with a 4-day history of fever and paleness. Family history was unremarkable. On physical examination she was weak, had fever 40 C, membranous tonsillitis and enlarged cervical lymphadenopathy.. Laboratory test on admittance were; hemoglobin 13 g/dL, WBC 5 × 109/L, and platelet count 117 × 109/L. ALT: 52U/L, AST: 95U/L, CRP: 16 mg/L, Than she was internalized due to prolonged fever, swolled eyelids, enlarged cervical LAM's, hepatosplenomegaly. She had leucopenia, thrombocytopenia, hypertransaminasemia, serological tests for hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), cytomegalovirus (CMV), EBV, were all negative. Blood and urine cultures were also negative (Table). The clinical and laboratory data were compatible with HLH Flow cytometric study revealed CD56: 7.5 % absolute CD56: 358 cells/micL, CD25(IL-2R): 1.2 % and absolute CD25: 57cells/micL. The second test for EBV and Parvovirus B1 was positive. The patient was HLH secondary to EBV and Parvovirus infections.

Topic 24: Pediatric Gastroenterology

No: 1242

Aminotransferase levels of children with rotavirus norovirus and enteric adenovirus gastroenteritis

Meltem Ugras[1], Oznur Kucuk[2], Suat Bicer[2], Ayca Vitrinel[2]

Yeditepe University Medical Faculty Ped Gastroenterology Hepatology Istanbul-Turkey[1], Yeditepe University Medical Faculty Pediatrics Istanbul-Turkey[2]

Background: In this study, we investigated the rates of increase in serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels of patients with rotavirus, norovirus and enteric adenovirus gastroenteritis.
Design and methods: Two hundred children with viral gastroenteritis were evaluated for hypertransaminasemia, retrospectively.
Results: A total of 200 children were enrolled in the study. The patients were between 0–17 years (mean ± SD: 5.10 ± 3.01) of age. ALT was elevated up to 67 IU/L in 7 (8.5 %) patients in the rotavirus group (n = 82), whereas it was elevated in 3 (4.0 %) and 1 (2.3 %) patients in the norovirus (n = 74) and adenovirus (n = 44) groups, respectively. AST was elevated up to 89 IU/L in 20 (24.4 %) patients in the rotavirus group, whereas it was elevated in 6 (8.1 %) and 1 (2.3 %) patients in the norovirus and adenovirus groups, respectively. Both transaminases were elevated in 6 (7.3 %), 1 (1.4 %), and 1 (2.3 %) patients in the rotavirus, norovirus, and adenovirus groups, respectively. The increases in ALT and AST levels were found to be significantly higher in the rotavirus group (n = 27) than in the norovirus (n = 9), and adenovirus group (n = 2) ($P < 0.05$). Mean serum ALT and AST levels in the rotavirus group were significantly higher than those in the norovirus and adenovirus group ($P < 0.05$).
Conclusions: Our study investigated the correlation between viral gastroenteritis and hypertransaminasemia. When evaluating a patient with hypertransaminasemia physicians should remember to consider acute gastroenteritis due to some viruses as a cause of elevated AST and ALT.

Topic 24: Pediatric Gastroenterology

No: 1508

Profile and outcome of acute liver failure in infants and young children in a tertiary pediatric hepatology centre in India

Seema Alam[1], Bikrant Bihari Lal[1], Vikrant Sood[1], Rajeev Khanna[1], Dinesh Rawat[1]

Institute of Liver and Biliary Sciences Pediatric Hepatology New Delhi-India[1]

Objective: (i) To study the etiological spectrum of Acute Liver Failure in infants and young children < 3yrs of age (ii) To evaluate outcome and identify factors predicting survival.
Methods: All infants and young children less than 3 years of age, admitted between January 2011 and July 2014 with ALF were included in the study. Poor outcome was defined as death or liver transplantation within 12 weeks of presentation. The etiological spectrum was studied and the factors affecting outcome were analyzed.
Results: There were a total of 31 children under 3 years of age with acute liver failure (ALF) with median age of 12.5 months. Fifteen of the 31 were infants. Metabolic liver diseases (MLD- 29 %) and hemophagocytic lymphohistiocytosis (HLH-16 %) together accounted for half of the ALF cases in this age group. Drug induced ALF and acute viral hepatitis A were other common etiologies. Drug induced liver injury (DILI) was seen in 5 (16 %): valproate, antitubercular therapy, acetaminophen and antibiotics (azithromycin and amoxiclavulanic acid) were the drugs implicated. Presence of grade 3-4 HE ($P = 0.001$), longer JE interval ($P = 0.023$) and higher lactate ($P = 0.04$) and MLD/HLH as etiology were associated with poor outcome on univariate analysis. On multivariate analysis, ALF associated with MLD and HLH had poor outcome (Survival with native liver of 11 % and 20 % respectively).
Conclusion: MLD and HLH in infants; whereas viral hepatitis, DILI and MLD in young children are commonest etiologies of ALF. ALF caused by MLD or HLH has poor outcome.

Topic 24: Pediatric Gastroenterology

No: 1213

Duodenal y roux fistula in child with portoenterostomy due to biliary atresia – case report

Marek Woynarowski[1], Violetta Wojno[1], Mikołaj Teisseyre[1], Maciej Dądalski[1]

Children's Health Memorial Institute Gastroenterology and Hepatology Warsaw-Poland[1]

Introduction: Kasai hepatoportoenterostomy is a treatment of choice in infants with biliary tract atresia. The bile is drained into the Y-roux intestinal loop and omits duodenum and upper part of jejunum.
Methods: This is a retrospective analysis of patient's case report.
Case report: We present a girl with biliary atresia treated with hepatoportoenterostomy at the age of 2 months. Patient developed splenomegaly and mild hypersplenism at the age of 1 year Patient started the endoscopy surveillance for portal hypertension at the age of 2 years (7 endoscopies done within subsequent 4 years of observation). The endoscopies showed increasing size of oesophageal varices and presence of deep ulceration of duodenal bulb wall. Patient underwent prophylactic endoscopic band ligation of oesophageal varices and received long term PPI therapy. Duodenal ulcer temporarily healed but reappeared after PPI discontinuation with further formation of small fistula to Y-Roux intestinal loop at the age of 6 years. The fistula allowed for the retrograde bile flow into the duodenal bulb and stomach.
Conclusion: To our knowledge this is the first in the literature report of duodenal-Y-Roux fistula in patient after hepatoportoenterostomy. The presence of the fistula may have a positive effect as it allow the partial bile flow into the duodenum. However with the increase of fistula size the duodenal content may omit upper jejunum what will shorten the alimentary passage and may lead to malabsorption.

Topic 25: Pregnancy and Liver

No: 1403

The rate of abcb4 and abcb11 mutations in intrahepatic cholestasis of pregnancy

Emel Ahishali[1], Gulcan Sahin[2], Can Dolapcioglu[1], Mehmet Sayiner[2], Ozdal Etlik[3], Tugba Baris[3], Abdulaziz Kural[1], Resat Dabak[2]

Dr. Lutfi Kirdar Kartal Education and Research Hospital Department of Gastroenterology Istanbul-Turkey[1], Dr. Lutfi Kirdar Kartal Education and Research Hospital Department of Family Medicine Istanbul-Turkey[2], Burc Genetic Diagnostic Center Department of Molecular Genetics Istanbul-Turkey[3]

Aim: Mutations in the genes coding biliary transport proteins play a role in the pathogenesis of Intrahepatic Cholestasis of Pregnancy (ICP). It is shown that ICP is associated with mutations in ABCB4 and ABCB11 genes that code multidrug resistance protein 3 and bile salt export pump proteins. We searched for ABCB4 and ABCB11 gene mutations in pregnant women that we follow with ICP diagnosis.
Method: In the last year, 2354 deliveries occurred in our hospital and ICP was diagnosed in 30 patients. ABCB11 gene polymorphism p.Val284Asp, p.Gln558His, p.Pro731Ser and ABCB4 rs2097937, rs31676, rs1149222, rs4148826, rs2109505, rs2302386 were analyzed by DNA sequencing analysis.
Results: Mean age of ICP patients was 27.17 ± 4.89 years. Mean time for ICP diagnosis was 31.47 ± 3.73 weeks of pregnancy. Fourteen (46.7 %) patients were multipara. In 6 multipara women there was a history of ICP in previous pregnancies. In all these 6 patients with previous ICP history, family history for ICP was positive and there was no family history in other patients.

No ABCB11 gene mutation was detected. The results of 6 polymorphism sequence analysis for ABCB4 gene are shown in Table 1. The results of control group composed of women experiencing a normal pregnancy are being studied in order to show the relation of these polymorphisms with Turkish ICP patients.

Conclusion: ABCB11 gene mutation was not detected in our ICP patients. The results of control group composed of women experiencing a normal pregnancy are waited to show the relation of ABCB4 gene polymorphism sequence analysis with Turkish ICP patients.
Note: ABCB4 gene polymorphism sequence analysis results of control.

Topic 25: Pregnancy and Liver

No: 2001

Monitoring results of 20 years related to the subjects having hbsag positive during pregnancy

Selma Tosun[1], Selda Erensoy[2], Sait Yucebilgin[3]

Izmir Bozyaka Research and Education Hospital Infectious Diseases Izmir-Turkey[1], Ege Univercity The Favculty of Medicine Microbiolgy Izmir-Turkey[2], Ege Univercity The Faculty of Medicine Gynaecolgy and Obstetrics Izmir-Turkey[3]

Aim: The aim of this study is to evaluate the monitoring results of 20 years related to the subjects having HBsAg positive during pregnancy in 1994.
Method: As a result of the examinations, the necessity of monitoring and its principles were explained in a detailed way by making face to face interviews with the pregnant women having HBsAg positive in 1994. The individuals were taken part in the regular monitoring process.
Results: The study included 38 pregnant women, but 6 of these women did not attend monitoring processes from the beginning and therefore were excluded from the study.It was detected that 4 out of the 32 monitored pregnant women had HBeAg and HBV DNA positive. It was observed that 2 of the pregnant women in the monitoring process could not continue the process due to moving to another city;and the remaining 30 women were monitored for 6 months or 1 year intervals.Except for one of the subjects,it was not necessary to make biopsy or to provide treatment fort he others.During the monitoring process, HBsAg disappeared in one of the subjects in the 7th year of the process and in the other subject,it disappeared in the 5th year of the process, and developed spontaneous antiHBs. None of the subjects developed cirrhosis or HCC.
Conclusion: It is important for HBsAg positive subjects to be monitored for a long term period and regularly.

Topic 25: Pregnancy and Liver

No: 2235

A case of acute fatty liver of pregnancy second trimester of pregnancy

Ramin Farajpour[1], Ali Ghavidel[2], Shiva Farajpour[3], Mohammadhosein Soomi[2], Mehdi Farhoodi[4]

Student Research Committee of Tabriz Medical University Faculty of Medicine Tabriz-Iran[1], Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences Liver and Gastrointestinal Diseases Research Centre, Tabriz University of Medical Sciences Tabriz-Iran[2], Vice Chancellor For Research and Technology of Tabriz Medical University Nsrcc(neuroscience Research Center) Tabriz-Iran[3], Nsrcc(neuroscience Research Center) Nsrcc(neuroscience Research Center) Tabriz-Iran[4]

In pregnancy, pathological conditions causing abnormality of liver function tests need to be differentiated from normal physiologic changes. Among various causes of pathological hepatic dysfunction, acute fatty liver of pregnancy (AFLP) is uncommon compared to pre-eclampsia and hemolytic anemia, elevated liver enzymes and low platelets (HELLP) syndrome. Early diagnosis and prompt termination of pregnancy is necessary for better maternal and foetal outcomes Acute liver failure during pregnancy may be due to fulminant acute viral hepatitis, liver toxicity or acute fatty liver of pregnancy. Acute fatty liver of pregnancy is a rare disease that occurs in the third trimester. The incidence is reported to affect 1 in 10,000 pregnancies. Maternal mortality rate is about 25 % and fetal mortality rate is estimated at 65 %. Early diagnosis and treatment can improve maternal and fetal outcomes.

We present a case report of a 18-year-old woman with AFLP complicated by sepsis and multiple organ dysfunction syndrome (MODS) requiring intensive care with catastrophic result.

Case report: A 18-year-old woman with a gestational age of 15 weeks was admitted with vomiting for days and unusual behaviors (aggression,) and involuntary movements (shaking hands to the hospital. Based on clinical and laboratory findings of the patient acute liver failure in acute fatty liver of pregnancy has been suggested patient with frequent seizures are not controlled by medication. Following the seizure, hypotension, bradycardia does not respond to resuscitation efforts the patient died.

Conclusions: All patients with persistent nausea and vomiting, epigastric pain and pregnancy are recommended to assess liver function tests, renal function tests and complete blood count to rule out the diagnosis of acute fatty liver of pregnancy.

Topic 25: Pregnancy and Liver

No: 1997

The importance of the researches on hbsag positivity in pregnant women

Fatma Eskicioglu[1], Selma Tosun[2], Tevfik Guvenal[3]

Merkez Efendi State Hospital Gynaecolgy and Obstetrics Manisa-Turkey[1], Izmir Bozyaka Research and Education Hospital Infectious Disease Izmir-Turkey[2], Celal Bayar University The Faculty of Medicine Gynaecolgy and Obstetrics Manisa-Turkey[3]

Aim: The aim of this study is to research the HBsAg of the pregnant admitted to Gynaecology and Obstetrics Clinic in the last four years, and to research the immunization status of their babies.

Method: HBsAg examination results of the pregnant who admitted to Manisa Merkez Efendi State Hospital Gynaecology and Obstetrics Clinic in the last four years were used for the study.Also, the cases related to vaccination + HBIG of the babies of carrier pregnants were also taken from the hospital data and pharmacy records. Repeated records regarding the numbers of pregnant admitted and examined were taken and the results of each pregnant were evaluated one by one.

Results: The number of pregnant examined in terms of HBsAg in the hospital between the years 2010-2013 was 8512, and HBsAg positivity was determined in 135 pregnant women(1.5 %).However,it was observed that the number of babies vaccinated HBV + HBIG during that period was found as 106. When the reasons for the difference between the number of HBsAg positive pregnant and HBIG numbers were studied, the reasons observed were that some pregnant gave birth at home, the birth was done at another hospital, or the pregnant was a guest subject.

Discussion: Pregnant's examination in terms of HBsAg and correct and appropriate immunization of the babies are of great importance, but in some cases, the subjects may be overlooked and disregarded. In order to prevent this issue, we believe that it would be effective for the Gynaecology physicians and Primary care physicians to work synchronized.

Topic 25: Pregnancy and Liver

No: 2162

Intrahepatic cholestasis of pregnancy in spontaneous and in vitro fertilization

Fusun F. Bolukbas[1], Cengiz Bolukbas[1], Yasemin H. Balaban[2], Emine Ergul[3], Cem Aygun[2], Seyda Ignak[4], Mehtap Yazicioglu[5], Osman C. Ozdogan[6], Suphan S. Ersahin[3]

Department of Gastroenterology, Bahcesehir University School of Medicine Gastroenterology Istanbul-Turkey[1], Department of Gastroenterology, Medipol Mega Hospitals Complex Gastroenterology Istanbul-Turkey[2], Department of Gynecology & Obstetrics, Medicalpark Bahcelievler Hospital Gynecology Istanbul-Turkey[3], Department of Medical Biology, Bahcesehir University School of Medicine Biology Istanbul-Turkey[4], Department of Gynecology & Obstetrics, Medicalpark Goztepe Hospital Gynecology Istanbul-Turkey[5], Department of Gastroenterology, Marmara University School of Medicine Gastroenterology Istanbul-Turkey[6]

Introduction: Intrahepatic cholestasis of pregnancy (ICP) is the most common liver disease in pregnancy. ICP characterized by maternal pruritus in the third trimester, raised serum bile acids and increased rates of adverse fetal outcomes. We investigated potential relationship between ICP and IVF/spontaneous pregnancies via evaluate the health condition of pregnants and newborns.

Methods: Pregnants with ICP (pruritus, elevated bile acids and/or transaminases levels) in three different hospitals between 2007 and 2014 were retrospectively reviewed. Extrahepatic biliary tract obstructions, viral and autoimmune hepatitis marker positivity, HELLP syndrome, and fatty liver of pregnancy were exclusion criteria. A total 55 women were included in this study. Clinical results of pregnant with ICP were analyzed from the aspect of age, fertilization type (spontan or IVF), multiple/singleton pregnancy, delivery week and biochemical tests.

Results: The mean maternal age at time of delivery was 30.13 ± 4.2 years. There was no difference between IVF and spontaneous fertilization groups in term of serum alanine aminotransferase, alkaline phosphatase, total bilirubin, direct bilirubin levels and platelet count. The delivery time in each group was similar. Serum bile acid levels were higher in IVF (34.5 ± 24 μmol/l) than spontaneous fertilization (20 ± 18 μmol/l). There was significant difference at multiple pregnancies in IVF (%75) and spontaneous (%10.26) group and multiple pregnancies determinate the delivery time.

Conclusion: Serum bile acid levels show a difference in spontaneous and in vitro fertilization (IVF) with intrahepatic cholestasis of pregnancy

Topic 25: Pregnancy and Liver

No: 1120

Pregnancy in a woman with budd chiari syndrome

Giuseppe Cerasari[1], Giuseppe Pisani[2], Antonio Starita[2], Maurizio Atzori[3], Alberto Cerasari[4], Saverio Cerasari[5], Rosa Chiodi[6], Claudio Giannelli[7]

San Camillo Forlanini Hospital Hepatology Rome-Italy[1], San Camillo Forlanini Hospital Ginecology Rome-Italy[2], San Camillo Forlanini Hospital Radiology Rome-Italy[3], Sant Rome-Italy[4], La Sapienza University Medicine Rome-Italy[5], San Camillo Forlanini Hospital Pediatrics Rome-Italy[6], San Camillo Forlanini Hospital Gastroenterology Rome[7]

Aim: Budd-Chiari syndrome (BCS) is a rare disorder caused by thrombotic or non-thrombotic obstruction of hepatic venous outflow. Many hereditary or acquired factors resulting in hypercoagulability confer predisposition to the development of BCS. Treatment options include anticoagulant therapy, surgical shunt or transjugular intrahepatic portosystemic shunt (TIPS) and liver transplantation.
Pregnancy is considered a thrombotic risk factor, and several cases of BCS have been described in women following pregnancy or during puerperium. In contrast, very few data are available about pregnancy outcome and management in women with known Budd-Chiari syndrome, since pregnancy is usually discouraged in these patients. Liver disease can cause significant morbidity and mortality in both pregnant women and their infants.
Methods: We describe the case of a young woman with known and treated BCS who had pregnancy, with good maternal and newborn outcome.At age 20, after taking estrogen-progestin pill for 3 months was diagnosed BCS, confirmed by histological diagnosis, and she has been subjected to stent placement in the right hepatic vein over and anticoagulant therapy. At age 32, detection of pregnancy. It was mantained the anticoagulant therapy with parnaparin 0.8 mg one vial per day. At 35 weeks of pregnancy was planned caesarean section. The baby is born healthy and in good condition. The new mother was subjected to ultrasound liver of control that did not reveal significant changes of flow.
Conclusions: Pregnancies are not absolutely contraindicated with appropriately treated disease. The mother should be counseled about the possible maternal and fetal unfavorable outcomes.