Official Journal of the Turkish Association for the Study of the Liver

ISSN 1307-5888
E-ISSN 2757-7392

HEPATOLOGY FORUM

Volume 3
Supplement 1
January 2022

AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

TASL

AASLD TASL DIGITAL HEPATOLOGY Meeting

14-15 JANUARY 2022

KARE

ISSN: 1307-5888 / E-ISSN 2757-7392

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Invitation

Dear Colleagues,

It is with great pleasure that the American Association for the Study of Liver Diseases (AASLD) and the Turkish Association for the Study of the Liver (TASL) announce our second joint conference to CONNECT physicians and health care providers in Turkey with experts from the USA and Turkey in hepatology.

AASLD is the global leader focused on advancing the science and practice of hepatology. Content delivered from our programs and journals, combined with local perspectives from experts in Turkey, have facilitated the incorporation of cutting edge research data into practice and offer the best possible atmosphere to encourage collaborative research between Turkish and American physicians.

This year, we have decided to take on the current challenges presented by the ongoing pandemic head-on and created a unique and exciting collaborative opportunity to link two meetings into a seamless, productive interactive experience. AASLD and TASL are working together to offer TASL attendees in our joint **AASLD-TASL Digital Hepatology Connect** to also register (at no additional cost) for **The Liver Meeting Digital Experience™ 2022**.

We truly believe that this arrangement for TASLD audience to participate in the two meetings will maximize learning about the latest liver disease research being presented at The Liver Meeting Digital Experience,™ followed, with the Hepatology Connect, by bringing the knowledge to life with more in-depth, case study-based discussions for state-of-the-art diagnosis and treatment approaches. The opportunity to interact with the unprecedented number of AASLD faculty and with local and regional experts in the science and practice of hepatology will make this a must-attend combination of events for the TASL audience.

We would be grateful to partner with organizations and companies that share our vision of collaboration and exchange. Support of this meeting is vital so that we can provide attendees with a quality meeting experience. Specifically, your support will help us deliver an exceptional scientific program via a digital platform that allows for large didactic lectures and smaller breakout sessions, as well as other opportunities for faculty and attendees to interact. Your participation will be mutually beneficial. There will be opportunities for satellite symposia and virtual exhibition space, and your involvement will provide exposure and brand recognition to extend your reach to hundreds of attendees.

On behalf of AASLD and TASL, we would like to thank you in advance for your financial contribution. Your support will play a crucial role in promoting liver health, providing quality patient care, and advancing the study and practice of hepatology in the region, especially in the area of viral hepatitis, chronic liver disease and hepatocellular carcinoma. It is because of supporters like you that we are able to plan and implement programs of this magnitude and collaboration on a global level. Your generosity directly allows us to carry out our mission to prevent and ultimately cure liver disease in Turkey, the US, and the world over.

Sincerely,

W. Ray Kim, MD
Board Liaison, AASLD Global Outreach Committee
Co-organizer, AASLD-TASL Connect

Ramazan Idilman, MD
President, TASL
Co-organizer, AASLD-TASL Connect

Content

OP-01

Characteristics of Wilson's disease in Turkey between 1993 and 2021: Preliminary Report of the Turkish Association for the Study of the Liver (TASL)/ Pediatric Liver Disease Special Interest Groups

Figen Özçay[1], Sinan Sarı[2], Zarife Kuloğlu[3], Çiğdem Arıkan[4], Khaled Warasnhe[5], Buket Dalgıç[2], Aysel Yüce[6], Hayriye Hızarcıoğlu Gülşen[6], Özlem Durmaz[7], Zerrin Önal[7], Mukadder Ayşe Selimoğlu[8], Fatma İlknur Varol[9]

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OBJECTIVES: Wilson's disease (WD) is a rare autosomal recessive disease caused by ATPB7 gene mutations that alter copper metabolism. Despite high prevalence, few studies have addressed the epidemiology and clinical characteristics of WD in Turkey. We analyzed data of 868 WD patients (Ferenci score >=3) diagnosed between 1993-2021 in 43 hepatology centers in Turkey.

MATERIALS & METHODS: A total of 868 patients (57.9% Male and 42.1% Female) were analyzed. 40 patients were adults. The mean diagnostic age was 118.78±65.734 months. The prevalence of consanguineous marriage was 59% (74.8% 1st degree, 19.4% 2nd degree and 5.8% >= 3rd degree). 45.8% of the patients had family history for WD (80.7% 1st degree, 8.5% 2nd degree and 10.8% >=3rd degree). 22.9% of the patients were diagnosed with family screening. Clinical manifestations, biochemical, genetic and histological findings are summarized in Tables 1, 2.

RESULTS: Zinc monotherapy was initiated in 11 patients (1.2%). 113 patients (13%) were treated with D-penicillamine (DP) alone.530 patients (61.1%) received combination of DP and zinc treatments. 23 patients (2.6%) only received Trientine treatment while 73 patients were treated with Trientine in combination with zinc (8.4%). DP side effects were reported in 8.5% of the patients. Main side effects were urticarial rash (2.3%),proteinuria (1.4%) and deterioration of neurological symptoms (0.7%). 87 patients (%10) underwent liver transplantation (LT) (63.1% living donor, 36.9% cadaveric donor). 31/70 (%44) of patients presented with acute liver failure (ALF) underwent LT. Mortality rate after LT was 7.1% (n 6). A total of 30 patients (3.6%) died during follow-up period.

CONCLUSION: WD should be always considered in patients presenting with asymptomatic elevation of transaminases. Medical treatment was successful in 90% of our patients. Combined treatment of zinc and DP was the most preferred treatment modality. Overall LT rate even in ALF presentation was low. Overall mortality rate was also low (3.6%) in our WD patients.

Keywords: Wilson's disease, liver transplantation, acute liver failure, chronic liver failure, children

Table 1. Clinical manifestations of WD patients

Hepatic involvement (92%)
- Isolated asymptomatic elevation of transaminases (54%) - Acute hepatitis (3.5%) - Cirrhosis (16.6%) - Acute liver failure (8.8%) - Hepatosteatosis (5%) - Hepatomegaly (4.2%) - Chronic hepatitis (7.9%)
Neurologic involvement (21%)
- Dysarthria (36.5%) - Dystonic syndrome (20.9%) - Ataxia (30.4%) - Parkinsonism (12.2%)
Psychiatric disease (5.1%)
Renal involvement (4.8%)
- Tubular disorders (4.8%) - Nephrolithiasis (2.3%) - Renal failure (3%)
Kayser–Fleischer ring (24.4%)
Hemolytic anemia (5.6%)

Table 2. Biochemical, genetic and histological findings in WD patients

Biochemical Profile of WD patients
- ALT 99.5 IU/L (13-1500)* - AST 114.5 IU/L (8-2100)* - Serum ceruloplasmin 10.49 ± 8.6mg/dL - Serum free copper 26 mg/dL (14-771)* - 24-hour urine copper 189 mg/dL (10-8795)* - Hepatic copper concentration 740 ± 656 mcg/g
Genetic Profile of WD patients (40%)
- One mutation (10.5%) - Two mutations (27%) - No mutations identified (2.5%)
Liver biopsy findings in WD patients (71.2%)
- Steatosis (62.8%) - Fibrosis (77.8%) - Chronic hepatitis (64.4%) - Cirrhosis (30.4%)

* *Levels expressed as median and range.*

OP-02

Liver injury after SARS-CoV-2 vaccination: Clinical and laboratory features, efficacy of corticosteroid treatment and outcome

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Mirta Peralta[17,18], Berat Ebik[19], Serkan Duman[20], Nurhan Demir[21],Yasemin Balaban[22], Álvaro Urzua[23], Fernando Contreras[24], Maria Grazia Venturelli[25], Yılmaz Bilgiç[26], Adriana Medina[27], Marcos Girala[27], Fulya Günşar[28], Maria-Carlota Londoño[29], Theodoros Androutsakos[30], Ayelen Kisch[31], Alper Yurci[32],Fatih Güzelbult[33] Yasir Furkan Çağın[26], Enver Avcı[34], Murat Akyıldız[35], Emine Kübra Dindar-Demiray[36], Murat Harputoğlu[26], Rahul Kumar[37], Sanjaya K. Satapathy[38], Manuel Mendizabal[18,39], Marcelo Silva[18,39], Stefano Fagiuoli[4], Stuart K. Roberts[40], Neşe Karadağ Soylu[41], James M. Crawford[42], Yoh Zen[43], Ramazan Idilman[20], Eric M. Yoshida[44], Aldo J. Montano-Loza[13], George N. Dalekos[45], Ezequiel Ridruejo[18,39,46], Thomas D. Schiano[47], Staffan Wahlin[48]

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OBJECTIVES: We aimed to evaluate clinical features, treatment response and outcomes of liver injury attributed to SARS-CoV-2 vaccination.

MATERIALS & METHODS: We collected data of cases that developed liver injury following SARS-CoV-2 vaccines (Pfizer-Biontech, Moderna and Oxford/AstraZeneca) from 18 countries. Study population was categorized according to given corticosteroid therapy.

RESULTS: We included 87 cases (63%, female) with a median age of 48 (range: 18-79) years at diagnosis of liver injury. Fifty-one (58.6%) cases attributed to Pfizer-Biontech (BNT162b2), 20 (23%) cases attributed to Oxford-AstraZeneca (ChAdOX1 nCoV-19) and 16 (18.4%) cases attributed to Moderna (mRNA-1273). Median duration from vaccination to diagnosis of liver injury was 15 (range, 3-94) days. The type of liver injury was predominantly hepatocellular (84%) and most cases (80%) showed laboratory features of autoimmune hepatitis (positive autoantibodies and/or elevated immunoglobulin-G levels). Corticosteroids were given to 46 (53%) patients. There was a positive trend with corticosteroid use and severity of liver injury, 36.8% in grade 1, 51.6% in grade 2 and 88.2% in grade 3, p=0.002. All patients showed resolution of liver injury while one case (1.1%) progressed into liver failure and underwent liver transplantation. Withdrawn of corticosteroids was attempted in 12 cases after complete resolution of liver injury. None patient had relapse during follow-up. Two cases with Oxford-AstraZeneca-induced liver injury received second Pfizer-BioNTech vaccine dose, without evidence of liver injury.

CONCLUSIONS: This international, multi-center study reveals that SARS-CoV-2 vaccination may cause to liver injury. The majority of cases had autoimmune phenotype and showed hepatocellular pattern. Corticosteroid therapy should be considered specifically in patients with severe features of liver injury. Patients generally have favorable outcome but fulminant liver failure due to SARS-CoV-2 vaccination may develop.

Keywords: Drug-induced liver injury, COVID-19, side effects, liver failure, autoimmunity

OP-03

Serum branched-chain amino acids and fructose in NAFLD spectrum

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OBJECTIVES: Serum branched-chain amino acids (BCAA) levels recently have been shown to be biomarker for obesity and Type 2 diabetes mellitus, and also might be biomarker of non-alcoholic fatty liver disease (NAFLD)/non-alcoholic steatohepatitis (NASH) (1, 2). Fructose is not only a junction molecule between metabolic pathways of carbohydrate, lipid and amino acid, it also plays a significant role in NAFLD/NASH pathogenesis.

MATERIALS & METHODS: NAFLD patients (105) and controls (27) were included. NAFLD patients were classified based on MR-PDFF and MRE as Steatohepatitis (SH), F1-F2 fibrosis, and F3-F4 fibrosis. Serum levels of fructose and BCAA were measured by GC-MS.

RESULTS: The median age in control and NAFLD group were 49 and 49 years (p=0.75),and respectively 33% and 46% of patient were male (p=0.21) (Table 1). The distribution of NAFLD patients in subgroups were 63 (60%) in SH, 29 (28%) in F1-F2 fibrosis, and 13(12%) in F3-F4 fibrosis. The metabolomic analysis revealed that NAFLD patients were similar to controls, although there were difference in some metabolic parameters (Fig. 1). There were significant differences between NAFLD and control groups for isoleucine (p=0.008), leucine (0.0001), but not for valine. Fructose level was found to be higher in NAFLD patients than controls (p=0.03), however, it was similar among subgroups of NAFLD (p=0.09). A positive, but non-significant correlation was found between dietary intake and serum levels of BCAA (r=0.23; p>0.05). The diatery intake of fructose did not correlated with serum levels of BCAA (p=0.28) or fructose (p=0.63).

CONCLUSION: Inspite of important role played by fructose in NAFLD pathogenesis and potential of BCAA as biomarker for NAFLD development, the serum levels of them were not correlated neither NAFLD spectrum nor their dietary intake. Since this might be due to type 2 statistical error, we believe that there is a need for studies including larger number of NAFLD patients.

Keywords: Branched chain amino acid, non-alcoholic fatty liver dieases, non-alcoholic steatohepatitis, fructose

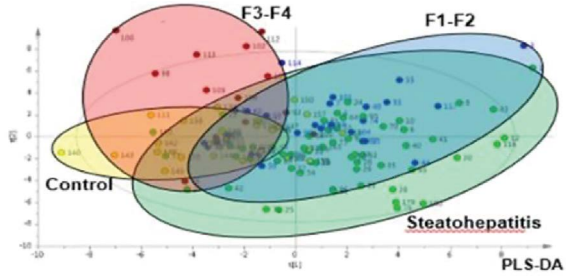

Figure 1. Metabolomic analysis of controls and NAFLD subgroups.

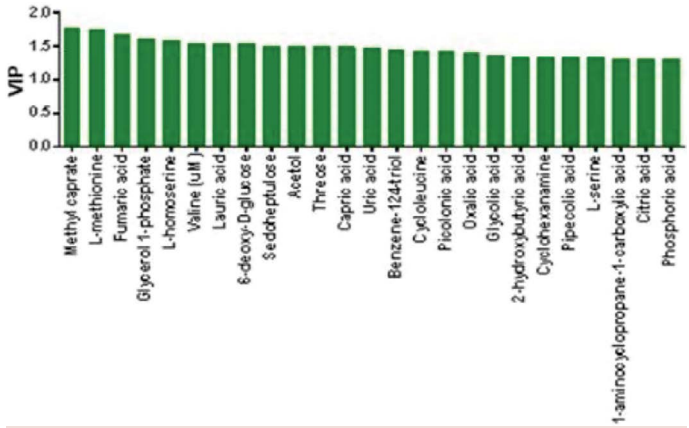

Figure 2.

Table 1. The demographic features and laboratory results

	Total n=132	Controls n=27	NAFLD n=105	P value*
Male; n (%)	58 (44)	9 (33)	49 (47)	0.21
Age; Median (Min.-Max.), years	54 (20-77)	49 (20-71)	49 (20-77)	0.75
Weight; Median (Min.-Max.), Kg	84 (44-138)	77 (44-113)	87 (54-138)	0.001
Waist circumference Median (Min.-Max.), cm	103 (60-135)	97 (60-130)	107 (65-135)	0.0006
Hip circumference Median (Min.-Max.), cm	111 (70-166)	104 (80-166)	116 (70-161)	0.002
BMI; Median (Min.-Max.), Kg/m^2	31.2 (18.6-50.1)	28.6 (18.6-48.3)	32.1 (19.8-50.1)	0.0008
Thrombocyte; Median (Min.-Max.), x10^3/ml	204 (36-151)	220 (89-403)	247 (36-161)	0.49
Neutrophil; Median (Min.-Max.), x10^3/ml	3.7 (1.0-7.9)	3.2 (1.6-2.9)	4.0 (1.0-7.9)	0.03
ALT; Median (Min.-Max.), IU/ml	35 (6-296)	18 (10-72)	40 (6-296)	>0.001
AST; Median (Min.-Max.), IU/ml	28 (13-131)	20 (13-33)	32 (13-131)	>0.001
GGT; Median (Min.-Max.), IU/ml	34 (10-241)	22 (12-241)	41 (10-220)	0.0006
Albumin; Median (Min.-Max.), gr/dl	4.35 (3.87-5.35)	4.39 (3.87-4.71)	4.47 (2.97-5.35)	0.15
Glucose; Median (Min.-Max.), gr/dl	101 (60-291)	95 (70-173)	100 (60-291)	0.056
TG; Median (Min.-Max.), gr/dl	132 (47-492)	105 (52-374)	150 (47-492)	0.02
LDL; Median (Min.-Max.), gr/dl	128 (41-275)	141 (70-175)	139 (40-222)	0.91
HDL; Median (Min.-Max.), gr/dl	50 (21-93)	53 (27-93)	47.2 (21-85)	0.03
Fructose; Median (Min.-Max.), µmol/ml	14.3 (4.5-61.0)	11.0 (6.0-23.8)	14.7 (4.6-61.0)	0.03
Valine; Median (Min.-Max.), µmol/ml	16.2 (4.8-33.1)	16.2 (9.5-26.2)	17.3 (4.9-33.1)	0.41
Leucine; Median (Min.-Max.), µmol/ml	55.0 (6.4-137.3)	48.4 (21.3-88.7)	60.2 (22.0-137.3)	0.008
Isoleucine; Median (Min.-Max.), µmol/ml	15.4 (6.1-30.6)	13.9 (7.7-20.8)	16.7 (6.1-30.6)	0.01

OP-04

Prediction of clinical outcomes in primary biliary cholangitis by FIB-4 score

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OBJECTIVES: In primary biliary cholangitis (PBC), assessment of the disease stage is useful for both prognostic and therapeutic reasons. Patients with more advanced disease have reduced survival than those in earlier stage. The aim was to assess the utility of baseline FIB-4 score in predicting transplant-free survival.

MATERIALS & METHODS: A total of 140 PBC patients (mean age 56.3 years, 82.9% females, median follow-up 36 months) were retrospectively assessed. FIB-4 scores were categorized into three groups: <1.45 (n=62, 44.3%), 1.45-3.25 (n=46, 32.9%), >3.25 (n=32, 22.9%). Receiver operator

characteristic (ROC) curve was used to assess the accuracy of FIB-4 to predict transplant-free survival. The influence of the biochemical and clinical variables on transplant-free survival was assessed with multivariable Cox proportional hazards' regressions. To assess the prognostic impact of baseline FIB-4 score, patients were stratified to FIB-4 >3.25 and FIB-4 < 3.25 score to estimate their survival with a Kaplan-Meier curve.

RESULTS: Seventeen patients (12.1%) reached a clinical endpoint: 4 (2.9%) required liver transplantation and 13 (9.3%) died without transplantation. On multivariate analysis, age (HR: 1.09; p=0.001) and bilirubin levels (HR: 1.19; p=0.009) were independent predictors of transplant-free survival. The transplant-free survival was poorer for patients with a FIB-4 score > 3.25 vs. patients with a FIB-4 score < 3.25 (67.7% vs. 96.2%; p<0.001) (Fig. 1). The AUROC for FIB-4 score for prediction of transplant-free survival was 0.868 (%95 CI 0.780-0.957) (Fig. 2).

CONCLUSIONS: In PBC, a FIB-4 score > 3.25 is associated with future risk of transplanta/on or death. This emphasizes the need to integrate baseline fibrosis stage in individual risk stra/fica/on in pa/ents with PBC.

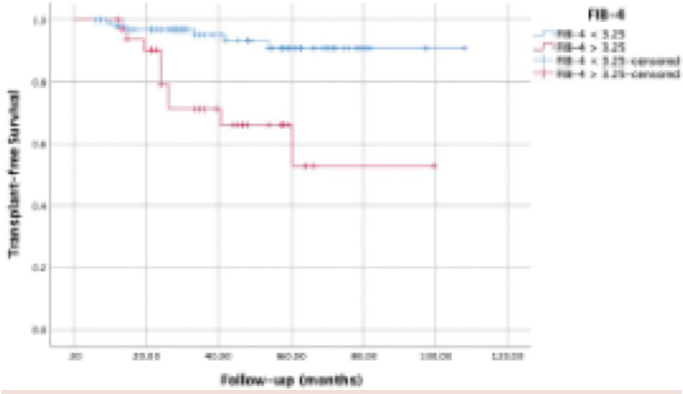

Figure 1. Transplant-free survival es/mates according to baseline FIB-4.

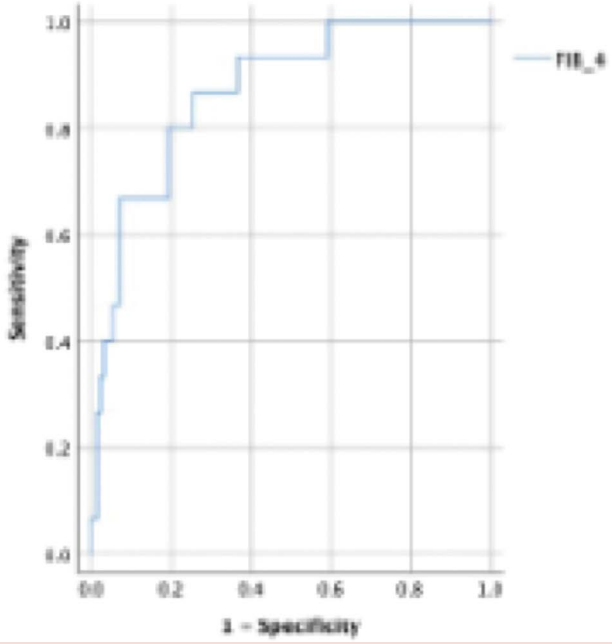

Figure 2. Accuracy of FIB-4 at baseline in predic/ng transplant-free survival.

OP-05

Real life efficacy and tolerability of tenofovir alafenamde fumarate in liver transplant recipients: A multicenter study

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OBJECTIVES: We aimed to determine the real-life efficacy and tolerability of tenofovir alafenamide fumarate (TAF) in liver transplant recipients.

MATERIALS & METHODS: This a multicenter retrospective study. A total of 196 recipients were enrolled into the study. The primary endpoints were virological and biochemical response at week 24 and 48 of the treatment, the secondary endpoint was tolerability of TAF. Median duration of the TAF treatment was 11.6 months (range: 6-60 months). A total of 108 recipients who had at least 6 months follow-up were included in the analysis. Mean age was 58±10 years, 74% were male. Of these, 80% were on tacrolimus-based and 38% on everolimus-based treatments. Median duration from.

RESULTS: LT to TAF initiation was 24.5 months (range: 0-252 months). Seventeen patients received TAF treatment as first-line therapy, whereas 91 patients switched to TAF treatment. Renal dysfunction and osteoporosis were the most common indications for TAF treatment. Baseline median serum ALT level was 25 IU/L (range: 10-96 U/L) and baseline median HBV DNA level was 890 IU/mL, respectively. Virological and biochemical response were 90% and 71% at week 24, and 100% and 92% at week 48, respectively. From baseline to the last follow-up, improvement in ALT at every 24 weeks compared by linear mixed model was significant; -3.226 IU/ml [95% CI: (-5.62) - (- 0.84); p=0.009]. After the switch to TAF treatment, none of the patients experienced HBV reactivation. TAF treatment was well tolerated. Renal functions and lipid profile remained stable during TAF treatment (Fig. 1). No serious adverse events were reported. No graft rejection was observed.

CONCLUSION: The present study indicates that TAF is effective and tolerable in liver transplant recipients.

Keywords: Tenofovir alafenamide fumarate, TAF, liver-transplant recipients

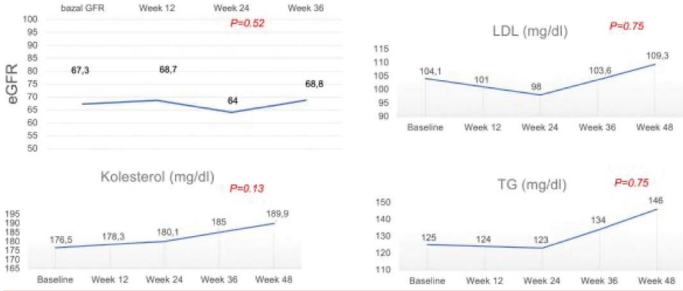

Figure 1. Change in estimated glomerular filtration rate (eGFR) and lipid profile.

OP-06

Trends and causes of etiology in adult liver transplant patients: Multicenter study

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OBJECTIVES: The indications to liver transplantation (LT) are changing in western population over the years. The aims of the present study were to determine etiological trends in LT in Turkey.

MATERIALS & METHODS: This is multicenter, retrospective study that evaluated the etiological factors of the patients with end-stage chronic liver disease who underwent LT between 2010 and 2020. A total of 5,080 adult patients with LT was included into the study. The time frame was divided as January 1, 2010 to December 31, 2014 (first period) and January 1, 2015 to December 31, 2020 (second period) (Table 1). The data from 11 LT centers was reviewed in this study.

RESULTS: Mean age was 50.3 years; their gender was predominantly female (69.5%). Chronic viral hepatitis (46.4%) was the most common etiological factors leading to transplantation in the overall cohort. The indications were categorized as viral hepatitis, alcohol-related liver disease (ALD), non-alcoholic fatty liver disease (NAFLD), autoimmune liver diseases (AIH, PBC, PSC) and miscellaneous factors. Hepatitis B virus (HBV) infection (35.2%) was the main etiology, followed by cryptogenic cirrhosis (23.5%), hepatitis C virus infection (8.2%), and ALD (6.2%). Hepatocellular carcinoma (HCC) was the LT indication for 939 patients (18.5%). In the second period, the proportion of viral hepatitis was decreased, whereas the proportion of NAFLD-related and ALD-related cirrhosis was increased. HCC also increased in second period (Table 1).

CONCLUSION: The present study reports that chronic viral hepatitis as the main cause in indication of LT in Turkey and suggest that the proportion of viral hepatitis is beginning to decline, while the prevalence of fatty liver disease is increasing.

Keywords: Liver transplantation, cirrhosis, etiology

Table 1. Demographic data and etiologic changes in adult liver transplant patients

	Periods	Periods	
Demographic and etiologic parameters	2010-2014 (n:1677)	2015-2020 (n:3403)	P
Age (year), mean±SD	49.95±1.92	50.68±5.75	0.707
Male/Female, n (%)	509 (%30.4) / 1168 (%69.6)	1037 (%30.5) / 2366 (%69.5)	0.930
Live LT/Deceased LT, n (%)	1244 (%74.2)/ 433 (%25.8)	2807 (%82.5) / 596 (%17.5)	<0.001
HCC, n (%)	277 (%16.5)	662 (%19.5)	0.011
Etiology, n (%)			
Viral Hepatitis			
HBV	668 (%39.8)	1125 (%33.1)	<0.001
HCV	196 (%11.7)	223 (%6.6)	<0.001
HDV	148 (%8.8)	110 (%3.2)	<0.001
Autoimmune liver diseases			
AIH	56 (%3.3)	167 (%4.9)	0.010
PBC	24 (%1.4)	64 (%1.9)	0.248
PSC	18 (%1.1)	97 (%2.9)	<0.001
NAFLD	5 (%0.3)	82 (%2.4)	<0.001
ALD	69 (%4.1)	250 (%7.3)	<0.001
Miscellaneous			
CC	347 (%20.7)	849 (%24.9)	0.001
WD	57 (%3.4)	65 (%1.9)	0.001
BCS	28 (%1.7)	103 (%3)	0.004
HC	3 (%0.2)	9 (%0.3)	0.761
AAD	3 (%0.2)	10 (%0.3)	0.564
Others	55 (%3.3)	245 (%7.2)	<0.001

OP-07

Novel isoxazole-piperazine derivatives inhibit the stemness of HCC cells

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OBJECTIVES: Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver and a leading cause of cancer-related death worldwide. Sorafenib is currently used as first-line therapy for advanced HCC. Unfortunately, heterogeneity plays a crucial role in developing resistance to Sorafenib which needs urgent solution. Cancer stem cells (CSCs) were reported to participate in therapeutic resistance in HCC. Therefore, it is essential to discover new therapeutics which target not only cancer cells but also CSCs. Here, we investigated

the anti-cancer activity of novel isoxazole-piperazine derivatives, especially focusing on their effects on stemness properties.

MATERIALS & METHODS: Cellular cytotoxicity of compounds was determined by NCI-SRB assay and RT-CES analysis. Flow cytometry was used for cell cycle analysis and detection of cellular apoptosis. Nuclear blebbing was visualized by Hoechst staining using fluorescence microscopy. Immunoblot analysis was performed to assess the levels of cell cycle and apoptosis-related proteins. CSC marker expression by flow cytometry and sphere formation assay was done to analyze the LCSC enrichment in HCC cells.

RESULTS: Among more than 50 compounds tested, two of them (1a and 1b) showed noticeable cytotoxic activities and selected to be screened against HCC cells. Both compounds were identified as auspicious anti-cancer agents and induced time- and dose-dependent growth inhibition and apoptosis involving Akt pathway inactivation due to cell cycle arrest in G1 and G2/M phases. The phosphorylation of Akt and Erk proteins were decreased upon 1a and 1b treatment. Furthermore, the expression of LCSC markers was decreased. Additionally, by decrease in the sphere size and sphere count indicated that LCSC enrichment was also disturbed.

CONCLUSIONS: Altogether, our findings show that these compounds can be considered as promising anti-cancer agents for liver cancer therapeutics with the advantage of elimination of CSCs in HCC.

This study was supported by Research Grants from TUBITAK (#214S062) and METU-BAP (TEZ-D-312-2021-10745).

Keywords: Cancer biology, medicinal chemistry, drug discovery, hepatocellular carcinoma, liver cancer stem cells

OP-08

The effect of clinicopathologic findings of hepatocellular carcinoma on posttransplant survival: A multicenter cohort from TASL liver transplantation special interest group

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OBJECTIVES: The aim of the present study was to determine the effect of clinicopathological findings of hepatocellular carcinoma (HCC) on posttransplant survival.

MATERIALS & METHODS: Based on the results of the study, viral hepatitis remains the most frequent etiology of HCC in Turkey. High serum AFP levels, poor histologic differentiation and microvascular invasion significantly affect the posttransplant outcome. Donor type does not significantly affect posttransplant survival in patients with HCC. This was a multicenter retrospective study of patients with HCC undergoing LT from 10 tertiary center in Turkey between 2002 and 2020. Datas were retrieved from standardized electronic case report forms in each center.

RESULTS: A total of 1428 patients with HCC underwent LT were included into the study. Viral hepatitis was the most common etiology accounting for 75.6% of patients. Hepatitis B infection was the most cause (58.6%) followed by hepatitis C (12.6%), and cryptogenic (13.8%). The mean overall survival (OS) was 178.2 months, whereas the mean progression free survival (PFS) was 44 months. The one and five-year estimated overall survival rate was found 89% and 80. Overall and disease-free survival did not significant differ between patients with Living Donor LT and patients with Deceased Donor LT (Log Rank for OS p=0.148 and for PFS p=0.137, respectively).

CONCLUSION: In univariate analysis, serum AFP level, histologic differentiation, tumor size, Milan and UCSF criteria, the number of tumors, the presence of microvascular and macrovascular invasion were significantly associated with patient survival (p<0.05).

Table 1. The demographics of the patients

Age	56.1 ±8.5
Gender (Male) (%)	79.7
Cirrhosis (%)	69.2
Etiology (%)	
Hepatitis B	58.6
Cryptogenic	13.8
Hepatitis C	12.6
Delta hepatitis	4.4
Alcohol	4.1
Nafld/Nash	2.6
Others	3.9
AFP	326±5548
Transplantation Type (Living donor/Cadaveric) (%)	66.9/33.1
MELD (0-14) (%)	67.4
MELD >14 (%)	32.6
Child Pugh Score	7.27±2.1
A (%)	44
B (%)	38
C (%)	18

Table 2. The comparison of recurring and non-recurrence groups

	Recurrence Group	Non-Recurrence Group	P value
Age	54.7 ±9.8	56.1±8.2	p>0.05
Gender (Male) (%)	87.9	84.2	p>0.05
Cirrhosis (%)	95.4	93.7	p=0.495
AFP	1825±16311	135.2±739.2	p<0.001
0-9 (%)	35.9	52.3	p<0.001
10-99 (%)	33.1	33.5	p<0.001
100-499 (%)	18.2	10.2	p<0.001
500-999 (%)	5.4	1.9	p<0.001
>1000 (%)	7.4	2.1	p<0.001
Transplantation Type Living donor/Cadaveric (%)	80.6/19.4	79.6/20.4	p>0.05
MELD (0-14) (%)	69.1	67.2	p>0.05
MELD >14 (%)	30.9	32.8	
Total Tumor Diameter	79.7±53.8	46.3±37.4	p<0.001
The Largest Tumor Diameter	53.8±38.6	33.1±24.4	p<0.001
Total Tumor Number	4±3.6	2.2±2.2	p<0.001
Milan (in/out) (%)	38.7/61.3	70.6/29.4	
UCSF (in/out) (%)	49/51	78.3/21.7	
Tumor Histopatology (%)			p<0.001
Poor differentiated	25	9.4	
Mild differentiated	57.3	50	
Well differentiated	17.7	40.6	
Lymph node invasion (%)	42.9	24.4	p<0.05
Microvascular invasion (%)	59.9	24.5	p<0.001
Macrovascular invasion (%)	44.1	17.2	p<0.001

PP-01

Gastric cancer presented with high AFP levels: A case report

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OBJECTIVES: Alpha-fetoprotein (AFP)-producing gastric cancer (AFP-GC) is a relatively rare type of gastric cancer (GC). Here we want to introduce a case of GC presented with high levels of AFP.

MATERIALS & METHODS: A 57-year-old postmenopausal female patient was found to have Hg: 7 g/dl in the examinations performed due to fatigue. In the gastrointestinal system scan, an ulcerovegetant mass lesion covering almost 1/3 of the wall of the stomach angulus was detected. The biopsy sample was reported as C-ERBB2 negative intestinal type adenocarcinoma. Abdominal CT showed hypodense lesions interpreted in favor of multiple metastases in the liver. The patient was considered to have metastatic stomach Ca to the liver, and chemotherapy was started with the XELOX protocol. However, in the tumor markers measured before the treatment, Ca 19-9 was normal, CEA: 4.15 (0-2.5) ng/ml, while AFP: 325.4 (0-8) ng/ml. Abdominal CT performed after the 5th cycle of XELOX showed both dimensional and numerical regression in liver metastases. In addition, AFP level decreased to 199 ng/ml. While the chemotherapy protocol was in progress, the patient who came to the Emergency Department after falling out of bed died due to trauma.

CONCLUSION: AFP commonly serves as an important tumor marker for HCC or yolk sac tumors. However, except these cancers, gastric cancer is the most common cancer that secrete AFP. AFPGC is a relatively rare type of malignancy, which comprises 2.7-8% of all GCs. AFPGC is characterized by a high incidence of metastases to the liver and lymph nodes, and had a poor prognosis.

Keywords: AFP, gastric cancer, liver metastasis

PP-02

Evaluation of lactate elevation in intensive care unit follow-up after hepato pancreato biliary surgery

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OBJECTIVES: Lactate elevation develops in post-op follow-up in patients undergoing Hepato Pancreato Biliary Surgery. In our study; We aimed to determine the time when serum lactate level decreased to normal limits with fluid therapy applied to patients who were followed up in our tertiary intensive care unit in the post-operative period and had an increase in serum lactate levels.

MATERIALS & METHODS: In the intensive care unit of Başakşehir Çam and Sakura City Hospital Organ Transplantation and Hepato Pancreato Biliary Surgery during a 10-month period. The records of 77 patients who underwent hepatectomy, major hepato biliary resection, whipple procedure, and distal pancreatomy were reviewed retrospectively. 51 (25 female, 26 male) patients whose lactate level was above 2 mmol/l in arterial blood gas tests were included in the study. The amount of fluid given to these patients (cc/kg) was calculated.

RESULTS: The median (borderline) age of the patients was 50 (2-81). In arterial blood gas analysis, the lactate level reached its highest level at the median ninth hour (8-12). The highest lactate level was found to be median seven (2-16). The median time for the lactate level to return to normal was 12 (4-30) hours.

CONCLUSION: Lactate serum lactate level, which indicates organ perfusion disorder, is high in patients who have undergone Hepato Pancreato Biliary surgery. In these patients, fluid replacement should be at the earliest and adequate level. We concluded that fluid replacement should be applied to the patient, just as in sepsis/septic shock.

Keywords: Fluid management, lactate, liver surgery

PP-03

Yubi-wakka" (Finger Ring) test and "o ring" test: A practical tool for detecting sarcopenia in end stage liver disease, a pilot study

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OBJECTIVES: Sarcopenia in patients with cirrhosis has been shown to be associated with poor prognosis and complications, independent of MELD score and other risk factors. There is a need for easily applicable tests to practically evaluate muscle mass status and strength in patients with cirrhosis. In this study, we aimed to investigate the utility of finger-ring test and O-ring test in the diagnosis of sarcopenia in cirrhotic patients.

MATERIAL & METHODS: A total of 16 cirrhosis patients, 10 males and 6 females, who applied to our outpatient clinic and underwent abdominopelvic tomography for various reasons and did not have pretibial edema, were included in the study. The muscle strength of the patients was evaluated with a hand dynamometer using three measurements on the non-dominant hand and taking the average. The 'Frailty Index' calculation was made. The muscle atrophy index of the patients was calculated by the ratio of the area of the psoas muscle measured at the level of the lumbar 3 vertebrae on the tomography to the square of the patient's height. Muscle strength and muscle atrophy indices were compared with finger-ring test (Fig. 1) and O-ring test (Fig. 2).

RESULTS: The mean body mass index was 26.6 kg/m². A statistically significant difference was found between those with small and normal finger circle tests in terms of Frailty Index and muscle atrophy index (p=0.000 and p=0.012, respectively). When those with weak O-ring test and those with normal tests were compared in terms of Frailty Index and atrophy index, a statistically significant difference was found (p=0.000 and p=0.012, respectively). A statistically significant difference was found between those with weak O-ring test and those with normal muscle strength measured by hand dynamometer (p=0.009).

CONCLUSION: Finger-ring test and O-ring test offer a practical approach to investigate the presence of sarcopenia in cirrhotic patients.

Keywords: Cirrhosis, sarcopenia, Yubi-wakka" (finger ring) Test and "O Ring" Test

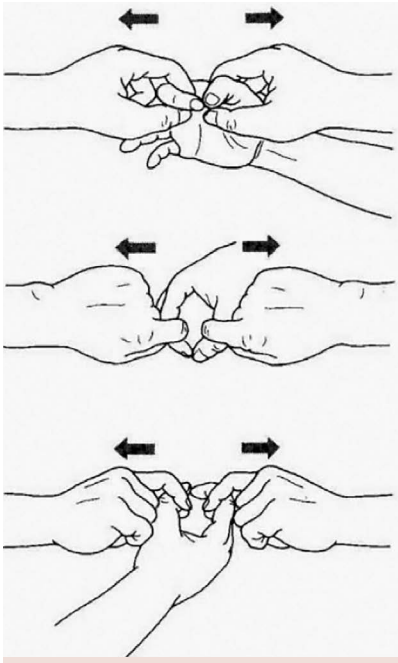

Figure 1. Finger O Ring Test.

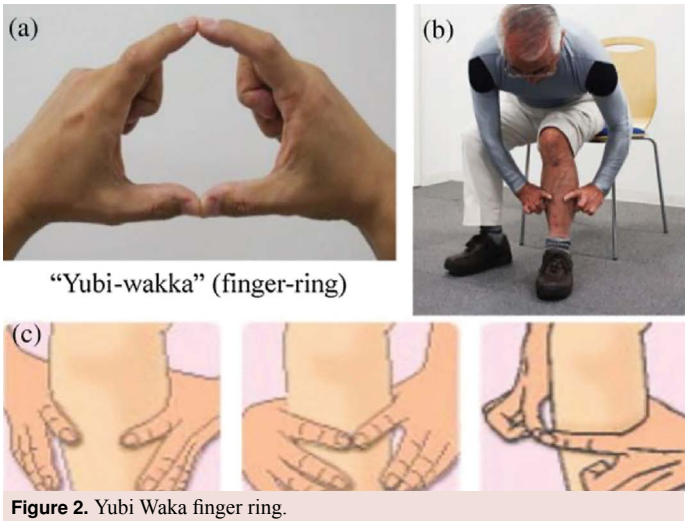

Figure 2. Yubi Waka finger ring.

PP-05

Evaluation of HBsAg (hepatitis b surface antigen) seroclirence in patients with hepatitis B

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OBJECTIVES: HBsAg loss is the most important endpoint, as it shows deep suppression of HBV replication and viral protein expression. This study was aimed to retrospectively evaluate the HBsAg seroclearance/seroconversion status in patients with acute or chronic hepatitis B (CHB) diagnosis.

MATERIALS & METHODS: Patients diagnosed with acute or CHB at the Harran University Faculty of Medicine Department of Gastroenterology between January 2012-December 2020 were included in the study. The study was designed as a retrospective historical cohort. Experimental analysis of the data was done with the help of the SPSS version 22.0 package program.

RESULTS: Of 1053 patients with positive HBsAg, 854 patients with sufficient data in their files were included in the study. The mean duration of illness was 86.13±72.92 months. In the 9-year follow-up of 854 patients, 65 (7.9%) of the last HBsAg test were negative and seroclearance had developed. The last anti-HBs test was positive in 49 (75.4%) of 65 patients who developed seroclearance, and it was found that seroconversion had developed. Twenty-seven of 30 (90%) of the patients who developed seroclearance had liver transplantation. Sixteen of 19 (84.2%) of them had acute hepatitis B, 14 of 477 (2.9%) were hepatitis carriers, 5 of 201 (2.5%) had e-negative CHB, 2 of 36 (5.6%) had cirrhosis, and 1 of 43 (2.3%) of them were delta hepatitis who developed seroclearance disease, none of the 38 e-positive CHB patients developed seroclearance.

CONCLUSION: In the 9-year follow-up of patients who were positive for HBsAg at their first admission, approximately one-tenth (7.9%) developed seroclearance, and two-thirds also developed seroconversion. After liver transplantation and acute hepatitis B, almost all patients developed seroclearance, whereas, in approximately three per cent of carriers (e-negative chronic hepatitis B and cirrhotic patients) seroclearance developed.

Keywords: Chronic hepatitis B infection, HBsAg, seroclearance/seroconversion

PP-06

A case with Wilson's disease showing atypic presentation

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Wilson's disease is a rare autosomal recessive inherited disease of copper metabolism and it causes various hepatic, neurological and psychiatric symptoms. It's caused by mutations in the ATP7B gene. Mutations in the ATP7B gene prevent the transport protein from working properly. As a result, an excessive amount of copper accumulates in the body. Copper mineral is essential for many cellular functions but it's toxic in excessive amounts. We present a case Wilson's disease who admitted to our hospital with elevated liver enzymes and low platelet count but, further examination showed severe liver injury with septal fibrosis without any hepatic copper deposition.

Keywords: Wilson's, hepatic fibrosis, restrictive diet

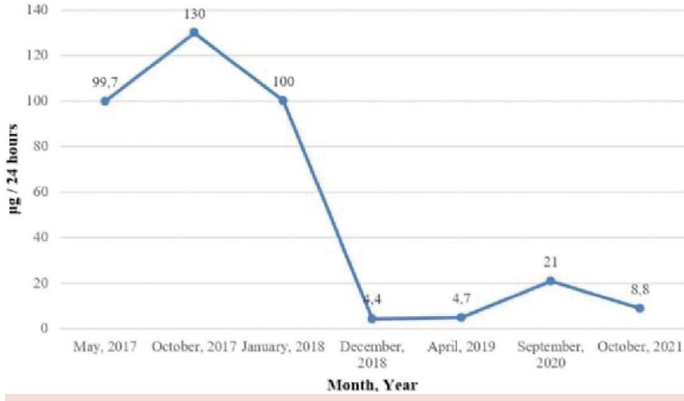

Figure 1. 24-hour urine copper levels.

PP-07

A single center experience: Liver biopsy results during a year

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OBJECTIVES: Liver biopsy is the gold standard method for the diagnosis and treatment of liver diseases. We aimed to evaluate the results of liver biopsies and we also aimed if these liver biopsies could reveal the etiology of liver disease in patients with elavations of transaminases or/and alkaline phosphatase levels or liver masses.

MATERIALS & METHODS: The patiens who had liver biopsies for persistantly elevated liver function tests, protocol biopsies after liver transplantation or liver masses in our hepatology clinic between 2011 and 2012 were included to the study. Liver biopsies were previously performed using classical percutaneous liver biopsy or ultrasonography-guided Sonocan® liver biopsy sets. The pathology results of liver biopsies and clinical data of the matching patients were obtained from the liver biopsy record archives and patient files, respectively.

RESULTS: 479 liver biopsy results (M=252, 52.6%; mean age 49±14.5) were evaluated in the study. Of these patients, 432 (M=228) underwent percutaneous liver biopsy and 47 (M=24) underwent Sonocan® needle biopsy. The most common histopathologic diagnoses in the percutaneous liver biopsy group were chronic hepatitis B (n=127; 29.3%), normal histopathological findings (n=50; 11.6% and 32 of them were protocol biopsies after liver transplantation), and non-alcoholic steatohepatitis (NASH, n=41; 9.4%). The most common histopathologic diagnoses in the Sonocan® group were 25 liver metastasis out of 29 liver tumors (n=25; 53.2% of all) chronic hepatitis B (n=5; 10.6%), and NASH (n=3; 6.4%).

CONCLUSION: In this study, diversity in liver biopsy results indicates the importance of histopathological evaluation. The most prevalant pathology in the liver biopsies was chronic hepatitis B as the most common chronic liver disease in Turkey. Metastatic liver tumor was the most common one among the liver masses.

Keywords: Liver biopsy, fatty liver, hepatitis, cirrhosis

Table 1. Liver biopsy results of the patients

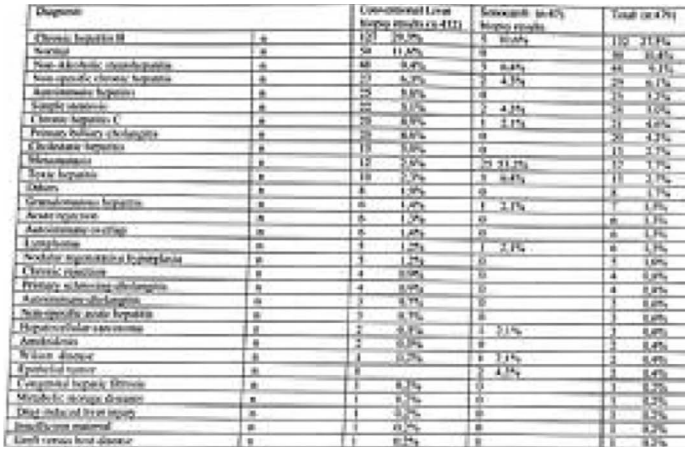

Table 2: The distributions of patients with normal histopathological liver biopsies

Reason for Liver biopsies	Number of patients
Protocol biopsies after liver transplantation	32
Elevated transaminase levels	13
HBV infection before renal transplantation	1
Variceal hemarage	1
Portal vein trombosis	1
Sjogren syndrome	1
Chronic Hepatitis B infection	1

Table 3 Fatty liver and Non-Alcoholic steatohepatitis rates in different liver disease

Diagnosis	Fatty Liver	NASH
Hepatitis B (n:132)	17 (12.8%)	1 (0.8%)
Hepatitis C (n:26)	4 (15.3%)	1 (3%)
Autoimmune hepatitis (n: 25)	1 (4%)	2 (8%)
Acute rejection (n:6)	1 (16%)	0
Primary biliary cholangitis (n:20)	1 (5%)	0

PP-09

A case of gastric adenocarcinoma presenting with liver mass and high AFP levels

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OBJECTIVES: Elevated alpha-fetoprotein (AFP) levels in adults are considered abnormal. AFP is mostly used in the diagnosis and follow-up of hepatocellular carcinoma and yolk sac tumors. Most common among other rare tumors with elevated serum AFP levels is stomach cancer. Here, we present a case with hepatic mass and elevated AFP, in which diagnosed as metastatic gastric adenocarcinoma.

CASE: A 65-year-old male patient was referred to us because of the detection of a mass lesion in the liver in an external center ultrasonographic examination. The patient has pain in the epigastrium and right upper quadrant for the last 1 month. In biochemical analysis AFP: 60, HG: 10.2, MCV: 73.8. Except these, all other blood tests were found normal. HBsAG and Anti-HCV were negative. At magnetic resonance examination non-enhancing, diffusion-restricting lesions (58 mm lesion in segment 4B and 14 mm lesion in segment 2) consistent with metastasis was seen. Also, a 62*49 mm mass lesion with heterogeneous contrast enhancement and diffusion restriction having exophytic extension from the head of the pancreas, which may be a primary focus, was detected. A 12 mm round lymph node was seen at the superior of the lesion. The spleen was normal size. At gastroduodenoscopy a 5-6 cm dimeter ulcerated-necrotic tumoral mass was detected on the posterior wall of the antrum. A similar 2-3 cm ulcero-necrotic lesion was sen at the bulbus as well, suggesting that the lesion in the stomach invades the bulb. Biopsies taken from both the stomach and bulbus were reported as adenocarcinoma. Result: Presence of high AFP levels together with liver masses showing metastatic features, especially in the absence of clinical signs of cirrhosis and viral infection serology, AFP-producing hepatoid gastric adenocarcinoma should be considered in differential diagnosis.

Keywords: AFP, gastric adenocarcinoma, liver mass

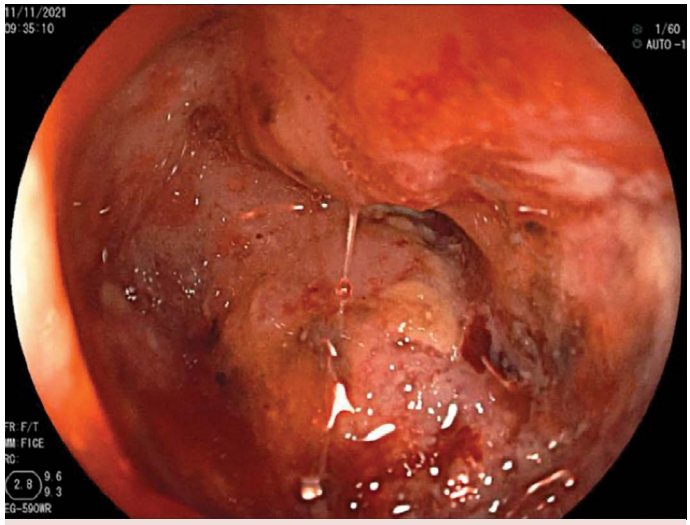

Figure 1. Ulcero-necrotic lesion at the antrum.

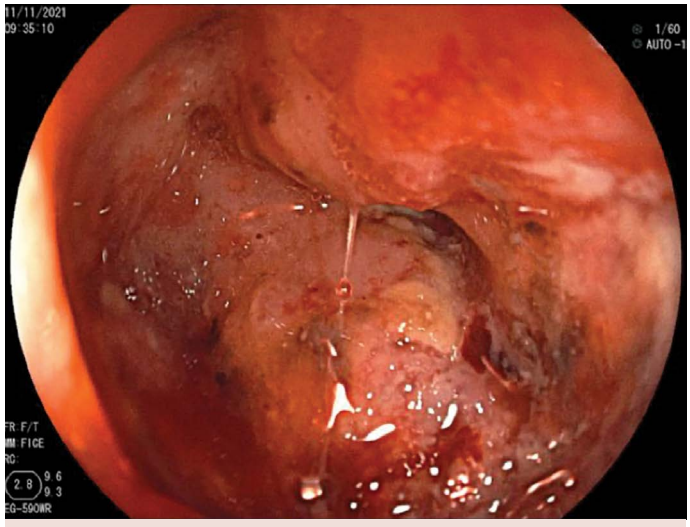

Figure 2. Ulcero-necrotic lesion at the bulbus.

PP-10

Efficacy and safety of tenofovir alefenamide in hepatitis B virus-infected patients with chronic hemodialysis and renal transplantation: A preliminary result

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OBJECTIVES: There are very limited data regarding the efficacy and safety of tenofovir alafenamide fumarate (TAF) in hemodialysis patients and renal transplant recipients. The aims of the present study were to assess the efficacy and tolerability of TAF treatment in hepatitis B virus-infected patients with chronic hemodialysis and renal transplant recipients.

MATERIALS & METHODS: This is a multicentric study. Between January 2019 and November 2021, HBV-infected patients with hemodialysis and renal transplantation from 17 tertiary centers of Turkey were enrolled. Data were entered in a standardized electronic case report form (CRF) from each center and collected from the CRF. The mean follow-up period was 13.4±5.1 and 14.8±6. months

RESULTS: A total of 77 HBV-infected patients were included into analyses: 16 patients were on hemodialysis and 61 patients had renal transplantation. The mean ages were 54.6±15.6 and 46.8±11.2 years, retrospectively. Male gender was predominant (62.5% vs 70.5%, respectively). Thirty-one patients (12 hemodialysis patients and 19 renal transplant patients) received TAF treatment as first-line therapy, while 46 patients had switched to TAF treatment. In renal transplant recipients, 82% were on tacrolimus-based, 23% were on cyclosporin-based and 15% on everolimus-based treatments. During the follow-up period, 12th month's virological response was 96% and biochemical response was 100%, for the renal transplantation group; whereas both of them were 100% for hemodialysis patients. None of the patients had clinical, biochemical, and serological evidence of HBV reactivation after the switch to TAF treatment. TAF treatment was well tolerated. Only one patient discontinued his treatment due to severe nausea.

CONCLUSION: From baseline to the end of the follow-up period, GFR was improved in renal transplant recipients (from 47.8±24.4 to 68.4±22.0) (p=0.001). Serum phosphorus levels and lipid panels did not significantly change.

Keywords: Tenofovir alefenamide, renal transplatation, hemodialysis

PP-11

Biliary complications and management in liver transplant recipients with duct to duct anastomosis: A single center experience

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OBJECTIVES: The aims of this study were to determine biliary complications in liver transplant recipients with duct to duct anastomosis in a single center

experience, to identify the factors affecting the development of biliary complications and to evaluate the success of endoscopic approaches in such recipients.

MATERIALS & METHODS: A total of 174 adult patients with liver disease who underwent liver transplantation (LT) between January 2013-May 2021 were included. Median posttransplant follow-up period was 26 months (4-78 months).

RESULTS: Median age is 54.0 years. Hepatitis B virus infection (32.8%) was the most common indication to LT. Living donor liver transplantation (LDLT) was performed in 86.8% of the patients. The overall prevalence of posttransplant biliary complications was 31% (n=54) among the recipients. Their mean age was 51.8±12.2 years, their gender predominantly was male (64.8%). Anastomotic biliary strictures were the most common biliary complications following LT (n=39, 72.2%), followed by biliary leakage (13%). Recipient age, gender, body mass index, primary etiology of disease, pretransplant MELD score, emergency transplant indication, acute kidney failure prior to LT, donor type and the presence of hepatocellular cancer did not affect on the development of BK (Table 1). Endoscopic retrograde cholangiopancreatography guided drainage and balloon dilation with/without stent placement were the most common treatment modalities in recipients with biliary strictures. The mean duration of endoscopic treatment following LT was 7.2 months with a mean 3±1.6 sessions. The overall complete success rate of endoscopic approaches was 65%. No significant difference in terms of the success rate between recipients with LDLT and deceased donor LT (p>0.05). Three recipients required surgical revision for repairing the biliary complications. Six patients died due to biliary sepsis.

CONCLUSION: Biliary complications were the most frequent complications following LT Biliary strictures and leakages were the most commonly seen. Endoscopic treatment was successful in the majority of such recipients.

Keywords: Liver transplantation, biliary complications, endoscopic retrograde cholangiopancreatography

Table 1. Liver transplantation, biliary complications, endoscopic retrograde cholangiopancreatography

	Patients without biliary complications (n=120)	Patients with biliary Complications (n=54)	p value
Age (Mean±SD)	51.2±12.3	51.8±12.0	0.383
Gender (%) (Female/Male)	%35/%65	%35.2/%64.8	0.136
Body Mass Index (Mean±SD)	26.8±5.2	27.5±4.9	0.352
Serum Albumin (Mean±SD)	3.08±0.56	3.06±0.54	0.156
Serum Creatinine (Median (Min-Max))	0.78 (0.35–3.85)	0.78 (0.36–2.27)	0.66
MELD Score (Median (Min-Max))	16 (6–40)	16 (6–41)	0.94
Emergency Transplant (n/%)	8/%6.7	3/%5.6	0.26
Deceased-Donor Transplantation (n/%)	17/%14.2	6/%11.1	0.17
Living-Donor Lobe-Segment (%) Right lobe/Left Lobe/Right Lateral segment	%88.5/%10.5/%1	%85.7/%12.3/%2	0.08
HCC (n/%)	28/%23	10/%19	0.126

Factors influenced on the development of biliary complications following LT

PP-12

Effects of autocrine secretion of Interleukin-6 on proliferation, migration and stemness of HCC cells

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OBJECTIVES: Irrespective of its etiology, hepatocellular carcinoma (HCC) always develops as a result of chronic inflammation. Evidence from various studies suggested that chronic inflammation is responsible for increasing the incidence and mortality of various types of cancers. Here, we investigated the possible effects of proinflammatory cytokine interleukin-6 (IL-6) in migration, proliferation and liver cancer stem cell (LCSC) populations.

MATERIALS & METHODS: Autocrine secretion of IL-6 in HCC cell lines was determined with ELISA. Effect of IL-6 and its receptor's inhibitor Tocilizumab on viability of HCC cells were determined with the NCI-SRB assay. Migration capacity was determined by both real-time transwell migration and wound healing assays. Flow cytometry and sphere formation assay were used to further investigate LCSC enrichment in HCC cell lines after treatment with IL-6 or Tocilizumab.

RESULTS: ELISA revealed that IL-6 was secreted by mesenchymal-like cells such as FOCUS and SNU182 cells but not in epithelial-like cells like Huh7. IL-6 stimulation and Tocilizumab treatment did not have a significant effect on proliferation in HCC cell lines. However, IL-6 significantly increased the migration capacity of HCC cell lines. CD133 and EpCAM were upregulated upon IL-6 treatment. Furthermore, IL-6 increased the sphere formation capacity of Huh7 cells significantly. Additionally, Tocilizumab inhibited LCSC enrichment by decreasing LCSC marker expression in FOCUS cells.

CONCLUSION: Altogether, IL-6 signaling pathway's effects on LCSC enrichment, sphere formation capacity and cell migration capacity indicated that IL-6 signaling pathway is an important pathway in the progression of HCC and in addition to conventional therapy methods, targeting IL-6 signaling pathway may be beneficial with the advantage of elimination of stem-like cancer cells and migration capacity of HCC cells.

Keywords: Proinflammatory cytokines, LCSC, inflammation, EMT

PP-13

Parameters predicting microvascular invasion and poor differentiation in hepatocellular carcinoma patients with normal AFP level

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OBJECTIVES: To evaluate the parameters which might be associated with the pathologically diagnosed microvascular invasion (MIVI) and poor differentiation, using complete blood count and routine clinical biochemistry tests results, in hepatocellular carcinoma (HCC) patients before liver transplantation

MATERIALS & METHODS: The data of the patients who underwent liver transplantation for HCC at Inonu University Liver Transplant Institue, between March 2006 and November 2021 was researched retrospectively. Demographic information of the patients, results of routine hematological and biochemical tests performed before transplantation, the recurrence rate after transplantation, pathological characteristics of primary tumor (maximum tumor diameter, number of nodules, degree of differentiation, presence of microvascular invasion) were recorded. The effects of these variables on the presence of microvascular invasion presence or poor differentiation were statistically analyzed by using univariate and multivariate analyses methods.

RESULTS: Incidence of microvascular invasion or poor differentiation rate, recurrences after liver transplantation and median recurrence rate, in patients with normal AFP level, were 28.6%, 9.3%, 12.1%, 13 months respectively. After univariate, and multivariate analyzes, Maximum Tumor Diamater (MTD) >4.5 cm and number of nodule >5 were found to be independent risk factors for MIVI, and number of nodule >4 and Mean

Platelet Volume (MPV) <=8.6 fL were found to be independent risk factors for poor differentiation. The serum AFP levels were still normal at the recurrence time, in the 53% of the patients who had recurrence after liver transplantation.

CONCLUSION: In HCC patients whose AFP level is normal before liver transplantation, independent risk factors of the presence of MİVİ, were, MTD and number of nodules, and independent risk factors of poor differentiation, were, MPV and number of nodules. Furthermore, serum AFP levels of 53% of the HCC patients whose AFP levels were normal before liver transplantation, were normal even at the recurrence time, but serum AFP levels were elevated 47% of the patients at recurrence time.

Keywords: Negative AFP, malignancy, living donor, relaps, microscopic

Table 1.

		Poorly differentiation			Poorly differentiation	
		Univariate			Multivariate	
Parameters	OR	95% CI	p	OR	95% CI	p
number of nodules	1.312	1.121-1.536	0.001	1.274	1.082-1500	0.004
Neu #	1.157	1.001-1.338	0.049			
MPV	0.552	0.355-0.859	0.008	0.579	0.363-0.923	0.022
Creatin	0.007	0.000-0.511	0.023			
		MIVI positivity			MIVI positivity	
MTD, cm	1.657	1.366-2.009	<0.001	1.492	1.230-1.810	<0.001
number of nodules	1.551	1.292-1.862	<0.001	1.417	1.134-1.771	0.002
Neu #	1.164	1.028-1.317	0.016			
Lym #	1.897	1.195-3.010	0.007			
Platelets	1.006	1.002-1.011	0.003			
AST	1.009	1.002-1.017	0.015			
ALT	1.006	1.000-1.013	0.044			

Univariate and Multivariate analysis of the parameters on the effect of poorly differentiation and MIVI positivity

Table 2.

Number of nodules	Poorly differentiation #	Poorly differentiation %	p
1 (n=82)	4/82	4.9	
2-5 (n=40)	3/40	7.5	
>5 (n=18)	6/18	33.3	0.002
MPV, fl	Poorly differentiation #	Poorly differentiation %	
>8.6 (n=96)	4/98	4.1	
<= 8.6 (n=39)	9/39	23.1	0.002
Number of nodules	MIVI positivity #	MIVI positivity %	p
1 (n=82)	15/82	18.3	
2-5 (n=40)	9/40	22.5	
>5 (n=18)	16/18	88.9	<0.001
MTD, cm	MIVI positivity #	MIVI positivity %	
<3 (n=76)	10/76	13.2	
3-5 (n=36)	8/36	22.2	
>5 (n=28)	22/28	78.6	<0.001

MIVI positivity and poorly differantiation rates according to number of nodules, MTD and MPV

PP-14

Synergistic effect of naproxen and sorafenib on hepatocellular carcinoma

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OBJECTIVES: Hepatocellular Carcinoma (HCC) which develops on a background of chronic liver inflammation, is one of the most prominent primary liver cancer type and a leading cause of cancer-related deaths worldwide. Due to the resistance to targeted therapies, combination therapy has become an important strategy to increase the efficacy of treatment. Recently, non-steroidal anti-inflammatory drugs (NSAIDs) possess anti-cancer activity in many cancer types. In this study, we aimed to find synergistic interaction between sorafenib and four different NSAIDs.

MATERIALS & METHODS: Cellular cytotoxicity of sorafenib in combination with naproxen, aspirin, ibuprofen and flurbiprofen was determined by NCI-SRB assay. Growth inhibition results were analyzed by SynergyFinder, which is a web-based application that analyzes synergistic interactions between drug pairs. Synergistic effect of sorafenib and naproxen was further investigated with Real Time Cell Electronic Sensing (RT-CES) analysis. Cells were stained with PI for cell cycle analysis or with Annexin-V/PI for analysis of apoptotic cells to determine the changes in cell cycle distribution and induction of apoptosis by flow cytometry.

RESULTS: According to NCI-SRB results that were analyzed by SynergyFinder tool, combination of sorafenib and naproxen synergistically inhibited growth of HCC cells. Although naproxen alone had no significant effect on cell viability, combination of 5 µM sorafenib and 400 µM naproxen resulted in higher growth inhibition in HCC cells compared to the effect of sorafenib alone. Moreover, upon combination of both drugs, apoptotic cell death was significantly increased and G1 arrest in HCC cells were enhanced compared to cells treated with Sorafenib alone.

CONCLUSION: Altogether, this study shows that naproxen synergistically enhances cytotoxicity of sorafenib on HCC cells, which could be a potential therapeutic option for HCC patients.

Keywords: HCC, synergy, sorafenib, naproxen

PP-15

An autoimmune-like herb related serious hepatitis case related with multi-ingredient herbal tea consumption

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OBJECTIVES: Liver injury due to herbal and dietary supplements (HDS) incorporate a variety of agents, primarily multi-ingredient nutritional or dietary supplements and body building products with anabolic steroids. Autoimmune-like DILI/HDS term has been used for cases of acute hepatocellular injury with elevated autoantibodies, female predominance and histological features resembling AIH that are timely associated with a drug, herb or supplement intake as a trigger.

MATERIALS & METHODS: A 66-year-old female patient was admitted to our hospital emergency unit with the complaints of darkening of the urine color for 10 days and yellowing of the eyes and nausea for 2 days. It was learned that the patient, who did not have any health problems in the past, was trying to lose weight

under the control of a dietitian and had consumed form teas of a famous brand for 2 months. The herbal teas that the patient drank were a mixture containing many herbs. Some of these were: alder buckthorn, birch, chamomile, cherry stalk, fennel, juniper, rose hip, senna, St. John's wort, stinging nettle, yarrow, etc. She did not have any disease in the past. Her BMI was 26. Anormal laboratory values were as follow: ALT 1696 U/L, AST 1528 U/L, GGT 242 U/L, ALP 244 U/L and total/direct bilirubin 6.48/5.8 mg/dl. Her viral markers were found negative. Her immunoglobulin levels were within normal limit. Anti-nuclear antibody was found positive. Other antibodies were negative. In the follow-up, bilirubin levels increased, and prothrombin time was prolonged. The patient was asked to undergo liver biopsy, but the patient refused. With the diagnosis autoimmune-like herb related serious hepatitis methyl prednisolone 40 mg/day was started. The patient recovered uneventfully.

CONCLUSION: We found it appropriate to present this case in order to emphasize the possible harms of widely used herbal teas containing many substances.

Keywords: Autoimmune-like DILI/HBS, hepatotoxicity, herbal tea

PP-16

Acute alcoholic hepatitis resulted in death of a new diagnosed cirrhosis patient

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OBJECTIVES: Alcoholic hepatitis is most likely to occur in people who drink heavily over many years. However, the relationship between drinking and alcoholic hepatitis is complex. Not all heavy drinkers develop alcoholic hepatitis, and the disease can occur in people who drink only moderately.

CASE: In our case a 57 yo male applied to ICU, because of extreme fatigue, unable to eat and jaundice. His lab counts are; wbc: 4500 plt: 48000 total bilirubin: 14.8 direct bilirubin: 11.6 inr: 2.33 and albumin: 2.1. He was taken to the gastroenterology unit. Patient was a heavy drinker for 30 years, drunk about 100-120 mg alcohol per day at least. Before his admission to ICU he drunk about 180 mg alcohol 3 days ago. His hepatobilier USG revealed that his liver is cirrhotic and he has the signs of portal hypertension such as splenomegaly. He was diagnosed as acute alholic hepatitis on chronic liver disease. Maddrey discriminant function was calculated as 41 points so steroid therapy was started. During follow up, his clinival status detoriated within day and bilirubin levels exceeded 24 mg/dl. Morever the patient became septic and wide spectrum antibiotics were started. Unfortunately the patient passed away 22. day of his admission.

Keywords: Acute, alcoholic hepatitis, cirrhosis

PP-17

Covid-19 patients with hepatitis B virus infection: Clinical course, mortality, biochemical flare after steroid treatment

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OBJECTIVES: We aim to determine the clinical course and biochemical flare in the COVID-19 patients with serum HBs Ag positive.

MATERIALS & METHODS: We collected data from all patente with COVİD-19 and serum HBs Ag positive admitted at the hospital between September 2019-March 2020. Patients were classified into chronic hepatitis B infection (CHBI) and chronic B hepatitis (CBH) groups according to viral hepatitis serology and treatment history. The primary endpoint in this study was to compare mortality between the CBHI and CHB groups. The secondary endpoint was biochemical flare, defined as an increase of serum ALT to at least two times ULN between 4-12 weeks after treatment in the CHBI group receiving steroid therapy. The steroid treatment was classified as group 1 (methylprednisolone >40 mg day, <=7 days) and group 2 (methylprednisolone >40 mg day, 8-21 days).

RESULTS: We evaluated data from 225 patients [mean age 53.7±15.4; female: 83 (36.9%) male: 142 (63.1)]. Fifty-eight (25.8%) patients needed supplemental oxygen treatment (SOT), 25 (11.1%) required mechanical ventilator support, and 45(%20) died. While serum AST were higher in CHB group (respectively; p<0.001 and p<0.001),there was no significant difference in serum ALT level, steroid treatment, and having more than one comorbid disease (respectively; p=0.356, 0.758 and 0.354). There was no significant relationship between SOT, intubation, or mortality (respectively; p=0.447, p: 0.067, and p: 0.092). Thirty percent of patients with CHIB received steroid treatment and, 51% of these patients died. Twenty-eight percent of patients with CBH received steroid treatment, 33% of these patients died. Biochemical flare was more common in group 2 steroid-treated patients than group 1. However, the data are insufficient in terms of statistical significance.

CONCLUSION: There is no difference in the prognosis of covid-19 between two groups. We need the large population cohort study to evaluate flare risk after steroid treatment in the patients with CBHI.

Keywords: COVID-19, steroid treatment, biochemical flare, hepatitis B infection, HBsAg

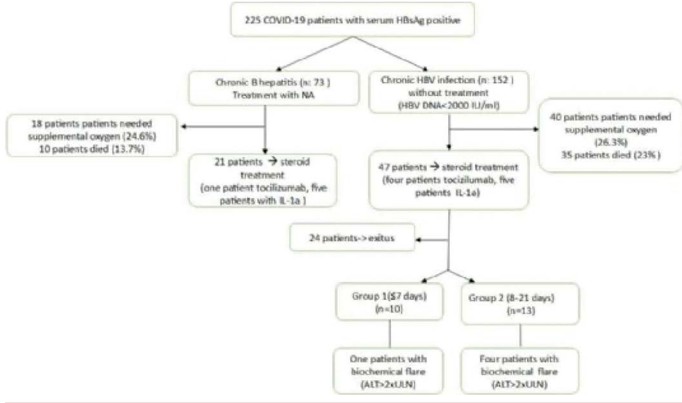

Figure 1.

PP-18

A rare cause of DIC in a patients with Wilson's disease: D-penicillamine

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OBJECTIVES: D-penicillamine therapy is considered an effective and safe treatment for Wilson's disease, although D-penicillamine treatment is a risk fac-

tor for several hematological side effects, such as thrombocytopenia, hemolytic anemia and development of thrombotic thrombocytopenic purpura. There is no report in the literature about the development of disseminated intravascular coagulation (DIC) with the use of the drug, except for one experimental study.

CASE: 24 years old female patient with Wilson disease, followed up with zinc and D-penicillamine treatment, was admitted to the emergency service because of oral mucosal bleeding and lethargy. There was no pathology in the brain tomography, hepatic encephalopathy (HE) stage 2 was diagnosed, and HE treatment was started. Initial laboratory tests showed hemoglobin 7.1g/dl (11.7-15.5), platelet 24x10^3/µL (159-388), total bilirubin 18 mg/dl (0.3-1.2), direct bilirubin 9.8 mg/dl (0-0.2), INR>10 (0.8-1.2), APTT 64.5sec (22.5-32), fibrinogen 23 mg/dl (180-350), factor 8% 26.4 (70-150) there were no acute infection or hepatotoxic injury as possible cause of acute on chronic liver failure. Melena, hematemesis and hematochezia were not present, and no active bleeding focus was detected on endoscopic evaluation. Upon meeting the DIC criteria, the patient underwent plasma exchange four times as for the treatment of acute on chronic liver failure. Haemocomplettan-P, Cryoprecipitate replacements were done as supportive treatment for the DIC. Since the clinical bleeding continued inspite of plazma exchanges and factor replacement treatment, D-penicillamine was switched to trientine (1250 mg/day). After this change, the mucosal bleeding stopped, DIC parameters improved. The factor replacement was no longer needed for last 4 months follow up period.

CONCLUSION: It is the first report of a patient presenting with DIC with possible association to D-penicillamine usage for Wilson's disease. We suggest that if hemorrhagic complications develops on D-penicillamine treatment, beside side effects of drug on platelets, the possibility of DIC induced by D-penicillamine activating the fibrinolysis should be considered.

Keywords: Wilson's disease, disseminated intravascular coagulation, D-penicillamine

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PP-19

An atypic hepatobiliary toxicity related with honey-herb mixture consumption

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OBJECTIVES: Liver damage due to herbal or dietary supplements (HDS) is a well-known phenomenon. However, idiopathic acute cholangitis together with bile duct dilatation due to HDS is not known.

CASE: A 23-year-old female patient presented to the emergency department with newly developed severe abdominal pain and vomiting. She had been using drospirenone/ethinylestradiol and metformin for 6 months due to polycystic ovary syndrome and insulin resistance. She had been consuming a supplement named "honey and herb mixture with bitter lemon" for 1.5 months due to her dyspeptic complaints. Some of the ingredients of this mixture are raw honey, bitter melon, lemon balm, chamomile, St. John's wort, frankincense resin, etc. She had occasional abdominal pain for last month. She admitted to emergency because his last pain was very severe. ALT was 757 U/L, AST 851 U/L, ALP 102 U/L, GGT 157 U/L and total/direct bilirubin were 3.6/2.3 mg/dl. All viral and auto-immune markers were negative. There were no significant findings other than mild common bile duct dilatation (8-9 mm) on imaging. She was discharged after spontaneous normalisation of laboratory. She re-admitted to the emergency with abdominal pain 4 days after her discharge. Her ALT was 517, AST 283, ALP 208, GGT 372 and total/direct bilirubin were 2.1/1.8. She was continued to consume abovementioned HDS. Progressive dilatation of the common bile duct was detected at tomography (10 mm) and MRI (12 mm) scans performed on consecutive days. There were no other significant findings. Endosonographic ultrasonography had similar findings. Enzymes normalized within 7 days. The common bile duct diameter was found to be normal in MRI.

CONCLUSION: The use of multi-ingredient HDS is becoming more and more common. It is possible to develop toxicity due to the substances they contain or other substances that are likely to be contaminated from the environments in which they are prepared.

Keywords: Bile duct dilatation, hepatotoxicity, herbal or dietary supplements

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PP-20

Amlodipine induced hepatitis

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OBJECTIVES: Amlodipine is a generic, well-known and commonly-prescribed dihydropyridine calcium channel blocker (CCB) used in the treatment of hypertension. Hepatoxicity due to CCBs is a known but uncommon adverse effect, sometimes can be serious. Resolution of clinical situation sometimes takes several months.

CASE: We herein present a case of nifedipine-induced hepatitis in a 54-year-old male with incidentally detected during preoperative evaluation for umbilical hernia repair. He had no prior history of liver or autoimmune disease, liver disease, intravenous drug use, excessive alcohol consumption, recent travel, infectious symptoms, or constitutional symptoms. He had no exposure to poisonous mushrooms or other common hepatotoxic agents. He was on medication for hypertension for 3 years with candesartan+ hydrochlorothiazide, 3 months ago his cardiologist added amlodipine 10 mg. Preoperative laboratory tests revealed elevations in liver enzymes, bilirubin, and LDH—all indicative of significant hepatocellular injury: • ALT 458 U/L • AST 427 U/L • ALP 320 U/L • GGT 264 U/L • Conjugated bilirubin 2 mg/dl • Total bilirubin 0.4 mg/dl • LDH 391 U/L • INR: 1.1. Complete blood count was within normal limits. Tests were also performed to rule out other viral, methabolic and autoimmune etiologies. Hepatobiliary ultrasound findings were normal. After complete evaluation, he was advised to stop the amlodipine and his Liver enzymes started to gradually improve over the 8 weeks.

CONCLUSION: Amlodipine is a member of dihydropyridine group of calcium channel blockers. It blocks the L-type calcium channels and thus prevents entry of calcium into vascular smooth muscle cells. This causes arterial/arteriolar dilatation and reduced blood pressure. It also causes coronary artery dilatation and improves myocardial blood flow. Idiosyncratic drug reactions can be unpredictable, non-reproducible and may have a variable latency period. We accepted this case as a idiosyncratic drug reaction. In current litarature there are few cases has been reported on amlodipine-induced hepatoxicity. Our case is an addition on this sparse group.

Keywords: Amlodipine, hepatotoxicity, DILI

PP-21

Prediction of transplant-free survival in primary biliary cholangitis by FIB-4 score

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OBJECTIVES: In primary biliary cholangitis (PBC), assessment of the disease stage is useful for both prognostic and therapeutic reasons. Patients

with more advanced disease have reduced survival than those in earlier stage. The aim was to assess the utility of baseline FIB-4 score in predicting transplant-free survival.

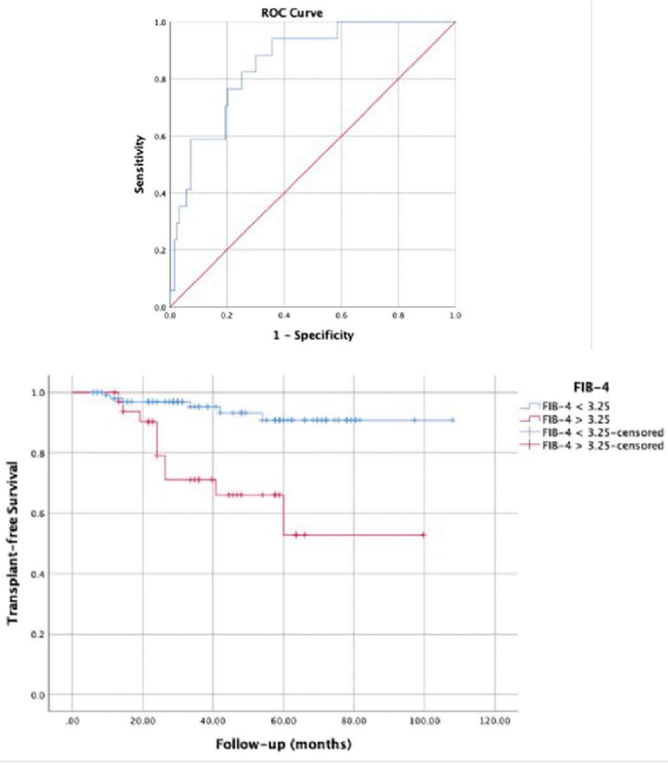
MATERIALS & METHODS: A total of 140 PBC patients (mean age 56.3 years, 82.9% females, median follow-up 36 months) were retrospectively assessed. FIB-4 scores were categorized into three groups: <1.45 (n=62, 44.3%), 1.45-3.25 (n=46, 32.9%), >3.25 (n=32, 22.9%). Receiver operator characteristic (ROC) curve was used to assess the accuracy of FIB-4 to predict transplant-free survival. The influence of the biochemical and clinical variables on transplant-free survival was assessed with multivariable Cox proportional hazards' regressions. To assess the prognostic impact of baseline FIB-4 score, patients were stratified to FIB-4 >3.25 and FIB-4 < 3.25 score to estimate their survival with a Kaplan-Meier curve.

RESULTS: Seventeen patients (12.1%) reached a clinical endpoint: 4 (2.9%) required liver transplantation and 13 (9.3%) died without transplantation. On multivariate analysis, age (HR: 1.09; p=0.001) and bilirubin levels (HR: 1.19; p=0.009) were independent predictors of transplant-free survival. The transplant-free survival was poorer for patients with a FIB-4 score >3.25 vs. patients with a FIB-4 score <3.25 (67.7% vs. 96.2%; p<0.001). The AUROC for FIB-4 score for prediction of transplant-free survival was 0.855.

CONCLUSION: In PBC, a FIB-4 score >3.25 is associated with future risk of transplantation or death. This emphasizes the need to integrate baseline fibrosis stage in individual risk stratification in patients with PBC.

Keywords: Primary biliary cholangitis, FIB-4, survival

Accuracy of FIB-4 at baseline in predicting transplant-free survival



AUROC:0.855 (0.772-0.938)

Transplant-free survival estimates according to baseline FIB-4

Figure 1.

PP-22

A rare cause of treatment failure in autoimmune hepatitis: Celiac disease

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OBJECTIVES: Autoimmune hepatitis is characterized by abnormal serum aspartate (AST) and alanine (ALT) aminotransferase levels, autoantibodies, increased serum IgG concentration, and interface hepatitis on histologic examination. In the treatment, steroids and azathioprine are the drugs used in the first step. In case of treatment failure, drugs such as cyclosporine, tacrolimus and mycophenolate mofetil can be used.

CASE: A 28-year-old female patient was admitted to the outpatient clinic with complaints of weakness and fatigue. In laboratory tests, Hb: 11,8 WBC: 8300 Platelet: 168000, Alb: 4,1 Globuline: 5,9 AST: 136 ALT: 158 ALP: 185 GGT: 104 T.bil: 0.8 and D.bil: 0.3 was detected. No significant finding except vitiligo was detected in the physical examination. Hepatitis panel was negative. No significant finding other than hepatosplenomegaly was detected in ultrasonography. In the autoimmune panel test, ANA (+) AMA (-) ASMA (+) IgG: 18 was detected. Liver biopsy revealed interface hepatitis, plasma cells and emperipolesis. The diagnosis of autoimmune hepatitis is made and the patient is planned to be treated with 48 mg/day methylprednisolone and 150 mg/day azathioprine. Since AST: 148 ALT: 142 IgG: 16.7 was detected in the first month of treatment, the patient's compliance with treatment was questioned first. After making sure of treatment compliance, mycophenolate mofetil was added to the patient's treatment. She had occasional diarrhea and anemia, and her tissue transglutaminase level was 135. Cracked soil appearance was observed in the duodenum in the endoscopy performed on the patient. In the biopsy taken, villus atrophy and increased lymphocyte level were detected. The patient was started on a gluten-free diet. In the 3rd month of the treatment, the patient's LFT values returned to normal.

CONCLUSION: In patients with autoimmune hepatitis, if LFT does not decrease despite effective immunosuppressive therapy, the preliminary diagnosis of malabsorption should be considered.

Keywords: Autoimmune hepatitis, treatment failure, celiac disease

PP-23

Evaluation of sarcopenia in non-cirrhotic chronic hepatitis C patients

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OBJECTIVES: Chronic hepatitis C (CHC) is one of the major causes of chronic liver disease. Extrahepatic manifestations, such as musculoskeletal involvement may occur in CHC. In this context, sarcopenia, which means loss of muscle tissue and muscle dysfunction, can be seen in these patients. This study aimed to evaluate sarcopenia in non-cirrhotic CHC patients treated in our department.

MATERIALS & METHODS: Patients admitted to the infectious disease

department in the last 5 years were reviewed retrospectively and 70 patients were found as positive for anti hcv and imagined with abdominopelvic CT. Any CT scans with artifacts, and patients who had diseases effecting muscle mass like malignancy, chronic kidney disease, cirrhosis were excluded. A control group was randomized from patients of similar age and gender, without systemic disease. On CT images, at the level of the L3 vertebra, the psoas area and total abdominal muscle area were calculated by the semi-automatic method. The mean density of the psoas muscles was measured in non-contrast-enhanced CT (Fig. 1). SMI (skeletal muscle index) and PMI (psoas muscle index) were calculated as dividing the cross-sectional areas by the squared height (cm^2/m^2) of patients whose height information was recorded.

RESULTS: 17 patients met the inclusion criteria and 16 controls were used in the study. When the patients and control group were compared, no statistically significant difference was found between the age, gender, psoas area, total abdominal muscle area, PMI and SMI values (p=0,809, p=1, p=0,063, p=0,855, p=0,062, p=0,382 respectively). However, psoas density mean values were significantly lower in CHC patients (p=0,005) (Table 1 and Fig. 2).

CONCLUSION: In this study, psoas density was found to be significantly lower in non-cirrhotic CHC patients. While previous studies showed that sarcopenia may present in cirrhotic patients; our study emphasizes that it may also present in non-cirrhotic patients. Further studies are needed.

Keywords: Chronic hepatitis c, sarcopenia, low muscle mass, non-cirrhotic

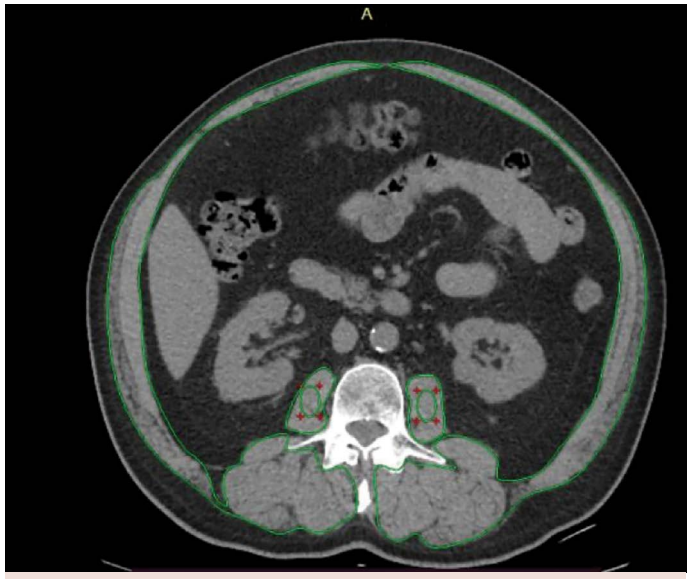

Figure 1. Axial abdominal computed tomography image at the level of third lumbar vertebrae. Skeletal muscle area, psoas area and psoas density was calculated with semi-automatic method.

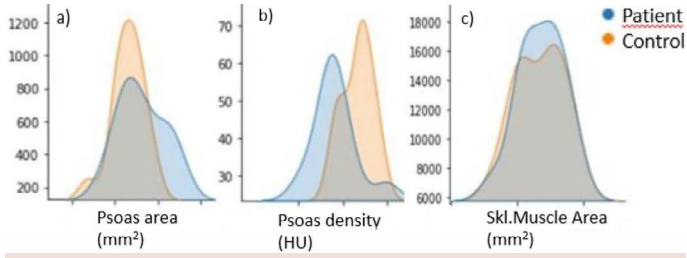

Figure 2. The peak mean value of the psoas area and psoas density were lower in patients than in the control group, but only the psoas density was statistically significant. There is no difference in skeletal muscle area between groups.

Table 1. General characteristics and compared mean values among patients and control groups

	Patients (n=17) (%)	Controls (n=16)(%)	p value
Age	57.71±3.147	56.63±3.105	0.809
Gender			1
female	6 (%50)	6 (%50)	
male	11 (%52.4)	10 (%47.6)	
Psoas area1	808.941±65.76	652.063±46.56	0.063
Psoas density 2	45.41±3.39	58.077±2.29	0.005
Total muscle area1	13551.24±821.07	13327.75±891.3	0.855
PMI3	30.94±3.34 (n=8)	23.39±1.08 (n=11)	0.062
SMI3	49.71±4.22 (n=8)	44.79±3.52 (n=11)	0.382

1 mm^2; 2Hounsfield Unit; 3 cm^2/m^2; PMI: Psoas muscle index; SMI: Skeletal muscle index

PP-24

Organic anion transporter polypeptide 1B1 polymorphism modulates the extent of hyperbilirubinemia during the treatment with paritoprevir, ombitasvir, ritonavir and dasabuvir (ROP/D) combination in chronivc HCV patients

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OBJECTIVES: Directly acting antiviral drugs (DAA) are known to be successful in the treatment of chronic hepatitis C (CHC). Among them, Paritoprevir, Ombitasvir, Ritonavir and Dasabuvir (ROP/D) combination has been routinely used in the treatment of CHC in Turkey, since the year 2016. There are some studies suggesting serum Bilirubin elevation up to 23 percent of patients with ROP/D combination. Normally, unconjugated bilirubin enters hepatocytes through the uptake transporters organic anion transporting polypeptide (OATP) 1B. Genetic mutations and drugs that interfere with this uptake mechanism may impede bilirubin disposition and cause hyperbilirubinemia. Several pharmaceutical compounds are known to cause hyperbilirubinemia via inhibition of OATP1Bs. We planned a study in our patient group who had CHC and treated with ROP D combination, whether the OATP1B1 gene polymorphism effect the hyperbilirubinemia status, or not, during ROP/D treatment.

MATERIALS & METHODS: All patients who were treated with ROP/D combination, and agreed to participate in the study in our hepatology clinic were included in the study. The blood samples were obtained from the patients 1 month later. The OATP1B1 polymorphism status and serum total-billirubin level were studied from this samples, in our medical genetics laboratory. OATP1B1 assessed as haplotypes 388A>G(AA,AG,GG), 521T>C(TT,TC,CC), 334T>G(TT,TG,GG), 699G>A(GG,GA,AA). The patients were categorized into two subgroups for each gene locus as homozygous haplotypes 388AA, 521TT, 334TT, 699GG and the all other heterozygous and homozygous haplotypes. The upper limit of normal total serum billirubin concentration was assessed as 1.2 mg/dl.

RESULTS: Totally 66 patients were included in the study. The mean-age was

59.00±15.11 years old. Of them, 37/66 were male, 29/66 were female. The hyperbilluribinemia rate was statistically lower in the homozygous haplotypes 334TT and 699GG groups than the all other haplotypes groups, by Chi Square test (p=0.021, and 0,02, respectively).

CONCLUSION: We concluded that the homozygous haplotypes 334TT and 699GG favors normo-billirubinemia during the ROP/D treatment.

Keywords: Hyperbilirubinemia, HCV, OATP1B1 polymorphism, ROPD

Table 1. Hyperbilirubinemia status in haplotype groups

Haplotype	Hyperbillirubinemia absent (n)	Hyperbillirubinemia present (n)	Total (n)
A334TT	4	5	9
A334TG	1	19	20
A334GG	5	32	37
Total	10	56	66
a699GG	2	0	2
a699GA	3	10	13
a699AA	5	46	51
Total	10	56	66

PP-25

A Case with Joubert syndrome diagnosed after abnormal liver tests

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OBJECTIVES: Joubert syndrome (JS) is a rare autosomal recessive disease characterized by partial or complete absence of the cerebellar vermis, with liver and kidney involvement. The diagnosis of the disease is made by characteristic clinical findings and magnetic resonance imaging (MRI).

CASE: 21 years old male patient applied to the adult neurology clinic due to worsening speech disorder complaints without mental retardation. At the age of 2, the cause of speech disorder was evaluated considering ischemic encephalopathy and he was not followed up. He was referred to our Gastroenterology clinic upon detection of abnormal liver tests. Firstly, the case was examined with the consideration of Wilson's disease because of the neurological findings. In the investigations laboratory findings were, ALT: 100 (U/L), AST: 52 (U/L), ALP: 241 (U/L), GGT: 392 (U/L), Total Bilirubin: 1.25 (mg/dl), Direct bilirubin: 0.65 (mg/dl). Inr, Albumin, Platelet levels were normal. Ophthalmological examination and screening tests (Ceruloplasmin and 24-hour urine copper) were normal for Wilson's Disease. Viral serology and autoimmune markers were unremarkable and no bile duct pathology was found in the abdominal MRI. With these findings we performed a liver biopsy. It was evaluated as a developmental or acquired biliary pathology (ductal plate malformation) in the biopsy. In the upper endoscopy small varices in the esophagus were observed. Simultaneous neurological examination with cranial MRI showed that the 4th ventricle was in the shape of a molar tooth and the inferior part of the cerebellar vermis was hypoplasic. Neuro-ophthalmological examination revealed see-saw nystagmus and tubing in the head. Findings in the patient, suspected of JS, were consistent with cerebellar pathology.

CONCLUSION: Although this case has exhibited neurological signs from the age of 2, JS was diagnosed at the age of 21 when cranial MRI was performed combining with the neurological findings. JS can usually cause both transaminase and cholestatic enzyme elevations and may lead to portal hypertension. In this rare case, we combined clinical and laboratory findings with a multidisciplinary approach to diagnose JS. JS should be considered in young patients with neurological findings, liver test abnormalities and portal hypertension.

Keywords: Joubert syndrome, speech disorder, abnormal liver tests

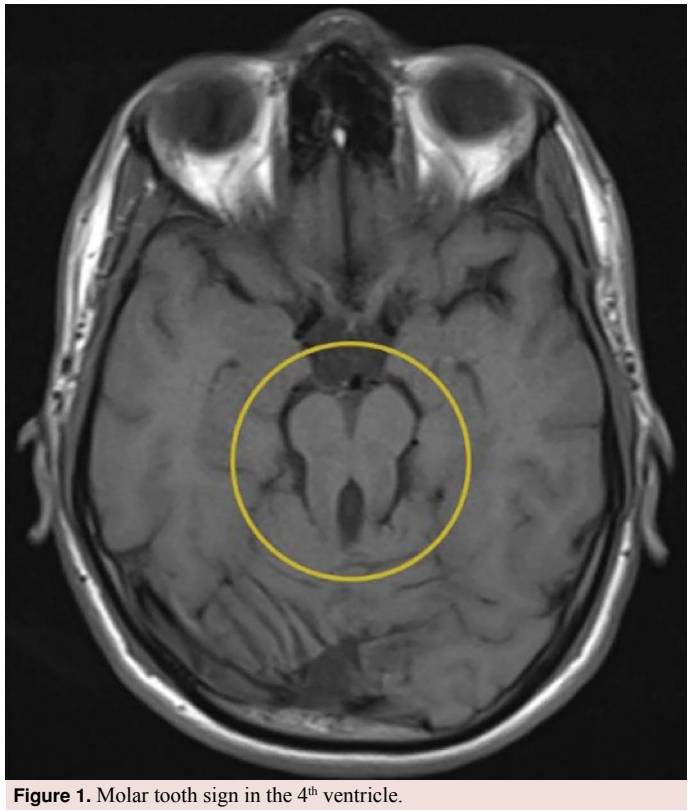

Figure 1. Molar tooth sign in the 4th ventricle.

PP-26

Clinical, demographic and laboratory predictors of elastographic fibrosis and steatosis

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OBJECTIVES: Liver fibrosis is the main cause of morbidity and mortality in chronic liver diseases. The liver biopsy is the gold standard in the diagnosis and staging of liver fibrosis. But it is an invasive procedure. We aimed to examine the relationships between fibrosis and steatosis determined by a noninvasive method fibroscan, and clinical, demographic and laboratory predictors.

MATERIALS & METHODS: Fifty patients who underwent elastography were

included in the study. Patients' clinical, demographic and laboratory parameters compared to fibroscan parameters to determine the fibrosis and steatosis predictors. Elastography controlled attenuation parameter values were classified between S0-S3 based on Li scale, and elasticity values were classified between F0-F4 based on Petroff's scale.

RESULTS: Of the 50 patients, 26 were male. The mean age was 49.9±13.4 years. The median body mass index (BMI) was 29.6. The most common comorbidities were hypertension 38%, diabetes mellitus 38% and hyperlipidemia 22%. Due to fibroscan results fibrosis and steatosis scores were as follows: 84% (n=42) F0-1, 4% (n=2) F2, 4% (n=2) F3, 8% (n=4) F4, and, 61.2% (n=30) S0, 2% (n=1) S1, 10.2% (n=5) S2, 6.1% (n=3) S2-3, 20.4% (n=10) S4, respectively. A significant correlation was found between BMI and triglyceride levels and those with steatosis grade 2 and above ($p<0.05$). The values of total cholesterol, HDL, ALT and GGT were significantly higher in patients with fibrosis level >=2 ($p<0.05$). The BMI value predicting the presence of S2 and above was found to be 29.6% with a sensitivity of 73.7% and a specificity of 65.5% (under the curve: 0.808, 95% confidence interval: 0.687-0.028).

CONCLUSION: In our study, BMI and triglyceride levels were found to be significant in S2 and higher steatosis, while total cholesterol, HDL, ALT and GGT levels were found to be significant in F2 and higher fibrosis.

Keywords: Elastography, steatosis, fibrosis

PP-27]

Development of reversion with low and moderate risk immunosuppressive therapy after the termination of antiviral treatment in a patient with HBsAg seroconversion with antiviral therapy

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CASE: 36 years old female patient has been taking 5-ASA treatment with the diagnosis of ulcerative colitis since 2009. The patient applied to our polyclinic for follow-up in 2015. Following detection of HBsAg (+) during the examination in October 2015, further analysis was requested here and HBsAg (+), anti-HBs (-), HBeAg (+), anti-HBe (-), HBV DNA: 403.600.000 (IU/mL), ALT >2x ONL (over the normal limits) finding. Liver biopsy: HAI: 13/18, stage: 3/6 were detected, and Tenofovir 245 mg 1x1 was started. In later follow-ups, HBeAg seroconversion was detected in May 2016; anti-HBe (+), anti-HBs (-), HBeAg (-), HBsAg (-), HBV DNA: <20 (IU/mL). The first HBsAg seroconversion was in February 2017; HBsAg (-), anti-HBs (+): 18 IU/L detected. Meanwhile, in May 2017: 2 mg/kg Azathioprine therapy was added due to UC activation. in January 2018, due to UC remission failure, Adalimumab 40 mg S.C. (every two weeks) treatment was started to the patient using Azathioprine + 5-ASA. In later follow-ups, anti-HBS (+), HBsAg (-) and HBV DNA (-) was contained for 1.5 years, and as anti-HBs (+): 133 IU/L, HBsAg (-), HBV DNA (-) values in June 2018, the treatment was discontinued. HBsAg (-), anti-HBs (+) was observed in 2019 and 2020; however, in follow-ups, initially, the values dated May 2021, HBsAg (+), anti-HBs (+): 11.2 IU/L, HBeAg (+), anti-HBe (-), HBVDNA: 38.500.000 (IU/mL) were detected, and reversion was considered, and tenofovirtherapy (245 mg 1x1) was started.

CONCLUSION: After HBsAg seroconversion, although it is a frequent method to discontinue antiviral therapy after a particular time, we should be more careful, especially in immune-suppressive/modulator treatment areas. Azathioprine and Adalimumab are presented in the low and moderate risk group in the guidelines, but intermittent HBVDNA, HBsAg and ALT follow-up is recommended, and as in this case, there are reversions over the years.

Keywords: HBsAg seroconversion, immunsupressive treatment, reversion

Table 1. Screening and management Guidelines for HBV reactivation

PP-28

HBV-associated intrahepatic cholangiocarcinoma

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OBJECTIVES: Hepatitis B virus (HBV) infection is a global public health problem with a prevalence of 240 million people, and its major sequelae are cirrhosis and hepatocellular carcinoma (HCC). Intrahepatic cholangiocarcinoma (ICC) is a malignant tumor arising from the peripheral intrahepatic bile duct epithelium. Its incidence and mortality have been increasing markedly in recent years, the reason for this increase is unclear and therefore alternative etiologies and pathogenetic mechanisms are being investigated. Recently, HBV infection has been implicated as a potential risk factor for ICC in areas where HBV is endemic.

CASE: 38-year-old male patient. He has chronic HBV infection for 8 years, has not received antiviral treatment. She presented with bloating and abdominal pain. Laboratory: HBsAg: positive, Delta antibody: Negative, HBVDNA: 1130 IU, Platelet: 111. 109/L, PT: 13.1 sec, AST: 65 U/L GGT: 216 U/ L Ca19-9: 36.5 U/ mL, AFP: 5.56 ng/mL. Abdominal MRI: Mass lesion in liver segment 5, subcapsular 29x16 mm, with mild hypervascular septal that creates diffusion restriction in the periphery. PET-CT: Increased FDG uptake in subcapsular 33 mm hypodense lesion in liver segment 5 (SUV_{max}: 6,9). Non-anatomical tumoral resection was performed for a tumoral mass of 3x2 cm in diameter in Liver Segment 5. Histology: Poorly differentiated intrahepatic cholangiocarcinoma, lymphovascular invasion were reported. The patient was started on chemotherapy in medical oncology.

CONCLUSION: ICC is intrahepatic bile duct carcinoma and is less common than HCC. Hepatolithiasis, primary sclerosing cholangitis, parasitic infection, fibropolycystic liver disease and chemical carcinogens are thought to be risk factors. HBV infection is a known risk factor for malignancy. Unlike HCC, little is known about the risk of non-HCC malignancy. Data on the risk of other malignancies such as pancreatic adenocarcinoma and intrahepatic cholangiocarcinoma are mixed. Identifying other risk factors can lead to prevention and early detection of ICC.

Keywords: Intrahepatic cholangiocarcinoma, HBV infection, antiviral therapy

PP-29

Clinical presentation and biochemical features of the autoimmune hepatitis in children: Is associated autoimmune diseases are more prevalent than expected?

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OBJECTIVES: Autoimmune hepatiti (AIH) is an inflammatory disease of the liver with variable clinical presentations from asymptomatic elevated liver enzymes to fulminant hepatic failure. 20-40% of the patients with AIH had another associated autoimmune disease. This study aimed to assess mode of presentation, biochemical features and outcomes in children with AIH, as well as to evaluate the frequency of concomitant autoimmune diseases (CAIDs) in children with AIH.

MATERIALS & METHODS: 17 children, aged 6 to 18 years were enrolled. The presenting symptoms, physical evaluation, accompanying autoimmune disease and family history of associated diseases were recorded. Biochemical parameters were evaluated either at time of submission and thereafter, according to mode of presentation and presence of the CAIDs. Remission induction and maintenance treatment, response, relapse were collected from the patient charts.

RESULTS: Fourteen patients had type-1 AIH (10 females, 4 males), and three (2 males, 1 female) had type-2 AIH. The mode of presentation was acute hepatitis in 53% and incidental enzyme elevation in 47% of them. There was an associated autoimmune or auto-inflammatory disease in 35% of the patients, 12% had vitiligo, 6% had celiac disease, 6% had juvenile idiopathic arthritis, 6% had Familial Mediterranean Fever, and one patient had both type 1diabetes mellitus and Hashimoto thyroiditis (HT). The subjects with CAIDs were females (6 patients) and all had insidious type of presentation. None of our patients had concomitant inflammatory bowel disease (IBD). Autoimmune diseases were observed in 24% of the parents of the children with AIH (3 had HT, 2 had vitiligo).

CONCLUSION: AIH is a rare but important cause of chronic liver disease in children. Frequent association with autoimmune or autoinflammatory diseases should be kept in mind as the clinical expression of the associated disease can be extremely variable therefore diagnosis and treatment delay may occur.

Keywords: Autoimmune hepatitis, children, concomitant autoimmune diseases

Table 1. Demographic and biochemical parameters according to the presence of associated autoimmune diseases in children with AIH

Parameter	No associated auto-immune disease	Associated autoimmune disease	p
Age (mean±SD) (years)	11.6±3.39	11.3±4.35	0.651
Sex (male/female)	5/6	0/6	
ALT (median (IQR) (IU/l)	672 (505)	456 (1456)	0.763
Total bilirubin (median (IQR) (mg/dl)	1.63 (4.95)	1.20 (7.77)	0.615
Conjugated bilirubin (median (IQR) (mg/dl)	0.70 (2.90)	0.80 (6.51)	0.580
GGT (median (IQR) (IU/l)	87.9 (71)	109 (113)	0.651
Albumin (median (IQR) (g/dl)	4.20 (1.05)	3.90 (1.00)	0.362
INR (median (IQR)	1.41 (0.55)	1.20 (0.31)	0.049
Total IgG (median (IQR) (mg/dl)	2433 (3759)	2197 (568)	0.447
Platelet (mean±SD) (/mm^3)	214.900±55.322	238.800±61.900	0.191
Hemoglobin (mean±SD) (g/dl)	12.1±1.64	11.9±0.95	0.650

Legend: SD, standard deviation; IQR: interquartile range; ALT, alanine aminotransferase; GGT, γ-glutamyl transferase; IgG, immunoglobulin G; INR, international normalized ratio

PP-30

HIV-associated acute decompensation in patient with alcoholic liver disease: A case presentation

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OBJECTIVES: Human immunodeficiency virus (HIV) infection is a chronic infection that gradually weakens the immune system with the effect of the causative virus. Recent studies report that it increases hepatic fibrosis. We present a case of chronic liver disease decompensated by HIV infection.

CASE: A 35-year-old male patient was admitted to the emergency service because of a fracture in the fourth metacarpal. An elevation is detected in liver function tests performed at the time of application. There is no pathology in the tests for the etiology. In the ultrasonography of the patient, it was seen that the liver dimensions increased (190 mm in diameter), and it was compatible with grade 3 hepatosteatosis. During the interrogation of the patient, it was learned that he had been using alcohol since the age of 18 and had increased it for about four years (about 40 g per day). Alcoholic-related chronic liver disease was considered in the patient. The patient presented with complaints of abdominal distension, pretibial edema, fatigue, and weakness approximately six months after the operation with appropriate treatment. Hyperbilirubinemia, hypoalbuminemia, and prolongation of prothrombin time were observed. After the patient's desired tests were found to be Anti-HIV positive, HIV RNA 1 637 241 copies/ml was detected, and "Elvitegravir + Cobicistat + Emtricitabine + Tenofovir" treatment was started. Sprinalactone 50 mg/day and furosemide 40 mg/day were added to his treatment. No esophageal varices were observed in the patient's endoscopy. As of the first week, significant clinical improvement, decrease in ascites, and regression in pretibial edema were observed. It was observed that the patient had almost complete biochemical and clinical recovery at the eighth week of the treatment.

Table 1. The course of the biochemical findings of the disease

Labaratory tests	Initial tests (1. visit)	Decompensation (2. visit)	4th week treatment (3. visit)	8th week treatment (4. visit)
Urea (mg/dl)	24		32	
Creatinine (mg/dl)	0.52	1.22	0.84	0.5
AST (U/L)	346	224	48	33
ALT (U/L)	103	64	40	27
ALP (U/L)	162	496	215	140
GGT (U/L)	2764	1183	305	262
T.protein/albumin (mg/dl)	7.3/4.6	7.6/2.8	8.3/4.1	7.8/3.9
T.bil/D.bil (mg/dl)	1.5/0.4	9.9/7.9	1.7/1.1	0.9/0.6
INR	1.1	1.4	1.4	1.1
hemoglobine	16.5	13.5	11.7	14.4
White blood cells /mm^3	11200	26850	8970	6740
Platelets /mm^3	188000	274000	311000	229000
Anti-HIV	Negative	Positive		Positive
Anti-HCV	Negative	Negative		Negative
HbsAg	Negative			Negative
HIV-RNA copy/ml		1637241		226
Abdomen USG	Liver parenchyma is compatible with grade 3 steatosis.Liver dimensions increased and the right lobe craniocaudal length was measured as 19 cm. No ascites	Liver right lobe CC size was measured 19.5 cm and increased. Its contour is slightly lobulated in places. The parenchymal echo pattern was homogeneous and the echo intensity increased diffusely secondary to grade 2 hepatosteatosis. The spleen CC size was measured 17 cm and increased. About 100 mm ascites	The liver is larger than normal with a CC of 195 mm, and the echo intensity of the parenchyma has increased secondary to grade 2 steatosis.The spleen size was 157 mm and it was larger than normal. No ascites.	

CONCLUSION: HIV-associated acute decompensation is not common in patients with liver cirrhosis. However, we know that HIV contributes to hepatic inflammation and fibrosis, by this mechanism HIV infection can also lead to hepatic decompensation.

Keywords: HIV, alcoholic liver disease, acute decompensation

PP-31

The evaluatuion of clinical parameters and multiparametric liver MRI findings in patients with wilson disease

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OBJECTIVES: Wilson's Disease (WD) is a rare genetic disorder with copper accumulation especially in the liver and brain. The Liver and brain MRI are the most common used radiologic imaging for diagnosis and follow-up of Wilson's disease. Multiparametric liver MRI is sensitive to pathophysiological processes such as fibrosis and steatosis in many liver diseases. We aimed to evaluate the correlation between clinical parameters, brain MRI and multiparametric liver MRI findings of patients with Wilson's Disease.

MATERIALS & METHODS: This prospective, cross-sectional, cohort study included patients with WD (43) followed at Hacettepe University, gastroenterology and neurology polyclinics. Brain and multiparametric liver MRIs were done, and demographic/clinical features as well as routine laboratuary tests were obtained from records.

RESULTS: The median age in WD patients were 32.8±10.7, and 44% of patient were male. Although, 88.4% of patients were strictly adhering to copper chelator treatment, the liver MRI revealed of 51.3% chronic liver disease and 30% of them are cirrhotisis. Similarly, neurological symptoms were clinically present in 46.5% of patients but brain MRI showed neurological involvement in 56.1% of the patients. The analysis of brain and multiparametric liver MRI finding and clinical paramaters will also be presented.

CONCLUSION: Both brain and liver MRI are more sensitive than clinical symptoms in order to detect organs' involment. We believe that multiparametric liver MRI has a potential to be used for routine follow up patients with WD in the feature.

Keywords: Wilson disease, multiparametric liver MRI, brain MRI

PP-32

Fontan associated liver disease is not rare during childhood: A cross-sectional evaluation

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Table 1. Patients' characteristics and laboratory datas'

*Sex (Male/Female)	15/7
*Age (years)	6.48 (1.2 to 13.7) years
Age of fontan operation	4.2 (0.42 to 7.82)
Post fontan duratio	1.4 (0.11 to 10.41)
*Antropometric measurements	
Weight SDS	-0.83(-2.32 to 1.2)
Height SDS	-0.785 (-2.02 to 1.7)
BMI SDS	-0.165 (-2.27 to 1.22)
Primer cardiac defects	(n)
Hypoplastic left heart syndrome	6
Double outlet right ventricule	3
Pulmonary valve atresia with intact ventricular septum	3
Tricuspid atresia	3
Unbalanced atrioventicular septal defect	2
Others	5
*Laboratory parameters	Median
Hemoglobin gr/dL	13.7 (11.7-15.9)
Thrombocyte /mm³	242.000 (107-535)
AST U/L	36 (22-105) U/L
ALT U/L	18 (12-34) U/L
LDH U/L	292 (123-504) U/L
GGT U/L	28 (13-77) U/L
Albumine g/L	45 (38-51)
Total bilirubin mg/dL	0.62 (0.47-1.54)
Direct bilirubin mg/dL	0,26 (0.16-0.53)
INR	1.2 (1.02-1.5)
Creatinine mg/dL	0.4 (0.2-0.6)
Pro-BNP pg/mL	167.5 (75-1042)
Bile salts pg/mL	5.6 (1-11.9)
Transient elastography**	(n)
F0 (<5 kPa)	0
F1 (5.1-7 kPa)	2
F2 (7.1-9 kPa)	4
F3 (9.1-15 kPa)	6
F4 (>=15 kPa)	4
Liver USG	(n)
Abnormal (granulaty, hepatomegaly, cycte, steatosis etc.)	6
Normal	9

**: Values were given in median and range; **: Garcovich et al. 2017*

OBJECTIVES: Fontan-associated liver disease (FALD) which included liver fibrosis, cirrhosis and hepatocellular carcinoma is a high frequency condition. The objectives of this cross sectional study were to determine liver abnormalities in children who underwent Fontan operation and related factors development of FALD.

MATERIALS & METHODS: Fontan patients followed up in our institution between August to December 2021 underwent a detailed hepatic assesment including liver ultrasound, transient elastrography and laboratory analysis at Division Pediatric GI and Hepatology. Subjects were excluded if there was a history of primary liver disease or other complications related to the Fontan physiology (eg. protein-losing enterpathy). The liver stiffnes measurements (LSM) were performed with Fibroscan device using M probe (Echosens, Paris, France). Patients cardiac and other data obtained from electronical data and patient's clinical charts.

RESULTS: The median age of 22 (M:F=15:7) recruited children was 6,48 (1,2-13,7) years. Patients demographic and laboratory data were given in Table 1. Median post Fontan duration was 1,4 (0,11-10,41) years. Overall FALD was detected in 87.5% of patients. Liver abnormalities were detected 40% and 87.5% by ultrasound and TE, respectively (Table 1). The median liver stiffness score, Aspartate/Platelet Ratio Index (APRI) and Fibrosis-4 (FIB-4) index were 10,3 (6-27,6) kpa, 0,3 (0,1-0,6), and 0,18 (0,09-0,77), respectively. Liver stiffness showed significant positive correlation with post-Fontan duration ($p<0,05$, $r=0,550$) and FIB-4 index ($p<0.05$, $r=0,7$) but not with APRI. Splenomegaly ($p<0,01$, $r=0,669$), APRI ($p<0,01$, $r=0,767$) and FIB4 index ($p<0,01$, $r=0,922$) were also found related to post-Fontan duration The age of patients' were correlated with APRI ($p<0,01$, $r=0,777$) and FIB4 index ($p<0,01$, $r=0,910$). AFP level was normal in all patients. Despite 10 patients had F3-F4 fibrosis, none of them showed liver failure during follow up.

CONCLUSION: Hepatic abnormalities are common in Fontan patients and not reflected by liver enzymes. A detailed hepatic assesment which included TE and non invasive fibrosis markers with cardiac indices should be a part of long-term follow up for surveillance of these children.

Keywords: Fontan surgery, Fontan associated liver disease, liver stiffness, pediatrics

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PP-33

A rare case of hepatocellular cancer on hepatoportal sclerosis

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OBJECTIVES: Hepatocellular carcinoma (HCC) is the most common form of liver cancer. Non-cirrhotic portal hypertension an infrequent cause of HCC.

CASE: A 36-year-old woman with a 2-year history of liver cirrhosis presented with esophagus varices admitted to our hospital. Serum aminotransferase levels were 1.5-2 times higher than normal. The viral hepatitis panel and autoimmune hepatitis panel were negative. Triple-phase CT scan demonstrated the increased caudate-to-right lobe ratio in the presence of preserved liver volumes with evidence of significant portal hypertension, including splenomegaly and varices. There were no portal vein or hepatic veins thrombosis. Non-cirrhotic portal hypertension was first considered in the patient. In the 2-years-follow-up, two liver lesions 8 mm x 4,5 mm in segment IVA and 6 mm x 7 mm in segment VIII were identified on triple-phase CT. The lesions had arterial enhancement, no wash-out on venous or late phase. In the dynamic MRI examination performed 2 years later, the size increase in the 20 mm lesion seen in Segment VIII includes a slightly hyperintense lesion in T2 sequence and diffuse enhancement in the arterial phase in contrasted sequences. It was observed that the contrast enhancement continued moderately in the portal and venous phases. Differentiation in favor of HCC was considered. Alpha feta protein was 3 ng/ml. RF ablation therapy was first applied to the patient who had no signs of metastasis, but multiple lesions were detected in the liver. Within two months, the patient underwent a living donor liver transplant. Well-differentiated HCC measuring 4 cm x 3 cm x 3 cm was seen, and also hepatoportal sclerosis was considered as the cause of non-cirrhotic portal hypertension in the explant pathology.

CONCLUSION: Non-cirrhotic portal hypertension, especially hepatoportal sclerosis, is an infrequent cause of HCC. Because of the liver nodules, patients with HPS must be followed carefully for HCC.

Keywords: Hepatoportal sclerosis, hepatocellular cancer, liver transplantation

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PP-34

Preliminary results of the effectiveness and safety of tenofovir alafenamide fumarate prophylaxis in HBV-Infected individuals, who received chemo/immunosuppressive therapy

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OBJECTIVES: There are very limited data regarding the efficacy and safety of tenofovir alafenamide fumarate (TAF) prophylaxis to prevent HBV reactivation in HBV-infected individuals undergoing chemo/immunosuppressive therapy. The aims of the present study were to determine the effectiveness and safety of TAF prophylaxis in HBV-infected individuals, who receive chemo/immunosuppressive therapy.

MATERIALS & METHODS: This is a multicenter, observational study. Data were entered in a standardized electronic case report form (CRF) from each center and collected from the CRF. TAF was administered at a dose of 25 mg/day at the initiation of the chemo/immunosuppressive therapy. The mean follow-up period was 17.1±7.8 months.

RESULTS: A total of 326 HBV-infected individuals with benign and malign diseases received TAF prophylaxis. Among these patients, 158 patients (M/F:83/75) with at least 6 months of follow-up were included into analysis. Mean age was 59.55±12.2 years. Thirty patients had detectable HBV DNA and 5% were HBeAg positive. Solid tumors were the most common primary disease (33.5%), followed by rheumatic diseases (32.9%) and myeloproliferative diseases (32.2%). Of these patients, 48% received cytotoxic chemotherapy, 17%

PP-34 Table 1. Laboratory changes during tenofovir alafenamide fumarate

n=158	Baseline	6-months	12-months	18-months	24-months	p value (pairwise comparisons vs baseline)			
	mean±sd	mean±sd	mean±sd	mean±sd	mean±sd	6-months	12-months	18-months	24-months
ALT, IU/L	34.38±67.32	24.48±21.7	27.01±36.85	-	30.07±30.22	0.040*	0.268	-	0.090
Blood phosphate, mg/dL	3.52±0.81	3.4±0.71	3.29±0.61	3.36±0.59	3.34±0.64	0.061	0.015*	0.069	0.150
GFR, mL/min	83.23±26.46	84.23±23.66	82.86±26.09	84.05±27.77	91.53±27.28	0.423	0.906	0.126	0.936
Total cholesterol, mg/dL	200.48±55.05	199.48±49.99	222.27±50.05	236.75±99.99	252.25±91.99	0.322	0.290	0.484	0.187
Triglyceride, mg/dL	147.46±90.11	179.3±111.7	165.17±106.72	168.9±95.53	168.7±77.73	0.050*	0.506	0.083	0.019*
HDL, mg/dL	46.15±14.54	45.57±11.49	53.05±16.29	54.57±20.94	60.13±21.66	0.755	0.165	0.754	0.244
LDL, mg/dL	125.79±43.82	119.53±35.26	146.63±39.81	149.33±90.73	140.5±91.32	0.788	0.318	0.502	0.877
Fasting glucose, mg/dL	110.73±37.06	117.57±37.68	122.87±61.55	112.41±38.09	102.95±22.54	0.095	0.033*	0.147	0.693

ALT: Alanine transaminase, GFR: Glomerular filtration rate, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

received B cell depleting therapy, 13% received anti-TNF therapy, 8% were received glucocorticoid therapy, and 12% patients were received other treatments. During the follow-up period, none of the patients had clinical, biochemical, and serological evidence of HBV reactivation under TAF prophylaxis. No HBV-related morbidity and mortality was observed. HBV DNA became negative in 77% of the patients with detectable HBV DNA. All patients maintained their chemo/immunosuppressive therapy without interruption. TAF prophylaxis was well tolerated. The renal function tests and lipid profiles, except triglyceride level did not significantly change from the baseline to the end of the follow-up period (Table 1). No serious adverse events were reported.

CONCLUSION: Based on the results of the study, TAF prophylaxis prevents chemo/immunosuppressive therapy-induced HBV reactivation in HBV-infected individuals receiving chemo/immunosuppressive therapy. TAF is safe and tolerable in such individuals.

Keywords: HBV reactivation, HBV prophylaxis, tenofovir alafenamide fumarate

PP-35

Development of metabolic disorders in liver transplant recipients

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OBJECTIVES: Survival following liver transplantation (LT) has increased over the last decades, focusing on the long-term metabolic complications of LT which is affected on patient morbidity and mortality. The aim of this study was to determine the development of long-term metabolic complications following liver transplantation.

MATERIALS & METHODS: Thirty and seven adult patients who underwent LT were included. All recipients had at least 1 year of follow-up period. Characteristics, anthropometric and metabolic data were collected from patients' hospital charts. The diagnosis of metabolic syndrome was defined based on the World Health Organization criteria. Median follow-up period after LT was 7.5 year (range; 1-20 year).

RESULTS: Mean age was 57±10 and 60% were male. Living donor LT was performed on 27 patients (72.9%). The most frequent indication for LT was hepatitis B virus-induced liver disease (37.1%). The majority of patients (88%) were on tacrolimus-based treatment. Metabolic data of LT patients are shown in Table 1.

CONCLUSION: Based on the preliminary results of the present study, metabolic disorders following LT are commonly seen in posttransplant follow-up period. Liver transplant recipients needed careful monitoring for development of metabolic disorders and its complications.

Keywords: Metabolic disorder, liver transplantation, metabolic syndrome

Table 1. Metabolic data of LT patients

	Prior to LT	Following LT
Glucose level mg/dL (mean±SD)	104.0±89.5	113.9±96.0
Cholesterol level mg/dL (median-range)	123 (39-230)	188 (104-350)
Triglyceride level mg/dL (median-range)	114 (27-449)	171 (46-514)
BMI kg/m^2	23.5	26.6
Obesity (%)	7	22.7
Diabetes Mellitus (%)	20.5	54.8
Hyperlipidemia (%)	22.2	45.4
Hypertension (%)	9.3	45.1
Metabolic syndrome (%)	11.7	52.9
Coronary heart disease (%)	12.5	21.8

PP-36

Presentation and outcomes of autoimmune hepatitis during pregnancy

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OBJECTIVES: The data regarding pregnancy in women with autoimmune

hepatitis (AIH) is limited. The aims of the present study were to determine the characteristics of patients with AIH, who had pregnancy and to describe disease and pregnancy outcomes.

MATERIALS & METHODS: This was a retrospective, multicenter cohort study. Between 1998 and 2020, patients with AIH presenting at least one pregnancy during follow-up were included into the study. The diagnosis of AIH was made based on the International AIH scoring system.

RESULTS: A total of 33 patients with AIH were included in the study. Their mean age was 39.8±13.2 years (range, 19 to 67 years). Sixteen patients (47%) accompanied concomitant extrahepatic autoimmune disease. Hashimoto's thyroiditis was the most common association (14.7%),followed by primary biliary cholangitis (8.8%), rheumatoid arthritis (5.9%) and systemic lupus erythematosus (5.9%). Jaundice was the most common presentation symptom (39.4%), followed by elevated serum aminotransferases levels (35.3%), itching (15.2%). Fort-five pregnancies were observed in 33 patients: One pregnancy in 24 patients, 2 pregnancies in 6 patients, and 3 pregnancies in 3 patients. During pregnancy, 53% of the patients modified their immunosuppressive treatment. There were 41 livebirths and 4 fetal lost. Six pregnancies resulted in an AIH flare. In these cases, their gestational week mean was 24 weeks (median 28±10.5 weeks). None of these flares required hospitalization. During pregnancy these patients didn't have any dose modification of their medical therapy of AIH. Two pregnant patients presented complications, premature membrane rupture and bleeding, during pregnancy. One to third of the patients had cesarean section. Seven women diagnosed with AIH during the pregnancy. No serious maternal complication was observed.

CONCLUSION: Based on the preliminary result of the present study, pregnancy is safe in patients with AIH. However, such patients needed careful monitoring for disease relapse and possible fetal and maternal complications during pregnancy.

Keywords: Autoimmune hepatitis, pregnancy outcomes, liver disease