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A. TRANSPLANT/LIVER SURGERY

001

INCREASED NASH INDICATION FOR LIVER TRANSPLANTATION IN RECENT YEARS RETROSPECTIVE ANALYSIS

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Introduction. Fatty liver disease affects 17-33% of the general population in Western countries, while non-alcoholic steatohepatitis (NASH) occurs in 6-17% and is directly related to obesity. In patients with NASH, the risk of developing cirrhosis is estimated to be up to 25%. Moreover, according to recent statistics, worldwide Mexico ranks second in adult obesity and first in childhood. Thus, an increase in candidates for liver transplantation owing to NASH is to be expected. **Material and methods.** We reviewed all transplants performed by our group from June 1999 to January 2013. The population was divided into two periods: 1999-2007 and 2008-2013. Indications for transplantation were compared using chi-squared. Kaplan Meyer curves were used for differences in survival according to the indication. **Results.** We analyzed 62 liver transplants in 61 patients. There were 39 (63%) transplants during the first period and 23 (37%) in the second. Globally, indications for liver transplant were as follows: HCV 19 (30.6%), OH 19 (30.6%), NASH 6 (9.7%), autoimmune hepatitis 6 (9.7%), others 12 (19.4%). When comparing the two study groups, the following differences were found: HCV 14 (36%) vs. 5 (22%), $p = 0.271$; OH 10 (25%) vs. 9 (39%), $p = 0.393$; NASH 1 (3%) vs. 5 (22%), $p = 0.023$; other 14 (36%) vs. 4 (17%), $p = 0.154$. Survival rates at 1 and 5 years were 84 and 70% respectively, with a mean follow up of 59 months. There was no significant difference in survival according to the indication for transplant (log-rank-test 0.919). **Conclusions.** Cirrhosis caused by NASH has increased in recent years as an indication for liver transplantation. No differences in survival of these patients were found when compared with other indications.

The authors declare that there is no conflict of interest.

002

TRANS-JUGULAR PORTOSYSTEMIC SHUNT (TIPS) FOR PATIENTS IN WAITING LIST FOR LIVER TRANSPLANTATION: SINGLE TRANSPLANT

CENTER AT HOSPITAL SAN JOSÉ-TEC DE MONTERREY

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Introduction. Trans-jugular portosystemic shunt (TIPS) was introduced in 1988 as an alternative treatment of variceal bleeding due to portal hypertension. Since then, many studies supporting its usefulness, especially after failure of endoscopic and pharmacological interventions, and it has been proposed as a useful option in treating refractory ascites and hydrothorax. **Objective.** To describe our experience and analyze the outcome of patients in the waiting list (WL) for liver transplantation (LT) who underwent TIPS. Demographic variables, pre-LT indications, surgical technique, use of blood in OR, vascular complications, renal dysfunction and LT post-operative mortality were analyzed. **Material and methods.** We retrospectively reviewed prospectively collected data of patients undergoing LT in our program. **Results.** 67 patients were included in the WL, 61 were transplanted and 6 died before transplant due to complications. TIPS was placed in 4 patients (5%), two women (50%) with a mean age of 52 years (46-60 years), etiology of cirrhosis was: PBC 1 (25%), NASH 2 (50%) and alcohol intake 1 (25%). Indications for TIPS were variceal hemorrhage 1 (25%), hepatic hydrothorax 2 (50%), refractory ascites 1 (25%). One patient with TIPS on WL died of sepsis, while 3 patients were transplanted and are still alive at 15, 8 and 4 months after surgery. There were no differences in the surgical technique, vascular complications, intraoperative blood consumption, renal dysfunction or operative mortality when compared with the rest of the evaluated patients. **Conclusion.** TIPS in patients on WL for LT is a safe procedure, which in our experience does not increase technical difficulty in surgery nor does it increase complications or operative mortality.

The authors declare that there is no conflict of interest.

003

MULTIDISCIPLINARY MANAGEMENT OF LIVER METASTASES IN A PATIENT WITH COLORECTAL CANCER

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Introduction. Liver metastasis from colorectal cancer is one of the most common causes of death in this group of patients. Their median survival rate without treatment is 6 to 12 months. The incidence of liver metastases (mets) goes from 50-60%; 25% of them presented at the diagnosis of colorectal cancer. The complete resection of the metastases (R0) is the only treatment with possibility of cure in selected patients. Unfortunately only less than 25% can be resected. The techniques of ablation with radiofrequency and cryotherapy have proved utility to raise the possibility of resection for multiple lesions. They are usually used as a complement for surgical treatment. **Objective.** To report a case with multidisciplinary management of liver metastasis in a patient with colorectal cancer. **Case.** 51-year-old male patient with diagnosis of right colon adenocarcinoma and 11 liver metastases. The colonoscopy reported a sessile tumor 5 x 3 cm without luminal obstruction, the TAC demonstrated bilobar lesions that ranged from 2-7 cm. The Pet-Scan didn't show any other site of disease. The patient took one cycle of chemotherapy with Folfox, and a second one with Avastin. The patient had good response to treatment. He was evaluated for resection with an Hepatic Volumetry that reported 34% of residual volume. It was performed a right hemicolectomy with an ileo-transverse anastomosis + left hepatectomy + local resection of a lesion in the V segment + radiofrequency of lesions in segment VI and VIII. After surgery, the patient had an adjuvant cycle of chemotherapy. 10 months after the procedure the patient has no evidence of disease. **Disclosure.** The current criteria for resection of mets are achievement of free margins (R0), preservation of at least two contiguous segments with vascular and biliary flow, and at least 20% of residual healthy parenchyma. The combination of surgery + ablative therapies increases the possibility of resecting all metastatic lesions leaving enough viable tissue. Our case is an example of multidisciplinary management for multiple liver mets. The authors declare that there is no conflict of interest.

004

TREATMENT OF FULMINANT HEPATIC FAILURE (FHF) WITH MARS (MOLECULAR ADSORBENT RECIRCULATING SYSTEM). PEDIATRIC CASE REPORT

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Introduction and aim. Currently, liver transplantation is the preferred treatment for FHF; however, the shortage of cadaveric donors has forced the use of replacement treatments of liver function such as MARS, procedure used as a bridge to transplantation. The aim of this work is to present a case of a pediatric patient with FHF successfully treated with MARS. **Case report.** Male patient, 11 years old, previously healthy, who entered with condition 25 days of evolution characterized by malaise, dark urine, jaundice and acolia, adding significant abdominal pain during the last 24 h. Was ruled out infectious, autoimmune and metabolic etiology, there was no history of drug intake. On admission, neurological impairment merited ventilation assistance and management in intensive care for eight days. Treatment consisted of administration of fresh frozen plasma, vitamin K, ursodeoxycholic acid (UDCA) and antiemetic measures.

Therapy was performed with MARS on 3 occasions and entered the waiting list for liver transplantation. Evolved with normalization of his consciousness, improvement of liver function tests and clotting times (Table 1). Was discharged home with omeprazole, spironolactone, UDCA, sodium benzoate, lactulose and neomycin without requiring liver transplantation. At 100 days after discharge, he is without clinical jaundice, receiving only UDCA. **Conclusions.** Decreasing ammonium and bilirubin levels, probably was determined by applying the MARS system, so it may be useful in pediatric patients with FHF. Studies remain to be conducted in children and determine the precise point during the course of the FHF to initiate this hepatic replacement therapy and evaluating its therapeutic action in relation to mortality. The authors declare that there is no conflict of interest.

Table 1. Changes in biochemical parameters with MARS therapy.

Biochemical parameters	Pre MARS	1st session	2nd session	3rd session	MARS post (100 days)
Total bilirubin (mg/dL)	35.15	23.09	20.10	18.65	1.8
Ammonia (mg/dL)	134.7	23.1	50.4	65.3	30

005

EXPRESSION OF CYTOKINES, CHEMOKINES, TGF-beta 1 AND COLLAGEN I AND III IN LIVERS FROM CHILDREN WITH END STAGE OF LIVER DISEASE

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Introduction. Cytokines play a critical role in communication and cellular activation, the liver is a source of cytokines involved in the development of liver disease, their receptors are found in hepatocytes. These proteins are key molecules in most acute and chronic liver disease. **Objective.** To evaluate gene expression of TNF- α , IL-10, CXCL-8, CXCL-10, IGFBP-1, TGF β -1, Col-1 and Col-3 in hepatic tissue from children with end stage of liver disease. **Material and methods.** We included 7 patients with end stage of liver disease (ESLD) of different etiologies: biliary atresia (3) fulminant hepatitis (3) and tyrosinemia (1), who underwent liver transplantation at Mexico City's Children's Hospital (Hospital Infantil de México). Five patients received a liver allograft from living relatives and two from deceased donors, informed consent was obtained and a liver biopsy from each subject. In each of the samples was carried out RNA extraction and obtaining cDNA and determined the gene expression of TNF- α , IL-10, CXCL-8, CXCL-10, TGF β -1, Col-1 and Col-3 by real time PCR. Data analysis was performed a Student T-test. **Results.** The average age of patients with ESLD (3 girls and 4 boys) was 3 ± 2 years. A control group of 7 people was included with mean age of 31 ± 14 years (3 women and 4 men). The expression of the genes was TNF- α (ng/mL) in ESLD = 3 ± 2 and CT = 2 ± 0.8 (p = 0.778). IL-10 (ng/mL) at ESLD = 6 ± 5 and CT = 0.3 ± 0.2 (p = 0.025). CXCL-8 was 53 ± 21 and 0.4 ± 0.3 for ESLD and CT, respectively (p = 0.048). CXCL-10 (pg/mL) was ESLD = 3 ± 0.4 and CT = 0.8 ± 0.2 (p = 0.043), TGF β -1 (ng/mL)

was ESLD = 7 ± 1 y CT = 1 ± 0.50 ($p = 0.002$). Col-1 expression (pg/mL) was ESLD = 15 ± 8 and CT = 8 ± 1 pg/mL (NS) and Col-III (pg/mL) was ESLD = 35 ± 2 and CT = 2 ± 1 pg/mL (0.032). **Conclusion.** In liver tissue of liver transplant recipients, the gene expression of proinflammatory cytokines and chemokines was increased, with higher transcriptional activity of CXCL8. Also the expression of genes related to the fibrogenic process is 7 times in the terminal stage of liver disease, regardless of etiology and patient age. The authors declare that there is no conflict of interest.

006

CASE REPORT: BILIO-PLEURAL FISTULA AFTER HEPATIC TRANSPLANT

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Disclosure. Biliary complications are still one of the main causes for morbidity despite the surgical advances on technique and graft preservation. A biloma or bilio-peritoneum is the most common presentation for a biliary leak. This report refers to an extraordinary presentation of biliary complications that could be related to the patient's history of thoracic ascites. The multidisciplinary management, with the use of endoscopic techniques and interventionist radiology allows resolution for most of these complications without conditioning the lost of the graft or the patient. The authors declare that there is no conflict of interest.

Introduction. A biliopleural fistula is an atypical presentation of biliary complications after hepatic transplant with complete graft, with higher incidence between living donor transplantation. They have been described more frequently as a complication for non-transplant related invasive radiologic procedures non-related with liver transplant. The global incidence of biliary complications after hepatic transplant ranges from 10-36%, from which biliary leaks represent 8%. The percentage of biliary complications in our center is about 16%. Half of them are biliary fistulas related to use of T tube.

Objective. To report an atypical presentation of a biliary fistula. **Case report.** 44-year-old male patient with history of orthotopic hepatic transplant for cirrhosis secondary to NASH. Complicated with refractory ascites, hydrothorax and recurrent spontaneous bacterial peritonitis. The patient was treated with TIPS in the pre-transplant period. The procedure was realized with a cadaveric graft, ABO identical with 9 h of cold ischemia. The biliary reconstruction was made with a choledoco-choledocostomy with an absorbable monofilament, without a T tube placement. The patient presented good evolution and was discharged 10 days after surgery with immunosuppression based on tacrolimus, MFF and prednisone. The patient came back 21 days later with abdominal pain, hyperbilirubinemia and right pleural effusion. An US guided thoracentesis was made and drained 3,400 mL of biliary fluid. The patient had a biliary scintigraphy that localized the leak on the site of the anastomosis. An ERCP was made confirming the diagnosis and was resolved with a stent colocation. The patient was discharged 5 days later, asymptomatic with normal liver function tests. The authors declare that there is no conflict of interest.

007

SUCCESSFUL IMMUNOSUPPRESSION SIROLIMUS IN LONG TERM LIVER TRANSPLANTATION. A ONE CENTER EXPERIENCE

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Introduction. Sirolimus (SIR) offers potential advantages over immunosuppression (IS) based on calcineurin inhibitors, preserves renal function, has antiproliferative and antiviral properties. **Objectives.** Evaluate efficacy and safety of SIR as an immunosuppressor in patients (px) with orthotopic liver transplantation (OLT). **Material and methods.** A retrospective study with 38 px postOLT converted from tacrolimus to SIR in the last five years. **Results.** Etiologies: HCV (9), OH (8), HAI (6), NASH (3), HCV + HCC (3) and others (9). SIR Main indications: renal dysfunction, neuropsychiatric symptoms and rejection. Pre-conversion glomerular filtration rate (preC) 52 ± 26 vs. 74 ± 2 mL/min postconversion (postC) ($P < 0.012$). 2 px with microalbuminuria (μ alb) preC: one progress to albuminuria (albU) postC mild (500 mg/dL), the other remained at μ alb and developed diabetes mellitus (DM) postOLT. 7 px developed proteinuria postC: 3px μ alb (30-180 mg/dL) without DM, 1 μ alb 100 mg/dL, DM preOLT, 1 mild albU 398 mg/dL, DM preOLT; 1 μ alb 30 mg/dL, DM postOLT development; 1 albU severe 1,272 mg/dL, DM preOLT. Urine protein: 130 ± 295 mg/24 postC. Triglycerides preC 199 ± 77 vs. 153 ± 92 mg/dL postC ($P = 0.058$). Cholesterol preC 165 ± 46 vs. 209 ± 116 mg/dL postC ($P = 0.004$). Mean time switch 15 ± 18 months (0-62 months), 10 px converted to SIR in 0-30 days postOLT (5 start), 9 px of 1-6 months (m), 5 of 6-12 m, 5 of 12-24 m, 3 of 24-36 m and 6 of 36-62 m. 4/38 (10%) experienced rejection postC: 2 used SIR start and experienced rejection at 6 days and 2 m postC, 2 were converted to SIR 2 and 6m post OLT, both experienced rejection postC 2-4 m. 3 px received SIR for rejection. Nine px died (24%), for reasons not attributable to the SIR. There were no thrombosis of the hepatic artery. Tracking postC is 52 ± 35 m. 13/38 px (34%) were able to reduce the dose of SIR to 1 mg/day or 1 mg/c/3 day as the only IS. **Conclusions.** SIR therapy can be safe in postOLT px, improved renal function and resolved neuropsychiatric manifestations. 10% experienced rejection postC. 18% developed proteinuria, mostly mild. There was an increase in cholesterol and triglyceride decrease over time. SIR IS decreased to minimum to long term was achieved in 34% of cases.

This work has been funded entirely by own resources. The authors declare that there is no conflict of interest.

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AUTOLOGOUS HEMATOPOIETIC STEM CELLS TRANSPLANTATION FOR IMPROVING POSTTRANSPLANTED LIVER GRAF FUNCTION. A CASE REPORT

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Case report. A 27 years old male patient, who underwent Orthotopic Liver Transplantation in 2001 due to cirrhosis related to hypoplastic biliary tract, initially presented with transient cholangitis episodes and persistent cholestasis evidenced by ALKP, GGT levels three times above upper limit of normal. Prednisone, tacrolimus and mycophenolate were used for immunosuppression. On May 2007 a liver biopsy (LB) showed chronic liver disease, 3/6 fibrosis, 5/18 activity, ductal proliferation, intracellular and intracanalicular cholestasis, and no acute rejection. On August 2007 after receiving three sessions of hepatic dialysis (MARS), great clinical improvement was achieved. On September 2007 Fibromax: F4 (0.74), A2-A3 (0.01). Ursodeoxycolic acid, SaMe and antioxidants were prescribed. His condition worsened gradually thereafter, peaking on 2012 by abnormal GGT 516, ALKP 429, TB 6.5, AST 521, ALT 271, total bile acids (TBA) (table), foetor hepaticus and ammonia 37 (30). On July 12, he received 4 sessions of MARS, followed by a 300 ug sc/d/x 5 days GM-CSF dosing until reaching 38,000 leucocytes. On August 1st an autologous CD34+ hematopoietic stem cells transplantation (AHSTC) was done through portal vein (24.7 x 10⁶/50 mL) (transhepatic) by interventional radiology, a LB was also done, and showed cirrhosis, lacking biliary ducts, cholestasis, cholangitis, chronic rejection could not be excluded. CD34+ Immunohistochemistry was negative. Six months follow-up showed an improvement in liver function, inflammatory mediators showed an increase in ICAM and IL6 (Table 1). **Conclusion.** The first successful AHSTC case post liver transplant is reported. This option could delay the need of retransplantation or be used as a bridge to it.

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009

EVALUATION OF THE NUTRITIONAL STATUS OF PATIENTS SUBMITTED FOR LIVER-TRANSPLANTATION EVALUATION AT THE INCMNSZ INSTITUTE AND ITS IMPACT ON MORTALITY

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Introduction. Undernourishment in patients with advanced liver disease prevails from 50 to 90%. It is associated with a

higher morbidity and mortality risk. **Objective.** Describing the nutritional status of patients submitted for Orthotopic Liver Transplantation (OLT) evaluation and their outcomes (deaths, alive, OLT). **Material and methods.** A prospective cohort study (August, 2011-August, 2012) included 48 patients submitted for nutritional evaluation within the OLT protocol at the INCMNSZ Institute. The following variables were obtained and analyzed: age, gender, validated body mass index (BMIv), MELD, weight (kg), height (cm), arm circumference (AC), and tricipital skin fold (TSF) with a body composition analyzer. The phase angle (PA) was calculated, and the body cell mass (BCM) and muscle strength (MS) were measured with a hand dynamometer. Undernourishment was considered with a BMIv in cirrhotic patients < 22 kg/m² without ascites; < 23 kg/m² with mild-moderate ascites; and < 25 kg/m², ascites to tension. The muscle reserve was measured as PA < 5.4, BCM < 35%, non-dominant arm's MS in females < 14Kg/F, in males < 30 kg/F, and arm muscle circumference (AMC) and TSF < 5th percentile. Non-parametric Spearman and Pearson's frequencies and correlations were analyzed. The statistical analysis was conducted using SPSS v17.0, with statistical significance p < 0.05. **Results.** Out of the 48 patients, 29 (60%) were males with a median age of 50 years (20-68); when measuring BMIv 40% of the patients were undernourished. 83% had a low BCM, 79% with a low PA and 81% with low MS, finding a significant correlation of (≤ 0.025), (≤ 1.032) and (≤ 0.05) with the BMIv. The outcomes are alive, dead, and OLT: 32 patients (67%) alive, 20% undernourished and with low MS; 5 (10%) dead, undernourished in 100% of cases, and with lower MS (median 8.6Kg/F) than in undernourished alive patients; and 11 (23%) OLT, with appropriate BMI and low MS. All of them with nutritional care and follow-up. **Conclusions.** Undernourishment and low muscle reserve are frequent in patients with advanced cirrhosis. The relationship between these 2 parameters (undernourishment by BMIv and MS, as per hand dynamometer, have a direct impact on the mortality of these patients. Thus, the nutritional intervention is very important.

The authors declare that there is no conflict of interest.

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CHOLESTASIS IN BILE DUCT INJURY

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Introduction. During bile duct injury level of hepatocytes and cholangiocytes performed a series of metabolic changes that are part of the pathophysiology of this scenario. In the

Table 1.*

	2 months PreTACH	PreMARS	PostMARS	TACH	Day 30	Day 60	Day 120	Day 180
T. bilirubin (mg/dL)	5.91	7.4	5.8	7.9	7.1	3.2	2.9	2.1
Albumine (g/dL)	3.8	2.8	2.6	3.5	3.4	4.9	3.3	3.3
AST (UI/L)	166	82	74	60	56	73	91	54
ALT (UI/L)	189	61	51	48	46	52	62	35
ALKP (UI/L)	310	295	275	328	447	649	587	376
GGT (UI/L)	788	78	-	273	175	192	159	98
ICAM (pg/mL)	-	4,652	-	3,972	5,345	5,229	4,339	3,969
IL-6 (pg/mL)	-	1,698	-	1,621	1,370	1,457	1,398	723
TBA (μmol/L)	246	-	-	-	-	159	77	-

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bile duct injury can find several scenarios and independently of these will develop cholestasis. The prevalence in the bile duct injury has variability according to several studies this is between 0.1 to 0.6% in cholecystectomies. The formation of bile is a vital function, and its impairment by drugs or infectious, autoimmune, metabolic or genetic syndrome result known as cholestasis. **Objective.** A review of the literature based on the pathophysiology of cholestasis and bile duct injury. **Development.** Cholestasis is a disorder of the colepoiesis and bile secretion by either a mechanical or functional obstruction to bile flow extrahepatic bile ducts. Jaundice may occur with or without jaundice. Cholestasis is associated with increased serum concentrations of compounds that are normally excreted in the bile, such as bile acids, bilirubin and enzymes alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT) and others. The result gives retention cholestasis bile acids, bilirubin, and substances that are removed with the bile. A submicroscopic level changes in cell membrane and adhesion structures and communication of hepatocytes called tight junctions. Damage in hepatocyte membranes and bile canaliculi causes increased permeability and reduced osmotic pressure gradient. **Conclusions.** Cholestasis is a phenomenon that occurs in the bile duct injury and management within a number of measures reported in the literature, specific as cholestyramine, UDCA, phenobarbital, rifampin. It has been demonstrated as a follower reliable monitoring alkaline phosphatase because this increases in duct obstruction and inflammation in the ductal epithelium. Even in the absence of obstructive processes therefore proposed to the FA and GGT for monitoring patients with biliary Rebuilding.

The authors declare that there is no conflict of interest.

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TOXIC EFFECTS OF WEEKEND ETHANOL CONSUMPTION ON BIOCHEMICAL PARAMETERS OF TWO DIFFERENT DOSES

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Introduction. Between 70 and 80% of deaths due to hepatic cirrhosis is attributable to the consumption of alcohol. In World Health Organization (WHO) reports (2000), hepatic cirrhosis-related mortality at the worldwide level was 797,000 inhabitants and morbidity was 14,856,000 inhabitants. But, to our knowledge, there are no reports on the damage occasioned by weekend ethanol consumption to the liver, because the Mexican Institute of Statistics and Geography (INEGI) indicates that > 20% of the population has chronic consumption of ethanol on weekends. **Objective.** To study the effect of weekend ethanol consumption on diverse biochemical parameters. **Material and methods.** We utilized male Wistar rats (weight 250 g) fed *ad libitum*. They were divided as follows: a) Control group, b) Group with ethanol (1.5 g/kg, concentration at 5%), and c) group with ethanol (1.5 g/kg, concentration at 40%). The ethanol was administered intragastrically (i.g.) twice weekly during 2 months. The rats were sacrificed and their serum was obtained, from which we quantified concentrations of glucose, cholesterol, triglycerides, albumin and enzyme activity glutamic-oxalacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT), by means of

spectrophotometric techniques. **Results and Discussion.** The activity of GOT as well as that of GPT increased significantly in both groups with ethanol in comparison to the control, this increasing higher in the group at 5%. Cholesterol levels decreased only in the group at 5% (30%). Triglycerides as well as glucose levels increased significantly in the group at 5% in comparison to the control. Albumin levels were not altered in any group with ethanol. The greatest biochemical alterations were observed in the group at 5%. **Conclusion.** We conclude that weekend alcohol consumption affects diverse biochemical parameters and that consumption of ethanol at 5% causes even greater damage.

The authors declare that there is no conflict of interest.

012

HEPATOPROTECTIVE EFFECT OF SILDENAFIL AND METFORMIN IN ISCHEMIA-REPERFUSION INJURY IN RATS LONG EVANS

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Introduction. Ischemia-reperfusion (IR) involves the formation of reactive oxygen species coupled with an excessive inflammatory response. Recent studies have demonstrated that sildenafil and metformin also reduces the damage induced by IR in heart and kidney, however there are no reported effect on liver. **Objective.** To evaluate the sildenafil and metformin effect in damage induced by IR in rat liver. **Material and methods.** A total of 20 male Long Evans rats (300-350g) were divided into 4 groups (n = 5). The first group (sham), only laparotomy was performed. The group IR was obstructed portal triad for 20 min and after a period of 60 min of reperfusion, blood samples were collected. The sildenafil group received 50 mg/kg orally 1 h before IR, the last group received metformin 500 mg/kg orally 1 h before IR. We quantified serum ALT, AST, LDH, IL-1 β , IL-6 and TNF- α . **Results.** Significant difference in ALT was found in Sham *vs.* IR (P = 0.03) and R/R *vs.* sildenafil + IR (P = 0.02), AST in Sham *vs.* IR (P = 0.03) and R/R *vs.* Met + IR (P = 0.01), LDH *vs.* Sham IR (P = 0.02), IR *vs.* sildenafil + IR (P = 0.006) and R/R Met *vs.* + IR (P = 0.002). IL-1b was the only one showing significant difference in the Sham group *vs.* IR and Met + IR (P = 0.005) and IR *vs.* Sildenafil (p < 0.05). In the Sham group and Met + IR did not find any correlation in the group IR: ALT with LDH (r = 1.000 P = 0.01) and in the group with sildenafil: AST with LDH (r = -0.885 P = 0.046). **Conclusions.** There is a marked decrease in the values of liver enzymes in the two types of treatment *vs.* IR group. Both drugs achieved a hepatoprotective effect by reducing levels of liver enzymes compared to IR group.

The authors declare that there is no conflict of interest.

013

PREVALENCE OF METABOLIC SYNDROME IN LIVER TRANSPLANTATION PATIENTS IN THE INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN (INCMNSZ): PRELIMINARY RESULTS OF 3 AND A HALF YEARS OF FOLLOW-UP
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Introduction. Metabolic disorders (MS) are frequently found in patients with orthotopic liver transplantation (OLT). The prevalence reported is 43-58%; systemic arterial hypertension (SAH), 40-85%; diabetes mellitus (DM), 13-61%; dyslipidemia (DLP), 40-66%; and obesity 24-40%. **Objectives.** Describing the prevalence of MS in liver transplantation patients in the INCMNSZ institute. **Material and methods.** Patients who received a liver transplantation at the INCMNSZ Institute, analyzed: gender, age at the time of transplantation, body weight (in kilograms), size (in centimeters), body mass index (BMI), lipid profile, fasting glucose, and blood pressure, as well as the pharmacological treatment for diabetes mellitus (DM), arterial hypertension (AHT) or dyslipidemia (DLP), pre-transplantation, at one year and at 3.5 years after liver transplantation. For MS diagnosis, the NCEP-ATP guidelines were used. **Results.** From 2005 to 2010, 30 patients were transplanted (16 men and 14 women), a median age of 52.8 years. Nineteen (63%) were transplanted due to HCV; five (16%) due to primary biliary cirrhosis; three (13%) with autoimmune hepatitis; and three patients (13%) due to other causes. Out of the patients diagnosed with VHC, 5 (26%) had hepatocellular carcinoma, 22 (73%) met the criteria for metabolic syndrome. Pre-transplantation, BMI (kg/m^2) had a median of 24.2 kg/m^2 (18.5-24.9). It did not change significantly at one year, but it did at 3.5 years of follow-up with $p < 0.05$. Triglycerides from 130.4, increased at one year to 153.6; and at 3.5 years, 167.3 mg/dL . HDL lipoproteins pre-transplantation, one and at 3.5 years- were found below the normal level. Blood pressure increased from pre-transplantation to one year from 112/70 to 122/76 mmHg, and it was maintained at 3.5 years. Out of the 22 patients that met the criteria for MS, 21 (95%) required pharmacological treatment at 3.5 years. **Conclusions.** Those patients transplanted due to HCV were those more associated to MS. Changes were observed at 3.5 years post-transplantation.

The authors declare that there is no conflict of interest.

014

SURVIVAL RATE AND FACTORS RELATED TO RELAPSE OF PATIENTS WITH PRIMARY BILIARY CIRRHOSIS (PBC) IN ORTHOTOPIC LIVER TRANSPLANTATION (OLT)

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Introduction. The influence of factors and relapse of PBC in post-transplanted patients is not clear, immune suppression with tacrolimus and older age of the donor have been associated to recurrence. **Objectives.** Describing factors related to relapse of PBC in transplanted patients. **Materials and methods.** Retrospective study included 15 recipients of a liver transplant, with PBC diagnosis in the INCMNSZ Institute. The following variables were analyzed: gender, age at time of transplantation, pre-transplant MELD, relapse of PBC, rejection, time of OLT at rejection, transplantation time at

last visit, immune suppression, infectious complications, type of infection and chronic complications. **Results.** From 1989 to 2010, 15 patients with PBC received an OLT. Median age of recipients was 46 years (41-49), and 93% were females. Pre-OLT MELD average was 14 (6-38). Age of donors was > 55 years old. Five patients had a relapse regarding PBC (33%); stage 2, (2); and stage, 3 (3). Time elapsed between the transplant and relapse was 2.8 years (2 months-10 years). Nine patients (60%) showed rejection with severity graded with Banff as grade 1 (33%), 2 (13%), and 3 (13%). Four individuals (44%) had early rejections; and 5 (56%), late rejections. Eight (53%) patients had infectious complications: 6 bacterial cases (3 pneumonias, 2 urinary tract infections, 1 cholangitic abscess), 1 cytomegalovirus, and 1 *Candida* infection. Relapse regarding PBC was more frequently observed in patients with infectious complications, and out of them, bacterial ones ($p = 0.04$). Relapse of PBC relapse also had a correlation with rejection ($p = 0.02$). Non-induction was more associated to rejection, and thus to relapse in relation to PBC. Post-transplant survival of these 15 patients in regards to PBC and graft is 80% at 10 years. **Conclusions.** Relapse in relation to primary biliary cirrhosis in post-transplanted patients was found to be associated to infectious diseases. Non-induction was associated to acute cellular rejection, and thus to the relapse in relation to PBC.

The authors declare that there is no conflict of interest.

B. CIRRHOSIS AND COMPLICATIONS

001

COMPARISON BETWEEN RIFLE AND AKIN CRITERIA IN THE EVALUATION OF ACUTE KIDNEY INJURY IN HOSPITALIZED CIRRHOTIC PATIENTS

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Background. Acute kidney injury (AKI) occurs in 50% of hospitalized cirrhotic patients and is associated with mortality. RIFLE and AKIN criteria assess renal risk and prognosis in intensive care units. It is unknown whether AKIN is superior to RIFLE to classify AKI in cirrhotic patients. **Material and methods.** Study of 53 hospitalized cirrhotic patients from April 2012 to March 2013. AKI was defined daily according to RIFLE and AKIN criteria. The glomerular filtration rate (GFR) was determined by Cockcroft-Gault, MDRD, and CKD-EPI equations. Comparison of means was performed using Student t test and P values < 0.05 were considered statistically significant. **Results.** When AKI was stratified by RIFLE at admission, 37.7% patients were found in risk, 13.2% in damage, and 1.9% in failure; within 24 h 5.7% were in risk and 1.9% in damage. After 48 h, 3.8% were in risk and 1.9% in damage. When AKI was defined by AKIN at admission, 9.4% were AKIN1 and 3.8% AKIN2; within 24 h 1.9% were AKIN1; and within 72 h 1.9% were AKIN1. When comparing GFR at admission in subjects with AKIN 1 and AKIN 2 they were not significant differences with any formula, but with RIFLE classification the differences did reach statistical significance (Table 1). **Conclusions.** RIFLE classification detected AKI more frequently and significant differences in admission GFR were

Table 1.* Comparison of admission glomerular filtration rate in patients stratified by AKIN and RIFLE criteria.

GFR ecuacion	AKIN stage	Median	SD	P value	GFR ecuacion	RIFLE stage	Median	SD	P value
COCKCROFT	1	41.165000	2.1700000	0.366000	COCKCROFT	R	80.822308	20.9617688	0.0030000
	2	45.585000	4.9200000	0.4090000		D	47.184000	7.9754893	0.0000000
MDRD	1	27.330000	3.9100000	0.4890000	MDRD	R	63.792222	17.8236155	0.0100000
	2	29.850000	1.6200000	0.5250000		D	33.490000	10.2757514	0.0030000
CKD-EPI	1	51.44	37.790	0.716	CKD-EPI	R	71.86	17.277	0.003
	2	40.55	0.910	0.555		D	47.53	12.720	0.002

* 001. COMPARISON BETWEEN RIFLE AND AKIN CRITERIA IN THE EVALUATION OF ACUTE KIDNEY INJURY IN HOSPITALIZED CIRRHOTIC PATIENTS.

found in subjects in risk or in kidney damage. In conclusion, RIFLE classification is superior to AKIN as a AKI prediction tool in hospitalized cirrhotic patients. Early identification of AKI will allow prompt targeted interventions and reduce mortality in this population.

The authors declare that there is no conflict of interest.

002

EFFICACY OF BIOELECTRICAL IMPEDANCE AND DYNAMOMETRY IN THE NUTRITIONAL ASSESSMENT OF AMBULATORY PATIENTS WITH CIRRHOSIS

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Background. Protein-calorie malnutrition is a common finding in cirrhotic patients, described in up to 80%, regardless of the stage disease. Malnutrition is associated with altered immunity, which increases the risk of complications and mortality. Because of this, it is considered a prognostic factor in chronic liver disease. **Objective.** To compare hand-grip strength against bioelectrical impedance phase angle to evaluate the frequency of protein-calorie malnutrition in ambulatory cirrhotic patients. **Material and methods.** Prospective study of 23 consecutive cirrhotic patients seen in an ambulatory clinic. Nutritional state assessment was performed through hand-grip strength and bioelectrical impedance phase angle. Statistical analysis was made with SPSS for Windows, version 17.0. Continuous variables were expressed as mean and standard deviation; categorical values as percentages. We used Wilcoxon's rank test and Student t test to compare means. P values < 0.05 were considered significant. **Results.** 52.2% of the study group were male. 34.8% were Child A; 39.1% Child B; and 26.1% Child C. Malnutrition was detected by dynamometry in 43% of the population, and in 39% by impedance. Those whose malnutrition was determined by dynamometry, 40% were classified as Child C, 30% Child B and 30% Child A. As expected, we found significant differences between gender in the dominant hand-grip strength (13.18 ± 14.71 in males and 47.82 ± 17.16 N in females $p > 0.001$); in their weight (67.76 ± 13.91 vs. 82.47 ± 17.47 kg, respectively $p > 0.001$), body fat percentage (34.77 ± 8.89 vs. 23.23 ± 5.67 $p > 0.001$), total body water (30.38 ± 5.28 vs. 46.05 ± 8.19 $p > 0.001$) and impedance measurements (603.91 ± 100.89 vs. 495.58 ± 75.79 Ω). **Conclusions.** Protein-calorie malnutrition was detected in 43% of the study subjects by dynamometry, and in 39% by bioelectrical impedance phase angle, which indi-

cates that both methods are effective for the evaluation of the nutritional state in cirrhotic patients. Up to 30% of Child A presented with malnutrition, which has an impact in their overall prognosis. It is necessary to consider nutritional support alternatives for this specific population.

The authors declare that there is no conflict of interest.

003

TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT (TIPS) DYSFUNCTION ASSESSED BY DOPPLER ULTRASOUND. A COHORT STUDY

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Background and aim. TIPS is a rescue intervention for refractory ascites or variceal bleeding and is a shunt between the hepatic vein and portal vein, it is considered a bridge for transplantation. Covered stents have lower dysfunction rates than bare ones. Surveillance after TIPS placement includes Doppler ultrasound to measure the flow within the prosthesis, speeds < 50 cm/sec or > 200 cm/sec are associated with dysfunction (stenosis or neointimal proliferation), low speeds are more specific for dysfunction of covered TIPS and high ones of uncovered TIPS. The aim of this study is to evaluate the usefulness of Doppler ultrasound to detect TIPS dysfunction. **Material and methods.** Prospective cohort of 15 patients (2006-2010). Doppler was performed at 24 h, 1 and 3 months, when results were suggestive of dysfunction (flow > 200 cm/sec, speed < 60 cm/sec, stenosis > 50%, recurrence of bleeding or ascites). To compare the groups Fisher's exact test and Mann Whitney test were performed. **Results.** 53% were men, median age was 48 (18-63). The etiology of portal hypertension was Budd-Chiari (4/15), alcohol (5/15), PBC (3/15), HCV (2/15) and AIH (1/15). TIPS indications were refractory ascites (67%), refractory bleeding (27%) and hydrothorax (7%). Flow in the inferior third at 24 h was 47 (43-51) and 98 (72-217) in patients who developed and didn't develop stenosis ($p = 0.02$). Flow in the upper third after 30 days was 136 (81-230) and 56 (53-123) in patients who had and didn't have stenosis ($p = 0.063$), portal flow was 43 (31-100) vs. 23(19-35) with $p = 0.04$. Regarding mortality, the presence of stenosis after the first month had an OR of 1.1 (CI0.7-7.1) when compared with those without a stenosis. After TIPS placement 47% developed encephalopathy, with 2 patients being difficult to treat. **Conclusions.** Altered flow in the lower

third of the TIPS at 24 h, and in the upper third and the portal vein after one month predict stenosis of the stent, and these suggests that these patients should be considered early for transplantation.

The authors declare that there is no conflict of interest.

004

QUALITY OF LIFE EVALUATION IN CIRRHOTIC PATIENTS IN HOSPITAL GENERAL DE MÉXICO

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Background and aim. Hepatic cirrhosis is the terminal stage of hepatic fibrosis that appears as a consequence in the chronic course of several liver diseases. It is an important health problem in the world, conditioning high rates of morbidity and mortality. In Mexico it is reported as the fifth cause of mortality, being the main etiologies alcoholic liver disease and hepatitis C virus infection. The chronic course is associated with an important morbidity with a negative impact in quality of life. In this work we look for evaluating the impact of certain clinical and demographic variables in the evaluation of quality of life using the SF-36 questionnaire in a sample of the patients treated in the Liver Clinic in Hospital General de México (HGM). **Material and methods.** Transversal, analytic and projective design. 29 patients were evaluated in the Liver Clinic of HGM using the SF 36 questionnaires. Descriptive statistics were used for demographic variables. Differences between groups were evaluated using the Kruskal Wallis Test for quantitative variables and χ^2 for qualitative variables. Spearman rho was used for establishing correlation between questionnaire items and variables. **Results.** 29 patients were evaluated, 15 men and 14 women (51.7 and 48.3%), 10 (34.5%) patients with liver disease classified as Child A, 10 (34.5%) Child B and 9 (31%) as Child C. The most frequent cirrhosis cause was alcoholic liver disease (51.7%), followed by chronic C hepatitis (13.8%). The lowest score in the questionnaire was found in the Child Pugh C group, without significant differences. Nor significant differences were found comparing groups by etiology. An inverse correlation was found in the physical component of the SF36 with the monthly spent attributed to the disease, MELD and Child Pugh classification. **Conclusions.** This analysis suggests that several clinical factors contribute in the patient's quality of life. The increment in the sample and the evaluation of other clinical factors could traduce important differences in the quality of life impact, allowing to establish opportune alternatives in therapy.

The authors declare that there is no conflict of interest.

005

BILIRUBIN AS A PREDICTOR OF SHORT TERM PROGNOSIS IN END STAGE-PATIENTS WITH CHRONIC LIVER DISEASE

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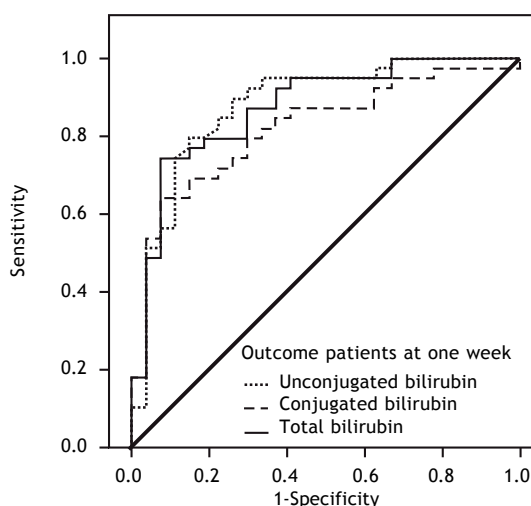


Figure 1. 005. ROC curve from bilirubin in predicting the one-week outcome of acute on chronic liver failure patients.

Background. Acute on chronic liver failure (ACLF) is characterized by a sudden deterioration of liver function which lead to end-organ dysfunction. Complex prognostic scores have been described to assess the prognosis of this lethal disease. Nevertheless, in order to find an accurate marker to predict outcome at end-stage cirrhosis, we proposed that bilirubin, a simple liver function marker which is widely used by prognostic scores in hepatology, might be a suitable marker to evaluate the outcome in ACLF patients. This could help to prioritize those patients in which liver transplantation is the only therapeutic choice. **Aim.** To investigate the role of bilirubin in predicting short term prognosis in ACLF patients.

Material and methods. We carried out a retrospective cohort study of patients with diagnosis of ACLF with at least 1 week follow-up during 7 years (2005-2012) in Medica Sur Hospital. Demographic, clinical and biochemical variables (creatinine, international normalized ratio, sodium, conjugated and unconjugated bilirubin and albumin) were analyzed to draw the receiver-operating characteristic-curves (ROC) at the first day hospital admission and the outcome patient at one week. **Results.** In a cohort of 66 patients, 32/34 (women/men), with an age average of 64 (range 25-87 years). Chronic liver failure was secondary to: hepatitis C virus infection (n = 20), cryptogenic cirrhosis (n = 27), alcoholic liver disease (n = 16) and hepatocellular carcinoma (n = 3). The majority of patients (59%) died within 1 week follow up. At the first day hospital admission, the AUCs data from conjugated bilirubin (0.757; 95%CI 0.636-0.877; P = 0.000), unconjugated bilirubin (0.731; 95%CI 0.606-0.857; P = 0.001) and total bilirubin (0.751; 95%CI 0.629-0.873; P = 0.001) were significantly higher. Accordingly to the outcome patient AUCs values, conjugated bilirubin (0.821; 95%CI 0.719-0.924; P = 0.000), unconjugated bilirubin (0.883; 95%CI 0.798-0.969; P = 0.000), total bilirubin (0.875; 95%CI 0.787-0.962; P = 0.000) were significantly higher (Figure 1) than the first day hospital admission values. Unconjugated bilirubin seems to be the most predictive outcome value in ACLF patients. **Conclusions.** Bilirubin could be a suitable marker in the prediction of short term prognosis in ACLF patients. High levels of unconjugated bilirubin may predict accurately the outcome of ACLF patients.

No potential conflict of interest relevant to this article was reported.

006

COMPARISON PROGNOSTIC SCALES IN DESCOMPENSATED CIRRHOSIS

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Introduction and objective. There are various prognostic scales in patients with liver failure, which is located between MELD, MELD-Na, MELD-integrated, each with different parameters to help improve the prognostic evaluation. MELD is important to its ability to accurately measure the severity and effectively assess mortality risk, prioritize organ allocation. MELD sodium proposal to improve the assessment of prognosis, since sodium levels associated with the severity of liver failure. To try to improve the accuracy of the scale parameter are added as in the case of integrated MELD. **Objective.** To determine which is the best prognostic scales to assess mortality in decompensated liver failure. **Material and methods.** 82 patients admitted to the Gastroenterology Service at Hospital Juárez de México with decompensated liver failure, period 2009-2012. We calculated MELD, MELD-Na and MELD-integrated admission. **Results.** 82 patients, 32 women and 50 men, mean age 55.5 years. By Spearman correlation analysis shows that there is a correlation between the three prognostic scales and mortality in the patient group. With a higher correlation between mortality and the MELD-Na-scale (392 $p < 0.000$), and integrated MELD (0.466 $p < 0.000$). **Conclusions.** These scales in liver failure are an important tool in determining prognosis; we can see that the scale-integrated MELD which uses sodium and age as variables, it is best to determine mortality in our population.

The authors declare that there is no conflict of interest.

007

MELD SCORE (INTEGRATED MELD MODEL) AS A PREDICTOR OF DECOMPENSATION EVENTS AND MORTALITY IN PATIENTS WITH CIRRHOSIS

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Introduction. The Model for End-Stage Liver Disease (MELD), was developed as a prognostic model to predict mortality in cirrhotic patients awaiting liver transplantation, replacing the Child-Pugh model. Additional variables have been added to the known models, improving forecast accuracy. The iMELD score (integrated MELD model) validated in Europe in 2007, being more certain prognostic showed that MELD and MELD-Na. In our population, there are no studies that validate this score. The objective was to determine the usefulness as prognostic score compared to those commonly used for one-year mortality and its relation to the number of events of decompensation in cirrhotic patients. **Material and methods.** Retrospective study was conducted based on an analysis of 97 cases of patients with decompensated cirrhosis of any etiology, who attended the Gastroenterology Department of

Hospital Juárez de México, from January 2008 to March 2012. We performed analysis of objective variables. Clinical variables included age, sex, cause of liver disease. Ascites and encephalopathy were not included. The biochemical variables included bilirubin, INR, sodium and creatinine. MELD, MELD-Na and iMELD score were calculated for each patient in the first episode of decompensation and mortality was assessed annually. Statistical analysis was performed using bivariate Spearman correlation coefficient. **Results.** Of a total of 97 patients, 57.7% were men; and after 12 months of follow-up 15 patients died (15.4%). The bivariate analysis using the Spearman correlation coefficient showed a positive correlation between the scales MELD (0.284 $p < 0.005$), MELD-Na (0.387 $P < 0.000$), iMELD (0.447 $p < 0.000$) with mortality. The scale iMELD not correlate with the number of events decompensation (0.177 $p < 0.083$). **Conclusions.** In our study, the iMELD score performed better than original MELD-Na in predicting mortality to 12-month mortality, but not correlated with the number of events of decompensation, however if the number of events correlated with mortality, this can be explained because the main cause death was variceal gastrointestinal bleeding. Prospective studies are needed with larger numbers of patients to validate this scale and its utility in our population.

The authors declare that there is no conflict of interest.

008

PREVALENCE OF ACUTE KIDNEY INJURY IN PATIENTS WITH VARICEAL BLEEDING IN THE GASTROENTEROLOGY SERVICE OF LA RAZA CENTRO MÉDICO NACIONAL

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Background and aim. Variceal bleeding is a severe complication of cirrhosis and portal hypertension, causing up to 70% of episodes of gastrointestinal bleeding, acute kidney injury occurs in up to 11% of these patients, is related to the severity of bleeding, degree of liver failure and this injury is progressive in 60% of cases and is currently considered one of the most important prognostic factors for recurrent bleeding and mortality. **Aim.** To determine the prevalence of acute kidney injury using AKIN criteria in patients admitted to our department with the diagnosis of variceal bleeding from January 2012 to January 2013. **Material and methods.** We reviewed medical records of patients admitted with a diagnosis of variceal bleeding, obtaining demographic, clinical and laboratory data at admission and within 6 months, to determine the presence of acute kidney injury using the AKIN criteria, we excluded patients with a previous diagnosis of chronic kidney disease, results were expressed in averages and percentages. **Results.** We included a total of 16 patients, 38% male and 63% female, mean age 57 years, the most common causes of cirrhosis were hepatitis C (25%), alcohol (25%) and cryptogenic (25%), 69% of them had a prior episode of variceal bleeding, 75% were on beta-blocker prophylaxis with MELD admission average of 14 and 75% of patients were in Child B, 19% A and 1% C. 31% had shock at admission and 63% required blood transfusion, was administered in 81% terlipressin or octreotide and 94% of them indicated antibiotic prophylaxis. Two patients (13%) had AKI being this AKIN II and III respectively,

reversible and both in Child Pugh B. No patient had early re-bleeding, or death during hospitalization. **Conclusions.** The prevalence of acute kidney injury in this study was 13% which is similar to that reported in previous studies.

The authors declare that there is no conflict of interest.

009

HEPATOCELLULAR CARCINOMA OF CLEAR CELL: CASE REPORT

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Introduction. The hepatocellular carcinoma is most common tumor lesion. It can be classified according to their histological lineage, which includes various cytological types, as: clear cell carcinoma is one of the rarer, and where the primary hepatocellular carcinoma of clear cell, represents a frequency of 2.2 to 6.7% of the reported in the world literature. **Case report.** Male 56 years of age, born and resident in area of Arsenicosis of mostly through drinking water. **Background.** With genetic cardiovascular disease type systemic arterial hypertension and cerebral vascular disease burden. It denies a cancer history in the family. Positive alcohol at a rate of 4.5 litres of beer (235 mL 14 beers). Every 21 days. Starts it so insidious for more than three months, with clinical picture characterized by pain type burning intensity 8-9/10 located at right, without irradiation, continuous, exacerbated with respiratory movements which ceded administration of anti-spasmodic as anticholinergic, later continued with accentuation of symptoms, as well as hyperoxia, until you reach anorexia, with pain postprandio, with irradiation at lumbar spine. As well as gag State, without vomiting, symptoms continues now with weight loss, concerns during this time weight loss of more than 12 kg. Concerned also over 38.5 °C febrile episodes, as well as profuse diaphoresis. Physical examination. Liver enlargement more than 5 cm below rim rib, with mass at epigastric painful, soft consistency on palpation with irradiation to lumbar spine. Severe. Laboratory. Hypoalbuminemia, leukocytosis with neutrophilia, important lengthening of the time of prothrombin, and rise to more than three times the normal alkaline phosphatase, LDH discreetly high. Computed tomography. Are they carried out two studies, the first concludes it's focal steatosis, and in the study carried out in our unit, it is heterogeneously tumor lesion in their densities, which can correspond to Hemangioma, or their malignant version, respects left lobe. Magnetic resonance. Not unlike the injury among the various types of liver injury. Evolution. It evaluates for using hepatectomy resective surgery, not find clinical and paraclinical criteria of inoperability, so it leads to surgery where is observed, that all the hepatic gland is taken, is decided to take biopsies with trucutt. Featuring a large bleed-

ing, which can inhibit. Pathological features. Hepatoacarcinoma clear cell. **Conclusion.** Being the primary hepatocellular carcinoma of clear cell injury, very rare, the possibility of arriving at diagnosis in prehistológica form, is extremely difficult, is presented to our understanding the first report of this injury in Mexico.

The authors declare that there is no conflict of interest.

010

CORRELATION BETWEEN FIBROTEST AND APRI, FORNS, FIBROINDEX AND FBI4 TO ASSESS LIVER FIBROSIS

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Background. Fibrosis is the outcome of chronic liver damage, and may result in development cirrhosis or revert this condition, so the evaluation is needed for treatment and monitoring of liver disease. Due liver biopsy disadvantages its necessary to have a non-invasive indicator of fibrosis. Some models are known like biochemical markers as APRI, FORNS, FibroIndex and FBI4 among others. The FibroTest is another model that uses biochemical parameters of hepatic synthesis so its sensitivity and specificity is higher. **Objective.** To correlate the results of FibroTest with APRI, FORNS, FibroIndex and FBI4 indices to predict the presence of fibrosis in Mexican patients with chronic liver disease. **Material and methods.** A cross-sectional study, we reviewed records with any diagnosis of chronic liver disease, which had Fibrotest, clinical and biochemical data for the models to predict fibrosis. Approved formulas were used to obtain results of APRI, FORNS, FibroIndex and FBI4. Spearman correlation was used 95% and ROC curves for sensitivity and specificity. **Results.** 76 patients were included, with the conditions listed in table 1. The Spearman correlation coefficient of 0.57 for APRI, FORNS 0.60, 0.77 FibroIndex FIB-4 compared to FibroTest 0.77 ($p < 0.0001$). Comparing advanced fibrosis and Fibrotest sensitivity and specificity of APRI index was 84 and 78%, FORNS 76 and 64%, FibroIndex 84% and 81%, FBI4 68 and 67%. The area under the curve with 95% CI was: APRI 0.871 (0.759-0.955), FORNS 0.754 (0.627-0.881), FibroIndex 0.871 (0.778-0.963) and FBI4 0.851 (0.755-0.947). **Conclusions.** With Fibrotest as reference, the model that best predicts fibrosis is FibroIndex, followed by APRI, FIB4 and finally FORNS. The authors declare that there is no conflict of interest.

011

NON VARICEAL GASTROINTESTINAL BLEEDING IN PATIENTS WITH LIVER CIRRHOSIS

Table 1.*

Gender	Age (years)	BMI (kg/m ²)	VHC	NASH	OH	Fatty liver	Criptogenic	CBP	VHB	HAI
50% male	59.6	27.4	27	16	10	9	5	5	3	1
50% women	(±13.6 SD)	(± 4.8 SD)								

* 009. HEPATOCELLULAR CARCINOMA OF CLEAR CELL: CASE REPORT.

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Introduction. Patients with liver cirrhosis (LC) may have upper gastrointestinal bleeding (UGB), associated or not to portal hypertension (PHT). It has been described that 25% of UGB in patients with LC belong to non-variceal etiology. **Objective.** To define the causes of UGB in patients with LC in a reference hospital. **Material and methods.** Observational retrospective study. Data collected from endoscopic studies performed in the Department of Endoscopies of Hospital de Especialidades, Centro Médico Nacional de Occidente, Instituto Mexicano del Seguro Social from March 2012 to February 2013 were used. There were included patients with clinical and biochemical diagnosis of LC, who presented UGB, showed up by hematemesis, melena or coffee grounds vomiting, who underwent endoscopy within the first 24 h after hospital admission. **Results.** 2,065 endoscopies were performed. Of which, 515 were performed in patients with LC. Of these, the indication for endoscopy in 48.2% (248) was clinical data of UGB, with an average age of 58.7 years, 51.6% (128) were male and 48.4% (120) female. 77% (191) of bleeding were attributed to causes associated with PHT: esophageal varices in 119 cases (62%), hypertensive gastropathy 48 cases (25%), gastric varices 22 cases (12%) and antral vascular ectasia in 2 cases (1%). 23% (57) not associated with PHT were reported: gastric ulcer 25 cases (44%), duodenal ulcer 8 patients (14%), erosive gastritis 7 cases (12%), esophagitis 4 cases (7%), Mallory Weiss, esophageal post banding ulcer and erosive duodenitis 3 cases each (5%), gastric angiodysplasia 2 cases (4%), gastric tumor and bleeding post sphincterotomy 1 case respectively (2%). **Conclusion.** About 20% of the causes of UGB in LC are due to diseases not associated with PHT, so early endoscopy must be performed to establish the differential diagnosis and direct the correct therapeutic.

The authors declare that there is no conflict of interest.

012

CARVEDILOL vs. PROPRANOLOL FOR PORTAL HYPERTENSION IN CIRRHOTIC PATIENTS, SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background. Carvedilol is a noncardioselective β -blocker with α -1 antagonism, it has been studied for the management of cirrhotic portal hypertension and appears to be more effective and well tolerated than propranolol. **Aim.** To analyze by systematic review and meta-analysis the benefit and harms of carvedilol vs. propranolol for portal hypertension treatment in cirrhotic patients. **Material and methods.** Randomised controlled trials comparing carvedilol vs. propranolol for portal hypertension in cirrhotic patients and esophageal varices with or without bleed history were included. The outcomes are expressed as odds ratio (OR), difference of means (DM) and confidence interval. **Results.** The search identified 14 citations, and 4 randomized controlled comparisons met the eligible criteria. The trials were conducted in Spain, India and Denmark, included a total of 161 patients, 82 underwent to carvedilol (6.5-50 mg/d) and 79 to propranolol (10-320 mg/d). Carvedilol was superior to get HVPG decrease $\geq 20\%$ from baseline value or to ≤ 12 mmHg (OR 2.92; 95% CI 1.26-6.74) (Figure 1). The magnitude of reduction of HVPG was greater with carvedilol (DM-2.22; 95% CI -2.82 to -1.60 mmHg). The rate of orthostatic or symptomatic hypotension was no different (OR 1.6; 95% CI 0.64 - 4.02). Renal function, including glomerular filtration rate, serum creatinine and plasma renin activity were not different between the treatments. Adverse events leading to withdrawal occurred with the same frequency (OR 0.52; 95% CI 0.18-1.54). Finally there was no difference about variceal bleeding or mortality.

Conclusions. This systematic review and meta-analysis showed that carvedilol is more effective than propranolol for hemodynamic response of portal hypertension in cirrhotic patients and there are no important differences about adverse effects.

The authors declare that there is no conflict of interest.

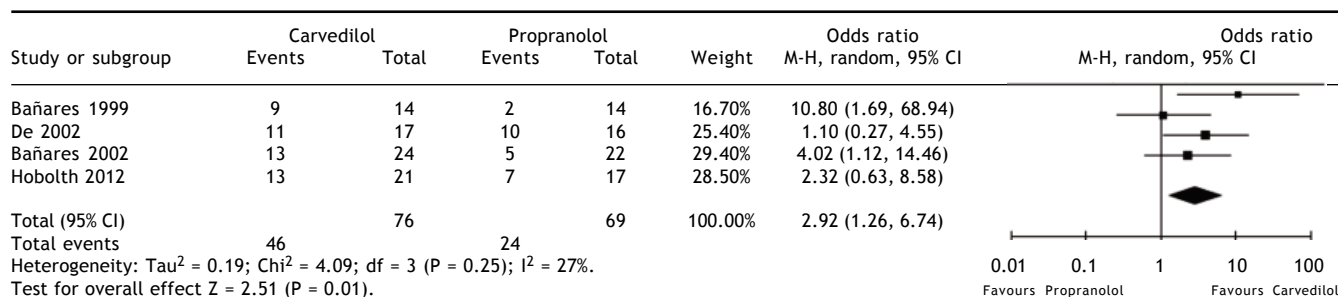
013

NON INVASIVE PARAMETERS AS PREDICTORS OF HIGH RISK ESOPHAGEAL VARICES BLEEDING IN CIRRHOTIC PATIENTS

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Figure 1.* HVPG decreases $\geq 20\%$ from baseline value or to ≤ 12 mmHg.



* 012. CARVEDILOL vs. PROPRANOLOL FOR PORTAL HYPERTENSION IN CIRRHOTIC PATIENTS, SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS.

Background/Aim. The prevalence of esophageal varices in cirrhotic patients is approximately 60-80% and the risk of bleeding 25-35%, therefore, all patients with cirrhosis are recommended to undergo an evaluation to predict the presence of varices through noninvasive parameters to avoid invasive procedures. **Material and methods.** We recruited 99 patients with cirrhosis from February 2011 to February 2013. Parameters assessed include Child-Pugh class, platelet count, spleen size, portal diameter, portal vein flow, portal congestion index, and esophageal varices size in relation to history of bleeding. The relationship between this parameters and variceal bleeding was evaluated using univariate and multivariate approaches. **Results.** 99 cirrhotic patients (56 women and 43 men) were enrolled. Mean age was 57.8 (± 12.2). 46 patients (46.5%) had history of variceal bleeding. Of patients who had previously bleeding, 80% had thrombocytopenia, 82% presented large varices, 59% splenomegaly, 53% portal dilatation, 49% congestive index increased. Comparative analysis between characteristics of patients with and without previous bleeding reported that large varices (38.8 *vs.* 16.2%, $P < 0.0001$), portal diameter (12.9 ± 2.5 *vs.* 11.3 ± 3.3 , $P 0.01$), spleen size (13.6 ± 2.6 *vs.* 12.4 ± 2.9 , $P 0.04$), congestion index (0.135 ± 0.51 *vs.* 0.109 ± 0.60 , $P 0.02$) were significantly higher in patients with previous variceal bleeding, while Child Pugh class, platelet count and portal vein flow were no significant. Also multivariate analysis to determine which variables were associated with variceal bleeding confirmed large varices [OR 11.1 (3.9-31.8, CI 95%), $P < 0.0001$] an portal diameter [OR 5.0 (1.1-21.7 CI 95%) $P 0.03$] as independent predictors of esophageal varices bleeding. **Conclusion.** Nowadays, the gold standard of measurement of portal venous pressure is the hepatic venous pressure gradient, but this is an invasive procedure not always available. We confirmed that variceal size is one of the best clinical predictors for variceal bleeding. About Doppler ultrasound only portal diameter seems to be associated with variceal bleeding, parameters as portal vein flow, portal congestion index, thrombocytopenia, splenomegaly are not good predictors for variceal bleeding. In our patients, Child Pugh class neither was significant. The authors declare that there is no conflict of interest.

014

PERITONEAL TUBERCULOSIS IN A SECONDARY BILIARY CIRRHOSIS PATIENT: A CASE REPORT

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Introduction. The reported incidence of tuberculous peritonitis (TBP) among all forms of TB varies from 0.1-0.7% worldwide. The risk of TBP is increased in patients with underlying liver cirrhosis, and the percentage of underlying cirrhosis among patients with TBP could be as high as 50%. The mortality rate may exceed 50% without prompt treatment. **Case report.** A patient of 50 years old, underwent laparoscopic cholecystectomy in 2009, complicated with biliary lesion, in September 2011 a Roux en Y hepatoyeyunoanastomosis was performed, during surgery the liver was observed with macroscopic characteristics compatible with cirrhosis and was performed a liver biopsy reported as incomplete septal fibrosis. We evaluated patient because of ascites, associated to abdomi-

nal pain, occasional fever and altered liver biochemical tests, the initial ascites analysis showed glucose 0 mg/dL, LDH 6,763 U/L, leucocytes 22,500 mm^3 , the liver US compatible with cirrhosis and septated ascites, glucose: 159 mg/dL, creatinine: 2.07 mg/dL, total cholesterol 32 mg/dL, albumin: 2.2 g/dL, AST: 83, ALT: 61, ALP: 192, total bilirubin: 38.19, direct bilirubin: 26.26 mg/dL, Na: 126 mmol/L, K: 4.8 mmol/L, hemoglobin: 9.9 g/dL, leucocytes: 7,200 mm^3 , platelets: 91,000 mm^3 . With the high suspect of TBP was solicited ADA, reported 36U/L. The patient was evaluated by the infectious diseases service and a scheme of isoniazid 250 mg QD, rifampin 600 mg QD, ethambutol 800 mg QD and pyrazinamide 1 g QD was started. However, the natural history of cirrhosis was observed in the patient and intermittent hepatic encephalopathy is the reason of previous hospitalization. **Discussion.** In this case we used ADA for diagnosis due the sensibility and specificity of the test reaching 100 and 97% respectively, and the results are not affected in patients with cirrhosis, this test is rapid and cheap contrary to PCR that is limited by high cost and low sensibility (60-80%). The incidence of drug-induced hepatitis may be greater and the implications of hepatotoxicity for patients with cirrhosis are potentially serious. The evidence in this group of patients indicates hepatotoxicity in 26%. The authors have not declared any conflict of interest.

015

FACTORS RELATED TO COEXISTENCE BETWEEN CHRONIC PANCREATITIS AND ALCOHOLIC LIVER CIRRHOSIS

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Introduction and aim: There a correlation between excessive alcohol consumption for many years and the risk of chronic pancreatitis (CP) and liver cirrhosis (LC). $< 5\%$ who are alcoholics develop CP and 2-35% will have LC. The concomitant presentation CP and LC is rare and has been poorly studied. The objective is to determine the frequency of CP in patients with LC secondary to chronic alcohol abuse (CA) and evaluate the factors related. **Materials and methods:** We reviewed reports of autopsies performed in Hospital General de Mexico from January 1999 to December 2007 looking for diagnosis of LC secondary to CA. We recorded demographic data, coexistence of PC, smoking, time drinking, Child Pugh scale and pancreatic pain and diarrhea. Quantitative variables were expressed as mean and standard deviation (SD) or median and range according to their distribution; and qualitative variables as proportions and percentages. **Results:** We review data from 7,258 autopsy reports, 193 were diagnosed by LC for CA. Of these 54 (28%) had CP. Mean age 51.77 ± 11.34 in LC + CP *vs* 54.9 ± 13.88 no CP in LC ($p = 0.14$). In terms of gender 47 (87%) males and 7 (13%) women in CP + LC *vs* 112 (80.5%) men and 27 (19.5%) women in LC without CP ($p = 0.39$). Years of alcohol consumption 28.18 ± 11.74 in LC + CP *vs* 33 ± 14.72 in LC without CP ($p = 0.06$). 23 (42.6%) had smoking history in LC + CP *vs* 40 (28.8%) in LC without CP ($p = 0.06$) [odds ratio 1.5 (95% CI 1.0 to 2.4)]. Child Pugh Classification: 1 (1.8%) stage A, 9 (16.7%) B and 44 (81.5%) C in LC + CP and 6 (4.3%) A, 28 (20.2%) B and 105 (75.5%) C in LC without CP ($p = 0.53$). 6 (11%) had a history of pancreatic pain and 1 (1.8%) of chronic diarrhea. **Conclusions:** We found coexistence of LC and CP in 28% of cases. This is more frequent in males and in the 6th decade of life. In the

data analyzed do not exist statistically significant differences, although the history of smoking and years of alcohol consumption tend to significance. When we calculated the odds ratio for smoking, it may be a risk factor, however, requires a larger sample size. **Conflict of interest:** The authors declare that no competing interest exist.

016

PREDICTIVE VALUE OF THE METHACETIN-13C BREATH TEST IN PATIENTS WITH LIVER CIRRHOSIS

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Background: The methacetin-13C breath test (PAM-13C) is a non-invasive tool that allows for the measurement of the functional capacity of the hepatocytes, and for the prediction of liver cirrhosis, there is no information on its potential utility to predict survival in patients with liver disease. **Objective:** To evaluate the ability of the methacetin-13C breath test to estimate survival in patients with liver cirrhosis. **Material and methods:** Patients from 18 to 75 years of age diagnosed with chronic liver disease were selected. All patients underwent a physical examination, hematic biometry, blood chemistry, clotting time, tests of liver function and methacetin-13C breath test at the beginning of the study. Death was recorded during the three-year of follow-up. **Results:** 151 patients were included (age, 56 ± 13 years). The cause of liver disease was hepatitis C virus infection in 60 (39.7%), excessive alcohol ingestion in 22 (14.6%), and other causes in 69 (45.7%). According to the Child-Pugh index, patients were classified at stage A ($n = 78$), B ($n = 57$) or C ($n = 16$) at the beginning of the study. Methacetin-13C oxidation was significantly higher in patients with a Child-Pugh score A [7.34% (0.14 - 31.49%)] vs. B [3.7% (0.38 - 22.35%)], and vs. C [0.76% (0.11 - 7.75%)]. A significant inverse correlation was found between methacetin-13C oxidation and the Child-Pugh score ($r = -0.349$ $p < 0.0001$). Regarding complications, 125 patients were considered decompensated, of which 30 died; the survival probability was 61.3% in a follow-up period of 36 months (33.9 - 38.1); The predictive variables for mortality were creatinine [HR = 3.19 (1.11 - 9.13)], total bilirubin [HR = 1.14 (1.08 - 1.24)], hematocrit [0.91 (0.84 - 0.98)], and methacetin oxidation [HR = 0.88 (0.78 - 0.97)]. **Conclusion:** Our results confirm the utility of PAM-13C as simple, non-invasive tool for assessing the functional capacity of the hepatocytes and as a predictor of survival in patients with decompensated cirrhosis. This work was partially supported by CONACYT and IMSS.

017

PREVALENCE OF MINIMAL HEPATIC ENCEPHALOPATHY AND QUALITY OF LIFE IN PATIENTS WITH DECOMPENSATED CIRRHOSIS

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Background: Minimal Hepatic Encephalopathy (MHE) affects more than 30% of patients with cirrhosis, and it has been suggested that, despite no recognizable clinical symptoms, it might affect the health-related quality of life.

Objective: To determine the prevalence of minimal hepatic encephalopathy and evaluate the quality of life in patients with decompensated liver cirrhosis. **Study design:** Analytical cross-sectional. **Methodology:** Patients diagnosed with liver cirrhosis of any given etiology attending the Research Laboratory in Gastroenterology at Centro Médico Nacional Siglo XXI were selected. The diagnosis of cirrhosis was made according to liver biopsy, clinical characteristics and/or liver reserve measured by methacetin-13C breath test. Selected patients underwent complete clinical evaluation to identify those with decompensated liver cirrhosis, and psychometric tests were applied to evaluate the presence of MHE, as well as a quality of life using the chronic liver disease questionnaire (CLDQ).

Results: 126 patients were included (age: 55.1 ± 12.3 years). According to the Child-Pugh score, 57 patients were staged as Child Pugh A, 50 as B and 19 as C. The prevalence of MHE was 44.4% ($n = 56$). In patients with MHE a significant reduction in the domains of activity (3.80 ± 1.59 vs 4.58 ± 1.65), systemic symptoms (4.15 ± 1.30 vs 4.68 ± 1.15), emotional function (3.82 ± 1.38 vs 4.29 ± 1.23), and global scoring (3.89 ± 1.12 vs 4.33 ± 1.03) were observed when compared to patients without MHE ($n = 70$). **Conclusion:** Our results suggest that MHE is a factor that affects quality of life in patients with decompensated liver cirrhosis. **Conflict of interest:** This work was partially supported by research fund of Mexican

Social Security institute (FIS-IMSS).

C. LIVER TUMORS

001

PREVALENCE AND TYPE OF SOLID LIVER LESION DIAGNOSED BY IMAGING AND ITS CORRELATION WITH LIVER BIOPSY

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Introduction. Liver masses are often identified by imaging modalities such as ultrasound (US) and computed tomography (CT). Hepatocellular carcinoma (HCC) is the most common malignancy in cirrhotic liver. In noncirrhotic patients the most common malignant liver tumor is metastasis. Enhanced CT provides information about tumor vascularity. **Objective.** Describe the prevalence and type of liver masses that are diagnosed by radiological imaging and its correlation with liver biopsy. **Material and methods.** We performed a cross-sectional study. Results of 44 liver biopsies were analyzed from January 2010 to March 2013 and its corresponding radiological imaging. The size, number of lesions per US, CT or MRI was described. We used descriptive statistics; quantitative variables are expressed as mean and standard deviation (SD) and qualitative variables as proportions and percentages. **Results.** The most common liver tumors were metastatic adenocarcinoma $n = 23$ (52%) and hepatocellular carcinoma $n = 11$ (25%), other $n = 10$ (23%). The average age at diagnosis was 53 years. Predominance of females $n = 23$ (52). In HCC

multiple lesions were predominated $n = 6$ (54%) as in adenocarcinoma $n = 15$ (65%). The predominant mode of study was enhanced CT $n = 25$ (57%), Doppler US liver (41%) and MRI (2%). CT diagnosed 87.5% of cases of HCC confirmed by biopsy and only 54% of metastasis adenocarcinoma. **Conclusion.** The diagnosis of HCC was accurate with enhanced- CT overdiagnosis however in adenocarcinoma, probably because the size of the lesion, occur alone, or their hypervascular peripheral enhancement in the arterial phase, mingling with the phenomenon wash in-wash out. It is important to the proper conduct of enhanced-CT for accurate diagnosis of liver lesions, especially hepatocellular carcinoma.

The authors declare that there is no conflict of interest.

002

PERSISTENT HEPATIC ENCEPHALOPATHY SECONDARY TO A SPONTANEOUS PORTO SYSTEMIC SHUNT OCCLUDED WITH AN AMPLATZER DEVICE: A CASE REPORT

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Background and aim. Decompensation of hepatic encephalopathy by spontaneous portosystemic shunt is rare, the incidence is unknown in the presence of cirrhosis. The evidence obtained to determine its management is based on a review of published case series. Here we present the successful management of a long spontaneous shunt with an Amplatzer II device.

Case report. A 57 years old, previously healthy male, started in 2006 with asthenia and adynamia. On medical evaluation, liver function tests showed elevated transaminases (ALT 75 U/L, AST 97 U/L, AF 119 U/L, GGT 195 U/L). After approach, the diagnosis of cryptogenic cirrhosis with no hemorrhagic portal hypertension was established. On June 2011 he presented the first event of hepatic encephalopathy and lactulose therapy was started. During the next year the patient developed 15 episodes of hepatic encephalopathy that required hospitalization. L-ornithine-L-aspartate, rifaximin, zinc and magnesium were added to treatment. The serum ammonium was 169.9 mcg/dL. In October 2012 he developed a new hepatic encephalopathy episode, which was classified as persistent and severe (grade II-III). The EEG and brain MRI ruled out other etiologies of neurological impairment. A thoracoabdominal CT was done which demonstrated the presence of a shunt with reperfusion of the umbilical vein into the right femoral vein, with a diameter of 12.34 cm (Figure 1). The case was evaluated with the Interventional Radiology department and decided to occlude the shunt with an Amplatzer II device in the umbilical vein.

Results. Two weeks after the procedure the patient was evaluated. The serum ammonium levels were reduced to 60 mcg/dL. The patient was listed for liver transplantation, with a B Child Pugh score and MELD of 18 points. **Conclusions.** The presence of persistent hepatic encephalopathy despite the proper treatment and patient compliance should force to rule out spontaneous shunts. The use of Amplatzer devices for closing spontaneous shunts is rarely described in the literature. Closure of large collaterals is technically challenging and is a low risk procedure. Assessment of the etiology and triggering factors of the persistent hepatic encephalopathy allows selec-

ting patients who will benefit from shunt closure, as in this case.

003

THE PROTECTIVE ROLE OF Nrf2 IN A HEPATIC CANCER CELL LINE

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Introduction. It is well known that Nrf2 transcription factor can induce a protective effect to cells exposed to cytotoxic compounds, this could be happen also in cancer cells, conferring survival and drug resistant. In order to evaluated this response we have used HepG2 cells to address the expression of Nrf2-related proteins and the relation in cell cycle and proliferation. **Material and methods.** HepG2 cells were exposed to 2.5, 5, 10, 15 and 20 μ M for 24, 48 and 72 h of cisplatin. We evaluated the proliferation and viability by cck8 kit; subsequently by Western blot technique we analysed the content of cytoprotective proteins: HO-1, NQO1, γ -GCS, and Nrf2. Nrf2 localization was monitored by confocal microscopy. Cell cycle analysis was performed by flow cytometry as well by Western blot. **Results.** Show increased expression of HO-1, NQO1, γ -GCS and Nrf2, at 2.5 and 5 μ M of cisplatin in HepG2. It was observed by confocal microscopy the nuclear translocation of Nrf2 induced by cisplatin, suggesting the activations of this transcription factor as a consequence of chemotherapeutic compound. The cell cycle analysis showed an arrest in S phase at concentrations of 2.5 and 5 μ M of cisplatin. In conclusion our data suggest a cytoprotective mechanism driven by Nrf2 in HepG2 cells exposed to cisplatin, this result pinpoint Nrf2 as a therapeutic target in liver cancer treatment. Supported by CONACYT # 153902 and SEP-PROMEP 912011-14611762.

004

ACETYLCHOLINESTERASE (AChE) EXPRESSION IN Huh-7 HCC CELL LINE AT DIFFERENT CELL DENSITY

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Introduction. Acetylcholinesterase (AChE) catalyzes the hydrolysis of acetylcholine, its main function is to control cholinergic neurotransmission. AChE also have not-catalytic functions acting as a tumor suppressor. It has been reported that AChE is involved in apoptosis, where is crucial in the activation of the apoptosome. Recent studies showed that the AChE is involved in arresting the cell cycle and in differentiation, opening the possibility that not only it is involved in apoptosis, but could regulate the cell cycle to control death processes particularly in tumors, where cell-cell interaction is high and affects regulatory functions. **Objective.** To deter-

Table 1.* Tumor characteristics and survival.

Histology type/ Stage	Poorly differentiated / II	Moderately differentiated / III B	Well differentiated / IVB	Moderately differentiated / I	Well differentiated / II	Moderately differentiated / IIIB
Localization/ Surgery	Intrahepatic/ Right hepatectomy	Hylar/ Left hepatectomy	Intrahepatic/ Left hepatectomy	Intrahepatic /-	Intrahepatic/ Right trisegmentectomy	Hylar/ Right hepatectomy
Chemotherapy/ Radiotherapy	-/-	+/-	-/-	-/+	-/-	+/+
Survival	*	57 months	*	4 months	50 months	8 months

* 007. CHOLANGIOCARCINOMA, A LOW INCIDENCE MALIGNANCY. EXPERIENCE OF SIX YEARS AT HOSPITAL SAN JOSÉ TEC DE MONTERREY.

mine whether levels of synthesis and enzymatic activity of acetylcholinesterase change at different cell densities. **Material and methods.** Huh-7 HCC cells were seeded in at different densities 47×10^3 cells/cm², 105×10^3 cells/cm², 147×10^3 cells/cm² and 283×10^3 cells/cm². Synthesis of acetylcholinesterase was determined by Western blot. The enzyme activity was assayed by Ellman's method, and mRNA was identified by RT-PCR in one-step. **Results.** The synthesis of acetylcholinesterase was increased due that to was increased density cellular, regardless of whether the cells were plated with Williams containing serum or serum-free. We found changes in enzyme activity, being relevant at high cell density. We found no changes in the alternative splicing of mRNA, but we found that the R-form of mRNA transcription was increased to a high cell density. **Conclusions.** Our data show that the increment of acetylcholinesterase synthesis at high density could suggest that acetylcholinesterase participates in cell cycle arrest. We also show that Cyclin D1 decreases its synthesis at high-density which was related to a p27 increment. Supported in part by CONACYT # 153902 y SEP-PROMEP 912011-14611762.

005

A HIGH CHOLESTEROL DIET ACCELERATES THE N-DIETHYLNITROSAMINE-INDUCED HEPATOCARCINOGENESIS

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Background and aim. Hepatocellular carcinoma (HCC) is the predominant type of primary liver cancer rated as fifth among all cancers in incidence and as third in mortality. Recently obesity has been recognized as an important risk factor for HCC. The principal hepatic manifestation of obesity is non-alcoholic fatty liver disease (NAFLD). NALFD has the potential to progress to non-alcoholic steatohepatitis (NASH) which can lead to cirrhosis causing major complications like HCC. Recent findings show that cholesterol accumulation, more than any other type of lipid, sensitizes hepatocytes to damage. The aim of this project was to determine the effect of the steatosis induced by a hypercholesterolemic diet over the induction and progression of liver cancer produced by a chemical hepatocarcinogen. **Material and methods.** 14 days-old

C57BL/6 male mice were fed with a hypercholesterolemic diet (DHC, 2% cholesterol and 0.5% sodium cholate), or with balanced chow diet (DCW). At day 16 mice were injected with N-diethylnitrosamine (DEN, 10 µg / g body weight, i.p.). Mice were sacrificed at different times and blood serum was collected for biochemical testing, protein was isolated from tissue samples to perform Western blot assays and pieces of tissue were embedded in paraffin for H&E routine staining and Masson's trichrome staining. **Results.** Liver neoplasia appeared in DHC mice since 3 months after DEN treatment while in DCW mice appeared after 5 months. At 8 months DHC mice had larger tumors, in greater number and more vascularized than DCW mice. Western blots revealed that the STAT3 pathway was activated since 3 months after DEN administration whereas ERK pathway doesn't seem to be involved in the proliferation of DHC tumors. **Conclusions.** Liver cholesterol overload acts as a tumor promoter generating fibrosis and activating proliferation and survival pathways such as STAT3.

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006

CHOLANGIOMA (BENIGN LESION OF THE BILE DUCTS)

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Introduction. Benign lesions of the bile ducts, intra, and extrahepatics, they are extremely rare, one can call it in the absence of a histological confirmation, as cholangiomas. **Clinical case.** Male. August 2008. symptomatology; loss of 10 kg in 1 month, jaundice of skin and intense itching. Referred by cancer of biliary tract *vs.* head of pancreas cancer. Ultrasound shows dilation of the bile duct. TAC: Hepatic common conduct bile, with image of aspect of mass of 1.8 cm, located at the level of the joint of the liver right and left, with decrease of the caliber of common bile duct near the pancreas. Laboratory. Bilirubin total of 3.15 mgrs, with 1171 UI/dL GGT, ALP of 592 UI/dL. CPRE: observe ampulla no abnormal features, via biliary 11 mm distal and proximal of 17 m with area of stenosis which measures 1.4 mm, regular concentric level common bile duct middle portion, allowing passage of guide wire. It dilates mechanical and hydrostatically driven to 8 mm. Biopsy is taken by brushing. Biliary prosthesis is placed succe-

ssfully. With diagnosis to the end of the procedure of likely tumor of Klastkin. Histological examination: biopsy reports negative for malignancy. Evolution: two years later decides, be magnetic resonance cholangiogram, as well as image of the tumoral lesion. Magnetic resonance cholangiopancreatography (MRCP) (August 2.010), the tumoral lesion, is assessed between 3.6 and 4.5 cms in its major axis. (MRCP) (2011 August) The tumoral lesion, presents an increase of approximately 50% with respect to the study of the previous year, in either of the two studies observed data of metastatic activity, not nodes, or tumor lesions on liver can be seen. Its evolution to the present time, is entirely satisfactory, **Conclusions.** Negativity of the cytological, shows lesion benign, and for which, there much information for its handling, since a resection of the lesion, with reconstruction of the bile duct, seems excessive. According to our knowledge, the report of benign lesions of the bile ducts, is extremely rare, and we have news of a similar report in Mexico.

The authors declare that there is no conflict of interest.

007

CHOLANGIOCARCINOMA, A LOW INCIDENCE MALIGNANCY. EXPERIENCE OF SIX YEARS AT HOSPITAL SAN JOSÉ TEC DE MONTERREY

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Background and aim. The cholangiocarcinoma is a malignancy of the biliary tree with low incidence and poor prognosis due to late diagnosis. Clinical presentation varies from non-specific symptoms to biliary obstruction. The treatment of choice is tumor resection. The aim is to recognize the clinical characteristics and outcome of patients with cholangiocarcinoma at our hospital. **Material and methods.** We identified the pathology report of 6 patients treated at the Hospital San José Tec de Monterrey from the years 2006 to 2011. Clinical characteristics, test results, postsurgical status and hospital stay, where analyzed in retrospective through their clinical files. The survival and outpatient evolution was obtained contacting the treating physician. Descriptive statistics, medians and ranges were used. **Results.** The patients, 5 men (83.3%) and 1 woman (16.7%), presented with abdominal pain and weight loss (66.7%). Median age was 60.5 years (range 42-81). Histopathology diagnosis was obtained by percutaneous liver biopsy. Moderately differentiated cholangiocarcinoma was reported in 50% of patients; 33.3% well differentiated and 16.7% poorly differentiated. Surgical treatment was offered to 83.3%; 33.3% received adjuvant chemotherapy and in 16.7% was combined with radiotherapy. Survival ranged from 4 to 57 months with median of 30.5 months, follow up was lost in two patients (Table 1). **Conclusions.** Most of the cases were observed in men (80%). Age of presentation was similar to the reported in the literature. Half of the cases were moderately differentiated cholangiocarcinoma. Survival in 40% of surgically treated patients reached 50 months, and this could be influenced by stage lower of IV at diagnosis.

The authors declare that there is no conflict of interest.

008

ARTERIAL EMBOLIZATION OF GIANT HEPATIC HEMANGIOMA

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Introduction. Hepatic hemangioma is the most common benign liver tumor, with prevalence of 5-20%, is more common in females. Most of these lesions are small and treatment or follow-up are not necessary. Only giant hepatic hemangioma, > 5 cm of diameter, can provide mechanical complications requiring intervention. **Case report.** A 44 year old woman with a history of blood transfusion 20 years ago, negative test for viral hepatitis, she presented severe abdominal pain in the right upper quadrant for two months, constant, a physical examination felt painful hepatomegaly with normal laboratory parameters. Abdominal ultrasonography was performed and show a heterogeneous tumor in the right lobe of 10.7 x 9.4 x 10.5 cm without vascular flow. MRI was performed reporting a tumor located in VI and VII segments of 10 x 9 x 9 cm corresponding to a cavernous hemangioma. Angiography confirmed the diagnosis and show it was originated right hepatic artery, anatomical variant of the right hepatic artery. Arterial embolization was performed successfully with gel-foam. The patient has had no symptoms and decrease the size of the lesion seen on CT. **Conclusion.** Hepatic hemangioma is a vascular malformation, due to cavernous vascular channels lined by a single layer of endothelium, separated by fibrous septum, with a clear correlation between their genesis and female hormones, the diagnosis is most frequent in women (60-80%), without symptoms, with age between 30 to 50 years. They are usually found in imaging studies done for another diagnosis, ultrasonography show a homogeneous and hyperechoic lesion. The CT and MRI are conclusive studies for diagnosis, with 95% sensitivity and specificity close to 100%, showing an image with centripetal enhancement on portal venous phase. The indications for treatment are giant hemangiomas are progressive abdominal pain, increase in size, difficulty in excluding malignancy, or rupture. It can be treated with surgical resection option, enucleation, hepatic artery ligation, liver transplant, arterial embolization or conservative.

The authors declare no conflict of interest

009

HEPATOSPLENIC GAMMA/DELTA T-CELL LYMPHOMA: CASE REPORT

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Introduction. Hepatosplenic gamma-delta T cell lymphoma is a mature neoplasia, rare, with infiltration into spleen, liver and bone marrow, which presentation is most common in adolescents and young adults, predominantly men more, characterized by symptoms B, hepatosplenomegaly, abdominal pain, anemia and thrombocytopenia, which express the receptor of T cells, gamma-delta. With an average survival of 16 months with the regime based cyclophosphamide, doxorubi-

cin, vincristine and prednisone. **Material and methods.** Male 28 years old without previously known pathologies, who started with clinical symptoms of 6 months duration with fever quantified at 39 degrees Celsius, myalgias, arthralgias, and sore throat, with multiple antibiotic regimens for respiratory infections, then the fever is mainly in the evening, adding profuse diaphoresis, epigastric pain and heartburn. With unintentional loss of 12 kg in the same time duration. Investigated as fever of unknown origin, with initial general laboratories highlighting alterations in liver function tests with AST 129 U/L, ALT 129 U/L, DHL 824 U/L, TORCH, bacilli resistant to alcohol and acid, throat swab, stools, urine and blood cultures without abnormalities, with USG and CT of the abdomen reporting hepatosplenomegaly. During his hospital stay presents with jaundice, gastrointestinal bleeding with hematochezia, with upper endoscopy and colonoscopy without obvious changes and reporting intestinal transit loss of morphology in the jejunum and ileum, underwent capsule endoscopy with jejunal ulcers report and nodular lymphoid hyperplasia. Progresses to pancytopenia with severe neutropenia. Subjected to laparotomy protocol. **Results.** Surgical specimen, spleen, and liver wedge biopsy, with immunohistochemistry, reported hepatosplenic gamma-delta T cell lymphoma. **Conclusions.** We report the case of a young male patient with B symptoms, who from the beginning showed an elevated LDH, who finally arrives in the diagnosis of hepatosplenic gamma-delta T cell lymphoma, with immunohistochemistry. This tumor is less than 1% of lymphoid neoplasms. Wherefore should be suspected in this neoplasia in male patients and/or youth with B symptoms, elevated LDH and hepatomegaly or splenomegaly. The authors declare no conflict of interest

010

MALIGNANT HISTIOCYTOSIS. CASE REPORT

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Male patient aged 67 with alcoholism for 9 years as the only pathological history, consumed 30 g per week during that period. Ailment began 3 months before admission with malaise, weight loss, fever predominantly nocturnal, jaundice, ascites and productive cough. On admission to the hospital in good general health, with conjunctival jaundice, without respiratory distress, cough only occasionally, the abdomen showed hepatomegaly painful 4-3-2 cm below costal margin. Ultra-

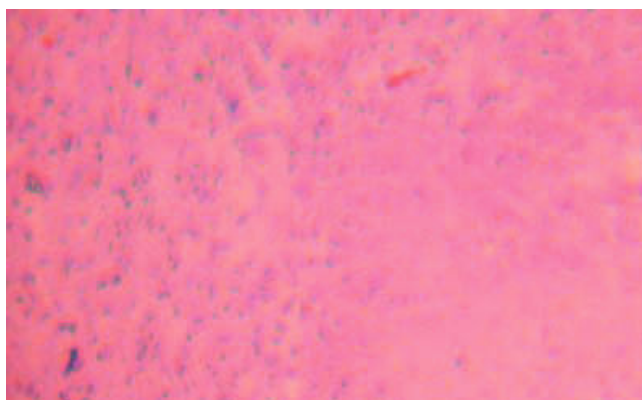


Figure 1. 010. MALIGNANT HISTIOCYTOSIS. CASE REPORT.

sound was performed which documented steatosis and simple cyst in segment VII, without dilatation of the bile duct. Abdominal CT was requested, which corroborated the ultrasound data was not conclusive so liver open biopsy was performed with histopathological report granulomatosis and cholestasis. We began to study protocol entities including infectious tuberculosis, rheumatic diseases, immunological and neoplastic with negative results. During his hospital stay showed progressive deterioration with increasing jaundice and acute liver failure later, renal failure, respiratory distress and finally the patient died. The results of autopsy showed conglomerate nodal level hepatic hilum and parenchymal infiltration by multiple hepatic and splenic nodules being the definitive diagnosis of malignant histiocytosis (Figure 1). The authors declare no conflict of interest.

011

PRIMARY HEPATIC CARCINOID TUMOR. CASE REPORT AND REVIEW OF THE LITERATURE

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Primary Hepatic Carcinoid Tumors (PHCT) are rare malignancies that represent a challenge in diagnosis and treatment. There are approximately 95 cases reported in the literature. They represent 1-2% of the digestive system malignancies. The exact incidence of primary hepatic neuroendocrine tumors is unknown. We present a case of a 35 year old asymptomatic female who during a check-up ultrasound was diagnosed with a hepatic right lobe tumor. CT revealed an 18 cm hyper vascular tumor who involved the whole right hepatic lobe suggesting a fibrolamellar carcinoma. She was treated with a right hepatectomy without incidences. Histopathological examination confirmed a neuroendocrine origin malignancy (carcinoid) of 24 x 14 x 10 cm. Chromogranin (+). Serological markers 5 hidroxyindolacetic acid (5-HIAA) and Chromogranin A were negative. 18F-FDG PET-CT did not evidenced metastatic disease or another primary origin. The authors declare no conflict of interest.

D. MOLECULAR AND CELLULAR BIOLOGY

001

PREVENTION OF CHOLESTEROL GALLSTONES FORMATION BY TWO EXTRACTS OF *RAPHANUS SATIVUS* L. VAR NIGER IN MICE

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Background. Cholesterol gallstones formation results from an imbalance in lipid components of bile through dysregulation of biliary transporters. Glucosinolates are active metabolites of *Raphanus sativus* L. var niger (blackradish), whose main therapeutic effects have shown to be hypolipidemic and

Table 1.* Effect of black radish extracts in gallstones formation and biliary lipids.

Experimental group, n = 7	Incidence of gallstones (%)	Bile salts	Biliary lipids (mmol/L) Phospholipids	Cholesterol
ND	0	148.7 ± 1.2**	15.81 ± 0.6	7.8 ± 0.1**
LD	100	170.1 ± 2.2	8.85 ± 0.4	31.9 ± 1.4
UDCA	0	167.6 ± 4.0	15.1 ± 0.7	20.6 ± 0.7
H ₂ O 1000	42.9	154.6 ± 2.9	12.1 ± 0.4	24.0 ± 1.1
MeOH 10	28.5	158.4 ± 2.1	16.3 ± 0.5**	20.0 ± 0.6**
MeOH 100	0	166.6 ± 3.5**	34.2 ± 1.7**	21.3 ± 0.5
MeOH 1000	0	174.7 ± 2.92	27.38 ± 1.38**	8.41 ± 0.24**

* 001. PREVENTION OF CHOLESTEROL GALLSTONES FORMATION BY TWO EXTRACTS OF *RAPHANUS SATIVUS* L. VAR NIGER IN MICE.

** Values indicate significant differences ($p < 0.05$) between groups versus LD group. One-Way ANOVA with Tukey *post-hoc*.

antioxidant effects. **Aim.** Investigate the effects of two extracts of black radish in the prevention of cholesterol gallstones formation in mice. **Material and methods.** 63 male adult mice (C57BL/6Nhsd) were administered with aqueous (H₂O) or methanolic (MeOH) extract from black radish intragastric 10, 100, 1,000 mg/kg plus lithogenic diet during 40 days. As control groups, animals were fed with normal diet (ND) or lithogenic diet (DL) or ursodeoxycholic acid (UDCA) plus lithogenic diet. Animals were sacrificed. In serum, total cholesterol, bile salts, triglycerides and cholesterol were measured; in bile, bile were determined salts and phospholipids. Biliary transport protein expression of Abcb11, Abcb4, Abcg5, Abcg8 was evaluated by western blot. Cholesterol gallstones formation was determined by microscopic analyses of the gallbladder. **Results.** MeOH extract (10, 100, 1000 mg/kg) inhibited cholesterol gallstones formation and these effects can be related with a decreased expression of hepatic Abcg5/8. In these groups, Abcg8 and Abcg5 decreased their expression, being dose dependent in the former. Mice that received MeOH extracts (10 and 100 mg/kg) showed a lower expression of Abcb11 in comparison with lithogenic diet group. Abcb4 increased its expression with H₂O extract (1,000 mg/kg) and MeOH extract (10 and 100 mg/kg) however, MeOH extract (1,000 mg/kg) diminished its expression (Table 1). **Conclusions.** Black radish may have important antilithogenic properties for prevention of cholesterol gallstones, by regulating components in bile through a modulation in expression of biliary transporters.

The authors declare no conflict of interest.

002

GPBAR1 EXPRESSION IN PATIENTS WITH ACUTE BILIARY PANCREATITIS

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Background and aim. GPBAR1 is a membrane-bound G protein-coupled receptor for bile acids detected in many tissues. Its deletion in mice has been associated with gallstone disease prevention and reduction of inflammation and hyperamylasemia in induced pancreatitis in vitro, thereby playing an important role in pathogenesis of biliary disease. GPBAR1 gene expression in patients with acute biliary pancreatitis is suggested be increased when compared with cholelithiasis. **Material and methods.** We studied patients with diagnosis

of acute biliary pancreatitis and cholelithiasis from Hospital Dr. José E. González. Patient data as medical history, demographics were expressed as mean, and standard deviation was calculated. Blood samples and gallbladder tissue were collected postcholecystectomy. GPBAR1 analysis expression was performed using an Applied Biosystems® 7500 Real-Time PCR System. GPBAR1 expression was normalized using an endogenous gene as GAPDH, matched by age and gender using $\Delta\Delta Ct$ method. All tests were performed in triplicate. Populations were compared using the Mann-Whitney U-test. Data was analyzed with SPSS software (version 20.0; SPSS, Chicago, IL). **Results.** We studied 54 patients, divided in 2 groups with 27 patients each. Mean age was 40.52 years (SD ± 17.54). 42 were women (80.76%). By calculating $\Delta\Delta Ct$ GPBAR1 expression level was higher in gallbladder tissue contrasted to blood sample levels. Comparing the two groups, blood samples showed a tendency to overexpression in pancreatitis group being 91.48 (SD ± 204.65) ($p = 0.026$). GPBAR1 expression in blood of women with pancreatitis had an average of 110.51 (SD ± 231.04) vs. gallbladder tissue, 287361.33 (SD ± 1285006.1). In men, there were no statistically significant differences in the groups of pancreatitis and cholelithiasis regarding GPBAR1 expression. **Conclusions.** Our population has an increased GPBAR1 gene expression levels in patients with acute biliary pancreatitis compared with gallstone disease, especially in blood. It is noteworthy that these variations may be specific to genetic variation within GPBAR1 gene. This project has been partially subsidized by Fundación Mexicana de la Salud A.C. and Fundación Mexicana para la Salud Hepática A.C. It won the Ángeles Espinosa Yglesias Award in 2011.

003

CHOLESTEROL OVERLOAD IN THE LIVER ENHANCES THE DAMAGE INDUCED BY CCL₄

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Introduction. Lipids overload, particularly cholesterol non-esterified, sensitizes the liver to toxic stimuli damage. It is known that it is due to particular overproduction of reactive oxygen species. The toxic effect of CCL₄ in the liver is due to its biotransformation to the radical CCL₃, causing fatty acid oxidation and lipid peroxidation, this damage triggers a repair process mediated by growth factors and cytokines, which allow activation of transcription factors, that provide survival, repair and proliferation signals through routes like Erk and STAT3. **Aim.** To study the effect of hypercholesterolemic

diet (HC) and a second aggression with CCl_4 in the hepatic reparation process. **Material and methods.** C57BL/6 mice were fed with an atherogenic diet (2% cholesterol and 0.5% sodium cholate) or normal control diet (Chow) for two days. After that, mice were injected with CCl_4 and sacrificed at different times. Biochemical tests like aspartate aminotransferase (AST) and alkaline phosphatase (ALP) were also performed. Different proteins were analyzed by Western such as ERK 1/2, STAT3 and β -Catenin. **Results.** Liver/body ratio in CCl_4 mice creases from 48 to 168 h, whereas in mice with the Chow diet seems to have decreased ratio at 24h. Levels of AST and ALP are slightly increased from 12 h in mice HC. The animals fed with HC diet show a decrease in the ERK 1/2 activation from 6h, it was also observed an increase in the STAT3 activation. **Conclusion.** The data suggest that the HC diet alone is causing liver damage, which is exacerbated by CCl_4 ; the data suggest a survival compensatory response by STAT3 pathway. This work was supported in part by CONACYT 166042. PROMEP-SEP 912011-14611762.

004

CAFFEINE PREVENTS EXPERIMENTAL HEPATIC FIBROSIS BY BLOCKING THE EXPRESSION OF TGF- β AND DOWNSTREAM EFFECTOR CTGF ATTENUATING THE INFLAMMATORY PROCESS

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Background. Caffeine (1,3,7-trimethylxanthine) is a purine alkaloid present in many popular beverages, including coffee. There is a growing body of evidence that caffeine has beneficial effects on the liver. However, the molecular mechanisms by which caffeine exerts beneficial effects on the liver are poorly defined. **Aims.** This study was performed to evaluate the antifibrotic properties of caffeine in a model of liver damage induced by repeated administration to thioacetamide (TAA) in male Wistar rats. **Material and methods.** Liver cirrhosis was induced by thioacetamide 200 mg/kg, (i.p.) three times a weekly for 8 weeks. One group of rats concomitantly received caffeine 20 mg/kg (p.o.) daily, by 8 weeks; the control group received the vehicle only (saline, i.p.). Liver injury was assessed by serological analysis, as well as Hematoxylin and eosin (H&E) and Masson's stains. Oxidative stress was evaluated by lipid peroxidation and glutathione peroxidase (GPx) activity. Whole liver lysates, were investigated for TGF- β , CTGF, α -SMA and IL-10 by Western blot and RT-PCR. MMP-2 and 9 were analyzed by zymography. **Results.** TAA administration elevated serum alkaline phosphatase, γ -glutamyl transpeptidase and alanine aminotransferase, liver lipid peroxidation, collagen content, depleted liver glycogen and glutathione peroxidase (GPx) activity. Additionally increased levels of a number of proteins were detected including TGF- β , CTGF and α -SMA, IL-10, MMP-2 and 9. Interestingly, administration of caffeine suppressed most of the changes produced by TAA. Histopathological analysis was in agreement with biochemical and molecular findings. **Conclusions.** Our results show that caffeine prevents experimental cirrhosis; the action mechanisms are probably associated with its antioxidant properties and mainly by its ability to block the elevation of the profibrogenic cytokine TGF- β and its downstream effector CTGF and therefore a reduction in the proliferation and activation of the HSCs. Thus, this reduction in the levels of TGF- β may be linked to attenuation of the inflammatory and fibrotic

processes. These findings support earlier findings suggesting a beneficial effect of caffeine on the liver. However, more basic and clinical studies must be performed to confirm the present finding.

The authors declares that there is no conflict of interest.

005

EFFECT OF ALPHA-BETA BLOCKERS COMPARED CHEMICAL SYMPATHECTOMY WITH 6-HYDROXYDOPAMINE IN LIVER REGENERATION IN HAMSTERS WITH CIRRHOSIS

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Background. Liver cirrhosis is a condition caused for some chronic liver diseases with the production of fibrotic tissue causing damage. Among liver cells, the stellate are the major producers of cirrhosis/fibrosis and important targets for addressing the treatment. These cells express the alpha-1 adrenergic receptors that allow its activity modulation. **Objective.** We analyze the effect of alpha and beta receptors inhibitors on the evolution of hepatic cirrhosis and its possible regeneration, through the study of hepatic stellate and oval cells. **Material and methods.** We study four groups of hepatic cirrhotic hamsters induced with CCl_4 : 1) 6-hidroxydopamine-treated (30 mg/kg), 2) Carvedilol-treated (beta inhibitor, 0.04 mg), 3) Doxazosin-treated (alpha-1 inhibitor, 0.013 mg) and 4) Without treatment (control). The 4 group was also useful to observe the possible regeneration without CCl_4 after 6 weeks. Liver samples were fixed with paraformaldehyde (4.5% in PBS) and stained with trichrome Masson technique. Immunohistochemical analyzes were developed for anti-synaptophysin antibody against hepatic stellate cells and anti-chromogranin antibody against oval cells. **Results.** After 6 weeks of treatment with: 6-hidroxydopamine, carvedilol and doxazosin; we observed the reduction of interlobular amount of collagen fibers. We also found that doxazosin-treated group showed high level of cirrhosis reversion; we based these observations in: 1) Reduction of deposits of collagen at portal triads and parenchyma, 2) Decrement of synaptophysin-positive cells, 3) Increment of chromogranin-positive hepatic cells (oval) at portal systems. **Conclusion.** We observed in cirrhotic hamsters the regeneration process of hepatic parenchyma highly damaged after blockade of hepatic stellate cells by sympathectomy or by alpha-beta receptors inhibitors. In this way, the cirrhosis regeneration process were associated to the presence of hepatic oval cells.

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006

CHOLESTATIC DAMAGE IS ENHANCED BY CHOLESTEROL LIVER OVERLOAD IN BILE DUCT LIGATION

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Introduction. Nonalcoholic fatty liver disease is defined by the deposition of fat in more than 5% of hepatocytes. It is well known that lipid overload, particularly cholesterol, sensitizes to hepatocellular damage. Cholestasis is the condition in which the bile flow from the liver is slowed or blocked, causing bile salts, bilirubin, and lipids to accumulate in the blood stream and in the liver. We were focused to figure out the effect of a high cholesterol diet (HC, 2% cholesterol and 0.5% sodium cholate) in liver damage after bile duct ligation (BDL) and the involvement of c-Met receptor in the repair process. **Material and methods.** C57Bl/6 mice were fed with the HC diet, parallel animals were fed with regular rodent diet (Chow) for two days and after that BDL was performed. Liver function tests, and bile acids in tissue were evaluated. Western blotting of main survival pathways were analyzed and confocal immunofluorescence for c-Met was performed in primary mouse hepatocytes isolated by the two-step collagenase perfusion. **Results.** Data show that HC animals were more susceptible to both insults, all animals in the HC-BDL group (n = 6) died during the first 72 h after surgery, while Chow-BDL mice presented a 100% of survive (n = 7). Liver macroscopic inspection of HC mice showed the characteristic pale color in steatosis and changes in gallbladder. Although AST, ALT and ALP were increased as a consequence of BDL, animals fed with the hypercholesterolemic diet increased significantly these values (ranging from 20- to 200-fold), these data were in agreement with an elevation on bilirubin and bile acids, suggesting an exacerbation of cholestatic damage. Examination of the main signaling pathways involved in repair process, such as Akt, Stat3 and Erk1/2 in HC animals showed a downactivation in Erk1/2 and Akt, but some compensatory effect in Stat3 was observed. In vitro analysis of c-Met activation by Western blotting and immunofluorescence in cultured hepatocytes from HC animals revealed a delayed activation of this receptor after HGF treatment. **Conclusion.** Our data suggest that cholesterol overload in hepatocytes aggravates cholestasis and impairs signaling pathways involved in liver repair such as c-Met/HGF. Work supported in part by CONACYT #166042 and 131707, and PROMEP-SEP 912011-14611762.g

007

GENE EXPRESSION OF TNF- α , IL-10, CXCL-8 AND Col2 IN LIVERS FROM CHILDREN WITH END STAGE OF LIVER DISEASE

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Introduction. Cytokines play a critical role in communication and cellular activation, the liver is a source of cytokines involved in the development of liver disease, their receptors are found in hepatocytes. **Objective.** To evaluate gene expression of TNF- α , IL-10, CXCL-8 and Col2 in hepatic tissue from children with end stage of liver disease. **Material and methods.** Seven patients with end stage of liver disease (ESLD) of different etiologies: biliary atresia (3) fulminant hepatitis (3) and tyrosinemia (1), who underwent liver trans-

plantation at Mexico City's Children's Hospital (Hospital Infantil de México), a liver biopsy from each subject. In each of the samples was carried out RNA extraction and obtaining cDNA and determined the gene expression of TNF- α , IL-10, CXCL-8 and Col2 by real time PCR. **Results.** The average age of patients with ESLD (3 girls and 4 boys) was 3 ± 2 years. A control group of 7 people was included with mean age of 31 ± 14 years (3 women and 4 men). The expression of the genes was TNF- α (ng/mL) in ESLD = 3 ± 2 and CT = 2 ± 0.8 (p = 0.778). IL-10 (ng/mL) at ESLD = 6 ± 5 and CT = 0.3 ± 0.2 (p = 0.025). CXCL-8 was 53 ± 21 and 0.4 ± 0.3 for ESLD and CT, respectively (p = 0.048). Col2 expression in ESLD (pg/mL) was 210 ± 70 and for CT was 3 ± 1 (p = 0.025). The ratio CXCL-8/IL-10 was 8.8 and 1.3 in ESLD and CT, respectively, indicating that the inflammatory process in patients is almost 8 times that of the donor tissue. **Conclusion.** Gene expression of IL-10, CXCL-8 and Col2 is increased in liver tissue from liver transplant recipients. This shows the involvement of cytokines in end-stage liver disease, independent of etiology and patient age.

The authors declare that there is no conflict of interest.

E. VIRAL HEPATITIS

001

CHEMOKINES DETERMINATION ON CHRONIC HEPATITIS C

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Introduction. Chronic infection with hepatitis C virus (HCV) is one of the most common etiologies of liver fibrosis in Mexico. Cirrhosis is the latest stage in the progression of liver fibrosis. Recently, some chemokines (CXCL-9 and CXCL-10) have been related with the progression of liver fibrosis. **Aim.** To determine CXCL-9 and CXCL-10 levels in serum of patients with chronic HCV. **Material and methods.** A cross-sectional and observational study was conducted. 21 patients with chronic HCV without any other hepatopathy and 40 healthy participants as a control group were included. CXCL-9 levels were evaluated by ELISA assay; CXCL-10 levels were evaluated by Luminex (Biorad) technology. The statistic analysis was performed with SPSS 15.0 version software, using U Mann-Whitney test. **Results.** CXCL-9 concentration levels (pg/mL) didn't show differences between both groups 1025 ± 962 y 747 ± 745 for patients and control group respectively (p = 0.162). CXCL-10 concentration levels (pg/mL) in patients were higher than control group with 88.9 ± 13 y 22.6 ± 13.1 respectively (p < 0.001). **Conclusion.** Our study didn't show differences between patients and control group in CXCL-9 levels. Recent studies in African population report CXCL-9 levels were not associated with fibrosis stage on initial or later biopsy. CXCL-10 is secreted in response to IFN γ , which mayor function is the macrophages activation in HCV infection. Our study shows higher levels of this protein in patients with chronic HCV infection, suggesting it could be used for evaluating the presence of this pathology on risk population. This work has been sponsored by Institute of Science and Technology of Mexico City. Project PIFUTP08-176 and SEP/PROMEP.

002

IDENTIFICATION OF MUTATIONS IN THE POLYMERASE GENE OF HEPATITIS B VIRUS (HBV) IN MEXICAN PATIENTS

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Background and aim. Therapy with nucleoside analogs (NAs) inhibits viral replication, but the resistance to antiviral drugs is one of the major concerns with the use of these treatments. To determine the presence of mutations in the reverse transcriptase domain (RT) of viral polymerase gene in Mexican patients with HBV infection. **Material and methods.** A blood sample was obtained from patients with chronic hepatitis B from the center and west of the country. RT region of the viral polymerase gene was amplified using PCR, the amplified products were sequenced by dye termination technique. **Results.** 11 samples have been sequenced. 82% corresponding to genotype H and 18% to genotype G; in 3/11 (27.3%) samples, were identified amino acid changes at sites identified as RT drug resistance. In a patient treated with LMV and infected with genotype H, I169M mutation was found instead of I169T as has been previously reported as primary resistance to ETV and secondary resistance to LMV. Also in two naive treated patients, drug mutations were found: in one patient infected with genotype G, the mutations M204V and L180M characteristics of primary resistance and compensatory to LMV were found; in the other patient infected with genotype H, the change identified was Q215E instead of Q215S as reported previously, which is a site of secondary resistance to LMV and ADV. **Conclusions.** New mutations (Q215E and I169M) were identified in the HBV genotype H in sites of antiviral resistance in naive and treated with NAs patients. Also, the classical mutations of LAM resistance in a naive treated patient with HBV genotype G were found. *In vitro* studies are needed to evaluate the effect of the mutations identified in genotype H in the viral replication and antiviral response. Resistance mutations may be present in untreated patients placing them in a risk group for empirical treatment failure.

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003

DISTRIBUTION OF SNP rs738409 [I148M] PNPLA3 GENE (ADIPONUTRIN) IN PATIENTS WITH HCV AND ITS IMPACT ON THE RESPONSE TO ANTIVIRAL TREATMENT

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Background. Hepatic steatosis is a clinically important in patients with HCV because it can accelerate the progression of hepatic fibrosis and reduce the response to antiviral therapy. **Aim.** To determine the distribution The SNP rs738409 G/C [I148M] PNPLA3 gene. GG is described as the risk genotype in patients with HCV treatment peg-IFN/RBV. **Material and methods.** 75 patients with HCV-1 and 15 HCV-treated peg-IFN/RBV \neq 1. rs738409 [I148M] was genotyping by Real-Time PCR LightCycler^{v2} and melting curves PCR-TR Light-Cycler ^{v2}. Descriptive statistics, medias and Kruskal-Wallis test $p < 0.05$ significant. SPSS v.15 (Table 1). **Conclusions.** The GG genotype of SNP rs738409 [I148M] associated with the development of hepatic steatosis, is of low prevalence in the cohort studied. However, it was observed that the CC genotype of this SNP, keeps significantly elevated levels of viral load during the first 12 weeks of treatment, should mention the SVR rate (40%) in this subgroup (CC) is at the expense of that 5/12 patients with SVR are carry HCV \neq 1, so it is important to assess the real impact on a larger number of patients with HCV -1 and rs738409 [I148M] PNPLA3 genotype CC. The authors declare that there is no conflict of interest.

004

CONTRIBUTION INOSIN TRIPHOSPHATASE (ITPA) GENE IN THE DEVELOPMENT OF HAEMOLYTIC ANEMIA, SECONDARY TO RIBAVIRIN IN HCV PATIENTS WITH ANTIVIRAL THERAPY

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Table 1. Genotypes of SNP rs738409[I148M] PNPLA3 (adiponutrin) in HCV with peg-IFN/RBV.

n = 90 (%)	Load viral Baseline	(RNA-HCV UI/mL)			ALT UL/L	AST U/L	Weight (kg)	Steatosis/*Activity/ *Fibrosis (*Metavir)	RVS (%)
		Week-4	Week-12						
GG (4.4)	4.55 E ⁵ ± 4.55 E ⁵	4.44 E ⁴ ± 5.96 E ⁴	6.93E ³ ± 5 1.38 E ⁴	P < 0.05 0.05	93 ± 48	104 ± 54	58.3 ± 7	2.5/3/3	50
GC (61.6)	1.89 E ⁶ ± 2.59 E ⁶	1,37 E ⁵ ± 3.37 E ⁵	8.36E ⁴ ± 3.44 E ⁵	0.01	86 ± 85	66 ± 45	71.2 ± 12	1.2/1/1	56
CC (34)	1.37 E ⁶ ± 2.05 E ⁶	1.37 E ⁶ ± 2.05 E ⁶	8.19 E ⁵ ± 4.02 E ⁶	0.865	78 ± 48	79 ± 72	70.8 ± 17	1/1.5/:2	40
P* < 0.05	0.377	0.345	0.98		0.122	0.122	0.020	0.101/ 0.096/0.116	

003. DISTRIBUTION OF SNP rs738409 [I148M] PNPLA3 GENE (ADIPONUTRIN) IN PATIENTS WITH HCV AND ITS IMPACT ON THE RESPONSE TO ANTIVIRAL TREATMENT.

Background. The peg-IFN/RBV is the standard care in HCV patients, however haemolytic anemia secondary to RBV compromises the SVR. Functional variants of the inosin triphosphatase (ITPA) gene could have a protective effect. **Aim.** Determine the contribution of genetic variants of SNP rs1127354 and rs7270101 ITPA gene in the development of haemolytic anemia in HCV patients in peg-IFN/RBV therapy. **Material and methods.** 88 patients with HCV, 38 men 50 women, age 55 ± 11.5 years baseline Hb of 15.8 g/dL. All patients were genotyped for SNP by PCR and real-time melting curves Light-Cycler v2. SPSS v15 for statistical analyses. **Results.** Distribution of genetics variants of rs1127354 SNP were; CC = 87.50%, CA = 12.50% and AA = 0%, frequency allele C = 0.93 and A = 0.062. The distribution of SNP rs7270101 were AA = 89.77% AC = 10.22% and CC = 00%, the frequency for allele A = 0.94 and C = 0.051. All patients reduced their Hb during the first 12 weeks of therapy but only 6.81% of the patients were homozygous for both risk alleles of SNPs (CC/AA) and developed hemolytic anemia severe (Hb < 10 g/dL), all are women, with HCV-1. The SNP rs1127354 CA has a PPV on SVR of 75%, with a specificity of 93.3% and the likelihood ratio of 3 on SVR while rs7270101 has a VPP of 86.74% on RVT, with sensitivity of 92% and likelihood of 4 on RVT. **Conclusions.** The results suggest that the simultaneous presence of risk alleles (homozygous) of both SNPs (CC/AA) is a precondition for the development of severe hemolysis. rs1127354/CA SNPs and SNP rs 7270101/AC of ITPA are protector genotypes but are very low prevalence in our population. However if the Hb basal is < 15 g/dL can reduce the risk of severe haemolytic anemia during antiviral therapy.

The authors declare that there is no conflict of interest.

005

SAFETY AND RESPONSE OF THERAPY WITH PEGINTERFERON ALFA 2B + RIBAVIRIN + BOCEPREVIR IN PATIENTS WITH CHRONIC C HEPATITIS, GENOTYPE 1 AND FAIL TO PREVIOUS TREATMENT

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Introduction. The recommended treatment in the patients with lack of response to dual therapy with peginterferon plus Ribavirin (Peg/R) is the triple combination that includes Peg/R and an inhibitor of protease (IP), with rates of sustained viral response (SVR) superior to 30%. Unfortunately in the initial studies of the IP the evaluation of Latin subjects is practically void. **Objective.** To evaluate the safety profile and response to triple therapy with Peg/R plus Boceprevir (BOC) in patients with prior treatment failure and advanced fibrosis (F3-F4) during the first 24 weeks. **Material and methods.** 20 patients were included (H: 18, M: 8, average age 51 years), 15 with genotype 1B and 5 1A. We excluded coinfecting patients and those with contraindications for Peg/R. The assessment of fibrosis was determined by liver biopsy and/or documentation of portal hypertension (esophageal varices). Twelve patients with fibrosis F4 and 8 with F3. The doses used for each drug, adjustments, duration of treatment and futility rules were re-

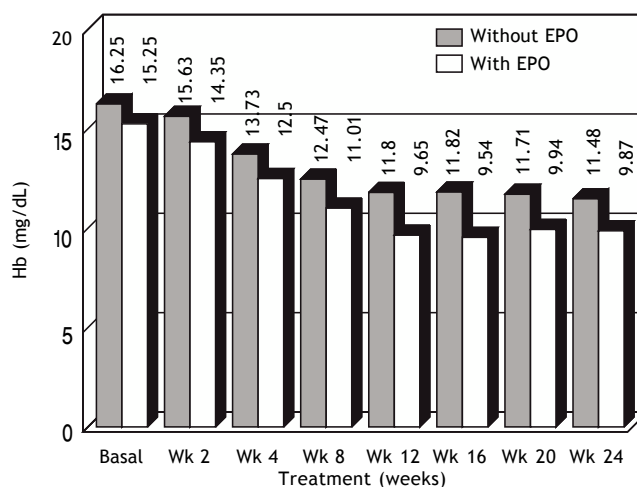


Figure 1. 005. Hemoglobine during triple therapy.

commended internationally. In addition to the adverse effects previously described for therapy with Peg/R, the most frequent side events were anemia (Hb < 10 g/dL, N = 6/20), dysgeusia (N = 12/20) and anorectal symptoms (N = 8/20). Figure 1 shows the hematologic evolution during treatment. 7/20 merited the use of erythropoietin in dosages of from 12,000 to 24,000 IU/wk. In 5/20 discontinued treatment, 1 withdrawal of consent and 4 futility rules, there were no serious adverse events or to warrant the suspension of therapy. Extended viral response was obtained in 15/20 patients. **Conclusions.** In this preliminary report, the use of triple therapy in Mexican patients with advanced fibrosis, failure to a previous scheme with Peg/R, showing a safety profile and viral response was similar to that reported in other ethnic groups. Studies related to genetic factors as predictors of response are ongoing.

The authors declare that there is no conflict of interest.

006

EFFICACY OF ENTECAVIR THERAPY IN PATIENTS WITH CHRONIC HEPATITIS B

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Introduction. Hepatitis B is a worldwide health issue, it's estimated that between 350 and 400 million people worldwide are surface antigen carriers. The first line therapy it's with tenofovir and entecavir, achieving virological response of 76 to 88% after 5 years of treatment. **Objectives.** Know response rate in our population on entecavir monotherapy treatment. **Material and methods.** In retrospective study, we included all patients with chronic hepatitis B treated with entecavir monotherapy for at least 12 months, from August 2010-February 2013, assessing HBV DNA, liver function tests and HBV serology, in 6th and 12th month of treatment, valuing virological, biochemical and serological response according the definition in EASL 2012 Guidelines. **Results.** We included a total of 19 patients, 7 were excluded for not meeting the inclusion criteria. 10 (83%) male patients, mean age of 48 years (range 25-73 years). 4 patients (33.3%) with E antigen (HBeAg)

negative. At 6 months of treatment 2 (16.6%) were non-responders, 7 (58.3%) with partial virological response and 3 (25%) with complete virological response. All patients had biochemical response and none had serologic response. At 12 months of treatment 3 (25%) were non-responders, 4 (33.3%) had complete virological response, and 5 (41.6%) remained with partial virological response. At the end of 12 months of treatment, all patients showed biochemical response and no patients had serologic response. In patients with HBeAg-negative complete virological response was 75% compared with 12.5% HBeAg-positive population. **Conclusions.** Treatment with entecavir monotherapy achieved a high biochemical response rate and moderate virological response rate at 12 months of therapy. Although it is known that the response rates are directly proportional to the length of treatment, reaching higher response rate after 5 years of treatment.

The authors declare that there is no conflict of interest.

007

COMPARISON OF ABBOTT IMX & AXSYM IN PREDICTING VIREMIA IN HCV POSITIVE PATIENTS THROUG THE S/CO RATIO OF THIRD GENERATION ELISA

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Background. The IMx and AXSYM assays for VHC were designed for the detection of antibodies against structural and no structural proteins of the HCV genome. The utility of the S/CO cut ratio of the ELISA techniques to predict viremia was recently described, however, in this cases it is indicated that the prevalence of the anti-HCV and the characteristics of the population of study must take into account. **Objective.** Investigate the S/CO cut ratio utility of the third generation ELISA in two ABBOTT equipment to predict viremia. **Material and methods.** A differential study was realized between the S/CO ratio of HCV negative subjects (n = 106) vs. HCV positive (n = 60) by using the ABBOTT IMx and AXSYM to analyze the samples, later, it was established if there was a correlation between the S/CO ratio and the viral load in each of the 60 HCV positive samples including the patients who requested their studies in the liver unit during June 2007 to March 2013, statistical analysis of the data was performed by student T test and Pearson's correlation analysis, the data was classified according to detection and no detection of HCV RNA by PCR. **Results.** The results of the S/CO in the groups with or without HCV, as well as the correlation of S/CO with the viral load in patients with HCV are shown on the table 1. **Conclusions.** It was established that in the analyzed patients by the IMx there was no relationship between the S/CO with the presence or absence of viremia as high S/CO (> 40) pre-

sented positive PCR and some others negative, however with AXSYM was established that patients with an S/CO > 20 always had positive PCR. Regarding the usefulness of the equipment to discard the presence of anti-HCV both showed S/CO < 1. Because currently monitoring the presence or absence of HCV is carried through of molecular biology techniques, which are expensive and complex, ELISA test could be useful for monitoring patients with HCV that get in antiviral therapy.

This work has been funded entirely by own resources

008

DIFFERENTIAL EXPRESSION IN MONONUCLEAR CELLS FROM ADIPONECTIN RECEPTORS ADR1 AND ADR2 DEPEND OF VIRAL GENOTYPE IN PATIENTS WITH HCV

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Background. Response to treatment of hepatitis C is highly variable and depends on viral and host factors. Adiponectin (ADQ) is an adipokine with hepatoprotective activity as it acts as a hormone involved in inflammatory and repair liver damage. It has been reported to inhibit TGF β 1 synthesis, decreases estosis and hepatomegaly. ADQ receptor has two isoforms ADR1 expressed in liver and ADR2 in muscle. **Objective.** To evaluate the association between ADQ expression of their receptors and leptin in peripheral blood of mononuclear cells (MNC) with biochemical and virological characteristics of patients with different genotypes of hepatitis C virus (HCV) treated with PEG-IFN + RBV. **Material and methods.** We included two study groups: 1) Patients with HCV infection (genotypes 1, 2 and 3) (n = 38, 14M and 24F), 2) Healthy control group (HC) (n = 27, 10M and 17F). mRNA expression of ADQ, ADR1 and ADR2 was determined in CMN by RT-PCR and ADQ and Leptine plasma levels by ELISA assay. We evaluated clinical, biochemical and virological parameters in the study groups. **Results.** ADQ mRNA expression was not found in MNC of both study groups. The ADQ protein values were similar between the different genotypes, showing a lower tendency in genotype 2b and 3a. ADR1 and ADR2, expression was higher in genotype 2b. ADQ levels were higher in women than in men. There was a positive correlation between body mass index and ADQ levels in all genotypes. The ADQ and leptin levels were higher in patients with HCV compared to the healthy group and Leptine high values were observed in genotype 1b. **Conclusions.** There is a difference in ADR1 and ADR2 expression in patients with genotype 2b, and leptin levels in genotype 1b. It is important to increase the number of subjects to establish an association with viral ge-

Table 1.*

Study group	n	S/CO IMx	S/CO Axsym	P	r
HCV negative	53	0.41 \pm 0.15	0.38 \pm 0.18	0.412	N/A
HCV positive	30	53.53 \pm 13.52	72.02 \pm 46.83	0.062	IMx r = 0.131, P = 0.48 Axsym r = 1, P < 0.001

* 007. COMPARISON OF ABBOTT IMX & AXSYM IN PREDICTING VIREMIA IN HCV POSITIVE PATIENTS THROUG THE S/CO RATIO OF THIRD GENERATION ELISA.

notype and to know more as these receptors are involved in the pathogenesis of the disease. This work was supported by CONACYT-CB2010-01-155082 (Rivas A.M.).

009

CLINICAL VALIDATION FROM THE MFAP-4 PROTEIN AS A MARKER OF HEPATIC SPECIFIC FIBROSIS

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Background and aim. Fibrosis is a response of the liver to injuries produced by variety chronic aggressions. Great interests exist to establish a noninvasive method for diagnosis and monitoring that provides alternatives to physicians and patients about the dynamic control of the disease. In an experimental model analyzed by expression microarray we detected the RNA of MFAP-4 protein, which normally favors pulmonary gas exchange (by binding to surfactant proteins); however, it has also a high expression level in the liver damage patients' sera. The aim of this work was determine the MFAP-4 serum level in patients with lung (chronic) and liver (acute and chronic) diseases, to validate it as a potential marker of liver specific fibrosis. **Material and methods.** We determined the presence of MFAP-4, by immunohistochemistry to establish its origin and cellular localization, measuring its expression level by ELISA in the serum from healthy individuals, CTL (n = 100) and patients with: idiopathic pulmonary fibrosis IPF (n = 32), AHA amebic liver abscess (n = 32) and hepatitis C, HCV (n = 30, F1-F4, Knodell). The results were analyzed with t test and Mann-Whitney, and compared the groups among them to determine the specificity and sensitivity of detection, using ROC curves. **Results.** The protein expression in human sera (ELISA) was heterogeneous. In subjects with HCV, fold change (FC) oscillated between 3.5 (F-0, F1) and 6.5 (F-IV). In patients with IPF, the FC was 1.5, a smaller value than the one detected in persons with minimal liver damage (F1 p < 0.001); while serum from patients with AHA showed similar levels to normal individuals (p < 0.001). Area under curve (AUC) analysis of comparisons (ROC) established: Ctl/F1 (0.994), Ctl/F4 (1.00), F1/F4 (0.942), FPI/F1-F4 (0.957) and AHA/F1-F4 (0.991), where sensitivity and specificity ranged from 93-100% and 84-100% respectively. **Conclusion.** Increased expression shown in serum of patients with chronic liver damage (ELISA) and the result of the assessment of sensitivity and specificity (> 90%), supports that MFAP-4 is valid as a noninvasive marker in liver specific fibrosis. This work was supported by funds provided by UNAM/PA-PIIT IN-205210 and SEP/CONACYT 84837.

010

EVALUATION OF ANTIOXIDANT SYSTEMS IN HUMAN HEPATOCARCINOMA CELLS INFECTED WITH THE HEPATITIS C VIRUS (HCV)

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Background. The mechanisms of cell damage caused by HCV have not been fully described. Oxidative stress plays an important role in HCV chronic infection. The cell has antioxidant systems such as glutathione and superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx) to counteract this action. **Aim.** Evaluating the modulation of antioxidant systems by using an in vitro model of HCV infection. **Materials and methods.** The human hepatoma cell line Huh7.5.1 was used. The viral production was performed using JFH-1 RNA transfection. Infected and uninfected Huh7.5.5 cells with HCV were lysed and total RNA and protein were extracted at 0-72h. The expression of viral proteins (core and NS3) and SOD system (SOD1 and SOD2) were detected by western blot, and further gene expression of SOD1, SOD2, CAT and GPx were detected by real time qPCR. Experiments were performed in triplicate. **Results.** A decrease in the SOD1 and SOD2 protein expression was observed from 48 h. In addition there was a decrease of 50% (p ≤ 0.05) for SOD1 at 72 h in infected cells, and at the same time there was an increase in the expression of viral proteins (core, NS3). There was no significant change in mRNA expression of SOD1, SOD2 and CAT enzymes; GPx mRNA decreased after 24h, subsequently at 72h showed a decline of over 50% (p ≤ 0.05). **Conclusion.** The presence of viral particles modifies protein expression profiles and antioxidant systems in infected cells, especially the SOD1 protein levels were down-regulated in infected cells and GPx mRNA levels showed the same pattern, while increasing expression of viral proteins (core, NS3). These findings demonstrate in part that the presence of viral particles alters the redox balance in infected cells and could be explained by the decrease of these systems that are essential in antioxidant defense.

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011

DIFFERENTIAL REGULATION OF COX-2 IN HEPATOCYTE CELL LINES PROMOTE DIFFERENT CELLULAR PERMISSIVENESS ASSOCIATED TO CAPACITY OF HCV REPLICATION

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Introduction. It has been reported an increase in mRNA of cyclooxygenase-2 (COX-2) in cells expressing HCV proteins compared to normal cells, suggesting that HCV regulates COX-2 transcription. **Objective.** To evaluate the involvement of viral structural proteins (E2) and nonstructural (NS5A) HCV in regulating expression of COX-2 in different hepatocytes cell lines. **Material and methods.** Transfection assays were performed in cell lines Huh-7 and HepG2 cells with the plasmids pFK1, pNS5A and pE2. Total proteins were extracted at 0-48h post-transfection. We performed cotransfection with pCOX-2 and expression was evaluated at 36h by Western blot. In addition, we evaluated the expression at transcriptio-

nal level by real-time PCR using Taqman and Sybergreen probes, GAPDH was measured to normalization. All assays were performed by triplicate. **Results.** We observed a differential regulation of COX-2 in both cell lines. The COX-2 expression increased compared to respective controls in both cell lines transfected with pFK1, pNS5A and pE2. Cotransfection of Huh7 cells with pFK1 and pCOX2 increased COX2-RNA, HCV-RNA and COX-2-protein levels, whereas in transfected HepG2 cells, COX-2 protein and HCV-RNA levels were lower than the COX2-RNA levels found in Huh-7. In cotransfected Huh-7 cells with pNS5A and pCOX2 we found increasing levels of COX2-RNA, NS5A-RNA and COX-2 and they were directly proportional to the quantity of plasmid used, unlike what was observed in transfected HepG2 cells where we found that levels of COX-2 and RNA were lower. Huh-7 cells cotransfected with pE2 and pCOX2 decreased RNA-E2 and COX-2, however in HepG2 cells RNA-E2 levels and COX-2 protein were higher compared with those found in Huh-7. **Conclusions.** HCV proteins differentially regulate the transcription of COX-2 in the two cell lines. The HCV-NS5A protein increased the level of COX-2 in Huh7 cells compared to HepG2, while E2-HCV decreased COX-2 levels in Huh7 compared to HepG2. Each of the cell lines differentially regulated signaling pathways of COX-2 in response to the presence of HCV. No conflicts of interest between the authors. This work was subsidized by CONACYT CB2010-01-155082 awarded to PhD. AM Rivas.

012

EFFECT OF ACETYLSALICYLIC ACID ON PROTEIN/HELICASE NS3/4 PROTEASE ACTIVITY OF HEPATITIS C VIRUS (HCV)

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Background. Hepatitis C virus (HCV) infects approximately 3% of the world population. Persistent infection is associated with chronic hepatitis, fatty liver, liver cirrhosis and hepatocellular carcinoma. HCV is a virus of enveloped RNA of positive polarity, which encodes a polypeptide containing 10 individual proteins. Current therapy is the use of alpha-PEG interferon and ribavirin plus one of the NS3 protease inhibitors, but not all the patients get cured, for this reason new therapies are required. The NS3/4A protein is an ideal therapeutic target since it has two independent activities involved in the replication of the virus, protease and helicase activity. It was noted that acetylsalicylic acid (ASA) inhibits the replication of the virus but its mechanism of action is not known. **Aim.** To determine if there was an effect of ASA on the protein NS3/4A protease and helicase activities. **Material and methods.** *In vitro* assays for the determination of the effect of different concentrations of AAS activities were carried out using different concentrations of the pure protein and were measured by a specific ELISA assay. In addition, we assessed the effect that different concentrations of AAS had on the protease/helicase activity in Huh7 replicon cells at different time of exposition by using ELISA assay. **Results.** Our ELISA data showed that there is not an inhibition by acetylsalicylic acid in any of the two activities helicase/proteinase of the NS3/4A protein *in vitro*. On the other hand, experiments performed on Huh7 replicon cells showed an inhibition of the protease activity of

around 20% and a decrease in the helicase activity of 5% when the cells were exposed to different concentrations of acetylsalicylic acid until 72h. **Conclusion.** It can be concluded that the mechanism of action of AAS on viral replication is not directly on the NS3/4A protein, however, in the cell line expressing HCV proteins, both activities were affected, indicating that the effect exerted by the AAS is an indirect effect.

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013

S-ADENOSULMETHIONINE (SAM) EFFECT ON THE HCV REPLICATION AND ANTIOXIDANT ENZYMES EXPRESSION IN HUH7 REPLICON CELLS

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Background and aim. HCV can cause cellular damage by increasing oxidative stress and reactive oxygen species generation. Liver antioxidant enzymes, like superoxide dismutases (SOD1 and SOD2) and catalase, counteract this damage. Recently it was reported that S-adenosylmethionine (SAM), decreases the levels of HCV RNA and proteins, however, the mechanism involved remains unknown. The aim of this study was to evaluate the effect of SAM on the levels of viral RNA and proteins, and antioxidant proteins such as, SOD1, SOD2 and catalase in cells expressing HCV. **Material and methods.** Replicon Huh7 cells were pre-treated for 2 h with SAM 800 nM, and then added the standard treatment, PegIFN- α (1,000 IU) and RBV (50 μ M). Total RNA and protein was extracted at 24-72h. cDNA was synthesized and qPCR was performed to quantify the HCV RNA using TaqMan probes and the $\Delta\Delta C_t$ method. GAPDH was used as normalizing gene. Protein expression was assessed by western blot using anti-NS5A, anti-SOD1, anti-SOD2, anti-catalase and anti-actin as control. **Results.** At transcriptional level, SAM reduces the viral RNA at 24 h, similar to standard treatment. By combining this treatment the effect is enhanced and decreased stays at 48 and 72 h post-treatment. At translational level, there is a decrease in viral protein NS5A in SAM treatment and is comparable to standard treatment. By combining the treatments, there is a greater effect in the three times studied. Antioxidant proteins, SOD1 and SOD2 expression increased in the presence of SAM, standard treatment and / or combined, compared with the untreated control. The catalase expression is not altered by the treatment. **Conclusions.** SAM modified HCV expression, at transcriptional and translational level, and this effect is comparable with the standard treatment. The antioxidant proteins SOD1 and SOD2 might be involved in the mechanisms of antiviral action of SAM, changing cellular oxidative stress levels.

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014

EVALUATION OF THE EFFECT OF THE GALLIC ACID ON THE REPLICATION OF HEPATITIS C VIRUS (HCV)

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Background. Gallic acid (GA) is a phenolic compound present in natural sources including plants, fruits and vegetables. It has various applications in industry, where it is used mainly as an additive to prevent oxidative food deterioration. In addition, it is used in pharmaceutical industry as an intermediate for the manufacture of trimethoprim. Furthermore, it has various biological effects such as anti-inflammatory, antibiotic, anticancer, antiviral and cardiovascular protection. **Aim.** We investigated the GA effect in the negative regulation of hepatitis C virus (HCV) by using the subgenomic replicon cell system (Huh7-HCV-replicon) that expresses HCV-nonstructural proteins and the Huh7 parental cell line. **Material and methods.** Cells were exposed to 300 μ M GA at different times (0-72 h). We evaluated GA cytotoxicity in both cells lines by MTT assay. Also, we analyzed the expression of NS5A HCV-nonstructural protein and HCV-RNA post-treatment by western blot and real-time PCR, respectively. Reactive oxygen species (ROS) production were measured to evaluate oxidative stress. In addition, we tested the GA cytotoxicity in human blood cells. Whole blood hemolysis levels were assessed by spectrophotometry in order to evaluate GA toxic effect. Peripheral blood leukocytes were treated with different concentrations of GA, and cell viability was determined. Experiments were performed in triplicate and analyzed using a Tukey test ($P < 0.05$). **Results.** Blood cells treatment with GA showed an LD_{50} of $2.360 \pm 4.3 \mu\text{g/mL}$ without statistically significant hemolysis. We observed that GA treatment did not generate toxicity in the Huh7 cell lines. NS5A protein showed a decreased expression compared to the control without GA at 48 h. Furthermore, GA modulates virus replication (HCV-RNA) negatively (nearly 50%) at 48-72h. We found that GA treatment decreased ROS production in the HCV subgenomic replicon cell system like the cells treated with a potent oxidant (PDTG). **Conclusions.** These results suggest that GA treatment reduce the *in vitro* expression of HCV-RNA and NS5A protein, and at the same time it decreases oxidative stress without affect cell viability. For this reason GA could be a potential candidate as adjuvant in the treatment of chronic HCV infection.

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015

PREDICTIVE VALUE OF THE RAPID VIRAL RESPONSE AND CORRELATION WITH SUSTAINED VIRAL RESPONSE IN MEXICAN PATIENTS UNDERGOING NAÏVE ANTIVIRAL TREATMENT WITH CHRONIC HEPATITIS C GENOTYPE 1

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Introduction. The genotype of hepatitis C is considered a predictor of effectiveness of antiviral treatment. Response rates are lower in genotypes 1 and 4. The rapid viral response (RVR) is a predictor of sustained viral response (SVR) when compared with viral load and genotype. **Objectives.** To determine the correlation of RVR with SVR in Mexican patients undergoing naïve antiviral treatment for chronic hepatitis C genotype 1. **Material and methods.** The study was clinical, descriptive, transversal, and prospective. Patients with chronic hepatitis C genotype 1 were analyzed for: RVR, rate of end of treatment response (ETR), and SVR. Viral load determinations were performed using a Real-Time PCR method (TaqMan Cobas, Roche Diagnostic), with a 50 UI cutoff. Biochemical characteristics and viral kinetics were compared between groups. We used Fisher's exact test for nominal variables and used Student t test for quantitative variables. **Results.** In total, 23 treatment-naïve patients with chronic hepatitis C genotype 1 were treated with pegylated interferon and ribavirin. The average age was 47.6 years; 100% underwent at least 80% of the total dose. Women accounted for 73.9%, while 78% had a history of previous transfusions. The mean body mass index was 28.3 m2SC. The mean baseline viral load was 1,772,770 Log 5.5, and 43.4% had high viral load ($> 400,000$ IU). The RVR was achieved in 47.8%, SVR in 78.2%, relapse in 4.3%, and 17.4% were not responded. Of the patients who achieved RVR, 43.5% achieved SVR, whereas inpatients who did not achieve RVR, only 34.8% achieved SVR. **Conclusions.** The RVR as predictor of sustained virological response in our population was lower compared to the literature, as it has a negative predictive value of 80%. The authors declare no conflicts of interest.

016

ANALYSIS OF THE FUNCTIONAL RESTORATION OF T LYMPHOCYTE CD3+CD8+ IN PATIENTS WITH HEPATITIS C UNDER STANDARD TREATMENT

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Background and aim. Standard treatment for the infection with hepatitis C virus (HCV) is the administration of pegylated interferon and ribavirin; however, it is only successful in 40% of the patients. The quantity of T lymphocyte (TL) CD3+CD28- and CD3+CD279+ is higher in chronic infection and its associated with cellular dysfunction. It has been demonstrated that without dysfunction, TL CD3+CD8+ are able to clear the virus during acute infection. The aim of this study is to determine the treatment effect over the functionality of LT and its relation with the genotype and viral load in patients HCV+ under standard treatment by monitoring LT functional markers. **Material and methods.** An observational pilot study is performing with HCV+ patients under standard treatment. A basal blood sample is collected and 3 samples more are collected corresponding to 4, 12 y 24 weeks of treatment ($\pm 1, \pm 2, \pm 3$). The population of TL CD3+CD8+ CD28- and CD279+ are determined by flow cytometry, viral load and genotype are determined by commercial tests. **Results.** The average of percentage basal of LTCD3+CD8+ CD279+ y CD28- in our patients is 45% and 35% respectively. By the mo-

ment, the LTCD3+CD8+CD28- not shows differences. The LTCD3+CD8+CD279+ in *t1* decreases a 15-20% respect of basal value in the 40% of the patients. In *t2* this same population decreases a 30-60% respect of basal value in the 90% of the patients until now included. The genotype and basal viral load could be related with the response in *t1*, however it is necessary a higher size sample for a suitable analysis. **Conclusions.** The functional restoration of LTCD3+CD8+ could be related with the success of the treatment and the dimension or irreversibility of this damage could be one of the reasons of the genotype-associated failure. Whereby, the generation of adjuvant therapies that restores the cellular function could increase the success of standard treatment. Authors declare no interest conflict.

017

FREQUENCY OF RAPID VIRAL RESPONSE AND ITS CORRELATION WITH SUSTAINED VIRAL RESPONSE IN MEXICAN PATIENTS WITH CHRONIC C HEPATITIS GENOTYPE 2 AND 3 UNDER STANDARD TREATMENT

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Background. Chronic hepatitis C virus (HCV) is a major cause of liver disease and a public health problem. The chances of achieving sustained viral response (SVR) ranging between 76-84% for genotype 2 and 3. Having tools to assess the possibilities of response to treatment, such as rapid viral response (RVR) can improve the management of these patients. **Objectives.** To evaluate the frequency of RVR and its correlation with sustained viral response in Mexican patients with chronic hepatitis c genotype 2 and 3. **Material and methods.** All the patients with genotype 2 and 3 who started standard treatment with pegylated interferon (IFN) alpha 2a 180 µg/subcutaneous/week and pegylated interferon alpha-2b 1.5 µg/kg/subcutaneous/week and ribavirin 800 mg/day fixed dose, during January 2009 and August 2011. We determined the presence of RVR (undetectable viral load at week four of treatment) of the end of treatment response (ETR undetectable viral load at the end of antiviral therapy) and the presence of SVR (undetectable viral load six months after completion antiviral treatment), all viral load determinations were performed using Real-Time PCR method Cobas TaqMan, Roche Diagnostic, with a cutoff of 43 IU. **Results.** 32 patients with mean age of 54.46 years, all met at least 80% of the dose of PEG IFN and ribavirin, 56.3% were women, 93.7% were genotype 2 and 6.3% genotype 3, the mean baseline viral load was 1,621,662 IU LOG 5.59 and 62.5% had high viral load (> 400,000 IU). The RVR was achieved in 68.75% of patients and SVR in 65.6% of cases, relapse in 25% and 9.37% of the cases

were non-responders. Of the patients who achieved RVR reached 72.7% SVR and patients who did not achieve RVR 50% presented therapeutic failure. **Conclusions.** Rapid viral response is achieved less frequently in our population as well as sustained viral response than that reported in the literature of patients with genotype 2 and 3.

Authors declare no interest conflict.

F. CHOLESTASIS AND CHRONIC AUTOIMMUNE LIVER DISEASE

001

OVERLAP SYNDROME OF AUTOIMMUNE HEPATITIS AND PRIMARY BILIARY CIRRHOSIS WITH ATYPICAL INITIAL PRESENTATION AS ACUTE LIVER FAILURE

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Background & aim. Acute liver failure is an uncommon condition in which rapid deterioration of liver function results in altered mental status and coagulopathy in individuals without known pre-existing liver disease. Most frequent causes include drug-induced liver injury, and viral hepatitis. Autoimmune hepatitis (AIH) and primary biliary cirrhosis (PBC) are two well-described distinct autoimmune mediated liver diseases, and called overlap syndrome (OS). Development of acute liver failure as the initial presentation has been reported for cases of AIH, while no cases for PBC alone. Here, we present a case of OS of AIH and PBC presenting to our hospital due to acute liver failure. **Case report.** A 37 year-old male present to the hospital with painless jaundice, and he developed grade 3-4 hepatic encephalopathy seven days after onset of jaundice requiring admission to the intensive care unit for intubation and mechanical support. Laboratory test showed AST: 3377 IU/L, ALT: 7,541 IU/L, total bilirubin 7.6 mg/dL, prothrombin time (PT) 44/11.9 sec. Imaging studies of the biliary tree showed absence of dilatation. Serological test for hepatitis A, B and C were negative. Serology for CMV and EBV were negatives too. Antinuclear antibodies were positive titles of 1:160 with speckled immunofluorescence staining pattern, and the antimitochondrial antibodies were positive titles of 1:80. Also, IgG levels were high in 1,810 mg/L. Liver biopsy showed interface hepatitis with lymphocytic infiltrate, with biliary ductal damage and cholangiocyte proliferation. Using the simplified criteria score for AIH, the patient had 6 points. The patient received prednisone 60 mg/day. Being discharged from the hospital 28 days length of stay with normal liver bio-

Figure 1.*

ANA	IFI (%)	AMA ELISA (%)	IFI (%)	LKM ELISA (%)	IFI (%)	ELISA (%)
Sensitivity	78	90	82	59	100	100
Specificity	73	64	58	85	100	100
PPV	88	80	35	92	100	100
NPV	56	80	92	95	100	100

* 004. UTILITY OF THE TECHNIQUE ELISA IN THE DETERMINATION OF AUTOANTIBODIES IN AUTOIMMUNE LIVER DISEASES.

chemistries. Currently, two years the episode of acute liver failure he is asymptomatic, with no clinical or biochemical finding suggestive of chronic liver disease, and only receiving ursodeoxycholic acid for treatment. **Conclusions.** Acute liver failure initial presentation of overlap syndromes of autoimmune hepatitis and primary biliary cirrhosis is extremely rare. This case report emphasizes that in cases of acute liver failure of unclear etiology, OS although rare, might be considered as potential treatment responsive condition. Authors declare no interest conflict.

002

AUTOIMMUNE HEPATITIS-PRIMARY BILIARY CIRRHOSIS OVERLAP SYNDROME: A RETROSPECTIVE STUDY IN A THIRD LEVEL HOSPITAL IN MEXICO

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Background and aim. Overlap syndromes do not have straight forward diagnostic criteria or therapeutic recommendations. Autoimmune hepatitis-primary biliary cirrhosis overlap is 7-13% of all autoimmune hepatitis cases, and is suspected when a patient with AIH has antimitochondrial antibodies, cholestasis or bile duct injury in biopsy. Paris Criteria's sensibility and specificity for AIH/PBC overlap are 92 and 97%. Other autoimmune diseases are found in 43% of these patients, they have ASMAs in 10%, IgM elevation in 42% and positivity for both, ds-DNA and antimitochondrial antibodies in 47%, with specificity of 98%. In Mexico the MHCDB1*07 is capable of distinguishing patients with overlap from those with AIH-1, more information is needed about these patients in our country. **Material and methods.** Observational, retrospective study. An search was performed regarding hospital records looking for HAI/PBC overlap, we found 24 cases. **Results.** AIH/PBC diagnosis was based on AIH with cholestasis (alkaline phosphatase ≥ 2 ULN and/or GGT ≥ 5 ULN) and a concordant biopsy, PSC was excluded with a biliary tract study. The median for age at diagnosis was 49 years (23-67), 88% were female. None of the patients had cirrhosis (F4). Total bilirubin levels were 3.5mg/dL (0.3-31), alkaline phosphatase 449U/L (58-2219), GGT 439 (24-1665), antimitochondrial antibodies were positive in 9/24 with levels of 83 (5-258), IgM 537 mg/dL (16-1710), ALT 125, AST 132 and albumin 3.5 g/dL. One third had positive ANAs with no predominant pattern, one patient had ASMA. Concerning symptoms 38% had pruritus, 58.3% fatigue, 17% arthralgias and jaundice each, one case had hyperpigmentation, one Sjögren and one Crest. Mean follow-up period was 38 months (7-93), two patients died of complications related to their hepatopathy (progression). All patients received prednisone and ursodesoxycholic acid. **Conclusions.** A low prevalence of ASMA and autoimmune comorbidities was found. Diagnosis was mainly based on the cholestatic pattern found in most of these patients. It is necessary to compare the characteristics of these population with those of patients with either AIH or PBC in order to validate diagnostic criteria for this condition in our country and to determine if there is any additional marker that can help us distinguish between these entities (HAI/PBC) when approaching a patient with HAI and cholestasis. Authors declare no interest conflict.

003

CD138: NEW MARKER FOR DIAGNOSIS AND EVALUATION OF AUTOIMMUNE HEPATITIS (AIH)

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Background. In AIH biochemical and immunological alterations are insufficient for diagnosis. Liver biopsy is needed. The histological characteristic finding, is interface hepatitis. In addition to portal plasma cells (PC) and lymphocytes. Being the formers the most useful diagnostic criteria. It has been reported that 34% of patients do not have PC and in Mexican patients it is presumed, that may be higher for unknown reasons. PC use to be determined only with hematoxylin-eosin stain (HE), is currently unknown role of CD138 (PC immunohistochemical marker) in the assessment of HAI. **Objectives.** To determine whether differences exist between the number of CP determined by HE and CD138. To establish the association between the degree of CP found with CD138 and disease progression. **Material and methods.** This is a retrospective study; we reviewed liver biopsies diagnosed with HAI from 2008 to 2011. Clinical data were collected from the records. **Results.** 39 biopsies were reviewed, in the HE group the mean was 5.28 CP, in the group of CD138 was 14.48 CP. The T student reported $p < 0.0001$, 95% CI 7.04-11.35. Comparing the level of IgG with the value of CD138 in 16 patients, the T student stated $p < 0.0001$, 95% CI 2054.64-3209.61. We followed 21 patients for 6 months, 22 patients for 12 months and 16 patients for 36 months, the value of CD138 was divided into ≤ 10 and > 10 and related to treatment response, defined as transaminases < 60 UI/mL, found χ^2 with Yates correction of 0.039 (p 0.84), 0.002 (p 0.96) and 0.08 (p 0.77) respectively. In 37 biopsies we calculated the degree of fibrosis (1-4) and correlated with the value of CD138, finding a Spearman correlation of 0.35. **Conclusions.** The marker CD138 allows for greater identification of CP compared with H&E. CD138 is associated with the IgG levels, but it was not associated with the degree of fibrosis and we require a larger sample to determine if it is associated with treatment response. This is the first study to evaluate the role of CD138 in patients with AIH. There are others antibodies who are reported to be useful like CD138, further research must be done. The authors declare that there is no conflict of interest.

004

UTILITY OF THE TECHNIQUE ELISA IN THE DETERMINATION OF AUTOANTIBODIES IN AUTOIMMUNE LIVER DISEASES

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Background. Autoimmune hepatitis is a hepatocellular inflammation often associated with polyclonal hypergammaglobulinemia, various circulating autoantibodies as immunogenetics predisposition. Usually used indirect immunofluorescence technique for detection of autoantibodies and if they are positive is recommended more specific tests to determine which antigens are directed against autoantibodies, and therefore used as the ELISA test. **Objective.** Investigate if both techniques are reliable and comparable for the detec-

tion of autoantibodies. **Material and methods.** We conducted a descriptive study comparing two diagnostic techniques (ELISA and indirect immunofluorescence) for the detection of antinuclear antibodies (ANA), anti-mitochondrial antibodies (AMA) and anti-liver-kidney microsome antibodies (LKM). We included 123 patients (256 samples) diagnosed with autoimmune hepatitis, 91 (74%) subjects were female and 32 (26%) male, aged 18 years. ANA was determined in 78 patients, AMA in 84 and LKM in 85 by both techniques. **Results.** The autoantibody LKM was more sensitivity, specificity and concordance (100%) between the two techniques discussed, followed by the ANA. The ANA counted by ELISA with a sensitivity of 90%, and a specificity of 64%. The AMA by ELISA had a sensitivity of 59%, with 82% of specificity (Table 1). **Conclusions.** It was established that the ELISA is a useful methodology for ANA and LKM favoring lower costs for determining these autoantibody. The LKM was autoantibody more sensitivity, specificity and agreement between the two techniques, followed by ANA and established that the AMA ELISA technique was useful only in subjects with high titers by IFI. This work has been supported by PAICYT.

005

FEBRIL SYNDROME INICIAL PRESENTATION OF WILSON DISEASE. CASE REPORT AND REVISION OF LITERATURE

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Introduction. The Wilson disease (WD) is an autosomal recessive genetic disorder associated with copper metabolism protein with impaired ATP7B and they have discovered more than 200 mutations of the responsible gene. The possibility is 1 in 3000 individuals, with a genetic variation of 0.3% and 0.7%. With a hepatic manifestation in 42%, from mild elevation of aminotransferases in asymptomatic individuals and occasionally full liver damage, neurological in 34%, Hematological in 12%. The clinical diagnostic and the laboratories findings are low ceruloplasmin serum even though it could be normal in 5-15% of the patients acute phase, Increasing the level of copper in the urination and the hepatic contents. The histology is little specified. The treatment with a chelating agent is (penicillamine or trientine) through out there whole life and liver transplantation in patients with fulminant disease. **Clinical case.** 36 yr old male, with history of two cases of jaundice syndrome at 10 and 12 years. Initiated with febril syndrome at 38-39 degrees, Diaphoresis, arthralgias and myalgia of 3 month of evolution. 7 days previous to his ingress with generalized jaundice, coluria without acoli. To his admission to jaundice with renal failure and anemia with BT of 11.4 mg/dL. AST 36 U/L ALT 33U/L, with normal coagulation, HB of 6.2 mg/dL, HTO 18 mg. Performed with serum ceruloplasmin value of 24 mg/dL, Copper in urine of 359 µg/24 h. Negative coombs. Hepatic biopsy with a positive

report of orcein staining. The ring of Kayser Fleischer absent. It initiate treatment with penicillamine with the majority of symptomatology and normalization of biochemical patterns. **Conclusions.** The disease of Wilson is a rare hereditary disorder, with a hepatic affectation, with neurological symptom and on Kayser Fleischer that are present in 55 to 70% of the patients with hepatic disease. Neurological symptoms and rings of Kayser Fleischer. That presented in 55-70% of the patients with hepatic disease. The symptomatology is the result of any bodily organ where copper deposits. The clinical manifestations are varied by the diagnostic is difficult and delayed. Hence the importance of presenting our case and ictericia, syndrome febril with normal levels of ceruloplasmin serum. The authors declare that there is no conflict of interest.

006

CHARACTERISTICS OF OVERLAP SYNDROME IN MEXICAN POPULATION. LIVER CLINIC, HOSPITAL GENERAL DE MÉXICO

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Introduction. The overlap syndrome include autoimmune hepatitis (AIH), associated with primary biliary cirrhosis (PBC) or primary sclerosing cholangitis (PSC). With prevalence of 4.8 to 19% of patients with PBC and 5 to 8.3% of patients with AIH. Presents cholestatic pattern and hepato-cellular, positivity for autoantibodies: antinuclear (ANA), anti-smooth muscle (SMA) and mitochondrial (AMA), more PBC, AIH histology or PSC, progressive evolution to liver failure. Nonspecific symptoms, fatigue, arthralgia and myalgia. To diagnose criteria used Chazouillères, *et al.* Empirical therapy is ursodeoxycholic acid plus corticosteroids and/or azathioprine. **Objective.** Characterizing Mexican patients with overlap syndrome. **Material and methods.** Cross-sectional study were collected and analyzed data from patients who met diagnostic criteria Chazouillères, *et al.*, for overlap syndrome Liver Clinic, Hospital General de México from 2009-2012. Descriptive statistics were used. **Results.** Of 3,800 patients first identified 10 cases (0.26%), all with PBC more AIH, none PSC. 90% female, age at diagnosis was 43.7 ± 9.73 years, adynamia and asthenia in 90%, arthralgia 80%, nausea 70%, 50% jaundice and itching 40%; biochemical parameters are shown in table 1. Two patients had both AMA and SMA positive, IgG is present at twice the upper limit of normal in 70%. Liver biopsy in 4 patients showed interface hepatitis, lymphoplasmacytic infiltrate, plasma cells, bile duct injury and granulomas 3 scleroderma patients had dermatomyositis. **Conclusion.** Similar to published frequency overlap syndrome is very low (0.26%), the prevalence was in women with a 9:1 ratio, the association was always AIH+ PBC, we find PSC, most of our patients had antimitochondrial antibodies and positive antinuclear while SMA occurred only in a small proportion, hypergammaglobulinemia was a distinctive finding in most of our patients. It is not rare asso-

Table 1.

ALT (U/L)	FA (U/L)	GGT (U/L)	BT (mg/dL)	AMA	ANA	SMA
185 ± 85	417 ± 273	440 ± 380	4.3 ± 6.2	90% +	70% +	30% +

* 006. CHARACTERISTICS OF OVERLAP SYNDROME IN MEXICAN POPULATION. LIVER CLINIC, HOSPITAL GENERAL DE MÉXICO.

ciation of this syndrome with other autoimmune diseases, as evidenced by our series of cases.

The authors declare that there is no conflict of interest.

007

ANALYSIS FROM CHARACTERISTICS OF MEXICAN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS TREATED WITH URSODEOXYCHOLIC ACID

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Background. Primary biliary cirrhosis (PBC) is a chronic progressive cholestatic liver disease that affects interlobular and intraseptal bile ducts. ursodeoxycholic acid (UDCA) seems to be the drug most effective to treat these patients. **Aims.** To describe the characteristics from Mexican patients with primary biliary cirrhosis treated with UDCA, and to compare changes in liver function tests (LFT) between basal, six months, and one year after treatment with UDCA. **Material and methods.** We analyzed retrospectively data from 40 patients with PBC, data was expressed as media and standard deviation for numeric variables and as proportion and percent for categorical variables. In 17 patients also we compare changes in LFT between baseline, six-month, and one-year after treatment with UDCA. **Results.** We included 40 females with PBC, age 56.1 ± 12.4 years, BMI 24.4 ± 4 kg/m². Main symptoms: pruritus 31 (77.5%), jaundice 5 (12.5%), fatigue 4 (10%). One woman had history of fractures associated with osteoporosis. Ultrasonography shown cirrhosis 21 (52.5%), steatosis 14 (35%), normal 5 (12.5%). Ascites was present in 23 (57.5%), small esophageal varices in 14 (35%) and large in 13 (32.5%). Within patients with varices, 3 (11.1%) had history of variceal bleeding. Changes in LFT are showing in table 1. **Conclusions.** Main changes in LFT with UDCA treatment seems to occur on GGT and AP, that are markers form cholestasis. Interestingly, changes in bilirubin were not observed.

The authors declare that there is no conflict of interest.

Table 1. 007. ANALYSIS FROM CHARACTERISTICS OF MEXICAN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS TREATED WITH URSODEOXYCHOLIC ACID.

LFT	Baseline(A) n = 17	Six months after (B) n = 17	One-year after (C) n = 17	P value Comparison between A and B	P value Comparison between A and C
BT (mg/dl)	3.6 \pm 7.5	2.6 \pm 5.0	2.2 \pm 4.2	0.17	0.13
AP (U/L)	438 \pm 383	310 \pm 187	237 \pm 126	0.14	0.03
GGT (U/L)	238 \pm 203	215 \pm 202	158 \pm 122	0.04	0.01

AP: alkaline phosphatase. GGT: gamma glutamil transpeptidase.

Table 1.* Early biochemical response according to treatment (1 month).

	Group I: UDCA (n = 55)		Group II : pre-UDCA era (n = 38)	
	Baseline characteristics	Post-treatment characteristics	Baseline characteristics	Post-treatment characteristics
Alkaline phosphatase (IU/mL)	497.8 (137-2,166)**	396.0(74.0-1,898.0)**	549.1 (190-3773.4)**	310.5 (77.0-1,678.0)**
Albumin (g/dL)	3.5 (2.1-4.8)**	3.4 (2.2-4.7)**	3.5 (2.0-4.9)**	3.5 (0.3-4.6)**
Bilirubin (mmol/L)	1.8 (0.4-14.4)**	1.4 (0.33-19.4)**,**	2.0 (0.4-26.5)	3.5 (0.7-21.4)**
AST (IU/mL)	99.0 (29.0-797.0)**	77.0 (23.0-262.0)**	115.3 (28.8-849.2)	83.0 (29.0-215.0)
ALT (IU/mL)	91.0 (14.0-867.6)**,**	69.0 (20.0-194.0)**	114.7 (35.3-838.2)**,**	88.5 (20.0-249.0)**

* 008. URSODEOXYCHOLIC ACID THERAPY IMPROVES SURVIVAL OF NON-CAUCASIAN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS WITH LIMITED LIVER TRANSPLANTATION AVAILABILITY ** p < 0.05 (Wilcoxon test). Baseline vs. post-treatment. *** p < 0.05 (U Mann Whitney test). Group I vs. group II.

008

URSODEOXYCHOLIC ACID THERAPY IMPROVES SURVIVAL OF NON-CAUCASIAN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS WITH LIMITED LIVER TRANSPLANTATION AVAILABILITY

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Introduction. Survival information of primary biliary cirrhosis (PBC) patients and the response do to the introduction of ursodeoxycholic acid (UDCA) treatment is limited. **Aim.** To compare the survival of patients with PBC using UDCA *vs.* other treatment prescribed. **Material and methods.** 93 patients were included, diagnosed with clinical, histological and immunological criteria. Patients were followed at least for 5 years after the initial diagnosis and death related to liver disease was recorded during this time. Patients were divided into two groups: group I (n = 55) received treatment with UDCA (15 mg/kg/per day); group II (n=38) received other treatment (Colchicine, Cholestyramine, Penicillamine, Azathioprine, or prednisolone) before introduction of UDCA in Mexico. For survival analysis, Kaplan Meier method was used for survival curves, log-rank test for univariate comparisons, and Cox proportional hazard model for multivariate analysis. **Results.** The mean age in Group I was 45.0 ± 12.6 yr and 48.4 ± 10.5 yr in group II. 18% of Group I had cirrhosis at the moment of diagnosis and 13% of the group II. No differences were found at baseline in cholestatic clinical and biochemical characteristics. After 1 month of treatment, the group I show response at the very early period of treatment, having a significant decrease of the levels of bilirubin and AST; while in both groups the concentrations of ALT diminish (Table 1). After 5 years of follow-up, the survival probability was 82.6% in patients treated with UDCA while was only 42.5% in patients who received any other treatment (p = 0.0001) (Figure 1). Only group of

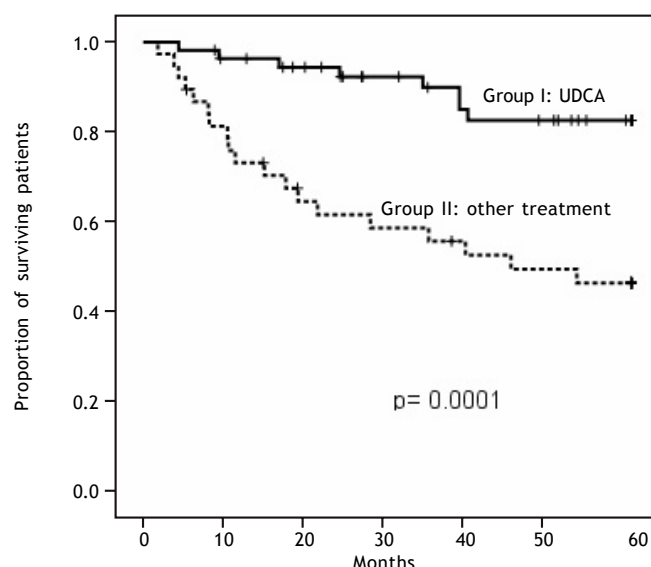


Figure 1. 008. PBC patient survival according to UDCA treatment. Cumulative probability of survival in PBC for 5 years according to treatment.

treatment was predict variable for mortality in the patients with PBC (HR 4.339, 95% CI: 1.89-9.9; $p = 0.0001$). **Conclusions.** The study suggests that the use of UDCA improves survival in patients with PBC free of transplantation. The authors declare that there is no conflict of interest.

009

BIOCHEMICAL FACTORS PREDICTORS OF HEPATIC OSTEODYSTROPHY IN PATIENTS WITH CIRRHOSIS PRIMARY BILIARY HOSPITAL GENERAL DE MÉXICO

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Introduction. Chronic liver disease, particularly primary biliary cirrhosis (PBC) are often associated with osteopenia and osteoporosis with a prevalence of 37%. Have been identified as risk factors associated with cholestasis, female menopause, smoking and steroids. Assessment of fracture risk using biochemical parameters is uncertain. **Objective.** To describe the prevalence of bone disease (EO) in CBP Liver Clinic HGM. Identify if there are relevant predictors of biochemical hepatic osteodystrophy. Knowing association between the severity of bone disease with severity of liver disease through May Score, Child-Pugh and MELD. **Material and methods.** Patients with CBP HGM Liver Clinic. They excluded patients with congenital bone disease or kidney failure. Parametric data were obtained, lab results, bone densitometry (DO) and biochemical assessment of bone metabolism (25-OH vitamin D (VitD), bone alkaline phosphatase (FAO) and parathyroid hormone (PTH). Prognostic scales were calculated Child-Pugh, and MELD Score May. retrospective. correlation level was calculated using the Spearman correlation coefficient using

GraphPad Prism Software V5.0. **Results.** 12 patients, female, with mean age of 60.33 (40-84) and BMI of 24 (19-34). Liver disease severity: CPT A 33.3% B 50% and C 16.6%. May Score average is 6.58 (4.10) and MELD of 12.33 (7-25). 0.77 mg/cm² and mean BMD T-score of -2.24 (-1.25 - 4.33), 100% had hepatic osteodystrophy (66.6 and 33.3% osteopenia osteoporosis). No correlation was found between BMD with age, BMI and biochemical parameters of the CBP (BT, FA and GGT). No association with disease severity. Significant correlations with markers of bone metabolism. **Conclusion.** We describe the prevalence of EO in this sample of Mexican patients with PBC. There was no correlation between the severity of liver disease and the severity of EO. Were found biochemical factors (VitD, FAO, HPT) predictors of EO. There was no correlation of BMD with age and BMI as risk factors. It was confirmed that there is no correlation between BMD and BT, FA and GGT would be interesting to increase the sample size to confirm the lack of statistical significance. This suggests biochemical predictors of bone disease in patients with PBC.ations in CBP. The authors declare that there is no conflict of interest.

G. PEDIATRIC HEPATOLOGY

001

CHOLEDOCHAL CYST, POSTOPERATIVE EVOLUTION IN CHILDREN IN HOSPITAL PEDIÁTRICO, CMN

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Background and aim. Choledochal cyst is dilatations of the biliary tree. Recognition and surgical treatment are important because of the significant long term risks of developing lethal complications like acute cholangitis, portal hypertension, pancreatitis, malignancy of the biliary tract and biliary cirrhosis. The aim of the study was to known characteristics of patients with choledochal cyst. **Material and methods.** Records were identified with a diagnosis of choledochal cyst, at the period from August 2006 to August 2012. The data reported in frequency and percentage or in median and range. Type of study was transversal, retrospective, descriptive. **Results.** There were 24 children (18 girls and 6 boys), with a female: male ratio 3:1. The 91% affected by a cystic dilatation type I, 8.3 type IV of Todani classification. The age group, infants 62.5%, preschool (20.8%), and similarly in children and adolescents with 4.2%. The 62.5% of patients with score Z of 0. The clinical manifestation was jaundice in 50% of patients, abdominal pain (20.8%), fever and vomiting in 16.7%, palpable mass in 8.3%, and coluria 4.2%. The method diagnosis most useful was abdominal ultrasound in 79.2%. Surgery performed in all patients was Hepatoyeyuno Roux-Y anastomosis. The complications reported were: pancreatitis in 25%, 16.7% sepsis, electrolyte imbalance in 8.3%, and 4.2% of choleretic diarrhea. The 45.8% of patients had cholangitis one event during follow-up (mean 1 year 6 months), only one had two events. Using the classification of Metavir found 41.6% had some degree of fibrosis in liver biopsy. **Conclusions.** Choledochal cyst has similar demographic profile as the see in Asia. Are more frequently in girls. The results showed that patients

had a satisfactory clinical and metabolic. However, factors such as the presence of fibrosis on liver biopsy at the time of diagnosis, nutritional status, birthplace, alkaline phosphatase, gamma glutamyl transferase could be factors influencing complications in these patients.

The authors declare that there is no conflict of interest.

002

PEG-INTERFERON, RIBAVIRIN AND AMANTADINE IN PRIOR NON-RESPONDERS TO PEG-INTERFERON AND RIBAVIRIN THERAPY WITH CHRONIC HEPATITIS C (GENOTYPE 1)

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Introduction and objectives. Despite the advances in the treatment of chronic Hepatitis C virus (HCV), the disease persists after treatment with pegylated interferon (Peg-interferon) and ribavirin in almost half the patients with genotype 1 infection and other effective therapeutic options were lacking until the arrival of boceprevir. We investigated the efficacy of retreatment with antiviral therapy including amantadine. **Material and methods.** Is a prospective and open study that began between November 2003 to June 2004. 21 patients with chronic HCV, genotype 1, who were non-responders to Interferon alpha 2b (3 million units three times a week) and ribavirin (1,000 mg daily), were included. The patients were given repeat treatment with Peg-interferon alpha 2a (180 µg once a week), ribavirin (1,000 mg daily) and amantadine (1-adamantanadine sulphate, 200 mg daily) for 48 weeks. **Results.** Ribonucleic acid of HCV (HCV-RNA) was undetectable in two patients, detected by polymerase chain reaction (PCR) in week 48, both patients with basal viremia > 6 log at the beginning of treatment. In two patients the HCV-RNA was undetectable in week 24, one with high viremia > 6 log and this patient maintained this condition at week 48, and the other patients had a low viremia at the beginning of treatment < 5.1 log (129,000 copies), but this patient maintained positive viral load at the end of treatment. The probability of response at the end of treatment was 9.55 and 4.7%, respectively. In one case treatment was finished in week 24 because of neutropenia and positive viral load. **Conclusions.** In patients with chronic HCV genotype 1 without response to Peg-interferon and ribavirin, triple antiviral therapy with Peg-interferon, ribavirin and amantadine is not useful. Actually are in use other triple therapies like Peg-interferon, ribavirin and boceprevir that show better results.

The authors declare that there is no conflict of interest.

003

DESCRIPTION PEDIATRIC PATIENTS WITH GALLSTONES UNDERGOING SURGERY AND POSTOPERATIVE EVOLUTION IN A TERTIARY HOSPITAL CARE

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Background. Cholelithiasis is defined as the presence of solid material in the biliary tract, usually in the gallbladder. Studies in Mexico have shown a prevalence of 0.35%. The clinical manifestations are different in concordance with the age group; treatment for pediatric patients with typical symptoms

is cholecystectomy. There is few data in children related to postoperative outcome of patients operated with either open or laparoscopic technique. **Aim.** To describe the etiology, clinical presentation, diagnosis method, type of surgical procedure and outcome in Mexican children with cholelithiasis in a third level Pediatric Hospital. **Materials and methods.** Study population. Pediatric patients undergoing gallstone surgery from January 2006 to December 2011. **Study design.** Retrospective, descriptive and transversal. Description. All patients with cholelithiasis diagnosis were included; data was obtained from the clinical chart including demographic variables (age and gender), anthropometric [weight, height, body mass index (BMI) and corresponding percentile according to the WHO classification]; clinically relevant data, biochemical tests and imaging studies, type of surgical procedure: laparoscopic or open cholecystectomy either elective or emergency, operative time; outcome: complications, morbidity, recovery time for discharge and morphological findings of the gallbladder and stones. **Results.** Thirty patients were studied, 66.7% were female. Mean age at the diagnosis was 63.3% were over 11 years of age. The main etiology was idiopathic. Clinical features were abdominal pain, nausea or vomiting in 76.7%. Diagnosis was made by ultrasound in all cases. Macroscopic description reported yellow stones in 50%. Laparoscopic cholecystectomy was performed in 60% of patients. There was no difference from the surgical procedure laparoscopic or open cholecystectomy related to bleeding volume, postoperative resumption of power and high postoperative time. **Conclusions.** In our population cholelithiasis occur primarily in females, mainly in adolescents. The etiology was idiopathic in most cases, the clinical picture was abdominal pain. Abdominal ultrasound showed gallbladder stones in all cases. We found that from 2006 laparoscopic cholecystectomy was preferred, lower volume of bleeding observed, fasting shorter and shorter high, in concordance with that observed in open cholecystectomy.

The authors declare no conflict of interest.

004

SMALL INTESTINAL BACTERIAL OVERGROWTH FREQUENCY IN PEDIATRIC PATIENTS WITH CIRRHOSIS

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Background. Liver cirrhosis is the end result of all chronic liver disease and is characterized by fibrosis and loss of normal hepatic architecture. Small intestinal bacterial overgrowth (SIBO) occurs when bacterial counts are abnormally high in small intestine (more than 10⁵ CFU/mL, from intestinal aspirate), this test is considered the gold standard although is invasive and difficult to perform. Noninvasive methods had been used for the diagnosis most frequently the breath test, this test measures the abnormal production of gas by products of bacterial fermentation. In concordance with the literature bacterial overgrowth is common in adult patients with liver cirrhosis, however, there are no data available in children with cirrhosis. **Aim.** To determine the frequency of bacterial overgrowth in pediatric patients with liver cirrhosis. **Material and methods.** Study design. Cross-sectional study. During the last year we studied all patients diagnosed by biopsy with liver cirrhosis. In all cases physical exam, clinical evaluation, Child Pugh score, PELD and MELD score and

hydrogen breath test with lactulose were done. Statistical analysis: mean \pm standard deviation, parametric or non-parametric tests. **Results.** Eleven patients were included, 7 were female (63.6%). Child-Pugh class A was found in 45.5% of the cases. Breath test was positive for Intestinal bacterial overgrowth in 72.7%. Bacterial overgrowth was present more frequently in patients with decompensated cirrhosis. Patients with serum bilirubin ≥ 1.4 mg/dL (83%) and low serum albumin < 3.2 g/dL (100%) showed a high frequency of bacterial overgrowth detect by breath test. **Conclusion.** In this study bacterial overgrowth diagnosed by the lactulose breath test was a common finding in children with liver cirrhosis, more frequently observed in those with decompensate liver disease. Prospective studies are required to evaluate more patients with breath test; clinical and biochemical parameters such as albumin, serum bilirubin and ascites should be explored as predictors of SBI.

The authors declare no conflict of interest.

H. ALCOHOLIC LIVER DISEASE AND FATTY LIVER

001

QUANTIFICATION OF TNF- α , IL-6, IL-8 E IL-10 IN BOTH ALCOHOLICS AND CIRRHOTIC BY ALCOHOL SUBJECTS

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Background. In Mexico the most abused drug is the alcohol. Alcoholism leads to alcoholic liver disease (ALD) ALD is characterized by lesions as steatosis, steatohepatitis, fibrosis and cirrhosis, and both in vitro and animal models has been associated with production of cytokines (TNF- α , IL-6, IL-10) and chemokines (IL-8) by Kupffer cells which are the initiators of the pathogenesis of ALD. **Objective.** Quantify and compare serum levels of cytokines IL-6, IL-10 and TNF- α and chemokine CXCL8 (IL-8) in alcoholic, cirrhosis by alcohol and control subjects. **Materials and methods.** Were included subjects who met the alcoholism OMS criterias and were classified in 40 alcoholics, 40 cirrhotic by alcohol and 40 controls subjects. A medical history and alcohol consumption surveys were and took 10 mL of peripheral blood by Bioplex were quantified IL-6, IL-8, IL-10 and TNF- α . Descriptive statistics and ANOVA with

orthogonal contrasts. **Results.** Results expressed as mean \pm standard deviation. P value is result between alcoholic and cirrhosis by alcohol groups (Table 1). **Conclusions.** This is the first study in Mexican population and cirrhotic alcoholic alcohol demonstrating the involvement of these molecules in liver damage. We can say that the chemokine CXCL8 contributes to inflammation and IL-6 may be involved in counteracting the damage its protective activity. The proinflammatory cytokines were higher in cirrhotic as are anti-inflammatory which probably reflects a compensatory role in the damage caused by alcohol.

The authors declare that there is no conflict of interest.

002

PREVALENCE STUDY OF NAFLD IN MEDICAL RESIDENTS IMSS PACHUCA, HIDALGO

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Background. Obesity is a pandemic associated with NASH, the most common cause of impaired PFH, including steatosis, steatohepatitis, fibrosis, cirrhosis and liver neoplasia. Is asymptomatic, lack of diagnostic suspicion, the overall prevalence is between 10 and 24% in the general population and 80% in obese people. There are few data on medical residents, being a group intervention to identify susceptible. **Objective.** To identify the prevalence of non-alcoholic hepatic steatosis and its associated factors in IMSS medical residents in Hidalgo. **Material and methods.** Cross, IMSS HGZMF1 description in Hidalgo, in the period March to June 2011 in Resident Physicians registered at the date of the study, were excluded for alcohol intake, previous liver disease, intake of hepatotoxic. Were removed by positive viral panel, not to use the diagnostic tests, specialty low. Risk factors were identified by history and physical examination. Statistical analysis. Descriptive statistics, univariate analysis obtained with prevalence, measures of central tendency and dispersion, as bivariate prevalence ratio with 95% CI and χ^2 . **Results.** 48 women resident physicians 64.6% and 35.4% men, mean age 29 and 33 years, respectively, 54.2 and 45.8% of normal weight and overweight obesity. 25% made moderate activity and 75% sedentary. 62.5% with abdominal circumference of 37.5% low risk and high risk. Was identified 25% with fatty liver and 42% with data steatohepatitis. Overweight and obesity increases 13 times the risk of fatty liver (RP13, IC2.865-218 184, p 001), dyslipidemia increases 3.57 times the risk (OR 3.57, CI 1.1513-40.806, p 007) and hyperglycemia was associated with RP 2.68, CI 036-1045, p .042. **Conclusions.** The prevalence of NASH among Resident Doctors was 25%, higher than expected, associated factors were overweight and obesity, dyslipide-

Table 1.* Demographic data.

Variable	Controls	Alcoholic	Cirrhosis by alcohol	p
Age	47 \pm 6	29 \pm 13	49 \pm 13	
Gender (female/male)	2/38	5/35	3/37	
Audit	2 \pm 1.8	18 \pm 7	21 \pm 10	< 0.001
IL-6 (pg/mL)	0.57 \pm 0.7	1.8 \pm 2	129 \pm 512	0.001
IL-8 (CXCL8) (pg/mL)	2.5 \pm 2.5	7 \pm 11	33 \pm 59	0.011
IL-10 (pg/mL)	4.5 \pm 16	4 \pm 19	13 \pm 36	0.189
TNF- α (pg/mL)	0.43 \pm 0.65	0.41 \pm 1.2	6.3 \pm 32	0.262

* 001. QUANTIFICATION OF TNF- α , IL-6, IL-8 E IL-10 IN BOTH ALCOHOLICS AND CIRRHOTIC BY ALCOHOL SUBJECTS.

mia and hyperglycemia. This study serves basis for future intervention studies seeking to prevent progression to irreversible forms in a timely manner.

The authors declare that there is no conflict of interest.

003 CLINICAL PRESENTATION OF PATIENTS WITH ALCOHOLIC HEPATITIS

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Introduction. The typical patient with alcoholic hepatitis (HA) has a history of alcohol consumption averaged over 80 g daily for a period of five years. Abstinence requires more than three months to exclude other diagnoses. The 50-60% of patients have concomitant cirrhosis. Urinary tract infections, spontaneous bacterial peritonitis, pneumonia, tuberculosis and sepsis are often associated. Withdrawal symptoms may be present. **Objective.** To describe the clinical presentation and underlying liver cirrhosis as well as alterations in blood chemistry of patients hospitalized with HA in a period of four years. **Material and methods.** A descriptive, retrospective and cross study was performed. We reviewed records of patients admitted with a diagnosis of the HA since January 2008 to December 2011. We recorded the clinical manifestations of hospitalization and liver function tests, blood chemistry and coagulation. Descriptive statistics, quantitative variables were expressed as mean and standard deviation (SD) and qualitative variables as proportions and percentages. **Results.** We analyzed 109 cases of patients with HA. The average age of presentation was 42 years (26-70), predominantly male $n = 93$ (85%). 65 patients (59%) were Child-Pugh C. 38 patients (35%) had grade II hepatic encephalopathy in West Haven scale. 29 patients (26%) had grade 2 ascites, 43 (39%) presented with small esophageal varices $n = 20$ (18.3%), 21 patients had initial gastrointestinal bleeding (19%) and 52 (48%) were admitted with renal failure. 23 patients (21%) had urinary tract infection, 6 (5.5%) spontaneous bacterial peritonitis, 5 (4.5%) candidiasis and 2 (1.8%) pneumonia. 5 (4.5%) presented with symptoms of alcohol withdrawal. **Conclusion.** Most patients admitted with severe HA. Predominance of the disease persists in males. It is frequently observed with concomitant liver cirrhosis complications. It should identify and treat associated infections that may contribute to the development of renal failure and disease severity.

The authors declare that there is no conflict of interest.

004

HEPATOCELLULAR BALLONING IN NASH

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Introduction. Hepatocellular ballooning is an important histological parameter in nonalcoholic steatohepatitis (NASH) diagnosis, as well as a component of NASH scoring systems (Brunt and Kleiner), which indicate a greater risk of disease progression. Multiple studies have attempted to associate the accumulation of fat droplets in ballooned hepatocytes with several pathogenic mechanisms in NASH including oxidative injury, abnormalities of the cytoskeleton, apoptosis and inflammation. **Objective.** The aim of this study was to deter-

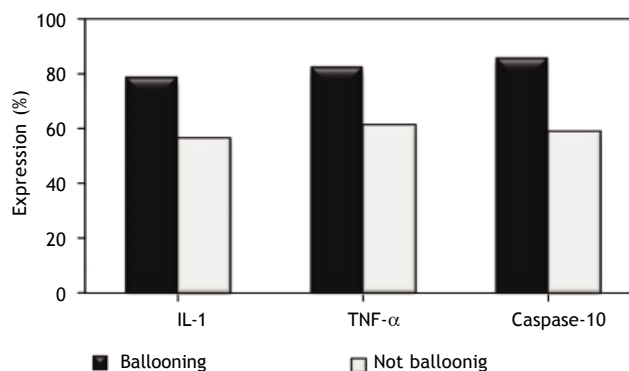


Figure 1. 004. Biomarkers expression in hepatocellular ballooning.

mine the expression of Interleukine-1 (IL-1), IL-6, IL-18, tumoral necrosis factor-alpha (TNF- α), caspase-10 and cytokeratin-18 (CK-18) in biopsies of patients with NAFLD diagnosis and their association with hepatocellular ballooning in order to associate this histologic feature with alterations in specific disease processes and to explore more objective criteria for diagnosis of hepatocyte ballooning. **Material and methods.** The present study included 69 biopsy-proven NAFLD (28 biopsies with hepatocellular ballooning and 41 with not-ballooning). H&E staining was employed to identify hepatocellular ballooning and lipid content was evaluated by oil red staining. Several NASH biomarkers were characterized by immunohistochemistry; TNF- α , IL-1, IL-6 and IL-18 which play a key role in inflammation, caspase-10 as an apoptosis marker, and CK-18 which determines hepatocyte integrity. **Results.** The presence of hepatocellular ballooning was significantly associated to cells TNF- α^+ ($P = 0.01$) and IL-1 $^+$ ($P = 0.05$) in comparison to liver biopsies without ballooning. Caspase-10 expression showed a statistical tendency of association with ballooning presence ($P = 0.06$). We did not find any statistical difference between CK-18 expression and ballooning or non-ballooning biopsies (Figure 1). **Conclusion.** These data suggest that NAFLD severity and hepatocyte ballooning present an association with pro-inflammatory cytokines such as IL-1 and TNF- α , therefore probably associated with caspase-10 related to an early apoptosis event. Future studies should evaluate whether ballooning can predict liver disease progression, independently of established histological scores and biomarkers related.

The authors declare that there is no conflict of interest.

005

PREVALENCE OF HYPOTHYROIDISM IN NON- ALCOHOLIC FATTY LIVER DISEASE AT INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN

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Background. Hypothyroidism it is characterized by changes in lipid metabolism and it seems to be associated with the aetiology and progression of non-alcoholic fatty liver disease (NAFLD). Several studies have shown that 21% of NAFLD patients present hypothyroidism, being more frequent in case

of steatohepatitis. Due these, recent NAFLD guidelines about diagnostic and therapeutic have considered hypothyroidism as an emergent condition of study. **Aim.** To describe the prevalence of hypothyroidism in NAFLD patients and their main characteristics. **Material and methods.** A cross-sectional study from Cohort of 129 NAFLD patients was conducted during 1 year. NAFLD diagnosis was made according laboratory test, ultrasound or liver biopsy. Hypothyroidism diagnostic was made by shifts in thyroid scan parameters. The Statistical package (SPSS v.16) was used to analyze descriptive and dispersion parameters. Groups were compared using χ^2 and student's t-test. **Results.** Prevalence of hypothyroidism in NAFLD patients was 23.5% (n = 30). Mean age was 47 ± 9.6 years, and 77% were women. The commonest comorbidities were hypertriglyceridemia (46.7% of the cases), hypercholesterolemia (23.3%), increased ALT (23%) and increased AST liver enzymes. Being more frequent the AST elevation in subjects with hypothyroidism (56.7 vs. 43.4%, $p < 0.05$). 93.3% of cases presented abdominal obesity with a mean percentage of body fat of 38.68 ± 12.4 . According the body mass index, 50% of the patients were obese, 43% overweight and 7% have normal weight to the height. **Conclusion.** Around 2 of 10 patients with NAFLD presented hypothyroidism; this report is one of the firsts made in Mexican population. It is important to consider this inter-relationship in order to provide a multidisciplinary treatment. Due this study was made in a third level of medical attention hospital, this prevalence might be not representative of general population.

The authors declare that there is no conflict of interest.

006

DETERMINATION OF PNPLA3 POLYMORPHISM AND ITS CORRELATION WITH THE ACTIVITY DEGREE AND LIVER BIOPSY FIBROSIS, CAP AND NAFLD SCORE

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Introduction. Non-alcoholic fatty liver (NAFL) is a common cause of chronic liver disease. There are genetic factors related to the development of fatty liver and its severity, such as: adipo-nutrin polymorphism (PNPLA3) located in chromosome 22, especially variable rs738409 C/G. **Objectives.** Determining the polymorphism variety of adipo-nutrin CC, GC, GG in patients with steatosis/steatohepatitis and correlation with fibrosis degree and liver biopsy activity (LB), NAFLD score and CAP (controlled-attenuation parameter) determined by means of a transition elastography. **Material and methods.** 27 patients with diagnosis of steatosis/steatohepatitis were included. All patients had a LB by means of a percutaneous tap of the liver. A transition elastography was conducted; in 16 of them, the CAP was determined (to measure liver fat percentage). M and XL transducers were used in accordance to the patients' adipose panicle. A high CAP was considered > 222 . The SNP of PNPLA 3 [1,148M] vs. 738,409 was analyzed in order to genotype as: GG, GC and CC by real-time PCR, hydration probes and melting curves. The NAFLD score was estimated for 26 patients. Non-parametric Spearman and Pearson's frequencies and correlations were analyzed. All 3 polymorphisms were compared with CAP, NAFLD score, and LB fibrosis and activity level. The statistical analysis was conducted using

SPSS v17.0. The statistical significance was $p < 0.05$. **Results.** Out of 27 patients, 18 (67%) presented the CC variety polymorphism; 7 (25%) CG; and 2 (8%) GG. CAP showed a positive correlation with the presence of steatosis and polymorphism; it was found high in 15 out of 16 patients. The highest values were in patients with G/C polymorphism. A tendency towards statistical significance was found in the different types of polymorphisms, steatosis and fibrosis ($p = 0.06$). The NAFLD score did not show any correlation with polymorphism, CAP or LB. **Conclusions.** The presence of adipo-nutrin polymorphism shows a trend towards significance with steatosis, fibrosis and high CAP. The NAFLD score did not show any correlation with any of our variables. The trend towards correlation and lack of statistical significance is explained by the size of the sample.

Authors hereby declare that there is no conflict of interest.

007

EFFECT OF HEPATOCYTE GROWTH FACTOR (HGF) IN CELLULAR REDOX STATE REGULATION IN HYPERCHOLESTEROLEMIC HEPATOCYTES

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Introduction. Lipid overload in the hepatocytes produces reactive oxygen species (ROS), which could trigger oxidative stress, an inflammatory response and tissue damage. Hepatocyte growth factor (HGF)/c-Met signaling play an important role in maintaining normal redox homeostasis in the liver. **Objective.** To evaluate the effect of HGF on the oxidative stress produced by lipid overload in hepatocytes of mouse with a high cholesterol (HC) diet. **Material and methods.** CD1 male mice were fed with high cholesterol diet (HC, 2% cholesterol and 0.5% sodium cholate) or normal diet (Chow) for two days. Primary mouse hepatocytes were obtained by the method of two-step perfusion. Cell primary cultures were pretreated or not with 50 ng/mL HGF for 3, 6, 12 and 24 h. ROS were detected with DCFH-DA by spectrofluorometric method. Protein oxidation was determined using OxyBlot™ kit. Antioxidant enzymes content were assayed by Western blot. Enzyme activities were performed by spectrophotometric methods. **Results.** An increase in ROS generation (1.6-fold) and protein oxidation (1.9-fold) in HC hepatocytes were found. HGF pretreatment reverted oxidation damage in HC hepatocytes in a time-dependent manner. HC cells presented 1.5 fold increase in catalase and superoxide dismutase content (SOD1) vs control hepatocytes. HGF induced superoxide dismutase (SOD1), however its activity decreased in 80%. HGF decreased catalase content and enzyme activity in HC in 50%. On the other hand, HGF increased the contents of antioxidant enzymes as glutathione peroxidase (GSHPx), glutathione-S-transferase (GST) and glucose-6-phosphate dehydrogenase (G6PD) (2.4, 2.8 and 3.3 fold respectively) after 24 h of HGF treatment in HC hepatocytes. **Conclusion.** The results show that an overload of lipids in the hepatocytes produces oxidative stress. HGF protects against oxidative stress in hypercholesterolemic hepatocytes by a mechanism mediated by the expression of antioxidant enzymes related with GSH system.

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008

OBESITY AND DIABETES, ASSOCIATED WITH CIRRHOSIS

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Introduction. Obesity and diabetes are a public health problem in Western countries. In Mexico, 70% of the population is overweight and 52% obese. The two entities are a risk factor for chronic liver damage type of nonalcoholic steatohepatitis (NASH) term applied by Ledwig et al., In 1980, which is characterized by a metabolic disorder where the liver is fatty change lobar accompanied by an infiltration of polymorphonuclear cells with Malory bodies and can evolve to steatosis, fat necrosis, fibrosis, cirrhosis and eventually to hepatocellular cancer. Moreover Diabetes Mellitus type II is the leading cause of death in Mexico to effect its complications is related to obesity has been associated with steatosis, steatohepatitis, fibrosis and cirrhosis, no other risks such as viruses, alcohol, autoimmune diseases, congestive and metabolic consequence of chronic liver damage by these entities. **Objective.** To assess the relationship of obesity and diabetes as probable etiology of liver cirrhosis in patients from western Mexico. **Design.** Cohort study. **Material and methods.** We studied 88 patients with cirrhosis and obesity and diabetes in a period of 3 years in the regional hospital Valentin Gomez Farias (ISSSTE). Relying for studying obesity with a body mass index above 30, diabetic glucose above 126 mg / dl (twice) at 200 or above outlet and biochemical studies with cirrhosis with ALT, AST, ELISA third generation, histological (Metavir classification), molecular and endoscopic, with support from the pathology department of the Hospital Civil Juan I. Menchaca. **Results.**

ETIOLOGY associated cirrhosis DM 11 AND OBESITY

- HCV Viral42 (48%),
ODDS Ratio 5.44
- Diabetes + obesity 26 (30%)
RR 2.85 <OR <10.46>
- Alcohol.....20 (22%)
- In this group found that 26 of the 88 patients with these risk factors who had cirrhosis without any other cause organic etiology demonstrable, that obesity and diabetes. We suggest a wide studies demonstrating this relationship affects a large percentage of the population.

The authors declare that there is no conflict of interest.

009

ASSOCIATION OF GENETIC POLYMORPHISMS OF METABOLIZING IN ALCOHOLICS AND CIRRHOTIC

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Introduction. The alcohol metabolism enzymes have several genetic polymorphisms that have been associated with enzyme activity¹ and susceptibility to liver disease². **Objective.** To investigate the frequency of genetic polymorphisms of ADH1B, ALDH2 and CYP2E1 in alcoholics and their relationship with the presence of liver damage. **Material and Me-**

thods. Inclusion criteria: 190 patients were included (OH) to Liver Clinic of General Hospital of Mexico with alcoholism criteria according to WHO. Developed detailed history of each patient. The control group (CT) consisted of 226 subjects who did not consume alcohol (<10g/day). Blood samples were taken on a single occasion (10ml) for determination of genetic polymorphisms ADH1B: exon 3, ALDH2: exon 12 and CYP2E1: 5' region (RsaI), intron 6 (DraI) and intron 7 (TaqI). We obtained written informed consent. **Results.** We included a CT 226 AUDIT <5, mean age 37 ± 13 years. Patients were classified as alcoholics (47) and cirrhosis (143). Mean age was 46 ± 13 and 49 ± 11 years, respectively. The average grams of alcohol per day for CT was 3 ± 3 while for alcoholics was 307 ± 198 g and 315 ± 198 g. Average years of consumption was similar in both groups (28 years). RFLPs: Allele frequencies in significant difference was obtained in the ADH1B * 2 allele (OH 0% vs CT 5% p = 0.001). ADH1B * 2 allele and ALDH2 * 2 allele has a frequency same (0%) to Western populations, in contrast to groups Asians. For CYP2E1 to the promoter region; c1, 16% OH vs 79% CT p = 0.001, for DraI in the most frequent allele C with 82% OH and 18% CT with p = 0.001 and TaqI; A2, with 18% OH vs 13% CT p = 0.51, but showing differences between alcoholics and cirrhotic patients (p = 0.015). **Conclusion.** In our population polymorphisms ADH1B * 1, CYP2E1* c1 and CYP2E1* C are associated with high ability to metabolize and therefore alcoholic dependence, and CYP2E1* A2 with associated with liver cirrhosis.

The authors declare that there is no conflict of interest.

010

INTERRELATIONSHIP BETWEEN THE PATTERN OF ALCOHOL CONSUMPTION AND LYMPHOCYTE PROFILE IN YOUNG PEOPLE

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Introduction. In Mexico the group with higher alcohol consumption per occasion was aged between 18 and 29 years. This consumption is associated with social, family and health problems¹. It has been demonstrated that alcohol alters the immune system. **Objective.** Study the pattern of alcohol consumption and lymphocyte profile in young people. **Material and Methods.** College students were included with informed consent. Test AUDIT, CIDI and Craving was applied, along with a survey of their alcohol consumption. From each subject was calculated BMI and biochemical studies were performed and immunophenotype. Individuals were classified into two groups: Risk Drinking (OH) and Control (CT), at the same time the OH group was subdivided: Risky (R), Abuse (A) and Dependency (D). For statistical analysis we performed an ANOVA and orthogonal analysis correlations. **Results.** We included 252 participants, where 68% OH and 43%CT were men. In the OH group mean values were higher than group CT: age (22 vs 21 years) (p<0.001), alcohol consumption/occasion (108 vs 31gr) (p<0.001). Total Craving score was moderate for OH and mild for CT (p<0.001). In lymphocytic profile we found differences between OH and CT percentage of CD45+ (81 vs. 67) (p<0.001) and NKT cells (4.4 vs 3) (p<0.01), being higher in OH. In subgroup D, the percentage of NK and NKT cells was higher than in CT (p <0.02) and in

B lymphocytes was lower ($p < 0.01$). In other subpopulations changes were not observed. We found that AUDIT score is directly related with alcohol consumed per occasion, total Craving, are older, BMI, high hemoglobin levels, GGT, AST, and the percentage of CD45 +, NK and NKT cells. **Conclusions.** The results showed that the higher drinking per occasion had differences in behavioral, biochemical and lymphocyte profile, in particular CD45 +, NK, NKT and B cells being the first change that happens in risky alcohol consumption in young people. **Referencias.** 1. ENA (Encuesta Nacional de Adicciones). 2008. "This work has been partially subsidized by: Macroproyecto UNAM SDEI-PTID06-3"

011

ASSOCIATION OF KUPFFER CELLS IN THE PROGRESSION OF NAFLD

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Background. Nonalcoholic fatty liver disease (NAFLD) has a complex pathophysiology coursing by steatosis (E), steatohepatitis (EH), cirrhosis (C) and hepatocellular carcinoma. It has been described that Kupffer cells (KC) can participate in the pathophysiological processes of NAFLD. However, the mechanisms and pathways that guide the progression of NAFLD are not completely understood. Aim. Evaluate the association of KC to the pathophysiological mechanisms related to the progression of NAFLD. Material and Methods. Retrospective study of 117 patients, 51% female, 49% male, with liver biopsy and positive diagnosis: E ($n = 66$), EH ($n = 40$) and C ($n = 11$). Interleukin IL-1, IL-6, IL-18, as well as caspase-3 expression, were evaluated by immunohistochemistry using a tissue microarray. The KC were determined by expression of the marker CD68 and CD163 in mononuclear cells. Results. 40% of the population had metabolic syndrome, 65% were overweight or obese, 24% diabetes, 73% hypertriglyceridemia, 38% hypercholesterolemia, 38% hypertension and elevated AST, ALT and GGT in 54%, 56% and 65 %, respectively. An increase in the expression of CD68 between E vs EH (77% vs 100%), E vs C (77% vs 36%) and EH vs C (100% vs 36%) ($P < 0.01$) was shown. Biopsies CD68+, were significantly associated with the expression of IL-1, IL-6, IL-18, TNF- α and Caspase-3 ($P < 0.05$) (Fig.1). In biopsies CD163+, an association with TNF- α ($p < 0.01$) and caspase-3 ($p < 0.02$) was observed, whereas in biopsies CQ-18+ (cytokeratin-18) there was no correlation with any marker. Conclusions. The KC were related to NAFLD stages, which confers a prognostic value to CD68, and major involvement of KC in inflammation and apoptosis mechanisms.

The authors declare no conflict of interest. "This work was subsidized entirely by Medical Sur Clinic Foundation."

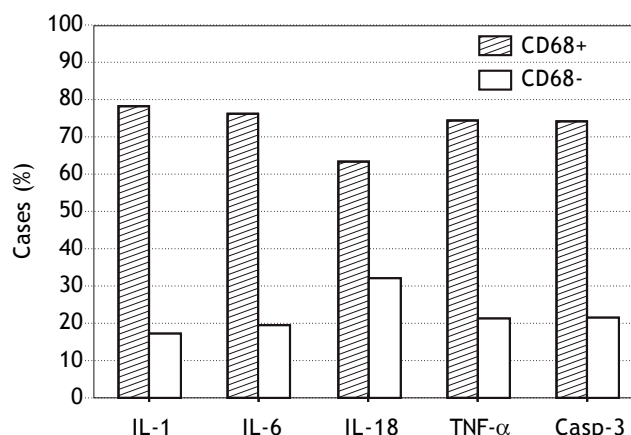


Figure 1. Association of CD68+ biopsies vs markers of inflammation and cell death. * $p < 0.05$.

012

ROLE OF OXIDATIVE STRESS IN THE ALCOHOLIC LIVER DISEASE.

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Background The involvement of free radical and the oxidative stress plays an important role in the pathogenesis of alcoholic liver disease¹, this has been demonstrated by several lipid peroxidation markers and the imbalance of antioxidant defenses in animal model^{1,2}, but little is known about this process in the human. Aim: Evaluate the role of oxidative stress through the quantification of carbonyl groups in patients with ALD. Material and methods: In our study we include patients with alcoholism according to WHO criteria, and a control group consisting of subjects with an ethanol consumption ≤ 10 g/day and AUDIT ≤ 8 . The carbonyl groups for each patient medical history and informed consent was obtained.

Results.

Control Alcoholics Cirrhotic

Gender F/M 15/21 1/4 2/50

Age (years) 39.6 60.2 48.9

BMI 27.5 19.7 27.8

Consumption OH (g/day) 4.7 140.8 320.5

Carbonyls (nmol Carb /mg prot) 0.10 ± 0.02 , 0.57 ± 0.21 , 0.74 ± 0.18 a.

Table 1. 012. ROLE OF OXIDATIVE STRESS IN THE ALCOHOLIC LIVER DISEASE.

	Control	Alcoholics	Cirrhotic
Gender F/M	15/21	1/4	2/50
Age (years)	39.6	60.2	48.9
BMI	27.5	19.7	27.8
Consumption OH (g/day)	4.7	140.8	320.5
Carbonyls (nmol Carb /mg prot)	0.10 ± 0.02	0.57 ± 0.21	0.74 ± 0.18 a

Values expressed as mean \pm S.E. "a" Means significantly different from control group at $P < 0.01$.

Levels of carbonyls were increased in alcoholic patients with cirrhosis ($P < 0.01$) but not in alcoholic patients without liver damage, comparing with control group. **Conclusions.** Our study shows that oxidative stress participates in the development of cirrhosis by alcohol consumption. These results suggest that carbonyls quantification in serum may be useful in the diagnosis of cirrhosis, however would be necessary to increase the number of patients without cirrhosis in our study to make more evident this effect.

Our work does not have any relationship that poses a conflict of interest.

013

CHOLESTEROL IN HEPATOCYTES ENHANCES ENDOPLASMIC RETICULUM STRESS INDUCED BY ETHANOL AND ACETALDEHYDE TREATMENT.

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Introduction. Disturbances in the normal functions of the endoplasmic reticulum (ER) is a result to cell stress and it is called as endoplasmic reticulum stress, which is aimed initially at compensating for damage but can eventually trigger cell death if ER dysfunction is severe or prolonged. Currently in our country, obesity is a serious public health problem. In addition, the National Addiction Survey reveals that drinking starts at an earlier age. To date the effect that high lipid content and the ethanol produce on ER stress and its relationship with the liver pathophysiology is unknown. Objective: To characterize the ER stress produced by an overload of cholesterol and the biotransformation of ethanol in primary cultured hepatocytes. Methods: Mice of the strain C57BL / 6 were treated with high-cholesterol diet (HC), hepatocytes were isolated and then treated with ethanol (EtOH) or acetaldehyde (Ac) for 24h (100mM and 200mM respectively). Cell viability was determined by crystal violet assay. The content of cytochrome P450 2E1 (CYP2E1), PERK and eIF2- α phosphorylation was determined by Western blot. ATF6 localization was assessed by confocal microscopy. Results: Cell viability decreased in hepatocytes treated with HC and HC+ EtOH, but decreases to 50% in HC+ Ac. CYP2E1 content increased 2.1 and 2.3 fold in HC and HC + EtOH respectively. ER stress markers as PERK increased 2.9 and 2.7 times its content compared to the control diet in HC and HC + Ac respectively, phosphorylation of eIF2- α increased in HC and HC+Ac hepatocytes. Furthermore, ATF6 was translocated to the nucleus in the presence of HC diet and / or treatment with EtOH and Ac. **Conclusion.** Cell viability indicates that Ac and EtOH potentiate cell damage generated by cholesterol. The data suggest that HC diet and exposure particularly to Ac produced ER stress because a significant increase was observed in the content of PERK, phosphorylation of eIF2- α , and translocation of ATF6. Also the increase in the content of CYP2E1 indicates a greater oxidative damage and its possible role in the generation of ER stress in hepatocytes lipid overloaded and EtOH or Ac treated.

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014

THE OVERLOAD OF CHOLESTEROL IN THE LIVER INDUCES OXIDATIVE STRESS DUE TO MITOCHONDRIA DYSFUNCTION IN MICE FED WITH AN ATHEROGENIC DIET

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Introduction. NAFLD is defined as infiltration of fat (fatty acids, triglycerides and cholesterol) in hepatocytes, by more than 5% in the absence of alcohol consumption. The accumulation of fat in the liver induces cytotoxicity and sensitizes the organ to a second aggression. Mitochondria are organelles with a very low content of cholesterol and are considered the main source of reactive oxygen species (ROS). Alterations in mitochondrial function leads to energy depletion, and oxidative stress, playing a prominent role in liver damage and the progression of NAFLD. Objective: The aim of this work was to determinate mechanism of ROS generation in the liver of mice fed with a high cholesterol diet. **Methods.** C57/BL6 male mice were fed with high cholesterol (2% cholesterol and 0.5% sodium cholate) or normal diet (Chow) for thirty days. Liver function markers were analyzed in serum. Lipids content were performed by spectrophotometric assay, by Oil Red and filipine staining. Protein oxidation was determined using OxyBlot kit. Primary mouse hepatocytes were obtained by the method of the two-step collagenase perfusion. Potential membrane mitochondrial was detected using MitoRed by confocal microscopy. Mitochondrial antioxidant enzymes content were assayed by Western blot. Results: Mice fed with HC diet presented an increase of 4-fold in transaminases (ALT, AST) and phosphatase alkaline. HC liver and cells showed an increased content of lipids (7-fold). HC liver exhibited protein oxidation increment. A decrease in hepatic function in HC cells were found. On the other hand, the cholesterol overload induced mitochondrial uncoupling and an decreased the contents of antioxidant enzymes glutathione peroxidase 1 (GSHPx), superoxide dismutase 2 (SOD2) and B-cell lymphoma 2 (Bcl-2) (0.36-, 0.23- and 0.25-fold respectively). Conclusion: The results show that an cholesterol overload in the liver causes tissue and functional damage. Our data suggest that an increase oxidative stress generation is due a decrease the expression of mitochondria antioxidant enzymes and a mechanism mediated by mitochondrial uncoupling.

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015

RESPONSE TO STANDARD AND TRIPLE THERAPY OF INFECTION BY HEPATITIS C IN THE HOSPITAL 71 SPECIALTY OF THE IMSS, TORREÓN, COAH."

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INTRODUCTION: Ribavirin and pegylated interferon therapy reaches 55-60% sustained viral response rates. There are few data about the triple treatment with amantadine in patients not responders or relapsing. **MATERIAL AND METHODS:** Measurement of ALT and viral load by quantitative

PCR initial and subsequent antiretroviral treatment week 12, and 24 weeks of suspension of the therapy.

RESULTS: We found 88 patients without prior antiretroviral treatment and 11 patients not responders to standard therapy. Of the 68 patients selected 39 (59.1%) male and 27 (40.9%) of the female gender, in ranges in age from 22 to 71 years. Fifty-seven patients (86.4%) relate to patients naive by which used standard treatment with interferon and ribavirin. And 11 (13.6%) patients which are not responders to standard treatment used triple treatment which includes amantadine. The genotype most commonly found was 1 in 53 patients (80%), genotype 2 in 9 patients (13.2%) and genotype 3 in 4 patients (6.2%). The viral load found in patients was low in 8 patients (12.1%), intermediate in 26 patients (39.4%) and high in 32 patients (48.5%). ALT met initially high at 93.2% of patients and normal values in the 6.8%. The good response to therapy in week 12 was found in 49 patients (85.96%) under standard treatment and in 8 patients (88.90%) under triple treatment which includes amantadine. ALT and PCR reported in week 12 and 24 weeks of suspension of the therapy presented normalization of up a 67.90% in patients with standard therapy with a 66.66% in patients under treatment triple.

DISCUSSION: In our study observed that the response to triple therapy with amantadine reaches therapeutic response in week 12 and 24 after finish therapy similar to standard treatment in patients with Hepatitis C chronic, expressed in decrease in viral load to levels as low as 50 copies/ml and standardization of the value of alanine aminotransferase in large proportion of patients.

The authors declare that there is no conflict of interest.

016

ADVANCED FIBROSIS DETECTION BY NON INVASIVE METHODS IN OVERWEIGHT PATIENTS WITH NON ALCOHOLIC FATTY LIVER DISEASE

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Background. Non alcoholic fatty liver disease is the most common liver disease worldwide; in Mexico it is present in 26% of population. It is unknown the prevalence of fibrosis among population affected by this disease. **Aim.** To determine the prevalence of advanced fibrosis in an overweight population that goes for screening check up and to determine factors associated with fibrosis. **Methods.** Advanced hepatic fibrosis was determined by NAFLD score, Fibroscan®, and combination of both methods. Patients were randomly assigned to the noninvasive methods of fibrosis detection. Risk factors were determined from clinical record, biochemical and anthropometric data. **Results.** A total of 299 patients were randomized, 234 were men (78%), with a mean BMI 30 ± 3 Kg/m². The overall prevalence of advanced fibrosis ranges from 1% to 5.3% according to the method used (Figure). Obesity ($p=0.006$), and hyperglycemia ($p=0.02$) were factors associated with fibrosis detected by Fibroscan®, while thrombocytopenia was associated with fibrosis detected by NAFLD score ($p=0.04$). **Conclusion.** The prevalence of advanced fibrosis overweight patients with non alcoholic fatty liver disease is high and it can vary according to the non invasive method used for it detection. The authors declare that there is no conflict of interest.

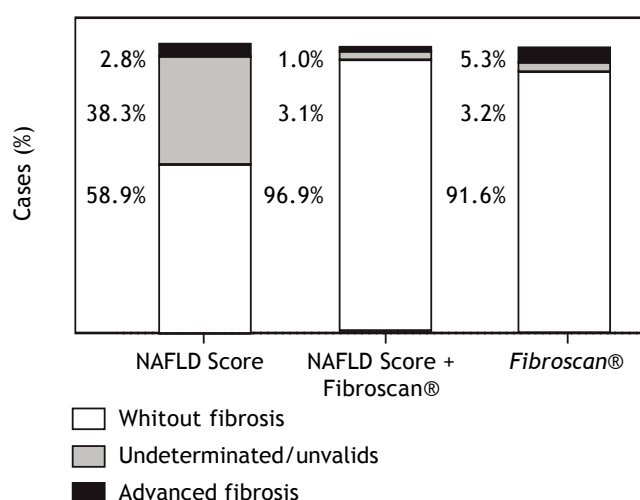


Figure 1. 016. ADVANCED FIBROSIS DETECTION BY NON INVASIVE METHODS IN OVERWEIGHT PATIENTS WITH NON ALCOHOLIC FATTY LIVER DISEASE. Advanced fibrosis detection by non invasive methods.

I. DRUG-INDUCED LIVER DAMAGE

001

EPIDEMIOLOGY OF DRUG-INDUCED LIVER INJURY IN HOSPITALIZED PATIENTS FROM INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN. ANALYSIS OF 24 YEARS: 1987-2011

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Background. Drug-induced liver injury (DILI) remains an important disease in clinical practice. It is difficult to predict, diagnose and manage. **Aim.** To identify the proportion, causes and the nature of DILI in a retrospective cohort of inpatients. **Material and methods.** We performed a search of toxic liver damage and related diagnoses in our computerized database of discharges that includes data since 24 years ago. Based on CIE-9 and CIE-10 coding as well as to the demonstration of a 3-fold times elevation in liver enzymes, eligible cases were subjected to the CIOMS criteria. Clinical chemistry, liver parameters and the exclusion of any disease-related causes for the liver injury were evaluated. Only the cases classified as highly probable, probable, or possible were diagnosed as DILI. Clinical data related to the diagnosis, possible etiology, drug posology and clinical outcome were analyzed. **Results.** 141 patients represented prevalent cases, 47% were men and 53% were women. Acetaminophen ($n = 37$, 26.2%), antibiotics ($n = 17$, 12%) and chemotherapy ($n = 12$, 8.5%) were the top three causes of DILI. Mean ingested dose for acetaminophen was $7.5 \text{ g/d} \pm 3.5 \text{ g/d}$ with mean ALT levels $1,128.4 \text{ UI} \pm 537.3 \text{ UI}$. 54 patients (38%) had metabolic syndrome and 88 (62%) had overweight/obesity. Hepatocellular pattern was observed in

60% cases, 11% had cholestatic pattern and 29% had mix pattern. 20 cases (15%) were classified as definite, 90 (64%) cases were probable and 31(21%) were possible. Peak ALT values were higher in patients with malignancy than patients without it (671.5 ± 71.6 UI *vs.* 302.5 ± 30.6 UI, p 0.01). 133 drugs and 8 herbs were found associated with DILI. There were 8 (11.3%) deaths all but one due to Acetaminophen. **Conclusion.** There was a prevalence of 1.2 cases of DILI per 1000 discharge, DILI was most frequently caused by acetaminophen and antibiotics without differences in phenotypic expression related to sex and age. Lean patients and non-malignancy patients could have better prognosis. An online warning for diagnosis of DILI and a checklist of minimum elements required for diagnosis of DILI may both be helpful for improving DILI diagnosis rates and future DILI research. The authors declares that there is no conflict of interest.

002

DRESS SYNDROME WITH ACUTE LIVER FAILURE INDUCED BY PHENYTOIN. CASE REPORT

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Introduction. DRESS syndrome (drug rash, eosinophilia and systemic symptoms) is an idiosyncratic drug's reaction. It's characterized by severe rash, hematologic disorders and organ involvement. Its associated with use of anticonvulsants. Its mortality is around 10%, it usually is outcome to liver failure. Early diagnosis and management with immunosuppressant drugs have been shown to reduce mortality. We report a female, 46 years, no history of consumption of hepatotoxic; one month prior to admission had subarachnoid hemorrhage, clipping to the affected vessel was realized, and starts consumption of phenytoin. Since the beginning of the drug she noted maculopapular lesions on both hands that resolved spontaneously, after 3 weeks lesions were extended to the trunk, arms and legs, fine flaking, itching, jaundice and fever. On her admission she had cervical lymphadenopathy, hepatomegaly, without evidence of hepatic encephalopathy, eosinophil 800/L, creatinine 5.6 mg/dL, total bilirubin (TB) 8.6 mg/dL (BD 5.6 / BI 3), alanine aminotransferase (ALT) 171 U/L, aspartate aminotransferase (AST) 333 U/L, alkaline phosphatase 751 U/L, GGT 1814 U/L, DHL 587 U/L, TP 38%, INR 1.8, negative cultures were obtained, viral hepatitis B and C was negative; ultrasonography of liver without evidence of bile duct dilatation or vascular changes. Management was initiated with prednisone weight 1 g/kg. The second day of hospitalization she presented hepatic encephalopathy, we added to her management N-acetyl cysteine (NAC) 140 mg/kg orally followed by 17 doses of 70 mg/kg and 10 mg vitamin K per day. The patient progressed favorably with reversal of acute liver failure and the probable interstitial nephritis associated with this syndrome and decreased maculopapular lesions. On the sixth day of treatment eosinophils 1,170 U/L, creatinine 1.1 mg/dL, BT 9.6 mg/dL (BI 3.7/BD 5.9), ALT 80 U/L, AST 106 U/L, TP 76%, INR 1.1. **Conclusions.** DRESS syndrome is a severe reaction to drugs; early identification and use of high doses of immunosuppressive drugs are considered the first line of management to prevent fatal outcomes. Concomitant use of NAC may improve clinical outcomes and avoid the need for transplantation in case of acute liver failure. The authors declare that there is no conflict of interest.

003

EVALUATION OF HEPATOTOXIC AND HEPATOPROTECTIVE EFFECT OF DIETARY SUPPLEMENTS AND/OR HERBAL MEDICINES THROUGH AN *IN VITRO* MODEL IN PRECISION CUT RAT LIVER SLICE

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Introduction. About 80% of the population uses complementary and alternative medicine and 30 to 80% of liver clinic patients uses herbal remedies. **Objective.** Evaluate the hepatotoxic and hepatoprotective activity from 3 dietary supplements and herbal medicines commonly used to treat liver disease through *in vitro* model. **Material and methods.** The compounds studied were: aloe vera, milk thistle and boldo in 3 different presentations. Aloe vera: Omnilife, Herbalife and GNC. Milk thistle: GNC, Liver Med and Legalon. Boldo: tea (Therbal), capsule (Botnatura) and tablet. The strategy consisted in obtaining liver slices of Wistar rats with a Brendel rebandor Vriton. Were established study groups ($n = 5$ slices): control (untreated slices), positive control of toxicity (Acetaminophen slices treated with 15 mM) and the various study groups that were treated slices each of the three presentations 3 different from those mentioned products more Acetaminophen 15 mM. **Results.** The results of experiments to evaluate hepatotoxicity through the levels of ALT, AST were: 1) Aloe vera (ALT): Control < GNC < Omnilife < Herbalife, (AST): GNC < Control < Herbalife < Omnilife. 2) Boldo (ALT and AST), 3) Milk thistle (ALT and AST): Control < Liver Med < Legalon < GNC Therefore chosen products to evaluate hepatoprotection were aloe vera (GNC), Boldo (Therbal tea) and milk thistle (Legalon). It was found that aloe vera (GNC) and milk thistle (Legalon) were those that showed greater

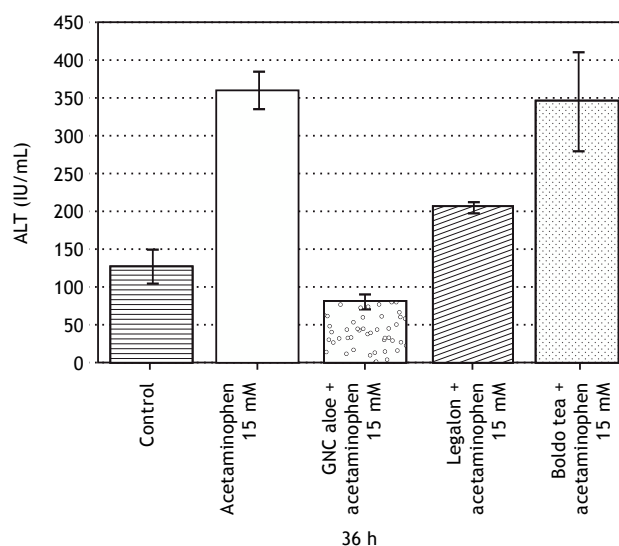


Figure 1.* 003. EVALUATION OF HEPATOTOXIC AND HEPATOPROTECTIVE EFFECT OF DIETARY SUPPLEMENTS AND/OR HERBAL MEDICINES THROUGH AN *IN VITRO* MODEL IN PRECISION CUT RAT LIVER SLICE.

protection against liver damage our inductor (acetaminophen) in the levels of ALT (Figure 1).

Conclusions. Of the 9 natural products which showed lower toxicity were aloe vera of GNC, tea Boldo of Therbal and Legalon of Nycomed. However, only showed hepatoprotection aloe vera of GNC and Legalon of Nycomed. The experimental model proved to be useful for the assessment of toxicity and/or hepatoprotection of natural products.

This study was supported by resources of the departments involved.

J. MISCELLANEOUS

001

CYTOKINES AND ADHESION MOLECULES LEVELS IN PATIENTS WITH NASH AND HCV

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Background. Cytokines actions interact in all inflammatory and immunoregulatory process, increased seric levels of them have been reported in liver cirrhosis, which represents the final stage of both, the inflammatory process and the chronic immunity activation. **Objective.** To compare the levels of IL-6, TNF- α , VEGF and ICAM in patients with steatohepatitis (NASH) and chronic hepatitis C virus (CHCV). **Material and methods.** 60 patients from the Liver Unit outpatient clinic were included, NASH (30) and CHCV (30), NASH was diagnosed by liver biopsy and CHCV by qualitative/quantitative PCR. Both groups were evaluated regarding demographics, anthropometrics, biochemical profile, fibrosis grade, and steatosis, as well as cytokines levels (ELISA). **Results.** When comparing both groups, statistical differences were founded regarding to the 4 studied markers, the biochemical profile, age and BMI (Table 1). In NASH correlations between TNF- α with VEGF ($r = 0.515$, $p = 0.004$), cholesterol ($r = -0.395$, $p = 0.034$), and IL-6 with total bilirrubine ($r = -0.429$, $p = 0.020$) were found. ICAM correlated with cholesterol ($r = -0.395$, $p = 0.034$); and within their liver profile: AST with ALT ($r = 0.568$, $p = 0.002$), ALKP ($r = 0.540$, $p = 0.003$) and GGT ($r = 0.491$, $p = 0.009$), also GGT with ALT ($r = 0.406$, $p = 0.036$), ALKP ($r = 0.458$, $p = 0.016$). In the HCVC group, correlation was found between TNF- α -VEGF (0.447 , $p = 0.013$) and within their liver profile: AST with ALT ($r = 0.872$, $p < 0.001$), GGT ($r = 0.696$, $p = 0.001$); and ALKP with GGT ($r = 0.676$, $p = 0.001$). **Conclusions.** NASH group exhibited a higher inflammatory response than the HCVC group. There was no correlation within most of the cytokines and biochemical parameters studied, it was only found within the liver profile in each group. This work has been supported by SEP and PAICYT.

Table 1.*

Group	ICAM (pg/mL)	IL-6 (pg/mL)	TNF- α (pg/mL)	VEGF (pg/mL)	AST (UI/L)	TGL (mg/dL)	AGE (years)	BMI (kg/m ²)
NASH	5,482 \pm 612	2,430 \pm 1,505	3,686 \pm 1,409	2,267 \pm 486	53 \pm 31	166 \pm 77	40 \pm 13	30 \pm 3
HCVC	2,038 \pm 838	720 \pm 747	336 \pm 470	365 \pm 472	101 \pm 79	100 \pm 49	53 \pm 11	27 \pm 5
p	< 0.001	< 0.001	< 0.001	< 0.001	0.010	0.002	0.001	0.007

* 001. CYTOKINES AND ADHESION MOLECULES LEVELS IN PATIENTS WITH NASH AND HCV.

002

THE HEPATOCYTE GROWTH FACTOR (HGF), INDUCES THE ACTIVATION OF THE DIFFERENT ISOFORMS OF THE NADPH OXIDASE IN MOUSE HEPATOCYTES

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Background. Evidence suggests a role for intracellular reactive oxygen species (ROS) as mediators of normal and pathological signal transduction pathways. A growing list of recent reports has demonstrated rapid and significant increases in intracellular ROS following growth factor or cytokine stimulation. The NADPH oxidase is a membrane bound enzymatic complex, now we know that they are present in many cellular types including the hepatic cells. No function is completely clear in non-phagocytic cells, but the evidence shows that the activity of the enzyme is related to signal transduction events. **Aim.** To determine the contribution of ROS in HGF/c-Met-induced Nox activation in primary mouse hepatocyte culture. **Material and methods.** Primary mouse hepatocytes were isolated by the two-step collagenase perfusion technique from male C57Bl6 mice. Cell primary cultures were pretreated or not with 50 ng/mL HGF for different times and with diphenyleneiodonium (DPI) a NADPH oxidase inhibitor. We utilized 2 dyes, 2',7'-dichlorofluorescein diacetate (DCFH-DA) and dihydroethidium (DHE), which measure hydrogen peroxide (H₂O₂) and superoxide anion (O₂⁻) respectively. To confirm the O₂⁻ production *in vivo* we determine the 2-hydroxyethidium bound to DNA by confocal microscopy. **Results.** We determine the ROS contribution by non-phagocytic NADPH oxidase by the stimulus of HGF in mouse hepatocytes, in the production of H₂O₂ we found a maximum peak at 30 min, moreover in the production of O₂⁻ we find a peak at 15 min, this finding was confirmed by detecting the O₂⁻ by confocal microscopy which shows an increase at 15 min that is maintained at 60 min. **Conclusion.** It is widely reported that different Nox isoforms produced different ROS, Nox 1 and 2 mainly produce the O₂⁻ while Nox 4, DUOX 1 and 2 produce H₂O₂, this result suggests that there is an activation and differential co-regulation of the NADPH oxidase isoforms by HGF and c-Met receptor. This work has been partially subsidized by CONACYT 131707.

003

HEPATIC AMYLOIDOSIS SECONDARY TO MULTIPLE MYELOMA

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Introduction and objectives. The secondary hepatic amyloidosis is a rare entity in our hospital and related to multiple myeloma occurs in 15%. Our objective is to review the issue and presentation of clinical case. **Case report.** Male 60 years, personal history nonpathological and pathological irrelevant. Clinical become with fatigue, weakness, epigastric pain, radiating to the right upper quadrant and no other accompanying symptoms, unintentional weight loss of 10 kg in two months. Physical examination: Patient alert and oriented, with no palpable lymphadenopathy, unaltered cardiopulmonary, abdomen globose with hepatomegaly 8cm below the costal margin, hepatalgia without peritoneal irritation, no peripheral edema. Labs: WBC 8000, 13.2 g/dL hb, hct 39.6%, platelets 737.000, TP 15.6 seg/77%, TTP 30 sec, INR 1.18 98 mg/dL glucose, BUN 11 mg/dL, Cr 0.76 mg/dL, BT 0.47 mg/dL, SGPT 128 U/L, AST 207 U/L, FA 2,434 U/L, LDH 814 U/L. Abdominal ultrasonography hydrocholecystitis, hepatomegaly without dilatation of intrahepatic or extrahepatic bile duct. The approach was to cholestasis and abnormal weight loss. Requesting: IgG 3,026 mg/dL, IgM 87 mg/dL, and anti-HCV AgsVHB: non reactive IgM cytomegalovirus, Epstein Barr and herpes simplex: negative, AFP1.89 U/mL, APE 3.65 ng/mL, CA19-9 138 U/mL. CT abdomen: hepatomegaly, dilated bile duct normal without intra or extrahepatic bile ducts. The patient continued with hepatalgia and cholestasis, liver biopsy was decided Q337-13: amyloidosis with sinusoidal pattern. Associated diseases were ruled out: bone marrow biopsy Q-722-13: multiple myeloma (lambda light chains). Concluding hepatic amyloidosis associated with multiple myeloma IgG, starting cycle melphalan, prednisone and thalidomide. **Discussion.** Systemic amyloidosis is a group of diseases characterized by amyloid deposits in the extracellular matrix or in the walls of the vessels in kidney (46%), heart (30%), liver (9%), spleen (5-10 %) and gastrointestinal (7%). The most common forms are the primary and secondary. Hepatic infiltration reported in half the cases. The clinical picture is characterized by fatigue, weakness and elevated alkaline phosphatase. The treatment of choice is melphalan, cyclophosphamide and prednisolone. **Conclusions.** Multiple myeloma secondary amyloidosis occurs by 15%. Treatment is with melphalan, prednisone and cyclophosphamide. The prognosis is poor for three months.

The authors declare that there is no conflict of interest.

004

HEPATOPROTECTIVE EFFECT OF TWO SUPPLEMENTS DONORS HYDROGEN SULPHIDE (SADSHTI AND SADSHTII) IN A MODEL OF ISCHEMIA-REPERFUSION INJURY IN RATS LONG EVANS

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Background. H₂S is involved in cytoprotection and inflammation, tissue damage is due to oxidative stress and subsequent inflammatory response. Hence the importance of this molecule with potential antioxidant and free radical scavenger. **Objective.** Evaluate the hepatoprotective effect of two supplements donors H₂S in I/R. **Material and methods.** After anesthesia with sodium pentobarbital (60mg/kg) and laparotomy was performed tubal Pringle maneuver. 16 male Long

Evans rats (300-350 g) were divided into 4 groups (n = 4). Group (sham), only laparotomy without the procedure of I/R. Group I/R was obstructed portal triad for 20 and 60 min of reperfusion. SADSHTI group received 111.42 mg/kg orally 1 h before I/R, and group SADSHTII 156.42 mg/kg orally 1 h before I/R. We quantified serum ALT, AST, LDH, IL-1 β , IL-6, MCP and TNF α . Data analysis was performed using SPSS V15.0 software. **Results.** Enzymes: ALT significant difference Sham vs. I/R (P = 0.05) and I/R vs. SADSHTII+I/R (P = 0.02); AST in Sham vs. I/R (P = 0.048), Sham vs. SADSHTI+I/R (P = 0.038); LDH in Sham vs. I/R (P = 0.01), Sham vs SADSHTII+I/R (P=0.029), I/R vs SADSHTI+I/R and SADSHTII+I/R (P = 0.01). Correlation Sham group: AST with IL-6 (r = 1, P = 0.01), ALT with LDH, FNT and IL-1 (r = -1, P = 0.01), LDH with ALT (r = -1, P = 0.01), LDH with TNF and IL-1 (r = 1, P = 0.01), TNF with IL-1 (r = 1, P = 0.01); IR: AST with TNF (r = -1, P = 0.01), ALT with IL-6 (r = 1, P = 0.01), LDH with MCP (r = -1, P = 0.01) and IL-1 (r = 1, P = 0.01), MCP with IL-1 (r = -1, P = 0.01); SADSHTI: AST with LDH e IL-1 (r = -1, P = 0.01), ALT with MCP (r = 1, P = 0.01), LDH with IL-1 (r = 1, P = 0.01), TNF with IL-6 (r = 1, P = 0.01); SADSHTII: AST with ALT and TNF (r = 1, P = 0.01), ALT with TNF (r = 1, P = 0.01), LDH with IL-1 (r = 1, P = 0.01) and IL-6 (r = -1, P = 0.01), IL-1 with IL-6 (r = -1, P = 0.01). **Conclusions.** We showed decrease in ALT, AST and LDH in the two types of treatment vs. I/R group. Cytokines: SADSHTI decreased the levels of MCP, TNF and IL-1 with regard to I/R, SADSHTII decreased MCP and IL-1 but increased TNF. The IL-6 increased significantly in both supplements respect to I/R.

This study was supported by department Liver Unit and Transplant Service.

005

COMPARE THE HEPATOPROTECTIVE EFFECT OF LEGALON AND LIVERMED IN ISCHEMIA-REPERFUSION INJURY IN RATS LONG EVANS

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Background. Studies have reported the hepatoprotective effect of silymarin. This is used to treat liver diseases, drug and natural products intoxications, this due to the antioxidant effect. **Objective.** Compare the hepatoprotective effect of two commercial compounds in a model of ischemia-reperfusion (I/R). **Material and methods.** After anesthesia with sodium pentobarbital (60 mg/kg) and laparotomy was performed tubal Pringle maneuver (portal triad), depending on the group. 16 male Long Evans rats (300-350 g) were divided into 4 groups (n = 4). Group (sham), laparotomy was performed without the procedure of I/R. Group I/R was obstructed portal triad for 20 min and after a period of 60 min of reperfusion. Legalon group received 3 mg/kg orally 1 h before I/R, the last group received livermed 9.8 mg/kg orally 1 h before I/R. We quantified serum ALT, AST, LDH, IL-1 β , IL-6, MCP and TNF α . Data analysis was performed using SPSS V15.0 software. **Results.** Enzymes: ALT significant difference Sham vs. I/R (P = 0.05) and Sham vs. livermed+I/R (P = 0.029); AST in Sham vs. I/R (P = 0.032) and Sham vs. livermed+I/R (P = 0.001); LDH in Sham vs. I/R (P = 0.013), Sham vs. legalon+I/

R ($P = 0.048$), I/R *vs.* livermed+I/R ($P = 0.013$) and legalon+I/R *vs.* livermed+I/R ($P = 0.047$). Cytokines: IL-1 β , IL-6, FNT α and MCP, the only one showing significant difference in Sham group *vs.* I/R ($P = 0.012$) was IL-6. Correlation between variables Sham group: IL-6 whit MCP ($r = 1$, $P = 0.01$) and IL-1 with LDH ($r = -1$, $P = 0.01$); I/R: IL-6 whit MCP ($r = 1$, $P = 0.01$), MCP and IL-1 whit LDH ($r = 1$, $P = 0.01$), TNF whit AST ($r = 1$, $P = 0.01$), LDH with IL-6 ($r = -1$, $P = 0.01$); legalon: MCP and FNT whit ALT, AST and LDH ($r = 1$, $P = 0.01$), ALT with AST and LDH ($r = 1$, $P = 0.01$), AST with LDH ($r = 1$, $P = 0.01$); livermed: MCP with ALT ($r = 1$, $P = 0.01$). **Conclusions.** Decrease in liver enzymes ALT, AST and LDH in the two types of treatment *vs.* I/R group. However, with the livermed decrease was more pronounced. Livermed only decreased levels of MCP, TNF α and IL-1 β *vs.* I/R. The IL-6 increased with both treatment groups with respect to I/R. This study was supported by Liver Unit, Hospital Universitario Dr. José E. González, Universidad Autónoma de Nuevo León, Monterrey, Nuevo León.

006

TRANSCRIPTIONAL REGULATION OF NADPH OXIDASE INDUCED BY HGF AND ITS RECEPTOR C-MET IN PRIMARY MOUSE HEPATOCYTES

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Introduction. HGF is a dimeric protein which is produced by stromal cells in the liver. This acts through its receptor called, c-Met, which is a RTK. c-Met is a transmembrane protein composed of extracellular and intracellular domains which contain the catalytic domain. Once the ligand binds performs dimerization of c-Met and many tyrosines are phosphorylated in the intracellular domain. NADPH oxidase is an enzyme that is linked to membrane, which catalyzes the reduction of oxygen to superoxide anion. Nox family consisting of several catalytic proteins membrane bound (NOX1-5, DUOX1-2) and some regulatory proteins (p67, p47, p40, Rac, etc.). These latter are located in the cytoplasm under normal conditions and these are translocated to the membrane after appropriate stimulation to assemble NOX complex. The exception is p22, which is a subunit required for activation and stabilization of NOX1-4. The aim was determine which of the NADPH oxidase subunits are transcriptionally deregulated in times long for the effect of HGF in liver tissue. **Material and methods.** Primary mouse hepatocytes were isolated by the two-step collagenase perfusion technique from male C57Bl6 mice. Cell primary cultures were pretreated or not with 50 ng/mL HGF for different times. The study of genes expression is performed by RT-PCR. **Results.** Our data revealed that HGF induce a deregulation in the subunits of the NADPH oxidase, As NOX4 that after 12 h of treatment with HGF undergoes a decrease in its expression. Similarly NOX2 undergoes a decrease in its expression at 6 h after treatment with HGF, but this subunit begins to normalize basal levels at 24 h. Meanwhile, p22 expression disappears almost completely at 12 h after treatment with HGF, although their basal expression levels begin to recover after 24 h. **Conclusion.** Our data provide evidence that HGF induce a deregulation in the subunits of the NADPH oxidase at long times of incubation. Conacyt 131707. SEP PROMEP 912011-14611762.

007

SECONDARY TO CHOLESTATIC HEPATITIS HEPATITIS A, HANDLED WITH PENTOXIFYLLINE

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Introduction. Secondary to cholestatic hepatitis viruses HAV, prevalence is unknown in Mexico and optimal management, some trials suggest brief dose corticosteroids for treatment, the most common cause is HAV but other viruses can cause HCV, HBV, HEV, VHD and autoimmune. The prognosis is favorable, but to consider fulminant hepatic failure. **Case report.** Women 10 years of age, admitted with jaundice box, acolia, dark urine, hepatomegaly, with papular vesicular lesions in extremities, conscious with a month earlier. The blood count normal, bilirubin 7.1 mg/dL, direct bilirubin 13.28 mg/dL, total bilirubin 19.56 mg/dL, SGOT 80 U/L and ALT 64 U/L, cholesterol 325 mg/dL, alkaline phosphatase 275 U/L, IgM positive hepatitis A. The following week increased its total bilirubin, alkaline phosphatase 223 U/L, GGT 220 mg/dL and total cholesterol 199 mg/dL; managed initially with pentoxifylline 400 mg IV every 8 h, cholestyramine and ursodeoxycholic acid. In 10 days posteriores direct bilirubin 10.79 mg/dL, total bilirubin to 11.90 mg/dL bilirubin 1.11 mg/dL and alkaline phosphatase 160 U/L, add prednisone 20 mg every 12 h, in three weeks after dramatically decrease: total bilirubin and transaminases. **Conclusions.** Cholestatic hepatitis is a rare entity in our environment and can evolve favorably however fulminant hepatitis neck should be discarded. The use of pentoxifylline was considered, as not used in these patients knowing their antioxidant and anti-inflammatory effects among others. In this patient decreased bilirubin, liver enzymes and jaundiced tint, so its utility should be investigated in the future.

008

FREQUENCY OF INFECTION WITH HEPATITIS C VIRUS IN TLAXCALA-ISSSTE

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Introduction. Chronic infection with hepatitis C virus (HCV) is a public health problem worldwide. In Mexico is reported in 1.4% of the population, with 35% of active infection. In the center of the country reported 1.1% and 0.51% in Tlaxcala. **Objective.** To determine the frequency of HCV infection in ISSSTE population-Tlaxcala. **Material and methods.** 1,300 patients were surveyed like a outpatient over a 6 months period. The survey included risk factors for hepatitis C (transfusions prior to 1995, intravenous drugs use, unsafe sex, relationship with a cirrhotic patients, tattoos, piercings, or health worker). Was performed for patients with risk factors qualitative rapid test for HCV in blood (TM RAPID anti-HCV test). Patients who presented reactive test it was confirmed by PCR. **Results.** 1,300 surveys were conducted, finding 1,144 patients with risk factors. 30.9% were female (363 patients), and 69.1% were male (791 patients). Of these 5 patients (0.43%) were reactive. These patients were confirmed with PCR, resulting in all them positive. The age group that

predominated understood the risk factors of 46 to 55 years (29.4%), and the lowest risk in those under 18 years (2.2%). Reactive patients were in the age range 36 to 55 years. Importantly, the statistical for the frequency of infection by hepatitis C virus in our State is 0.51%, reported by the State Center for transfusions. Conclusions: In patients surveyed found a high percentage of risks factors (88% for all factors with 38.7% for transfusions) however, only 0.43% of these were reactive, with average below the region and nearby the State percentage (0.51%). In this study the quick test reactive was 100% specific (confirmed by PCR).

The authors declare that there is no conflict of interest.

009

PORTAL HYPERTENSION SECONDARY TO CHRONIC MYELOFIBROSIS: A CASE REPORT

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Introduction. It is a very rare disease whose incidence is estimated less than one case per 100,000 population. Chronic idiopathic myelofibrosis is disease characterized by clonal proliferation of hematopoietic stem cells and phenomenon of secondary progressive fibrosis if the marrow and extramedullary hematopoiesis development and organ infiltration and extramedullary sites such as liver and spleen. **Case report.** 52 year old female with a history of smoking at 20 cigarettes a day for 40 years. Enter the gastroenterology service to be treated by a week of evolution with melena evacuations and hematemesis, is hospitalized in the unit and performed upper endoscopy with report esophageal varices Soehendra grade IV. Later study protocol is performed including abdominal ultrasound report splenomegaly longitudinal diameter 20 cm, portal veins of 13 mm, enlarged liver echogenicity diffuse infiltration areas, moderate free fluid cavity. Laboratory test: leukocytes 14,000, neutrophil 10,300, lymphocytes 2,110, Hb 8.0 g/dL hto 24%, platelets 800,000 AST 40 U/L, ALT 60 U/L, DHL 473 U/L, albumin 4.2, total bilirubin 1.06 mg/dL. Negative hepatitis viral panel, normal immune profile. Liver biopsy: chronic hepatitis with hepatic fibrosis grade 1. It is done by bone marrow aspiration report finding trombocytosis with increased proliferation of megakaryocytes, myeloid metaplasia with chronic idiopathic myelofibrosis. **Conclusions.** Chronic idiopathic myelofibrosis has no specific symptoms or signs. Most patients are asymptomatic and the diagnosis is usually made when one discover splenomegaly or abnormal blood counts during a systematic exploration trombocytosis especially in early stages. Among the complications seen in the course of the disease: portal hypertension with esophageal varices and ascites, which occurs in 20-20% of patients, as a result of marked increase in vascular blood flow in the spleen erythropoiesis extramedullary, liver failure and liver fibrosis mass myeloid metaplasia is seen in 10-15% of cases.

The authors declare that there is no conflict of interest.

010

RELIABILITY OF TRANSIENT HEPATIC ELASTOGRAPHY

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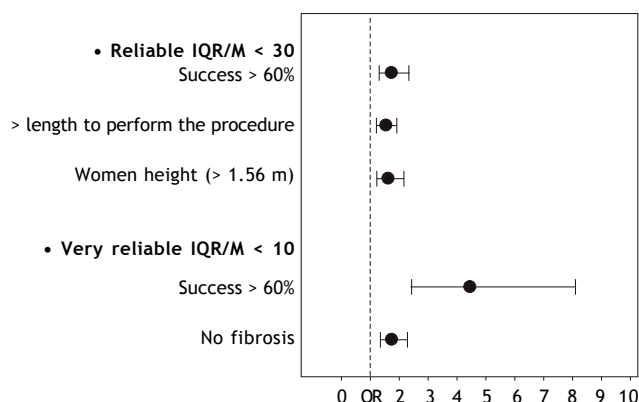


Figure 1. 010. RELIABILITY OF TRANSIENT HEPATIC ELASTOGRAPHY. Factors affecting the reliability of transient elastography.

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Background. Transient hepatic elastography is a non invasive method for fibrosis detection in chronic liver disease. However its reliability is variable and the factors associated with good accuracy are unknown. **Aim.** To determine transient hepatic elastography reliability and factors associated with it. **Material and methods.** A total of 1251 transient elastography measurements were performed from 2009 to 2013. Reliability was determined according to the interquartile range/median (IQR/M < 0.3-reliable; IQR/M < 0.1 very reliable). Also was determined percentage of success (> 60%) and length of the procedure. Factors that could affect reliability of the procedure were analyzed by logistic regression. **Results.** The sample included 649 (52%) of women, with a mean age of 50 ± 14 years, the prevalence of advanced fibrosis was 37%. The prevalence of reliable procedures was 61%, and it was associated with the percentage of success and with an over the average length to perform the procedure (Figure 1). The percentage of very reliable procedures was 21%, and it was associated with percentage of success and absence of fibrosis (Figure). The successful rate was related with a below the average length to perform the procedure (OR 0.118, 95%CI 0.083-0.169), BMI > 27 kg/m² (OR 0.677, 95%CI 0.477-0.960), and perform the procedure for screening (OR 0.611, 95%CI 0.433-0.861). Finally perform transient elastography for screening purposes was related with a below the average length to perform the procedure (OR 0.705, 95%CI 0.527-0.943) and with less number of reliable procedures (OR 0.748, 95%CI 0.577-0.969). **Conclusion.** Transient hepatic elastography reliability is variable. There are several factors related to the operator. Very reliable procedures are the minimum; improvements in the quality of this procedure are mandatory. The authors declare that there is no conflict of interest.

011

NORMAL VALUES OF TRANSIENT ELASTOGRAPHY IN RURAL PEDIATRIC POPULATION

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Introduction. Transient elastography (TE) has been studied extensively in adults. There is little information on normal values in pediatric populations. Particularly in Hispanic population. **Objective.** Set the parameters of normality in a pediatric population of Mexico. **Material and methods.** Children from the general population of Tlapa de Comonfort, Guerrero, were invited through their parents. Clinical data were obtained, anthropometric measurement, and TE was realized, we excluded patients with history or clinical liver disease. Data are described as median values and interquartile ranges. The values were compared using Student t-test. **Results.** We studied a pediatric population, 48 women (40%) and 66 men (55%). The subjects were divided by age, in group A (1-5 years, n=18), group B (6-10 years, n = 68) and group C (11-16 years, n = 38). Subjects were categorized according to body mass index, showing the following distribution: malnutrition 8% (n = 10), normal weight 60% (n = 72), 11% overweight (n = 14) and 11% obese (n = 14). According to age (Figure 1), group A had a median of 4 (3.8-4.9) kPa, the group B of 5.3 (4.5-6.1) kPa, and group C of 6.6 (4.8-7.7) kPa, being different between groups ($P < 0.05$). According to BMI subjects with malnutrition, had a median of 4.8 (4.3-6.1) kPa, the group with normal body mass index of 4.8 (4.1-5.9) kPa, overweight subjects of 6.7 (6.1-7.7) kPa, and the group with obesity of 5.5 (4.8-7.4) kPa, the values between patients with normal weight

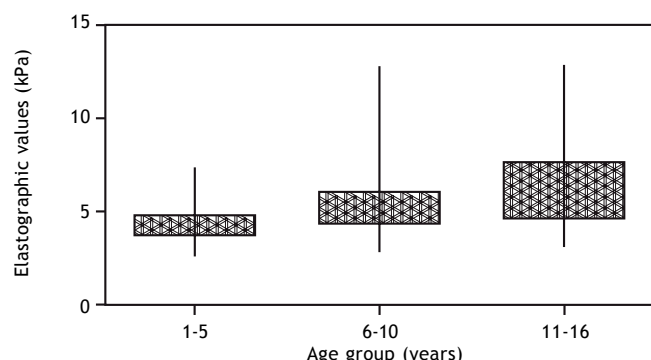


Figure 1. 011. NORMAL VALUES OF TRANSIENT ELASTOGRAPHY IN RURAL PEDIATRIC POPULATION. Distribution of fibrosis stages by ages.

and overweight population were different ($P < 0.05$). By gender, for men was 5.5 (4.5-6.6) kPa, and for women 5 (4.2-6.4) kPa. **Conclusions.** In this pediatric population of Mexico TE values are different from those published worldwide. Showing differences according to age, gender, and body mass index. The authors declare that there is no conflict of interest.

012

PREVALENCE OF FIBROSIS BY TRANSIENT ELASTOGRAPHY IN VULNERABLE POPULATION

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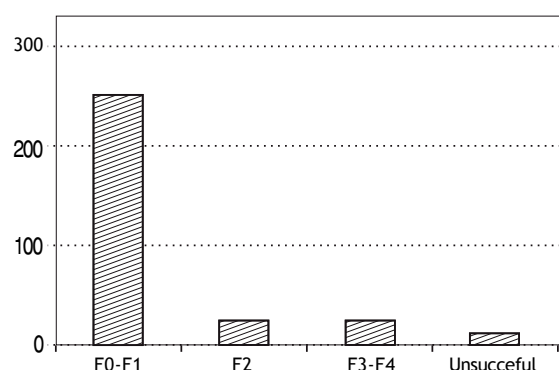


Figure 1. 012. PREVALENCE OF FIBROSIS BY TRANSIENT ELASTOGRAPHY IN VULNERABLE POPULATION. Distribution of fibrosis stages.

Introduction. Transient elastography (TE) is a noninvasive alternative for the detection of hepatic fibrosis. There are few studies analyzing the prevalence of fibrosis stages in the general population. **Aim.** To study the prevalence of liver fibrosis by TE in general population of regions socially vulnerable and geographically isolated. **Material and methods.** Through open invitation to the adult population of Tlapa de Comonfort, Guerrero, patients were studied using TE, data for clinical history, physical examination and anthropometric measurements were collected. The data are described by measures of central tendency and dispersion. **Results.** We included 299 patients, 187 women (62%), their ethnicity was Náhuatl, Mixteca and Tlapaneca, with an age range of 16 to 100 years, and a range of body mass index of 17-44 kg/m². In the study population 243 (81%) had normal values of TE, 24 (8%) had values compatible with F2 fibrosis, and 22 (7%) individuals with TE values compatible with advanced fibrosis F3-F4, and 10 (3%) studies were unsuccessful (Figure 1). An increase in TE values was noticed with increasing body mass index. **Conclusions.** In socioeconomically vulnerable populations advanced fibrosis prevalence is high. TE values increase with body mass index. The authors declare that there is no conflict of interest.

013

THE HEPATOCYTE GROWTH FACTOR (HGF) INDUCES NADPH OXIDASE ACTIVATION BY A MECHANISM MEDIATED BY PKC δ IN PRIMARY MOUSE HEPATOCYTES

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Introduction. Several differentially localized and expressed enzymatic systems contribute to reactive oxygen species (ROS) formation in the liver, including endothelial NO synthase, cytochrome P450 monooxygenases, and NADPH oxidases (Nox). We propose that NADPH oxidase-derived ROS oxidize Keap1 in order to activate transcription factor Nrf2 which drives expression of antioxidants genes providing cell survival. **Aim.** To address the main kinase involved in HGF/c-

Met-induced Nox activation in primary mouse hepatocytes in order to determinate the signaling pathway implicated in this process. **Material and methods.** Primary mouse hepatocytes were isolated by the two-step collagenase perfusion technique from male C57Bl6 mice. Cell primary cultures were pretreated or not with 50 ng/mL HGF for different times and with diphenyleneiodonium (DPI) a NADPH oxidase inhibitor. Nox activity was assayed by spectrophotometry and ROS production by spectrofluorometry labeling with DCFH. We determine by immunoprecipitation the interaction between PKC δ and p47phox in order to determinate the phosphorylation and the Nrf2 activation was determined by confocal microscopy. **Results.** Our data revealed that HGF induce NADPH oxidase activity at early time points peaking at 30 min and this result was related to ROS increase at the same time. We found by immunoprecipitation that PKC δ is involved in the p47phox phosphorylation and therefore in the NADPH oxidase activation, finally we found by oxyblot assay that ROS produced by NADPH oxidase are involved in the Keap1 oxidation that consequently allows Nrf2 activation that provides cell survival. In conclusion our data provide evidence that HGF induce p47phox phosphorylation mediated by PKC δ resulting in NADPH oxidase mediated cell survival. Conacyt 131707.

014

SEROPREVALENCE HBV, HCV AND HIV AND CAUSES OF REJECTION IN THE BLOOD BANK OF HOSPITAL UNIVERSITARIO DR. JOSÉ E. GONZÁLEZ, UANL

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Introduction. In Mexico there are few studies that show the prevalence hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV). **Objective.** To investigate the seroprevalence of viral markers for human immunodeficiency virus, hepatitis B and C viruses as well as the causes of rejection in blood donors at the Hospital Universitario (HU) Dr. José E. González, UANL, Monterrey, N.L. **Material and methods.** Data was recorded on blood bank forms in 104,381 of which 77,451 were blood donors of HU, over a period of eight years (January 2003 to December 2010), whom underwent to serological tests for HBV, HCV and HIV, seroty-

pes 1 and 2, using an enzymatic immunoassay of third generation in human serum or plasma (AxSYM Abbott); the seroprevalence rate of seropositive donors were calculated and stratified by sex. 26,930 were rejected. **Results.** The seroprevalence for positive cases was 1.13% (872); for HCV was 0.8% (623), for HBV, 0.09% (71), and 0.22% for HIV (172). For males, HBV was 0.08% (45), HCV, 0.88% (507), and HIV, 0.25% (143). For females, HBV was 0.13% (26), HCV was 0.58% (116), and HIV was 0.14% (29). HIV-positive men had a 4.1 times higher ratio than women. The most prevalent HCV, followed by HIV and HBV (Table 1). Coinfection was presented during this time in 6 donors (HIV/HBV-2, HIV/HCV-2 and HBV/HCV-2). **Conclusions.** The seroprevalence of viral markers was similar or lower than that reported in national and international literature, low hemoglobin was cause for rejection in most cases. The highest seroprevalence was HCV. This study was supported by departments involved.

The authors declare that there is no conflict of interest.

015

FACTORS ASSOCIATED WITH LIVER INFECTIONS FOUND IN AUTOPSY

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Introduction. Primary infections of the liver parenchyma are rare. The blood supply makes it susceptible to infections of intestinal, systemic origin and the biliary tree provides another via for parasites and bacteria to access the liver parenchyma. Some infections have high mortality if not are treated promptly. **Objectives.** To describe the clinical factors associated with the presence of liver infections detected during the autopsy. **Material and methods.** We reviewed the autopsy reports conducted from January 1th, 2003 to December 31, 2007 looking for viral, bacterial, fungal and parasites liver infections. **Results.** We reviewed data from 3616 autopsies performed in 5 years. Liver infections were found in 117 patients (3%), with age of 50 years (\pm 18.24), 57 (49%) were women and 60 (51%) were men. As for the type of infection 63 (54%) were hepatic tuberculosis, 26 (22%) pyogenic abscesses, 4 (3.5%) histoplasmosis, 3 amebic abscesses, 3 cholangitis abscesses, 3 leptospirosis, 2 cryptococcosis, 2 aspergillosis, 2 candidiasis, 1 leishmaniasis, 1 coccidioidomycosis, actinomycosis 1, 1 case of *Yersinia* sp., 1 nematode, 1 cytomegalovirus, 1 hepatitis C virus and 1 hepatitis B virus. The most important was the pre-

Table 1.* Seroprevalence of HBV, HCV, HIV and coinfections during the period 2003-2010.

	Study population	Seropositive			
		HBV	HCV	HIV	Coinfected
2003	6,288	4 (0.06%)	56 (0.89%)	15 (0.24%)	1 (0.02%)
2004	9,117	19 (0.21%)	88 (0.97%)	15 (0.16%)	0 (0.00%)
2005	9,617	10 (0.10%)	74 (0.77%)	17 (0.18%)	0 (0.00%)
2006	9,852	4 (0.04%)	82 (0.83%)	33 (0.33%)	1 (0.01%)
2007	9,662	7 (0.07%)	81 (0.84%)	26 (0.27%)	2 (0.02%)
2008	9,665	9 (0.09%)	52 (0.54%)	11 (0.11%)	1 (0.01%)
2009	11,530	10 (0.09%)	104 (0.90%)	26 (0.23%)	1 (0.01%)
2010	11,720	8 (0.07%)	86 (0.73%)	29 (0.25%)	0 (0.00%)
Total	77,451	71 (0.09%)	623 (0.80%)	172 (0.22%)	6 (0.01%)

* 014. SEROPREVALENCE HBV, HCV AND HIV AND CAUSES OF REJECTION IN THE BLOOD BANK OF HOSPITAL UNIVERSITARIO DR. JOSÉ E. GONZÁLEZ, UANL

sence of concomitant infection in other organs in 110 patients (94%). Regarding patients with hepatic TB 62 (98%) were associated with miliary TB, sepsis in 41 (35%), DM 30 (26%), alcohol 30 (26%), smoking 26 (23%), hypertension 14 (12%), hematologic malignancies 11 (9.5%), chronic kidney failure 9 (8%) and history of abdominal or pelvic surgery 7 (6%). The median to the time of onset of symptoms was 30 days (1-548 days). Fever was found in 44 (38%), abdominal pain in 39 (33%), fatigue-debility in 34 (29%) and hepatomegaly in 22 patients (19%). **Conclusions.** Liver infections are so rare. In our country the most common liver infection is tuberculosis of the liver, which represents over 50% of liver infections, followed by pyogenic liver abscesses. Other important clinical factors found in these patients were sepsis, diabetes mellitus and a history of chronic alcohol abuse and smoking. The authors declare that there is no conflict of interest.

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MALIGNANT PERIPHERAL NERVE SHEATH TUMOR. CASE REPORT

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Introduction. Malignant peripheral nerve sheath originate from neurofibromas in 5% of cases. Most are presented in a more peripheral nerve in a limb, however, can develop at any level, be diagnosed at abdominal sporadically, usually present as painful masses with local invasion and metastasis. We report a patient of 24 years with abdominal pain, weight loss and abdominal distension secondary to large tumor simulating a hepatic tumor, so percutaneous biopsy was performed with report of a tumor malignant peripheral nerve sheath tumor. **Case report.** A female patient was 24 years old, previously healthy, who began his condition two months before admission with malaise and weight loss involuntary, 13 kg in 2 months, diffuse abdominal pain of medium intensity and persistent nausea. Physical examination showed cachectic, pale, with 40 spots latte widespread distribution, the largest in the thorax and abdomen of 13 cm in diameter. The presence of freckles was documented in Axilla. A indurated mass in the right hypochondrium of 14/12/10 cm below the costal margin was palpated, with irregular edges, not painful on palpation. Ultrasound was performed with reported liver tumor, to rule out hepatocellular carcinoma. Tomography of the abdomen confirmed the mass, unable to determine etiology of the lesion, so percutaneous liver biopsy was performed with a report of malignant peripheral nerve sheath tumor. The patient was not a candidate for surgery and started chemotherapy using epirubicin/ifosfamide for 6 cycles, with improvement of symptoms. Currently the patient is no tumor activity.

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HEPATIC ACTINOMYCOSIS. CASE REPORT

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Introduction and objectives. Actinomycosis is a rare, indolent and slowly progressive infection, liver involvement is con-

sidered rare (< 5%) and is often confused with hepatic tumors. We present a case of hepatic actinomycosis simulating a hepatic neoplasm. **Case report.** 42 year old female with a history of a twin with schizophrenia, uncle with apparent pulmonary tuberculosis. Depressive disorder with carrier-based medical management serotonin reuptake inhibitors and benzodiazepines. Intrauterine device carrier for over 13 years. Sent to our unit with 8 months of malaise, involuntary weight loss, abdominal pain, ascites, jaundice and fever with a diagnosis of cirrhosis and imaging studies reported diffuse hepatocellular carcinoma. However evolving data regarding sepsis and history of IUD actinomycosis is suspected in what is given by management with third-generation cephalosporins and clindamycin with torpid and after 19 days of medical management, the patient dies from severe sepsis, occlusion intestinal and kidney failure. Was performed *post-mortem* study showing multiple liver abscesses, fistula duodenum, colon and terminal ileum with areas of stenosis, uterus and vaginal canal abscesses and purulent ascites and pleural fluid, with histological evidence of sulfur granules and as Gram positive, concluding disseminated actinomycosis as a cause of severe sepsis and death. **Conclusion.** We present the first case reported in the IMSS UMAE Puebla, with disseminated actinomycosis and liver involvement, we believe it pertinent to remind the actinomycosis as a diagnostic potential in patients with abdominal sepsis and risk factors for this entity.

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SECONDARY PROPHYLAXIS FOR VARICEAL REBLEEDING IN NONCIRRHOTIC PORTAL VEIN THROMBOSIS

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Background and aim: Variceal bleeding is usually the first manifestation of portal thrombosis in the non-cirrhotic liver; as a matter of fact, the prevalence of esophageal and gastric varices is of 80-90% and 30-40% in these patients, respectively. There is insufficient data regarding secondary prophylaxis among these patients, and international consensus guidelines advice to extrapolate the recommendations followed in cirrhotic patients (dual therapy: endoscopic treatment and beta blockers). In a randomized controlled trial of propranolol versus placebo, Kiire et al., found a risk reduction for rebleeding of 60% at one-year follow up; in a non controlled study using sclerotherapy in pediatric patients, Vleggar et al., showed a five-year rebleeding rate of 28%; Spander et al., reported a five-year rebleeding rate of 37% with endoscopic ligation. Moreover, given the excellent hepatic function in these patients, some authors have used devascularization or portosystemic shunt procedures as methods of primary or secondary prophylaxis, with overall good results. The objective of this study is to compare rebleeding rates between patients with secondary prophylaxis based on endoscopic ligation and patients with dual prophylaxis (ligation and beta blockade) in non-cirrhotic portal hypertension secondary to portal thrombosis. **Material and methods:** This is an observational, retrospective study. An electronic search of the portal hypertension database at our hospital was performed looking for the diagnosis of portal thrombosis in the non-cirrhotic liver. We analyzed 17 cases with secondary prophylaxis either with monotherapy

(endoscopic ligation) or dual therapy (ligation plus beta blockade). **Results:** A total of 17 cases were analyzed. Mean age was 39 years ($SD \pm 10.9$), 65% (8/17) were men, with a mean follow-up of 106 months ($SD \pm 121$). Five patients had an intrahepatic thrombosis, twelve an extrahepatic one, and amongst the latter, three had extension to either the inferior vena cava or the mesenteric vein. A prothrombotic condition was found in 35% of cases, the most frequent were antiphospholipid syndrome and protein C resistance. Secondary prophylaxis with monotherapy (endoscopic ligation) was used in 4 patients (24%), and dual therapy (ligation plus beta blockade) was used in 13 (76%). Despite prophylaxis, rebleeding occurred in 71% of patients (12/17): 100% (4/4) of patients with monotherapy and 67% (8/13) of patients with dual therapy ($p = 0.26$). The mean propranolol dose of both,

patients who had rebleeding and patients who did not was 80mg ($p = 0.62$). Five patients had a successful secondary prophylaxis and did not rebleed during their follow-up, in two of them a portosystemic shunt had been performed early after the diagnosis of portal hypertension (one mesocava shunt and one abdominal Sugiura), the other three were under secondary prophylaxis with dual therapy. The anatomic distribution of the thrombosis was not found to be an independent predictor for rebleeding. **Conclusions:** Regarding our results rebleeding rate in this group of patients seems to be high and independent of the chosen secondary prophylaxis strategy. Alternative therapies such as surgical portosystemic shunts should be considered in an early fashion in these patients. More studies with more patients are needed to confirm these results.