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TRANSPLANT/LIVER SURGERY

001

USE OF A COLLAGEN MATRIX AS A SCAFFOLD FOR THE HEPATIC TISSUE

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INTRODUCTION AND OBJECTIVES: Recently, biomedicine has incorporated the use of biomaterials as scaffolds for the functional and structural recovery of damaged tissues. These kinds of materials are amply used in orthopedics, maxillofacial surgery and dentistry. Most of these materials favor cellular induction and conduction in the tissue, and enable cell proliferation in the tissue where they have been grafted. The Institute of Research on Materials from the National Autonomous University of Mexico have developed a novel collagen based matrix that has shown mechanical and compositional properties that would allow it to become a scaffold for different tissues. This material has been successfully used in the urinary tract; however it has not been use elsewhere. The purpose of our work was to test the biocompatibility of this novel collagen matrix in the fibrotic hepatic tissue and its possible use as a hepatic scaffold. **MATERIAL AND METHODS:** Male Wistar rats weighing 240 ± 20 g were administered CCl₄ (33% v/v in olive oil) bi-weekly for 10 weeks. Animals were distributed in two groups: partial hepatectomy (n = 6) or partial hepatectomy + scaffold (n = 6). All animals were subject of surgery after sedation-anesthesia with Xylacine-Ketamine. A piece of 1 cm³ was excised from the ventrolateral segment of the liver, in the case of the scaffold group the piece was substituted by the sterile material. 10 days after the surgery, animals received an excess of anesthetics and livers were obtained. The areas of interest were excised. Tissue was collected, fixed and paraffin embedded. 5 µm sections were obtained and stained with Hematoxyline-Eosine or Sirius Red. **RESULTS:** Surgeries were successfully developed. Rats in the scaffold group did not show any post-surgical alteration. The area of interest in the liver was located by unabsorbable suture stitches. At the macroscopic level, the scaffold grafted was difficult to identify since new tissue had grown on the material. Histological sections revealed the development of new tissue in both groups. The partial hepatectomy + scaffold livers showed cellular growth over the scaffold and no signs of rejection towards the material were observed. **CONCLUSIONS:** The novel collagen based matrix exhibited biocompatibility with hepatic tissue and was able to allow cellular growth

functioning as a scaffold while it was incorporated into the tissue. **CONFLICT OF INTEREST:** The authors have no relationship to disclose.

002

AUTOLOGOUS TRANSPLANTATION OF HEMATOPOIETIC CELLS. CASE REPORT

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INTRODUCTION: Orthotopic liver transplantation can improve survival of patients with liver failure and is currently the treatment of choice for patients with poor prognostic signs. However, its clinical use is limited because donor organ shortage and high costs associated with the procedure. New therapeutic strategies for this cases are being investigated. Autologous transplantation of hematopoietic cells (ATHC) could be a therapeutic alternative for these patients. **AIM:** Describe the evolution of a patient with sub-acute autoimmune hepatitis with autologous hematopoietic stem cells transplantation. **METHOD AND PATIENT:** Report of a case. A female of 20 year old who presented in date 7/30/2008 asthenia, headache, anorexia, nausea and vomiting. On 08/02/2008 started with jaundice and dark urine or itching without acolia. She was admitted in the intensive care unit 08/04/2008 TB 13 mg/dL, DB 7.3 mg/dL, AST 3533 IU/L, ALT 2582 IU/L, ALP 158 IU/L, GGT 223 IU/L, negative viral markers HCV and HBV, PT 20 s, PTT 37.6 s, INR 1.81, aerobic and anaerobic blood culture negative. 08/07/2008 AFP 2.93 ng/mL, V factor 74.8%, VII factor 37.8%, AMA (-), EBV (-), AML 66.5 U (+), AMHR (-) CMV (-), ammonium 1.48 µg/mL (Hepatic encephalopathy, G1), Ceruloplasmin 25 mg/dL, PT 19.4 s, TTP 36.5 s, INR 1.62, ferritin 1106 ng/mL, negative HFE (C282Y, H63D and S65C), TB 20.7 mg/dL, DB 15.9 mg/dL, IB 4.8 mg/dL, TP 6.2 g/dL, AST 1,008 IU/L, ALT 1946 IU/L, ALP 124 IU/L, GGT 154 IU/L, liver Doppler ultrasound was performed reporting splenomegaly. Liver biopsy reported necrosis 60-70%, acute hepatitis and autoimmune hepatitis interface, had no source data toxic hepatitis. Was diagnosed with severe sub-acute hepatitis of autoimmune origin, candidate for transplant without donors available. Was started meticorten 50 mg, celcept 2 g, vit E 1200, samyr 1,500 mg, Pantozol 40 mg. On 08/11/2008 was performed ATHC after stimulating with neupogen dose of 300 µg/2/4 days and 52.6x10⁶ CD34 + cells were obtained in a volume of 100 mL. This cells were placed percutaneously into the portal vein and only referred pain in right upper quadrant and bloating. The following days she was gradual improvement in biochemical and clotting time. She was discharged 7 days post ATHC with the following studies: PT 13s, TTP 13.1 s, INR 0.99, TB 3.2 mg/dL, DB 2.1 mg/dL, IB 1.1 mg/dL, TP 5.7g/dL, AST 31 IU/L,

ALT 88 IU/L, ALP 103 IU/L, GGT 174 IU/L. IL-6, TNF α , IL-1 β , haptoglobin, AFP, biochemical profile and clotting times were performed on 1, 4, 5, 6 months post ATHC and were normal. During this period the patient was asymptomatic. On sixth months post-ATHC cellcept decreased to 500 mg for 15 days, suspended and starts Inmuran 50 x 1. One year before post-ATHC liver biopsy showed cholestasis without activity, or inflammation or evidence of regeneration. On 10/01/2009 asymptomatic, PBN and autoantibodies (-). On 10/09/2010 asymptomatic with Fibrotest F0 and A0. On 2 years 8 months post-ATHC the patient was completely asymptomatic and leading a normal life. Currently in treatment Inmuran, autrin 600 x 1, vit E 400U each 3 days. **CONCLUSION:** Autologous transplantation of hematopoietic stem cells may be a treatment strategy for patients with severe liver disease, however a larger study is needed to confirm these results. This work was sponsored entirely by own resources of participating departments.

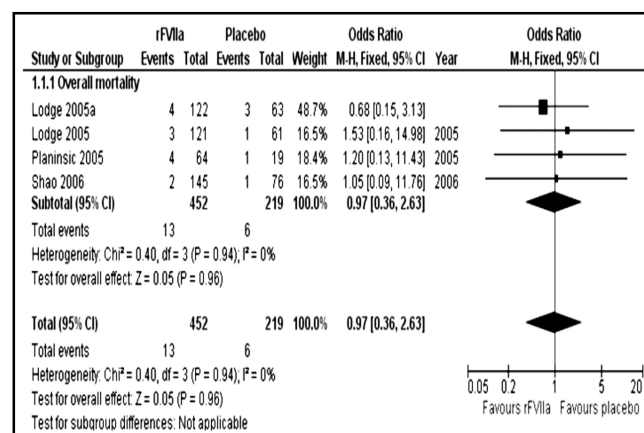
003

RECOMBINANT ACTIVATED FACTOR VII FOR HEPATIC RESECTION AND LIVER TRANSPLANTATION META-ANALYSIS AND SYSTEMATIC REVIEW

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BACKGROUND: Hepatic resection and orthotopic liver transplantation are associated with intraoperative blood loss. Recombinant activated coagulation factor VII (rFVIIa) is a coagulation protein that induce homeostasis directly activating factor X. There is no clear information regarding the use of rFVIIa in liver surgery, specifically liver resection and liver transplantation. **OBJECTIVES:** The aims of this study were to assess the effect of rFVIIa to manage bleeding in hepatic surgery and prevent mortality. **MATERIAL AND METHODS:** *Data sources.* Relevant randomized trials were identified by searching The Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library, MEDLINE, EMBASE, and Science Citation Index. *Study eligibility criteria.* Randomized clinical trials comparing different rFVIIa therapy with placebo or no intervention to prevent or treat bleeding in hepatobiliary surgery. *Participants and interventions.* Adults undergoing liver resection, partial hepatectomy and OLT. *Study appraisal and synthesis methods.*



Dichotomous data were analyzed calculating the odds ratio (OR) for each trial, expressing the uncertainty with 95% confidence intervals (CI). **RESULTS:** We included 4 randomized controlled trials designed to evaluate rFVIIa in liver surgery. There were no significant differences in mortality rate (OR 0.97; 95%CI 0.36-2.63) or adverse event rate (OR 1.55; 95%CI 0.97-2.49). Only one trial demonstrated a reduction in the requirements of red blood cells (Figure 1). *Limitations.* Few studies available and any assessing mortality as primary outcome. **CONCLUSIONS:** The current information shows no benefit on significant outcomes. Available information is insufficient to draw evidence-based conclusions.

CIRRHOSIS AND COMPLICATIONS

001

HEPATIC HYDROTHORAX: PRESENTATION OF A 5 CASES AND REVIEW OF THE LITERATURE

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INTRODUCTION AND OBJECTIVES: The hepatic hydrothorax (HH) is a rare manifestation of portal hypertension, present in the 5-12% of cirrhotic patients. On the other hand, spontaneous bacterial empyema is an uncommon complication of hepatic hydrothorax, occurring in 13% of patients with HH. It can occur in the absence of spontaneous bacterial peritonitis or even ascites. In order to increase and actualize our knowledge, we report 5 cases and review pertinent literature. **MATERIAL AND METHODS:** This is a descriptive study. In short time around 2 months we can observe clinic presentation of hepatic hydrothorax and spontaneous bacterial empyema in 5 hospitalized patients of INCMNSZ, with etiology, evolution and outcomes diverse. We not only analyze clinic and paraclinic evolution but also outcomes. **RESULTS:** We report the case of 5 patients that developed hepatic hydrothorax as the first complication of liver cirrhosis which was treated with thoracentesis, diuretics and antibiotics also in one case albumin infusion improved renal dysfunction. Due to the lack of response to diuretics diverse treatment were used, with diverse outcomes despite optimal treatment. In order to increase and actualize our knowledge, we review pertinent literature related to pathophysiology, clinical manifestations, treatment and prognosis of hepatic hydrothorax and spontaneous bacterial empyema. **CONCLUSION:** These conditions, despite being infrequent, require a high suspicion index because of its therapeutic and prognostic implications, being very similar to spontaneous bacterial peritonitis and different from other pleural effusions and classic empyema.

002

SURVIVAL AFTER TIPS (TRANSJUGULAR INTRAHEPATIC PORTO SYSTEMIC SHUNT) FOR REFRACTORY ASCITES IN CIRRHOSIS AND BUDD CHIARI SYNDROME

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INTRODUCTION: Refractory of ascites is a condition that affects survival and quality of life in patients with cirrhosis. Treatment is based on the accomplishment of repeated paracentesis, nevertheless in cases that do not tolerate this procedure or requires it frequently (3 or more per month) TIPS should be considerate with a carefully patient selection, that includes a Child score < 12 points or MELD < 20. It has been observed that this maneuver has little impact in survival of these patients if they are not transplanted. **OBJECTIVE:** Describe survival after TIPS placement in patients with refractory ascites in Budd Chiari syndrome or decompensate cirrhosis. **MATERIAL AND METHODS:** The cases were reviewed in which a TIPS was placed for treatment of refractory ascites in our Institute. Survival was analyzed. Demographic and biochemical variables were obtained. Descriptive statistic was realized. **RESULTS:** A total of 17 patients were identified to whom TIPS performance was indicated for the treatment of refractory ascites, six men and eleven women. The diagnoses were syndrome of Budd Chiari (SBC) in eight patients, cirrhosis by alcohol in four, cirrhosis for hepatitis C virus in three cases and primary biliary cirrhosis in two. The median of Child score was of 11, 5 (max-min 10-13) and for MELD score was of 19, 5 (12-30). The mean creatinine value before the TIPS was $1.92 \pm \text{mg/dL}$. Ascites was resolved in 15 of 17 patients, all these responders patients had a porto-cava gradient less than 10 mmHg after TIPS placement. Encephalopathy appeared subsequent to the TIPS in 13 patients (75%) that was of grade II in all except two cases that presented grade IV of encephalopathy and that responded with lactulose and L-ornitina L-aspartate. The mean follow up was of 6, 5 months (1-50). We identified two different survival groups: Patients with SBC have a mean survival of 12 months (6-50) and patients with cirrhosis have mean survival was of 5 months (1-24). For the moment in which the study was realized only remained alive three patients (1 SBC and 2 with cirrhosis (1 with liver transplantation). Patients with cirrhosis and survival < 1 month after TIPS had higher creatinine levels and higher MELD score. **CONCLUSIONS:** Refractory ascites is resolved in 90% of cases with TIPS placement, although a survival impact is difficult to demonstrate because mortality is high in the first year, especially in patients without liver transplantation and with high basal creatinine levels (hepato-renal syndrome type 2). Nevertheless, our data suggest that patients with SBC have major benefit in survival which could be translated in a greater time of bridge to the transplant. They are required of more cases to demonstrate this impact in the survival.

003

CASE REPORT

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CASE REPORT: This is the history of 23 yr old male with no previous medical history, presenting to the ER for upper gastrointestinal bleeding characterized by bright red hematemesis. Tables 1 and 2 shows the laboratory test in the ER. Hemodynamic status is handled by requiring transfusion of 2 packed red blood cells in the emergency department and upper endoscopy was performed found the presence of medium to large esophageal varices and the presence of fund varices Sarin

type II without stigmata of recent bleeding. In the radiology workup ultrasound was performed reported normal liver echogenicity, the diameter of the portal vein was normal and spleen was 18 cm without ascites. Because sonographic suspicion of thrombosis of the splenic vein Angio-CT of the portal system was requested (Figure 1). The report was presence of splenic vein thrombosis at the body of the pancreas, the presence of spleno-renal shunt and large gastric varices. Especial examinations (Table 3) was investigated for pro-thrombotic states. Ac anti lupic coagulant was positive, Ac Anti cardiolipin and mutation of coagulation factor V were negative, with this most likely diagnosis was primary anti phospholipid syndrome. Fibro scan and gradient portal pressure was performed with liver biopsy via trans-jugular puncture the portal pressure gradient was 12 mm/Hg which means that the source of the portal hypertension is sinusoidal or post-sinusoidal, on the biopsy we observed the presence of minimal expansion of triads, sites with low and incomplete septa without evidence of inflammatory infiltrate on the scale of Metavir Activity: 0 Fibrosis 1. In Fibro scan we obtain 9 k Pa being representative of a F1-F2 stage of the Metavir. On the follow-up the patient was seen by service of rheumatology and gastroenterology and he began on anticoagulation therapy base on warfarin. As apart of the evaluation and management general surgery department performed splenectomy and devascularization of the varicose veins of the fund. Catheterization was repeated 3 months after the surgery reported a gradient of 12 mm/Hg. **DISCUSSION:** The patient as already mentioned is a young man who had primary anti-phospholipid syndrome and portal hypertension with large fundic varices and secondary hypersplenism. We thought in the first place that presence of the splenic thrombosis was origin of portal hypertension, but the measure of the portal pressure gradient pre and post surgery and liver biopsy with hepatic sinusoidal expansion in the absence of fibrosis tells us of a probable concomitant liver disease in the pathophysiology of portal hypertension, these patients may develop post-sinusoidal vascular events or autoimmune liver disease in future.

004

BLEEDING GASTRIC VARICES: EXPERIENCE OF ENDOSCOPIC INJECTION WITH CYANOACRYLATE AT CENTRO MÉDICO NACIONAL DE OCCIDENTE

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INTRODUCTION: Portal hypertension is the main complication of cirrhosis, and variceal bleeding constitutes one of the principal morbidity and mortality causes of cirrhosis. Gastric varices (GV) are less prevalent and present less bleeding risk than esophageal varices, but usually their clinical presentation massive gastrointestinal bleeding, with high recurrence rate (up to 80%) and can be lethal. Endoscopic injection with N-butyl-cyanoacrylate is one of the most widely accepted for their treatment. **OBJECTIVE:** To report effectiveness and security of endoscopic injection with cyanoacrylate for bleeding GV and its eradication in a tertiary center. **MATERIAL AND METHODS:** Endoscopic reports and medical records of patients presented in Gastroenterology Service, IMSS CMNO, who received endoscopic injection with cyanoacrylate for bleeding GV from January 2006 to Decem-

ber 2010 were achieved. Periodic monitoring was performed until its obliteration or death; we included those with complete clinical records. Endoscopic treatment consisted in intravariceal administration of cyanoacrylate + lipoidal 1:1. Periodic endoscopic follow-up was accomplished and new injection was performed depending on findings, until its elimination or hardening. Radiologic control was taken only in patients with clinical suspicion of embolic complications. The monitoring finished with variceal eradication or death. **RESULTS:** 55 cases of bleeding GV (active bleeding or recent stigmata) with endoscopic injection with cyanoacrylate were collected; 10 were excluded because incomplete clinical records. 45 cases were included, 18 (40%) male and 27 (60%) female, with a mean age of 52.2 years. About child-pugh distribution, 11 (24.4%) belonged to class A, 24 (53.3%) to class B and 10 (22.2%) to class C. Among the most common cirrhosis etiologies were HCV infection in 21 cases, alcoholic in 12 cases and steatosis in 4 cases. All patients presented upper gastrointestinal bleeding showed as hematemesis and melena. In 33.3% of cases, this event was the debut of cirrhosis. There were reported GOV-2 in 26 (57.7%) cases, IGV-1 in 15 (33.3%) and GOV-1 in 4 (8.8%). Variceal eradication was achieved (elimination or hardening) in 40 (88.8%) patients. Of which, 1 (2.5%) presented pulmonary embolism, that resolved with medical management; 4 (10%) presented active jet bleeding during the procedure, that resolved with a second endoscopic injection with cyanoacrylate. During follow up, 10 (25%) patients presented rebleeding in spite of 1 or 2 previous cyanoacrylate applications, but continued sclerotherapy sessions, achieving eradication. 1 to 4 sessions were required to achieve eradication of GV, with an average of 1.8 sessions per patient; 1 to 6 ampullas of cyanoacrylate were applied to achieve eradication, with an average of 2.4 ampullas per patient. The 5 (11.1%) patients who didn't achieve eradication in spite of 1 to 3 sessions of endoscopic injection with cyanoacrylate (1 to 5 ampullas) had upper gastrointestinal bleeding with fatal ending, reporting death for bleeding complications. **CONCLUSIONS:** In our center, endoscopic injection with cyanoacrylate proved to be an effective therapy (88.8%) in eradicating bleeding GV and have a low rate of major complications. **CONFLICT OF INTEREST:** This work presents no conflict of interest.

005

EFFICACY AND SAFETY OF TWO SCHEMES OF TREATMENT WITH TERLIPRESSIN IN ESOPHAGEAL VARICEAL BLEEDING AFTER SUCCESSFUL LIGATION: EARLY RETIREMENT AGAINST STANDARD SCHEMA

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INTRODUCTION AND OBJECTIVES: At esophageal variceal bleeding endoscopic therapy with banding is the recommended treatment and its effectiveness improves with the previous use of pharmacological therapy. Continue pharmacological therapy after successful band ligation may

increases costs, but it has been considered that the early withdrawal may increase risk. The objective of the study was to compare the efficacy and safety of the retirement scheme of terlipressin after successful band ligation against a scheme of 72 h. **MATERIAL AND METHODS:** Prospectively we selected patients older than 18 years with digestive bleeding from esophageal varices who were managed under established care protocol that included pharmacological therapy from their income (terlipressin 2 mg initial bolus followed by 1 mg every 6 h) and digestive endoscopy in the first 24 h from income. Informed consent was obtained in those patients with successful banding ligation of esophageal varices and they were randomly assigned to suspend terlipressin (Group 1 = G1) or receive terlipressin until complete 72 h period (Group 2 = G2). Both groups were monitored in hospital at least three days with similar management and medical surveillance and at discharge non-selective beta-blocker was initiated. Patients were followed 4 weeks. Efficacy was evaluated by variceal bleeding control, safety was assessed by complications or death by cause of bleeding or pharmacological therapy, both in the immediate (3 days) and medium (4 weeks) period. The results were compared and applied statistical tests (χ^2 and Student, Biostat 2009 Professional 5.8.0, Analyst Soft.Inc t). **RESULTS:** Between June 2009 and October 2010 60 patients were included (30 in each group). There was no difference between groups in age, gender, etiology of liver cirrhosis, comorbid, prior esophageal variceal bleeding and use of beta-blocker, vital signs, level of anaemia and thrombocytopenia, degree of hepatic insufficiency (Child Pugh, MELD), time from admission to endoscopy, grade and stigmata of variceal hemorrhage. **Effectiveness:** in the first three days of monitoring there were no differences between groups in evolution of vital signs, level of hemoglobin, platelet, biochemical parameters, and no patient had rebleeding. The four weeks of follow-up study found no difference in rebleeding events (G1 = 3, G2 = 2, $p = 0.64$), requirements of globular package units (G1 = 2.1 ± 1.6 , G2 = 1.7 ± 1.3 , $p = 0.33$), days of hospitalization (G1 = 4.6 ± 2.1 , G2 = 4.2 ± 1.2 , $p = 0.37$), events of re-hospitalization (G1 = 2, G2 = 2, $p = 1$). **Security:** There were no differences between groups in the number of terlipressin side effects (G1 = 1, G2 = 2, $p = 0.55$), cirrhosis complications in hospitalization (G1 = 4, G2 = 3, $p = 0.69$) or in the 4 weeks follow-up (G1 = 5, G2 = 3, $p = 0.44$). In the first three days follow-up there was no significant difference in mortality but 1 death, presented by hypertensive crisis and myocardial infarction on the third day of the 72 h terlipressin scheme (G1 = 0, G2 = 1, $p = 0.31$); the overall mortality in 4 weeks of the study did not differ between groups (G1 = 4, G2 = 2, $p = 0.38$). **CONCLUSIONS:** The rate of mortality with both interventions is lower than that reported in the current literature, acute variceal bleeding patients benefit from administration of terlipressin prior to endoscopy. No significant differences in efficacy and safety between suspend terlipressin immediately after endoscopy with successful banding ligation or continue the treatment for 72 h. Events of rebleeding with both schemes may occur. Terlipressin can cause serious side effects. **CONFLICT OF INTEREST:** This work was performed by Social Security resources; there were no conflicts of interest.

006

CORRELATION DEGREE OF FIBROSIS BETWEEN FIBROTEST® AND TRANSYUGULAR BIOPSY SPECIMENS INTERPRETED WITH METAVIR SCALE

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BACKGROUND AND AIM: Liver biopsy is the gold standard for the measurement of fibrosis in patients with cirrhosis. Fibrotest® (Biopredictive, Mexico) is a panel of biochemical markers of fibrosis that originally validated in a cohort of hepatitis C patients that is now available for other etiologies of liver cirrhosis, which in turn is a non-invasive method for the determination of liver fibrosis. The aim of this study was to identify the relation between Fibrotest® score with the degree of liver fibrosis determined by liver biopsy in patients with liver fibrosis. **MATERIAL AND METHODS:** We performed a prospective study in consecutive CIRRHOTIC patients attended at Hospital Universitario de Monterrey between August 2010 and March 2011. All patients underwent measurement of hepatic vein gradient pressure (HVGP) and a liver biopsy was obtained during the procedure. Fibrotest was obtained before the invasive procedure. Demographic, clinical, laboratory variables were collected and liver biopsies were interpreted by an expert pathologist by using the Metavir scale. Descriptive statistics were performed and Kappa correlation was used to determine the relationship between Fibrotest and Metavir scores. **RESULTS:** A total of 58 patients were studied, 56.9% (n = 33) were male, and mean age found was 52.5 ± 12 years. The most common etiologies were cryptogenic 36.2% (n = 21) and alcoholic 34.5% (n = 20). Child-Pugh B status was found in half of the patients. Mean HVGP was 17.1 ± 7 mmHg, with 86% (n = 50) of patients above 10 mmHg of HVGP, of which 96% (n = 48) had esophageal varices. Of biopsies, 21% (n = 12) were inadequate for analysis, but 89% (n = 41) of remain revealed Metavir F3-F4 fibrosis. Fibrotest demonstrated F3-F4 fibrosis in 82.6% (n = 38), and the concordance with the Kappa index between transjugular biopsy and Fibrotest was 0.556 (p = 0.001). Moreover, an association between the presence of Fibrotest F2-F4 fibrosis and HVGP > 10 mmHg was found (p = 0.001) as well as with the presence of varices (p < 0.0001). **CONCLUSION:** Fibrotest is an alternative to liver biopsy for the evaluation of fibrosis degree in patients with cirrhosis. Moreover, patients with a Fibrotest > F2 has a high probability to present clinically significant portal hypertension (HVGP > 10) and esophageal varices. **ACKNOWLEDGE:** We appreciate the support given by Laboratorios UCB de México in the realization of this research.

007

COMPARISON OF THE NUTRITIONAL STATUS IN PATIENTS WITH ALCOHOLIC LIVER CIRRHOSIS AND OTHER ETIOLOGIES OF CIRRHOSIS

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INTRODUCTION: Cirrhosis is considered as a public health issue worldwide. In subjects with cirrhosis of any etiology, nutritional deficiencies are common and give rise to a poor prognosis. Approximate figures have found out that 50% of

patients with cirrhosis have malnutrition. Malnutrition is more related with the liver damage than with the cause. Nevertheless, alcohol consumption is capable to produce malnutrition before the symptoms of liver insufficiency because alcohol consumption decreases the ingestion of nutrients.

OBJECTIVE: Comparison of the nutritional status in patients with alcoholic liver cirrhosis and other etiologies of cirrhosis. **MATERIAL AND METHODS:** Cross sectional study. The protocol was approved by the Hospital Committee for Clinical Investigations, informed consent was obtained from all subjects; the sampling was not probabilistic. The inclusion criteria were: female or male, age 18 or older, diagnosed with alcoholic liver disease or other etiology of cirrhosis. Subjects that assisted to the Liver Clinic disease at CMNO, HE, IMSS and had cirrhosis with Child-Pugh A, B, or C with no complications. Anthropometric measurements were made such as weight, height, triceps skinfold, middle arm circumference. Also we took from the medical record the most recent results of albumin and blood count. In addition, we did a comparison between the two groups. Paired and unpaired t tests, chi-square test, and analysis of variance were used for statistical analysis. The study was made in a period of five months.

RESULTS: In the study we included 39 patients, of whom 10 patients belonged to the group of alcoholic liver cirrhosis and 29 liver cirrhosis group of other etiologies. The anthropometric and biochemical results are shown in table 1. We observed a significant difference in fat mass area, the patients with alcoholic liver disease had less fat mass area in the arm (21.54 ± 16.74) and the other etiology (38.35 ± 22.69) p = 0.039. Also there is a significant difference in the percentage of fat mass area, the patients with other etiology of cirrhosis (47.79 ± 13.43) and alcoholic liver cirrhosis (34.35 ± 12.97) p = 0.009.

Table 1. Anthropometric evaluation of the patients with liver cirrhosis.

	Other etiology Media \pm SD	Alcoholic Media \pm SD	p* value
Height cm	157 \pm 1	165 \pm 3	0.016
Weight (kg)	74.8 \pm 22	75.9 \pm 25	0.938
TSF (mm)	25.8 \pm 11	17.9 \pm 9.2	0.060
MAMC (cm)	30.2 \pm 6.7	26.7 \pm 6.0	0.156
BMI (kg/cm ²)	30.1 \pm 7.96	27.4 \pm 8.14	0.361
AMA	37.8 \pm 17.4	37.9 \pm 14.7	0.998
AMA Z score	-1.78 \pm 0.9	-2.22 \pm 0.64	0.172
AFA	38.36 \pm 22.69	21.54 \pm 16.74	0.039
Fat mas area Z score	0.33 \pm 1.68	-0.74 \pm 1.67	0.513
% AFA	47.79 \pm 13.43	34.35 \pm 12.97	0.009
% AFA Z score	0.60 \pm 1.68	0.63 \pm 1.44	0.957

SD: Standar desviation. TSF: Triceps skinfold. MAMC: Midarm muscle circumference. BMI: Body mass index. AMA: Upper-arm muscle area. AFA: Upper-arm fat area. *Paired and unpaired t tests.

DISCUSSION: Liver cirrhosis is characterized by a significant reduction in muscle mass and fat with redistribution of body water. The most significant losses of fat mass happen in the initial stages followed by an accelerated loss of muscle mass in the final stages. The results of this study are similar to this; patients who participated in the study were in stages of compensated liver cirrhosis (stage A or B of the Child-Pugh scale) they had a less fat mass and a lower percentage of this in the arms. Malnutrition data of this study suggest that nutritional deficiencies in patients with cirrhosis are similar to those found world wide. **CONCLUSIONS:**

The patients with alcoholic liver disease have a higher degree of malnutrition compared to the patients with cirrhosis of other etiologies because the fat mass area and the percentage of fat mass area were less. **CONFLICT OF INTEREST:** The authors declare that they have no competing interests.

LIVER TUMORS

001

CLINICOPATHOLOGICAL FEATURES OF HEPATIC TUMORS IN A THIRD LEVEL HOSPITAL IN NORTHEAST OF MEXICO. EXPERIENCE OF 12 YEARS

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INTRODUCTION: Hepatocellular carcinoma (HCC) is one of the leading causes of cancer deaths, and its incidence has increased in the last decades. There are well recognized risk factors for HCC: infection with hepatitis B and C virus (HBV and HCV) and alcoholism. Although in up to 5-30% of cases, neither risk factors or etiology are identified. It's considered that most of them could be related to non-alcoholic fatty liver disease (NAFLD) which is a manifestation of the metabolic syndrome (MS). This syndrome has been related with several types of cancer, HCC among them. It is estimated that in the year 2050, NAFLD will surpass infectious etiology as risk factor for HCC. **AIM:** To describe the clinical, biochemical and histopathologic features of hepatic tumors, all of them with histopathological confirmation, in a third level Hospital in Northeast of Mexico. **METHODS:** This is a retrospective, descriptive study that included all liver tumors with histopathological confirmation, reviewed at the Pathology Department of Hospital San José Tec de Monterrey (HSJ) from January 1999 to February 2011. All hospitalized patients with diagnosis of hepatic tumor by clinic data or imaging were included. A descriptive analysis with a Minitab 16.01 software was done. **RESULTS:** Sixty five patients with hepatic tumors were included. In 30 (46%) the diagnosis was metastatic tumors and 35 cases (54%) corresponded to primary hepatic neoplasms. In the primary hepatic neoplasm group the mean age was 67.48 ± 15.77 years and 29 (83%) were males. Clinical manifestations included: abdominal pain in 8 (27%), malaise in 6 (20%), weight loss in 2 (7%), 17% (3) cirrhotic stigmata, 3% (1) palpable mass and 50% (15) were asymptomatic. In 90% imaging studies established the diagnosis of HCC. The most frequent neoplasm found was HCC in 85.7% (20 were well differentiated, 3 moderately differentiated and 4 undifferentiated). In 11.4% (4) the diagnosis was cholangiocarcinomas and only 1 adenoma was found. In 3/16 patients with available alpha-fetoprotein levels they were greater than 400 ng/mL. Three HCC had HBV infection and other three had HCV. In 50% (n = 15) of

the biopsies, cirrhosis was documented by histological examination. From these, 5 patients had been previously diagnosed as cirrhotic: 2 with HCV, 1 with HBV infection and 2 patients had no risk factor for cirrhosis. In the remaining 10 patients (30%) there were no risk factors or previous history related to liver cirrhosis. **CONCLUSIONS:** In this case series that includes only hepatic tumors with histological diagnosis, hepatic primary neoplasms were more frequent than metastatic. Well differentiated HCC comprised the majority of neoplasms. In 50% of the HCC, cirrhosis was documented by histology. From these, only 33.3% were known as cirrhotic, and the remainder 66.7% had no risk factor for HCC. This data suggest that a significant proportion of the HCC detected could be associated with metabolic factors in absence of previously diagnosis of cirrhosis or any other identified risk factor. Further investigation linking NAFLD and HCC in our media is warranted. **CONFLICT OF INTEREST:** The authors have no relationship to disclose.

002

HEPATOCELLULAR CARCINOMA COMBINED WITH CHOLANGIOCARCINOMA DIAGNOSED THROUGH PERCUTANEOUS BIOPSY

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INTRODUCTION: Combined hepatocellular and cholangiocellular carcinoma is a rare neoplasm that accounts for between 1.0 and 4.7% of the primary neoplasms in the liver. Two types have been described: collision tumors originating from different cells, and transitional tumors that probably originate from a single cell and that show both histological patterns mixed. A mixed tumor case diagnosed through a percutaneous biopsy is described. **CLINICAL CASE:** A 67 year-old male with intense alcoholism for 30 years and type 2 diabetes mellitus with 10 years of evolution. Four months before his admission, he presented with intermittent abdominal pain in the right hypochondrium, jaundice, generalized itch, weight loss (10 kg), weakness, and adynamia. Physical examination indicated he was emaciated, with generalized jaundice and hepatomegaly with pain to deep palpation. The laboratory tests showed the following results: glucose 227 mg/dL, total bilirubin 2.1 mg/dL, direct bilirubin 0.8 mg/dL, alkaline phosphatase 228 U/L, gamma-glutamyltransferase 818 U/L, α -fetoprotein 28 ng/dL, CA19-9 464 U/L, CA-125 76 ng/dL, and ACE 17 ng/dL. An abdominal tomography revealed an ovoid hepatic tumor with irregular edges of 14 x 11.2 x 10 cm in segments IV and V, with mixed attenuation from soft tissue density and liquid component, with strengthening in phase contrast and invasion of the portal vein. A percutaneous biopsy was performed using an ultrasound-guided Trucut needle and the patient was diagnosed with primary mixed hepatocellular and cholangiocellular carcinoma. Due to the advanced stage of the condition, the patient received palliative treatment. **DISCUSSION:** Mixed hepatic carcinomas are generally diagnosed through analysis of autopsy reports or examination of partial resections of hepatic tissue removed by hepatectomy. Needle biopsy diagnosis is rarely established, because of the small size of the obtained samples. Only one journal (*J Gastroenterol & Hepatol* 1998; 13: 34-40) has reported that 8 out of 21 cases were diagnosed through a percutaneous biopsy.

003

CHOLANGIOCARCINOMA: EXPERIENCE AT THE GENERAL HOSPITAL OF MEXICO

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INTRODUCTION: Cholangiocarcinoma is a tumor originating in the epithelial cells of the bile duct and it represents the second most common malignant neoplasm in the liver. The main risk factors include, among others, primary sclerosing cholangitis, common bile duct cysts, and hepatolithiasis. Short-term prognosis is bad and the therapeutic options are few. **OBJECTIVE:** To determine the demographic, clinical and survival characteristics in a group of patients diagnosed with cholangiocarcinoma. **MATERIAL AND METHODS:** A search for autopsy and biopsy reports with a histopathological diagnosis of cholangiocarcinoma was carried out among the archives from 2003 to 2010 of the Pathology Department of the General Hospital of Mexico. A total of 16 cases were found, 8 autopsies and 8 biopsies (7 percutaneous biopsies and one laparotomy biopsy). The histological diagnosis of cholangiocarcinoma was confirmed by a pathologist from the Pathology Service, supported by the clinical signs and the laboratory and imaging parameters. Demographic, clinical, biochemical, treatment and survival characteristics are shown. Descriptive statistics was used and the nominal variables are expressed as proportions, whereas the numerical variables are expressed as medians (minimum-maximum). Mann-Whitney's U test was used to compare the numerical variables between patients with intrahepatic tumors and those with extra hepatic tumors. **RESULTS:** Out of the 16 patients diagnosed with cholangiocarcinoma, 12 (75%) had intrahepatic tumors and 25% had extrahepatic tumors. The average age at the time of diagnosis was 63 (39-86) years. Seven patients (43.8%) were female and nine (56.3%) were male. Risk factors were identified in only one patient (6.25%), who had congenital bile duct cysts. Other associated risk factors recently described were alcohol consumption (50%), liver cirrhosis (31%), hepatitis C virus infection (12.5%), bladder lithiasis (37.5%), and diabetes mellitus (31%). The average time from symptom onset to diagnosis was 4.7 (1-12) months. The first symptom observed was abdominal pain (66%) in intrahepatic cases and jaundice (75%) in extrahepatic cases. The main manifestation at the moment of diagnosis was abdominal pain (81.3%), of which 23% (3) had manifestations of associated cholangitis. Another important finding was weight loss in 62% of the cases. Patients with extrahepatic tumors had higher total bilirubin levels (30.4 vs. 3.3 mg/dL, $p = 0.005$). The CA19-9 value of 86% of the cases was above 150 U/mL. The most frequent location of intrahepatic tumors was the right lobe (58.3%), followed by the left lobe (8.3%), and both (33.3%). All extrahepatic tumors were hilar. The most frequent stage was IIA (50%), followed by III (31.3%). Only two (12.5%) cases were treated with hepatectomy and four (25%) underwent a percutaneous bypass of the bile duct. The global survival median was 1.4 (0.5-6) months. **CONCLUSIONS:** Cholangiocarcinoma is a rare neoplasm diagnosed in most cases at an advanced stage, with no option of curative surgical treatment. The increase in frequency of intrahepatic tumors reported in recent literature is a finding from our study. In Mexico there is not enough information about these tumors.

004

HEPATIC EPITHELIOID HEMANGIOENDOTHELIOMA: A SIMULATOR OF METASTASES. CASE REPORT

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INTRODUCTION: Hepatic hemangioendothelioma is a rare tumor in adults, of unknown etiology that most often affects women. Its importance lies in that diagnostic imaging studies simulating liver metastases and this leads to misdiagnosis. **CASE REPORT:** 62-year-old man with history of type 2 diabetes mellitus and benign prostatic hypertrophy who developed chronic renal failure and for this reason was abdominal ultrasound finding of multiple metastatic liver lesions and small kidneys. Laboratory tests reported normochromic normocytic anemia, elevated azo function tests. Required peritoneal dialysis since it showed worsening of chronic kidney disease. CT scan of abdomen showed injuries can correspond to tomographic hepatic metastases, the rest of the CT scan was normal report without finding a primary neoplasm. In our department, study protocol began searching for primary neoplasia undergoing upper endoscopy findings gastropathy chronic biliary, colonoscopy found only uncomplicated diverticular disease. A CT scan of the chest with mediastinal and lung window Reporting normal. Was requested Alfa fetoprotein, carcinoembryonic antigen, CA 19-9 and prostate-specific antigen in all normal parameters, and viral hepatitis panel B and C negative. Clinically, the patient was not with wasting syndrome and no evidence of primary tumor imaging studies, we decided to perform laparoscopic liver biopsy, richly vascularized tumor was found and biopsy to massive bleeding requiring conversion to open surgery to perform to achieve hemostasis, the postoperative course was satisfactory to be graduated at 48 h. The report of the biopsy was benign liver epithelial hemangioendothelioma. The patient remained on surveillance for a year in an asymptomatic, with no changes in liver function tests and CT scan no change in relation to the original. **CONCLUSIONS:** We report a case of hepatic tumor metastases suggesting that clinically and biochemically not for a patient with advanced malignant hepatic neoplasia. Hence the importance of liver biopsy in this clinical setting to rule out benign neoplasm simulating liver metastases.

005

SUSTAINED VIRAL RESPONSE IN PATIENTS WITH HEPATIC C VIRUS, FOLLOWED FOR 10 YEARS

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INTRODUCTION: Sustained viral response is more objective parameter to assess the antiviral response in patients with hepatic C virus. Is defined as undetectable levels of hepatitis C virus by molecular biology studies HCV RNA PCR. Six months after stopping treatment. This response is estimated to range from 30 to 55% in patients with chronic hepatitis C and 30 to 46% in patients with liver cirrhosis, however, is not common practice to continue this study because they are considered virtually viremia. As a study tracking 10 years in the Hospital Valentín Gómez Farías ISSSTE, Zapopan, Jalisco. **OBJECTIVE:** Evaluate sustained viral response in patients with he-

patic C virus in a 10 year period. **MATERIAL AND METHODS:** Study design: Retrospective cohort. In the Gastroenterology, Hospital of the ISSSTE Valentín Gómez Farias, Zapopan, Jalisco. In a period of 10 years were followed up patients with SVR. Bearers of liver cirrhosis and chronic hepatitis C virus persistence is evaluating 115 patients with chronic hepatitis C virus and 180 with hepatitis C, diagnosed by biochemical studies, histological, serological and molecular characteristics of hepatitis C, which are given 180 µg pegylated interferon and ribavirin subcutaneous week 400 to 1,200 mg according to weight and genotype over a period of 48 weeks. Statistical analysis averages, percentages and t student. **RESULTS:** There was a sustained viral response in 55% in patients with hepatitis, with genotype 1 and in patients with cirrhosis with a response of 43%, this number of patients were followed for over 10 years finding the following: average patients (Table 1). **CONCLUSIONS:** a) In our study we found that most patients are women. b) Age is significantly higher in patients with cirrhosis than in hepatitis. c) Genotype 1 prevailed over the rest in both groups but the monitoring of sustained viral response was average 7.4 years and 6.9 in hepatitis cirrhosis. d) As we conclude the SVR is similar in both groups and that relapse in patients with cirrhosis is significantly higher in patients with hepatitis.

Table 1.

Average	n	Year	Gender	Genotype	Pcr RNA VHC	YEARS RVS VHC	Patient Relapse
Hepatitis	33	51.7	F 25(75%) M 8(25%)	1ab (72%) 2ab (28%)	358.000 UI/mL	7.4	n 1
Cirrhosis	17	64.4	F 14(82%) M 3(18%)	1ab (76%) 2ab (24%)	399.000 UI/mL	6.9	n 8 P<0.05

006

EMBRYONAL LIVER SARCOMA IN A 16 YEARS OLD PATIENT IN THE HOSPITAL OF MEDICAL SPECIALTIES "LA RAZA", MEXICO

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INTRODUCTION: The embryonal liver sarcoma was first reported in 1978 by Stocker, *et al.* Since then, only about 150 cases have been reported in world literature. In Mexico there are about 4 cases in adults reported in international literature. So we consider this case is important for the epidemiology of our country. **OBJECTIVE:** The aim of our study is to describe the case of 16 years old patient, with an hepatic lesion which was diagnosed as an embryonal liver sarcoma. **MATERIAL AND METHODS:** The description of the case of a 16 years old boy, of the Gastroenterology Service of the Hospital of Medical Specialties "Dr. Antonio Fraga Mouret" La Raza in Mexico who was studied because of an hepatic tumor. **RESULTS:** The patient had not pathological history; and begun with pain in right upper quadrant, significant weight lost and jaundice. He had a painful palpable liver that was able to be detected from upper right quadrant to right iliac fossa. The significant laboratory findings included: the antinuclear antibodies which were positive in a dilution of 1:80, alkaline phosphatase of 227 U/L, LDH 1109 U/L, GGT 293 U/L,

hemoglobin of 9.5 g/dL, the alfa feto protein was of 01.83 UI/mL, CA 125 of 99.7 U/mL, with no other significant anomaly. A simple fase TC of abdomen was taken, in which a large, heterogenic tumor was corroborated (Figure 1). Then an US percutaneous guided liver biopsy was performed which reported hystologic changes according to embryonal liver sarcoma (Figure 2). After the liver biopsy, the patient presented tachycardia, polypnea, asthenia and adynamia. New laboratories were taken, in which the hemoglobin descended to 6.5 g/dL. So he was transfused 4 globular concentrates. A new TC was taken, in which no evidence of acute hemorrhage was found. After that, the patient, had a improvement of the vital signs and overall physical status, his last hemoglobin control was of 9.9 g/dL. Finally, his whole clinical condition deteriorated again and the patient died before any oncologic intervention could be done. The total follow up was of one month. **CONCLUSION:** We conclude that this tumor may be underdiagnosed or under reported in adults in our country, but still must be thought as a differential diagnosis for hepatic lesions.

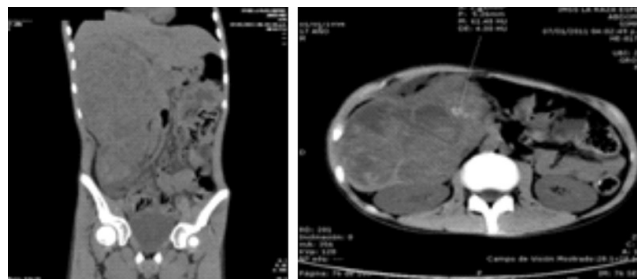


Figure 1. Simple face TC that shows hepatomegaly secondary to a tumoral heterogenic lesion in right lobe of the liver which measured about 24 x 12 x 14 cm.

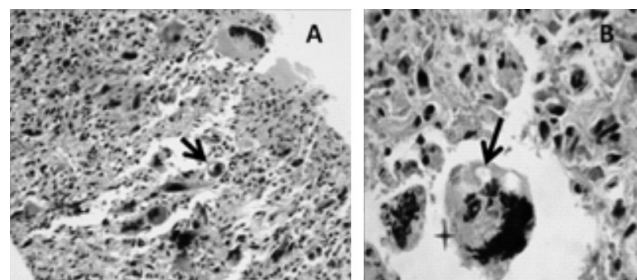


Figure 2. The cells of the tumor vary from small tapered, spindle and bizarre multinucleated giant cells, with hyperchromatic nuclei and atypical mitosis, with eosinophilic globules (star) and intracytoplasmic vacuoles (arrows), in a collagenous stroma (hematoxylin and eosin stain, original magnification A x 10, B x 40).

007

HEPATIC ANGIOSARCOMA DIAGNOSED BY AUTOPSY. REPORT OF 4 YEARS IN THE GENERAL HOSPITAL OF MEXICO

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BACKGROUND: Hepatic angiosarcoma (HA) is a rare primary tumor 0.5-2.5 cases c/10,000,000, accounts for only 2% of all malignant primary liver tumors, it's the most common type of hepatic sarcoma. It has a poor prognosis and is rapidly progressing tumor. In men appears between 2nd and 8th decade of life and the peak incidence between the 6th and 7th decade. The risk factors are exposure to thorium dioxide, vinyl chloride and arsenic. The hemochromatosis or Von Recklinghausen's disease, cyclophosphamide treatment, steroids and oral contraceptive agents have been also related. However in over half of patients the origin remains uncertain. Initial symptoms, clinical and laboratory findings are not specific, these includes: abdominal pain, weakness, weight loss and jaundice, thrombocytopenia, hemolytic anemia and intravascular disseminated coagulation. The imaging findings have a large dominant mass measuring 8-14 cm or multiple small nodules scattered measuring < 3 cm, hypoattenuating, heterogeneous, in the right lobe and 80% has necrosis. Most patients have metastatic lesions at the time of diagnosis, the most common site is the lung and spleen. The median survival for patients without treatment is < 6 months. The majority is unresectable; palliative chemotherapy could be an option. More than 35% of diagnoses are obtained in necropsies. **OBJECTIVE:** To describe clinical and pathological findings in cases of HA diagnosed at autopsy in a period of 4 years in the General Hospital of Mexico (HGM). **MATERIAL AND METHODS:** We collected information of all cases of HA in autopsy during the period January 2007 to December 2010 in the HGM. The clinical records were reviewed, to search for intentionally background and clinical characteristics that might be relevant to the diagnosis. **RESULTS:** We reviewed 2894 autopsies and found 5 (0.17%) cases had a diagnosis of primary HA. 4 cases were male (80%), the average age was 56 years (range 36-78). No patients had a history of exposure to specific carcinogens, 80% with smoking and IT > 10, 1 diabetic and 1 patient with chronic alcoholism and liver failure secondary. 80% right upper quadrant abdominal pain was the most common presenting symptom, 60% developed jaundice, on physical examination 3 patients had hepatomegaly, 80% had anemia and lymphopenia at admission, 2 patients with thrombocytopenia and all patients with hypoalbuminemia; 60% had elevated total bilirubin predominantly direct, 100% with elevated transaminases and alkaline phosphatase. Tomographic findings were hypodense lesions, 4 with compression of vascular structures, and extrahepatic metastatic were found only in 1 patient in the suprarenal gland. **CONCLUSIONS:** HA is a rare tumor of difficult diagnosis with rapidly progressive and fatal. All of cases had nonspecific symptoms, without evidence of liver failure in most of them, clinical and pathological findings are consistent with the reports, only found one case with metastatic in an unusual site. Because of its low incidence has not defined specific characteristics for early diagnosis. Possibly the HA is a neoplasm frequently underestimated due to low suspicion as a differential diagnosis in liver tumors. **CONFLICT OF INTEREST:** Non conflict of interest.

008

INTRAHEPATIC CHOLANGIOCARCINOMA: A DIAGNOSIS TO CONSIDER IN PATIENTS WITH LIVER CIRRHOSIS

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BACKGROUND AND AIM: Cholangiocarcinoma (CC) accounts for 10 to 15% of hepatobiliary tumors in cirrhotic patients. Several recent studies have reported an increase in both incidence and mortality in this group of patients. The aim of this study is to present our 5 year experience in two third-level centers of Monterrey, Mexico. **MATERIAL AND METHODS:** A retrospective (5 year) search of records was performed in Christus Muguerza Alta Especialidad and Hospital Universitario "Dr. José E. González" of patients with histological confirmed diagnosis of hepatocellular carcinoma, biliary tract adenocarcinoma and CC. Studied variables included genre, age, presence and etiology of cirrhosis, tumoral markers, MELD score at the moment of diagnosis, involvement of the tumor at diagnosis, diagnostic approach of tumors, therapeutic decision, and mortality. Descriptive statistics were used to portray findings. **RESULTS:** A total of 151 patients were included, of which 113 (74.8%) had hepatocellular carcinoma. Eighteen patients (11.9%) had biliary tract adenocarcinoma and 20 patients (13.2%) had CC. Of this subset of patients, most were male (n = 11, 55%) with a mean age of 64.4 years. Seven patients (33%) had confirmed diagnosis of cirrhosis. Most of patients with CC (90%) had intrahepatic involvement. **CONCLUSION:** CC is an uncommon disease that seems to be rising among cirrhotic patients. In our series, although hepatocellular carcinoma is the most frequent tumor, CC accounts 13.2% of all hepatobiliary carcinomas. High index of suspicion is required to diagnose this entity of poor prognosis in cirrhotic patients with imaging findings incompatible with hepatocellular carcinoma or normal alpha-fetoprotein.

009

NUTRITIONAL RISK IN ONCOLOGIC PATIENTS WITH METASTATIC DISEASE OF LIVER

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INTRODUCTION: Nutritional risk is defined as the likelihood of complications, coupled with malnutrition during anti-neoplastic treatment. Liver disease is common to see malnutrition broadly and lack of nutrients, especially when a serious hepatocellular dysfunction, as the caused by metastatic disease that occurs in 40-50% of adult patients with primary neoplasms, being the most frequent the originating in breast, lung, colon and rectum, kidney. **OBJETIVE:** Know the nutritional risk of patients carriers of liver metastases secondary to some form of cancer, to assess whether they are likely to more or less of complications related to their degree of malnutrition, during the course of his cancer treatment. **MATERIAL AND METHODS:** It is a retrospective descriptive longitudinal study series of consecutive cases which took place from July 1st, 2009-July 1st, 2010 which included oncologic patients, carriers of liver metastases who undergoing nutritional assessment on the basis of their anthropometric and biochemical parameters and their functional class Child-Pugh. The nutritional risk index was calculated with the following formula: $NRI = (\text{current weight/weight normal} \times 0.417 \times 100) + (15.1 \times \text{serum albumin})$. If this is more than 97.5 points are defined as low risk, if you are 97.4 to 83.5 points is intermediate risk and if it is below 83.5 is high risk. **RESULTS:** In-

cluded a total of 20 patients with liver metastases: 60% were men, 40% were women. The most frequent cancer diagnosis associated with metastases was colorectal (35%) followed by renal cancer, a patient had liver metastases of unknown origin. 85% of patients had stage Child-Pugh A and 15% stage B, none presented stage C. The proportion of patients with malnutrition was 25% (15% with intermediate nutritional risk and 10% with high nutritional risk); 60% of the patients presented overweight and obesity. The condition frequently associated was systemic hypertension (25.8%) followed by type 2 diabetes mellitus (9.7%), five patients (25%) had no weight loss. The average weight loss in the rest of patients was $10.6 \pm 7.6\%$. The average index of nutritional risk was 98.9 ± 11.2 (Table 1).

Table 1. Clinical study population characteristics.

Clinical feature	n = 20
• Size (m)	1.62 ± 0.11
• Normal weight (kg)	71.7 ± 11.4
• Current weight (kg)	66.6 ± 12.1
• Ideal weight (kg)	59.7 ± 2.6
• BMI (m/kg^2)	25.1 ± 2.6
• Percentage of loss of weight (%)	10.6 ± 7.6
• Nutritional risk index	98.9 ± 11.2
• Nutritional diagnosis	
◦ Overweight/Obesity	12 (60%)
◦ Normal	3 (15%)
◦ Malnutrition	
◦ Intermediate nutritional risk	3 (15%)
◦ High nutritional risk	2 (10%)

CONCLUSION: On liver metastatic disease, we can find some degree of overweight and obesity and even normal nutrition in absence of descompensation of hepatic function. Presenting a high nutritional risk is increased susceptibility to suffer complications of malnutrition in cancer treatments: surgical, chemo or radiotherapy, such as dehiscence of anastomosis, haematological toxicity translated in cytopenias, susceptibility to infections, increased risk of sepsis and multiple organic failure, increase in days of hospitalization, decompensation of comorbidities, risk of bleeding due to deficiency of coagulation factors, factors that worsen their prognosis and quality of life.

MOLECULAR AND CELLULAR BIOLOGY

001

AD-MMP8 ADMINISTRATION IN SKELETIC MUSCLE IS AN EFFECTIVE THERAPY AGAINST EXPERIMENTAL LIVER CIRRHOSIS

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INTRODUCTION: Diverse therapies to induce regression of experimental liver fibrosis have been reported. Gene therapy has been useful as an important tool in hepatic gene delivery. Adenoviral vectors containing *MMP8* gene have

demonstrated considerable fibrosis reduction when sistemically administered. In fact, liver is seriously affected during liver cirrhosis, resulting in a diminished transduction rate when compared to a healthy liver. **OBJECTIVE:** To evaluate fibrosis regression through adenoviral gene therapy intramuscularly administered utilizing *MMP8* gene. **MATERIAL AND METHODS:** Liver cirrhosis was induced in Wistar rats through chronic intoxication with tioacetamide administered during 7 weeks. At the beginning of the 5th week, adenoviral vector was administered intramuscularly. Rats were sacrificed after one, two and three weeks. Fibrosis index was evaluated, together with the expression of pro and antifibrogenic genes, proinflammatory genes and hepatic liver function tests. We made 4 groups: healthy rats, TAA, TAA+AdMMP8 and TAA+AdGF<p. **RESULTS:** After adenovirus administration with Ad-GFP, its expression was observed until 21 days *in vivo*. Fibrosis index in rats treated with Ad-MMP8 was significantly lowered, 18.3, 23.4 and 10.9%. Profibrogenic genes significantly lowered during three weeks ($p < 0.05$). Antifibrogenic genes *MMP-1* and *MMP9* increased in the second week 10.8, 2.8 times respectively ($p < 0.05$). AST significantly lowered in the second week 320.5 ± 137.4 ($p < 0.05$). **CONCLUSIONS:** Adenoviral transduction in skeletal muscle was efficient during up to 21 days. Ad-MMP8 treatment prevented the expression of profibrogenic genes. It was observed that *MMP8* was capable to act in liver and degrade extracellular matrix proteins preventing fibrosis development.

002

CELLULAR SENESCENCE IN A MODEL OF EXPERIMENTAL FIBROSIS: DETERMINATION OF TELOMERE LENGTH AND TELOMERASE PRESENCE

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INTRODUCTION: In chronic liver diseases, the ongoing damage and concomitant regeneration accelerate telomere shortening, specifically in hepatocytes, which eventually become senescent and stop recovery. The telomere hypothesis proposes that the chronic liver injury induces a continuous wave of destruction and regeneration of the organ, resulting in critical telomere shortening, which in turn culminates in replicative senescence or death of hepatocytes and ultimately in cirrhosis. It is known that an early metabolism intermediate must be attached to proteins cytochrome P450-mediated forming acetylilmidolisina derivatives, responsible for the toxic effect. According to the dose-response, the TAA leads different types of liver damage (necrosis, regeneration, cirrhosis) and promoted as the ultimate cause malignant transformation. **OBJECTIVE:** Determine whether telomere shortening is involved in the cirrhotic process as a result of continuous liver regeneration, or is a mechanical factor that drives the development of cirrhosis, and if presence of telomerase justifies the appearance of the neoplastic process in the model. **MATERIAL AND METHODS:** Cirrhosis was induced in male Wistar rats weighing 150-200 g fed ad libitum with water and purine, intraperitoneally injected, TAA (200 mg/kg body weight) in saline twice a week for 15 weeks. To determine the telomere shortening by qPCR technique we used the total liver DNA from treated animals, and telomerase was located by indirect immunohistochemistry on sections of paraffin-em-

bedded liver tissue. We used the Pearson correlation test to quantify the significance of the results. **RESULTS:** Determination of telomere shortening by qPCR revealed that there is a significant gradual decrease from the second phase with a $p > 0.0005$ and a slight recovery of telomere size in the last two phases, which was expected since apparently there are some regenerative nodules with clear presence of dysplastic cells (4th and 5th stages). The telomerase immunohistochemistry assay indicated the gradual presence (qualitative) of this enzyme in the last three phases of the experimental model showing the likely activity, which explains the telomere size recovery in representative animals liver of this phase. **CONCLUSION:** In a previous study results suggested that liver cirrhosis induced by TAA is associated with alterations in the organization of the cell cycle related regulatory proteins, and regeneration of hepatocytes was responsible for the expression of these proteins in response to liver damage. With the results obtained in this work we suggest that the mechanism by which senescence reverses is the gradual increase of telomerase expression resulting in telomere size recovery of certain structures (some neoformed cholangioles, dysplastic nodules, with the lack of regulation of p16, p21, and p53 proteins). Sponsorship: This work was supported by funds provided by UNAM, PAPIIT IN-205210, and SEP-CONACYT 84837.

VIRAL HEPATITIS

001

TOTAL ANTI-HBC ANTIBODIES IN THE SCREENING OF ASYMPTOMATIC BLOOD DONORS IN A THIRD LEVEL HOSPITAL IN MEXICO CITY

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INTRODUCTION AND AIM: Clinical utility of isolated detection of total anti-HBc is controversial. Although it could be the only serological detectable marker in some subjects. Recently, it has been suggested the inclusion of this marker into the screening panel of volunteers in blood banks, however, there are not enough data to support this recommendation for its generalized inclusion in our media. The aim of this study was to evaluate the usefulness of total anti-HBc detection in asymptomatic blood donors in our institution. **MATERIAL AND METHODS:** All consecutive subjects that attend and were accepted for blood donation at INCMNSZ in 2010, were screened for HBV infection. Total anti-HBc and HBsAg determinations were done by chemiluminescence method (Vitros ECiQ, Ortho Clinical Diagnostics, Withchurch Cardiff, R.U.). Total anti-HBc positive serums were confirmed in a second sample. In all this cases (Total anti-HBc positive and HBsAg negative) a clinical evaluation, liver function tests and HBeAg, Anti-HBe, Anti-HBs, Anti-HBc IgM, HBsAg (ARCHITECT, Abbott Laboratories, Wiesbaden, Germany) and HBV-DNA by RT-PCR (Specialty Labs, San Juan Capistrano, California, EUA, ILD: 29 UI/mL) were performed. **RESULTS:** During 2010, 9,461 subjects attend as candidates for blood donation. From these, 7670 after a pre-donation inter-

view were accepted (81.06%). Ten anti-HBsAg positive subjects were detected (0.13%). In the primary evaluation, 41 cases (0.53%) of blood donors with total Anti-HBc and HBsAg negative were identified. None of the patients with had detectable HBV-DNA. In 7 patients the Anti-HBe and Anti-HBs were positive, and 4 were positive for anti-HBs suggesting previous exposition to HBV. **CONCLUSION:** Our result suggests that adding total anti-HBc testing to the traditional screening panel does not increase the safety of blood derivatives in our media. This could be associated to the low HBV chronic infection prevalence in Mexico and that the blood donors constitute a low risk population. These results must be validated and confirmed in a larger Mexican population. **CONFLICT OF INTEREST:** The authors have no relationship to disclose.

002

NK CELL ACTIVATION IN PATIENTS WITH CHRONIC HEPATITIS C BY MILD HYPERPROLACTINAEMIA

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INTRODUCTION: Natural killer (NK) cells play a central role in HCV infection. Its quantity and activity are decreased in chronic hepatitis C (CHC), therefore NK cell reactivation could be an option in order to clearance of the virus (*Cell Immunol* 2010; 262: 96). Prolactin (PRL) is a hormone with additional functions over the immune system and can activate NK cells *in vitro*. **AIM:** To analyze if the induction of mild hyperprolactinaemia is able to activate peripheral NK cells of patients with CHC. **MATERIAL AND METHODS:** 11 patients HCV-RNA+ treatment-naïve without cirrhosis were included. Patients received Levosulpiride (L) 75 mg/day plus Cimetidine (C) 1,600 mg/day. HB, LFTs, viral load and lymphocytes count were done before and after therapy. Additionally, NK cells count and TRAIL, NKG2D and CD16 expression was measured over NK dim and bright subpopulations in FACS.

Table 1.

	Before	After	p
PRL (ng/mL)	6.0 ± 2.8	38.5 ± 15.0	0.001
Lymphocytes/DI	1,861 ± 664	2,166 ± 765	0.006
TRAIL (MFI) over NK	517 ± 216	1,337 ± 393	0.005
% NK Dim TRAIL ⁺	8.009 ± 4.6	4.6 ± 3.35	0.048

MFI: Median fluorescence intensity.

RESULTS: Significant results in PRL, lymphocytes, TRAIL expression over NK and NKdim TRAIL⁺ were observed (Table 1). No significant changes in NK percentage, NKG2D and CD16 expression were observed. Viral load decrease was observed in 6 patients (before = $1.53 \times 10^6 \pm 1.39 \times 10^6$ UI; after = $0.82 \times 10^6 \pm 0.79 \times 10^6$ UI; $p = 0.05$). **CONCLUSIONS:** Mild hyperprolactinaemia by 15 days of L plus C in patients with CHC was able to increase peripheral lymphocytes and activate

NK cells to express TRAIL. TRAIL can induce apoptosis in infected hepatocytes and activated hepatic stellate cells, so this type of activation could be promising as a combined immunotherapy. Sponsorship: This work was supported by CONA-CyT 134341.

003

ADVERSE EFFECTS OF ANTIVIRAL TREATMENT WITH PEGINTERFERON ALFA + RIBAVIRIN IN CHRONIC HCV INFECTION PATIENTS. IMPACT ON DOSIFICATION AND TREATMENT RESPONSE

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INTRODUCTION: Almost all those patients treated with Peginterferon-Alfa and Ribavirin present one or more adverse effects during the treatment course and are the main reason for which patients reject or suspend treatment. From 10 and 14% of patients will have to suspend treatment due to severe adverse effects or laboratory abnormalities. Moreover, from 9 to 15% of patients will need a Peginterferon or Ribavirin dose reduction, mostly as a result of laboratory abnormalities, which can affect the treatment efficacy. **AIM:** To determine the frequency of antiviral treatment adverse effects in patients with chronic hepatitis C virus (HCV) infection and to investigate their impact in dosification, treatment continuity and treatment response. **MATERIAL AND METHODS:** This is a descriptive, retrospective and comparative trial including chronic HCV infection patients with complete record, treated with Peginterferon-Alfa + Ribavirin in the Department of Gastroenterology, Hospital de Especialidades, Centro Médico Nacional de Occidente, IMSS, from January 2003 to December 2009. The frequency of adverse effects was determined, as well as the frequency and cause of drug dosage adjustments and/or treatment suspension. The magnitude of drug dosage reduction was quantified and the Sustained Viral Response (SVR) rate was determined in the subgroup of those patients treated with reduced dosage, which subsequently was compared with the global SVR. **RESULTS:** 210 cases with complete record were reviewed. All the patients reported adverse effects. The flu-like symptoms, leucopenia and neutropenia occurred in more than 50% of cases. Depression was reported by 41.4% of patients. Antiviral treatment had to be suspended in 27 patients (12.8%), due to the presence of adverse effects or due to treatment-contraindicating comorbidities. The most frequent causes of treatment suspension were infections, depression, thrombocytopenia and neutropenia. Three patients suspended treatment due to intolerance to adverse effects and 7 abandoned their treatment with the cause ignored. 40 patients (19%) required Peginterferon and/or Ribavirin dosage adjustment. In 2 patients, both drug dosages were adjusted due to anemia and neutropenia. Four patients required dosage reduction due to anemia, while 34 patients (16%) required Peginterferon dosage reduction due to neutropenia and/or thrombocytopenia, or severe adverse effects. 75% of those patients who required drug dosage reduction received 70% (or more) of the recommended dosage of adjusted drug. The SVR for the subgroup of patients treated with reduced dosage was 52.5%. The genotype distribution (main response prediction factor) among the subgroup of patients managed with reduced dosage and the total of revised cases (210) was compared; no differences were found [χ^2 1.051 (3df), p NS]. Moreover, the SVR rate among the subgroup of patients managed with re-

duced dosage and the SVR of the evaluated cohort were compared, with no differences found (52.5 vs. 52.84%, χ^2 0.019 (1df), p NS). **CONCLUSIONS:** The frequency of treatment suspension due to adverse effects and drug dosage adjustments in our population is similar to those reported in international literature. In our population, a reduction in SVR among the group of patients requiring dosage reduction was not observed, possibly explained due to the fact that 75% of them received dosages \geq 75% of the recommended dosification according to the genotype.

004

RESPONSE TO TREATMENT IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION TREATED WITH PEGINTERFERON-ALFA AND RIBAVIRIN AT THE DEPARTMENT OF GASTROENTEROLOGY, CENTRO MÉDICO NACIONAL DE OCCIDENTE

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INTRODUCTION: The current treatment for chronic HCV (hepatitis C virus) is the combination of peginterferon-alfa-2a or 2b plus ribavirin, with a response rate between 42 and 82%, depending on the genotype. Several factors affecting the treatment response have been identified, among which the race is included. Some authors have reported inferior response rates in Latino patients; nevertheless, there are few publications about treatment response in this ethnic group, an underrepresented population in multicenter trials. In 2009, the results of a trial comparing the treatment response between Caucasian and Latino patients infected by HCV genotype 1 were published, reporting a lower rate of Sustained Virologic Response (SVR) among Latino patients (34 vs. 49%). **AIM:** To determine the rate of SVR in a group of Mexican patients with chronic HCV infection treated with Peginterferon-Alfa and Ribavirin, and to identify the factors associated to SVR. To determine the treatment response rate to antiviral treatment in patients with chronic HCV infection and to identify those factors associated to SVR. **MATERIAL AND METHODS:** This was a descriptive, retrospective, and comparative trial, with chronic HCV infection patients treated with peginterferon alfa-2a or alfa-2b, plus ribavirin, by the Department of Gastroenterology, Hospital de Especialidades, Centro Médico Nacional de Occidente, IMSS, between January 2003 and December 2009. The SVR rate was determined, and subsequently, the responder patients were compared with the non-responders in order to identify the differences. Moreover, a logistic-regression analysis was performed to identify those factors associated to SVR. **RESULTS:** A total of 210 medical records with complete information were obtained. 50.95% of the cases were women and 49.05% were men, with a mean age of 44.4 years \pm 13.06. Infection by HCV genotype 1 was more frequent: 129 patients (61.42%), followed by genotype 2 with 62 patients (29.52%), genotype 3 with 18 patients (8.57%), and genotype 4 with 1 patient (0.47%). Treatment was suspended in 27 patients (12.8%), due to adverse reactions or due to detection of treatment-contraindicating concomitant diseases and 7 patients (3.3%) abandoned treatment with the cause being ignored. In 29 of the patients (13.8%) with genotype 1 infection, treatment was suspended due to response failure. A total of 147

patients (70%) completed their treatment according to their genotype, of which 110 patients (62.5%, 110/176) presented the End-of-Treatment Response. Subsequently, relapse was observed in 17 cases (9.65%), while 93 patients (53%, 93/176) presented SVR. 43% of patients with genotype 1 infection reached SVR, compared to 68% of those with genotype 2 and 3 infection. Comparison between the responder and non-responder patients showed differences only for genotype distribution ($p < 0.05$) and basal platelet count ($p < 0.01$). The logistic-regression analysis identified two factors independently associated to SVR: infection by genotypes 2 or 3 [OR 2.8; 95% confidence interval [CI], 1.45 to 5.4; $p < 0.01$] and a basal platelet count $< 90,000$ [OR 0.30; 95% (CI), 0.10 to 0.92; $p < 0.05$], the latter negatively associated to SVR. **CONCLUSIONS:** The efficacy of antiviral treatment for our population is comparable with the data reported by international literature. The inter-racial differences in response rates to treatment deserve major research, ideally with prospective trials. Infection by genotypes 2 and 3 is associated to SVR, whereas those patients with a basal platelet count $< 90,000$ show a lower probability of presenting SVR. We consider that the thrombocytopenia seen in these patients is related to portal hypertension and cirrhosis, the latter identified by previous trials as a factor diminishing the probability of SVR.

005

RETREATMENT WITH HIGHLY PURIFIED nIFN- α (MULTIFERON®) IN MEXICAN NON-RESPONDERS PATIENTS WITH CHRONIC HEPATITIS C

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INTRODUCTION: nIFN- α (Multiferon®) is a mixture of interferons produced from pooled units of human leukocytes, used as monotherapy in patients with hepatitis C treatment-naïve. **AIM:** To evaluate the virological response and presence of adverse events to nIFN- α in genotype 1 chronic hepatitis C previously non-responder Mexican patients. **MATERIAL AND METHODS:** 39 patients received a 4 week induction phase of 5 days/week of nIFN- α 6 MU plus weight based RBV, followed by 3 MU three times a week of nIFN- α for 44 weeks. The relationship between viral response and incidence of adverse effects was analyzed regarding age, gender, BMI, blood glucose, diagnosis of cirrhosis, genotype 1 subtype a, b, ab and number of previous treatments. **RESULTS:** Early viral response (EVR) was age- and gender-dependent, older male patients being less responsive. Overall, EVR was 0.47-0.76, with 95% confidence interval. Sustained viral response (SVR) was evaluated according to: a) ITT analysis, b) 48-weeks treatment and 24-weeks of follow up (16 patients) and c) EVR cases (11 patients). None of the factors considered in groups a) and b) were significantly different; however, in group c), there was better response in younger patients and in patients 50 and older with a marked viral load decline. Five out of 16 (31%) of patients who completed 48 weeks of treatment and 24 weeks of follow up presented a SVR. Adverse events were not

associated with any of the variables. The most common adverse event was asthenia in 27% of patients. **CONCLUSION:** nIFN- α (Multiferon), may be an strategy for retreatment some genotype 1 chronic hepatitis C previously non-responder patients. Confirmation of this data in a larger population in guaranteed.

006

PREVALENCE OF SEROLOGICAL MARKERS OF VIRAL HEPATITIS IN A REFERENCE OF NORTHEASTERN MEXICO DURING THE PERIOD 1999-2009

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INTRODUCTION: In Mexico, cirrhosis and liver diseases represented the fourth leading cause of death. Currently describes several viral agents causing hepatitis, among the most common are hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV) and Hepatitis E virus (HEV), each having different transmission mechanisms, incubation period and clinical patterns. **AIM:** To determine the prevalence of viral hepatitis markers in a population with clinical suspicion of hepatitis during the period 1999 to 2009. **MATERIAL AND METHODS:** This was a observational, descriptive and retrospectively study and were studied 3,383 patients who came to the Laboratory of the Liver Unit, Department of Internal Medicine, University Hospital "José Eleuterio González", who were requested two or more viral markers for HAV, HBV and HCV (Anti hepatitis A virus IgM antibody: anti-HAV IgM, anti hepatitis A virus IgG antibody: anti-HAV IgG, hepatitis B surface antigen: HBsAg, antibody to hepatitis B virus core IgG: anti-HBc IgG, antibody to HBV core IgM: anti-HBc IgM, hepatitis B e antigen: HBe Ag, antibody hepatitis B e antigen: anti-HBe and antibody to HCV: anti HCV). All serological markers were measured by enzyme-linked immunosorbent assay. **RESULTS:** During this period 2,875 patients were included. In these patients the following viral markers were positive: 81% anti-HAV IgG (240/295), 27% anti-HAV IgM (116/424), 8% HBsAg (122/1539), 13% anti-HBc IgG (181/1444), 6% anti-HBc IgM (16/280), 25% HBeAg (30/120), 42% anti-HBe (44/106) and 13% anti VHC (190/1481). The rate positive viral markers according age were: 0-9 years, 55% anti-HAV IgG (16/29), 63% anti-HAV IgM (56/89), 1% HBsAg (1/75), 8% anti-HBc IgG (3/39), 100% HBeAg (1/1), and 8% anti VHC (4/49); 10-19 years 71% anti-HAV IgG (25/35), 59% anti-HAV IgM (35/59), 7% HBsAg (5/72), 4% anti-HBc IgG (3/70), 4% anti-HBc IgM (1/23), 50% HBeAg (3/6), 25% anti-HBe (1/4) y 10% anti VHC (6/60); 20-39 years 71% anti-HAV IgG (55/77), 14% anti-HAV IgM (17/118), 9% HBsAg (39/427), 11% anti-HBc IgG (44/390), 9% anti-HBc IgM (8/87), 20% HBeAg (6/30), 56% anti-HBe (15/27) and 16% anti VHC (62/400); 40-59 years 95% anti-HAV IgG (108/114), 1% anti-HAV IgM (1/82), 9% HBsAg (41/468), 13% anti-HBc IgG (66/496), 4% anti-HB c IgM (3/67), 24% HBeAg (10/42), 47% anti-HB e (16/34) and 13% anti VHC (59/455); 60-90 years 0% anti-HAV IgG (0/1), 0% anti-HAV IgM (0/34), 7% HBsAg (18/257), 17% anti-HBc IgG (43/258), 7% anti-HBc IgM (2/28), 26% HBeAg (7/27), 35% anti-HBe (8/23) and 12% anti VHC (28/240), respectively. According to gender: Male 83% anti-HAV IgG (126/152), 30% anti-HAV IgM (63/144), 10% HBsAg

(96/951), 15% anti-HB c IgG (146/943), 5% anti-HBc IgM (8/147), 26% HBeAg (19/73), 46% anti-HB e (32/69) and 14% anti VHC (142/983); female 80% anti-HAV IgG (112/140), 25% anti-HAV IgM (53/216), 5% HBsAg (46/870), 9% anti-HBc IgG (72/803), 6% anti-HBc IgM (8/143), 23% HBeAg (9/39), 34% anti-HBe (10/29) and 13% anti VHC (106/832), respectively. **CONCLUSION:** In this analysis, it was observed that the marker viral more requested was HBsAg. In the adult study population highlights the high prevalence of IgG antibodies against HAV and HAV IgM antibodies in children and adolescents, which coincides with our country is an endemic area for this viral infection. With regard to chronic infections in the total population, the markers for HBV and HCV showed the same percentage of positivity during the study period. The marking chronic HCV was more positive in adults (greater than 20 years). According to gender not differences were observed in percentage of majority viral markers. We emphasize the need to monitor viral hepatitis especially immunization, to prevent the development of chronic diseases that affect the quality of life of the individual. This work was sponsored entirely by own resources of participating department.

007

POTENTIAL ANTIVIRAL EFFECT OF INDUCIBLE NITRIC OXIDE SYNTHASE (iNOS) GENE SILENCING ON HEPATITIS C VIRUS (HCV) EXPRESSION INDUCED BY ACETYSALICYLIC ACID (ASA) AND iRNA-iNOS GENE

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INTRODUCTION: We have previously demonstrated that ASA decreases HCV-RNA and viral protein levels (~ 50%, F, p < 0.05) but the mechanisms has not been yet elucidated. In endothelial cells, it has been demonstrated that ASA induces nitric oxide (NO) through the generation of epi-lipoxins. This molecule plays an outstanding role in immunological defense mechanisms as an antimicrobial agent. **OBJETIVE:** Our major aim was to evaluate the participation of inducible-Nitric Oxide Synthase (iNOS) enzyme in the negative regulation of HCV-RNA levels induced by ASA and using RNA-interference technology against iNOS gene (iRNA-iNOS). **MATERIAL AND METHODS:** Huh7 cells expressing non-structural HCV proteins were exposed to 4mM ASA and incubated at the same times that we reported HCV-down regulation (24-72 h), iNOS-mRNA and protein levels were measured by real time PCR and western blot, respectively. Furthermore, inhibition of iNOS gene by RNA interference (iRNA) and the role of ASA in the modulation of iNOS promoter activity (luciferase reporter assay) were evaluated. The results were carried out in triplicate and were analysed by a one-way analysis of variance (ANOVA) and Dunnett test. P < 0.05 was considered statistically significant. **RESULTS:** Upon cell treatment with ASA we found a decreased levels of iNOS-RNA (90%, p < 0.05), and proteins (30%), and a slightly decrease in protein-nitrosylated levels at 48-72 h. ASA exposure also reduced the

transactivation of the iNOS promoter in HCV-replicon cells (60%, p < 0.05). Furthermore, inhibition of iNOS gene expression by iRNA silencing decreased HCV expression (70%, p < 0.05) which mimics the antiviral effect of ASA. **CONCLUSIONS:** ASA reduces iNOS expression at transcriptional and translational levels at the same time that it decreases HCV expression and decreases iNOS-promoter activity. iNOS silencing decreased HCV replication. Recently, we detected that ASA increased the activity and expression of SOD enzyme, suggesting that the antiviral activity of ASA is mediated at least in part by its antioxidant properties. The modulation of reactive nitrogen and oxygen species by a pharmacology pathway could be used as an adjuvant in the treatment of chronic HCV infection. Sponsorship: Conacyt BASICA-2006 CB2006-1-58781. **CONFLICT OF INTEREST:** Authors declare no interest conflict.

008

TRANSCRIPTIONAL SIGN OF ANTIVIRAL EFFECT OF ACETYSALICYLIC ACID (ASA) ON HEPATITIS C VIRUS (HCV) IN HEPATOCARCINOMA CELLS (HUH-7)

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INTRODUCTION: It have been demonstrated that ASA treatment could down-regulate *in vitro* HCV expression (~ 50%, F, p < 0.05). However, the signaling pathway induced during ASA antiviral effect has not been elucidated. cDNA-microarray analysis let us to evaluate expression of multiple genes to identify differentially-expressed genes between two or more experimental condition. **OBJETIVE:** To obtain a transcriptional expression profile of Huh-7-HCV-replicon cells in presence or absence of ASA in order to elucidate the signaling pathway and the molecular mechanisms involved into the antiviral effect induced by ASA on HCV expression. **MATERIAL AND METHODS:** Huh-7-HCV-replicon cells were exposed to 4 mM ASA during 24, 48 and 72 h. Total RNA was isolated, quantified and validated by capilar electrophoresis to evaluate quality and quantity. After that, we performed a retrotranscription *in vitro* analysis to get cDNA. Synthesized transcripts were marked with biotin, purified, fragmentized and hybridized in HG-U133 Plus 2 Gene Expression. The hybridization signals were captured with Gen Chip 3000 7G Scanner and analyzed by Expression Console and Dchit Software. **RESULTS:** After normalization, we obtained hierarchical maps with differentially-expressed genes. At 24 h upon ASA exposure we detected 21 genes, at 48 h 98 genes and at 72 h 439 genes. Among genetics targets over-expressed we could stand out Interleukine-8, Cytochrome P450 and Methallothioneins genes. Among down-regulated genes we identified Ribonucleotide Reductase gene. These genes have been previously associated with oxidative stress regulation. **CONCLUSIONS:** AAS modulate the expression of genes associated with antioxidant role as methallothioneins. This study provide a tool for identifying novel host factors involved in antiviral effect regulated by ASA against HCV and improve our understanding of regulatory mechanism of HCV replication. Sponsorship of work: Conacyt BASICA-2006 CB2006-1-58781. **CONFLICT OF INTEREST:** Authors declare no interest conflict.

009

ALGORITHM FOR TWO-DIMENSIONAL GELS (2-D) ELECTROPHORESIS INTERPRETATION TO EVALUATE ANTIVIRAL EFFECT OF ACETYSALICYLIC ACID (ASA) ON HEPATITIS C VIRUS (HCV) IN ORDER TO IDENTIFY A PROTEIN EXPRESSION PROFILE

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INTRODUCTION: ASA reduces HCV-RNA levels in hepatocarcinoma cells (~50%; F, $p < 0.05$). Identification of a proteomic sign could be useful to suggest new therapeutic targets against this virus. Through 2-D gels is possible to analyze many proteins simultaneously. The results of 2-D electrophoresis can be evaluated using the principal component analysis (PCA) in order to evaluate proteins with major relevance into the studied conditions. The expression: $C^k = a_{k1}X^1 + \dots + a_{kj}X^j + \dots + a_{km}X^m$ (C^k = the score on principal component k ; a = the regression coefficient for observed variable k ; X = the score on observed variable k) describes a procedure to calculate around 100% of accumulated variance (AV), which is an important parameter in the PCA. **OBJECTIVE:** Our major aim was to establish *in silico* parameters for 2-D gels to identify a protein profile expression involved in down-regulation induced by ASA in hepatocarcinoma cells expressing the non-structural proteins of HCV (Huh-7-HCV-replicon cells). **MATERIAL AND METHODS:** The total proteins were isolated from Huh-7-HCV-replicon cells treated with ASA 4 mM during 24, 48 y 72 h upon exposure. 2-D gels were performed to separate proteins by molecular weight (MW) and isoelectric point (pI). Densitometric analysis was performed with PD-QUEST software and was selected a PCA as mathematic algorithm ($X_{ij} = a_{i1}Z_{1f} + \dots + a_{ik}Z_{kj} = \sum a_{is}Z_{sk}$; X = factor matrix; a = coefficients; Z = standardized matrix), to determine factorials coefficients using Unscrambler 9.8 software. **RESULTS:** The explained variance ($EV = 1/n \cdot X^T X$) with two principal components (CP^1 and CP^2) for each time were as follow: at 24 h we observed EV of 86 and 12%, at 48 h the EV was 57 and 32%; and at 72 h was of 64 and 28% respectively. Among over-expressed proteins we identified: a protein of 35.04 KDa, pI 8.89 ($\Delta = 3.67$); a protein weighting 10.26 KDa, pI 4.81 ($\Delta = 9.34$); a protein of 87.51 KDa, pI 6.3 ($\Delta = 4.72$); a protein of 16.15, pI 5.23 ($\Delta = 8.27$); and a protein of 6.83, pI 4.31 ($\Delta = 5.51$). Among the down-regulated proteins that we could stand out we found a protein of 79.91 KDa, pI 5.61 ($\Delta = 0.16$) and a protein of 16.4, pI 7.34 ($\Delta = 0.18$). **CONCLUSIONS:** ASA treatment modified protein expression profile in Huh-7-VHC replicon cells showed mainly in proteins weighting MW < 100 KDa ($t, p < 0.05$) and wide range of pI. It is important to emphasize that proteomic signs could help us to develop personalized treatments against this viral agent. Sponsorship of work: Conacyt BASICA-2006 CB2006-1-58781. **CONFLICT OF INTEREST:** Authors declare no interest conflict.

010

EFFICACY OF COMBINED ANTIVIRAL TREATMENT IN CHRONIC HEPATITIS C PATIENTS INMATES IN FEDERAL CENTERS FOR SOCIAL REHABILITATION IN MEXICO. PRELIMINAR REPORT

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INTRODUCTION: It is considered that chronic hepatitis C (HCV) affect more than 1.5 million people in México. However, there are some high risk groups that are understudied in which the prevalence could be higher. Inmates in Federal Centers for Social Rehabilitation belongs to a special population in those the anti-HCV treatment could limit infection transmission and liver disease progression. At present, information regarding HCV prevalence and the efficacy of antiviral treatment in these particular population is scarce. **AIM:** To evaluate the efficacy of combined antiviral treatment (PegIFN alfa y Ribavirin) in chronic hepatitis C patients, inmates in Federal Centers for Social Rehabilitation in México. **MATERIAL AND METHODS:** Prospective study begun in 2004. All subjects were screened with anti-VHC, HBsAg and Anti-VIH serology at admission. All anti-HCV-positive inmates were evaluated for evidence of chronic HCV infection, including the presence and extent of chronic liver disease and candidacy for antiviral therapy, including HCV genotype and quantitative HCV-RNA (Real time PCR, Quest Diagnostics, San Juan Capistrano). Direct observed combined antiviral therapy was assigned according to HCV-genotype (PEG-IFN alfa 2b 1.5 mcg/Kg/sem plus Ribavirin 800-1,400 mg/d). Statistics analysis was performed using SPSS 12.0 software. **RESULTS:** In this preliminary report we included 42 patients who finalized the treatment and a follow up at least 6 months post therapy to evaluate Sustained Virological Response (SVR). All patients were male with a mean age of 40 years ($SD \pm 7.90$ y). Body Mass Index was 26.68 ($SD \pm 2.98$). Twenty six of them (62%) were genotype 1, five (12%) genotype 2, ten (24%) genotype 3 and only one (2%) had genotype 4. Global SVR was 74%. In genotype 1 SVR was achieved in 16/26 patients (62%), in genotype 2 and 3 SVR was 100% (5/5 and 10/10 patients respectively). Genotype 4 patient was a non responder. **CONCLUSIONS:** In present study, genotype 1 was the most prevalent, similar to the information obtained in HCV Mexican infected population. Although preliminary, the SVR obtained with direct observed combined antiviral therapy in genotype 2 and 3 was 100 and 62% in genotype 1. This data confirms the efficacy of PegIFN and Riba treatment in HCV patients inmates in Mexican Federal Centers for Social Rehabilitation and suggests that the implementation of direct observed treatment could improved the SVR in this special population. **CONFLICT OF INTEREST:** Authors have nothing to disclose.

011

DISTRIBUTION OF RS12979860 IL28B GENE POLYMORPHISM IN MEXICAN PATIENTS WITH CHRONIC HCV INFECTION

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INTRODUCTION: In patients with chronic hepatitis C a single nucleotide polymorphism (SNP) has been identified

(rs12979860) located in chromosome 19, Three kb upstream of the IL28B gene that encodes IFN- λ 3. The variant of this SNP has been divided in three different genotypes: T/T, C/T and C/C. It has been reported that carriers of C/C are 2 times more likely to develop viral response (SVR) to standard antiviral therapy and up to 3 times more likely to achieve spontaneous clearance of virus during primary infection. In contrast, T/T polymorphism is associated to non-response to Peg-IFN/Riba treatment. **OBJECTIVE:** To determine the distribution of genotypes of IL28B rs12979860 genetic variant in a cohort of Mexican patients with chronic HCV infection. **MATERIAL AND METHODS:** We selected 291 patients with chronic HCV infection: 121 male, 170 female, mean age: 52.7 ± 11.26 years. Peripheral blood was obtained from each patient and DNA extraction was performed with QIAamp DNA Blood Kit (Qiagen®). The rs12979860 variant was genotyped for the IL28-B in 50 ng of genomic DNA using hybridization Taq-Man probes by real-time PCR and dissociation curves of the amplified product. We determined the frequency of the variant and its distribution in the study cohort. **RESULTS:** Of 291 patients 52 (17.9%) were T/T genotype for rs 12979860, 178 (61.1%) C/T and 61 (21.0%) C/C. The distribution according to HCV genotype is shown in table 1. **CONCLUSIONS:** In this group of Mexican chronic hepatitis C patients, the genotype rs 12979860 of IL-28B most prevalent was C/T and only 21% were carriers of C/C, the genotype associated with better HCV depuration (spontaneous or treatment induced). Moreover, these results suggest that the high frequencies of genotypes T/T and C/T in our patients, contribute to reported lower SVR rate obtained with antiviral therapy in our population. **CONFLICT OF INTEREST:** The authors have no relationship to disclose.

Table 1.

IL28B Genotype (rs 12979860)	HCV -1	HCV genotype patients HCV -2	HCV -3	HCV- 5
T/T	38 (18.5%)	13 (178%)	0	1
C/T	127 (62.0%)	42 (57.6%)	9	0
C/C	40 (19.5%)	18 (24.6%)	3	0
Total	n = 205	n = 73	n = 12	n = 1

012

ANTI-TRANSGLUTAMINASE ANTIBODY PREVALENCE IN MEXICAN PATIENTS WITH CHRONIC HEPATITIS C

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INTRODUCTION AND AIM: The chronic infection with hepatitis C virus (HCV) represents a public health problem, with a reported seroprevalence of positive anti-HCV of 1.4% and is the second most frequent disease leading to cirrhosis that is taken care of at third level hospitals. HCV infection is associated with multiple endocrine diseases such as hypothyroidism, diabetes and hypogonadism. It has been recently described that the prevalence of celiac disease in this group of patients might be 1-1.3 vs. 0.4% in healthy volunteers. Some

studies found that the prevalence of celiac disease in healthy Mexican population is 0.5-2.6%. The objective of this work is to determine the prevalence of anti-transglutaminase antibodies in patients with chronic infection with HCV. **MATERIAL AND METHODS:** Seventy-six consecutive patients diagnosed with chronic HCV infection (anti-HCV positive and HCV-RNA detected in serum) from the viral hepatitis clinic from the period of May to December 2010 were included regardless of previous treatment and response to it. All of them agreed to participate. We performed anti-endomysium antibodies (IgG/IgA) by indirect immunofluorescence (the binding site, Ltd, Birmingham, UK) and anti-transglutaminase IgA with ELISA (Orgentec, Diagnostika, GmbH, Germany) to all the patients. Reference values for anti-transglutaminase antibodies were previously established using 99 percentile in 100 healthy volunteers (reference value > 3.2 U/mL). Demographic and viral characteristics were analyzed, comorbidities and previous treatment. Parametric or non-parametric tests were used accordingly using SPSS V. 15.0. **RESULTS:** In total there were 53 (69.7%) women and 23 (30.2%) men. 68 patients had been previously treated with combined antiviral therapy, 15 (19.7%) had diabetes, 32 (42.1%) dyslipidemia and 18 (23.6%) hypothyroidism. 100% of patients had negative anti-endomysium-antibodies (IgG and IgA). Of the 76 patients 6 (7.89%) had positive anti-transglutaminase antibodies. Of the 6 patients 1 did not received previous treatment and the other 5 had been previously treated with pegylated interferon and ribavirin. **CONCLUSIONS:** In this patients cohort with chronic hepatitis C virus infection we found a prevalence of 7.89% of positive anti-transglutaminase antibodies; this is 3 times greater to the highest prevalence reported in Mexican population. Additional evaluation is ongoing to establish clinical relevance of this finding. **CONFLICT OF INTEREST:** The authors have no relationships to disclosure.

013

PARTIAL CHARACTERIZATION OF THE PROTEOMIC EXPRESSION PROFILE OF HCC CELLS IN PRESENCE OF HEPATITIS C VIRUS (HCV) AND ACETYLSALICYLIC ACID (ASA)

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INTRODUCTION: HCV is considered a public health problem and it is estimated that affects approximately 3% of the world population. Nowadays, there is not an effective and specific treatment against HCV, then the search for new therapeutic options is in constant development. Recently, it was demonstrate that ASA has a suppressor effect in HCV proteins and RNA levels; although, it is not known the molecular mechanisms involved in this antiviral effect. The use of wide-scale proteomic strategies makes easier the identification of new pharmacologic targets against this virus. **AIM:** To analyze and characterize the proteomic expression profile of hepatocarcinoma cells (HCC) in absence and presence of non structural proteins of HCV and ASA. **MATERIAL AND METHODS:** We use Huh7 parental and Huh7-HCV replicon cell lines (which express constitutively the HCV non structural

proteins). Cells were cultured, treated with ASA 4 mM and harvested at 24-72 h, and then total protein was extracted by cell lysis and solubilization. Protein extracts integrity was verified by SDS-PAGE. Protein separation was made by bidimensional electrophoresis, using 17 cm IPG strips at pH 3-10 for the first dimension separation, followed by SDS-PAGE for the weight molecular separation. Gels were revealed with silver staining, digitalized with GS-800 (Bio-Rad) densitometer and analyzed with PDQuest (Bio-Rad) software. Statistics analysis included t-test. **RESULTS:** Proteins resolved in a bidimensional pattern, showed a distributing in range of 10-132 kDa and a value of 3.4-9.8 for the pI. Densitometric analysis demonstrated expression profiles between 736 ± 37 proteins in cells without treatment and 792 ± 70 proteins in cells exposed to ASA. When we compared the protein profile of cells that express non structural proteins of HCV in presence or absence of ASA, we were able to detect 57 proteins differentially expressed. We also estimated the experimental MW and pI by the use of molecular markers to define the corresponding coordinates. **CONCLUSIONS:** Under the established conditions, we obtained differential expression profiles of Huh7 parental and HCV-replicon cell lines treated and untreated with ASA. Partial identification of differentially expressed proteins during ASA treatment suggests the possible participation of proteins related with antiviral activity. Thus, bidimensional electrophoresis represents a useful approach in the separation and generation of a dynamic profile of the proteins expressed under certain conditions. Research of variation in protein expression makes possible the study of molecules related with viral pathogenesis and replication, being the most important application the identification of protein signatures for the definition of biomarkers and new therapeutic targets. Sponsorship of work: Conacyt BASICA-2006 CB2006-1-58781 and Conacyt-health-2008-01-86996 to Dra. AM Rivas. **CONFLICT OF INTEREST:** No conflicts of interest by any of the authors.

014

GEOGRAPHICAL DISTRIBUTION OF THE DIFFERENT GENOTYPES OF HEPATITIS C VIRUS

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INTRODUCTION AND OBJECTIVES: Global studies of hepatitis C virus (HCV), have documented a high genetic variability. HCV has major genetic groups called genotypes that have been designated 1 through 6, as well as over 90 subtypes. This is very important because the response to treatment varies according to the genotype. The purpose of this study was to investigate the prevalence of the different genotypes of HCV in a group of patients of the medical service of Petróleos Mexicanos in 14 states of México in 22 different hospitals. **MATERIAL AND METHODS:** This is a retrospective study in which it was reviewed records of patients diagnosed with HCV infection with genotyping (which was made by RT-PCR in real-time using FRET probes and analyzing melting curves), investigating their place of origin. For purposes of analysis 3 zones were considered: north (Nuevo León, Jalisco, Hidalgo, Tamaulipas and Guanajuato), center (Estado de México and Distrito Federal) and south (Veracruz, Tlaxcala, Tabasco, Oaxaca, Yucatán, Campeche and Puebla). **RESULTS:** 168 patients were analyzed, in the northern zone in total 24 patients, of whom 20

(83.3%) genotypes correspond to genotype 1a/b, 2 (8.3%) patients with genotype 2b and 1 (4.16%) genotype 2a/c and one (4.16%) with genotype 3a. In the center zone in total 89 patients, of whom 69 (77.52%) with genotype 1a/b, 7 (7.9%) patients with 2a/c, 11 (12.4%) with 2b and two (2.2%) patients 3a. In the southern zone 55 patients in total, of whom 48 (87.3%) correspond to genotype 1a/b, three (5.5%) patients 2a/c, one (1.8%) 2b, and three patients (5.5%) genotype 3a. **CONCLUSIONS:** Genotype 1 is the most common genotype in any region (137 cases 81.5%). It was found difference of genotype 2b that is much less prevalent in the southern zone (1.8%) in comparison with the other regions (northern zone 8.3% and center zone 12.3%); genotype 3 is the least prevalent.

CHOLESTASIS AND CHRONIC AUTOIMMUNE LIVER DISEASES

001

SURVIVAL WITH MARS AFTER 27 HOURS OF ANHEPATIC PHASE. FIRST CASE IN MEXICO

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INTRODUCTION: Orthotopic Liver transplantation was described in 2 stages in the 80's to stabilize patients with fulminant hepatic failure (FHF) or primary graft failure (FPI). The donor shortage is accentuated when liver transplantation (OLT) is urgent. **CASE REPORT:** Female patient 16 years old with FHF due to antifimic drugs. The patient presented with a history of 6 months with fever, positive Coombs +, over-reactive bone marrow. On January 6-10 at cervical lymph node biopsy granulomas were found, she was treated with rifampicin, isoniazid, pyrazinamide and moxifloxacin. On February 6-10 liver function tests (LFT's): ALT 71 U/L, AST 137 U/L, ALP 167 U/L, GGT 223 U/L, ALB 2.4 g/dL, DHL 197 U/L. Laparoscopic cholecystectomy was performed on February 7-10, she developed postoperative ascites. On February 12-10 presented generalized erythema multiforme secondary to drugs in skin biopsy. Antifimic drugs were discontinued for 1 week upon restarting LFT's worsen: ALT 1337 U/L, AST 1530 IU/L, DHL 764U/L. She received gangciclovir for CMV-PCR-positive. On February 18-10 she presented hepatic encephalopathy (HE) GII. Liver biopsy showed massive hemorrhagic necrosis of centrilobular predominance. The patient was started on N-acetyl cysteine, s-adenosylmethionine, L-ornithine, lactulax and was transfer to adult intensive care unit (UCI) presenting transient improvement, ammonium 1.79 $\mu\text{mol/L}$. On February 19-10 she was connected on MARS 8 h, without improvement, ammonium rose to 2.79 $\mu\text{mol/L}$, factor V 27.8%, factor VII 5.26%, HE progressed GIII-IV for an OLT, lactate increased to 8 mmol/L, MAP 83 mmHg. She was in high degree of medical urgency, the family did not accept related living donor liver transplantation. She underwent a prolonged anhepatic phase, performing hepatectomy on February 20-10, remained anhepatic for 27 h, connected to MARS. An hepatectomy was performed with preservation of the retro-hepatic vena cava, hepatic veins were sutured with surjete, portacaval anastomosis was performed end to side. She received OLT from a 22 year donor, on February 21-10.

OLT was performed with the piggy back technique. Persistent abnormal bleeding and was left packaged. The patient developed compartmental syndrome in 24 h abdomen was decompressed, ischemic graft regained its color, the bleeding was controlled, cavity was closed without packaged. AST 5286 UI/L, ALT 2003U/L, DHL 6616U/L. Kidneys suffered ischemia with transient anuria, diuresis resumed, but development tubulo interstitial damage, and hemodialysis was started. Tacrolimus dose was suboptimal due to renal failure; in addition she received mycophenolate and steroids. On fifth day post-OLT a liver biopsy showed acute cellular rejection and preservation injury, metil prednisolone 500 mg/3 dosis was administrated to patient with adequate response. She was extubated 7th day pos-OLT, and 48 h was re-intubated for hypoxemia. Liver function was stable. On 9th day post-OLT antifimic treatment was initiated for pulmonary infiltrates suggestive of PTB, with negative AFB, the patient received etambutol, diamino-diphenyl sulfone, clarithromycin, and she showed initial improvement, but subsequently developed pancytopenia and hemophagocytic syndrome, Direct Coombs + + +, the dose of metil prednisolone 2 g/day and 50 mg of prednisone was increased on March 8-10. Pulmonary infiltrates increased and decreased O₂ saturation of 74-74%. Her clinical condition deteriorated sharply. On March 15-10 began isoniazide and rifampicin with improvement in O₂ saturation to 91%, nevertheless the patient died on March 16-10. **CONCLUSIONS:** This is the first report in Mexico of prolonged anhepatic phase maintained by MARS, this may represent an option for severe cases, given the scarcity of donors.

002

PROGNOSTIC MODEL OF SURVIVAL IN PRIMARY BILIARY CIRRHOSIS

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INTRODUCTION: Primary Biliary Cirrhosis (PBC) is a chronic cholestatic disease, initially described as non-suppurative destructive cholangitis. Etiology of PBC is thought to be due to a combination of genetic predisposition and environmental triggers. Disease progression is usually slow. Anti-mitochondrial antibodies (AMA) are the most widely used diagnosis tool. Bilirubin had been shown the most sensitive parameter in PBC prognosis; it is included in most objective models Mayo prognostic model (MPM) which has been applied to predict spontaneous survival. Treatment with ursodeoxycholic acid (UDCA) in early stages of PBC improves life expectancy in these patients. **OBJECTIVE:** The aim of this study was to determine the frequency of PBC in our population, assess the data to estimate survival using MPM and the model of end stage liver disease) and the impact of treatment with UDCA. **MATERIAL AND METHODS:** Between 1981 and 2008, 2,485 patients were seen in The Liver Unit Hospital Universitario "Dr. José Eleuterio González" for different liver diseases, and 162 patients (6.5%) was attended for autoimmune liver diseases. Clinical, biochemical, and histological data were recovered. MPM, MELD and Child Pugh (CP) were calculated on admission and the follow-up. The patients were grouped according CP and compared between them. **RESULTS:** 32 (19.8%) patients were diagnosed as PBC, 29 (91%) were female. The median age at diagnosis was 49 ± 8. The follow-up time was 55 ± 57 months (range 12-278). Twenty five pa-

tients with PBC exhibited a positive AMA, 24 on admission and one patient in the follow-up period, (17, 1:40; 2, 1:80; 6 > 1:80); 17 patients had AMA2 determined of whom 8, < 1:40; 5, 1:40; 1, 1:80, 3 > 1:80. Liver biopsy was available in 29 patients; 13 (45%) were classified as early (Stages I and II), and 16 (55%) as late (Stages III-IV). Some patients had a combination of stages: 2 (I-II) and 3 (III-IV). Bilirubin level in patients with PBC was < 1 mg/dL on admission in 17 patients (53%) and > 1 mg/dL in the remaining 15 patients (47%). Ten patients exhibit a MPM risk score of > 5, 8 (80%) of these patients were cirrhotic, 3 (30%) of them died and 2 (20%) received an orthotopic liver transplantation (n = 2). Six of 22 (27%) that exhibited a MPM risk score of < 5 were cirrhotic on admission, and one further patient developed cirrhosis during follow-up. No patients with MPM < 5 died during follow-up period. On admission, 25 patients (78%) were CP-A and 7 (22%) CP-B with MELD 8.9 ± 2.9. At follow-up 23 patients (72%) were CP-A, 8 (25%) CP-B and 1 (3) CP-C with MELD 9.7 ± 5. All patients received UDCA 10-15 mg/kg, and seven patients received prednisone, azathioprine and/or S adenosyl-methionine. **CONCLUSION:** MPM identified on admission at cut-point of 5 more cirrhotic patients, who had higher mortality compared with those with the lowest score on admission to (< 5). In contrast, the CP classification and MELD score at admission were low, progressing to more advanced stages in the follow-up. MPM was superior to CP and MELD in identifying cases with poor prognosis in patients with PBC. This project was supported by resources of the participating departments, PAICYT and CONACYT.

003

NON-INVASIVE MODELS IN AUTOIMMUNE LIVER DISEASES AS PREDICTOR OF ADVANCED FIBROSIS

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INTRODUCTION: Autoimmune Liver Diseases (AILD) are characterized by chronic and progressive inflammation. AILD include autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC), autoimmune cholangitis, primary sclerosing cholangitis, and overlap syndrome, when patients may demonstrate features of two or more AILD. In our population, as well as AILD patients, obesity and overweight are increasing, this complicates further the conditions of patients, coupled with their immune factor, may have components of metabolic syndrome and in turn, trigger liver damage. It is important to assess fibrosis and progression to cirrhosis. Liver biopsy is the gold standard; however, it is an invasive procedure, adverse effects may occur. Prognostic models have been developed for assessing liver fibrosis which have been applied to different etiologies, based on biochemical parameters, including Fibrotest, Fibromax, Forns, APRI, AST/ALT ratio, and platelets account. Other models such as the NAFLD fibrosis score and BARD had been focused on diseases such as nonalcoholic steatohepatitis (NASH). **OBJECTIVE:** The aim of this study was to apply non-invasive methods to assess fibrosis to a group of patients with AILD and compare against liver biopsy. **MATERIAL AND METHODS:** The cohort study included AILD patients diagnosed according to international criteria; which had data recorded to apply non-invasive methods APRI, NAFLD fibrosis score, Forns, BARD and FIB4 were: age, gender, weight, height, body mass index (BMI), AST, ALT, GGT, albumin, platelets account, glucose, and cholest-

rol, not more than 1 month apart respect to biopsy date. The diagnosis value (DV) was assessed by calculating the area under the receiver operating characteristic (ROC) curves (AUC). Reference value was liver biopsy using METAVIR scale. Patients were ungrouped like non-advanced cirrhosis (F0, F1 and F2) and advanced fibrosis (F3 and F4). Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for each method. **RESULTS:** 92 patients were included; 51 (54%) AIH, 27 (30%) PBC, and 14 (16%) OS. In the total group, 54 (59%) patients had BMI > 25 and 32 (35%) BMI > 28. For AIH 60%, PBC 59%, and OS 50% had BMI > 25. APRI showed a better performance for AILD with DV 0.71 and AUC 0.751, sensitivity 78% and specificity 61%. For AIH the APRI with DV 0.995, AUC 0.771, sensitivity 73%, and specificity 71%; in PBC NAFLD fibrosis score with DV -1.615, AUC 0.813, sensitivity 86%, specificity 77%; and OS APRI with DV 0.490, AUC 0.542, sensitivity 83% y specificity 50%. 11/ 92 biopsies (12%), showed steatosis: 8 (9%) < 30%, 2 (3%) with 40% and 1 with > 70%. None of the patients showed features of NASH in the liver biopsy. **CONCLUSIONS:** Non-invasive methods aimed to detect advanced fibrosis in patients with NAFLD or NASH showed acceptable sensitivity (73% - 86%) in AILD, APRI had the best performance for both the overall group and for AIH (sensitivity 73%) and OS (sensitivity 83%), while NAFLD fibrosis score showed a higher sensitivity in PBC with 83%. Liver biopsy remains a useful tool in AILD to confirm diagnosis. However, these non-invasive methods can be used as an alternative for monitoring patients in the follow-up before indicating a new liver biopsy. This project was supported by resources of the participating departments, PAICYT and CONACYT.

004

PREVALENCE OF FRACTURES IN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS AND PATIENTS WITH ULCERATIVE COLITIS

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OBJECTIVE: Osteoporosis is characterized by structural deterioration of bone tissue and low bone mass, leading to bone fragility and an increased susceptibility for fractures. Both Primary Biliary Cirrhosis (PBC) and Ulcerative Colitis (UC) are strongly associated with loss of bone mass. The purpose of this study was to examine the prevalence of fractures in PBC and UC patients. **MATERIAL AND METHODS:** Retrospective study that included patients with PBC and UC diagnosed between 2000-2010, currently being treated as outpatients at our hospital. Patients were matched by age and gender. Medical records were reviewed and clinical, biochemical and demographic data were assessed such as age, gender, body mass index (BMI) tobacco and alcohol use, use of medications including steroids, clinical behavior, radiographic and densitometry studies. χ^2 , T-test, Mann-Whitney U and ANOVA were used to compare categorical variables and means between the groups. Data was analyzed with SPSS 17. **RESULTS:** 102 patients were evaluated (51 with PBC and 51 with UC). T scores were significantly decreased in patients with PBC, with a mean value of -1.44 for femoral and -1.98 for vertebral (p = 0.010 and p = 0.001). More patients in the PBC group had osteopenia when compared with UC (p = 0.001 OR: 4.37, IC 95% 1.85-10.31), osteoporosis was similar

in both groups. There were no differences in BMI between both groups, but more patients in the UC group had previous steroid and tobacco use. Fractures were more common in patients with PBC than UC (p = 0.003 OR: 5.41 IC 95% 1.66-17.64), the sites of fracture were the arm in 1 patient in the PBC group and 4 patients in the UC group (p = NS), wrist in 5 PBC patients (p = 0.013 OR: 2.13 IC 95% 1.10-2.65) and vertebral fractures in 4 patients in the PBC group (p = 0.028 OR: 2.11, IC 95% 1.70-8.61). Vertebral fractures were also associated with osteoporosis (p=0.002 OR: 3.95 IC 95% 2.55-53.45). **CONCLUSIONS:** In both PBC and UC, presence of osteoporosis was similar, but fractures were more frequent in patients with PBC, underscoring the importance of detection and prevention of fractures in these patients.

005

COMPARISON OF SIMPLIFIED CRITERIA OF AUTOIMMUNE HEPATITIS WITH THE ORIGINAL SCORE SYSTEM GROUP OF AUTOIMMUNE HEPATITIS IN A GROUP OF PATIENTS IN CMN "LA RAZA"

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INTRODUCTION: Autoimmune hepatitis (AIH) is a necro-inflammatory disease that affects both genders. The presentation of this disease is heterogeneous and no isolated biochemical, clinical or histologic alterations diagnosed the illness. That is the reason a score was created by an international panel in 1993 and updated in 1999 (Gold Standard-GS) which give the clinician a guide to the diagnosis of AIH and classified it as "definitive" or "probable". Even though it has a sensitivity of 97-100%, it's limited because it is complex (includes 15 parameters and its clinical application is not simple), then the international group of HAI design a simplified diagnostic scale (SC) which is useful in routine clinical practice based on 4 components (auto-antibodies, IgG, histology and exclusion of viral liver disease) this scale defined as "probable AIH" with a score of 6 and "HAI possible" with a score of ≥ 7 . This scale showed a sensitivity of 88% and specificity of 99% in U.S., Japan and Europe, but there is no record in Mexico. **OBJECTIVE:** To compare the original with the simplified criteria of HAI in Mexican population of the Gastroenterology department in the Hospital de Especialidades "La Raza". **MATERIAL AND METHODS:** We included patients with a diagnosis of AIH based on the revised criteria for HAI 1999, attended at the Gastroenterology Service CMN "La Raza", IMSS. They were retrospectively assessed with the results of biochemical, immunological and histological features when they were available. HAI was defined as "definitive" when the score was > 15, and "probable" when the score was between 10 and 15 before treatment. These patients were assessed with the gold standard before receiving treatment and re-staged with HAI simplified criteria as "definitive" when the score was ≥ 7 , and "probable" with a score of 6. For statistical analysis, we employed descriptive statistics. We evaluated the sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of simplified criteria compared with the GS. **RESULTS:** Twenty three patients (n) were included retrospectively of the Gastroenterology Department in the Hospital de Especialidades "La Raza" diagnosed with HAI

consecutively from 2006-2010. We found that 91% (21n) were females, with ages ranging between 17-70 years. Ninety six percent (22n) had ANA (+) while 52% (12n) had AMAs (+). The 61% (14n) showed elevation of IgG (range 1,810-4,190, mean 2,451) and 35% (8n) had association with another autoimmune disease: 5n (62.5%) had thyroid disease. Comparison of GS vs. SC: With the GS, 16n had a definitive diagnosis and 7 probable. Of the 16 patients with definitive diagnosis, 12 had definitive diagnosis and 4 probable with SC. Of the 7 patients with probable diagnosis using the GS, 3 were definitive, 2 probable and 2 didn't reach the criteria using the SC classification. Applying the SC 15 patients had definitive diagnosis, 6 probable and 2 didn't reach the criteria; of the 15 patients with definitive diagnosis, 12 were definitive and 3 probable applying the GS. Of the "probable" diagnosis using the SC 4 were definitive and 2 probable applying the GS. Comparing the results obtained in our simplified criteria has a sensitivity of 75%, specificity 71%, PPV of 70% and NPV of 66% with a diagnostic accuracy of 70.5%. **CONCLUSION:** Comparing our results with those obtained in other studies, in our population the sensitivity, specificity of the simplified criteria are lower.

006

CAROLI'S SYNDROME. A CASE REPORT AND A REVIEW OF THE LITERATURE

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INTRODUCTION: Caroli's syndrome consists in the coexistence of Caroli's disease and congenital hepatic fibrosis. Pathogenesis is related with a ductal plate malformation at different levels in the intrahepatic biliary tree. It is an autosomal recessive inherited malformation associated to mutations of the PKHD1 and ARPKD genes. Clinically it presents as a combination of Caroli's disease with recurrent cholangitis episodes and gallstones formation, and congenital hepatic fibrosis with symptoms associated to portal hypertension. Demonstration of sacular and ductal communication is elemental for diagnosis of the Caroli's disease component which is possible by ultrasound, computed tomography, magnetic cholangiography, or endoscopic retrograde cholangiopancreatography (ERCP). Hepatic fibrosis diagnosis is established by biopsy. Treatment consists in drainage procedures with ERCP or percutaneous cholangiography. Surgical options consist in lobar or segmentary hepatic resection. Transplantation represents the only one curative option in Caroli's syndrome, which is considered in recurrent cholangitis attacks or if a malignant transformation suspicion is present. **OBJECTIVE:** To report the presence of a representative case of Caroli's syndrome and to review in the literature the characteristic features of this disease. **CASE REPORT:** This case is about a male patient, 18 years old, who was admitted in Hospital General de México in February of 2009, with recurrent episodes of fever, nausea, vomit, malaise as the only pathological antecedent. At admission, with fever, jaundice, choloria, acholia, constant epigastric and right hypochondrium pain, without irradiation, abdominal bloating, nausea, vomit, and with 2 episodes of melena, without hemodynamic repercussion. At physical examination: blood pressure of 120/90, hearth rate of 100 bpm, respiratory rate of 30 rpm, and temperature of 38.4 grades. Awake, dehydrated, jaundiced. The neck and thorax

without abnormalities. Abdomen bloated and collateral vein circulation. Abdominal tenderness in right hypochondrium, 3 hepatomegaly of 3 cm, irregular and firm liver surface. Splenomegaly was found. The rest of physical examination resulted without abnormalities. Laboratory findings: WBC 13100, neutrophils 95%, platelets 97 mil, creatinine 1.5, alkaline phosphatase 277, total bilirrubin 5.2, direct bilirrubin 3.6, GGT 270, AST 77, ALT 81, PT 15.6, aPTT 42.8. Computed tomography reported hepatomegaly, and intrahepatic biliary dilatation, predominantly in the right side. With this finding, a percutaneous cholangiography and a liver biopsy was done, in the former, right biliary tract dilatation was found with cystic images related to perihilar abscesses. A mixed biliary drainage catheter was placed. The histological study reported sacular dilatations, with periportal fibrosis, consistent with congenital hepatic fibrosis with Caroli's disease associated. Posterior to drainage, the patient continued with an adequate evolution, actually considering as a treatment option partial resection, due to the segmentary affection. **CONCLUSION:** Case report is illustrative about pathologies, that even when not common, they allow to consider them at the moment of diagnosing, so that an opportune treatment can be initiated, improving prognosis.

ALCOHOLIC LIVER DISEASE AND FATTY LIVER

001

POLYMORPHISMS OF ALCOHOL-METABOLIZING ENZYMES IN YOUNG UNIVERSITY STUDENTS

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INTRODUCTION AND OBJECTIVE: Chronic alcohol consumption causes a variety of biochemical and physiological changes in various organs as brain, liver and pancreas. Genetic polymorphisms of alcohol-metabolizing enzymes (alcohol dehydrogenase, ADH; acetaldehyde dehydrogenase, ALDH; Cytochrome P450E1, CYP2E1) have been reported as a possible association with alcoholism and alcoholic liver injury in different populations (Montaño A, 2006; Chambers GK, 2001; Chao YC, 1997; Goedde HW, 1992; Novoradovsky A, 1995; Osier MV, 2002; Reed T, 1996). However, the association of these genetic polymorphisms in subjects without alcohol-induced hepatic or pancreatic injury has not been studied. The objective was to analyze the genotypic and allelic frequencies of ADH1B, ALDH2 and CYP2E1 genes in a university young population and their association with alcohol consumption patterns. **MATERIAL AND METHODS:** University students with ethanol consumption (OH) and an age- and scolarity- matched control group (CTL) teetotalers or alcohol consumers of < 10 g per day. Both groups were classified according to AUDIT (Alcohol Use Disorders Identification Test) and CIDI (Composite International Diagnostic Interview). OH group was subdivided into 3 categories: alcohol abuse (AB), al-

coholic dependency (DE) and risk consumption (RI). Craving questionnaire was applied for assess (measure) the wanting for drinking and behavioral lack of inhibition. Both groups gave their written informed consent. Body Mass Index (BMI) and peripheral blood were obtained from each participant. Liver function test (GGT, AST, ALT), hematic biometry, DNA extraction and restriction fragment length polymorphisms (RFLP's) of ADH1B, ALDH2 and CYP2E1 were performed. **RESULTS:** 146 CTL and 106 OH (DE: 51%, RI: 27% and AB: 22%) subjects were included. CTL group with BMI of 23.5 ± 3.6 kg/m². OH group with BMI of 24.5 ± 3.6 kg/m². Statistically significant differences between CTL and OH groups in alcohol consumption (gr OH/day), AUDIT, Craving and age were found ($p < 0.05$), as well as in Hb, Hto, MCV, lymphocytes, AST and ALT (these differences weren't observed within OH group). RFLPs: The most frequent allele for ADH1B and ALDH2 was wild type (CTL = 98% vs. OH= 99%, CTL= 98% vs. OH = 100%, respectively); for DraI was C/C (CTL = 82% vs. OH = 82%); for RsaI was c1/c1 (CTL = 84% vs. OH = 84%) and for TaqI was A2/A2 (CTL = 83% vs. OH = 81%). Both groups were in Hardy-Weinberg equilibrium. **CONCLUSIONS:** In a young consuming alcohol population, we found differences in biochemical parameters between groups, which can be orientated towards primary care. The polymorphic frequencies of ADH1B, ALDH2 and CYP2E1 between CTL group and OH group were similar. We conclude that genetic polymorphisms aren't determinants or have no influence on the alcohol consumption patterns in young consumers' alcohol. This project was sponsored by "Macroproyecto UNAM: MP16-14 SDEI-PTID-06-3".

002

ASSOCIATION OF GENETIC POLYMORPHISM OF ALCOHOL DEHYDROGENASE ENZYMES AND ALDEHYDE DEHYDROGENASE WITH ALCOHOLISM IN A GROUP OF MEXICAN MESTIZOS

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INTRODUCTION: In the liver occurs of 99% of alcohol metabolizing (Kirdesley D, 2001). Key enzymes for alcohol metabolism are alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) (Pocock G, 2005; Deitrich RA, 2007). Alcohol affects major organs also includes central nervous system (Gisbert Calabuig JA, 2005). It is proposed that certain genetic variations in the metabolism of alcohol and acetaldehyde, confer individual risks for alcohol dependence or organ damage related to alcohol (Yoshihara E, 2000; Harada S, 2001; Stinson F, 2001). Several polymorphisms of genes encoding alcohol-metabolizing enzymes (ADH, ALDH) have been reported for their association with alcoholism and liver damage by alcohol in different populations (Chambers GK, 2001; Chao YC, 1997; Goedde HW, 1992; Osier M, 2002; Reed T, 1996). **OBJECTIVE:** To investigate the frequency of genetic polymorphisms of ADH1B and ALDH2 in alcoholic and non-alcoholic population and its relationship with liver damage. **MATERIAL AND METHODS:** Inclusion criteria: We included 170 chronic alcoholic (OH) patients that subsequent

CAPRA consulting the General Hospital of Mexico with alcoholism according to WHO criteria (> 70 g/day in men, > 50 g/day in women over the past 5 years). They were classified according to the absence or presence of alcohol liver damage. Detailed history was drawn from each patient. The control group (CT) consisted of 149 teetotalers or alcohol consumers of < 10 g per day. Blood samples were taken in one occasion for analyzed the restriction fragment length polymorphisms (RFLPs) of ADH1B/MaeIII, ALDH2/MboII. **RESULTS:** We included a CT group (149), with mean age of 36 ± 5 years, IMC 26 ± 5 years, and AUDIT < 5 . The OH group was classified by presence (122) or absence of liver damage (48). The mean age was 49 ± 11 and 45 ± 12 years respectively, BMI 27 ± 4 kg/m² both groups. The average grams of alcohol per day in liver damage patients were 290 ± 22 g while that without liver injury was 350 ± 31 g. The average years of consumption was similar in both groups (28 years). RFLPs: We found significant differences in ADH1B*2 allele (OH: 0% vs. CT: 5% $p = 0.002$). The allele ADH1B *2 and ALDH2*2 have a similar allele frequency (0%) that Western populations; in contrast the Asians ethnic groups the frequency of these alleles is about 85 and 40%, respectively. It should be noted that the alleles ADH1B*2 and ALDH2*2 allele is considered protective for the development of alcoholism. The Hardy-Weinberg equilibrium was achieved. **CONCLUSION:** Alcoholic group have a low prevalence of ADH1B*2. The allele ADH1B*1 is indicative of an increased capacity to metabolize alcohol. Our results showed that this allele was associated with chronic alcohol consumption in this group of Mexican mestizos.

003

ASSOCIATION OF GENETIC POLYMORPHISMS OF CYP2E1 (DRAI, RSAI AND TAQI) WITH ALCOHOLISM IN A GROUP OF MEXICAN MESTIZOS

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INTRODUCTION: The liver has the ability to metabolize alcohol 8 to 10 g/h in an adult. Standard alcoholic beverage contains 13 to 14 g of alcohol (Williams MH, 2002). When the liver exceeds its capacity to metabolize activates the mitochondrial oxidative system of ethanol by the cytochrome P450 (CYP2E1) (Lieber CS, 1999). Several polymorphisms of the enzyme have been associated with susceptibility to alcoholic liver disease (ALD) in caucasians, one is located in the promoter region (RsaI), and others in intron 6 and 7 (DraI and TaqI respectively) (Ingelman-Sundberg, *et al.*, 1996). **OBJECTIVE:** To investigate the frequency of genetic polymorphisms of CYP2E1 (DraI, RsaI and TaqI) in the alcoholic population and their relationship to the presence of liver damage. **MATERIAL AND METHODS:** We included 170 chronic alcoholic (OH) patients consulting the General Hospital of Mexico with alcoholism according to WHO criteria (> 70 g/day in men, > 50 g/day in women for 5 years). We made detailed clinical history from each patient, they were classified according to the absence or presence of liver damage of alcohol. The control group (CT) consisted of 149 teetotalers or alcohol consumers of < 10 g per day. Blood samples were taken in one occasion for analyzed the restriction fragment length polymorphisms

(RFLPs) of CYP2E1: promoter region (DraI), intron 6 (RsaI) and intron 7 (TaqI). We obtained written informed consent. **RESULTS:** We included 149 CT, AUDIT-5, average age 36 ± 15 years and a BMI of 26 ± 5 kg/m². Alcoholic subjects were classified by presence (122) or absence of liver damage (48). The average age was 49 ± 11 and 45 ± 12 years respectively, BMI 27 ± 4 kg/m² for both groups. The average for gram of alcohol per day for those with liver damage was 290 ± 22 g while that without injury was 350 ± 31 g. The average years of consumption were similar in both groups (28 years). RFLPs: The wild type allele was more common (c1) for the promoter region: OH 86% vs. 81% CT, and TaqI, (A2), with 81% OH 84% vs. CT. While for DraI the most frequent was the mutant allele C with 82% OH vs. 77% CT, no significant differences between groups. In the subgroups of OH with and without liver damage were significant differences in TaqI polymorphism ($p = 0.032$). The Hardy-Weinberg equilibrium was achieved. **CONCLUSION:** Our results showed that the higher frequency of the variant A1 allele in individuals with liver damage reflects an increased risk of developing alcoholic liver disease.

004

SEVERITY OF ALCOHOLIC CIRRHOSIS AND CYP2E1*C2/CYP2E1*5B. POLYMORPHISMS OF GENES CODING FOR ETHANOL METABOLIZING ENZYMES IN WESTERN MEXICAN PATIENTS

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INTRODUCTION: Alcoholic cirrhosis constitutes a major worldwide health problem. ADH1B and ALDH2 are the main ethanol metabolizing enzymes; meanwhile, CYP2E1 is activated in individuals chronically ingesting alcohol. Polymorphisms of genes coding these enzymes may play an important role in the developing of cirrhosis, as alcohol represents the major etiological factor of this nosological entity, but controversial results have been reported. **OBJECTIVE:** To determine the association of ADH1B*2, ALDH2*2, and CYP2E1*c2 with cirrhosis. **MATERIAL AND METHODS:** 90 clinically healthy individuals as control (C) and 41 patients with alcoholic cirrhosis (AC) were included. Genotypes were determined through PCR-RFLP's in genomic DNA isolated from peripheral leukocytes. MaeIII, Ksp632I and RsaI were utilized to characterize ADH1B, ALDH2 and CYP2E1 polymorphisms, respectively. Besides, clinical, biochemical and histopathological assays were performed. Pearson chi-square was applied to analyze frequencies. Levene and Kolmogorov-Smirnov tests were utilized to evaluate variance homogeneity and variable distribution, respectively. Student's t test was employed to analyze quantitative data. Also, multifactorial analysis was performed in order to determine variable interaction. **RESULTS:** Genotype distribution in patients with AC was 1.6% ADH1B*2, 0.0% ALDH2*2, 19.5% CYP2E1*c2; C individuals presented 6.1% ADH1B*2, 0% ALDH2*2, 10.6% CYP2E1*c2. Frequency of the polymorphic allele CYP2E1*c2 was statistically higher ($p < 0.05$) in AC patients than in C individuals. CYP2E1*c2 carrying AC patients showed higher hepatic decompensation than those carrying wild type alleles regarding to total bilirubin and prothrombin time ($p <$

0.05). Cirrhosis severity evaluated through Child-Pugh score and mortality were higher in patients carrying de polymorphic c2 allele, though not attaining statistical significance. **CONCLUSIONS:** Association of CYP2E1*c2 with cirrhosis was observed; meanwhile, association with ADH1B*2 or ALDH2*2 was no shown. The population studied presented monomorphism for ALDH2*1, as polymorphic allele was not present in AC nor C either. AC severity was associated to CYP2E1*c2, probably due to oxidative stress promoted by this polymorphic allele. Induction of CYP2E1 expression by obesity, fasting as well as diet composition has been reported, probably exacerbating liver damage. Nevertheless, ulterior studies are needed in order to clearly establish the utility of CYP2E1*c2 determination as a prognostic marker for liver damage in patients with AC.

005

PREVALENCE OF AUTOANTIBODIES IN NON ALCOHOLIC FATTY LIVER DISEASE

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INTRODUCTION: Non-alcoholic fatty liver disease (NAFLD) is now one of the commonest liver disorders. It is closely associated with features of the metabolic syndrome, particularly obesity and diabetes. It is comprised of a spectrum of liver disease ranging from simple steatosis to full-blown steatohepatitis that is characterized by steatosis, lobular inflammation, ballooning, and fibrosis. Although low titer autoantibody (AAb) positivity can be seen in up to 33% of patients with NAFLD, some studies have reported more severe histological damage in these patients. In patients with suspected NAFLD and positive AAb, a liver biopsy may be considered to exclude the presence of autoimmune hepatitis. **OBJECTIVE:** The aim was to study the prevalence of AAb in a group of NAFLD patients and to compare AAb positive and negative patients. **MATERIAL AND METHODS:** Data base was developed and patients diagnosed as NAFLD and follow information was recovered: age, gender, body mass index, Diabetes Mellitus (DM), insulin resistance, glucose resistance, arterial hypertension, HOMA-IR Quicki, liver function test, glucose, cholesterol triglycerides, LDL, HDL, fibrosis degree, NAFLD and autoimmune hepatitis histological features. Liver biopsy was available in 51 (65%) cases. Patients were ungrouped as AAb positive (AAb-pos) when the result of ANA, AMA, LKM, or ASMA was more than 1:40 and AAb negative (AAb-neg) if all the results were minor than 1:40. Data were statistically compared using SPSS 15.0 program. **RESULTS:** 79 patients with NAFLD diagnosis were included, which 15 (19%) were catalogued as AAb positive (AAb-pos) and 51 (71%) as AAb negative (AAb-neg). In the group of AAb-pos, 7 patients had ANA positive ($n = 4$, 1:80, $n = 1$, 1:320 and $n = 2$, 1:40); 8 ASMA positive ($n = 5$, 1:40, $n = 1$, 1:320 and $n = 2$, 1:80); 5 AMA positive ($n = 4$, 1:40 and $n = 1$, 1:80). No patient presented LKM positive. In 5 patients more than one AAb was positive. In the liver biopsies diagnosis of NAFLD was confirmed, without features of autoimmune liver disease. There was a significant difference between age ($p = 0.017$), triglycerides ($p = 0.003$) comorbidities of diabetes mellitus (insulin resistance) ($p = 0.002$), hypertension ($p = 0.022$), GGT ($P = 0.034$), and the degree of fibrosis ($p = 0.014$). **CONCLUSION:** The incidence of AAb in this patient group was 19%, age and triglycerids and GGT were significantly higher in

AAb-pos group as well as a greater incidence of comorbidities like diabetes mellitus, hypertension and greater degree of fibrosis in this group of patients, thus supporting the theory that the presence of AAb in NAFLD could mean a more severe disease.

006

FIBROMAX POSITIVE PREDICTIVE VALUE IN THE DIAGNOSIS OF NASH

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BACKGROUND AND AIM: Non-alcoholic fatty liver disease is an entity that have been employed to describe many clinical and histological features from simple steatosis, inflammatory activity, fibrosis and cirrhosis. Biopsy specimens describe ballooning degeneration and advanced fibrosis. However, there is a high rate of false negative results since fatty infiltrate are not homogeneous. **AIM:** To determine the sensitivity, specificity, prevalence, positive predictive value (PPV) and negative predictive value (NPV) of fibromax test in patients with no-alcoholic steatohepatitis. **MATERIAL AND METHODS:** Crossover design From March 2009 to September 2010, where 35 patients with non-alcoholic steatohepatitis were evaluated to calculate the degree of fibrosis, steatosis and necroinflammatory activity fibromax via and compared with a biopsy specimen. Sensitivity (Sn), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were determined respectively. **RESULTS:** To detect fibrosis, Sn, Sp, PPV and NPV were 59, 25, 93 and 3%, respectively. To detect steatosis, Sn, Sp, PPV and NPV were 96, 25, 96 and 25%, respectively. To detect necroinflammatory activity, Sn, Sp, PPV and NPV were 59, 25, 93 and 3%, respectively. To detect non-alcoholic activity, Sn, Sp, PPV and NPV were 96, 25, 96 and 25%, respectively. **CONCLUSION:** Fibromax as non invasive biomarker of hepatic fibrosis and necroinflammatory disease has a limited specificity compared with biopsy specimen.

007

EFFECT OF AN ATHEROGENIC DIET IN LIVER REGENERATION AFTER PARTIAL HEPATECTOMY

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INTRODUCTION: The non-alcoholic fatty liver disease (NAFLD) is the hepatic manifestation of metabolic syndrome, defined by the deposition of fat (fatty acids, triglycerides and cholesterol) by more than 5% in hepatocytes. It has been reported that the presence of lipids, mainly cholesterol, induces cell sensitization to injury. Liver regeneration after partial hepatectomy is a process of compensatory hyperplasia that involves all of the remaining liver cell types and depends on the interplay of different regulatory pathways that directly or indirectly control the successful restoration of liver mass. HGF and its receptor c-Met regulate various processes in the

liver, including mitogenic regulation, motogenesis and morphogenesis, as well as a stimulator of liver regeneration, being a potent inducer of DNA synthesis, as many other growth factors. **OBJECTIVE:** The aim of this work was to study the effect of high cholesterol diet in the hepatic repair process in a in vivo model. **MATERIAL AND METHODS:** Mice of the strain C57BL/6 were used and were fed with an atherogenic diet (2% cholesterol and 0.5% sodium cholate) or normal diet (Chow) for two days. Subsequently, a partial hepatectomy was performed and the animal sacrifice was done at different times, doing a hematoxylin and eosin staining, measuring the free cholesterol by HPLC. The primary culture was treated with HGF at different times, to obtain total protein and use it in Western Blot against active and total forms of c-Met. **RESULTS:** It was observed that the liver mass ratio between the total mass of mice increases progressively over time, recovering at the fifth day, but the liver mass of the mice fed with a high cholesterol diet continues increasing as the time passes. In hematoxylin and eosin staining we observed that mice fed with a balanced diet the cell proliferation ceases on the seventh day, whereas in mice fed a high cholesterol diet the proliferation continues. The free cholesterol levels in the liver are increased in mice with high cholesterol diet. By Western Blot we found in cells isolated from these animals, HGF shows a delayed activation of its receptor c-Met. **CONCLUSION:** our data suggest that cholesterol affects the process of liver regeneration, altering the cell cycle. HGF activates its receptor belatedly; which may impact on a proper repair response. This may have implications in terms of initiation of an uncontrolled proliferative process that can affect diseases such as cancer. CONACYT 61544 y 131707, NNL is scholarship holder of CONACYT # 234219.

008

TRANSIENT ELASTOGRAPHY (FIBROSCAN) FOR THE DIAGNOSIS OF SECONDARY HEPATIC FIBROSIS TO SEVERE REGURGITATION OF TRICUSPID VALVE. SERIES OF CASES

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INTRODUCTION AND AIM: The use of transient elastography as an auxiliary diagnosis method of hepatic fibrosis has been widely studied in different chronic liver diseases such as virus C and B, cholestatic, autoimmune, by toxins, and so on. The aim of this study was to investigate the utility of Fibroscan in the assessment of hepatic fibrosis secondary to severe regurgitation of tricuspid valve. **MATERIAL AND METHODS:** We studied patients with diagnosis of tricuspid regurgitation and important hemodynamic repercussion (valued by the physical check-up and transthoracic echocardiography); of any etiology and that they fulfill with the inclusion criteria, in the order of how they get hospitalized and applying the sequential techniques. They were invited to participate in the investigation and once they've accepted, they were invited to sign a letter of agreement with the investigation, where they authorize the realization of the hepatic biopsy and Fibroscan. All the patients were negative to hepatitis B and C by serology and autoimmune diseases. All patients with a record of high alcoholism and with other possible reasons of hepatic fibrosis were excluded of this research. They

were made evaluations of the anatomy and the physiology of the liver such as clinical evaluations, functioning tests, complete blood count, hepatic ecography and gammagrama. We also apply a hepatic biopsy, and with the microscopic description, the Masson Trichrome Stain and Morphometry we obtain the pathological results. They were also applying to all the patients a fibroscan using the METAVIR scale, from FO (absence of fibrosis) on to F4 (cirrhosis). We compare the relationship of the results of the biopsy and the fibroscan. **RESULTS:** Five patients fulfill the inclusion criteria. Three of them were women and two men. The minimum age was 33 and the maximum age 56 years old. Four of them, have a diagnosis of Inactive Rheumatic Cardiopathy with mitral affection and severe tricuspid regurgitation. One of them, his diagnosis was mitro-tricuspid regurgitation. In three of them the histological diagnosis of the biopsy was cirrhosis, and the result of Fibroscan was F4. In one of them the histological diagnosis of the biopsy was passive congestion, and the result of Fibroscan was F1. **CONCLUSIONS:** The results obtained by Fibroscan were related with the ones of the biopsy in all of patients of the study, that's why we must consider the use of this tool in the valuation of the secondary hepatic fibrosis to severe regurgitation of tricuspid valve. This work was supported by Médica Sur Clinic and Foundation.

009

SERUM CORTISOL LEVELS ARE RELATED TO THE PRESENCE OF METABOLIC SYNDROME FEATURES, BUT NOT WITH THE PRESENCE OF NAFLD

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INTRODUCTION AND AIM: Several studies have compared the similarities between Cushing's syndrome and Metabolic Syndrome (MS). Recent studies on metabolic syndrome, have pointed out the importance of cortisol in its pathophysiology, especially on the activity of tissular 11β hidroxyesteroid deshydrogenase, which is the enzyme that regenerates cortisol from cortisone. In patients with MS, has been observed that tissular cortisol and 11β hidroxyesteroid deshydrogenase expression, are closely related to visceral fat content, insulin resistance, dyslipidemia, type 2 diabetes mellitus and hypertension. A recent study carried out by our group showed that female patients with polycystic ovary syndrome (PCOS) and nonalcoholic fatty liver disease (NAFLD) have higher serum cortisol concentrations. The aim of this study was to compare serum cortisol levels in patients with and without NAFLD. **MATERIAL AND METHODS:** We carried out a cross sectional study in the University Hospital, in Mexico City. We studied 78 women including 53 with NAFLD and 25 without NAFLD. The presence of NAFLD was established through ultrasonography. Anthropometric, metabolic, dietary and biochemical variables were measured in all patients. Serum cortisol levels were determined and compared between the groups. **RESULTS:** Age, body mass index (BMI), waist-to-hip ratio, body fat percentage, fasting glucose, HOMA-IR and insulin were significantly higher in patients with NAFLD. Serum cortisol concentration was similar between patients with (10.98 ± 3.9) and without NAFLD (10.20 ± 4.0). Serum cortisol level is related to BMI and insulin, and had a negative correlation with HDL, also it has a trend with serum glucose levels. **CONCLUSIONS:** In

this study, as in others recently published we observed that there is a correlation between serum cortisol levels and several features of metabolic syndrome including HDL, BMI and insulin, but not with HOMA-IR. On the other side we did not observed significative differences in cortisol levels between patients with and without NAFLD. This might be related to the effect observed in other studies, for this reason another important feature to be considered in this study is to measure tissular concentration of cortisol and tissular expression of 11β -hydroxyesteroid deshydrogenase, since is probable that we observe a difference in patients with and without NAFLD. This work was supported by Médica Sur Clinic and Foundation.

MISCELLANEOUS

001

FREQUENCY OF HEPATIC INVOLVEMENT IN PATIENTS WITH INFLUENZA AH1N1

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INTRODUCTION: In 2009 we experienced an influenza H1N1 pandemic. There have been reports of association with this infection and the appearance of hepatic damage, in some cases severe, especially in those with comorbidities or immunosuppression. **OBJECTIVE:** The aim of this study was to analyze the frequency of hepatic involvement (abnormal liver function test) in those patients that were admitted at two hospitals in northeast of México. **MATERIAL AND METHODS:** This is a retrospective, observational and descriptive study that included all confirmed cases of influenza A H1N1 (RT-PCR), admitted in two hospitals: San José Tec de Monterrey (HSJ) and Hospital Metropolitano Bernardo Sepúlveda (HM), from March 2009 to February 2010. Medical History, laboratory reports at admission and clinical evolution as well as liver related or non liver related complications were collected. Descriptive statistical analysis using a Minitab 16.0.1 program was performed. **RESULTS:** A total of 221 cases with confirmed diagnosis of influenza A H1N1 were reviewed. One hundred and eighty-three (83%) patients from HSJ and 38 (17%) from HM. One hundred and twenty four (56.2%) females and 97 (43.8%) males, with an mean age of 34.68 ± 14.11 ys, (min: 8 months-max: 73 ys). Mean in hospital stay was 4.68 ± 4.86 days (1 to 40 days). Detected comorbidities included: obesity and overweight in 32% (n = 70), systemic hypertension in 7% (n = 16), pregnancy in 7% (n = 15), diabetes mellitus in 6% (n = 13) and asthma in 5% (n = 11). At admission we found a threefold (ULN) elevation of AST in 34% and ALT in 31%. Twelve percent (n = 28) required admission to a intensive care unit. There were 5 non liver related complications: aseptic meningitis (n = 1), acute myocardial infarction (n = 1) and 3 deaths. There were no cases of liver failure. In this particular group abnormal AST and ALT levels were present in 42 and 29%, respectively. Serum ALT and AST values at admission in all patients with abnormal results according to age are shown on table 1. A favorable clinical outcome was presented in 87% of cases (n = 193).

Table 1. Serum levels of ALT/AST at admission in patients with confirmed diagnosis of influenza H1N1 and abnormal liver function test (mean \pm SD).

Age group	AST	ALT
0-19 (n = 6)	42.5 (\pm 5.5) IU/L	49.17 (\pm 43.5) IU/L
20-29 (n = 15)	190.27 (\pm 302.7) IU/L	410.2 (\pm 1134.2) IU/L
30-39 (n = 12)	63.33 (\pm 42.82) IU/L	67.33 (\pm 36.87) IU/L
40-49 (n = 7)	72.14 (\pm 37.32) IU/L	41.6 (\pm 19.27) IU/L
Older than 50 (n = 15)	67.27 (\pm 45.5) IU/L	45.9 (\pm 24.9) IU/L

CONCLUSIONS: In this retrospective study a high frequency of hepatic involvement was identified, higher than the reported in other series. It could be related to: present study only included those patients that required in-hospital management; to an elevated frequency of associated comorbidities or/and the specific search of liver enzymes abnormalities. The pathogenesis of extrapulmonary involvement of influenza H1N1 virus infection is under investigation. **CONFLICT OF INTEREST:** The authors have no relationship to disclose.

002

FROM THE BASIC RESEARCH TO THE CLINIC: PRELIMINARY ANALYSIS OF A HEPATIC FIBROSIS MARKER FROM EXPERIMENTAL MODELS

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INTRODUCTION: Fibrosis is a common complication of most chronic liver diseases. The limitations of available analytical methods require using non-invasive tests for the evaluation of early stages of the disease. The different experimental models used to reproduce the fibrosis-cirrhosis, generate genetic patterns resulting from stimulus own inductor, which analyzed as a whole can characterize different stages of development of liver fibrosis, which could reasonably be extrapolated human suffering. **OBJECTIVE:** Using experimental models of hepatic fibrosis induction (bi-weekly injections of carbon tetrachloride (CCl₄) and thioacetamide (TAA), to locate, identify and validate, MFAP4 protein expression obtained by microarray analysis, in the animal models sera and in alcoholic patients sera with different degrees of liver damage with dx by USG. **MATERIAL AND METHODS:** Developed two experimental models of cirrhosis in Wistar rats, one with TAA, and the other with CCl₄, injected intraperitoneally biweekly for 15 and 20 weeks respectively. The techniques used were, microarray technology, qPCR and ELISA. Were

used serum samples from animals belonging to the experimental models developed and alcoholic patients. For data analysis were applied statistical and bioinformatics tools and DAVID, SAM and Pearson correlation tests for the significance of the results. **RESULTS:** We identified an extracellular matrix glycoprotein, Mfap4 by microarray technology, which was validated by qPCR and ELISA to establish the gene and protein expression in experimental models. Likewise, the ELISA performed in alcoholic patients showed an increase in exchange rates up to 4 times compared to controls. **CONCLUSIONS:** In a previous proteomic study carried out with sera from cirrhotic patients Dr. Mölleken, *et al.* proposed the MFAP4 as a potential biomarker for liver fibrosis. Simultaneously we identified the same molecule in our experimental models using expression microarrays in total rat liver. We can say that our data are confirmatory to previous reports regarding the Mölleken group, and significantly related to our induction of fibrosis stages in the models. So we can conclude that there is a high correlation between the pathophysiology of fibrotic process in animal and human disease. This work was supported by funds provided by UNAM, PAPIIT IN-205210, SEP-CONACYT 84837.

003

HEPATIC TUBERCULOSIS IN NECROPSY, REPORT OF TEN YEARS AT HOSPITAL GENERAL DE MÉXICO

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INTRODUCTION: Gastrointestinal involvement is the sixth site of extrapulmonary tuberculosis. Hepatic tuberculosis counts for less than 1% of tuberculosis reported cases, and is most frequent in men between 30 to 50 years. Tuberculosis can affect the liver in three different ways: the most common are miliary tuberculosis (59-80%), hepatic symptoms or signs are uncommon; the second form of affection is granulomatous disease with fever, mild jaundice and hepatomegaly; finally located hepatic tuberculosis, which may or may not have involvement of biliary tract. *Mycobacterium tuberculosis* is the etiological agent most frequently isolated. Patients can have abnormal transaminases, alkaline phosphatase and gamma glutamyltranspeptidase. Diagnosis should be considered in any patient with chronic pain on right superior quadrant and hepatomegaly, especially if fever and weight loss are present. For definitive diagnosis is mandatory the histological examination, finding caseificant granulomas is characteristic. **OBJECTIVE:** To determine the prevalence of hepatic tuberculosis in a ten year-period in death patients who underwent necropsy in Hospital General de México O.D. **MATERIAL AND METHODS:** We reviewed reports of necropsy performed from January 1998 to December 2007, searching intentionally for diagnosis of hepatic tuberculosis. We used measures of central tendency (mean) and dispersion (standard deviation) for quantitative variables, the nominal variables are expressed in terms of proportions (%). **RESULTS:** In a ten year-period was performed 7,258 necropsies, finding that 3,254 (44.83%) presen-

ted some type of liver disease, 1,602 (49.23%) were male and 1,652 (50.76%) were female. From those 7,258 total necropsies performed in our hospital, hepatic tuberculosis represents 1.86%. From those 3,254 necropsies with some liver disease, 135 (4.14%) presented hepatic tuberculosis, from these 81 were men (60%) and 54 were female (40%), mean age of death was 53 ± 19.6 years, in men was 56 ± 18 years and in female was 50 ± 21 years. From these 135 necropsies with hepatic tuberculosis, 134 (99.25%) were associated with miliary tuberculosis, and 1 (0.74%) patient had only hepatic disease. In one case the etiological agent was atypical mycobacterium. **CONCLUSIONS:** Hepatic tuberculosis is a rare finding on necropsies performed in our hospital, with a low prevalence of 1.86% in ten years if we consider all causes of mortality. When we consider only those cases with some liver disease, prevalence is still low, representing 4.14% of all hepatic disease. Similar to that reported in literature, the most cases were associated with miliary tuberculosis and the etiological agent was *Mycobacterium tuberculosis*. **CONFLICT OF INTEREST:** Authors declare no interest conflict.

004

ACUTE FATTY LIVER OF PREGNANCY, PRESENTATION OF TWO CASES AND LITERATURE REVIEW

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INTRODUCTION: Acute fatty liver of pregnancy (AFLP) is a complication that occurs in the third trimester. There is a deficiency of long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD), which is associated with mutations G1528C and E474Q. This condition affects 1 in 13,000 pregnancies. The clinical presentation may include acute liver failure (IHA) severe coagulopathy, coma and renal failure. It has a mortality rate of 18% and a fetal mortality rate of 23%. **OBJECTIVE:** To report two autopsy cases with clinical and histopathological AFLP classic. **MATERIAL AND METHODS:** Two cases occurred in young primigravida during the third trimester of pregnancy, attended with jaundice, IHA, hepatic encephalopathy, hyperbilirubinemia, moderate elevation of aminotransferases, hypoglycemia, prolonged clotting times more thrombocytopenia, leukocytosis and anemia. The two died. Autopsy was performed. **RESULTS:** Case 1: Woman, 18 years old, primigravida, with stillbirth at 33 weeks of pregnancy, jaundice, metabolic encephalopathy and hemorrhagic syndrome. Died under these conditions the fifth day of hospitalization. Laboratories: direct bilirubin 11.9 mg/dL, indirect 2.1 mg/dL, AST 860 U/L, ALT 967 U/L, alkaline phosphatase 554 U/L, albumin 2.7 g/dL, prolonged clotting times, platelet count 120,000; glucose 81 mg/dL. The liver histological H & E, which showed microvesicular steatosis, predominantly in centrilobular hepatocytes, microvesicular steatosis which gave an appearance of hepatocytes affected "sparkling." Case 2: Male, 21 years old, primigravida with pregnancy of 36.5 weeks with unique product alive and final condition of a week earlier with vomiting, weakness and jaundice. Laboratories: direct bilirubin 3.2 mg/dL, indirect 1.8 mg/dL, AST 84 U/L, ALT 100 U/L, alkaline phosphatase 320 U/L, albumin 1.2 g/dL, prolonged clotting times, platelet 94,000; glucose 70 mg/dL. He

died the second day of hospitalization. The liver histological H & E which demonstrates the preserved architecture and predominantly centrilobular microvesicular steatosis with small vacuoles located at the periphery of hepatocytes, the nucleus retained its central position. **CONCLUSIONS:** Approximately 50% of these patients also show signs of preeclampsia, although usually not severe hypertension. The AFLP is most commonly seen in nulliparous women or multiple gestation. The strongest evidence is liver biopsy, although not always be performed by the alterations in coagulation. The histopathological findings revealed hepatocytes with edema, pale in the central area with microvesicular fatty infiltration. Imaging studies, including ultrasound and computed tomography (CT), are inconsistent in the detection of fatty infiltration. Therefore, the diagnosis of AFLP is usually done with the clinical and laboratory findings. Delivery should be considered as soon as possible. However, many laboratory abnormalities may persist after birth and initially may worsen during the first week postpartum. In rare cases, patients progress to fulminant IHA need for liver transplantation. Finally, patients should be examined for defects in fatty acid oxidation and subsequent relapse in children is 25%, and recurrence of AFLP in the mother is also possible, so that appropriate follow-up is suggested.

005

ACUTE PANCREATITIS SECONDARY TO HEPATITIS A VIRUS IN ACUTE LIVER FAILURE. CASE REPORT AND REVIEW OF THE LITERATURE

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INTRODUCTION: Although hepatitis A virus has a strong tropism for hepatocytes, viral antigens have also been detected in other tissues such as pancreas and gallbladder. Several viruses have been implicated as etiological factor of pancreatitis. Most secondary cases of viral hepatitis have been reported in association with acute liver failure and rarely in non-fulminant acute viral hepatitis have been documented. The incidence of acute pancreatitis in the context of acute liver failure in serological studies and autopsy is 3.7 to 34% and only case reports of its association with hepatitis A had been described. **OBJECTIVE:** To report a case of acute pancreatitis secondary to hepatitis A virus in a patient with acute liver failure. **MATERIAL AND METHODS:** A 33-year-old man with a sporadic history of alcoholism and smoking and frequent street food intake presented with 8 days of evolution of frontal headache, retro-orbital pain, epigastric pain radiating to the back, bloating, fever of 39°C and vomiting of gastric contents. After 3 days of evolution jaundice and itching were added. Laboratory reported: leukocytes, 28,100/ul, with increased neutrophil count, creatinine, 3.7 mg/dL and urea, 128 mg/dL. Hemoglobin, 9.1 g/dL, normal platelets, PT 27.6 s, INR 2.4, total bilirubin 80.9 mg/dL, direct bilirubin 63.2 mg/dL, indirect bilirubin 17.7 mg/dL, GGT 416 U/L, ALP 255 U/L, ALT 1,892 U/L, AST 993 U/L, cholesterol 152 mg/dL, triglycerides 232 mg/dL. Negative HBsAg, negative anti HCV, negative anti HIV, negative anti-core IgM and positive anti hepatitis A IgM. Amylase 950 U/l, lipase 1063 U/l. Duodenoscopy with normal greater papilla and spontaneous biliary output. **RESULTS:**

During his evolution presented oliguria and refractory metabolic acidosis so hemodialysis was indicated. Abdominal pain persisted and elevated pancreatic enzymes were reported, so acute pancreatitis diagnosis was integrated. Abdominal ultrasound reported normal liver, bile duct 3 mm, portal vein 8 mm, anechoic gallbladder, normal pancreas and kidneys. Abdominal tomography showed enlarged pancreas without evidence of necrosis or collections, hepatomegaly and bilateral pleural effusion. Developed altered mental state and hepatic encephalopathy, so required intensive care management, with continuous hemodialysis, mechanical ventilation and anti cerebral edema measures. Presented a satisfactory evolution, with progressive normalization of coagulation times, improvement of encephalopathy and successful extubation, renal function improved without requiring hemodialysis and adequate diet tolerance. He was subsequently valued with normal renal function with creatinine clearance of 84 mL/min and normal liver function tests. **CONCLUSIONS:** After biliary, alcoholic, metabolic and pharmacological etiologies were ruled out, we concluded acute pancreatitis secondary to hepatitis A virus in acute liver failure, of which only few cases have been reported in the literature. In the setting of viral hepatitis A, acute abdominal pain should be evaluated to rule out acute pancreatitis. Although pancreatitis in a patient with hepatitis A is usually mild, threatening life complications can occur, such as acute renal failure and acute hemorrhagic pancreatitis. This patient had a satisfactory outcome with conservative management without requiring liver transplantation and total resolution of symptoms without chronic renal damage. **CONFLICT OF INTEREST:** This work presents no conflict of interest.

006

TYPHOID HEPATITIS AND ENTERITIS, REPORT OF A CASE AND REVIEW OF THE LITERATURE

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INTRODUCTION AND OBJECTIVE: It is common to find abnormalities in liver function in patients with typhoid fever, but a clinical picture with fever and frank alteration in liver function tests, characterized the course of a small group of patients. The aim is to present the case of a patient presenting with clinical symptoms of acute hepatitis and terminal ileitis by *Salmonella typhi* and review of the literature. **MATERIAL AND METHODS:** Female 29 years old with a history of recent travel. His suffering starts 15 days before admission, with myalgia, arthralgia, fever of 39 °C predominance evening, colicky epigastric pain, accompanied of nausea and vomiting gastrointestinal content. Added 72 h before admission diarrheal stools, initially melena and later hematochezia. The following studies were conducted: WBC 3,384, hemoglobin 9.8 g/dL, platelets 163,000, DHL 714 U/L, ALP 1,214 IU/L, GGT 803 IU/L, AST 654 U/L, ALT 541 U/L. Index ALT/DHL was 0.29. Colonoscopy reported multiple injuries excavated 3 mm, the largest of 5 mm covered with fibrin in the distal ileum and ascending colon segmentally. The biopsy reported chronic nonspecific ileitis. Febrile reactions: Tiphyc "O" 1:160, tiphyc "H" 1:160. Blood culture was negative and mielocultivo shown growth of *Salmonella typhi*. Panels of viral hepatitis A, B and C was negative. **CONCLUSIONS:** *Salmonella* infections remain a serious problem throughout

the world in developing countries. Involucres liver in typhoid fever varies from a mild elevation in transaminases and alkaline phosphatase at a more dramatic presentation with a clinically indistinguishable from acute viral hepatitis in 1 to 26% of cases (Table 1). Typhoid hepatitis is associated with significant morbidity, but the disease is curable with a very good response to appropriate antibiotic therapy. Our patient had typical clinical symptoms, which led to the suspicion of typhoid hepatitis. This was corroborated by an index ALT/DHL from 0.29 and the mielocultivo+. The patient showed improvement in all parameters following the initiation of therapy with 3rd generation cephalosporins. Liver biopsy was not performed because the patient did not accept the procedure. The clinical picture of salmonella hepatitis may be indistinguishable from acute viral hepatitis. The lack of suspicion and an appropriate test to detect salmonella infection can lead to failure to diagnose and delay in treatment. The routine practice of obtaining cultures in patients with fever helps establish the diagnosis. The treatment is adequate fluid replacement, electrolyte and third generation cephalosporins.

Table 1. Clinical and biochemical differential aspects between viral hepatitis and salmonella hepatitis.

	Salmonella hepatitis	Viral hepatitis
Recent travel history	Yes	No
Fever	More than 39°C	Less than 39°C
Transaminases	Further increase of 5 to 8 times normal upper limit	Further increase of 10 times normal upper limit
ALT/DHL index	Less than 4	More than 4
Bandas	Increased	Normal
Enteric manifestations	Diarrhea to lower gastrointestinal bleeding	Diarrhea

007

ICTERIC LEPTOSPIROSIS. A CASE REPORT AND A REVIEW OF THE LITERATURE

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INTRODUCTION: Leptospirosis is a zoonosis caused by the spirochetes *Leptospira*. It has a world distribution, with an annual incidence estimated in 0.1-1 cases per 100,000 people. Infected mammals constitute the reservoir, eliminating the microorganism by urine. It introduces into the body by abrasions and by mucous membranes; the incubation period occurs between 2-20 days. Clinical characteristics varies from a sublinic course to a severe disease, potentially lethal. It has a wide range of manifestations like hepatic compromise, which includes hepatomegaly and jaundice (Weil's Syndrome). The diagnosis is based in culture isolation or seroconversion, with

a 4-fold increase in antibody titers. Treatment consists in antibiotics including oral doxycycline for mild infections and G penicillin, or 7 days intravenous ceftriaxone or cefotaxime in severe infections. **OBJECTIVE:** To report the case of a patient with jaundice associated to leptospirosis diagnosis. **METHODS AND MATERIALS:** We present a female patient, 47 years old, from a Michoacan rural community, exposed to overcrowding conditions, without basic services, in contact with dogs, sheep, and cattle. She had the antecedent of an hospitalization in a different medical center 2 years before her admission in our hospital. She was discharged with type A hepatitis diagnosis. The patient was then admitted in February of 2011 with clinical manifestations characterized by arthralgia, myalgia, malaise, weakness, not related with meals vomit, weight loss of 10 kg, jaundice and choluria. She affirmed the presence of pruritus, and intermittent fever 8 months before admission. At physical examination cachexia was found, patient awake, jaundiced and with cutaneous hyperpigmentation. In abdomen, 4 cm tender hepatomegaly, splenomegaly and inguinal, axilar and cervical not deep painful adenopathies. Hypotrophic lower and upper extremities. At admission with Hb 8.1 g/dL, Hto 23.5%, WBC 4,100/uL, NEU 2,700/uL, LIN 1,200/uL, platelets 83,000/uL, total bilirubin 37 mg/dL, direct bilirubin 22.9 mg/dL, AST 38U/L, ALT 23U/L, ALP 251U/L, GGT 189U/L, PT 21", PTTa 41.5". Hepatitis B and C serology negative. Expectoration acid fast rod negative. Liver and biliary tract US with hepatosplenomegaly and diffuse liver disease. Magnetic cholangiography showed hepatomegaly, without alterations in biliary tract. Liver biopsy showed regeneration related data. In lymphatic node biopsy neither infiltrative nor granulomatous lesions were found. In panendoscopy corporal and antral chronic gastropathy was observed. A bone marrow aspirate was realized, with normal results. Dark field microscopy study for *Leptospira sp* was realized, resulting positive. Anti-*Leptospira* antibodies with titers of IgG 1:80, IgM 1:20 were reported. **CONCLUSIONS:** Leptospirosis is an infrequent pathology, clinically characterized by a wide range of manifestations. Jaundice is not a common presentation, and when is associated it is called Weil's syndrome. However, clinical suspicion must be present when other frequent etiologies of jaundice were eliminated in a patient with risk factors. **CONFLICT OF INTEREST:** Authors declare no interest conflict.

008

USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE IN PATIENTS WITH LIVER DISEASE IN A LIVER UNIT

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INTRODUCTION: The use of complementary and alternative medicine (CAM) has increased significantly in recent years. According to WHO more than 80% of the world's population uses CAM and has been reported that up to 30% of patients who received treatment in liver clinics use herbal remedies. **OBJECTIVE:** To define the type of CAM used in patients with liver disease of a Liver Unit and describe in the case of medicine herbal, which is the main compound used in the treatment of liver diseases. **MATERIAL AND ME-**

THODS: A questionnaire (14 questions) based on international benchmarks for the use of CAM, patients older than 18 who were seen at the Liver Unit of University Hospital "José E. González" for the past 6 months. We recorded demographic data, level of education and for CAM: frequency of use, cost, category of the CAM used, type of herbal medicine and applied what liver disease. **RESULTS:** Questionnaire was applied to 100 patients, 13 first time and 87 subsequent. Of which 60% were women and 40% men. 75% were from the northeast region (Coahuila, Tamaulipas, Nuevo León), 19% of the center (San Luis Potosí, Durango, Mexico City, Puebla, Veracruz, Guanajuato, Morelos), 4% of the South (Tabasco, Campeche, Nayarit) and 2% from U.S. Regarding education: 38% were higher-level, 16% technical education, 15% postgraduate school, 13% elementary school, 11% college, 6% high school and 1% none. The 64% reported using some type of CAM with a frequency of 33% occasional, 17% daily, 13% weekly, 1% monthly and 36% spoke no longer use. The investment cost by 64% of patients referred using MAC was less than 500 pesos in 73%, from 500 to 1,000 pesos by 16%, from 1,000 to 5,000 pesos by 1.6%, higher at 5,000 pesos 4.7% and none 4.7%. The extent to which patients used at least one type of CAM was 22%, two types 17% and more than two types of CAM 61%. The CAM type used was herbal remedies (90%), followed by exercise or walking (34%), homeopathy (28%), vitamins (26%) and acupuncture (25%). The most widely used herbal remedy was the chamomile (60%), followed by cinnamon (41%), green tea (25%), honey (25%), garlic (20%), peppermint (20%). Herbal remedies for liver disease was referred to aloe vera 17%, followed by milk thistle (13%), boldus (5%), tooth of lion (5%) and mullein in 3%. The CAM was recommended in 78% of cases by a familiar or friend, 6% by a doctor of CAM, 5% by internet and 8% by allopathic doctor. In 3% of patients had unwanted effects from the use of CAM, such as abdominal pain and weight loss. **CONCLUSIONS:** 64% of patients treated at the Liver Unit in a period of 6 months using some type of CAM, herbal remedies is the most common type of CAM and the most widely used remedy was chamomile. The aloe vera was the most commonly used for treatment of liver diseases.

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HEPATIC ISCHEMIA/REPERFUSION INJURY IS DIMINISHED BY SPIRONOLACTONE

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INTRODUCTION: Temporal occlusion of the hepatoduodenal ligament (Pringle's maneuver) is often used during liver surgeries in order to reduce blood loss. This results in ischemia/reperfusion injury (I/R), a condition that also occurs during transplant procedures. Recent studies have shown that spironolactone reduces damage induced by I/R in brain, heart and kidney, but has not been reported in liver. **AIM:** To investigate the effects of spironolactone (Spr) on hepatic I/R injury induced in liver of rats. **MATERIALS AND METHODS:** Experiments were performed in three groups of 5 male Wistar rats for each group with an average weight of

200-250 g. These groups were: sham group, in which the intestines were handled but there is no ischemia, group I/R, in which this was induced by clamping in pringle maneuver for 20 min, followed by 60 min of reperfusion and Spr treatment group (2.6 mg/kg, orally), which was administered 20 h before induction of I/R. The rats were killed after the indicated period of reperfusion, and blood and tissue samples were taken for analysis. Was determined in serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), interleukin-1 (IL-1) and interleukin-6 (IL-6), tumor necrosis factor alpha (TNF- α), total serum antioxidant, measured of lipid peroxidation (malonaldehyde, MDA) and catalase. It also conducted a histopathological analysis. For statistical analysis, t test was used to determine differences between groups and was performed using SPSS 11.0 software. **RESULTS:** After I/R, there was evident tissue injury characterized by extensive acute inflammatory infiltrate, hemorrhage, disruption of hepatic trabeculae as well as presence of apoptotic bodies. Also, AST, ALT and LDH levels increased significantly in I/R group compared with sham group ($1, 407 \pm 787$ U/L vs. 149 ± 63 U/L; 673 ± 409 U/L vs. 54 ± 6 U/L; $24, 747 \pm 13,878$ U/L vs. $5,245 \pm 5,345$ U/L, $p < 0.05$), respectively. Serum concentrations of IL-1, IL-6 and TNF- α were increased in I/R group vs. sham group (1.27 ± 0.31 ng/mL vs. 1.07 ± 0.49 ng/mL; 0.68 ± 1.53 ng/mL vs. 0.14 ± 0.31 ng/mL; 1.08 ± 0.76 ng/mL vs. 0.89 ± 0.58 ng/mL, respectively) but not was significant. Sham group had MDA concentrations and catalase activity of 10.62 ± 0.71 μ M/mL; 8.95 ± 15.03 nmol/min/mL, respectively. In IR group, MDA levels and catalase activity were increased (13.22 ± 0.34 μ M/mL and 177.22 ± 84.46 nmol/min/mL, respectively). All these alterations histological and serum levels of AST, ALT described for the group I/R were prevented by treatment with Spr. At the histological level the Spr group showed preserved cellular architecture, isolated foci of acute inflammation and isolated apoptotic bodies. Serum levels of AST, ALT and LDH were significantly diminished in Spr group compared with I/R group (559 ± 176 U/L vs. 1407 ± 787 U/L; 260 ± 128 U/L vs. 673 ± 409 U/L and $14,195 \pm 12,793$ U/L vs. $24,747 \pm 13,878$ U/L, respectively). No significant changes in the concentrations of pro-inflammatory cytokines, total serum antioxidant, MDA levels, catalase activity. **CONCLUSIONS:** Pretreatment with Spr reduce the damage induced by ischemia-reperfusion in rat liver. Spironolactone is indicated for the treatment and prevention of heart failure as an adjunct in the treatment of hypertension, ischemia and treatment of metabolic syndrome. However, future research is needed to determine the clinical value of these results. This work was sponsored entirely by own resources of participating departments and PAICYT.

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SYSTEMIC AND PULMONARY HEMODYNAMICS IN NON CIRRHOTIC PORTAL HYPERTENSION. A STUDY IN A GROUP OF PATIENTS WITH EXTRAHEPATIC PORTAL VEIN OBSTRUCTION (EHPVO)

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INTRODUCTION: EHPVO is a vascular disorder of the liver and is defined as an obstruction of the extrahepatic portal vein. It can occur either with or without cirrhosis. Clinical manifestations are caused by pre hepatic portal hypertension.

Variceal bleeding it the most common clinical presentation followed by complications caused by ectopic varices (portal duodenopathy, portal biliopathy). Hemodynamically, the hepatic vein pressure gradient is within normal limits which indicate the presinusoidal nature of the block. Intrasplenic pressure is significantly elevated. This obstruction causes circulatory changes in splanchnic circulation. There is scanty literature information about systemic and pulmonary hemodynamic of EHPVO in noncirrhotic patients. **OBJECTIVE:** To describe systemic and pulmonary hemodynamic in non-cirrhotic portal hypertension caused by extrahepatic portal vein obstruction. **MATERIAL AND METHODS:** We undertook a prospective study to measure systemic and pulmonary hemodynamics in patients with EHPVO and without cirrhosis from June 2009 to December 2010. Demographic, clinical, biochemical and complementary studies (upper endoscopy and echocardiography with contrast-enhanced bubbles technique) are described. A transjugular approach was done to measure wedge and free hepatic vein pressures. Transjugular hepatic biopsy was done in all patients. Then the catheter was advanced into the right heart and the pulmonary artery to measure the rest of pressures. Mean arterial pressure, right atrial pressure, pulmonary free and wedge capillary pressure, cardiac output, systemic and pulmonary vascular resistance were obtained by Fick's principle. Statistics for normal distribution variables was done. **RESULTS:** Five patients were recruited. Most of them were males (80%). Mean age at diagnosis was 34 years. Mean time between thrombosis and hemodynamic measure was 6 years. The cause of thrombosis was identified in one patient. All of patients had portal portal vein cavernoma transformation. Thrombosis outside portal system occurred in one patient and this patient is the only one with ascites. The most common clinical presentation was variceal bleeding (40%) and the most common hematologic finding was thrombocytopenia (60%). All patients had normal liver tests. Esophageal varices were found in all patients. One of them had gastric varices (20%) and one patient had portal duodenopathy and portal biliopathy (20%). None of the liver biopsies showed fibrosis or inflammation. All patients had normal anatomic and heart function at echocardiography and a negative contrast-enhanced bubbles test. Mean systemic and pulmonary hemodynamic showed low systemic vascular resistance (SVR 784 ± 301 dynes \times sec \times cm), high cardiac output (CO: 11.2 ± 6.9 L \times min) and a high cardiac output index (COI: 6.1 ± 3.4 L \times min \times m²) which demonstrates hyperdynamic circulatory syndrome in the absence of cirrhosis. **CONCLUSIONS:** EHPVO in non-cirrhotic patients causes a persistent state of systemic vasodilatation accompanied by a compensatory increase of the cardiac output, similar to what is observed in patients with cirrhosis. No pulmonary disturbances (porto-pulmonary hypertension/hepato-pulmonary syndrome) were found in this group of patients.

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AUTOIMMUNE LIVER DISEASE AND ITS ASSOCIATION WITH RHEUMATIC DISEASES

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INTRODUCTION AND OBJECTIVE: The autoimmune liver disease (HAI) are handled independent of rheumatic diseases, but share characteristics; 30% of patients with autoimmune liver diseases have concurrent rheumatologic disease.

In contrast, 25% of patients with rheumatic diseases have liver dysfunction and these may be wrongly classified and treated as primary liver disease. The aim of this study is to determine the frequency of autoimmune liver diseases in association with rheumatic diseases in the outpatient HJM from 2005 to 2010. **MATERIAL AND METHODS:** A nonexperimental, longitudinal, retrospective, transversal, and clinical. We reviewed 25 cases of patients who met clinical, biochemical and histopathological HAI and rheumatic diseases from 2005 to 2010. We used frequency measures were expressed in terms of proportion. **RESULTS:** Of the 25 cases reviewed were 23 women (92%) and 2 men (8%) with mean age 45 (21-69). The clinical onset was arthropathy in 10 patients (40%), jaundice in 7 (28%), mucous membrane or integument manifestations in 5 (20%) and liver failure in 3 (12%). The association is shown in table 1. **CONCLUSION:** Autoimmune liver disease and rheumatic diseases share pathophysiological features and antibodies, so that a considerable proportion of patients may present as a rheumatic disease on the basis of autoimmune liver disease. Moreover, it is common to elevated liver function tests in rheumatic diseases without forgetting that the treatment drugs can be hepatotoxic and it is important to suspect this association, not overlook the performance testing

liver and antibodies routinely allow the differential diagnosis and treatment.

Table 1. Association of autoimmune liver disease with rheumatic diseases.

Autoimmune liver disease	Total cases	Associated rheumatic disease
Autoimmune hepatitis	14	Rheumatoid arthritis: 6; SEL: 2; AFS: 2; Sjögren syndrome: 3; Esclerodermia: 1.
Primary biliary cirrosis	3	Sx. Sjögren: 1; CREST: 1; Scleroderma: 1.
Primary sclerosing cholangitis	1	Rheumatoid arthritis: 1.
Elevated liver enzymes without	7	SEL: 4; rheumatoid arthritis: 3.
ALD confirmed		

ALD: Autoimmune liver disease. SEL: Sistemic erythematosus lupus. AFS: Antiphospholipid syndrome.