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ABSTRACT SECTION

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Poster Presentations

A. CASE REPORT

001

FIRST CASES OF ACUTE HEPATITIS HBV/HDV IN ARGENTINA. CASE REPORT

CARLOS REMONDEGUI,* SUSANA CEBALLOS,* JORGE GONZALEZ**
*SERVICIO DE INFECTOLOGÍA & MEDICINA TROPICAL. HOSPITAL SAN ROQUE. JUJUY. ARGENTINA.
**SERVICIO HEPATITIS Y GASTROENTERITIS, DEPARTAMENTO VIROLOGÍA, INEI-ANLIS. ARGENTINA.

The prevalence of HBV infection in our region is relatively high. The Jujuy province is located northwest in Argentina, in a Subtropical Region, bordering with Bolivia and Chile. Inside our province in the Yungas biosphere, there were foci of high prevalence HBsAg 4%, antiHBc 26% in blood donors. Now days this percentages decreased substantially to 1 and 9% respectively, due to national vaccination against HBV since 14 years ago. According to our previous publication HBV genotype F seems to be prevalent also in our province, *J Clin Virol* 2008. This region population is Amerindians belonging to Guaraní culture mixed with Europeans. In Latin America, western Amazonia is a highly endemic area where hepatitis D is prevalent. Non-safe sexual activity seems to be the most important transmission route. There are no reports of HDV circulation in our region neither description of acute cases of HBV/HDV coinfection in Argentina. However there are scarce published studies of HDV prevalence in blood donors and Amerindian communities from Northeast region of Argentine. We here describe two young patients with severe acute hepatitis coinfection. Both from Yungas area, belonging to mixed ethnia, without family history of hepatitis neither personal history of hepatitis. The female patient acquired virus infection via transfusion and the male patient via unsafe sex apparently (Table). **Comments.** We describe evidence of circulation of HBV/HDV in our region and the first cases definition of severe acute coinfection HBV/HDV in Argentina. The female was treated with LAM 3 months. None needed liver transplant and they normalized their lab after 21 days. Both seroconverted HBeAg and then HBsAg at 3 months of follow-up. It is well known, that HBV/HDV coinfection is associated with a higher rate of severe even fulminant acute presentation comparing with HBV infection alone. We used to see 35% of acute cases of HVB with severe clinical presentation reported at XX Congress ALEH 2008. Now we have to think in HBV/HDV coinfection as a probably cause of this high percentage of severe acute presentation.

Table. (001) Sex.

	Male	Female
Age	23y	28y
Tattoo	yes	no
Days of symptoms	20	10
ALT increased UL	x38	x37
AST increased UL	x32	x18
MELD	24	28
HBsAg	pos	pos
aHBc IgM	pos	pos
aHBc IgG	pos	pos
HBeAg	pos	neg
aHBe	pos	pos
aHDV	pos	pos
LAM	no	yes

002

SOFOSBUVIR, RIBAVIRIN AND PEGINTERFERON AS A SUCCESSFUL TREATMENT FOR FIBROSING CHOLESTATIC HEPATITIS AFTER LIVER TRANSPLANTATION: A CASE REPORT IN A MEXICAN TRANSPLANT CENTER

E. NEGRETE-CARBALLO, J.M. ANTOLINEZ-MOTTA, J. AGUIRRE-VALADEZ, L.R. VALDOVINOS-GARCÍA, A. RAMIREZ-POLO, A. CONTRERAS-SALDIVAR, M. VILATOBA-CHAPA, I. GARCÍA-JUÁREZ
DEPARTMENT OF GASTROENTEROLOGY, INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MEXICO CITY, MEXICO.

Introduction. Hepatitis C virus (HCV) recurrence after liver transplantation (LT) is universal. Fibrosing cholestatic hepatitis (FCH) is a severe form of recurrent HCV marked by an aggressive progression of cholestasis and development of fibrosis leading to accelerated graft loss and/or death. Pegylated interferon (PEG) and ribavirin (RBV) as combined therapy has been used in selected LT recipients with moderate to severe recurrent HCV but is limited by frequent side effects and low antiviral efficacy. Sofosbuvir (SOF), an inhibitor of the HCV NS5B polymerase has been shown to be effective in combination with RBV, with or without PEG, in patients with HCV infection of all genotypes (GT). **Material and methods.** We report a case of a patient with FCH following LT, SOF/RBV/PEG therapy was elected, so far 14 of 24 weeks are completed. **Results.** A 61-year-old man with cirrhosis related to a HCV GT2 infection resistant to standard therapy who developed hepatocarcinoma during pre-transplantation period underwent LT in November 2013. At the time of LT, his HCV RNA level of 322,222 IU/mL. Four weeks after he developed jaundice and the liver function tests (LFT) were noted to be

abnormal with a total bilirubin 6.94 mg/dL, aspartate aminotransferase 389 U/L, alanine aminotransferase 850 U/L, alkaline phosphate 299 U/L, gamma-glutamyl transpeptidase 1317 U/L and HVC RNA level 3,000,000 IU/mL. A MRI cholangiography and ERCP were performed showing evidence of a biliary stricture and a 10F plastic stent was placed. Liver biopsy revealed four portal tracts with mild portal and centrilobular inflammation, pericholangitis, cholestasis and focal endothelitis. The LFT remained abnormal, his HVC RNA level increased reaching 13,000,000 UI/mL and a new liver biopsy showed features of FCH. On February 2014 SOF/PEG/RBV was initiated. The patient developed anemia, leukopenia (requiring GCSF), thrombocytopenia, dyspeptic symptoms and severe malaise; mycophenolate mofetil was stopped and the dose of PEG and RBV were adjusted. His liver tests began to improve by week one and were normal at week 10 as his general condition. After 12 weeks of treatment, the HVC RNA level was undetectable. During treatment blood levels of tacrolimus remained stable. Further follow-up will be given at the meeting. **Conclusion.** We report the first case of a Mexican patient with cholestatic HCV recurrence following LT treated with the promising SOF-based regimen which resulted in notable clinical improvement, disease stabilizer and rapid suppressor agent of HCV replication lacking of interaction with immunosuppressive medications as reported in previous literature.

003

ATYPICAL BEHAVIOR OF HEPATOCELLULAR CARCINOMA: SPONTANEOUS REGRESSION, TWO CASE REPORT

A. RAMÍREZ-POLO,* L. VALDOVINOS,* J. AGUIRRE-VALADEZ,* E. MUÑOZ,* M. VILATOBÁ,** A. TORRE,*** A. GONZÁLEZ,**** I. GARCÍA-JUÁREZ**

*DEPARTAMENTO DE GASTROENTEROLOGÍA. **DEPARTAMENTO DE TRASPLANTES. ***DEPARTAMENTO DE HEPATOLOGÍA. ****DEPARTAMENTO DE RADIOINTERVENCIÓN, INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y DE LA NUTRICIÓN SALVADOR ZUBIRÁN, MÉXICO, D.F.

Background. Hepatocellular carcinoma (HCC) is the most common liver tumor; it is the second leading cause of death in patients with cancer and the fifth leading cause of cancer in men and the seventh in women. Prevalence is high in regions where Hepatitis B virus (HBV) infection is endemic, with sub-Saharan Africa and East Asia prevalence reports to 20 cases per 100,000. In Mexico, the incidence is 5 and 4.9 cases per 100,000 habitants, for male and female respectively. In North America and Europe regions, principal risk factor is hepatitis C coinfection (HCV). Between 80 to 90% of HCC cases are related to cirrhosis. Frequently, typical radiologic findings are diagnostic for HCC. The triphasic liver computed tomography (CT) shows an enhanced lesion in arterial phase with completed washing out in portal venous phase images. Current metastatic lesions, number and size of hepatic tumors determines the treatment. The options can be orthotopic liver transplant (OLT) or radiointervention techniques. HCC spontaneous involution is a rare phenomenon, only 70 case reports are described in the medical literature. The spontaneous regression of a cancer lesion is defined as partial or complete disappearance of a malignancy in the absence of treatment or in the presence of therapy that is considered inadequate to exert any significant influence. Causes are unknown, but some involution cases are related with tumoral hypoxia or systemic inflammatory response, previously it has related to needs for transfusions and decreased alphafetoprotein (AFP) levels. **Case report.** We describe two HCC spontaneous involution cases in two patients. The first case was a 72 years-old man with liver cirrhosis by hemochromatosis. He had a typical HCC lesion on RMN of 14 mm at VII liver segment. This lesion was not visualized on CT previous to RFA. The second one, was a 52 years old man with cryptogenic cirrhosis, the CT demonstrated a 5 cm typical lesion in segment II. In the second CT, the lesion reduce to 3 cm. Previously PEI procedure, the lesion disappeared. The AFP levels reduction and absence of metastatic disease was demonstrated in both cases. The patients continues ambulatory monitoring, with radiologic and laboratory surveillance, without HCC. **Discussion.** The spontaneous regression of HCC lesion is a rare phenomenon. The surveillance and the radiology approach previously any treatment is very important because it could demonstrate the lesion involution.

004

JAUNDICE AND ABNORMAL LIVER FUNCTION TEST AS FIRST MANIFESTATION OF DIFFUSE LARGE B CELL LYMPHOMA. A CASE REPORT

M.A. PEÑALOZA-POSADA,* G. BARRANCO-LAMPON,** C. RAMOS-PEÑAFIEL,** E. PÉREZ-TORRES*

*GASTROENTEROLOGY DEPARTMENT. HOSPITAL GENERAL DE MÉXICO EDUARDO LICEAGA. MÉXICO, D.F.

**HEMATOLOGY DEPARTMENT. HOSPITAL GENERAL DE MÉXICO EDUARDO LICEAGA. MÉXICO, D.F.

Introduction. Diffuse large B cell lymphoma (DLBCL) is the most common form of no-Hodgkin lymphoma. The average age at time of diagnosis is 60 years, more frequently in men. Often is a painless rapid swelling in the neck, armpit, or groin which is caused by enlarged lymph nodes, with night sweats, fever and weight loss. Is an aggressive (fast growing) lymphoma and is fatal if left untreated, but with timely and appropriate treatment, 60% of all patients can be cured. 10% of the cases developed hepatic dysfunction and jaundice as manifestation with alcohol consumption and viral hepatitis as associated risk factors. Anthracycline-based chemotherapy cannot be safely administered in these setting, so an alternative regimens are required. Successful use of dexamethasone, cytarabine and cisplatin (DHAP) as part of initial therapy is use until hepatic function normalized and standardar treatment can be administrated known as CHOP. **Case report.** Female 57 years old. History of moderate to heavy alcohol consume and arterial hypertension. Presented with jaundice, fever, asthenia, adinamia and significative weight loss, abnormal liver function test with total bilirubine of 8.29 md/dl, a alanine aminotransferasa (ALT) of 205 U/L, a aspartate aminotransferasa (AST) of 194 U/L, alkaline phosphatase (AP) 623 U/L and gamma glutamyltransferasa 592 U/L. Viral hepatitis serology was negative. A neck lymphadenopathy of 2 x 3 cm was explore, with biopsy revealing diffuse large B cell lymphoma, bacause of the elevated bilirubin and transaminases DHAP was administered. CT with multiples lymphadenopathies and hepatomegalia. The patient tolerated chemotherapy without complication and within 3 weeks the total bilirubin, AST, ALT, and AP had decreased to 4.1 mg/dL, 37 U/L, 45 U/L and 324 respectively and the estándar treatment was administrated with excellent response. **Discussion.** DLBCL, typically do not result in hepatic dysfunction. This fact may delay diagnosis, contributing to the poor prognosis. Establishing a diagnosis of malignancy as the cause of liver failure is difficult and requires a high index of suspicious. Given the poor prognosis

associated with late or missed diagnosis and the benefits of early chemotherapy, lymphoma should be considered. DLBCL advances very quickly and it requires immediate treatment, but in patiens that have hepatic dysfunction the estándar treatment has resulted in further liver damage, and also hepatitis reactivation and fulminant hepatitis after initiation of therapy. Thats the importance of using DHAP as firts line treatment until hepatic function normalized.

005

HEPATITIS C INFECTION-AUTOIMMUNE HEPATITIS OVERLAP SYNDROME: CASE REPORT AND LITERATURE REVIEW

E. CANTÚ-LLANOS, J. CASTRO GÓMEZ, D. RUIZ-ROMERO, C. GUERRERO-VELÁZQUEZ, E. NEGRETE-CARBALLO, J. SÁNCHEZ-ÁVILA, I. GARCÍA-JUÁREZ
DEPARTAMENTO DE GASTROENTEROLOGÍA, INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN. CIUDAD DE MÉXICO, MÉXICO.

Introduction. Hepatitis C infection (HCV) and autoimmune hepatitis (AIH) overlap syndrome is a unique condition and represents a diagnosis challenge. The appropriate treatment for this entity has not been clearly standardized. The following case illustrates the biochemical and histological findings in a HCV and HAI overlap syndrome. **Case report.** A 58 years old woman was referred to our institution due to a two year history of fatigue and abnormal liver tests. At admission, her studies revealed the following: BT 1.77 mg/dL, AST 61 U/L, ALT 37 U/L, AP 296 U/L, IgG 2808 mg/dL, ANAs 1:320, SMA 1:80 and 69,000 platelets A viral load of 672,363 copies confirmed infection. The genotype 1b was found. An ultrasound revealed surface nodularity and splenomegaly. Upper gastrointestinal tract endoscopy exhibited small esophageal varices. Liver biopsy showed cirrhosis, with intense activity and plasma cell infiltration predominance. Due to the histological findings the patient was started on prednisone. Prior to the following visit, the patient attended another institution. She was told to suspend the prednisone and was started on INF-α2a and ribavirin. Rapid virology repose (RVR) was achieved. Unfortunately, at week 18 she presented severe sepsis due to pneumonia. Antiviral treatment was suspended. Currently, the patient has a viral load of 284, 135, BT 2.17 mg/dL, ALT 57 U/L, AST 108 U/L and AP 135 U/L. **Discussion.** It's burdensome to discriminate if the autoimmune findings are due to HCV or HAI. The findings of interface hepatitis in HCV infection is rare (5.2%). Serum antibodies are frequently positive in HCV infection: ANA (10-33%), SMA (13-66%) and LKM (0-3%). Due to histological changes we decided to start the patient on prednisone, but without our consensus the patient changed to antiviral treatment. Since RVR was achieved we decided to continue the antiviral treatment. The current strategy includes treating the dominant disease. Patients with HAI predominance are those with ANA $\geq$ 1:320, SMA and ANA $\geq$ 1:40 and compatible histological findings. HCV dominant cases are defined as ANA $\leq$ 1:320, HCV viremia and histological findings of steatosis with lymphoid aggregates or duct damage. **Conclusion.** The correct diagnosis and management of patients with HCV-HAI overlap syndrome remains controversial. The decision to treat based on the predominant histological behavior may dictate the initial treatment. The correct timing to treat the second disease remains unclear. A second biopsy could impact on the treatment strategy; however more studies are needed to establish precise recommendations.

006

CONGENITAL LIVER FIBROSIS ASSOCIATED TO INTESTINAL PERFORATION BY ASPERGILLUS

M. JIMENEZ-LUEVANO, M. JIMÉNEZ-PARTIDA, R. AGUILAR-RODRÍGUEZ, L. RIGGEN-MARTINEZ, A. FÉLIX-GUZMÁN, M. GUTIÉRREZ-MEDRANO, R. FRANCO-TOPETE, T. LEÓN-ESCOBEDO, A. BRAVO-CUELLAR
ISSSTE, ZAPOPAN, JALISCO, MÉXICO.

Introduction. Congenital liver fibrosis is a rare condition with a 1/100,000 prevalence in newborns. Its etiology its congenital, of origin autosomal recessive and it can be found as typical familiar form or as an sporadic case and be linked/related to poliquistic renal disease in up to 50% of cases. It generates an overproduction of embryonic bile ducts in the portal tracts which persistence conduces to portal hypertension along with its clinical complications during childhood and adolescence. The relation between congenital liver fibrosis and intestinal perforation due to aspergillus it rare and uncommon; it clinical symptoms and signs are found prevalently in patients with neutropenia, and previous use of corticosteroids and high spectrum antibiotics. **Material and methods.** Ten year old infant, who is admitted to pediatric services on June/2013 showing abdominal distention, jaundice and general discomfort, this clinical condition has three months of evolution. At physical examination the patients is found with icteric conjuntive, general paillnes, hepatosplenomagaly 7 cm under rib cage, and a perception of liquid in abdominal cavity. Labs: HB 6.9 g/dL, leukocytes 9.27 miles/μl, platelets 367 mil, neutrophils 4.50%, eosinophils 15.5%, AST 70U/L, ALT 38U/L, FA 254U/L, proteins 6.6 g/dL, albumin 2.5 g/dL, total bilirubin 6.8 mg/dL, direct 4.20 mg/dL, INR 2.59. Treated with multiple medical regimens showing no improvement. The patient undergoes multiple exams; biochemical studies: negative serological for VHA, VHC, VHB, metabolic diseases, study endoscopic, molecular, radiographic chest plate, TAC, eco Doppler, and histological. During his hospital stay develops a pneumonic process which does not respond to several treatments. Develops hypoxemia, undergoes assisted ventilation two weeks after admission, and shows signs of acute abdomen. Reason for which laparotomy is used as a method for diagnosis finding intestinal perforation. One week posterior to laparotomy the patient develops disseminated intravascular coagulation and cardiorespitatory arrest. **Results.** Histological studies showed congenital liver fibrosis and intestinal aspergillosis. **Conclusion.** The predominant complications found on congenital liver fibrosis are from portal hypertension. However; micotic infestations in atypical places as in this case, should be considered in the future. Considering the fact that; these fungal infections are more predominant in patients with immunosuppression, as well as exogenous sources, especially in the respiratory tract.

007

BENIGN RECURRENT INTRAHEPATIC CHOLESTASIS: A CASE REPORT AND LITERATURE REVIEW

D. RUIZ-ROMERO, J. CASTRO-GÓMEZ, C. GUERRERO-VELÁZQUEZ, E. CANTÚ-LLANOS, E. NEGRETE-CARBALLO, A. TROLLE-SILVA, E. LÓPEZ-MENDEZ, J. SÁNCHEZ-AVILA, I. GARCÍA-JUAREZ
DEPARTAMENTO DE GASTROENTEROLOGÍA, INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, CIUDAD DE MÉXICO, MÉXICO.

Introduction. Benign recurrent intrahepatic cholestasis (BRIC) is an autosomal recessive disorder, associated with mutations in the gene ATP8B1 and ABCB11. It was first described by Summerskill and Walshe in 1959. Ten years later, Tygstrup and Jensen defined its diagnostic criteria's: 1) Recurrent episodes of jaundice and pruritus fluctuating with symptom free intervals, 2) Absence risk factors related to intrahepatic cholestasis, 3) Normal extrahepatic and intrahepatic bile ducts documented by cholangiography and 4) Canalicular cholestasis noted thru histology. The diagnostic confirmation is obtained by identifying the mutated genes. **Case report.** A 32 years old woman was referred to our institute for a two month history of jaundice and severe pruritus. The year prior to admission she suffered a similar event that lasted 3 months and resolved spontaneously. Family history of liver disease, herbal products, over the counter medication, illicit drugs or alcohol use was denied. Her liver tests at admission were the following: total bilirubin of 34.5 mg/dL, direct bilirubin 16.9 mg/dL, indirect bilirubin 17.6 mg/dL, alkaline phosphatase 426 UI/L, gamma-glutamyl tranferase (GGT) 27 UI/L, alanine aminotransferase 40UI and aspartate aminotransferase 47UI/L. The viral hepatitis panel, anti-nuclear antibodies, anti-mitochondrial antibodies, ferritin, saturation index, ceruloplasmin and immunoglobulins were negative or in normal range. Total bile acids (265 μmol/L) and chenodeoxycholic acid (63.7 μmol/L) levels were also measured. An endoscopic cholangiography was performed showing normal extrahepatic and intrahepatic bile duct architecture. The liver biopsy revealed canalicular cholestasis. **Discussion.** BRIC or Summerskill-Walshe-Tygstrup syndrome is characterized by cholestasic syndrome with normal or slightly elevated GGT. This case describes a young woman with a recurrent cholestasic syndrome where biliary obstructive disease, viral hepatitis and other immunologic or genetic entities had been discarded. The liver biopsy findings were also distinctive. Our case meets the criteria proposed by Tygstrup and Jensen making the diagnosis of BRIC highly possible. Treatment options include ursodeoxycholic acid (UDCA) or rifampin with an adequate response. Some cases BRIC can progress to chronic liver disease, making liver transplantation the only option. Our patient was started on UDCA with clinical and biochemical resolution. The specific mutations were requested, but results are still pending. **Conclusion.** This case represents an extraordinary cause of cholestasic syndrome. Although, confirmation thru genetic testing hasn't been obtained, the case meets the clinical, morphological and histological criteria to support our diagnosis. BRIC should be considered in a cholestasis syndrome with normal GGT. Its proper diagnosis can lead to proper treatment and resolution.

008

THERAPEUTIC MANAGEMENT OF SEVERE CHOLESTATIC HEPATITIS WITH PENTOXIFYLLINE AND PRENDISONE

M. JIMÉNEZ-LUEVANO,[*,**] P. RODRÍGUEZ-VILLA,[**] S. RAMÍREZ FLORES,[**] M. JIMÉNEZ PARTIDA,[*] E. OROZCO-CHÁVEZ,[*] E. AGUILAR-RODRÍGUEZ,[*] L. RIGGEN-MARTÍNEZ,[*] A. FÉLIX-GUZMÁN,[*] J. RAMÍREZ-JAIMEZ,[*] R. FRANCO-TOPETE,[*] S. LEÓN-ESCOBEDO,[**] M. GUTIÉRREZ-MEDRANO,[**] A. BRAVO-CUELLAR*
[*]ISSSTE (VALENTÍN GÓMEZ FARÍAS). ZAPOPAN, JALISCO, MÉXICO.
[**]CENTRO UNIVERSITARIO DE CIENCIAS DE LA SALUD. GUADALAJARA, JALISCO, MÉXICO.

Introduction. Cholestatic hepatitis is a severe clinical entity which could be acute or chronic and has a mutiple etiology; furthermore, it entails an elevated morbi-mortality. It is manifested with a decrease of the canalicular bile flow that produces accumulation of biliar substances in blood and extrahepatic tissues. Two weeks later of the acute presentation; there is an elevation of bilirubin in adults > 10 mg/dL. Its incidence is 3 per 375 patients with jaundice. The medical treatment is based in corticosteroids; however, the possibility of a fulminant liver must be always present. So here is presented a case of a severe cholestatic hepatitis treated with pentoxifylline and prednisone. **Case report.** An 8 years old, was admitted to the emergency department of ISSSTE on February 2014 for jaundice 3 months duration, accompanied by malaise, acholia, choluria and pruritus; managed with multiple treatment without response. As an important history data is resulted from a twin pregnancy, with a gestational age of 25 weeks, birth weight of 680 g and received multiple transfusions; brother with hereditary spherocytosis. The patient had severe generalized jaundice, temperature 38 °C, hepatalgia and hepatosplenomegaly of 4 cm. The laboratory upon admission have: BT: 63.8 U/dL, BD: 60.2 U/dL, BI: 3.5 U/dL, TP: 24.4, INR 2,047, TPT: 37.1, glucose: 56, GGT: 127.3, GOT: 1567.1, GPT: 1169.1, FA: 236 and LDH: 761. Presented during the stay an INR: 2,047 being handled with pentoxifylline 100 mg/24 h, methylprednisolone 60 mg/m^2/24 h, urodesoxicolic acid 100 mg/24 h, vitamin E/24h responding favorably until the discharge; having TP: 20.2, INR 1.81, PTT: 54.2, glucose: 73, GPT: 68, GOT: 58, BT: 4.80, BD: 2.33, BI: 2.47, LDH: 483, FA 483. Diagnosis: cholestatic hepatitis in pre-cirrhotic phase; with autoimmune etiology. **Discussion.** Intrahepatic cholestasis is a clinical entity which could have a favorable evolution; nevertheless, in especial conditions can develop fibrosis, chronic liver disease, cirrhosis and death. Traditional medical treatment has been based on corticosteroids; however, in a patient with hyperbilirrubinemia of 63.8 U/dL; pentoxifylline (IV) was added, responding beneficially; apparently for their anti-inflammatory, antioxidant, anti-fibrotic and anti NF-kb effects; so it is suggested multicenter studies to verify its true effectiveness; due to obtain a positive response in the patient.

009

HEMORRHAGE DUE TO DUODENAL ECTOPIC VARICES

PATRICIA L. PÉREZ-IXCOY, EDUARDO PÉREZ-TORRES
HOSPITAL GENERAL DE MÉXICO, CIUDAD DE MÉXICO, MÉXICO.

Introduction. Ectopic varices are defined formed by portal hypertension abdomen except the region of the gastroesophageal varices are the cause of bleeding in 1 to 5% of patients

with intrahepatic portal hypertension and in 20 and 30% of patients with extrahepatic portal hypertension and 2 to 5% of variceal bleeding. Duodenal varices are most commonly caused by portal hypertension secondary to cirrhosis, make up 17% of all ectopic varices bleeding. They have a prevalence of 0.2 to 0.4% in all patients undergoing upper endoscopy. Treatment should be individualized and depends on the experience and local resources, In case of acute bleeding vasoconstrictor drugs will be administered, and if have an endoscopist with experience, you can try to endoscopic therapy. Local treatment (ligation, sclerotherapy, embolization) providing to control bleeding in most cases; but is associated with a high rate of rebleeding due to the persistence of portal hypertension. **Case report.** We report a case of ectopic varices as atypical presentation of duodenal gastrointestinal bleeding in a patient with liver cirrhosis and portal hypertension. A 44-year-old man with alcoholic cirrhosis AND portal hypertension was admitted with hematemesis and hematochezia. His hemoglobin was 5.9 mg/dL, requiring blood transfusions, with esophagogastroduodenoscopy evidencing large esophageal varices with endoscopic variceal ligation, ultrasound is performed which shows images compatible with liver cirrhosis, portal vein 16.8, splenomegaly and splenic collateral, six months later, the patient was readmitted for melena and hematochezia EGD without any source of bleeding found. Endoscopic capsule was performed evidencing angiectasia small suspicious lesions, vascular ectasia and colon, However, recurrent bleeding occurred 2 days later enteroscopy was performed showed a duodenal varix with stigmata of recent bleeding, therefore, injection sclerotherapy, three months later the patient presented again upper gastrointestinal bleeding with hypovolemic shock and died in critical care. **Discussion.** Duodenal varices are typically located in the first or second portions of the duodenum. Most cases occur secondary to portal hypertension, we observed that in the case of patient local treatment with sclerotherapy, achievement control bleeding; however to associate a rebleeding due to the persistence of portal hypertension.

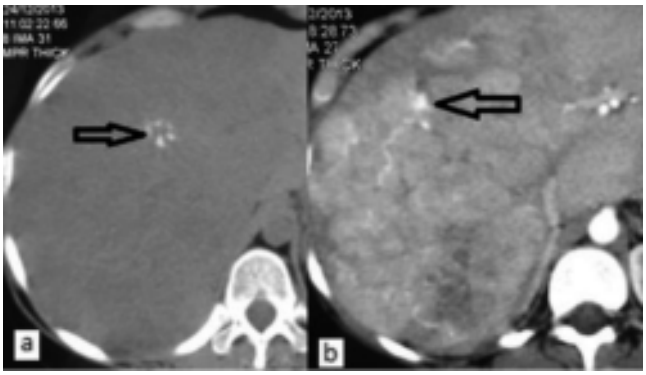

Figure 1. (010) CT without (A) and with contrast (B) wherein hypervascular liver tumor, calcified central scar is observed (arrows).

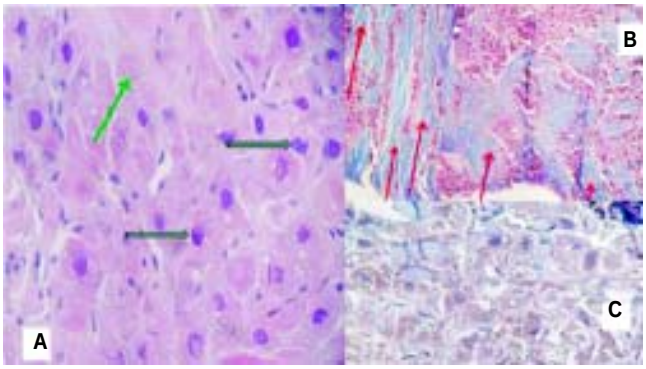

Figure 2. (010) A. FLC with eosinophilic cells with prominent nuclei and nucloeolos and intracytoplasmic pale bodies (green arrows). B. Masson staining evidence the fibrin strands (red arrows).C. Cytokeratin 7 staining positive.

010

FIBROLAMELLAR HEPATOCELLULAR CARCINOMA: A CASE REPORT

G. PARRA-TORRES,* A. MONTAÑO-LOZA,* C. DÁVALOS-COBIÁN,* M. ROSALES**

**DEPARTMENT OF GASTROENTEROLOGY AND **DEPARTMENT OF ANATOMIC PATHOLOGY, WESTERN NATIONAL MEDICAL CENTER SPECIALTY HOSPITAL; INSTITUTO MEXICANO DEL SEGURO DEL SOCIAL, GUADALAJARA, JALISCO, MÉXICO.*

Background/Aims. Fibrolamellar carcinoma (FLC) is an aggressive primary neoplasm of liver that has been reported to represent 8.6% of all hepatocellular carcinomas (HCC) in Mexico (Moreno-Luna, *et al*. *BMC Cancer* 2005; 5: 142). FLC occurs more frequently in children and young adults, and controversy exists whether FLC has a better prognosis than HCC, since is not associated with chronic viral infection and cirrhosis (Torbenson M. *Scientifica* 2012; 2012: 743). Surgical resectability is one of the most important prognostic features for FLC (Stipa. *et al*. *Cancer* 2006; 6: 106). Their etiology is unknown and efforts aimed at elucidating its molecular characteristics are a research priority. FLCs have an overall low cure rate. This report describes a patient with FLC with no feasible therapeutic options. **Case report.** A 24-year-old woman sought medical attention for abdominal pain, malaise, anorexia, and diarrhea for two-months. She was found to have hepatomegaly and ascites on physical exam, and a computed tomography (CT) scan revealed a 18 cm heterogeneous tumor involving both hepatic lobes, with early arterial enhancement, portal venous washout and hyperdense calcified central scar (Figure 1). Serum α-fetoprotein, Ca 19-9 and carcinoembryonic antigen levels were normal. HBsAg and HCV-Ab were negative, and liver biochemistries showed elevation of aminotransferases and alkaline phosphatase, and normal bilirubin. Tru-cut needle biopsy showed a FLC with immunoreactivity to Hep-par 1, alpha-fetoprotein and cytokeratin 7 (Figure 2). Because of the tumor size and vascular invasion the patient was not candidate for surgical resection. Unfortunately, there are no known effective chemotherapies for FLC that cannot be surgically resected. Patients with unresectable disease have poor prognosis, with median survival between 3 to 7 months, and they should be enrolled in clinical trials as there are no effective systemic options. **Conclusions.** FLC should be part of the differential diagnosis of a liver tumor in young adults who are otherwise healthy. Pathogenesis of FLC is not known and efforts aimed at elucidating its molecular characteristics are a research priority. Surgery can provide long-term disease control and should be performed where possible. Liver transplantation and ablative therapies may be considered, although there is no prospective data to evaluate its efficacy.

011

NON-HFE HEMOCHROMATOSIS, CASE REPORT

E. PÉREZ-REYES,* G. ARISTI-URISTA,** B. MARTÍNEZ-SALDÍVAR,*** E. PÉREZ-TORRES*
**GASTROENTEROLOGY DEPARTMENT, **PATHOLOGY DEPARTMENT, ***LIVER CLINIC, HOSPITAL GENERAL DE MÉXICO DR. EDUARDO LICEAGA, MÉXICO D.F.*

Introduction. Hemochromatosis is a disorder of progressive tissue iron deposit, without treatment it causes damage where it's deposited. It's an autosomal recessive disorder, predominantly in white people, with prevalence of one case in 300. The alteration in HFE gen is the most frequent, C282Y mutation occurs in 90% of patients, the second one is H63D. The absence of these doesn't rule out the disease. Cases in which HFE gene are not documented; alterations at genes related in pathways involved in the regulation of iron homeostasis are present. **Case report.** Male, 32 years old, without a family history of importance. Allergies, alcoholism and transfusions were negatives. He had an ocular surgery because of congenital cataract at 2 years old. Smoking index 0.35 cigarrets/year. He had skin progressive pigmentation by 1 year, and he suddenly presented jaundice and fatigue. Doppler liver ultrasound showed hepatosplenomegaly with biliary sludge. Magnetic resonance showed gallstones and a hypointense liver on T2, splenomegaly of 20 cm with hypointensity on T2. Laparoscopic cholecystectomy was performed, and a liver biopsy was taken, it was compatible with hemochromatosis. Iron kinetic showed high ferritin (911.5 ng/mL) and percentage of transferrin saturation (532%). HFE gene mutations were looking for being homozygous normal for both mutations. Complementary studies: HIV, VHB, VHC, and direct Coombs test negatives; bone biopsy normal, but with high intracellular and extracellular hemosiderin. Echocardiogram and endoscopy were normal. Phlebotomy treatment is initiated by Hematology department. **Discussion.** Non-HFE hemochromatosis is a rare disease, it is distributed in various parts of the world no matter the race, usually as the HFE hemochromatosis patient has elevated serum ferritin and transferrin saturation percentage. Non-HFE hemochromatosis is classified according to the mutation found. Hemojuvenil and hepcidin mutation are pooled in the same group, considered as hemochromatosis type 2, 2A and 2B respectively, occurs in patients under 30 years accompanied by cardiomyopathy and hypogonadism. Transferrin receptor 2 mutation (T*f*R2) or type 3 hemochromatosis is clinically similar presentation to the Hemochromatosis with HFE mutation or type 1 (fatigue, lethargy, skin pigmentation, liver damage, diabetes mellitus, endocrine disruption, cardiomyopathy and hypogonadism). Mutation in ferroportin or type 4 has same features that type 1, but with less intense symptoms, anemia and low tolerance to phlebotomy can be present. **Conclusion.** The absence of HFE mutation doesn't rule out the disease. Clinically the patient may correspond to type 4, in this moment our patient has an adequate response to treatment, with normal synthesis function liver.

012

HEPATIC ACTINOMYCOSIS, A CASE REPORT

I. LÁZARO-PACHECO, G. ROJAS-LOUREIRO, B. MARTÍNEZ-SALDIVAR, PEREZ-TORRES E
HOSPITAL GENERAL DE MÉXICO. MEXICO CITY, MEXICO.

Introduction. Actinomycosis is a granulomatous disease of slow evolution. Its incidence is estimated between 0.3-1 episodes/100,000 habitants predominantly in men (3:1) between 30-50 years. The causative organism is a gram positive bacillus, Actinomyces israelii, identified with Grocott Gomori technique, measuring about 1 micron of diameter, are strict anaerobes, and require a minimum temperature of 30 ºC to grow. Clinically present with fever, abdominal pain, anorexia and weight loss. In some cases nausea, vomiting, abdominal pain and diarrhea. Histopathologically it is characterized by the presence of yellow granules of 1 to 2 mm in diameter called "sulfur granules" by their gross appearance. Their locations are: orofacial (56%), thoracic (15%) and abdominal (20%). Actinomyces is part of the normal flora of the oropharynx, gastrointestinal tract and female genitalia, in pathological circumstances this bacterium can cause disease in humans. **Case report.** Male 50 years old, history of obesity, diabetes mellitus 2, left pyelolithotomy, extracorporeal shock wave lithotripsy and exploratory laparotomy for left renal abscess. He started with fever, 38-39 ºC, associated with abdominal pain and left flank pain. At the time of admission with surgical wound was draining, characteristic appearance in sulfur granules, hepatosplenomegaly, leukocytosis, anemia and alterations in liver function tests, contrast abdominal CT scan was performed with residual image of left renal abscess, not meriting drainage, and multiple ovoid lesions with heterogeneous attenuation pattern, predominantly hypodense , with ring enhancement. Liver ultrasound images with multiple lesions rounded. Skin biopsy of surgical wound and Liver biopsy, stained positively with Gram's, periodic acid-Schiff and Gomori's methenamine silver stains, and started treatment based on penicillin G sodium. **Conclusions.** Actinomycosis is a rare, uncommon cause of liver abscesses, which usually develop in the context of disseminated disease. A liver lesion is present in 5% of cases of actinomycosis and in 15% of abdominal cases. Usually with a nonspecific clinical presentation, so it is important to consider this diagnosis in differential etiology as occupying lesions of the liver, especially in immunocompromised patients.

013

GIANT FOCAL NODULAR HYPERPLASIA IN A PEDIATRIC PATIENT. A CASE REPORT

M.A. PEÑALOZA-POSADA,* G. ARISTI-URISTA,** R. PEÑALOZA-RAMIREZ,** E. PÉREZ-TORRES*
**GASTROENTEROLOGY DEPARTMENT, **PATHOLOGY DEPARTMENT. HOSPITAL GENERAL DE MÉXICO EDUARDO LICEAGA. MEXICO CITY.*

Introduction. Focal nodular hyperplasia (FNH) is a common non-malignant hepatic tumor that is not of vascular origin. Corresponding to 8% of non-malignant tumors, at second place after hemangioma. In childhood 10% of hepatic tumor are benign, and 0.02 to 2% are FNH. The FNH is seen in both sexes an throughout the age apectrum, although it is found predominantly in women between the ages of 20 and 50 years, with a diameter less than 5 cm. Is believed to occur as a result of a localized hepatocyte response to an underlying congenital arteriovenous malformation, with an hyperplasic process with abnormally organized pattern. In 80% the clinical course is silent, and FNF is incidently discovered during imaging test. For the optimal evaluation of FNH a helical CT scan with 3-phase study should be performed; the lesión becomes hyperattenueating in the arterial phase with a hypoattenuating stellate central scar that becomes hyperattenueating in delayed phase. If the image lesion is not typical a needle biopsies are helpful for the diagnosis. Surgery

only if syntomatic, complication or compression of adjacent organs. **Case report.** Male, 9 years old with no patological hystory. Initiated prior to hospitalization with diarrhea and being documented by pedriatician with hepatomegaly, starting study protocol with Doppler ultrasound and abdominal helicoidal CT showing a circular mass of 12 x 10 cm, with hyperattenueating in the arterial phase and without stellate central scar. The liver function test was within the reference range and no clasical images pattern was shown, so an hepatic biopsy was taken to determinate de etiology. Nodular overgrowth of normal hepatocytes, abnormal architecture and fibrous tissue was found at biopsy positive for β-catenin. Because of the size of FNH a right hepatic lobectomy was made and the patient is now following-up at regular medical dates. **Discussion.** Although this tumor is quite common in women at the third decade, it have to be suspected in every age. The image studies are helpfull at diagnosis, with high sensitivity and specificity, but in cases like these its very important to determine the histopathology by hepatic percutaneous biopsy with β-catenin or glutamine synthetasa as markers. It can be less invasive with magnetic resonance or scintigraphy using Tc-sulful colloid. The importance of determine with certainty a FNH is that malignant transformation has not been reported and the treatment and follow-up is different than the malignant tumors, avoiding unnecessary surgery or hazardous treatments.

014

HEPATIC ABSCESS IN THE NEONATAL PERIOD

S. GIRALDO-LORA,* M. OSORIO-RUIZ*
FACULTAD DE SALUD. ESCUELA DE MEDICINA. DEPARTAMENTO DE PEDIATRÍA. UNIVERSIDAD DEL VALLE, CALI, COLOMBIA.

Introduction. Neonatal liver abscess is a rare clinical entity which differs in its cause significantly between children and adults. About 50 cases of neonatal solitary liver abscess have been reported. Newborns may have a relatively higher risk due to immaturity of the immune system, particularly adhesion and chemotaxis of neutrophils decreased. Other risk factors are described systemic sepsis, contiguous infection, umbilical catheterization, prolonged parenteral nutrition, prematurity and necrotizing enterocolitis, abdominal surgery and immune deficiencies. Liver abscess is particularly rare in neonates, in most cases fatal and its diagnosis and management are difficult by the lack of clinical suspicion. Ultrasound diagnosis could be the first imaging study in newborns. Treatment of single liver abscess in neonates usually been managed with drainage by laparotomy with antibiotic therapy, but percutaneous drainage is less invasive and is often preferred as first-line treatment. **Material and methods.** A case of a newborn patient who is diagnosed with liver abscess and wide spectrum antibiotics treatment were administered for 43 days, with follow-up ultrasound. Risk factors of this patient were: umbilical catheter, parenteral nutrition, necrotizing enterocolitis with subsequent sepsis. **Conclusion.** Contribution is made to the case in the management of liver abscess in newborn, which could be done only with wide spectrum antibiotics, including vancomycin, with follow-up with serial ultrasound imaging without surgical treatment. Clinical evolution was satisfactory.

015

BUDD-CHIARI SYNDROME DURING PREGANACY: THE IMPORTANCE OF AN EARLY DIAGNOSIS

C. JARAMILLO-BUENDÍA,* A. MONTAÑO-LOZA,* C. DÁVALOS-COBIÁN,* J. RAMÍREZ-GARCÍA,* S.M. GONZÁLEZ-HUERTA,** J.G. VÁZQUEZ-HUERTA**
**DEPARTMENT OF GASTROENTEROLOGY, **DEPARTMENT OF ANATOMIC PATHOLOGY, WESTERN NATIONAL MEDICAL CENTER SPECIALTY HOSPITAL, INSTITUTO MEXICANO DEL SEGURO SOCIAL, GUADALAJARA, JALISCO, MÉXICO.*

Background/Aims. Budd-Chiari syndrome (BCS) is a manifestation of hepatic venous outflow obstruction at any level from the small hepatic veins to the junction of the inferior vena cava and the right atrium regardless of the cause of obstruction. The clinical presentation depends on the extent and rapidity of hepatic-vein occlusion and on whether a venous collateral circulation has developed to decompress the liver sinusoids. The development of thromboembolic events during or after pregnancy is not uncommon; however, chronic liver failure after pregnancy attributable to BCS has rarely been reported. This report describes a patient with chronic hepatic failure in pregnancy attributable to BCS. **Case report.** A 24-year-old pregnant woman was admitted to medical Institution with history of ascites for two-years. She developed ascites for first time during her week seven of pregnancy. There was no history of venous thrombosis, and no prior history of liver disease. She was well until one week before admission to another hospital, when she felt pain in the right upper quadrant and noted rapidly increasing abdominal girth and she had a spontaneous abortion. For two years she was treated conservative with diuretics, non-selective B-adrenergic blocking agent and no diagnosis was established. Subsequently, she had several admissions to the hospital due to massive ascites, episodes of spontaneous bacterial peritonitis, and acute kidney failure. After transfer to Institution, physical examination showed stigma of chronic liver disease, enlarged and tender liver and tense ascites. BSC was diagnosed with Doppler US. The patient was assessed for liver transplantation; however, she developed another episode of acute kidney failure due to hepatorenal syndrome and hypotension, requiring hemodialysis and vasopressor and ventilation support. Patient conditions deteriorate and she died due to liver failure. An autopsy was performed corroborating the diagnosis of BCS and cirrhosis. **Conclusions.** The key imaging findings in BCS are occlusion of the hepatic veins, inferior vena cava, or both; caudate lobe enlargement; inhomogeneous liver enhancement; and the presence of intrahepatic collateral vessels and hypervascular nodules. Early diagnosis of BCS is important for appropriate treatment, as medical treatment with diuretics, anticoagulation, and decompression with TIPS or surgical shunts may improve prognosis; however, once patients develop decompensated cirrhosis, liver transplantation is the only feasible treatment option. This case illustrates that early diagnosis is thus of prime importance to initiate appropriate treatment, and the challenges involved in the management of delayed diagnosis of BCS.

016

HEPATIC HAMARTOMA: A CASE REPORT

K. RODRIGUES-DO-Ó.,* L. SPIELMANN,** D'ALBUQUERQUE E CASTRO***
*HOSPITAL SÃO LUCAS, **HOSPITAL SANTA TERESA, PETRÓPOLIS, RIO DE JANEIRO, BRASIL.
***HOSPITAL GERAL DE PALMAS, TOCANTINS, BRASIL.

Background and aims. Hepatic Hamartoma is a very rare benign tumor that arises from the mesenchyme of the portal triad. It is formed by cystic dysplastic bile ducts and periportal embryonic precursors. Maresh was the first to describe this disease in 1903 which was initially known as a mesenchymal tumor pseudocyst biliary fibroadenoma and tumor cavernous until Edemondson in 1956 named mesenchymal hamartoma. This lesion is uncommon and represents 5% of all pediatric liver tumors and, most reports in literature are descriptions of isolated cases. Although cases appear in adults, this disease is identified in children under 2 years old and 80% are diagnosed in the first year of life. **Material and methods.** Case report: female, 64 years old, born in Sobral/Ceará; denies viruses in childhood, denies smoking, denies alcohol consumption; denies use of illict drugs; history of dyspepsia and pain in the right hypochondrium. **Results.** Abdominal ultrasound showed a picture of heterogeneous liver, gallbladder and bile ducts was performed normal. Resonance magnetic showed thal liver presenting countless nodular lesions with diameters no larger variables that 0.5 cm, scattered in all segments associated with hepatic bile hamartomas.

017

HEPATIC AMYLOIDOSIS

J.J. GUERRERO-ANGUIANO, M. CASTILLO-BARRADAS, H.J. RUIZ-MORALES, A. PÉREZ-MENDOZA
CENTRO MÉDICO NACIONAL LA RAZA, MEXICO CITY.

Background. Amyloidosis belongs to a group of diseases structural proteins and results from the ability of some of them to adopt a stable tertiary structure of the polymerization leading to amyloid fibrils in the extracellular space of various tissues. It can be classified in amyloidosis AL (light chain), amyloidosis AA, genetic and the associated to hemodialysis. Liver disease varies depending on the type of amyloidosis generally more common in type AL with 54% of affected individuals. The criteria for liver disease are: hepatomegaly, absence of heart failure and alkaline phosphatase > 1.5 times upper normal limit. It can be associated with encephalopathy, jaundice and ascites. In laboratory abnormalities, ALT and AST are usually elevated < 2 times the upper normal limit. With imaging studies demonstrating hepatomegaly. **Material and methods.** Female patient, 40 years of age with no history of relevance, with pregnancy of 24 weeks gestation, introduced labor with uterine unsuccessful inhibition, product yield 650 g. Who referred study from previous 7 days with fever and chills. Laboratories detected by increased transaminase, laboratory study protocol were initiated with AST 130 and ALT 132, alkaline phosphatase 773 and GGT 469. On physical examination revealed hepatomegaly of 3 cm below the right costal margin, immunological, infectious, oncologic causes are ruled out; liver biopsy was performed, resulting in acute fatty liver of pregnancy, with good performance is discharged. However for outpatients with fever persists and the case resumes. **Results.** Immunohistochemistry was performed, which was observed to deposit positive lambda and kappa chains, along with gamma protein electrophoresis peak; concluding severe chronic hepatitis with extensive deposits of lambda light chains (hepatic amyloidosis). **Conclusions.** This is a case of female patient 40 years with no history of relevance, pregnant, with recent symptoms, referred to as fever, hepatomegaly, cholestasis, diagnosed as acute fatty liver of pregnancy, without good expected performance for this pathology related disengage, reaching immunohistochemical diagnosis of hepatic amyloidosis. So you have to think this disease when evolution is unsatisfactory in pregnant women with liver disease in pregnancy.

018

EXOTIC ASSOCIATION BETWEEN CIRRHOSIS AND GASTRIC KAPOSI SARCOMA IN A NEGATIVE HIV PATIENT

CELY HERNÁNDEZ,* J.D. MARTÍNEZ,*,** A.F. NORIEGA,*** M.A. GARZÓN,* N. HORMAZA,* J. LIZARAZU,* J.C. MARULANDA,* J.C. MOLANO,*1 M.H. REY*
*UNIDAD DE GASTROENTEROLOGÍA, HOSPITAL UNIVERSITARIO DE LA SAMARITANA-UNIVERSIDAD EL ROSARIO. BOGOTÁ, COLOMBIA
**UNIVERSIDAD NACIONAL DE COLOMBIA.
***UNIVERSIDAD DE LA SABANA-BOGOTÁ, COLOMBIA.

Background. Kaposi sarcoma (KS) commonly develops in patients with immunosuppressed condition, for example acquired immunodeficiency syndrome (AIDS) and sometimes in patients without AIDS with variable immunologic abnormalities after corticosteroid, cytotoxic, or immunosuppressive therapy for malignancies, tissue transplants, or autoimmunity. KS has four main clinical presentations: human immunodeficiency virus (HIV), immunosuppressed patients, classic type (sporadic) and endemic (African). The association with cirrhosis is exceptional and generates a clinical diagnosis challenge. **Material and methods.** We reported a case of a 66-year-old male with long-standing alcoholic cirrhosis. Who was admitted to emergency room with decompensated cirrhosis as ascites with isolated haematemesis. An evacuatory paracentesis was performed (2 L). Upper gastrointestinal tract endoscopy showed two small varices without bleeding. Abnormal vascular lesions finding on fundic and major curvature of the stomach, between 5-10 mm, biopsies were obtained. **Results.** Histology of gastric biopsies showed a Kaposi sarcoma. HIV ELISA and viral hepatitis B and C were negative. Child-Pugh score was 9 points and MELD score was 13 points (Model for End stage Liver Disease). *Mycobacterium tuberculosis* ascites culture was negative. **Conclusions.** Kaposi sarcoma (KS) associated to cirrhosis is extremely rare. Typical endoscopic findings in cirrhotic patients such as gastric antral vascular ectasia and hypertensive portal gastropathy might be mistaken for GSK. In fact, therapeutic options for these patients are limited due to high risk of hepatotoxicity.

019

PRIMARY HEPATIC AMYLOIDOSIS: REPORT OF CASE

E. RODRÍGUEZ-NEGRETE, A. ÁLVAREZ-DE-LA-O
HOSPITAL DE ESPECIALIDADES CENTRO MÉDICO NACIONAL SIGLO XXI, IMSS, MÉXICO.

Introduction. Amyloidosis is an uncommon disease that results from the extracellular deposition of amorphous, fibrillar

protein. Progressive deposition of amyloid compresses and replaces normal tissue, and this leads to organ dysfunction and a wide variety of clinical syndromes. Amyloidosis is usually observed in a systemic form although 10-20% of cases are localized. The primary amyloidosis has been associated with a monoclonal plasma cell dyscrasia, as at least 30% of those patients will eventually progress to multiple myeloma. Median survival time is 1.5 years. Amyloid protein deposition can be seen in a variety of organs, symptomatic hepatic involvement, including rupture, portal hypertension or hepatic failure, is rare. Hepatomegaly and a borderline abnormal liver function test are the most frequent findings in patients with hepatic amyloidosis. **Material and methods.** Male 45 years old with a history of importance: Chronic degenerative: questioned and denied. Alcoholism: from 15 to 40 years old (36 g alcohol per month). Present illness: home in October 2012 with fatigue, weakness, pain in epigastrium poorly systematized, intensity 3/10 without irradiation, gastric fullness and unintentional weight loss (15 kg in 6 months). In February 2013 he presented hematemesis event (approximately 50 cc) and subsequently intermittent melena stools for 1 month (not specifying number). Subsequently edema predominantly in lower limbs and general waekness seeking medical attention. Physical examination: hepatic gland is palpable 4 cm below the right costal margin. Limbs with soft dominance in lower limbs ++/++++ edema auxiliary diagnosis: glucose 119, 7.74 creatinine, urea 127, Hb 12.8, 181000 platelets , leukocytes 6800, AST 37, ALT 19, GGT 479, FA 345. CT of the abdomen: hepatomegaly. Urine protein electrophoresis in 24 h: elevated gamma fraction and normal bone marrow aspirate. Liver biopsy ultrasound-guided with report of primary hepatic amyloidosis. **Conclusions.** According to the WHO classification, our case belongs to the primary hepatic amyloidosis. Staining of hepatic tissues with Congo Red is often regarded as the "gold standard". Pharmacological therapy should aim to rapidly reduce the supply of misfolded amyloidogenic AL. High-dose intravenous melphalan and autologous stem cell transplantation appear to be the most appropriate therapy but controversies still exist.

020

ASCITES AS THE MAIN MANIFESTATION OF DISSEMINATED TUBERCULOSIS BIOLOGICAL THERAPY

J.A. MÁRQUEZ-RODRÍGUEZ, P. BENNEMANN, A. AMOROS-TENORIO, L. DÍAZ-HERNÁNDEZ, I. REDONDO-ZAERA, E. BORJA-GUTIÉRREZ
APARATO DIGESTIVO. HOSPITAL UNIVERSITARIO NUESTRA SEÑORA DE LA CANDELARIA. SANTA CRUZ DE TENERIFE. SPAIN.

Introduction. Infection with *Mycobacterium tuberculosis* (TB) should be included in the differential diagnosis of ascites. In developed countries, tuberculous peritonitis is associated with alcoholic cirrhosis in ≈ 50% of cases. The use of "biological therapies", widely used in patients with rheumatic and autoimmune digestive diseases, may favor the reactivation of latent tuberculosis (LTB). Therefore, the use of these drugs requires discarding LTB, and give chemoprophylaxis in affected patients. **Case report.** A 56-year-old woman was admitted to our service for digestive abdominal discomfort and progressive abdominal distension. She had a history of ankylosing spondylitis in long-term treatment with Adalimumab. Ultrasound examination was performed finding moderate ascites with signs of chronic liver disease, later confirmed by CT scan. An ascites sample showed a transudate liquid (proteins 0.6 g/L) with 1,005 leucocytes (95% lymphocytes), negative cytology and high serum-ascites albumin gradient (2.4 mg/dL). She underwent transjugular liver biopsy with measurement of portosystemic gradient (4 mmHg, no portal hypertension), revealing a "focal granulomatous hepatitis" without acid fast bacilli (AFB) present. Suspecting a neoplastic origin, a colonoscopy was performed which displayed "[...] a large excavated ulcer in terminal ileum" which was biopsied. Awaiting for the histological result a gynecological study was performed (transvaginal ultrasound and pelvic MRI), which showed a uterine mass (27 x 17 x 23 mm) with non-neoplastic appearance, abundant pelvic ascites and diffuse peritoneal thickening that suggested peritonitis. An endometrial aspiration proved a "granulomatous endometritis" with a "positive AFB staining". Likewise, the pathology result for ileal ulcer was "non-necrotizing granuloma" with a "positive AFB". A bronchoscopy + lavage were performed with positive smear and PCR of M. Tuberculosis sensitive to rifampicin. With the diagnosis of disseminated TB, treatment was started and supervised by the Infectious Diseases Unit. In a second interrogation it was found that the patient had received treatment with isoniazid 6 months before the income because of a positive Mantoux test (10 mm). Treatment was irregularly accomplished because of gastric distress. She reported intermittent fever with multiple courses of antibiotics during this period. **Discussion.** We present a rare case of disseminated TB secondary to treatment with Adalimumab, whose main symptom was ascites. In our opinion, this case highlights two important aspects: TB as a cause of ascites and the importance of chemoprophylaxis in LTB in patients who will undergo biological treatment.

021

HEPATIC METASTASES FROM CARCINOMA OF THE UTERINE CERVIX: AN EXTREMELY RARE SITE OF METASTASIS

Z. DEL REAL-ROMO,[**] C. RODRÍGUEZ-MONTALVO,[*,**] E. FLORES-VILLALBA,[**] L. TIJERINA-GÓMEZ,[**] P. CUEVAS-ESTANDÍA,[*] F. BOSQUES-PADILLA[*]
[*]CENTRO DE ENFERMEDADES HEPÁTICAS, DIGESTIVAS Y NUTRICIÓN, HOSPITAL SAN JOSÉ-TEC DE MONTERREY, MONTERREY, N.L., MÉXICO.
[**]CIRUGÍA GENERAL DEL PROGRAMA MULTICÉNTRICO DE ESPECIALIDADES MÉDICAS DE LA ESCUELA DE MEDICINA Y CIENCIAS DE LA SALUD DEL TECNOLÓGICO DE MONTERREY, MONTERREY, N.L., MÉXICO.

Background or Introduction. Cervical cancer is a frequent malignancy of the females. It still remains a leading cause of cancer-related death in women worldwide. Cervical cancers do not always spread, but those that do most often spread to the lungs, bladder, vagina and liver. Most common types of cancers that can spread to the liver include: breast cancer, melanoma squamous cell carcinoma of the anus and sarcoma. We present an extremely rare liver metastasis from the uterine cervix. **Material and methods.** Solitary hepatic tumor was diagnosed 4 years after a 60-year-old woman had undergone radical hysterectomy and postoperative irradiation for squamous cell carcinoma of the cervix. A 4 cm tumor in segment III was detected. Laparoscopic liver resection of metastatic tumor was achieved and squamous cell carcinoma from the uterine cervix confirmed. Two years following hepatic resection, this patient is doing well with no evidence of any recurrence. **Discussion.** Cervical cancer has been a leading cause of morbidity and gynecologic cancer deaths throughout the world in this generation despite the implementation of Pap smears. Metastases of carcinoma of the uterine cervix firstly

affect paracervical lymphatic vessels progressing to paraaortic lymph nodes and then cause distant lesions involving mainly the lungs, and infrequently liver and bones. Patients with distant relapse at sole/limited metastatic site(s) could undergo salvage treatment by chemoradiation, surgery plus radiotherapy/chemoradiation, or surgery alone to achieve prolonged survival. In recent years, technical improvements in liver resection and perioperative management have led to a dramatic decrease in morbidity and mortality associated with these procedures. Resection of liver metastases tumors is currently the treatment of choice when technically feasible. It has been estimated that liver metastases of gynecological cancer are less than 1% of the total liver metastases resected. **Conclusions.** Squamous cell carcinoma of the uterine cervix is a frequent malignancy of the females but it is exceptional when it metastasizes to the liver. However hepatic resection of metastases from gynecologic carcinomas can be performed safely and may help prolong survival in carefully selected patients.

B. VIRAL HEPATITIS (A, B, C, D, E AND OTHER VIRUS)

001

HOW TO OBTAIN AN ADEQUATE LIVER FRAGMENT IN CLINICAL PRACTICE TO ASSESS FIBROSIS STAGE IN CHRONIC HEPATITIS C

MARIA CHIARA-CHINDAMO, CRISTIANE A. VILLELA-NOGUEIRA, RENATA DE-MELLO-PEREZ, JOÃO MARCELO DE-ARAUJO-NETO, VERA L. NUNES-PANNAIN, HENRIQUE S. MORAES-COELHO
UNIVERSIDADE FEDERAL DO RIO DE JANEIRO, BRAZIL.

Introduction. In recent decades studies addressed on quality of liver biopsy adopted as optimal standards fragments 20 to 25 mm long and/or containing at least 11 complete portal tracts. However, most of the studies related to viral hepatitis therapy and serum markers of fibrosis have used suboptimal liver specimens. **Aim.** To present a methodology to perform a liver biopsy that allows obtaining adequate fragments for fibrosis analysis considering the current patterns. **Materials and methods.** We evaluated patients with chronic hepatitis C, submitted to liver biopsies at the Federal University of Rio de Janeiro, between March 2010 and March 2013. Procedures were guided by ultrasonography using 14 or 16 G Tru Cut needle 20 mm long. A second biopsy was performed at the same session if fragment visually presented less than 20 mm. Total fragment length was verified before and after paraffin inclusion. Portal tracts containing at least an element a portal vein and hepatic artery were considered for evaluation. Fixed samples were included for analysis when length ≥ 10 mm and containing ≥ 6 portal tracts. Fragmented specimens were excluded. **Results.** We analyzed 270 biopsies of which 15 (5.5%) were considered inadequate. Were included 255 biopsies with median length of 31 ± 8 mm before and 24 ± 5 mm after fixation, determining an average reduction of 23% from the original size (7 ± 6 mm). The mean number of portal tracts was 16.1 ± 6.2 which increased according to fragment size ($p < 0.001$). Tru-cut needle 14 was used in 80% of cases and no difference was found in fragment size according to the type of needle 14 or 16 both before (31 ± 9 *vs.* 32 ± 8 mm; $p = 0.86$) or after fixation (24 ± 5 *vs.* 24 ± 6 mm; $p = 0.403$), but a greater number of portal tracts was obtained with needle 14 (16.7 ± 6.3 *vs.* 14.0 ± 5.0; $p = 0.005$). One pass was done in 2% of patients, 2 passes in 54%, 3 in 34% and 4 in 10%, with no differences regarding type of needle ($p = 0.84$). When two pass were performed, the fragment length was respectively 30 ± 7 mm before and 24 ± 5 after fixation, and the mean number of portal tracts was 15.7 ± 6. The execution of more than one pass did not determine a risk of major complications as bleeding or death. **Conclusion.** It is possible to obtain adequate liver samples according to current patterns performing two passes of guided biopsies with tru cut 14 or 16 gauge needles that ensure fresh fragments of at least 3 cm long, without increase in morbidity.

002

USEFULNESS OF RAPID TESTS FOR ANTI-HBE DETECTION

H. MEDINA-CRUZ, J. CUSTÓDIO-MIGUEL, E. FERREIRA-DA-SILVA, L. LAURA LEWIS-XIMENEZ, E. LAMPE, L. MELO-VILLAR
OSWALDO CRUZ INSTITUTE, FIOCRUZ, RJ, BRAZIL.

Objectives. The use of rapid tests as a substitute for conventional diagnosis of hepatitis B virus (HBV) infection can provide advantages, such as: results of the test in a few minutes and availability at low infrastructure laboratories. The aim of this study was to evaluate the use of rapid test for detection of anti-HBe marker in individuals referred to Viral Hepatitis Ambulatory in Brazil. **Material and methods.** In this study, 166 patients referred to Viral Hepatitis Ambulatory at Oswaldo Cruz Foundation (Rio de Janeiro, Brazil) from 2009 to 2013 were included. These individuals donated serum samples that were tested to HBsAg, anti-HBc and anti-HBs using commercial EIAs. Samples were also submitted to two assays: electrochemiluminescence (ECLIA) Elecsys anti-HBe (Roche, France) and rapid test Imuno-Rápido anti-HBeAg® (Wama, Brazil). ECLIA is a conventional assay and was considered the gold standard. Although both tests require approximately the same sample volume (150 μL) and time to release the results (15-20 min), sophisticated equipment and highly trained personnel are necessary to execute ECLIA assay. **Results and conclusions.** Subjects presented mean age ± standard deviation of 45.3 ± 14.6 years and most of them were male (55.6%). In this study, 124 individuals were HBsAg reactive, 151 were anti-HBc reactive and 9 did not present HBV markers. Anti-HBe was detected by ECLIA in 113 samples and not detected in 53 samples. Sensitivity and specificity of rapid test were 76.99% (87/113) and 96.23% (51/53), respectively. Anti-HBe false negative samples by rapid test presented an average value of ratio of optical density to cut off (OD/CO) by ECLIA higher (0.264 ± 0.316) than those true positive samples by rapid test (0.025 ± 0.122). Sensitivity of rapid test was higher (84%) among patients with active HBV infection (anti-HBe reactive/HBsAg reactive) compared to individuals with HBV past infection (anti-HBe reactive/HBsAg non-reactive) (23.1%). We concluded that rapid test for anti-HBe detection could be a potential tool to identify individuals with active HBV infection and could be employed in low resource limited areas.

003

LOW PREVALENCE OF HEPATITIS C VIRUS MARKERS AMONG DIABETTES MELLITUS PATIENTS

L.M. VILLAR,* J.C. MIGUEL,* E.F. DA SILVA,* L.P. SCALIONI,* G.C. CALDAS,* A.C.J. VASQUES,** B. GELONEZE,** E. LAMPE*
*VIRAL HEPATITIS LABORATORY, OSWALDO CRUZ INSTITUTE, FIOCRUZ, RIO DE JANEIRO, BRAZIL.
**LABORATORY OF INVESTIGATION IN METABOLISM AND DIABETES, UNICAMP, CAMPINAS, BRAZIL.

Introduction. The liver is the primary site of hormone and glucose metabolism, and intercommunication between liver and diabetes has long been recognized. Many studies have suggested a connection between hepatitis C virus (HCV) infection and type 2 diabetes (T2D). However, the association of HCV infection with diabetes-related complications has not yet been clarified. The aim of this study was to determine the prevalence of hepatitis C virus (HCV) infection in T2D-patients in Brazil which has a high incidence of type 2 diabetes. **Material and methods.** Sera samples from 453 T2D individuals referred to reference hospitals from two distinct geographical areas from Brazil were recruited from years 2010 to 2012. Defining type 2 diabetes was done according to the American Diabetes Association guidelines. Demographic data recorded included age and gender. Measurements of fasting glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma glutamyltransferase (GGT) were performed following standard laboratory procedures. Insulin was determined by electrochemiluminescence method. Anti-HCV was done using commercial enzyme immunoassays following manufacturer's instructions. Anti-HCV reactive samples were submitted to HCV RNA detection using RT-PCR and genotyped using RFLP technique. **Results.** Most of individuals were females (62.0%) and mean age ± standard deviation was 55.6 ± 11.1 years. Mean ± SD values for laboratory data were 26.7 ± 27.3 U/L for ALT, 23.2 ± 12.9 U/L for AST, 44.5 ± 41.3 U/L for GGT, 158.7 ± 66.8 mg/dL for glucose and 15.4 ± 19.7 μU/L for insulin. Anti-HCV was detected among 7 individuals (1.54%), where 5 had HCV RNA detected and genotypes I (n = 4) and III (n = 1) were observed. **Conclusions.** HCV prevalence is low among type 2 diabetes patients and seems to be equivalent to general population in Brazil.

004

THE "ADITTIVE" EFFECT OF THE VHC WITH THE HSV TYPE I, II IN PATIENTS WITH CHRONIC HEPATITIS C?

ADELA TURCANU, VLADA-TATIANA DUMBRAVA, LUDMILA TFON-SCUTARU
THE STATE UNIVERSITY OF MEDICINE AND MEDICINE "N. TETSTEMITANU", CHISINAU, MOLDOVA REPUBLIC.

Background. The researchers suggest that the herpetic infection, by creating a specific state of immunodeficiency, may hasten the evolution of the hepatitis C. In turn, the viral hepatitis C, as alternates the balance Th1/Th2, would create favorable circumstances for the reactivation of the latent herpetic infection. **Material and methods.** In our study enrolled 144 patients with chronic hepatitis C: 103 patients with viral chronic hepatitis C, without the HSV; 41 patients with HCVC in association with the HSV I, II. Before giving the hepatitis diagnosis, a complex of laboratory, clinic and instrumental researches were performed. **Results.** After analyzing the given data, at the patients with HCVC associated with HSV I, II was established a correlations between level antibodies anti HSV I + II Ig M with activity of AST ($r = 0.65$, $p < 0.001$) and ALT ($r = 0.86$, $P < 0.01$); between the anti HSV I, II Ig M and the non-structured part of the virus C (NS5) ($r = 0.44$ $p < 0.01$). There have been found direct correlations between ALT and Ig G ($r = 0.62$, $p < 0.01$) and AST with Ig G ($r = 0.59$ $P < 0$, 01) and with Ig M ($r = 0.51$, $p < 0.01$). There have been found indirect correlations between ALT with CD4+ ($r = -0.36$ $p < 0.05$), CD3+ ($r = -0.49$, $p < 0.01$), AST with CD4+ ($r = -0.48$, $p < 0.05$), CD3+ ($r = -0.42$, $p < 0.01$). Our research highlights that for all the patients with HCV C + HSV I, II VHC is in a reactivation phase, which makes us concern that the herpetic infection might hurry the evolution of the chronic C hepatitis. **Conclusions.** Our results prove the presence of the role match bigger than it was previously known concerning immunological status at the VHC + HSV I, II patients. It is visible the presence of a correlation between immunological response and biochemical processes that take place in the liver at the HCVC + HSV I, II patients, possibly as a result of the inter stimulation action between VHC with HSV. The research of HSV type I and II in VHC positive patients is important because of at least 2 reasons: the diagnosis and the precocious treatment of this disease, which would prevent any other complications to the patients with VHC; and the patients with the infectious pathology detected may serve as target for the screening of chronic viral C hepatitis patients.

005

HEPATITIS A AND B SEROPREVALENCE IN 1,000 PATIENTS WITH CHRONIC HEPATITIS C (CHC) INFECTION ON A TERTIARY CARE CENTER IN SAO PAULO, BRAZIL

E.F. SILVA, D.F. MAZO, C.M. OLIVEIRA, R.P. MEDEIROS, F.J. CARRILHO, M.G. PESSOA
UNIVERSITY OF SÃO PAULO SCHOOL OF MEDICINE, SÃO PAULO, BRAZIL.

Background and aims. Patients with chronic HCV infection and superinfection by hepatitis A virus (HAV) or hepatitis B virus (HBV), have higher morbidity and mortality when compared with patients with only acute infection with HAV or HBV. For this reason, active immunization with vaccines against HAV and HBV has become mandatory in this population and hence markers for hepatitis A and B must be determined. The aim of this study was to evaluate the prevalence of serological markers of hepatitis A and hepatitis B infection in patients with chronic hepatitis C. **Material and methods.** 1.000 chronic HCV infected patients at the Liver Clinic at the University of Sao Paulo School of Medicine Hospital were evaluated for the prevalence of serological markers of hepatitis A and B infection. **Results.** Of the 1,000 patients evaluated, anti-HAV IgG was positive in 923 patients (92.3%), and negative in 77 (7.7%), not showing, in this case, prior contact with HAV. When patients were stratified by age, the anti-HAV IgG was found in 14 (61%) patients between 20 and 29 years, 58 (70%) between 30-39 years, 111 (85%) between 40-49 years, 279 (94%) aged 50-59 years, and 461 (99%) patients with more than 60 years. Anti-HBc IgG was positive in 244 (24%) of 1,000 patients and negative in 756 (76%), showing no previous contact with HBV. When patients were stratified by age, anti-HBc IgG was found in 1 (4.3%) patients 20-29 years 14 (17%) with 30-39 years, 27 (21%) with 40-49 years, 70 (24%) with 50-59 years, and 132 (28%) patients with more than 60

years. Of the 244 anti-HBc IgG positive patients, 8 patients (0.8%) were HBsAg positive, 85 (8.5%) were anti-HBc IgG isolated and 157 (16%) were also anti-HBs positive, demonstrating acquired immunity to HBV. **Conclusions.** The prevalence of anti-HAV IgG in patients with chronic HCV infection in our study was similar to that observed in the general population of São Paulo City. The prevalence of anti-HBc IgG was higher in patients with chronic HCV infection in our Outpatient Clinic compared historically to the general population of Western countries, suggesting similar risk factors for HBV and HCV infection, so emphasizing the importance of immunization programs in this population.

006

RESTING ENERGY EXPENDITURE IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS WITH AND WITHOUT NAFLD

T.P. OLIVEIRA,[*] R. ROCHA,[*,**] F.M. CASTRO,[*] F.R. NOBRE,[*] CHC DALTRO,[*,**] COTRIM H.P.[**]
[*]*ESCOLA DE NUTRIÇÃO-UNIVERSIDADE FEDERAL DA BAHIA, BRAZIL.*
[**]*NASH STUDY GROUP-PPGMS-FACULDADE DE MEDICINA-UNIVERSIDADE FEDERAL DA BAHIA, BRAZIL.*

Background. Chronic hepatitis C virus (CHC) is one the most frequent cause of chronic liver disease worldwide, and it associated a several conditions. One of the them is nonalcoholic fatty liver disease (NAFLD). However, there are some discussions if metabolic and nutritional characteristics of CHC patients may increase the risk for NAFLD. The present study aimed to compare the resting energy expenditure (REE) in CHC patients with and without NAFLD. **Material and methods.** Cross-sectional study including patients from the Hepatology outclinic at Federal University in Bahia, Brazil, from March 2011 to December 2012. CHC patients were included before antiviral treatment; all of them did not have history of ethanol ingestion ≥ 140 g/week. All the patients answered a questionnaire with clinical and anthropometric informations. The presence of NAFLD (steatosis or steatohepatitis) was observed on liver biopsy. Patients were submitted to indirect calorimetry to measure REE and bioelectrical impedance test for assessment of body composition. The results were analyzed between patients with CHC associated to NAFLD and those with CHC without NAFLD. **Results.** A total of 39 CHC patients were evaluated and 11 (28.2%) had NAFLD. Genotype 1 was present in 79.5% of patients. The mean age was 45.2 ± 9.4 year and 63.6% were women. Overweight was observed in 63.6% of the cases, 81.8% presented increased waist circumference and 90.9% did not refer to practice physical activity. These characteristics were the same as those found in CHC patients without NAFLD ($p > 0.05$). The REE of the patients with NAFLD was similar when compared to that of patients without NAFLD (1,100.0 ± 361.5 Kcal/day and 1,207.5 ± 319.7 kcal/day, respectively, $p = 0.37$). There was no difference between the two groups of patients regarding the BMI classification and body composition ($p > 0.05$). **Conclusion.** Patients with CHC associated or not with NAFLD had the same anthropometric and body composition characteristics. The resting energy expenditure was similar in CHC with or without NAFLD.

007

INSULIN RESISTANCE AND HYPERTRIGLYCERIDEMIA ARE ASSOCIATED WITH VITAMIN D DEFICIENCY IN HCV, HIV AND HIV/HCV COINFECTED PATIENTS

MÁRIO GUIMARÃES-PESSÔA,[*] MARIO PERIBAÑEZ-GONZALEZ,[†] GISELLE BURLAMAQUI-KLAUTAU,[†] MARIA C. MENDES-CORRÊA,[‡] LUCIANO GIACAGLIA,[§] ROBERTA SCHIAVON-NOGUEIRA,[||] DANIEL FERRAZ-DE-CAMPOS-MAZO,[*] FLAIR CARRILHO[*]
[*]*DIVISION OF GASTROENTEROLOGY AND HEPATOLOGY-UNIVERSITY OF SÃO PAULO SCHOOL OF MEDICINE, BRAZIL.*
[†]*OUTPATIENTS CLINIC OF INSTITUTO DE INFECTOLOGIA EMÍLIO RIBAS, BRAZIL.*
[‡]*DEPARTMENT OF INFECTIOUS DISEASES-UNIVERSITY OF SÃO PAULO SCHOOL OF MEDICINE, BRAZIL.*
[§]*ENDOCRINOLOGY UNIT-UNIVERSITY OF SÃO PAULO SCHOOL OF MEDICINE, BRAZIL.*
[||]*AIDS AND STD'S REFERENCE CENTER OF SÃO PAULO STATE, BRAZIL.*

Background and Aims. Vitamin D deficiency (VDD) is pandemic. It is associated with metabolic comorbidities and worst prognosis in HIV individuals, HCV patients and those with HIV/HCV co-infection. The aim of this study was to evaluate 25-hydroxyvitamin D levels among a population including HCV, HIV and HIV/HCV co-infected patients, and to describe metabolic factors associated to VDD. **Material and methods.** We collected 25-hydroxyvitamin D samples, demographic and clinical information data, also liver function tests and metabolic profile, assessing three distinct groups of patients; 1-HCV monoinfected, 2-HIV monoinfected , 3-HIV/HCV coinfected, followed at reference centers of São Paulo-Brazil. **Results.** 300 patients were included for analysis. From those, 129 belonged to group 1-HCV, 118 to group 2-HIV, and 53 to group 3-HIV/HCV. Mean levels of vitamin D were low in all groups, with more significance in group 2. In overall analysis, VDD (serum levels < 20 ng/mL) was associated with insulin resistance ($p = 0.034$ OR = 1.99 95%CI: 1.05-3.76) and total triglyceride levels > 150 mg/dL ($p = 0.001$ OR 2.49 95%CI: 1.43-4.34). When analyzed by groups, VDD was associated with: 1-insulin resistance in both HCV group ($p = 0.01$ OR = 6.45 95%CI: 1.57-26.4) and HIV/HCV group ($p = 0.028$ Fisher test). In HCV group, association remained after multiple regression adjustment for obesity ($p = 0.035$ OR = 4.85 95%CI: 1.12-21.1). 2-Triglycerides > 150 mg/dL in HIV group ($p = 0.01$ OR 3.06 95%CI: 1.27-7.35). **Conclusion.** This study found high prevalence of VDD at this specific population. Association between Insulin Resistance and Vitamin D deficiency has been demonstrated in other populations, but not previously described in HCV patients.

008

HISTOLOGICAL ASPECTS OF HBV/HDV CO-INFECTION IN PATIENTS FROM THE BRAZILIAN AMAZON

O.P. DE-ALVARENGA, M.L. C.R. SILVA, M. DA C. CASTILHO, C.M.C. DE OLIVEIRA, J.B. DE L. GIMAQUE, J.R. DE ARAÚJO, W.S. M. BRAGA
TROPICAL MEDICINE FOUNDATION DOUTOR HEITOR VIEIRA DOURADO, MANAUS, BRAZIL.

Background. Chronic hepatitis B and D virus coinfection or superinfection is perhaps the most intriguing amongst all the human viral hepatitis. In Brazil, HDV is highly endemic in the western Amazon region where the occurrence of severe cases of acute and chronic liver diseases are frequently observed. This study aimed to identify patterns of histological lesions and predictors of advanced disease. **Material and methods.**

Patients were selected consecutively, between January/2007 and December/2013 from the viral hepatitis outpatient's clinic at the Tropical Medicine Foundation Doctor Heitor Vieira Dourado (FMT-HVD) a referral Centre for liver diseases in Manaus, Western Amazon. The inclusion criteria was defined as diagnosis of compensated chronic disease, HBsAg, anti-HBC IgG, and anti-HD IgG, reactive, regardless of HBeAg status, HDV-RNA positive and having performed a liver biopsy in the past 12 months. Liver biopsy was performed using a Menghini-type needle guided by ultrasound. Liver fragments were fixed in paraffin-embedded and stained with hematoxylin-eosin, Picrosirius red, Persl, PAS and reticulin. Fibrosis and necroinflammatory activity was categorized according to the METAVIR score. **Results.** We analyzed cross-sectional data of 104 patients. Sixty-nine patients (66.3%) were male and 35 (33.7%) were female. The median age was 30 years (min 17-max 69). The METAVIR histologic scoring ranged as follows A0 (n = 3; 2.9%), A1 (n = 38; 36.5%), A2 (n = 26; 25%) and A3 (n = 37; 35.6%). Concerning fibrosis stages patients were classified as follow FO (n = 22; 21.2%), F1 (n = 31; 29.8%), F2 (n = 16; 15.4%), F3 (n = 26; 25%) and F4 (n = 9; 8.7%). Steatosis was present in 77 (74%) patients. Forty-three (41.3%) patients exhibited alterations in liver architecture. Regarding piecemeal necrosis, it ranged from mild to intense (n = 46; 44.3%). Studied subjects were extremely young; nevertheless all of them were already classified as compensated chronic liver disease patients, 61% presenting important necroinflammatory activity and 49% significant grade of liver fibrosis, suggesting a very aggressive process. **Conclusions.** Possibly, HDV in this region is being transmitted early in life superinfecting an already injured liver of an HBV carrier.

009

INNOVATIVE TREATMENT FOR HCV-G4 EGYPTIAN PATIENTS: A PILOT STUDY

IBRAHIM ABD EL ATY,* AHMED MONIS,** SALLY EMARA***
*ENGINEERING AUTHORITY OF MINISTRY OF DEFENSE, **AIN SHAMS UNIVERSITY, ***ABBASIA FEVER HOSPITAL, CAIRO, EGYPT.

Introduction. Egypt has the highest prevalence of HCV worldwide (15%). With a predominance of sub type 4a. The goal of hepatitis C treatment is to prevent the development of chronic infection, improve the patient's quality of life, and prevent morbidity and mortality. **Aim.** The primary efficacy objective is to assess the outcome after using Electro-Magnetic Signals treatment strategy for Individuals infected with HCV at the end of treatment period. The Outcome is defined by undetectable PCR at the end of treatment period (3 weeks treatment duration) and the Sustained Virological Response (SVR) defined as continued undetectable HCV viral load 24 weeks after completion of therapy. To assess the safety and addressing the serious adverse events experienced by the patients upon using this innovative treatment. **Material and methods.** 50 patients were enrolled in this study between May 12, 2013 till May 12, 2014. Full investigation was done include PCR before and at 1st-3rd week of treatment and after stopping treatment by 24 weeks, ILB28 was done for 29 patients and most of them CT, every patient exposed to extracorporeal exposure to electromagnetic signal every day for total 21 h. **Results.** Seven patients (14%; 95%CI, 4-24%) achieved undetectable PCR after first week of treatment and increased at the end of 3rd week of treatment, to 38 patients (76%; 95%CI, 63.7-88.3%) achieved undetected PCR. Out of the enrolled population, 47 patients (94%; 95%CI, 87.2-100.8%) achieved SVR defined as continued undetectable viral load 12 weeks after completion of therapy while 48 patients (96%; 95%CI, 90.4-101.6 %) achieved SVR, 24 weeks after completion of therapy. The mean ALT levels of eligible patients at baseline was 71.32 ± 39.48 IU/L but it was significantly decreased after 1 week ($p = 0.001$) by -11.3 ± 22.4 and after 3 weeks of treatment ($p < 0.001$) by -28.8 ± 36.5. **Conclusion.** The Innovative electro-magnetic signals treatment strategy is highly effective and totally safe as a therapy for infected individuals with HCV disease.

010

HEPATITIS E VIRUS SEROPREVALENCE: A REAPPRAISAL

A. URZÚA MANCHEGO, N. COVARRUBIAS RUZ, A. DÍAZ MOLINA, C. HURTADO HEIM, M. VENEGAS SANTOS, J. BRAHM BARRIL
HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.

Introduction. Reported seroprevalence of hepatitis E virus (HEV) in developed countries is between 0.3-53%. Published data relies on the assays used and its technical performance. Sensitivity on new available tests has improved, which has changed HEV seroprevalence in the world. **Objective.** To reevaluate the presence of anti HEV IgG on stored blood samples of patients previously studied. **Materials and methods.** Serum samples, stored at -20 °C of 178 patients with previous anti HEV IgG determination between 2009 and 2012 were reevaluate. Initial analysis was performed with ELISA kit Genelabs (Singapur), with 7.3% of antibody positivity. The reevaluation was done with ELISA kit AccuDiagTMHEV-IgG (Diagnostic Automation, United States), with a reported sensitivity and specificity over 99%. **Results.** With this new ELISA kit 32.6% of the 178 analyzed samples had a positive result. This is statistically significant when compared with the previous kit ($p < 0.001$). There were no sex differences. A not statistically significant trend was seen in older patients. **Conclusions.** Our results show that anti HEV IgG antibody seroprevalence using AccuDiagTMHEV-IgG is 4.5 times more common. This suggests that previous testing might have underestimated HEV seroprevalence in Chile, which should be reevaluated using the new available kits.

011

SEROLOGIC RESPONSE TO STANDARD HEPATITIS B VACCINATION IN HIV-POSITIVE PATIENTS

J.I. VARGAS-DOMÍNGUEZ,* F. FUSTER-SALDÍAS,† D. JENSEN-FERNÁNDEZ,* V. SARMIENTO-HERNÁNDEZ,† P. ACUÑA-VALENZUELA,§ F. PEIRANO-POZO,* S. SOTO-SEPÚLVEDA,|| W. JENSEN-REYES,‡ R. AHUMADA-MERCADO,‡ M. HUILCAMAN-PIZARRO,‡ M. BRUNA-PAEZ‡
*FACULTY OF MEDICINE. UNIVERSIDAD DE VALPARAÍSO, VALPARAÍSO, CHILE.
†DEPARTMENT OF HEPATOLOGY. HOSPITAL GUSTAVO FRICKE, VIÑA DEL MAR, CHILE.
‡DEPARTMENT OF INFECTOLOGY. HOSPITAL GUSTAVO FRICKE, VIÑA DEL MAR, CHILE.
§FACULTY OF MEDICINE. UNIVERSIDAD ANDRÉS BELLO, VIÑA DEL MAR, CHILE.
||ACLIN CLINICAL LABORATORY. VIÑA DEL MAR, CHILE.

Background. HIV-infected patients are at risk for HBV co-infection, which leads to increased morbidity and mortality. Immunisation with hepatitis B virus (HBV) vaccine is recommended to prevent infection in patients with HIV. Vaccine response is lower compared to immunocompetent individuals, ranging from 34% to 65% with standard scheme. Several

reports describe intensified schemes of vaccination to improve serological response, however, few data of response to the standard scheme are available in latinoamerican people. In our country, immunisation with HBV vaccine is not included in guidelines for management of HIV-positive individuals, therefore, there is no data available. **Objective.** Assess serological response to immunisation with HBV vaccine in HIV-infected patients, and associated variables. **Material and methods.** Single center prospective study of immunisation with HBV vaccine (Engerix-B, GlaxoSK, 20 ug at 0.1 and 6 months, intramusculary), who where regular attendants to HIV program controls, without history of previous HBV vaccination, and negative serological markers of HBV infection; from October 2012 to April 2014. Measurement of anti-HBs titers 4 to 8 weeks after complete the vaccination scheme. **Results.** 158 subjects completed the three-dose regimen, 68% where male and median age was 42 years. Undetectable HIV viral load was present in 82%, CD4 cell count was higher than 200/μl in 88%, and 94% were on HAART. The seroconversion rate (anti-HBs > 10 ui/mL) was 69% (109/158), with mean titers of 657 ui/mL. In those with positive response to vaccination, 90% (98/109) had titers of anti-HBs greater than 100 ui/mL. Vaccine response was associated with younger age, lower weight and triglycerides levels; higher mean CD4 cell count, CD4/CD8 ratio, and longer time receiving HAART. In logistic regression model, CD4 cell count and CD4/CD8 ratio > 0.55 retained their predicting value. **Conclusions.** In our study, response to immunisation for HBV with standard scheme in HIV-infected individuals attendants to HIV programme, was concordant with the rates previously reported. Variables related to immunological status at beginning of the vaccination scheme were asssociated with seroconversion.

012

SEROLOGIC MARKERS OF HEPATITIS B VIRUS IN HIV-POSITIVE PATIENTS WITH HBSAG-NEGATIVE AND RAPID TEST AS SCREENING FOR ANTI-HBC

J.I. VARGAS-DOMÍNGUEZ,* F. FUSTER-SALDÍAS,† D. JENSEN-FERNÁNDEZ,* V. SARMIENTO-HERNÁNDEZ,† F. PEIRANO-POZO,* P. ACUÑA-VALENZUELA,§ S. SOTO-SEPÚLVEDA,‖ W. JENSEN-REYES,‡ R. AHUMADA-MERCADO,‡ M. HUILCAMAN-PIZARRO,‡ M. BRUNA-PAEZ‡

*FACULTY OF MEDICINE. UNIVERSIDAD DE VALPARAÍSO, VALPARAÍSO, CHILE. ‡DEPARTMENT OF HEPATOLOGY. ‡DEPARTMENT OF INFECTOLOGY. HOSPITAL GUSTAVO FRICKE, VIÑA DEL MAR, CHILE. §FACULTY OF MEDICINE. UNIVERSIDAD ANDRÉS BELLO, VIÑA DEL MAR, CHILE. ‖ACLIN CLINICAL LABORATORY. VIÑA DEL MAR, CHILE.

Background. HBV co-infection in HIV-positive patients is frequent, therefore, assesment of HVB status is recommended in HIV patients. In many cases, anti-HBc is the only detectable serologic marker for HVB, that can be related to resolved infection or occult infection. Regional data are scarce about this condition. Rapid test for anti-HBc have been used as screening in various clinical scenarios, but with variable results as compared with anti-HBc by ELISA. It hasn't been tested in HIV-positive patients. **Objetives.** Describe the prevalence of anti-HBc in HIV-positive individuals who tested negative for HBsAg, and define serologic profiles of resolve infection and isolated anti-HBc. Evaluate rapid test for anti-HBc as screening. **Material and methods.** Single center prospective study. Anti-HBc were determined in HBsAg-negative subjects, and anti-HBs in those who tested positive for anti-HBc. Simultaneous rapid tests for anti-HBc were perfomed. Individuals with HCV-positive were excluded. **Results.** 192 subjects were included. Prevalence of anti-HBc was 42.7% (82/192). In anti-HBc positive individuals, anti-HBs was positive in 80.5% (66/82), with mean titers of 638 ui/mL, indicative of resolve infection. Serological pattern of isolated anti-HBc in 19.5% (16/82). Presence of anti-HBc positive was associated with male sex, drug use, men-sex-men, positive VDRL, longer time from diagnosis of HIV and no-use of HAART. Considering all individuals who were tested for anti-HBc, prevalence of isolated anti-HBc pattern was 8.3% (16/192), associated to detectable HIV viral load, less time from diagnosis of HIV, and no-use of HAART. DNA HVB has detectable in a minority. Rapid test for anti-HBc showed a low sensitivity (22.9%) and high especificity (100%) when compared to ELISA anti-HBc. **Conclusions.** Serological markers of HVB in HIV-infected individuals HBsAg-negative shows high prevalence of anti-HBc, accordant with previous reports. Most of these patients had serologic pattern consistent with resolve infection. In our study, proportion of patients with isolated anti-HBc was low, which could imply a low rate of occult HVB infection. Rapid test for anti-HBc was not as a good screnning test in HIV-positive patients with negative HBsAg.

013

CURRENT SITUATION OF HEPATITIS C VIRUS INFECTION IN PATIENTS OF HEMODIALYSIS UNIT

M. TORRES-ABREU, S. CORRALES-ALONSO, F. PONCE-RODRÍGUEZ

HOSPITAL UNIVERSITARIO CLÍNICO QUIRÚRGICO FAUSTINO PÉREZ HERNÁNDEZ. MATANZAS. CUBA.

Introduction. Patients with chronic renal failure undergoing periodical hemodialysis are a high risk group for contracting viral infections and hepatitis C virus (HCV) is one of the common complications in those patients. The study was conducted in the hemodialysis unit of the University Hospital in Matanzas to analyze the incidence of HCV infection among the patients treated by hemodialysis and the risk factors strongly associated with the infection. **Objective.** Establish a new educational interventionist proposal for the health staff who work in hemodialysis units to prevent the hepatitis C virus infection (HCV). **Material and methods.** A retrospective cohort analytical study was conducted in the hemodialysis unit in the period from December 2008 to December 2013 to analyze the incidence of HCV infection among the patients treated by hemodialysis and its casual association with different variables, such as: time of hemodialysis (THD), number of transfusions, base disease, sex and color of the skin. The period of study was divided into 5 strata. A sample of 93 patients was analyzed. **Results.** It was found that the global incidence rate was 1.01 per 100 months/patients. Males showed a higher relative risk (RR) with 5.2 (with statistical significance). The subjects that suffered from glomerulopathies had the greatest number of cases infected for an incidence density of 1.6 per 100 months/patients. The white patients prevailed and the THD showed an RR of 1.3. Blood transfusions represented the most remarkable evidence as a risk factor with an RR of 4.3, and a statistically significant $p < 0.05$. There is a high prevalence of VHC antibodies with a high positive of PCR and low race of ALAT and ASAT. There are epidemiological risk factors associated with the incidence of infection. **Conclusion.** It was concluded that the risk factors with the highest force of association with the HCV infection in hemodialysis patients are: the amount of blood transfusions, the presence of glomerulopathies and the male sex. The prevention of viral hepatitis in hemodialysis service is a strong need and it's es-

sential that medical staff acts on the epidemiological risk factors.

014

TREATMENT OF CHRONIC HEPATITIS C WITH CUBAN PEGILATED INTERFERON AND RIBAVIRIN

M. TORRES-ABREU,* S. CORRALES-ALONSO,*
C. RAMOS-PACHÓN,* H. CELESTRÍN-TÁPANES**
*HOSPITAL UNIVERSITARIO CLÍNICO QUIRÚRGICO FAUSTINO PÉREZ HERNÁNDEZ. MATANZAS. CUBA.
**HOSPITAL DOCENTE JOSÉ RAMÓN LÓPEZ TABRANE. MATANZAS. CUBA.

Introduction. At present it is the association of pegylated interferon and Ribavirin the therapy internationally approved for the treatment of chronic hepatitis C. In Matanzas, in 2011, it stars the application of this combination using a new medication made in Cuba, PEG-Heberon, which set up a new way in the therapeutic management of this disease. **Objective.** Describe the first results in the application of PEG-Heberon and Ribavirin in the treatment of chronic hepatitis C. **Material and methods.** Descriptive-prospective study. Universe: 109 patients from the provincial consultation of Hepatology in the period from December 2011 to December 2013. The studied variables were: sex, age groups, type of patient, way of presentation, adverse reactions and conduct for them, biochemical and virological answers to treatment, by means of tables. **Results.** Most of the patients were female (57.9%), average age 41.7 ± 9.2 years, virgins of treatment (73.7%) and with asymptomatic clinic patterns (68.4%)There were adverse reactions in all patients, all the clinics were classified as mild and among the hematologic ones 70.4% were light. There were neither serious events nor cancelations of treatment. There was a biochemical answer at the end of treatment in 84.2% and maintained in 78.9%. The virological answer was gotten in 73.7% at the end of treatment and in 57.6% of the patients six months after this. **Conclusion.** A high adherence of the combined therapy was gotten, being tolerated and safe for the patient, with acceptable rates of continuous virological answers.

015

CHRONIC HEPATITIS C - A 7-YEAR EXPERIENCE

J. VELEZ, A. MAIO, D. COUTINHO, S. NUNES, F. FREITAS, C. OLIVEIRA
CENTRO HOSPITALAR DO BAIXO VOUGA-EPE, AVEIRO, PORTUGAL.

Background. Chronic hepatitis C runs a silent clinical course, but has severe long-term complications (cirrhosis/ hepatocellular carcinoma). Therefore, its' timely diagnosis and appropriate treatment should be prioritized. **Material and methods.** Internal database review of all HCV positive patients, followed at the outpatient clinic from April/2007 to April/2014, with at least one positive HCV RNA sample and without HIV co-infection. **Results.** These criteria were fulfilled by 557 patients. Most were male (81%, 451/557), Portuguese (94%, 522/557) and born from 1961-1980 (70%, 387/ 557). Main risk behaviour was drug use, IV (71%, 394/557) or non-IV (7%, 39/557). Approximately 34% (188/557) admitted excessive alcohol intake, 41% (226/557) took some kind of psychiatric drug and 23% (128/557) were under substitution treatments. Genotype 1 was dominant (65%, 363/557), followed by genotype 3 (23%, 130/557), 4 (7%, 39/557) and 2 (2%, 9/557) - among the first, subtype 1a was most common (62%). Considering all patients, HCV viral load was usually over 600.000 UI/l (63%, 349/557) and HBV co-infection was rare (1%, 7/557). A fibrosis evaluation, either invasive, non-invasive or both, was performed in 68% (381/557) revealing: absent/mild disease in 67%, moderate disease in 18% and severe disease/cirrhosis in 15%. Half of all patients (280/557) didn't receive treatment, mostly because they abandoned follow-up. About 65% (255/391) of patients that did remain on follow-up were treated, with an overall SVR rate of 66% (169/255) in this group. SVR rates varied according to gender (male 64% *vs.* female 76%), genotype (1-59% *vs.* 2-100% *vs.* 3-78% *vs.* 4-61%), viral load (values > 600,000 UI/l always lead to lower SVR, except in genotype 2) and fibrosis stage (higher fibrosis always lead to lower SVR, except in genotype 2 and genotype 4 - in the latter, a small sample was analysed). Treatment consisted of peginterferon plus ribavirin, except for 22% (33/148) of genotype 1 patients who were included in clinical trials with newer DAA's (SVR rate in this subgroup was 82%). Failures were driven by therapeutic inefficacy (43%, 37/86), bad adherence/loss to follow-up during treatment (41%, 35/86) or suspension due to side effects (16%, 14/86). Therapeutic inefficacy exhibited variable failure patterns: partial response (38%, 14/37), relapse (27%, 10/37), null response (24%, 9/37) and virological breakthrough (8%, 3/37). **Conclusions.** Peginterferon plus ribavirin (as well as first-generation PI's), are no longer recommended treatment regimens. Nevertheless, in settings with economic constraints where newer drugs aren't readily available, selected and well-motivated patients may still benefit from their use.

016

RELATIONSHIP BETWEEN SERUM VITAMIN D LEVELS AND HEPATIC FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS C

G. GUALANO,* P. RODRIGUEZ,** R. ISLA,*** E. ALVAREZ,****
G. RUFFILLO,* E. MORATTO,** C. LAGÜES,**** N. DOMÍNGUEZ,*
G. LANDEIRA,* E. FASSIO*
*SECCIÓN HEPATOLOGÍA, **SECCIÓN ENDOCRINOLOGÍA DEL LABORATORIO CENTRAL, ***SERVICIO DE ANATOMÍA PATOLÓGICA, HOSPITAL NACIONAL PROF. A. POSADAS, EL PALOMAR, BUENOS AIRES, ARGENTINA. ****SECCIÓN HEPATOLOGÍA, HOSPITAL GENERAL DE AGUDOS DR. P. PIÑERO, BUENOS AIRES, ARGENTINA.

Introduction. It has been recently proposed that vitamin D (Vit D) has immunomodulatory, anti-inflammatory and antifibrotic properties. In patients with chronic hepatitis C (CHC), 2 studies have shown that decreased levels of Vit D are associated with higher grades of fibrosis, while other 2 papers have denied that finding. Vit D insufficiency might also contribute to insulin resistance and diabetes, factors that could influence fibrosis in CHC. The aim of this prospective study was to analyze relationship between serum levels of Vit D and grades of fibrosis in CHC. Secondary objectives were to assess relationship between Vit D levels and metabolic parameters (body mass index, waist circumference, glycaemia, insulin, HOMA-IR, triglycerides, HDL-cholesterol, arterial pressure), and between ethanol intake history, diabetes, demographic, virological, metabolic and biochemical variables and grade of fibrosis. **Material and methods.** 122 patients with CHC (male gender in 59, age 49.9 ± 10.9 years, chronic alcoholism in 31, diabetes in 22, genotype 1 in 86, viral load 5.67 ± 0.8 log) were studied. Exclusion criteria were co-infection with HBV or HIV; presence of auto-antibodies in high titers or liver biopsy suggesting autoimmune hepatitis; decompensated cirrhosis. All patients underwent complete clinical history, evaluating alcoholism, metabolic syndrome criteria, HOMA-

IR, liver function tests and 25-OH-Vit D levels by a chemoluminescence assay. Grades of inflammatory activity and fibrosis were assessed through METAVIR classification. Statistical analysis. ANOVA test and Pearson correlation were used to study relationship between Vit D and METAVIR stages and metabolic parameters, respectively. Univariate and multivariate analysis were performed relating all variables with severe fibrosis (METAVIR F3 + F4). **Results.** Vit D levels < 30 ng/mL (insufficiency) were found in 86 patients (70.5%) and < 20 (deficiency) in 65 (53.3%). Vit D levels were 26.5 ± 15, 20.4 ± 11, 24.3 ± 18 and 24.4 ± 15 ng/mL in METAVIR stages F1, F2, F3 and F4, respectively (NS). There was no significant correlation between Vit D levels and metabolic parameters. Univariate analysis showed that significant variables in relationship with severe fibrosis were alcoholism, grade of inflammatory activity, risk factors, glycaemia, HDL and LDL-cholesterol, total cholesterol, AST, ALT, AST/ALT, bilirubin and prothrombin activity. Logistic regression showed that prothrombin activity, alcoholism and total cholesterol are the significant variables that have a 78% global prediction of severe fibrosis. In conclusion, insufficiency of Vit D was found in 70% of our patients with chronic hepatitis C, but is not associated with the severity of liver disease.

017

CHRONIC HEPATITIS C: CLINICAL ASPECTS AND TREATMENT SEROLOGIC: 2 CARE CENTERS IN BOGOTA (COLOMBIA)

JHON E. PRIETO-O.,[*,**] SANTIAGO SÁNCHEZ-P.,[*] LEONARDO DÍAZ-R.,[*] SANDRA HUERTAS-P.[*]
[*]CLÍNICA UNIVERSITARIA COLOMBIA, BOGOTÁ, COLOMBIA.
[**]CONSULTORIO DE HEPATOLOGÍA, BOGOTÁ, COLOMBIA.

Introduction. Hepatitis C affects 170 million people worldwide, the World Health Organization (WHO) estimates a worldwide prevalence of 2%. It is known that the overall response to treatment in the era of dual therapy in genotype 1 is the order of 40%. In Colombia there are no studies to confirm these results, and there are no descriptions of the clinical aspects of the majority of those patients. **Material and methods.** We performed a review of medical records of patients diagnosed with chronic hepatitis C attending outpatient Hepatology Service of Colombia University clinic and an outpatient Hepatology Service of one of the authors during the period from January 1st 2010 to may 30 2013, in order to describe the clinical, and serological aspects and response to treatment of chronic hepatitis C. **Results.** We retrospectively reviewed the clinical records of 163 patients, 62% were female and 38% male, mean age was 58.2 years, the main risk factor for acquiring hepatitis C was history of transfusions before 1992 in 62% of patients. Therapy was started in 77 patients (47.2%), 86 (52.8%) were not considered to receive treatment for various reasons among which two major causes were advanced cirrhosis and advanced age in 44 patients that represent almost more than 50%, other reasons were minimum disease 4 patients (4.7%), minimum disease plus advanced age 9 (10.5%), spontaneous healing 12 (14%), little likelihood of response 3 (3.3%) and others 14 (16.3%). For the group of 62 patients with information related to previous treatments or recently treated 19 patients (30.6%) presented sustained virological response (SVR), (29.0%) were classified as "relapser", 5 (8.1%) had partial response, 12 (19.4%) had no response to treatment and 8 (12.9%) stopped treatment for intolerance. **Conclusions.** The most frequent risk factor to acquire the infection was transfusion history before 1992 in relation to gynecological surgery. Almost half of the patients are diagnosed late. Is an increased tendency to treatment of hepatitis C with SVR rates similar to those found in real life studies and reference. This series opens the door to further studies in order to define widely prevalence, risk factors and treatment response variables of this entity in our country.

018

THE CLINICAL AND IMMUNOLOGICAL PROFILE OF COINFECTION WITH HUMAN T LYMPHOTROPIC VIRUS TYPE 1 AND HEPATITIS C VIRUS

M. COSTA-SILVA, M.I. SCHINONI, R. PARANÁ
UNIVERSIDADE FEDERAL DA BAHIA-BRAZIL.

Introduction. Coinfection by hepatitis C virus (HCV) and human T-lymphotropic virus type 1 (HTLV-1) has been reported in multiple geographical regions and is a result of the similarity in the transmission pathway of both viruses. **Objective.** To assess and describe the clinical, epidemiological and immunohistopathological aspects of this coinfection. **Materials and methods.** We conducted a cross-sectional study of a sample of 23 patients who were coinfected with HCV and HTLV-1, 21 patients who were monoinfected by HCV and 20 patients who were monoinfected by HTLV-1. The cytokine profiles (TH1 and TH2 response) as well as the presence and frequency of autoantibodies were assessed in all three groups. **Results.** There were no clinical or anthropometric differences between the groups. On the other hand, there was a higher serum concentration of IFN gamma in serum samples from the coinfected group (HCV/HTLV-1) compared with the monoinfected group (HCV), with the monoinfected (HTLV-1) ($p < 0.01$). The group monoinfected HTLV-1 showed higher production of IFN gamma in relation to the other groups ($p < 0.001$) The coinfected group (HCV/HTLV-1) had a higher degree of hepatic steatosis than the monoinfected group (HCV) ($p < 0.01$). There was also a higher concentration of total protein and globulin in the coinfected group (HCV/HTLV-1) ($p < 0.01$). Statistical analysis of the four groups involved in the evaluation of the profile of cytokines INF gamma suggests a difference in the immune profile ($P < 0.0001$). Th1 response induced by HTLV-1 infection was less severe when associated with HCV. **Conclusion.** The results suggest that coinfection may result in a different pattern of HCV infection due to the immunological disorders associated with HTLV-1.

019

CHANGE IN THE DISTRIBUTION OF HEPATITIS C VIRUS GENOTYPES IN CHILE BETWEEN 1994-2012

A. URZÚA-MANCHEGO, M. VENEGAS-SANTOS, J. BRAHM-BARRIL
HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.

Introduction. Genotyping is important as predictor to antiviral treatment response in chronic hepatitis C (HCV), and could change in its distribution over tim. **Objective.** Description of changes in the distribution of HCV genotypes in Chile, during a long period of time. **Materials and methods.** HCV genotyping was done in 1766 patients from 1994 through 2012, using nested PCR technique, followed by restriction fragment length polymorphism assay. **Results.** The global genotypes distribution through the 18 years period was: 1a:

7.8%; 1b: 72.7%; 2: 1.9%; 3a: 16.5%; 4: 0.5%; 5a: 0.2% y 6: 0.06%. Genotype 1b was the most frequent, but has diminished from 88.24 to 70.6%. By contrast, 3a has rised from 8.33 to 15.13%, representing more than 20% on 2009 (22%) and 2011 (24%). Genotype 1a, that only represented a few cases at the beginning, being absent in 1994 and 1996, has maintained a stable proportion since 2003, representing nowadays 11.76%. Genotypes 4, 5a and 6 only represent a few cases. **Conclusions.** HCV genotypes distribution has changed in our country. Genotype 1b has been historically the most frequent, but has diminished its representation. Genotype 3a has gained importance, and is nowadays 2-3 times more frequent than at 1994, while 1a has stabilized. Other genotypes (4, 5a y 6) are still very uncommon. These changes are important in the era of direct acting antivirals, since they have shown better sustained viral response in genotype 1b over 1a, but also have worse results in genotype 3a, which has currently the second frequency in Chile.

020

ASSESSMENT OF RENAL FUNCTION DURING TREATMENT FOR CHRONIC HEPATITIS C WITH PROTEASE INHIBITORS

M. STUDART, P.M. YOSHIMURA, D.F. MAZO, C.P. MARQUES, F.J. CARRILHO, M.G. PESSÔA
CLINICAL HOSPITAL OF THE UNIVERSITY OF SAO PAULO, SAO PAULO, BRAZIL.

Introduction. The prevalence of HCV infection is estimated as 2-3% worldwide, affecting 130-170 million people. Adding direct acting-antiviral agents (DDA) as telaprevir (TVR) and boceprevir (BOC) to peg-IFN and ribavirin (RBV) increases the sustained virologic response (SVR) by about 30%. However, triple therapy with these protease inhibitors (PI) also increased the incidence of renal damage. This dysfunction is poorly understood and needs to be clarified. **Aims.** The purpose of the study was to evaluate the role of PI over renal function during triple therapy for hepatitis C. **Material and methods.** Thirty-four patients with chronic hepatitis C, genotype 1, were consecutively enrolled. They were referred to the outpatient HCV Clinic at the Division of Gastroenterology and Hepatology at a tertiary Hospital in Brazil, between July 2013 and May 2014. Twenty-seven patients received TVR in combination with peg-IFN and RBV for 12 weeks followed by peg-IFN and RBV, and 7 received BOC in triple therapy for 44 weeks after lead-in. Estimated glomerular filtration rate (eGFR) was prospectively evaluated for an average period of up to 35 weeks. MDRD and Cockcroft-Gault (CG) equations were used to calculate eGFR. **Results.** Statistically significant worsening of renal function in patients who received TVR was detected by an increase in serum creatinine ($p < 0.001$; OR 28.677; 95% CI 6.395-128.596) and decrease in eGFR, when calculated by CG (p 0.003; OR 10.779; 95% CI 2.271-51.153) and MDRD ($p < 0.001$; OR 8.333; 95% CI 2.770-25.066). A non-statistically significant increase in serum creatinine was seen with BOC (p 0.676; OR 1.312; 95%CI 0.367-4.696), as well as a decrease in CG (p 0.425; OR 2.793; 95%CI 0.224-34.783) and in MDRD (p 0.915; OR 0.922; 95%CI 0.208-4.082). It was also observed that the chance of having normal renal function after completion of 12 weeks of TVR was high and significant when studied by creatinine ($p < 0.001$; OR 7.916; 95%CI 3.307-18.948), CG (p 0.020; OR 3.491, 95% CI 1.219-9.996) or MDRD ($p < 0.001$; OR8.598; 95%CI 3.474-21.277). More than 90% of patients are still under treatment, precluding analysis of post-treatment for BOC. **Conclusions.** The association of TVR to the treatment regimen for genotype 1 HCV increased the risk of renal dysfunction, but it was likely to return to normal levels after discontinuation of PI, similarly as in recent publications. Further analysis is needed after completion of triple therapy in the majority of patients.

021

INITIAL EXPERIENCE OF TREATMENT OF HEPATITIS C TRIPLE THERAPY WITH THE FEDERAL DISTRICT, BRAZIL

ACP MORAES, LHL TAVARES, JDU BRITO, SM GERALDES, NPMV THOMAZONI, RC CAPELI, MG QUEIROZ, DF GAMA
UNIDADE MISTA DE SAÚDE DA COORDENAÇÃO GERAL DE SAÚDE DA ASA SUL (UMS/CGSAS), BRAZIL.

Introduction. In recent years, the development of new strategies to improve the rate of sustained virologic response (SVR) has been an important focus in the treatment of hepatitis C virus (HCV). Several direct-acting antivirals are in the final stages of study, however, only telaprevir and boceprevir are protease inhibitors (PIs) approved in Brazil so far. Unfortunately, this therapy may have many side effects and eventually compromise the treatment outcome. **Objective.** This observational study demonstrated the experience of the first year of treatment with triple therapy followed by standard dual therapy with pegylated interferon and ribavirin in usual doses for 48 weeks, patients chronically infected with HCV in the Federal District, one of 27 Brazilian federative units in 2013. **Results.** Sixty-four patients started triple therapy, 53 (82.8%) with telaprevir and 11 (17.2%) with boceprevir. Of the 64 patients who started the IPs, 19 (29.6%) had to stop triple therapy, 5 (7.81%) during the first 12 weeks. The main reasons for the suspension of treatment were: 2 (3.1%) deaths, 3 (4.6%) severe anemia, 6 (9.3%) skin rash, 4 (6.2%) virologic failure, 1 (1.5%) severe thrombocytopenia, 1 (1.5%) abandonment of therapy, 1 (1.5%), generalized weakness, and 1 (1.5%) for extensive pneumonia. At the moment, 35 (54.6%) patients are still under treatment, and 10 (15.62%) have completed 48 weeks, with undetectable viral load. **Conclusion.** Significant advances in the treatment of HCV have improved the effectiveness of SVR. However, triple therapy with PIs still has several adverse effects, leading to a large number of suspensions treatments when not properly conducted by experienced professionals.

022

EVALUATION OF QUALITY OF LIFE OF PATIENTS WITH HEPATITIS C IN AN ASSISTED OUTPATIENT REFERENCE IN THE MUNICIPALITY IPIAÚ-BA

L. PESTANA-BARBOSA,* M. COSTA-SILVA,** J. ANGÉLICA MESQUISTA**
**FACULDADE DE TECNOLOGIA E CIÊNCIAS, BAHIA, BRAZIL.*
***SECRETARIA DE SAÚDE DO ESTADO DA BAHIA, BRAZIL.*

Introduction. The term quality of life has improved its importance recently, bringing interest due probably its increasing need of doing a health planning. Several studies have already shown that patients with chronic Hepatitis C have the quality of life is significantly reduced and individuals infected with HCV may present a wide range of problems of neuropsy-

chiatric nature. **Objective.** Evaluate the quality of life of patients who have hepatitis C assisted on an ambulatory of reference at the city of Ipiaú-Bahia. **Material and methods.** The study has analyzed 67 patients carrying hepatitis C on an ambulatory of reference at the city of Ipiaú-Bahia, realizing a descriptive and cross-sectional study, characterizing the sample studied and relating the domains of the life's quality survey (SF-36) with gender and phase of medical monitoring. **Results.** Patients were mainly of the female gender (52.2%); the prevailing age group was between 50 and 59 years old; the genotype 1 was the most found (49.25%); the domain of the SF-36 that presented the lowest average was limitation by physical aspects (46.64%), the relations that obtained statistical significance were between the domains limitation by physical aspects, general state of health, vitality and limitation by emotional aspects with the phases of medical monitoring. **Conclusion.** Some domains of the survey SF-36 presented statistical significance when related with the phase of the medical monitoring. Posterior studies must be realized to establish possible relations here analyzed in a trusted way.

023

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF HEPATITIS E IN URUGUAY: CURRENT STATUS

V. MAINARDI,* S. MIRAZO,** A. ROCCA,* M. VALVERDE,* P. SCALONE,* N. RAMOS,** J. ARBIZA,* M. VIÑOLY,* S. GONZALEZ,* S. GERONA*

**UNIDAD BI-INSTITUCIONAL DE TRASPLANTE HEPÁTICO, HOSPITAL CENTRAL DE LAS FUERZAS ARMADAS-HOSPITAL DE CLÍNICAS, MONTEVIDEO, URUGUAY.*
***FACULTAD DE CIENCIAS, UNIVERSIDAD DE LA REPÚBLICA, MONTEVIDEO, URUGUAY.*

Background. Epidemiology of hepatitis E virus (HEV) infection varies with genotype and geographic area. In endemic areas, large outbreaks of acute hepatitis by genotype 1 and 2 frequently occur (through contamination of water, fecal-oral transmission), mainly in young adults. In developed countries, sporadic autochthonous cases of genotype 3 and 4 have been increasingly reported, presenting as mild to fulminant acute hepatitis, and chronic hepatitis in immunocompromised patients. There is a zoonotic transmission by consumption of undercooked meat (swine and deer). Genotype 3 is the most frequent in Latinamerica. Uruguay is considered a non-endemic area. Thirteen autochthonous cases were reported in 2010-2011 by Mirazo. All were immunocompetent adults, from urban area, unrelated, without risk factors for HEV infection, presented as self-limiting mild acute hepatitis. All belong to genotype 3. The strains were related to the diagnosed in Europe, but dissimilar to Southamerican isolates. None HEV infection has been detected in Uruguayan´s swine. The aim of this study was to update the epidemiological scenario of HEV infection in Uruguay. **Material and methods.** Since 2013 to the current date, acute and chronic hepatitis without clear etiology and acute liver failures (ALF) were tested for immunoglobulin M (IgM) and G (IgG) against HEV by line immunoassay in blood and HEV RNA by reverse-transcriptase nested polymerase chain reaction (PCR) in blood and stool. **Results.** From 3 mild acute hepatitis tested, one had positive IgM and PCR, genotype 1. It was an immunocompetent 26 years old man, from suburban area, without risk factors, and resolved spontaneously. 3 ALF were tested: one had positive PCR, genotype 3, negative IgM. It was a 16 years old girl, from urban area, without risk factors, presenting as cholestasic acute hepatitis with prothrombine time < 50%, without encephalopathy. She also had diagnosed criteria for Wilson's disease; with a favorable outcome with cooper chelating therapy, without antiviral. Other had positive IgG, negative IgM and PCR. The third tested all negative. The source of infection could not be identified in any. No cases of chronic hepatitis were tested. **Conclusions.** 1 of 3 acute hepatitis without clear etiology, and 1 of 3 ALF had HEV infection. All HEV infections reported in Uruguay presented as acute hepatitis, mild in immunocompetent patients; the one with underlying liver disease developed ALF. All except one were genotype 3 according to epidemiology in Latinamerica. The identification of genotype 1 suggests that HEV epidemiology may be changing in the region.

024

NATIONAL PROGRAM FOR CONTROL OF VIRAL HEPATITIS: SCOPE AND CURRENT DATA MINISTRY OF HEALTH DIRECTORATE OF AIDS AND STDS, ARGENTINA

G. VIDIELLA, E. CORONEL, J. SOLARI, R. AQUINO, K. ROITMAN, D. MARTINEZ MADRID, C. FALISTOCCO

PROGRAMA NACIONAL DE CONTROL DE LAS HEPATITIS VIRALES, DIRECCIÓN DE SIDA Y ETSS. MINISTERIO DE SALUD DE LA NACIÓN. REPÚBLICA ARGENTINA.

Objective. To present data on the results of provision of treatment by the National Program for Control of Viral Hepatitis (PNHV), since its formation. **Material and methods.** A database of patients without health insurance authorized for treatment of chronic hepatitis during the period of January 2012 to March 2014 was analyzed. Applications for treatment of chronic hepatitis were audited and approved for treatment for patients with hepatitis C, B and also C co-infected with HIV following the Program Guidelines. Available drugs are Peg-Interferon Alfa 2a and 2b, Ribavirin, Boceprevir, Telaprevir, GM Stimulating Factor, Erythropoietin, Entecavir, Tenofovir and Lamivudine. **Results.** 358 treatments for mono-infected patients (216 with Hepatitis C and 142 with Hepatitis B) and 148 HIV-HCV co-infected patients were authorized; requests for treatment increased 22 and 16% in 2013 compared to 2012 for mono and co-infected patients, respectively. 67% of the treatments were requested from the city and province of Buenos Aires, followed by Córdoba, Mendoza and Santa Fe. Of the patients treated for hepatitis B: 79% were male; 82% were naïve; 59% started treatment without a liver biopsy; 51% were HBeAg (-); 72% requested entecavir and 15% requested tenofovir. Of the patients treated for hepatitis C: 52% were male; 92% were naïve; 62% had genotype 1; 28% had genotype 3; 72% had fibrosis assessment: 33% had F0-F1, 48% had F3 or F4. The rate of sustained virological response (SVR) was 58% in 35 patients with genotype 1. Among patients co-infected with HIV and HCV: 70% were male, 92% were naïve; in 48% of the patients fibrosis was assessed before starting treatment: 89% by biopsy and 11% by elastography; 64% began dual therapy with F ≤ 2; 98% used HAART and had CD4 ≥ 250 cells/mL; 37% were G1a; 10% were G1b, 19% G1 without classification; 23% G3. 40 treatments with boceprevir and telaprevir were initially administered to patients with advanced fibrosis. These treatments began in March and April 2014, and therefore as of yet there are no details regarding SVR. **Conclusions.** The distribution of prescriptions for chronic hepatitis in Argentina is heterogeneous, with a higher concentration in several large urban centers. This also shows the heterogeneous distribution of professionals trained to treat these diseases. The low number of treatments requested in relation to the estimated prevalence of hepatitis B and C in

Argentina reinforces the need to promote access for diagnosis and treatment in the country.

025

EVIDENCE OF HEPATITIS E VIRUS INFECTION IN LIVER TRANSPLANT RECIPIENTS FROM BRAZIL

ADRIANO MORAES, MICHELE GOVEIA, MARIO PESSOA, EDSON ADDALA, DEBORA TERRABUIO, ARIANA FERREIRA, PATRICIA BONAZZI, LUIS D'ALBUQUERQUE, FLAIR CARRILHO, JOÃO RENATO
SAO PAULO UNIVERSITY, BRAZIL.

Background. Hepatitis E virus (HEV) has been recognized as an important cause of acute viral hepatitis worldwide. Nevertheless, several studies have recently suggested that HEV infection might result in chronic hepatitis in different cohorts of immunocompromised individuals, including recipients of organ transplants. There are no data regarding prevalence of HEV infections in patients submitted to liver transplantation in Brazil, where the circulation of this virus has been demonstrated by antibody detection in different groups of immunocompetent individuals with a prevalence of 2.6-17.7%. Moreover, HEV infection among pigs has been identified in different regions of the country. **Aim.** To determine the seroprevalence of anti-HEV IgG and IgM in patients submitted to liver transplantation at São Paulo University in Brazil. **Material and methods.** Two hundred eighty-four liver transplant patients were enrolled in this study. The mean age of the patients was 50.5 years old (19-78 years old) and 174 were male. Serum samples collected between January and May, 2013 were tested for the presence of IgG and IgM antibodies by enzyme immunoassay (ELISA) tests (recomWell HEV IgG and IgM, Mikrogen, Neuried, Germany). **Results.** Anti-HEV IgG were reactive in 23 (8.1%) among the 284 serum samples examined. A total of 230 samples were also tested to anti-HEV IgM and 6 (2.6%) were positive. Only one (4.3%) of the 23 anti-HEV IgG reactive samples also showed positivity to anti-HEV IgM. This patient was 69 y.o. male, with normal transaminases levels (ALT = 14 U/L; AST = 19 U/L). Chronic hepatitis C was the cause of liver transplantation in 13 (46.4%) of the 28 patients with antibodies to HEV. The mean AST and ALT levels in patients without any serological marker of HEV infection were 48 U/L (range from 5 to 1,039 U/L) and 42 U/L (range from 8 to 675 U/L), respectively. Patients with positive anti-HEV antibodies did not show extensive increase of ALT and AST levels. **Conclusions.** This study indicates that the prevalence of Anti-HEV antibodies is higher in liver transplant recipients than that previously observed in some immunocompetent populations in Brazil. These results suggest that HEV infection should be investigated as a possible cause of liver injure in the liver transplant population. The presence of HEV RNA will be investigate to determine more accurately the prevalence of HEV infection in this population and the occurrence of chronic infection.

026

TREATMENT WITH PEGYLATED INTERFERON MONOTHERAPY ALPHA 2A IN ACUTE C HEPATITIS: EXPERIENCE OF A TERTIARY CARE HOSPITAL

R. SANDOVAL-SALAS, M. DEHESA-VIOLANTE, R. MORENO-ALCANTAR
SERVICIO DE GASTROENTEROLOGÍA, HOSPITAL DE ESPECIALIDADES DEL CENTRO MÉDICO NACIONAL SIGLO XXI DR. BERNARDO SEPÚLVEDA, IMSS, MÉXICO, D.F.

Introduction. Chronic infection with hepatitis C virus (HCV) is considered a public health problem. The acute phase of this infection is a key point in the evolution of the disease, as it can evolve into chronicity or spontaneous resolution. Several situations that contribute to this disease be underdiagnosed, as; asymptomatic course and little clinical suspicion. Prompt treatment with pegylated interferon (PEG IFN) monotherapy has proved effective in achieving sustained viral response (SVR) in 90% higher rates. **Objective.** To evaluate the efficacy of PEG IFN alfa monotherapy 2A in patients with acute HCV infection. **Material and methods.** All clinic records were reviewed and patients with diagnosis of acute hepatitis C between 2006 and 2013 and start of antiviral treatment within the first 12 weeks after diagnosis and conclude the scheme based on monotherapy PEG IFN alfa 2A 180 μgr per week for 24 weeks regardless of genotype. Acute hepatitis C was considered when there was a risk factor for 2-12 weeks before the acute illness, elevation of AST and ALT, blood HCV RNA quantified by PCR and found entered in the previous record for HCV serology negative, besides other causes of hepatitis acute (HBV, HAV, toxic liver damage, autoimmuni-

Table. (026)

Patient	Age	Genre	ALT	AST	BT	Risk factor	Health personnel	Clinical manifestations	Comorbidity	Anti HCV negative before the acute hepatitis	RNA VHC (UI/mL)	Genotype
1	48	M	501	622	0.73	Accidental puncture	Physician	Symptomatic	No	No	51,500	2
2	21	M	1,618	1,003	1.36	Transfusion	No	Symptomatic	Acute lymphoblastic leukemia with chemotherapy	Yes	353	1b
3	44	F	1,028	2,438	8.4	Accidental puncture	Nurse	Symptomatic	No	No	912	1b
4	64	F	1,229	1,214	13.17	Any apparent	No	Symptomatic	DM2, HAS	Yes	2,240	1a
5	58	F	617	823	8.46	Accidental puncture	Chemical	Symptomatic	No	No	1,320,000	1b
6	74	M	832	516	5.6	Cystoscopy	No	Symptomatic	Prostatic cancer	No	139,000	1a
7	45	F	175	154	0.7	Transfusion and hemodialysis	No	Asymptomatic	CKD	Yes	170	1b

ty). **Results.** We identified 6 patients achievement of which 3 were male and 3 female, 5 with genotype 1 and 1 with genotype 2, the SVR achieved in 100% of cases **(Table). Conclusions.** Monotherapy with PEG IFN alpha 2A is effective in patients with acute hepatitis C to achieve a high rate of SVR. Our data are consistent with those reported in the literature to the difficulties diagnosed though our sample is small.

027

SERUM LEVELS OF TRANSFORMING GROWTH FACTOR BETA-1 AND SOLUBLE FAS (sFas) IN PATIENTS WITH OCCULT HBV INFECTION AND INFECTED WITH HIV

J.L.A. SILVA,[*] D.M. VASCONCELOS DE DEUS,[*,||] G.G.O.M. CAHÚ,[*,||] C.N.L. DE-MORAIS,[‡] R.C. MOREIRA,[†] M.R.C.D. COÊLHO[*,§,||]
[*]*VIROLOGY SECTOR, KEIZO ASAMI IMMUNOPATHOLOGY LABORATORY (LIKA), FEDERAL UNIVERSITY OF PERNAMBUCO (UFPE), RECIFE, BRAZIL.*
[†]*VIRAL HEPATITIS LABORATORY, ADOLFO LUTZ INSTITUTE, SÃO PAULO, BRAZIL.*
[‡]*DEPARTMENT OF IMMUNOLOGY, CENTRO DE PESQUISAS AGGEU MAGALHÃES (CPQAM), RECIFE, BRAZIL.*
[§]*DEPARTMENT OF PHYSIOLOGY AND PHARMACOLOGY, UFPE, RECIFE, BRAZIL.*
[||]*POST GRADUATE PROGRAM IN TROPICAL MEDICINE, CENTER OF HEALTH SCIENCES, UFPE, RECIFE, BRAZIL.*

Introduction. The transforming growth factor beta-1 (TGF-β1) and soluble fas (sFas) cytokines play an important role in the defense against viral infections, but they are rarely investigated in patients with occult hepatitis B and HIV infection. Occult HBV infection is characterized by the absence of surface antigen (HBsAg) together with the positivity of HBV-DNA plasma with very low viral load (< 200 IU/mL). **Objective.** To determine the serum levels of TGF-β1 and sFas in HIV treatment-naive patients with HBV occult infection. **Material and methods.** The study included 38 patients treated in two specialized care services for HIV/AIDS in Pernambuco, Brazil. The study of serological markers HBsAg, anti-HBc , anti-HBs (Bio-Rad Laboratories®) and serum levels of sFas and TGF-β1 (R&D Systems®) were measured by ELISA and HBV-DNA was quantified by qPCR. **Results.** 28.95% (11/38) of the patients had occult HBV infection. The HBV viral load was 2.56 log10 copies/mL, less than the patients without occult HBV infection (6.39 log10 copies/mL). In patients with occult infection, the median of sFas serum levels was 12,437 pg/mL and for TGF-β1 was 65,400 pg/mL. In the patients without occult infection the median value was 10,836 pg/mL for sFas and for TGF-β1 was 68,408 pg/mL, although without any statistical significance. There was no correlation between serum levels of these cytokines and HBV viral load in patients with and without occult HBV infection. **Conclusion.** The presence of occult HBV infection did not influence the development of liver damage in these patients.

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THE CELLULAR IMMUNE STATUS DISORDERS IN PATIENTS WITH ASTHMA IN ASSOCIATION WITH OCCULT HBV INFECTION

E. KIRVAS,[*] IU. LUPASCO,[*] V. DUMBRAVA,[*] I. ROMANCIUC,[*] G. HAREA[*]
[*]*STATE UNIVERSITY OF MEDICINE AND PHARMACY NICOLAE TESTEMITANU, CHISINAU, REPUBLIC OF MOLDOVA.*

Introduction. Asthma association with occult HBV infection had an impact on immunological disorders occurred in these diseases. **Aim.** Assessment of cellular immune status in patients with asthma in association with occult infection HBV. **Material and methods.** The study included 66 patients. The control group (group I) served 10 healthy individuals. Patients with asthma associated with occult HBV infection were 39 people and the group of patients with occult HBV infection without asthma presented 27 people. Group II-A represented patients with asthma in association with occult HBV infection with normal transaminase levels (NTL), group II-B consisted of patients with the same pathology with high transaminase levels (HTL). Group III-A presented occult HBV infected patients without asthma with NTL, while group III-B served occult HBV infected patients without asthma, with HTL. Clinical and laboratory examination was performed with assessment of serum markers of viral hepatitis HBV DNA PCR; biochemical data; humoral and cellular immune status; abdominal USG, spirometry, etc. **Results.** The elevated leukocyte blood counts were found in group II-B 8.19 ± 0.55 *vs.* 5.83 ± 0.53 in group I ($p < 0.01$); and in II group B *vs.* group III-B 6.11 ± 0.39 ($p < 0.01$). Reducing level of lymphocytes was presented in group II-B 24.97 ± 0.9% *vs.* 29.3 ± 1.57% in control group I ($p < 0.05$); group II-B *vs.* group III-B 33.94 ± 2.47% ($p < 0.01$). Elevated T helper lymphocytes (CD4) number was assessed in group III-B 947.61 ± 100.41 *vs.* group I 606.46 ± 55.74 ($p < 0.01$) and 47 ± 3.08% *vs.* 37.4 ± 2.93% ($p < 0.05$); group II-B 911.46 ± 68.12 *vs.* group I 606.46 ± 55.74 ($p < 0.01$) and 46.14 ± 2.1% *vs.* 37.4 ± 2.93% ($p < 0.05$). Elevated B lymphocytes (CD20) were established in group II-B 136.03 ± 15.66 *vs.* III-B group 66.82 ± 10.62 ($p < 0.001$) and 7.03 ± 0.79% *vs.* 3.5 ± 0.53% ($p < 0,001$); group II-B *vs.* 87.9 ± 17.57 group II-A ($p < 0.05$). **Conclusions.** The most pronounced cellular immune disorders were found in the group of patients with asthma in association with occult HBV infection with high levels of transaminases.

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THE HUMORAL IMMUNE STATUS DISORDERS IN PATIENTS WITH ASTHMA WITH OCCULT HBV INFECTION ASSOCIATION

E. KIRVAS, IU. LUPASCO, V. DUMBRAVA, I. ROMANCIUC, G.HAREA
STATE UNIVERSITY OF MEDICINE AND PHARMACY "NICOLAE TESTEMITANU" CHISINAU, REPUBLIC OF MOLDOVA.

Introduction. Immune disorders that develop in asthma and chronic viral hepatitis have a great role in both diseases progression and may explain the increased frequency of asthma association with occult infection in HBV. **Aim.** Assessment of humoral immune status in patients with asthma in association with occult HBV infection. **Materials and methods.** The study included 66 patients. The control group (group I) served 10 healthy individuals. The group of patients with asthma associated with occult HBV infection consisted of 39 people and the group of patients with occult HBV infection without asthma presented 27 people. Group II-A represented patients with asthma in association with occult HBV infection with normal transaminase levels (NTL), group II-B consisted of patients with the same pathology with high transaminase levels (HTL). Group III-A presented occult HBV infected patients without asthma with NTL, while group III-B served occult HBV infected patients without asthma, with HTL. Clinical and laboratory examination was performed with assessment of serum markers of viral hepatitis, HBV DNA PCR; biochemical data; humoral and cellular immune status; abdominal USG, spirometry, etc. **Results.** Elevation of serum IgE was observed in group II-B 226,97 ± 54,82 IU/mL *vs.* control

78.25 ± 38.73 IU/mL ($p < 0.05$). The same tendency was found in group II-B *vs.* group III-B 74.28 ± 27.03 IU/mL ($p < 0.05$), as well as in group II-A *vs.* group III-A ($p < 0.01$) independent of transaminase level. Increase of serum IgM was highlighted in group II-B 234,83 ± 23,05 mg/dL *vs.* control 129.9 ± 22.39 mg/dL ($p < 0.01$). Statistical difference between groups was also appreciated between II-B and III-B 115.25 ± 14.4 mg/dL groups ($p < 0.001$). Decrease serum IgA level was detected in group III-B 179.4 ± 18.32 mg/dL and in group III-A 190.36 ± 18.16 mg/dL *vs.* group I 248.7 ± 21.98 mg/dL ($p < 0.05$). At the same time IgA indices increase was observed in group I-B 247.24 ± 19.9 mg/dL *vs.* group III-B 179.4 ± 18.32 mg/dL ($p < 0.05$) with dislocation of immune answer (Th1) guided by HBV infection. **Conclusions.** The more significant humoral immune disorders were found in the group of patients with asthma in association with occult HBV infection with high transaminases levels.

030

OPTIMIZATION METHOD FOR DIAGNOSING CHANGES IN THE THYROID STATUS IN OCCULT HBV INFECTION

IU. LUPASCO, V. DUMBRAVA, I. ROMANIUC, E. KIRVAS, G. HAREA
STATE UNIVERSITY OF MEDICINE AND PHARMACY NICOLAE TESTEMITANU CHISINAU, REPUBLIC OF MOLDOVA.

Background. The Republic of Moldova is among the countries with high prevalence of chronic hepatitis B (CHB). Prevalence of CHB from 2005 to 2002 increased from 328.9 to 588.2 per 100 thousand population, which causes the growth of various forms of the disease, including occult HBV infection. Meanwhile, the thyroid profile in patients with occult HBV infection is studied insufficient. The aim was to study the thyroid profile in patients with occult HBV infection. **Material and methods.** It has been surveyed 225 people who had the presence of HBV in history, of which 72 patients were selected with different forms of chronic hepatitis and 28 with no signs of chronic hepatitis B, but with the presence of occult infection HBV. Both groups have investigated the level of T3, T4, TSH both fasting and in dynamics of the original euphyllin-glucose load test at 60 and 120 min (Method ELISA USA). The control served 62 healthy subjects. **Results.** The levels of T3 (1.39 ± 0.04 nmol/mL) and T4 (84.67 ± 5.26 nmol/mL) in patients with occult HBV infection were significantly lower fasting corresponding values in the control group (1.76 ± 0.03 nmol/mL), $p < 0.001$ and 101.15 ± 2.16 nmol/mL, $p < 0.001$). Meanwhile, the level of TSH (2.08 ± 0.11 iu/mL) exceeded the data of healthy persons (1.79 ± 0.09 iu/mL) ($p < 0.001$). Euphyllin-glucose load at 60 min of the test caused a significant decrease of T3 and T4 levels in normal 1.18 ± 0.04 nmol/mL, $p < 0.001$ and 84.08 ± 5.65 nmol/mL, $p < 0.001$, with a substantial increase of TSH in the same period 2.16 ± 0.03 iu/mL, $p < 0.001$. The curves of T3 and T4 in occult infection remained flat (1.38 ± 0.05 nmol/mL, $p > 0.05$ and 89.22 ± 5.53 nmol/mL, $p > 0.005$) with concomitant significant increase of TSH level at 60 minute of the test (1.62 ± 0.10 iu/mL, $p < 0.001$). **Conclusions.** The received data showed presence of hidden hypothyroid function in occult infection HBV that was not diagnosed by clinical examination. Euphyllin-glucose load test reveals depletion of reserve capacity of the thyroid gland and makes it possible to diagnose latent hypofunction. An identified change in thyroid function requires dynamic monitoring and appropriate correction to avoid further progression.

031

MUTATIONS ASSOCIATED WITH DRUG RESISTANCE AND ESCAPE VACCINE IN PATIENTS WITH CHRONIC HEPATITIS B INFECTION

MARIA I. MAGALHÃES-ANDRADE-DOS-SANTOS,* ANDREAS STOECKER,** SIDELCINA PACHECO-RUGIERE,* RAYMUNDO PARANÁ,*** MITERMAYER G. REIS,* LUCIANO K. SILVA*
**CENTRO DE PESQUISAS GONÇALO MONIZ, FIOCRUZ, SALVADOR, BRAZIL.*
***LABORATÓRIO DO SERVIÇO DE GASTRO-HEPATOLOGIA/DE PESQUISA EM INFECTOLOGIA (SGH/LAPI), HUPES-UFBA, SALVADOR, BRAZIL.*
****AMBULATÓRIO MAGALHÃES NETO, HUPES-UFBA, SALVADOR, BRAZIL.*

Background and Aims. The Brazilian public health system (SUS) has provided antiviral drugs for chronic hepatitis B treatment for over 10 years, but a system for monitoring for nucleos(t)ide resistance mutations during antiviral therapy is not available. We aimed to establish a monitoring routine at the Federal University Hospital (HUPES/UFBA), a reference unit for HBV treatment at Salvador-BA-Brazil. **Material and methods.** We screened for known HBV nucleos(t)ide resistance mutations in 81 patients with chronic hepatitis B. We amplified the HBV Pol/rt domain using PCR and sequenced the resulting products using ABI Prism 3730 (Applied Biosystems, USA). We submitted the sequences to the HBV drug resistance database (HBVrt DB, Stanford University, USA) to genotype each isolate and to identify any drug resistance mutations. **Results.** We determined that the HBV genotype A1 (85.2%) was the most prevalent followed by genotype A2 (4.9%), F (6.2%), and C1, D2 and D4 (1.2% each). Isolates from six patients (7%) exhibited resistance mutations to LAM, ETV and TDF: L180M + M204V (2) L80I + L180M + M204I (1); L80V + L180M + M204V (1); M204I (1); and, A194T (1). We only identified mutations in patients with genotype A (four A1 and two A2). When we analyzed the S gene we identified four (6%) vaccine escape mutations: sI195M (3), and W196L (1). Additionally, we tested for association of drug resistance mutations and laboratory results or treatment history. **Conclusions.** In this study we found a strong association between the occurrence of HBV resistance mutations and HBeAg positivity, co-infection with HIV and the history of antiviral for HBV and/or HIV treatment.
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032

EPIDEMIOLOGICAL, HISTOLOGICAL AND GENOTYPIC CHARACTERISTICS IN PATIENTS MONOINFECTED AND COINFECTED WITH HEPATITIS B AND CHRONIC HBV/HTLV I AND II, HBV/HCV AND HBV/HIV - PRELIMINARY RESULTS - AT THE UNIVERSITY HOSPITAL IN SALVADOR-BAHIA

V. MENEZES-JESUS,* M.I. MAGALHÃES SANTOS,** S. PACHECO-RUGIERI,** R.S FREIRE JUNIOR,* L. KALABRIC SILVA,** M. GALVÃO DOS-REIS,** R. PARANÁ,* M. ISABEL SCHINONI*
**HOSPITAL UNIVERSITÁRIO PROFESSOR EDGARD SANTOS, UFBA SALVADOR, BRAZIL.*
***CENTRO DE PESQUISAS GONÇALO MONIZ, FIOCRUZ, SALVADOR, BRAZIL.*

Introduction. Two billion people in the world have serological evidence of infection in the past or in the present by the HBV, and 350 million suffer from chronic infection and are at

risk of developing liver disease as cirrhosis and hepatocarcinoma. Studies on co-infection HBV/HTLV I and II, HBV/HCV and HBV/HIV show similarity in route of infection, as well as worse prognosis for patients co-infected. This study aims to describe the epidemiological characteristics, histolopathology and Genotype of patients mono and co-infected, in a reference service in Hepatology, Salvador-Bahia. **Material and methods.** A cross-sectional observational descriptive study. The statistical methods used for analysis were mean, standard deviation and frequency. The genotype studied by direct sequencing and analysis by Stanford. **Results.** Patients number was 217, 60.8% female, age: 45.4 ± 12.3 years, the race was 50.7% Mulatto, 34.6% Black, 13.8% White and 0.9% Oriental. Transmission risk factors: 53.9% dental treatment, 48.8% shared sharp instruments, 47.5% had used non-disposable syringes, HBV familiar; 24.4%, 13.4% transfused blood before 1993, 8.3% have tattoo, 7.4% already had accident with blood/secretions. Biopsy underwent: 42.2%, Metavir score was: 65% F0-F2, F3:14.2% and F4: 3.8%. HBsAg: 94.6%, HBeAg: 9.4%, anti-HBe: 86.2% anti-HBs: 3. Metavir F4 in HBeAg+: 0% and in anti-HBe+: 2,7%. Non cirrhotic: 97,3% of all the patients, 2.7% were co-infected HBV/HCV of these 100% were anti-HBe, HBV/HTLV I/II was 2.3% of these 83% were anti-HBe+. Co-infection HBV/HIV+ was 1.9 %, of these 60% anti-HBe and 40% HBe+. It was studied the genotypes of 85 patients of the sample: A1 (84.71%) was the most prevalent followed by genotype A2 (5.88%), F (5.88%), and C1, D2 and D4 (1.18% each). Of these 85 patients with HBeAg+ status: 78,6% were genotype A1, and in Anti-HBe+ status: 87.5% genotype A1. The genotype pacientes co-infected HBV/HIV: 40% A2: 20% A1 (40% missing). **Conclusions.** The most of these patients were Blacks, with predominance genotype A1, showing the African immigration to Bahia, genotype F had a slow prevalence (it was related), another genotypes were circulating in this city, the most of patients were not cirrhotic and was prevalent the anti-HBe status in mono and co-infected patients with the 3 virus. In patients with co-infection HIV the genotype A2 was more prevalent, the genotype A1 was present HBeAg+ and anti-HBe+ patients.

033

PHARMACOKINETICS OF THE NEW NS3/4A HCV PROTEASE INHIBITOR SIMEPREVIR IN MEXICAN PATIENTS ENROLLED IN THE PHASE III QUEST-1 STUDY

L.E. MUÑOZ-ESPINOSA,[*] A.M. CONTRERAS,[†] J.F. SANCHEZ-AVILA,[‡] I. JACOBSON,[§] J. MÉNDEZ-NAVARRO,[||] A. BROCHOT,[¶] M. PEETERS,[¶] J. WITEK,[¶] S. OUWERKERK[¶6]

[*]*DEPARTMENT OF INTERNAL MEDICINE, LIVER UNIT, UNIVERSIDAD AUTÓNOMA DE NUEVO LEÓN, MONTERREY, NUEVO LEÓN, MÉXICO.*

[†]*DEPARTMENT OF PUBLIC HEALTH, UNIVERSITY CENTER OF HEALTH SCIENCES, UNIVERSIDAD DE GUADALAJARA, JALISCO, MÉXICO.*

[‡]*GASTROENTEROLOGY DEPARTMENT, INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN (INCMNSZ), MÉXICO, D.F., MÉXICO.*

[§]*WEILL CORNELL MEDICAL COLLEGE, NEW YORK, NEW YORK, USA.*

[||]*REGIONAL MEDICAL AFFAIRS (MAF) HEPATITIS, JANSSEN LATIN-AMERICA, MEXICO CITY, MEXICO.*

[¶]*JANSSEN RESEARCH AND DEVELOPMENT (R&D), BEERSE, BELGIUM.*

Background. The assessment of pharmacokinetics is very important in the development of new molecules. In subjects with chronic HCV infection, steady-state pharmacokinetics of simeprevir (TMC435) have been evaluated following monotherapy or in combination with pegylated interferon-alpha (PegIFNa) and ribavirin (RBV) at doses between 75 mg qd and 200 mg qd. In healthy volunteers and patients, higher exposures were observed in Japanese subjects compared to Caucasians. Phase III study QUEST-1 evaluated the efficacy, safety and pharmacokinetics of simeprevir 150mg once daily, combined with pegylated interferon and ribavirin in 394 naïve patients with hepatitis C genotype 1 from USA, Europe, Australia, Mexico and Puerto Rico. **Objective.** To describe the pharmacokinetic data of simeprevir in Mexican patients enrolled in the QUEST-1 study. **Material and methods.** Sparse blood sampling was performed in all subjects to determine individual steady-state pharmacokinetic parameters of simeprevir (apparent clearance [CL/F], area under the concentration-time curve [AUC], predose plasma concentration [C0h], and the average steady-state concentration [Css]) using Bayesian feedback. Pharmacokinetic analyses of simeprevir were performed using population pharmacokinetic modeling to determine population model parameters and individual estimates of simeprevir CL/F, AUC, and C0h. Descriptive statistics were reported for these pharmacokinetic parameters as well as by subgroups, such as race. **Results.** A total of 5.3% subjects (21/394) in Quest-1 study were enrolled in Mexico. Simeprevir pharmacokinetic parameters were available from a total of 13 patients from Mexico who were randomized to the simeprevir-containing arm. Demographic baseline characteristics of the 13 Mexican subjects were: female 5/male 8; ethnicity 13 (100%) were Hispanic or Latino with Spanish as their primary language and were born in the Mexican Republic; age mean 39.6 (11.7 SD); weight (kg) mean 72.3 (14.3 SD); BMI mean 26.1 (3.4 SD). The arithmetic mean exposure (expressed as AUC24h) was 44,462 ng*h/mL (SD 52,827) in the Mexican patients, and 54,795 ng*h/mL (SD 55,627) in the overall population. For simeprevir trough concentration, values were 1,421 ng/mL (SD 2,194) for the Mexican patients and 1,825 ng/mL (SD 2,306) for the overall population. Compared to non-Mexican patients it was observed that the mean, median and range of the AUC24h of simeprevir of Mexicans was within the median, mean and range of the rest of study patients. **Conclusions.** By taking into account the intersubject variability, we conclude that the plasma exposure of simeprevir in Mexican patients is similar to that observed in the general population enrolled in the QUEST-1 trial.

034

ASSOCIATION OF INOSINE TRIPHOSPHATASE (ITPA) POLYMORPHISMS WITH TREATMENT-INDUCED REDUCTION IN HEMOGLOBIN IN BRAZILIAN PATIENTS DURING HCV THERAPY AND ALLELIC DISTRIBUITION IN HEALTHY INDIVIDUALS

NATHÁLIA DELVAUX,[*] VANESSA DUARTE-DA-COSTA,[*] MARISTELLA MATOS DA COSTA,[*] ADILSON JOSÉ DE-ALMEIDA,[**] CARLOS EDUARDO BRANDÃO-MELLO,[**] CRISTIANE ALVES-VILLELA-NOGUEIRA,[***] HENRIQUE SÉRGIO MORAES-COELHO,[***] ELIANE ESBERARD,[****] PRISCILA POLLO-FLORES,[****] ELISABETH LAMPE[*]

[*]*LABORATORY OF VIRAL HEPATITIS, OSWALDO CRUZ INSTITUTE, FIOCRUZ, RJ, BRAZIL.*

[**]*DEPARTMENT OF HEMATOLOGY, UNIVERSITY HOSPITAL GAFFRÉE GUINLE (HUGG), FEDERAL UNIVERSITY OF THE STATE OF RIO DE JANEIRO (UNIRIO). BRAZIL*

[***]*DEPARTMENT OF HEPATOLOGY, UNIVERSITY HOSPITAL CLEMENTINO FRAGA FILHO (HUCFF), FEDERAL UNIVERSITY OF RIO DE JANEIRO (UFRJ). BRAZIL*

[****]*DEPARTMENT OF GASTROENTEROLOGY, UNIVERSITY HOSPITAL ANTÔNIO PEDRO (HUAP), FLUMINENSE FEDERAL UNIVERSITY (UFF). BRAZIL*

Background. Treatment of patients with chronic hepatitis C virus infection (HCV) is a major challenge both in terms of

clinical success and cost-effectiveness. Ribavirin-induced hemolytic anemia is the most important hematological adverse effects in treatment of hepatitis C. Recently, inosine triphosphatase (ITPA) gene variants associated with protection against ribavirin-induced anemia were identified. **Aim.** Evaluate the association of SNPs rs7270101 and rs1127354 in ITPA gene with treatment-induced reduction in hemoglobin (Hg) and to evaluate the distribution in general population, considering the scarcity of studies in Brazil. **Material and methods.** Real-time PCR (Roche) and direct nucleotide sequencing. **Results.** In healthy individuals (n = 100), the distribution of genotypes AA, AC, CC of SNP rs7270101 was 87, 11, and 2%, respectively; and in rs1127354 genotype CC was found in 93% and AC in 7%. In HCV infected patients (n = 200), genotypes AA, AC, CC of rs7270101 were seen in 82.5, 16.5, and 1.0%, respectively; as to rs1127354 genotype CC was seen in 95% and genotype AC in 5%. Among those who completed the treatment (n = 97), the mean pretreatment Hg was 13.98 ± 1.57 g/dL, but a progressive reduction in Hg levels was observed at weeks 4 (12.46 ± 1.56), 8 (11.00 ± 1.38), and 12 (10.65 ± 1.54) after treatment beginning. The prevalence of anemia at week 12 was 84.5% (82/97), of which 85.4% (70/82) had AA genotype in rs7270101 and 100% (81/82) had CC genotype in rs1127354. **Conclusions.** These results demonstrate that AA genotype of rs7270101 SNP was associated with reduced levels of Hb for antiviral therapy. A relatively high proportion of healthy and HCV infected individuals harbor the unfavorable genetic variants of rs7270101 and rs1127354 which could explain the high rates of ribavirin-induced anemia observed during treatment of HCV in Brazilian population.

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035

SAFETY AND EFFICACY OF TERAP C, A THERAPEUTIC DNA-BASED VACCINE PREPARATION FOR HEPATITIS C, IN A PHASE II CLINICAL TRIAL

Z. DORTA-GURIDI,* M.I. CASTELLANOS-FERNÁNDEZ,* Z. CINZA ESTÉVEZ,** S. DUEÑAS-CARRERA,** C. VALENZUELA-SILVA,** G. MARTÍNEZ,** L. ÁLVAREZ-LAJONCHERE,** Y. AMADOR-CAÑIZARES,** M. NÚÑEZ,*** E. ARÚS-SOLER*

*NATIONAL INSTITUTE OF GASTROENTEROLOGY. HAVANA. CUBA.
**GENETIC ENGINEERING AND BIOTECHNOLOGY CENTER. HAVANA. CUBA.
***HERMANOS AMEIJEIRAS HOSPITAL. HAVANA. CUBA.

Background. Hepatitis C virus (HCV) infection affects an estimated 170 million individuals worldwide. Although treatment options using a combination of pegylated interferon and ribavirin (IFN/RBV) are available, sustained virological response (SVR) is only achieved in approximately 40% of individuals infected with HCV genotype 1. A breakthrough in the treatment of HCV was achieved with the introduction of direct-acting antiviral agents, but they are very expensive and also associated with substantial side effects. Development of new treatment alternatives is advised. One possible modality could be specific immunotherapy. **Material and methods.** TERAP C is a therapeutic vaccine candidate based on the mixture of pIDKE2, a plasmid encoding HCV structural antigens, with a recombinant HCV core protein, Co.120. Phase II clinical trial was carried out evaluating TERAP C plus IFN/RBV in 92 treatment naive patients, genotype 1, in two hospitals (National Institute of Gastroenterology and Hermanos Amejeiras Hospital) in Havana. The trial included five groups: control arm (30 patients treated with IFN/RBV and vaccine placebo for 48 weeks) and four experimental arms. Arms 2 and 3 were assessed with 6 and 9 doses, respectively of TERAP C administered concomitantly with the treatment with IFN/RBV. Arms 4 and 5 were assessed with 6 and 9 doses, respectively of TERAP C, 12 weeks after the start of treatment with IFN/RBV. **Results.** All patients showed some adverse events. Most of the adverse events were considered to be not probably associated with the administration of TERAP C. Only 18 (8%) out of 3,615 adverse events, were considered to be probably associated with the administration of TERAP C. The most common adverse events (≥ 65%) observed were: local pain, headache, asthenia, psychiatric disturbances, fever, and gastrointestinal symptoms. Regarding SVR, 20% superiority was observed in the groups that received concomitant treatments from the beginning of the study, compared to those who started immunization after week 12. **Conclusions.** Vaccination with TERAP C in HCV chronically-infected individuals was safe and well tolerated.

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IL28B DISTRIBUTION IN PATIENTS INFECTED WITH HEPATITIS C VIRUS (HCV): RESPONSE TO THERAPY WITH PEGINTERFERON AND RIBAVIRIN

K. RODRIGUES-DO-Ó,* F.D'ALBUQUERQUE E. CASTRO,** B.C. BERTHOL,*** J.J. BARROS,**** P.C. FRANÇA***

*HOSPITAL SÃO LUCAS, PETRÓPOLIS, RJ, BRAZIL.
**HOSPITAL GERAL DE PALMAS, TOCANTINS, BRAZIL.
***UNIVERSIDADE DA REGIÃO DE JOINVILLE, SANTA CATARINA, BRAZIL.
****LABORATÓRIO DE VIROLOGIA MOLECULAR, INSTITUTO OSWALDO CRUZ, RIO DE JANEIRO, BRAZIL.

Background and aims. Infection with the hepatitis C (HCV) is a global public health problem that affects 140 million people worlwide and, of these 130 million are chronically infected. HCV causes chronic hepatitis that progresses to liver cirrhosis and hepatocellular carcinoma. Factors inherent to th virus, host and environment have been related to disease progression; recent polymorphism of the IL28B gene has been associated with virologic response to therapy with pegylated interferon and ribavirin. Th presence of CC alleles increases at twice the likehood of response to treatment with pegylatd interferon and ribavirin. The T-allele is known as risk and shows lower probability of response. **Material and methods.** A total of 30 patients were enrolled in this study; all patints underwent blood sampling and survey single nucleotide polymorphism (SNP)rs12979860 extraction technique for peripheral DNA. The polymorphism was genotyped by PCR using specific primers. **Results.** Most patients were women (70%) and the average age was 54 years. Distribution of IL28B: 23(76.6%) patients, genotype CT, 02(6.66%) patient TT genotype, and 05(16.6%) patients genotype CC. **Conclusions.** Our study confirms that there is a difference in the impact of the IL28B polymorphism among the various genotypes. Moreover, patients with TT allele advanced fibrosis and high viral load possibly benefit from new therapies such as protease inhibitors added to pegylated interferon and ribavirin. Pharmacoeconomic studies are needed to evaluate the influence of the IL28B gene in deciding the treatment of chronic hepatitis C. A limitation of our study is retrospective considering only patients who underwent planned treatment.

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NATURAL HISTORY OF NON-TREATED CHRONIC HEPATITIS C PATIENTS: OUR EXPERIENCE

A. CAPRETTI, M.T. TADDEI, G. FANELLI
SAN CARLO BORROMEO HOSPITAL, HEPATOLOGY SURGERY, MILAN, ITALY.

Background. Hepatitis C virus is leading cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma, as well as the most common indication for liver transplant. Although the factors involved in the development and progression to cirrhosis are incompletely understood, many studies have identified variables contributing to progressive liver disease: alcohol, HCV infection age, inflammation and fibrosis degree on liver biopsy, HIV and HBV coinfection, comorbid conditions. From January 2004 till January 2008 we visited in hepatology surgery about 600 chronic hepatitis C patients. 368 HCVRNA positive were observed by regular follow up without therapy for several reasons: age, comorbilities, patient will, normality of examinations. **Aim.** To see natural history of hepatitis C in never treated patiens and confirm contingently risk factors. **Material and methods.** 199 of no-treated patients were males (median age 68 ± 9), 169 females (median age 64 ± 11), 6 were HBsAg positive, 58 HBcAb positive, 61 had chronic alcohol abuse, 32 both (HbcAb + alcohol), 0 HIV positive. We performed a follow up with 6 months blood examination plus clinical inspections, and annual ultrasound exam, for at lowest five years. We monitored AST, ALT, alfafetoprotein, platelet count, albumin dosage. **Results.** 120/368 pts showed a worsening disease, while 248/368 were stable. 40/368 became cirrothic (11%), and 30/368 (8.1%) of them were HBcAb positive plus chronic alcohol abusing, 4/368 occurred HCC (3 of them were HBsAg positive). **Conclusions.** Our results indicate that the majority of adults have persistent viremia without clinically demonstrable liver disease. In our experience 66% of pts are stable, regardless by genotype, viremia level, gender, race, comorbility. Only 33% of non-treated pts had a worsenining of disease: in particular HBV coinfection, pregressive HBVinfection, alcohol abuse, older age, seems influence cirrhosis evolution (11%) and hepatocarcinoma (1.1%).

038

SINGLE NUCLEOTIDE POLYMORPHISM (SNP) OF INTERLEUKIN 28B rs12979860 FREQUENCE IN RIO DE JANEIRO AND LDL-CHOLESTEROL CORRELATION IN GENOTYPE-1 CHRONIC HEPATITIS C

P. POLLO-FLORES, D.L.S. CÁSSERES, LBZ GOULART, T. GUARANÁ, E.B.C. ESBERARD
FACULDADE DE MEDICINA, UNIVERSIDADE FEDERAL FLUMINENSE, RIO DE JANEIRO, BRAZIL.

Backgrounds. Predictive factors for sustained virological response (SVR) in hepatitis C (HCV) genotype 1 treatment are extensively studied. Low density lipoprotein-cholesterol (LDL-C) is a significant predictor of SVR for heterozygous IL 28B genotype patients and our study had the purpose of describe frequencies of single nucleotide polymorphisms(SNPs) near the interleukin 28B gene (chromosome 19) in genotype 1 hepatitis C virus patients in Rio de Janeiro and investigates the correlation with Low density lipoprotein (LDL) cholesterol. **Materials and methods.** Prospective study in patients with chronic hepatitis C genotype 1 infection. Inclusion criteria were polymerase chain reaction for hepatitis C virus quantification measured (COBAS Taqman assay, USA), genotype 1. Exclusion criteria were fibrosis F4 (METAVIR score) by liver biopsy, statin use in the last year. All patients signed the written informed consent and were submitted to blood sample tests. The single nucleotide polymorphism 12979860 (SNP) was studied by extraction DNA in periphery blood and was genotyped by specifics primers (PCR). The study met the local institutional review board and Helsinki's declaration review of 2000. **Results.** 53 patients had performed IL28B polymorphism rs 12979860 test and results showed: 7 patients were (13.2%) C/C, 22 (41.5%) C/T e 24 (45.3%) T/T. 76.8% (n = 46) in the C/T and T/T group. LDL-C results in 25 patients presented (n = 25): 16 (64%) LDL < 110 mg/dL (minimum: 44-maximum: 105) e 9 (36%) ≥ 110 (minimum: 117-maximum: 154). The Table represents the correlation between the LDL-C and Il 28B polymorphism rs 12979860. **Conclusion.** The results showed the TT genotype in polymorphism rs 12979860 more frequently than the others CT and CC. Consequently, these patients are in majority poor responders to the therapy with pegylated interferon /ribavirin. The lower LDL-C was more correlated with the CT and TT genotypes of Il 28B. LDL-C is a marker of HCV role in lipid metabolism, mediated by host mechanisms. In literature, the best performance for LDL-C like a predictor factor of SVR is in heterozygous genotype Il28B and understanding the interrelation of lipoproteins and viral kinetics may help to better individualize treatment in the future.

Table. (038)

LDL ILB28	C/C = 4	C/T = 6	T/T = 10
≥ 110	3	3	3
< 110	1	3	7

n = 20.

039

EVALUATION OF PEGYLATED INTERFERON (UNIPEG®) FOR RESPONSE AND SAFETY IN PAKISTANI POPULATION (EUROP)

G.U.N. TAYYAB,[*,†] Z.Y. HASHMI,[‡,§] W.U. AHMED,[‖,¶] A.M. SIDDIQUI,[**] A. MOHSIN,[††] F.S.K. BHATTI,[‡‡] M.S. QURESHI,[§§] M.A. ANWAR,[‡‡] W. UDDIN[‖‖,¶¶]
[*]MEDICINE & GI, LAHORE GENERAL HOSPITAL, PAKISTAN.
[†]POST GRADUATE MEDICAL INSTITUTE, LAHORE, PUNJAB, PAKISTAN.
[‡]LIVER CENTER DHQ HOSPITAL, FAISALABAD, PUNJAB, PAKISTAN.
[§]ALLIED HOSPITAL, FAISALABAD, PUNJAB, PAKISTAN.
[‖]PAKISTAN MEDICAL RESEARCH COUNCIL, KARACHI, SINDH, PAKISTAN.
[¶]JINNAH POST GRADUATE MEDICAL CENTER, KARACHI, SINDH, PAKISTAN.
[**]ALLAMA IQBAL MEDICAL COLLEGE & JINNAH HOSPITAL, LAHORE, PUNJAB, PAKISTAN.
[††]SERVICES HOSPITAL, LAHORE, PUNJAB, PAKISTAN.
[‡‡]PAEC GENERAL HOSPITAL, ISLAMABAD, PUNJAB, PAKISTAN.
[§§]KRL HOSPITAL, ISLAMABAD, PUNJAB, PAKISTAN.
[‖‖]POF HOSPITAL, WAH CANTT, PUNJAB, PAKISTAN.
[¶¶]WAH MEDICAL COLLEGE, RAWALPINDI, PUNJAB PAKISTAN.

Background. According to a conservative estimate from the last sero-survey of Pakistan, HCV prevalence was 7.8 million (4.9%). To assess efficacy and safety of pegylated interferon alfa-2a 180 μg 20 kDa (Unipeg®) in combination with Ribavirin (Ribazole®) for treatment of chronic hepatitis C infection in Pakistani population. **Material and methods.** Phase-IV, single-arm, open-label, multicentre study, 67 patients from major Pakistani cities included in study from 8/2010 to

9/2013. All were interferon naïve, anti-HCV antibodies positive and PCR HCV-RNA positive. Patients were treated with Pegylated Interferon alfa-2a 180 μg 20 kDa subcutaneous weekly and 800-1,200 mg ribavirin once daily with varying doses for 24/48 weeks depending on genotype and bodyweight. Virological responses were evaluated: rapid virological response (RVR) at week 4, end treatment response (ETR) at week 24 or 48 and sustained virological response (SVR) at 6 months after therapy completion. **Results.** A total of 67 patients were enrolled and there were 3 dropouts. Male:female ratio was 1.3:1 with mean age of 35.4 ± 9.5 (range: 19-62) years. Out of 64 patients, 60 (93.8%) were genotype-3 and 4 (6.2%) patients were genotype-1. RVR achieved in 48 (75%) & not achieved in 16 (25%) patients. ETR achieved in 56 (87.5%) & not achieved in 8 (12.5%) patients. One patient was lost to follow-up and fifty-five patients completed the 6 months follow-up; 48 (87.3%) patients achieved SVR and 7 (12.7%) patients relapsed at 24 weeks post-therapy. Only 10 (15.6%) patients experienced expected adverse events of non-serious nature. **Conclusion.** The results showed pegylated interferon alfa-2a 180 μg 20 kDa in combination with ribavirin in chronic HCV infection is clinically effective, well tolerated with minimal adverse events similar to those reported in literature.

040

S-ADENOSYL METHIONINE (SAM) DOWN-REGULATES HCV EXPRESSION BY MODULATING THE ENZYMATIC ANTIOXIDANT SYSTEMS

S.A. LOZANO-SEPÚLVEDA,* P. CORDERO-PÉREZ,** L.E. MUÑOZ-ESPINOSA,** A.M. RIVAS-ESTILLA*
*LABORATORIO DE INFECTOLOGÍA MOLECULAR, FACULTAD DE MEDICINA, UNIVERSIDAD AUTÓNOMA DE NUEVO LEÓN, MONTERREY, N.L., MÉXICO.
**UNIDAD DE HÍGADO DEL HOSPITAL JOSÉ ELEUTERIO GONZÁLEZ, MONTERREY, MÉXICO.

Background and aim. In previous reports we demonstrated that S-adenosyl methionine (SAM) decreases HCV viral expression, but involved mechanisms remain unknown. The aim of this study was to evaluate the mechanism(s) implicated in HCV down-regulation mediated by SAM and the role of enzymatic antioxidant systems such as superoxide dismutases; SOD1 and SOD2, catalase and thioredoxin1 enzymes using a hepatoma cell line expressing HCV non-structural proteins. **Material and methods.** HCV hepatoma cells were treated with SAM 1mM alone or in combination with standard treatment pegylated interferon alfa (PEG-IFNα, 1,000 IU) plus ribavirin (RBV, 50 μM) from 0-72 h. Upon each time, total RNA and proteins were extracted, cDNA was synthesized and qPCR was performed to quantify the HCV-RNA levels using a TaqMan probe and further GAPDH normalization. Cellular and viral proteins expression were evaluated by western blot using antibodies against NS5A (viral protein), SOD1, SOD2, catalase, thioredoxin and actin as control. Furthermore, reactive oxygen species (ROS) levels were measured using the dichlorofluorescein method. In addition, cells were treated with 1mM SAM plus H2O2 or pyrrolidine dithiocarbamate, in order to compare with positive controls for damage and antioxidant activity respectively. ROS levels were measured at 0.5, 1, 3, 12, 24 y 48 h after treatment by fluorescent spectroscopy. **Results.** HCV-RNA levels decreased 50% upon 24 h, in the presence of SAM alone compared with untreated control. In cells treated with combined therapy (SAM + PEG-IFNα + RBV), HCV-RNA levels decreased 90% compared to control at 24 h. NS5A protein levels decreased between 50-60% in presence of SAM at 24-48 h upon monotherapy and combined treatment compared with the control. Regarding antioxidant protein expression, SOD1 and thioredoxin 1 expression increased upon 24-48 h in combined treatment. In contrast, SOD2 protein expression decreased in all the times and treatments evaluated. Catalase expression levels were not modified at any treatment. Otherwise, ROS level did not showed any change in SAM-treated cells compared with untreated cells upon different times of exposition. **Conclusions.** SAM decreases HCV-RNA and NS5A expression levels upon exposition to monotherapy and combined with PEG-IFNα + RBV in HCV hepatoma cells. In parallel, antioxidant proteins SOD1, SOD2 and thioredoxin1 are differentially regulated by SAM, suggesting a possible involvement of the antioxidant systems in the mechanism of action of SAM. Nevertheless, this mechanism may not involve the modulation of ROS levels. Further experiments are required to investigate the modulation of antioxidant enzymes in replicon cells treated with SAM. No conflicts of interest between authors.

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041

GALLIC ACID, A NATURAL ANTIOXIDANT, PRESENT ANTIVIRAL EFFECT AGAINST HEPATITIS C VIRUS (HCV), WHICH IS MEDIATED BY ITS ANTIOXIDANT ACTIVITY

M. GOVEA-SALAS,* A.M. RIVAS-ESTILLA,** S.A. LOZANO-SEPÚLVEDA,** R. RODRÍGUEZ-HERRERA,* C.N. AGUILAR-GONZÁLEZ,* A. ZUGASTI-CRUZ,* S.Y. SILVA-BELMARES,* J.A. MORLETT-CHÁVEZ*
*FOOD RESEARCH DEPARTMENT, SCHOOL OF CHEMISTRY. UNIVERSIDAD AUTÓNOMA DE COAHUILA, SALTILLO, COAHUILA, MÉXICO.
**DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR MEDICINE, SCHOOL OF MEDICINE, UNIVERSIDAD AUTÓNOMA DE NUEVO LEÓN. MONTERREY, NUEVO LEÓN, MÉXICO.

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 whether GA has antiviral effect against hepatitis C virus (HCV) and further investigate the mechanism(s) involved in the regulation of HCV mediated by GA by using a cell system that expresses HCV-nonstructural proteins and the parental cell line. **Material and methods.** Huh7 HCV-replicon cells were exposed to 300iM GA at different times for 0 to 72 h, and then total RNA and protein were extracted. RT-qPCR was performed to quantify HCV-RNA using TaqMan probes and further RNA viral levels were normalized based on the ratio of HCV/GAPDH-RNA. Cellular and viral protein expression was evaluated by Western Blot using antibodies against HCV-NS5A and actin. We evaluated GA cytotoxicity at the concentrations between 100-1000 μM in cells in both cells lines by MTT assay. Reactive oxygen species (ROS) levels were measured at 0.5, 1, 3, 12, 24 y 48 h after treatment in total cellular extracts by DCF-HDA assay to determine oxidative stress modulation. Hydrogen peroxide (H_2O_2, 2 μM) was used as a negative control and Pyrrolidine dithiocarbamate (PDTC, 5 μM) as a positive control. All the experiments were performed in triplicate ($P < 0.05$). **Results.** We found that GA does not produce statistically significant cytotoxicity in the Huh7 replicon cell line, and it was able to

down-regulates NS5A-HCV protein expression (around 55% upon 48 h of treatment). Furthermore, GA negatively decreased virus replication (HCV-RNA) (nearly 50%) upon 48-72 h of treatment. In addition, we found that GA treatment decreased ROS production in the HCV subgenomic replicon cell system in the same way to the cells treated simultaneously with a potent antioxidant used as a control (PDTC). **Conclusions.** Our results suggest that GA treatment modulates at transcription and translation level the *in vitro* expression of HCV (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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042

PEGYLATED INTERFERON ALPHA 2A PLUS RIBAVIRIN FOR CHRONIC HEPATITIS C IN A REAL-LIFE SETTING: THE PRACTICE STUDY IN A TUNISIAN COHORT

RIADH BOUALI
HOPITAL MILITAIRE DE TUNIS, TUNISIA.

Aim. To document in real life the characteristics and management of hepatitis C patients treated with pegylated interferon alpha 2a and ribavirin. To determine the efficacy of treatment: sustained virological response (SVR). **Material and methods.** This observational study enrolled hepatitis C patients initiating pegylated interferon alpha 2a and ribavirin treatment (from March 2008 until June 2010). **Results.** A total of 933 patients were included: mean age = 52.4 yr; 39.5% were male; 91.3% were treatment-naive, 82.8% had genotype 1, 14.8% G2 and 2.4% G3 infection; 31.2% and 21.6% had respectively F4 and F3 Metavir score. In total, 6.3% received less than 80% of treatment and 8.5% prematurely stopped treatment, mainly because of side effects. The global SVR rate (intent-to-treat population) was 49.4%: 45.1% in G1 carriers, 73.2% in G2 and 50% in G3 carriers. Predictive factors of SVR for G1 were: fibrosis stage < F4 (OR:2.8), naive patient (OR:3.1), hemoglobin > 10 g/dL at week 4 (OR:3.1), more than 80% of treatment received (OR:4.5), no viremia detected at week 4 (OR:6.1) and week 12 (OR:8.6). **Conclusion.** In patients treated in a real-life setting, adherence to therapy, SVR rates, predictive factors of SVR and safety results were close to those observed in randomized trials. New treatments, more effective and safer, must be available in our country to reduce the non response rate in selected patients.

043

PREVALENCE OF OCCULT HEPATITIS C VIRUS INFECTION IN MEXICAN POPULATION AT THE BLOOD BANK OF CENTRO MÉDICO NACIONAL LA RAZA

M.L. MARTÍNEZ-RODRÍGUEZ, G.M. CALDERÓN-RODRÍGUEZ, E. PRIETO-TORRES, O. ARROYO-ARROYO, L.O. URIBE-NOGUEZ, V. JACQUES-FLORES, L.A. URIBE-NOGUEZ
UNIDAD DE INVESTIGACIÓN EN INMUNOLOGÍA E INFECTOLOGÍA. HOSPITAL DE INFECTOLOGÍA. CMN LA RAZA. IMSS, MEXICO CITY.

Introduction. The hepatitis C virus (HCV), affected more than 150 million people around the world. In 2004 Castillo, reported a new type of infection. The occult hepatitis C infection (OHCV), defined as the presence of HCV-RNA in liver and in peripheral blood mononuclear cells (PBMc), in the absence of detectable viral RNA in plasma by standard assay. **Objective.** Determine the prevalence of the OHCV in Mexican open population. **Materials and methods.** 499 participants were studied, we obtained 16 mL of total blood with EDTA, it was separated by centrifugation, the RNA viral was obtained using RNA Amp kit (QIAgene) and the total RNA from leukocyte package using the RNA easy kit (QIA gene). RT and two PCR rounds were using, occult hepatitis C virus infection was positive when the product of 214 pb corresponding to 5'UTR region was amplified only in leukocytes, indicate a OHCV. **Results.** We obtain of 499 subjects between 18 and 64 years old and average of 35 years which 62.1% (310) are male and 37.9% (189) are female, the prevalence of occult hepatitis C infection was 5% (25). The female had the highest prevalence of 5.8% (11) meanwhile male get 4.5%. **Conclusion.** The prevalence founded through the PCR nested studied in Mexican population is 5%, therefore is necessary introduced the RT-PCR test on leukocyte packages as a diagnostic method, to detect and prevent opportunely cases of infection of occult hepatitis C virus infection in blood donors.

044

EVALUATION OF THE ROLE OF ANTIOXIDANT SYSTEMS IN HUMAN HEPATOMA CELLS INFECTED WITH FULL-LENGTH HEPATITIS C VIRUS PARTICLES (HCV)

J.A. MERINO-MASCORRO,* S.A. LOZANO-SEPÚLVEDA,**
A.R. RINCON-SÁNCHEZ,** A.M. RIVAS-ESTILLA*
**DEPARTAMENTO DE BIOQUÍMICA Y MEDICINA MOLECULAR, FACULTAD DE MEDICINA, UNIVERSIDAD AUTÓNOMA DE NUEVO LEÓN, MONTERREY, N.L., MÉXICO.*
***CENTRO UNIVERSITARIO DE CIENCIAS DE LA SALUD, UNIVERSIDAD DE GUADALAJARA, GUADALAJARA, MÉXICO.*

Background. Oxidative stress and its regulation by cellular antioxidant enzyme systems have been reported to play an important role in HCV infection; however, the mechanisms involved remain unknown. **Aim.** We evaluated the role of cellular antioxidant enzymes as superoxide dismutase (SOD1), SOD2, catalase (CAT) and glutathione-peroxidase (GPx) on HCV expression in human hepatocarcinoma cells harboring expression of HCV full-length replicon. **Material and methods.** Huh7.5.1 cells were infected with full-length HCV-viral particles at different times. Total RNA and proteins were extracted at 24 to 72h, and then cellular antioxidant enzymes levels were detected by Western Blot and RT-qPCR. Specific TaqMan probes were used to detect viral and cellular RNAs. Relative HCV expression was calculated by $\Delta\Delta$Ct method, using housekeeping genes (actin and GAPDH). HCV replication was evaluated in simultaneously HCV-infected, transfected (pSOD1; 100-500ng) and knocked-down cells with siRNA against SOD1-mRNA using the SG-replicon system. **Results.** SOD1 and SOD2 protein levels decreased more than 50% at 72h in Huh7.5.1 cells harboring HCV-Full Length replicon (infected), while mRNAs levels remained unchanged, compared to naïve cells at the same times. In addition, GPx expression levels of infected cells decreased around 60% at 72 h, while CAT expression showed no changes at the same time. In SG-replicon cells with inhibition of SOD1 expression by siRNA, HCV-RNA levels decreased approximately 50% at 48 to 72 h compared to controls. In addition, HCV protein and mRNA levels (NS5A) were increased in cells over expressing

SOD1 (500 ng) compared with controls. **Conclusions.** The presence of HCV particles on infected cell modifies expression of SOD1 and GPx protein levels. Silencing of SOD1 enzyme leads to a decrease in HCV-RNA while SOD1 over-expression up-regulates HCV protein expression. Our results suggest that SOD1 may play a dual role in HCV replication and this is related with antioxidant systems modulation.
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045

PREVALENCE OF AUTOANTIBODIES IN CHRONIC HCV-INFECTED PATIENTS REVEALS A PATTERN OF ASMA, ANA AND LKM1 REACTIVITIES SIMILAR TO THAT FOUND IN PATIENTS WITH AUTOIMMUNE HEPATITIS TYPE 1

L.M. NAVARTA,* C.A. ESPUL,* V. RIVERO,** N. ACOSTA-RIVERO*
*LABORATORIO DE VIROLOGÍA, HOSPITAL CENTRAL, MENDOZA.
**CIBICI_CONICET. FAC. DE CIENCIAS QUÍMICAS. UNC. ARGENTINA.

Introduction. Chronic viral infections such as hepatitis C virus (HCV) and human immunodeficiency virus (HIV) have been recognized with the ability of breaking tolerance to self-antigens, promoting self-reactivity, extrahepatic manifestations and autoimmune diseases. Thus, studying the prevalence of autoantibodies in sera of patients with chronic viral infection is relevant not only to search for optimal treatment options and diagnosis but also to elucidate the mechanisms of viral infection-related autoimmune diseases induction. **Objectives.** We aimed to study the prevalence of autoantibodies in sera of patients chronically infected with HCV as compared to healthy individuals and HIV-infected patients. The relationship between the presence of autoantibodies and biochemical markers of hepatic damage and viral titers was also investigated. **Results.** HCV infection was associated with a high prevalence of autoantibodies (87.67%). Interestingly, prevalence of autoantibodies was higher in HCV+ than in HIV+ patients (87.67 *vs*. 74.36%; p = 0,043, z test to compare proportions), particularly for Rheumatoid Factor (RF) (75.34% *vs*. 53.85%, respectively). Total autoantibodies and RF prevalence were associated with the female gender in HCV-infected patients. Antibodies specific for RF, SMA, ANA and TGP were associated with HCV infection. On the other hand, HIV infection was associated with reactivity for RF, ASMA, ANA and ANCA-MPO antibodies. Similar viral titers and levels of serum hepatic enzymes were observed in HCV-infected patients with or not reactivity against autoantigens. **Conclusion.** The observed pattern of positive ASMA and ANA reactivity and negative LKM1 reactivity, might predict development of AIH type 1 in these HCV-infected patients. So, further studies are required to determine the role of HCV infection in this pathology.

046

EXPRESSION OF ADIPONECTIN RECEPTORS ADR1, ADR2 AND LEPTIN LEVELS DEPEND OF VIRAL GENOTYPE IN PATIENTS WITH HCV

A.R. RINCÓN-SÁNCHEZ,* M.A. RÍOS-GUERRA,**,*** P. CORDERO-PÉREZ,*** L.E. MUÑOZ-ESPINOSA,*** M.C. ISLAS-CARBAJAL,* A.M. RIVAS-ESTILLA**
*DEPARTMENT OF PHYSIOLOGY, CENTRO UNIVERSITARIO DE CIENCIAS DE LA SALUD (CUCS), UNIVERSIDAD DE GUADALAJARA, GUADALAJARA, JALISCO, MÉXICO.
**DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR MEDICINE, MÉXICO.
***LIVER UNIT, SCHOOL OF MEDICINE, UNIVERSIDAD AUTÓNOMA DE NUEVO LEÓN, MONTERREY, N.L. MÉXICO.

Background. In the pathophysiology of patients with HCV infection, adipokines such as adiponectin and leptin play a crucial role. Adiponectin (ADQ) plays a hepatoprotective and anti-inflammatory role and is involved in the repair of liver damage, but the function of leptin in hepatic fibrosis is less clear. Furthermore, leptin concentrations rise as liver function deteriorates. Moreover, it is unknown whether there is a relationship between HCV genotypes and the liver injury, insulin resistance and steatosis. **Aim.** To evaluate whether there is a differential expression of ADQ receptors and adipokines in peripheral blood of mononuclear cells (MNC) from patients with different genotypes of HCV treated with PEG-IFN-alpha+ribavirin, compared with other hepatopathies. **Material and methods.** We included three groups: 1) Patients with HCV infection (HCV) (n = 38, 14M and 24F). 2) Patients with other hepathopathies (n = 34, 13M and 21F), and 3) Healthy control group (n = 27, 10M and 17F). mRNA expression of ADQ, AdipoR1 and AdipoR2 were determined in MNC by RT-PCR and ADQ and Leptine plasma levels were measured by ELISA assay. **Results.** ADQ mRNA expression was not detected in MNC of all study groups. In contrast, ADQ serum levels correlated with age mainly in women. Interestingly, ADQ serum values were similar between different HCV genotypes analyzed. There was a positive correlation between BMI and ADQ levels in all HCV genotypes. The ADQ and leptin levels were higher in patients with HCV compared to the healthy group. Interestingly, Leptin levels were highest for genotype 1b, in both men and women. In contrast, only women with HCV genotype 1a/1b showed high levels of leptin. Differential mRNA expression was observed in the receptors AdipoR1 and AdipoR2, being higher for genotype 2b. **Conclusions.** There is a difference in AdipoR1 and AdipoR2 mRNA expression in patients with genotype 2b, and leptin levels in the genotype 1b. It is not yet clear, if these differences play a role in the development of liver damage in these genotypes. Larger population studies are needed to elucidate the molecular mechanisms that define the participation of these receptors and adipokines in the pathogenesis of HCV.
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047

EVALUATION OF PROGRESSION TO SIGNIFICANT LIVER FIBROSIS WITH NON-INVASIVE MARKERS IN PATIENTS WITH CHRONIC INFECTION WITH HEPATITIS C VIRUS WITHOUT RESPONSE TO ANTIVIRAL THERAPY

M. CASTILLO-BARRADAS, H.J. RUIZ-MORALES, J.J. GUERRERO-ANGUIANO, A. PÉREZ-MENDOZA, M.T. RIZO-ROBLES, F. LÓPEZ-FUERTE
HOSPITAL DE ESPECIALIDADES, CENTRO MÉDICO NACIONAL LA RAZA, IMSS, MEXICO CITY.

Introduction. The failure to achieve sustained virological response in patients with chronic infection with HCV treated with pegylated interferon and ribavirin, the high cost of triple therapy with protease inhibitors and evolution to significant liver fibrosis, cirrhosis and its complications make them mandatory the evaluation for progression to significant fibrosis or cirrhosis, one way to do this is through non-invasive methods included the Forns Index, APRI and FIB 4, these are accessible, not harmful and have been little explored in Mexican population. **Material and methods.** This was an observational, retrospective, transversal and descriptive study with patients from the gastroenterology service at the Hospital "Dr. Antonio Fraga Mouret" treated with pegylated interferon and ribavirin during January 2007 to February 2012 and did not respond (null response, partial response and breakthrough), we included patients older than 18 years, liver biopsy perform prior treatment, it was considered a period of 24 months after failure to treatment to perform analysis. **Results.** From the database were review 255 subsequent patients with HCV, there were 30 patients eligible, however, 19 were excluded because lack of liver biopsy prior treatment and when the indexes were performed with basal data were positive to fibrosis > F2. Eleven patients were included, 6 were male, the mean age was 39.1 years, the mean BMI was 26.2, 10 were genotype 1, 8 patients had F0 at pretreatment biopsy. The most frequent type of failure to treatment was partial response (6 patients), followed by breakthrough (4). From de 11 patients none developed significant fibrosis at 24 months after treatment failure. The median score 24 months after treatment failure for Forns was 4.3 (cutoff for < F2 6.19), for APRI score 0.39 (cutoff for < F2 1.5) and FIB-4 0.96 (cutoff for < F2 0.96). **Conclusions.** In this study, the eleven patients included none progressed to further degrees of fibrosis, there were no divergences in discrimination between non-invasive indexes, these are easy to perform and need information with wide accessibility. Taking in count our resources available we advocate for the routine use in the following of these patients.

048

TRIPLE THERAPY WITH PROTEASE INHIBITORS FOR GENOTYPE 1 HCV INFECTED PATIENTS: OUR EXPERIENCE

S. BLANCO-SAMPASCUAL, F. MENÉNDEZ-BLÁZQUEZ, P. RUIZ-EGUILUZ, A. BARANDA-MARTÍN, A.B. DÍAZ-ROCA, J. ORTUZAR-AMESTI, M. MILAGROS ALVAREZ-LAVÍN, M. BAUTISTA-HENRÍQUEZ, V.M. ORIVE-CURA
HOSPITAL UNIVERSITARIO BASURTO. BILBAO, VIZCAYA, ESPAÑA.

Introduction. Chronic HCV infection is one of the most frequent causes of hepatic cirrhosis and hepatocellular carcinoma in Spain. Treatment with Pegylated Interferon and Ribavirin does not achieve good response rates, especially in patients infected with genotype 1 virus. The advent of triple therapy with protease inhibitors (Telaprevir and Boceprevir) has got a significant increase of sustained viral response (SVR) in these patients. The aim of our study is to evaluate our experience with triple treatment in patients with chronic genotype 1 Hepatitis C infection. **Material and methods.** In our hospital, we have treated 42 patients (36 with telaprevir/6 with boceprevir), between September 2012 and May 2014. 28 of them have finished treatment, either by completion of the scheduled therapy or by discontinuation due to lack of efficacy or adverse events. Twelve patients are still on treatment and 2 were transplanted while on therapy and are lost to follow-up. We review the results of those 28 patients who have finished treatment. 19 (68%) are men and 9 (32%) women, with a median age of 52.5; 54% with genotype 1a and 46% with genotype 1b, and 75% of them had a pretreatment viral load more than 800000 UI/ml. With respect to fibrosis, 57% had cirrhosis, 32% F3 and 11% F2 and only 18% had IL 28B genoype CC; 11 (39%) were naïve and 17 (61%) had been previously treated (7 relapsers, 3 partial responders and 7 null responders). **Results.** Fifteen (54%) patients completed treatment, but 23 (46%) had to discontinue it, 6 (46%) due to severe adverse effects (SAE), 3 (23%) according to stopping rules (non effective treatment) and 4 (31%) because of viral break-through during therapy. Thirteen (87%) of 15 patients who completed treatment achieved a sustained virological response (SVR), and 2 (13%) relapsed. Of patients who achieved SVR 62% were genotype 1b. Four of 5 patients IL28B CC were cured in opposition to 9 of 23 non-CC. SVR was clearly superior in patients F2 and F3 (100/ 66%) in contrast with F4 patients (25%); no patient null-responder achieved a SVR (0/7) while it was 64% in naïve patients, 57% in relapsers and 67% in partial responders. Side effects were frequent, and severe in some cases, especially anemia and cutaneous manifestations. One cirrhotic patient decompensated and another had a neutrophil count of 0, but we had no cases of severe infections or death. **Conclusions.** In our series, 46% of patients who initiated therapy achieved SVR, but excluding patients who discontinued treatment due to severe adverse events (21%), SVR was 59%. This rate of discontinuation and SVR reflects well the characteristics of our patients, who are difficult-to-treat patients, most of them cirrhotic, g1a with high viral load. In this population it is a good SVR, clearly superior to standard therapy. Results achieved in non responders are extremely poor in our experience. Tolerance is not good, with a high discontinuation rate due to SAE, again in relation with the type of patients treated; because of economic reasons, in our community treatment is restricted to F3/F4 patients or anyF relapsers. Results will probably improve if we are allowed to treat patients with less severe infection.

049

DISTRIBUTION OF GENOTYPES OF HEPATITIS C VIRUS AMONG THE INSURED POPULATION OF PETRÓLEOS MEXICANOS, USING RT-PCR IN REAL TIME BY ANALYSIS OF DISOCIATION CURVES BY FRET PROBES

J.L. PÉREZ-HERNÁNDEZ, N.A. SALGADO-GALÍCIA, M.R. VEJA-MARTÍNEZ, A. LUPIAN-SÁNCHEZ A., R. ESPINOSA-LÓPEZ
HOSPITAL CENTRAL SUR DE ALTA ESPECIALIDAD PETRÓLEOS MEXICANOS, MEXICO CITY.

Introduction and objective. The hepatitis C virus has the characteristic of presenting a high tendency to mutation,

which has led to describe genotypes and subtypes of this virus, which show differences in the response to treatment. For this reason, it is important determine the HCV by reliable and quick tests in order to establish the type and time of antiviral treatment. Introduction of PCR methodologies in real time has allowed laboratories of clinical diagnosis to have specific, sensitive and quick tests, very useful in viral genotyping. Bullock, *et al*. described a methodology consisting in carrying out a reaction of reverse transcription and PCR in real time (RT-PCR) by an analysis of dissociation curves (melting curve) with only one set of FRET probes (fluorescent resonance energy transfer) that correlates well with INNO-Lipa and sequencing by DupliType. **Objective.** To determine the distribution of genotypes of HCV using RT-PCR in real time by analysis of dissociation curves. **Materials and methods.** It is an observational, across study, in patients infected with HCV, processed from June 2005 to April 2014 in the Unit of Molecular Biology in the Hospital Central Sur de Alta Especialidad de Petróleos Mexicanos. For the genotyping it was made a retrotranscription with hexamer primers with random sequences, the DNA was amplified by means of a first PCR in real time using primers NAF and NAR1 using SYBRGREEN for its detection, later, it was carried out a semi-nested reaction, using the primers NAF1 and NAR3, and FRET probes (the anchorage probe marked with FITC and the detection probe marked with LCRed640), and later an analysis of dissociation curves in order to determine the fusion temperatures, that allows to rule out the genotypes 1a/b, 2a/c, 2b, 3a and 3b/4. **Results.** 205 tests were carried out with the following findings: the gender distribution was 139 women (67.8%) and 66 men (32.1%), with 55.6 year average age (rank 16 to 83). Of those genotypes determined, 160 (78%) correspond to the type 1; 32 (15.6%) to type 2 and 7 (3.4%) to type 3. The rank of viral loads goes from 741 UI to 7,210,00 UI of RNA-HCV. **Conclusion.** This methodology proved to be faster than the automated methodology for genotyping by INNO-LIPA, and although it does not detect all the genotypes nor differentiates subtypes, it allows discriminate those clinically relevant (1, 2, 3 and 4). The highest percentage corresponded to genotype 1 as expected.

050

UTILITY OF S-ADENOSYL METHIONINE IN THE TREATMENT OF MEXICAN PATIENTS WITH CHRONIC HEPATITIS C. A CONTROLED PILOT ESSAY

L.E. MUÑOZ-ESPINOSA,* L.A. PEREZ-ARREDONDO,* S.A. LOZANO-GARZA,** R.F. MARTINEZ-MACIAS,* P. CORDERO-PEREZ,* A. RIVAS-ESTILLA**
**UNIDAD DE HÍGADO, FACULTAD DE MEDICINA, UANL, MONTERREY, NUEVO LEÓN, MÉXICO.*
***DEPARTAMENTO DE BIOQUÍMICA Y MEDICINA MOLECULAR, FACULTAD DE MEDICINA, UANL, MONTERREY, NUEVO LEÓN, MÉXICO.*

Introduction. The current therapy for genotype (GT) 1 hepatitis C virus (HCV) infection is peginterferon-α (PegIFN-α) and ribavirin (RBV) plus direct-acting antivirals since 2011, improving considerably sustained virological response (SVR) rates. Nevertheless, its use has been limited in our population because of the high costs. In vitro studies suggest that S-Adenosyl-Methionine (SAMe) could enhance PegIFN-α+RBV antiviral effect. Furthermore, few clinical studies have suggested that the addition of SAMe could improve the antiviral response in previously non-responder patients up to 39%. **Material and methods.** This is an ongoing pilot clinical trial that evaluates patients with chronic HCV infection. Sixteen patients have been included, 9 from experimental group and 7 from control group. Experimental group received SAMe 500mg bid for an induction period of 4 weeks, at the end of which PegIFN+RBV were added. Control group received pegIFN-α2 a or b + RBV according to internationally recommended doses. Fibrosis was determined by either liver biopsy or FibroTest®. Viral load was determined in both groups as follows: at baseline (post-induction period at experimental group) and at weeks 2, 4, 8, 12, 24 and 48. Qualitative HCV PCR was determined 24 weeks after the end of treatment. **Results.** Genotype distribution: experimental group (GT1 = 7, GT = 2), control group (GT1 = 7). Currently, 8 patients have finished antiviral treatment in the experimental group: 2 had SVR, 1 relapsed, whereas 1 patient with end-of-treatment response is at week 65 of follow-up. The last 4 patients stopped antiviral treatment at week 24, 3 of them due to null response and 1 because partial response. All patients in control group reached week 72 of follow-up: 4 have SVR (57%) and 3 with treatment failure (2 relapses and 1 breakthrough). **Conclusions.** PegIFN-α+RBV+SAMe scheme has not shown superiority over PegIFN-α+RBV therapy so far. However, this is a pilot study and addition of more patients is guaranteed.

051

GENETIC VARIATION IN THE INTERLEUKIN-28B AND ITS ASSOCIATION WITH FIBROSIS STAGE IN PATIENTS WITH CHRONIC HEPATITIS C GENOTYPE 1

M. CASTILLO-BARRADAS, E.J. RUBALCABA-MACÍAS, J.J. GUERRERO-ANGUIANO, H.J. RUIZ-MORALES, A. PÉREZ-MENDOZA
HOSPITAL DE ESPECIALIDADES, CENTRO MÉDICO NACIONAL LA RAZA, IMSS, MÉXICO, D.F.

Background. Infection with hepatitis C virus (HCV) affects an estimated 180 million people globally. Is well established the main predictors of success on treatment wich are genotype HCV, Interleukin-28B and fibrosis stage. The natural history of chronic HCV infection is quite virable. Has been proposed the IL28B as predictor of hepatic fibrosis in patients with chronic HCV infection. **Objective.** Establish the association between genetic variation in IL28B and the stage of hepatic fibrosis in patients with chronic HCV infection. **Material and methods.** Retrospective study. Inclusion criteria comprise age 18 years or more, HCV RNA serum positive, diagnostic liver biopsy before antiviral treatment, genotype 1, with IL28B determination, between January 2004 and May 2013. Statystical analysis was calculated using frecuencies, percentagees, medians and ranges. In order to compare groups we used Pearson test and Logistic regression. **Results.** A total of 40 patients with chronic HCV infection were included in this study. Wich were 28 (70%) females, 12 (30%) males, the mean age was 50 years (IQR 44-57); median time of infection was 26 years (IQR 18 a 30). Regarding rs8099917 polymorfism, there was no difference between genotype and fibrosis stage (p = 0.835). Regarding rs 12979860, despite there was differen betwen genotypes and hepatic fibrosis stage, it was not statystically significant (p = 0.916). **Conclusions.** IL28B genotype was not associated with fibrosis stage in chronic HCV infected patients.

052

ACETILSALYCILIC ACID (ASA) DECREASES TRANSLATION RATES OF STRUCTURAL AND NONSTRUCTURAL PROTEINS GENERATED BY NEW HCV PARTICLES FROM HEPATOMA INFECTED CELLS

J.A. MERINO-MASCORRO,* C. FILLEBEEN,** A.R. RINCON-SÁNCHEZ,*** K. PANTOPOULOS,** A.M. RIVAS-ESTILLA*
*DEPARTAMENTO DE BIOQUÍMICA Y MEDICINA MOLECULAR, FACULTAD DE MEDICINA, UNIVERSIDAD AUTÓNOMA DE NUEVO LEÓN, MONTERREY, N.L., MÉXICO.
**LADY DAVIS INSTITUTE, MCGILL UNIVERSITY, CANADA.
***CENTRO UNIVERSITARIO DE CIENCIAS DE LA SALUD, UNIVERSIDAD DE GUADALAJARA, GUADALAJARA, MÉXICO.

Background. We have previously reported that in vitro, ASA treatment decrease HCV-RNA and protein expression levels in subgenomic (SG) replicon system (Huh7 HCV-replicon cells). Now the closest viral infection system useful to evaluate and study the HCV-pathogenic mechanisms is the full-length HCV replicon system, because it involves generation of complete viral particles capable of infecting naïve hepatocyes. **Aim.** We evaluated whether ASA is able to modify translation rates of viral proteins upon infection of hepatocytes (Huh7.5.1) with HCV full-length viral particles and further exposure to ASA at different times of new viral particles generation. **Material and methods.** Huh7.5.1-cells were transfected with HCV-JFH1 RNA, and then cells were cultured post-transfection for 15-30 days. Infective supernatant and total protein from transfected cells were collected at different times to detect HCV protein expression, and then this supernatant was used to infect naïve cells. Generation of new viral particles was evaluated and quantified during several days post-infection (0-15 days) to standardize experimental conditions. Upon new infections were confirmed, HCV-infected cells were treated with ASA at different concentrations (1mM-4mM), viability was measured by MTT assay and HCV expression was detected by Western Blot at 0-72h. GAPDH was used as housekeeping gene to normalize results. **Results.** Cells transfected with HCV-JFH1 RNA were able to produce high expression levels of new viral particles expressing structural (Core) and non-structural (NS3) viral proteins. Furthermore, supernatant from these cells were able to infect naïve cells. Huh7.5.1 infected cells treated with ASA 4mM showed decreased translational rates of HCV-NS3 protein levels (2-3 fold times) through a time course (24-72h). Decrease in translational rate was more dramatic for HCV-Core protein showing a decrease from 2 to up 200 fold times through the same time course (24-72 h), compared with non treated cells. Cell viability was decreasing with the time according ASA concentrations was increasing (from 1-4 mM). **Conclusions.** Full-length HCV infection system provides a tool for analyze HCV complete viral cycle and studying new alternative therapies in cell culture expressing complete HCV particles. ASA showed an antiviral effect in Huh7.5.1 HCV FL-replicon system, decreasing both, structural proteins (core) and Non-Structural proteins (NS3) in infected cells. There was a differential sensitivity of structural and non-structural proteins to ASA exposure, perhaps due to differences in its processing and function in viral cycle.

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053

THE EFFECTIVENESS OF PEGYLATED ALPHA 2B INTERFERON AND RIBAVIRIN TREATMENT OF CHRONIC VIRAL HEPATITIS C IN CHILDREN IN MOLDOVA

T. RABA, V. DUMBRAVA, IU. LUPASCO
STATE UNIVERSITY OF MEDICINE AND PHARMACY NICOLAE TESTEMITANU CHISINAU, REPUBLIC OF MOLDOVA.

Introduction. The standard combination antiviral therapy with PEG-IFN and ribavirin in children with chronic hepatitis C (CHC) leads to a sustained virological response and is comparable to the results in adults. Aim of this work was to present the effectiveness of PEG IFN alpha 2b and ribavirin in chronic hepatitis C in children in Moldova. **Materials and methods.** Twenty-eight patients of 3-18 years of age were treated using antiviral therapy with PEG IFN α2b, 1.5 mcg/ week plus ribavirin 15 mg/kg/day during 2011-2012 y. Duration of therapy was determined by the virus C genotype: 24 weeks (genotype 3a and 2) and 48 weeks (genotype 1b). Screening survey involved the classical scheme of clinical examination, determination of ARN VHC Real Time, IL28B, elastometry fibrosis assessment, blind liver biopsy. Viremia was determined at 3, 6, 9, 12 month of treatment and 6 months after discontinuation of therapy. **Results.** Vertical transmission of viral infection C was found in 11 (39%) of 28, 8 (29%) children with previous history of parenteral interventions, in 3 (11%) cases - blood transfusion, in 2 patients (7%) - dental procedures, in 4 (14%) cases route of infection could not be established. Genotype 1b was detected In 24 (86%) children, genotype 2 (4%) - in one case and genotype 3a – in 3 (11%) patients. In 12 patients was identified fibrosis F1, in 4 - F2, in 8 - F0-F1. 17 children (61%) had viral load above 600,000 Iu/ml. 17 (61%) children with CHC presented cytolysis. The expected positive virologic response with negative ARN VHC was noted in 15 patients (53.7%) of 28 children with chronic hepatitis C: in 1 patient with genotype 2, in 3 - with genotype 3a (100%), in 11 patients with genotype 1b (45%). 5 (20.8 %) of 24 patients with genotype 1b had partial virologic response with a decrease of viremia, and 1 (4.2%) child had relaps at 11 months of combined AVT. **Conclusions.** Standard combination antiviral therapy with PEG-IFN alpha-2b and ribavirin in children with chronic hepatitis C is effective and leads to a sustained virological response in 53.7% of cases. Among children with genotype 1b sustained virological response was observed in 45%, and in 20.8% of patients was achieved a partial virologic response.

054

PRELIMINARY RESULTS OF VHC GENOTYPE IN CHILDREN WITH CHRONIC VIRAL HEPATITIS C IN MOLDOVA

T. RABA, V. DUMBRAVA, IU. LUPASCO
STATE UNIVERSITY OF MEDICINE AND PHARMACY NICOLAE TESTEMITANU CHISINAU, REPUBLIC OF MOLDOVA.

Background. The genotype of viral C influence on the severity of chronic infection and virologic response to combination antiviral therapy (AVT). It has epidemiological significance, as the baby can be infected by several genotypes of VHC, which may affect the expected response of AVT. Genotype 1b has a direct relationship with nosocomial VHC infec-

tion, most often during the transfusion of blood and its compounds, while 3a and 1a - with parenteral administration of narcotic drugs. Aim of this work was to study the genotype structure in children with chronic hepatitis C in Moldova. **Materials and methods.** The genotype VHC has been investigated in 32 children with chronic hepatitis C, hospitalized in the period 2011-2013y. Genotyping VHC was evaluated using CORBETT RESEARCH ROTOR Gene 6,000 and diagnostic kits Amplisens equipment. **Results.** Age of surveyed children was 1.5 - 18 years, mean age – 12,7 years. 9 of 32 children were girls and 23 boys. Genotyping of surveyed patients revealed the prevalence of genotype 1b in 29 (90,6 %) cases, genotype 2 - in 1 (3%), genotype 3a - in 2 (6.3%) children. Vertical route of infection VHC was found in 21 (65.6%) of 32 born from mothers suffered from chronic hepatitis C genotype 1b - 19 children, genotype 2 - 1 , genotype 3a - 1. Parenteral route of transmission was established in 2 cases, blood transfusions and its components in 4 (genotype 3a – 2, genotype 1b -2), repeated operation of skin transplantation and reconstructive postburn surgery (genotype 1b -2), heart surgery (genotype 1b - 1), and in one case the route of infection could not be established. Genotype 1b predominated: boys (21 of 23) and girls (8 of 9), and in 2 cases was identified genotype 3a in boys, in 1 case - Genotype 2 in girls. **Conclusions.** The obtained results showed that in Moldova among children with chronic viral hepatitis C genotype 1b predominates in 90.6% of cases. The main route of VHC transmission in children is a vertical path established in 65.6 % of children born from viremic VHC mothers. Considering the effect of genotype 1b on a chronic VHC process and its high resistance to classic antiviral drugs, the results may be used to implement epidemiological surveillance, antiviral therapy and expected virological response in children with chronic hepatitis C.

055

USEFULNESS OF SALIVA SAMPLES FOR HBSAG AND ANTI-HCV DETECTION AMONG ALCOHOLIC PATIENTS

VANESSA FARIA-CORTES,* HELENA MEDINA-CRUZ,** MARJORIE PARRA-DE-LIMA,** ELISÂNGELA FERREIRA-SILVA,** JULIANA CUSTÓDIO-MIGUEL,** ELISABETH LAMPE,** LIVIA MELO-VILLAR

*CELULAR BIOCHEMISTRY LABORATORY, FEDERAL UNIVERSITY OF SÃO JOÃO DEL REI, MINAS GERAIS-BRAZIL.

**VIRAL HEPATITIS LABORATORY, OSWALDO CRUZ INSTITUTE, FIOCRUZ, RIO DE JANEIRO-BRAZIL.

Introduction. Hepatitis B and C virus diagnosis is made using serum samples, however blood sample collection is difficult among individuals with poor venous access, such as, drug users. **Aim.** The aim of this study is to evaluate the usefulness of saliva samples for HBsAg and anti-HCV detection among alcoholic patients using a modified commercial enzyme imunoassay (EIA). **Material and methods.** In this study, 46 individuals referred to chemically dependent treatment units from Southeast Brazil were included. All individuals presented alcoholic history that was identified by the questionnaire Alcohol, Smoking and Substance Involvement Screening Test (ASSIST). Blood samples were collected by venipuncture in tubes without anticoagulant and processed to obtain the serum. Saliva samples were obtained with the aid of the commercial collector Salivette (Sarsted, Germany). Serum and saliva samples were tested for HBsAg and anti-HCV using commercial EIAs (HBsAg One, Radim and Murex HCV Ab, Diasorin) following manufacturer´s instructions for sera samples. For anti-HCV detection among saliva, sample volume was nine fold increased compared to serum sample. For HBsAg detection among saliva, the same protocol recommended for serum was followed. ROC curve analysis was employed to define cut off (CO) value for both assays using saliva, where reactive samples for anti-HCV should presented an optical density (OD) value higher than 0.068) and for HBsAg, reactive samples should presented an OD value higher than 0.024). **Results.** All individuals included in this study were male with mean age (± standard deviation) of 33.5 ± 11.5 years. All sera and saliva samples were HBsAg non reactive giving 100% of specificity. One individual presented anti-HCV in paired sera and saliva giving 100% of sensitivity and among 45 anti-HCV non reactive serum samples, 42 were also negative at saliva samples giving 93.3% of specificity. **Conclusions.** This study shows the potential of saliva samples for HBsAg and anti-HCV detection among alcoholic patients using optimized EIAs what could increase the access of diagnosis in this population.

056

EVALUATION OF IGFBP-3 AND IGFBP-7 IN PATIENTS WITH CHRONIC HEPATITIS C ACCORDING THE FIBROSIS GRADE

D. ROSIQUE-ORAMAS,* D. LECHUGA,* Z. MEDINA-AVILA,* L. VERY-PINEDA,* C. GUZMÁN,* F. ARAGÓN-VALVERDE,* M. GALICIA-MORENO,* D. FALCON-CARRILLO,* Y. BEJAR,*** J. CHAVÉZ-MAYOR,*** P. CORDERO-PÉREZ,** L.E. MUÑOZ-ESPINOSA,** E. MONTALVO,*** D. KERSHENOBICH,*,**** G. GUTIERREZ-REYES*

*LABORATORIO HÍGADO PÁNCREAS Y MOTILIDAD. UNIVERSIDAD NACIONAL AUTÓNOMA DE MÉXICO, MEXICO.

**HOSPITAL UNIVERSITARIO. UNIVERSIDAD AUTÓNOMA DE NUEVO LEÓN, MÉXICO.

***HOSPITAL GENERAL DE MÉXICO, MÉXICO.

****INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN DR. SALVADOR ZUBIRÁN, MÉXICO.

Introduction. Hepatic fibrosis and cirrhosis are characterized by excessive extracellular matrix attributable to hepatic stellate cell (HSC). Hepatic fibrosis is also a common response to viral hepatitis. The IGF-binding proteins (IGFBP) modulate insulin growth factor (IGF)-1 activity, IGF-1 is produced by HSC (Willem Boers, *et al*. 2006) and IGFBP-7 is highly expressed in these cells, whereas a smaller induction is seen for IGFBP-3, but is responsible for binding of 70-90% of all circulating IGF-1 (Inge Mannaerts, *et al*. 2013). **Objective.** Evaluation of IGFBP-3 and IGFBP-7 levels in patients with chronic hepatitis C according to the grade of fibrosis. **Material and methods.** Blood samples were obtained from 47 patients with chronic hepatitis C (CHC) with Fibrotest score and 104 participants without CHC were included as a control group, and informed consent was obtained from all participants. IGFBP-3 and 7 levels were evaluated by Luminex (Biorad) technology. One-way ANOVA plus orthogonal analysis was used to determine the differences between in the groups. **Conclusions.** Studies in human liver tissue demonstrated that IGFBPs were associated with liver fibrosis. Our study showed differences between patients and control group in IGFBP 3 decrease and 7 increase levels and according to liver fibrosis. Levels of these proteins in patients with chronic hepatitis C, suggesting it could be used than biomarkers of this pathology. This work was supported in part by PROMEP-SEP.

057

DIFFERENCES IN HCV GENOTYPE DISTRIBUTION AND RISK FACTORS IN TWO GEOGRAPHICAL REGIONS OF MEXICO

L.E. MUÑOZ-ESPINOSA,* R.F. MARTÍNEZ-MACÍAS,* A.M. RIVAS-ESTILLA,** M.E. TRUJILLO-TRUJILLO,*** R. TORRES-VALADEZ,*** A.L. SILVERA-LINARES,* P. CORDERO-PÉREZ,* A. PANDURO,*** E. MARTÍNEZ-LÓPEZ,*** S.M. ROMÁN-MALDONADO***

**LIVER UNIT AND **DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR MEDICINE HOSPITAL UNIVERSITARIO DR. JOSÉ E. GONZÁLEZ, UANL, MONTERREY, NUEVO LEÓN, MÉXICO.*

****MOLECULAR BIOLOGY LABORATORY SERVICE, HOSPITAL CIVIL DE GUADALAJARA, U DE G, GUADALAJARA, JALISCO, MÉXICO.*

Introduction. Mexico has scarce information regarding the evolution of HCV genotype (GT) distribution, risk factors (RF) and prevalence over time. In this study, we assessed HCV-GT and RF through age groups among patients from Center-West (CW) and Northeast (NE) Mexico. **Material and methods.** Three-hundred and thirty-three patients with confirmed chronic hepatitis C (CHC) seen between 1987 and 2013 (NE n = 117; CW n = 153) were included in this retrospective, cross-sectional study. Baseline features collected were: demographics, date of medical interview, RF for HCV infection, HCV viral load, HCV-GT, cirrhosis status and antiviral treatment exposure. Patients with HIV and HBV were excluded. Spearman correlation test was used to detect variables prevalence trends according to date of birth (DOB). **Results.** We found that mean age was 48 ± 13 (4-76), relation between males/females was 123/207. The variables prevalence by age group shows in Table. Noteworthy, there were very few GT4 patients (n = 2) therefore, they were not analyzed. **Conclusions.** These results suggest that prevalence of GT3, male sex, IV drugs use, sexual promiscuity and tattoos increased as younger were the patients. Contrariwise prevalence of GT1b, female sex, blood transfusions and surgeries were increased while increasing age. Treatment rate did not increase among youths, and there was a high prevalence of cirrhosis in this study, mainly at an earlier DOB.

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Table. (057)

Variables	1930-1944 N = 35 (100 %)	1945-1959 N = 145 (100 %)	1960-1974 n = 95 (100 %)	≥ 1975 n = 55 (100 %)	r	p
Males	7 (20)	36 (25)	45 (47)	35 (64)	-0.31	<0.001
GT1	29 (83)	103 (71)	67 (71)	36 (65)	0.08	0.149
GT1a	14 (40)	54 (37)	44 (46)	26 (47)	0.07	0.182
GT1b	29 (83)	103 (71)	67 (71)	36 (65)	0.08	0.149
GT2	5 (14)	31 (21)	12 (13)	6 (11)	0.08	0.173
GT3	1 (3)	11 (8)	15 (16)	12 (21)	-0.18	0.001
Surgeries	20 (57)	94 (65)	50 (53)	19 (35)	0.18	0.001
Blood transfusion	26 (74)	101 (70)	43 (45)	15 (27)	0.34	<0.001
Sexual promiscuity	1 (3)	12 (8)	21 (22)	15 (27)	-0.24	<0.001
Tattoing	5 (14)	15 (10)	17 (18)	22 (40)	-0.21	<0.001
IV drugs	0	11 (8)	13 (14)	9 (31)	-0.29	<0.001
Cirrhosis	22 (62)	67 (46)	35 (36)	13 (24)	0.21	<0.001
Antiviral theraphy	13 (37)	64 (44)	38 (40)	16 (29)	0.06	0.228

058

INTERFERON-BASED THERAPY DELAYS BUT METABOLIC COMORBIDITY ACCELERATES CHRONIC HEPATITIS C PROGRESSION: LONG-TERM FOLLOW-UP OF MEXICAN PATIENTS

R.F. MARTÍNEZ-MACÍAS,* P. CORDERO-PÉREZ,* O.A. JUÁREZ-RODRÍGUEZ,* C.Y. CHEN-LÓPEZ,** FM MARTÍNEZ-CARRILLO,* G ALARCÓN-GALVÁN,** R. MERCADO-HERNÁNDEZ,*** L.E. MUÑOZ-ESPINOSA*

**UNIVERSITY HOSPITAL, LIVER UNIT, UANL, MONTERREY, NUEVO LEÓN, MÉXICO.*
***UNIVERSITY HOSPITAL, PATHOLOGY SERVICE, UANL. MONTERREY, NUEVO LEÓN, MÉXICO.*
****INFORMATICS DEPARTMENT, UANL SCHOOL OF BIOLOGY. MONTERREY, NUEVO LEÓN, MÉXICO.*

Introduction. Once hepatitis C virus (HCV)-related cirrhosis has developed, the annual incidence of hepatic decompensation (HepD), death or liver transplantation (LT), and hepatocellular carcinoma (HCC) among untreated (noRxG) patients or non-responders to antiviral therapy (NRs) with chronic hepatitis C (CHC) is ~4%, ~3%, and ~3% per year, respectively. However, there is scarce information on long-term follow-up in treated Mexican patients with CHC. In this study, we compared mortality and complications of CHC between treated and noRxG Mexican patients after long-term follow-up. We used a time-to-event analysis and identified the prognostic factors. **Material and methods.** Seventy-four patients with CHC were retrospectively followed-up for a median of 83 (6-195) months. They were ≥18 years of age and had a molecular diagnosis of CHC and ≥ 6 months of follow-up. Patients with neoplasia or those infected with HIV or HBV were excluded. Main baseline features: females (60%), median age 49 (18-76), treated (50%), cirrhotics (51%), diabetics (19%), high blood pressure (HBP, 19%), APRI ≥ 1.5 and MELD ≥ 18 in cirrhotics (63%, 5%, respectively). Kaplan-Meier analysis, log-rank test, annualized incidence per 100 person-years (p100py), and stepwise discriminant analysis (SDA) were used to analyze mortality and complications after the end of follow-up. Complications occurrences were sough on subgroups free from them at baseline (non-cirrhotics n = 36; cirrhotics n = 38: portal hypertension [PH] n = 19, HepD/HCC n = 28).

Results. The end-point of annualized incidence was lowest in sustained virological responders (4.4 to 11.1 times less than in the noRxG), intermediate in NRs (1.3 to 4.2 times less than noRxG) and highest among the noRxG (0.3-46.2 p100py). The absence of treatment impacted adversely on cirrhosis development, the occurrence of PH and HepD/HCC (log-rank, $p < 0.05$). Diabetes impacted adversely on liver-related death (LRD)/LT among noRxG (log-rank, $p < 0.05$). SDA showed that diabetes, HBP, and no retreatment predicted cirrhosis development (eigenvalue ≥ 0.8; $p < 0.05$). A MELD ≥ 18 and age ≥ 50 years predicted HepD/HCC (eigenvalue < 0.8; $p < 0.05$). APRI ≥ 1.5 predicted mortality/LT and LRD/LT (eigenvalue < 0.8; $p < 0.05$). **Conclusions.** This is the first long-term study of CHC among Mexican patients. We found that interferon-based therapy beneficially affected mortality/LT and HCV-related complications among Mexican patients with CHC after a long-term follow-up. The prognostic factors were metabolic comorbidities and no retreatment for cirrhosis development; APRI ≥ 1.5 for mortality/LT and LRD/LT; and older age and MELD ≥ 18 for DAGTP/HCC. DM was confirmed to impact adversely on LRD/LT in noRxG.

This study received no funding.

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VITAMIN D DEFICIENCY IS RELATED TO DEMOGRAPHIC AND LABORATORY FINDINGS AMONG CHRONIC HEPATITIS C VIRUS PATIENTS

LIVIA MELO-VILLAR,* ELISABETH-LAMPE,* ADILSON JOSÉ DE-ALMEIDA,* LIA LAURA LEWIS-XIMENEZ,* JULIANA CUSTÓDIO-MIGUEL,* LETICIA DE PAULA SCALIONI,* GABRIELA CARDOSO CALDAS,* NATHALIA DELVAUX,* JOSÉ ANTONIO DEL-CAMPO,** ISIDORA RANCHAL,** CRISTIANE ALVES VILLELA-NOGUEIRA,*** MANUEL ROMERO-GOMEZ**

*VIRAL HEPATITIS LABORATORY, FIOCRUZ, RIO DE JANEIRO, BRAZIL.
**UNIT FOR THE CLINICAL MANAGEMENT OF DIGESTIVE DISEASES AND CIBEREHD, HOSPITAL UNIVERSITARIO DE VALME, SEVILLE, SPAIN.
***HEPATOLOGY UNIT, CLEMENTINO AND FRAGA FILHO HOSPITAL, FEDERAL UNIVERSITY OF RIO DE JANEIRO, UFRJ, RIO DE JANEIRO, BRAZIL.

Introduction. The relationship between serum 25-hydroxy-vitamin D [25(OH)D] levels and laboratory data and response to antiviral therapy in HCV infection remains unclear. This work aims to determine pre-treatment serum 25(OH)D levels among Brazilian HCV-infected individuals and to evaluate the association between vitamin D status and laboratory and virological response data. **Material and methods.** Baseline serum 25(OH)D levels were measured in 237 chronic HCV infected patients (139 female, age 53.7 ± 11.2 years) using chemiluminescence immunoassay. Correlations between serum 25(OH)D levels, virological and laboratory data regarding HCV infection as well as sustained virological response (SVR) were evaluated. **Results.** Mean serum values of 25(OH)D was 26.2 ± 12 ng/mL and prevalence of vitamin D deficiency (< 30 ng/mL) was 66.2%. Advanced age (> 55 years), high mean values of LDL, total cholesterol, and HDL as well as low mean values of alkaline phospatase and hemoglobin were statistically related to vitamin D deficiency. One hundred and thirty three (56.0%) HCV patients underwent antiviral treatment and 44.3% of them achieved SVR. Most of individuals that presented SVR also presented 25(OH)D levels higher than 30 ng/mL (55.9%). SVR was related to lower mean values of LDL, total cholesterol, and platelets; higher mean values of ALT, AST, and lower fibrosis grade. No association between 25(OH)D status and SVR was found. **Conclusions.** A high prevalence of vitamin D deficiency was observed among Brazilian HCV infected patients and was related to advanced age and a number of laboratory findings. Pre-treatment serum 25(OH)D levels was not related to SVR.

060

IL28B POLYMORPHISMS ASOCIATED WITH THE RESPONSE TO PEG IFN AND RIBAVIRIN TREATMENT IN HEPATITIS C GENOTYPE 1 PERUVIAN PATIENTS

C. MORI-TORRES,* C. GARCÍA-DELGADO,* J. CABRERA-VALENTIN**

*SERVICIO DE GASTROENTEROLOGÍA, **UNIDAD DE CUIDADOS INTENSIVOS, HOSPITAL ALBERTO SABOGAL SOLOGUREN, CALLAO, PERÚ.

Objective. Study in a Peruvian population effects of polymorphism rs12979860 IL28B CC, CT and TT in response to PEG IFN and ribavirin treatment in patients infected with hepatitis C genotype 1 virus. **Material and methods.** The clinical records of patients diagnosed with chronic hepatitis C infection treated at the Department of Gastroenterology Alberto Sabogal Hospital, between 2010 and 2013, who received pegylated-interferon alpha 2a (PEGASYS Roche) 180 mcg subcutaneously once a week plus ribavirin (COPEGUS Roche) 1,000 mg/day if weight less than 75 kg and 1,200 mg/day if weight more than 75 kg for 24 to 48 weeks was analyzed. **Results.** The rate of the genotypes of IL28B rs12979860 polymorphism was CC: 18.8%, CT: 65.6% and TT: 15.6%; of patients with IL28B polymorphism CC 66.7% achieved a sustained virological response (SVR) compared with 38.5% with CC and TT genotypes. In multivariable logistic regression model, IL28B polymorphism CC predicted SVR and it had OR = 0.34 (IC95% 0.35-3.37). **Conclusions.** IL28B polymorphism CC was associated with a greater likelihood of sustained virological response in patients infected with genotype 1 VHC treated with PEG IFN plus ribavirin.

061

DISEASE BURDEN OF CHRONIC HEPATITIS C VIRUS (HCV) INFECTION IN BRAZIL

P.R.A. FERREIRA,* C.E. BRANDÃO-MELLO,† C. ESTES,‡ F.L. GONÇALES-JÚNIOR,§ H.S.M. COELHO,† H. RAZAVI,‡ H. CHEINQUER,|| M.L.G. FERRAZ,* M.G. PESSÔA,¶ M.C. MENDES-CORREA**

*FEDERAL UNIVERSITY OF SÃO PAULO, SÃO PAULO, BRAZIL.
†FEDERAL UNIVERSITY OF THE STATE OF RIO DE JANEIRO, RIO DE JANEIRO, BRAZIL.
‡CENTER FOR DISEASE ANALYSIS (CDA), LOUISVILLE, CO, U.S.A.
§UNIVERSIDADE ESTADUAL DE CAMPINAS, UNICAMP, SÃO PAULO, BRAZIL.
||HOSPITAL DAS CLÍNICAS DA UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, PORTO ALEGRE, BRAZIL.
¶UNIVERSITY OF SÃO PAULO SCHOOL OF MEDICINE, SÃO PAULO, BRAZIL.

Background. HCV infection is a major cause of cirrhosis, liver cancer, and liver-related deaths. To quantify the burden of HCV-related morbidity and mortality in Brazil, a modeling approach was used to examine disease progression. **Material and methods.** The infected population and associated disease progression in Brazil were modeled using 36 age- and gender-defined cohorts to track HCV incidence, prevalence, hepatic complications, and mortality. Baseline assumptions and transition probabilities were extracted from the literature. The impacts of two scenarios on HCV-related disease burden were considered: 1) Increased sustained virologic response (SVR), and 2) Increased treatment and SVR. **Results.** Under the base case, 12,000 new HCV infections occurred in Brazil in 2013. The viremic prevalence is estimated to have peaked in

1996 (2,282,100 individuals), declining 15% to 1,930,800 by 2013. In 2013, it is estimated that over 70% of the infected population was born between 1950 and 1975. By 2030, the infected population was projected to decrease to 1,205,500 individuals, a 38% decrease from 2013. Cases of compensated cirrhosis are projected to peak at 345,700 cases in 2027, a 57% increase from 2013, while decompensated cirrhosis cases will peak in 2030 at 47,500 cases, an 83% increase. Under Scenario 1, SVR and treatment eligibility increased to 90% and 95% (among 15-74 years with a fibrosis score ≥ F1) in 2017. Compared to the base case, there was a 4% reduction in prevalent cases, and a 5% reduction in liver-related deaths by 2030. Cases of liver cancer and decompensated cirrhosis decreased 5% and 6%, respectively, as compared to the base case in 2030. Under Scenario 2, the same increases in SVR and treatment eligibility were modeled, with gradual increases in the annual treated population through 2025 when 118,800 cases were treated as compared to 11,740 treated cases in 2013. Compared to the base case, this scenario decreased prevalent infections by 1,059,000 (88%) and decreased liver-related deaths by 83,200 (73%) by 2030. HCV-related liver cancer cases decreased by 73%, and decompensated cirrhosis decreased by 80%. By 2030, viremic prevalence of HCV decreased below 0.1%. **Conclusions.** While the prevalence of HCV in Brazil is decreasing, cases of advanced liver disease and liver-related deaths continue to rise. A scenario that considered increases in SVR and treatment had a much larger impact than the scenario which considered increased SVR alone. The projected impact of the scenarios will facilitate disease forecasting, resource planning, and rational strategies for HCV management in Brazil.

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PREVALENCE OF ANEMIA IN HEPATITIS C PATIENTS TREATED WITH TRIPLE THERAPY IN AN OUTPATIENT CLINIC REFERENCE IN HEPATOLOGY IN SALVADOR (BAHIA, BRAZIL)

S. MACEDO-BELMONTE,[*] A. REZENDE-GOMES,[*] V.L. MENEZES-JESUS,[*] V. SOUZA-VILANOVA,[*] M.I. MAGALHÃES-SANTOS,[***] V. SANTOS-SILVA,[*] T. REQUIÃO-ROCHA,[*] R. PARANÁ,[*,***] M.I. SCHINONI[**,***]

[*]FACULDADE DE MEDICINA, UNIVERSIDADE FEDERAL DA BAHIA, SALVADOR,BRAZIL.
[**]INSTITUTO DE CIÊNCIAS DA SAÚDE, UNIVERSIDADE FEDERAL DA BAHIA, SALVADOR, BRAZIL.
[***]AMBULATÓRIO MAGALHÃES NETO, HUPES-UFBA, SALVADOR, BRAZIL.

Introduction. The Adverse effects of dual therapy (peginterferon and ribaviriva) as anemia have intensified with the use of protease inhibitors (telaprevir and boceprevir) in the treatment of Hepatitis C (HCV), and result in low adherence to treatment. **Objective.** To evaluate the levels of hemoglobin Hb and serum creatinine in weeks 0.4 and 12 of the treatment and the rapid virological response in HCV patients treated with triple therapy (protease inhibitors) in an outpatient referral in hepatology in Bahia, Brazil. **Material and methods.** Descriptive cross-sectional study. The analysis was with mean, standard deviation and frequency. **Results.** Total 35 patients, 34.3 % female, race: 25.9 % white, 14.8 % black and 59.3 browns. Stage of fibrosis cirrhotic: 35.7 % and not cirrhotic 64.3 of the patients studied, 80.6 % used Telaprevir and 19.4 % Boceprevir. Group TelaprevirHb average week 0: 14.2 + 1.10, Week 4: 11.9 + 1.27 and week 12: 10.7 + 1.86 and Creatinine average week 0: 0.9 + 0.11 at week 4: 1.03 + 0.11 and 1.2 + week 12 12:12. Boceprevir group (started in week 4), HB average week 0 was 14.4 + 2.74, week 4: 12.8 + 2.21 and week 12: 10.3 + 1.33, creatinine media: Week 0 0.9 + 0.11, week 4: 1.03 + 0.11 and 1.2 + week 12 00:12. Cirrhotic patients (35.7%): average viral load (CV) at week 0 6.99 + 7.01 log it week 4: log 6.27 + log 6.58 and log 0.HB week 12 week average 0: 14.0 + 1.17, 11.3 + week 4 and week 12 1.16 11.0 + 1.38 Creatinine media: week 0: 0.9 + 0.20 at week 4 of 1 01 + 0.07 and + 1.2 at week 12 12:14. Patients without cirrhosis (64.3%) CV average week 0: 7.35 + 7.66 log, week 4 4.19 + 4.72 log, week 12 1.58 + 2.10 log average HB in week 0: 14.0 + 1.56, 12.2 + week 4 and week 12 1.55 10.3 + 1.86. Creatinine average: week 0 0.8 + 0.07, 0.96 + week 4 0.19 and week 12: 1.0 + 0.19. Among cirrhotic patients, 8 had CV in week 4. **Conclusion.** These preliminary data from an ongoing cohort study showed that there was no difference between the group of patients with hepatic cirrhosis and without cirrhosis in basal levels of hemoglobin and creatinine. Levels of HB had a similar drop during treatment in these 2 groups as well as in telaprevir and boceprevir group. The Creatinine showed slightly increase during treatment in cirrhotic patients as expected. These events were mild without necessity to suspend the drug and awaiting results of SVR.

063

THE PORTAL HEMODYNAMICS IN PATIENTS WITH CHRONIC HEPATITIS C, IN ASSOCIATION WITH HEPATIC STEATOSIS

G. HAREA, IU. LUPASCO, V. DUMBRAVA, E. KIRVAS, I. ROMANCIUC

STATE UNIVERSITY OF MEDICINE AND PHARMACY NICOLAE TESTEMITANU CHISINAU, REPUBLIC OF MOLDOVA.

Introduction. Hepatic steatosis, along with alcohol consumption, co-infections, is a known unfavorable factor of chronic hepatitis C (CH) progression. The more rapidly develops fibrosis the earlier appears portal hypertension. **Aim.** To study the portal hemodynamic's changes in patients with CH C in association with hepatic steatosis. **Material and methods.** 111 patients with CH C were investigated, 56 (50.45%)- with steatosis and 55 (49.55%)- without steatosis. The control group served 30 practical healthy individuals. Abdominal ultrasound was performed, with duplex Doppler of the portal system; with evaluation of diameter, velocities and blood flow volume of the portal, splenic and superior mesenteric veins, the hepatic and splenic arteries, as well as pulsatility and resistance indexes in these arteries. **Results.** In patients with CH C and steatosis was found the bigger size of liver caudate lobe (37.18 ± 1.63 mm) in comparison to patients without fatty liver (31.44 ± 1.78 mm, $p < 0.05$). The blood flow velocity in portal vein (10.96 ± 0.47 cm/s) and the volume of blood flow in portal vein (1,248.66 ± 47.63 mL/min) in patients with CH C with steatosis were lower than in patients without steatosis (13.11 ± 0.80 cm/s, 1,398.05 ± 54, 24 mL/min; $p < 0.05$). In women with concomitant steatosis, were observed significant changes in arterial blood flow: flow velocity in hepatic (90.27 ± 3.18 cm/s) and splenic arteries (93.18 ± 8.7 cm/s) was higher than in the comparison group (77.58 ± 4.70 cm/s, $\delta < 0.05$ and 69.89 ± 2.73 cm/s; $\delta < 0.05$ respectively), pulsatility index in hepatic (1.58 ± 0.09) and splenic arteries (1.19 ± 0,10) also was higher than in the group without steatosis (1.18 ± 0.1; $\delta < 0.01$ and 0.85 ± 0.04; $\delta < 0.01$, respectively). **Conclusions.** The presence of hepatic steatosis in patients with CH C has a negative impact on portal hemodynamics.

064

PREVALENCE OF IgG AND IgM ANTIBODIES TO HEPATITIS E VIRUS (HEV) AND HEV RNA IN HIV-INFECTED PATIENTS

A.C. FERREIRA,* M.S. GOMES-GOUVÊA,* M.C.J. MENDES-CORREA,**,*** C. PICONE,*** J.R.R. PINHO*

*LABORATORY OF GASTROENTEROLOGY AND HEPATOLOGY, SÃO PAULO INSTITUTE OF TROPICAL MEDICINE AND DEPARTMENT OF GASTROENTEROLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF SÃO PAULO, BRAZIL.

**DEPARTMENT OF INFECTIOUS DISEASES, UNIVERSITY OF SÃO PAULO MEDICAL SCHOOL, SÃO PAULO, BRAZIL.

***HIV/AIDS OUTPATIENT CLINIC, CLINICAS HOSPITAL, SCHOOL OF MEDICINE, SÃO PAULO UNIVERSITY, SÃO PAULO, BRAZIL.

Introduction. HEV infection is recognized as a significant public health problem in different world regions. Although characterized as benign infection with a self-limited course, there are increasing data showing its evolution to chronicity and liver cirrhosis in immunocompromised individuals. There are no data regarding prevalence of HEV infections in HIV-infected patients in Brazil, where the circulation of this virus has been demonstrated in different groups of immunocompetent individuals. Moreover, HEV infection among pigs has been identified in different regions of the country. **Aim.** To evaluate the frequency of anti-HEV IgG and IgM antibodies and HEV RNA among HIV-infected patients followed up in São Paulo, Brazil. **Materials and methods.** Serum and plasma of HIV-infected patients (n = 359) followed at "Casa da AIDS-São Paulo-Brazil" were included in this study. These samples were collected between 2007 and 2013. Anti HEV IgG and IgM were detected by ELISA using RecomWell kit (Mikrogen, Dusseldorf, Germany). Some of these results were confirmed by IMMUNOBLOT using kit RecomBlot (Mikrogen, Dusseldorf, Germany). Two hundred forty two samples were also tested to HEV RNA by a One-Step Real Time PCR assay targeting a fragment of ORF 3. **Results.** Anti-HEV IgG were detected in 39 (10.9%) of the 359 patients and Anti-HEV IgM in 6 (1.7%) but only two of these IgM positive was concomitantly positive to IgG. HEV RNA was detected in only one of the 216 HIV-positive patients tested. **Conclusions.** In Brazil the prevalence of anti-HEV antibodies is higher than that previously found in immunocompetent individuals, as has been found in some countries in Europe. However, in our country additional studies are needed to determine if it is due differences in the sensitivity of ELISA tests utilized in the different studies. No case of current or chronic HEV infection was detected in this study.

065

AUTOANTIBODY FREQUENCES IN PATIENTS WITH HEPATITIS DELTA IN THE BRAZILIAN AMAZON: PILOT STUDY

B. MATTOS-CAVALCANTE,* C.M. OLIVEIRA-LOBATO,** A. STOECKER,* M.I. SCHINONI,* R. PARANÁ*

*UNIVERSITY FEDERAL OF THE BAHIA, SALVADOR-BAHIA. BRAZIL.

**UNIVERSITY FEDERAL OF THE ACRE, RIO BRANCO-ACRE. BRAZIL.

Introduction. The chronic hepatitis D virus (HDV) infection is currently a global health problem that affects 18 million people worldwide. In South America, This infection has been associated with large splenomegaly when compared with splenomegaly observed in liver cirrhosis of other hepatic etiologies, regardless the portal hypertention. Since the 80s the hepatitis delta virus has been associated with autoimmune phenomena, especially with anti-LKM-3 antibody, however, these studies were conducted in other populations of patients, mostly genotype 1, with different genetic profiles found in the Brazilian population. Due to the prior history of autoimmunity phenomenon associated with hepatitis delta virus, this study aimed to evaluate the presence of nonspecific autoantibodies in patients with delta hepatitis, genotype 3 in the Brazilian Amazon. **Materials and methods.** A total of 38 patients, 23 patients HDV-positive and 15 HBsAg-positive, were screened from the HUPES Gastrohepatology Service database associated with the Service "Serviço Especializado do Acre (SAE)". **Results.** The sample was composed of 38 subjects, 71% of which were males. In HDV positive group the average age was 39.8 ± 12.7 years and in AgHBs-positive group the average age was 44 ± 13 years. In both groups not found positivity rate for ANA, anti-smooth muscle, anti-mitochondrial and anti-LKM. Splenomegaly was observed in 20% of AgHBs-positive group and 52% in HDV-positive group. **Conclusion.** These findings indicate that there seems to be a higher frequency of non-specific autoantibodies (ANA, anti-smooth muscle, anti-mitochondrial and anti-LKM) in the studied population of carriers of hepatitis D virus in the Brazilian Amazon. Moreover, this study confirms the higher prevalence of splenomegaly among patients HBV/HDV compared to monoinfected with HBV, a fact that deserves further discussion of its pathogenesis in future work.

066

ANTIVIRAL TREATMENT FOR HEPATITIS D INFECTION: A SYSTEMATIC LITERATURE REVIEW WITH META-ANALYSIS

R. PARANÁ,* J.M. VILLALOBOS-SALCEDO,** M. PEZZOTO-LAURITO***

*MEDICINE SCHOOL OF FEDERAL UNIVERSITY OF BAHIA, GASTRO-HEPATOLOGY UNIT OF HOSPITAL UNIVERSITY. BAHIA, BRAZIL.

**FEDERAL UNIVERSITY OF RONDONIA; FIOCRUZ-RONDONIA.

***BRISTOL-MYERS SQUIBB S.A, BRAZIL.

Background/aims. Hepatitis D virus (HDV) replication and its association with hepatitis B virus (HBV) make this disease a difficult target for antiviral therapy. This study aims to evaluate the efficacy of therapeutic regimes offered to HDV patients with a systematic literature review and meta-analysis. **Material and methods.** Electronic searches were performed using the terms "hepatitis D" and "therapy" until June 2013. Outcomes of interest were sustained virological response (SVR) and biochemical responses. **Results.** Meta-analysis was estimated using Dersimonian and Laird's method and involved 533 infected patients included in 18 studies, treated with interferon (IFN), pegylated interferon (PEG-IFN), ribavirine (RBV), lamivudine (LAM), famciclovir and entecavir. Seven studies evaluated IFN treatment and virological and biochemical response rate were 50% (CI 95%: 0.38-0.63) and 41% (CI 95%: 0.31-0.51), respectively, at the end of treatment. PEG-IFN treatment, analyzed in 5 articles, demonstrated virological response rate of 30% (CI 95%: 0.19-0.40) and biochemical response of 32% (CI 95%: 0.17-0.47). Therapy with LAM was evaluated among six studies and the combined virological and biochemical responses rate were 25% (CI 95%: 0.03-0.47) and 49% (CI 95%: 0.26-0.72), respectively. At the end of follow-up, SVR or combined responses do not achieve a satisfactory efficacy rate in most of the studies, regardless the type of treatment. It was not possible to perform combined analysis of therapeutic responses for adefovir dipivoxil, RBV,

famciclovir and entecavir. **Conclusions.** There is not enough evidence in literature to establish precise guidelines for treatment of HDV infection, therefore additional randomized trials with high scientific quality are needed.

067

SYSTEMATIC REVIEW OF HEPATITIS DELTA EPIDEMIOLOGY IN BRAZIL

R. PARANÁ,* J.M. VILLALOBOS-SALCEDO,** M. PEZZOTO LAURITO***
*MEDICINE SCHOOL OF FEDERAL UNIVERSITY OF BAHIA, GASTRO-HEPATOLOGY UNIT OF HOSPITAL UNIVERSITY. BAHIA, BRAZIL.
**FEDERAL UNIVERSITY OF RONDONIA; FIOCRUZ-RONDONIA.
***BRISTOL-MYERS SQUIBB S.A., BRAZIL.

Background/aim. Hepatitis delta virus (HDV) is a defective RNA viral, which can lead to severe forms of acute or chronic liver diseases. In Brazil, is endemic in Brazilian Amazonia, but has been reported in other parts of the country. Their genotypes are geographically distributed and may influence the natural history of the disease. The aim of this study was evaluate the HDV epidemiology, natural history and genotype distribution in Brazil. **Material and methods.** A systematic literature review was conducted by June 2013 through electronic databases. Brazilian data of HDV epidemiology and clinical features were selected. Results: In Brazil, HDV infection occurs mainly in the Amazon Basin region. Among subjects from Labrea rural population and from western part of Acre state, HDV prevalence can reach 13.5% among HBsAg carriers. Among Indians living in Amazonas state communities, subjects from Labrea´s area and/or riverine communities of Acre and Purus rivers, HDV prevalence (HBV carriers) were 13.4, 41.9 and 66.6%, respectively. Other HDV genotypes than HDV-3 were reported. HDV-3 was found in all western Amazonia; HDV-1 in large Amazonian cities, but not in remote areas; and HDV-8, to date considered restricted to Africa, was also recently described in Brazil (Maranhão state). HDV-3 appears to be the most aggressive genotype and is often associated with a peculiar and severe acute hepatitis. In Amazonia, the fulminant hepatitis outbreak has been associated with HDV-3. **Conclusions.** HDV is endemic in specifics Brazilian regions, with mainly HDV-3 genotype, which seems to be associated with fulminant hepatitis.

068

PREVALENCE OF HEPATITIS E VIRUS ANTIBODIES IN PATIENTS WITH CHRONIC HEPATITIS C AT A TERTIARY CENTER IN SÃO PAULO, BRAZIL

S.K. FANTINI, M.S. GOMES-GOUVÊA, D.F. MAZO, A.C. FERREIRA, F.J. CARRILHO, J.R. PINHO, M.G. PESSÔA
UNIVERSITY OF SÃO PAULO SCHOOL OF MEDICINE, BRAZIL.

Introduction. The prevalence of serum IgG anti-hepatitis E (HEV) antibodies in the Brazilian general population varies from 0 to 7.5% in different regions. In addition, in selected high risk groups for viral diseases, this prevalence can be as high as 38%. However, the presence of serum IgG anti-HEV antibodies in patients with chronic hepatitis C virus (HCV) infection in our region is not known as yet. **Objectives.** To investigate the prevalence of serum IgG and IgM anti-HEV antibodies among patients with chronic HCV infection, naïve to interferon treatment. **Material and methods.** Samples from 90 adult patients with chronic HCV (51F/39M) were collected between January and November 2013 after informed consent and tested for the presence of IgG and Igm antibodies by enzyme immunoassay (ELISA) tests (recomWell HEV IgG and IgM, Mikrogen, Neuried, Germany). **Results.** Anti-HEV IgG antibodies were positive in 11 (12.2%) among the 90 serum samples of chronic HCV patients examined. Only one (9.1%) of the 11 anti-HEV IgG reactive samples also showed positivity to anti-HEV IgM. The mean age of our whole population was 51.7 years compared to 57.4 years on the 11 HEV IgG positive patients. The mean ALT levels of the 11 anti-HEV IgG positive was 66.1 U/L (range from 20 to 228). The mean ALT levels in patients without any serological marker of HEV infection was 65.3 U/L (ranging from 11 to 221). **Conclusions.** Our findings suggest that the prevalence of HEV in HCV patients is higher than it was previously described in the general population in Brazil and warrants further investigation in this group of patients in order to establish possible interactions on HCV disease severity.

069

BUDD-CHIARI'S SYNDROME SECONDARY TO A DEFICIENCY OF S PROTEIN

MARISOL GÁLVEZ-MARTÍNEZ,* ILCE BELINDA LÁZARO-PACHECO,* XAIRA RIVERA-GUTIÉRREZ,** EDUARDO PÉREZ-TORREZ*
*HOSPITAL GENERAL DE MÉXICO, CIUDAD DE MÉXICO, MÉXICO.
**FACULTAD DE MEDICINA. UNIVERSIDAD DE VERACRUZ, MÉXICO.

Introduction. Budd-Chiari's syndrome affects 1 in 2.5 million people annually, commonly women in the third or fourth decade of life and 87% of cases have an inherited or acquired prothrombotic risk factor. Myeloproliferative disorders are the most common cause, followed by rare causes as paroxysmal nocturnal hemoglobinuria, antiphospholipid syndrome and deficiency of S and C protein in 3% of the cases, 10% of all the cases are idiopathic. Clinically there may be a fulminate, acute, subacute or chronic evolution, depending on the extent and rapidity of occlusion of the hepatic veins, all characterized by abdominal pain, hepatomegaly and ascites. While nausea, vomiting, jaundice and encephalopathy are more frequent in fulminant and acute forms, splenomegaly and gastroesophageal varices are presented in chronic forms. USG Doopler, abdominal CT and hepatic venography are used for diagnosis. Treatment consists of medical therapy with thrombolysis, surgical or endovascular therapy, depending on the case. **Case report.** A 41 years old female without previous history of diseases, presents with 1 month of evolution of intermittent generalized cramped abdominal pain, with intensity score of 8 out of 10, associated with progressive increase of waist circumference and 5 kg of weight. On admission with generalized pallor and painless 2 cm below costal margin hepatomegaly with dullness in flanks. In the initial laboratory findings were with hemoglobin 11 g/dL, platelet count 180,000/uL, albumin 3.4 g/dL, alanine aminotransferase 77 U/L, aspartate aminotransferase 64 U/L, total bilirubin 1.2 mg/dL, alkaline

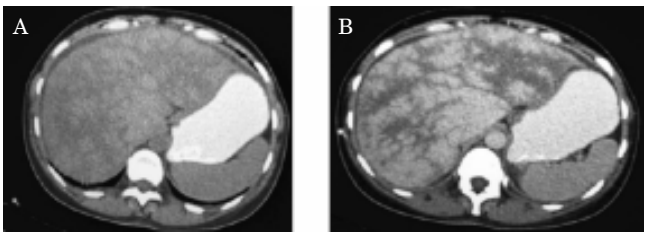

Figure 1. (069) CT scan.

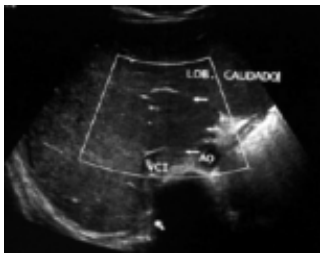

Figure 2. (069) USG Doppler.

phosphatase 70 U/L, glutamyltransferase 40 U/L, ascites fluid total protein 2, GASA 1.9, upper digestive endoscopy was negative for esophageal varices, abdominal CT scan showed hepatic congestion, supra hepatic vein thrombosis and free fluid in cavity (Figure 1). USG Doppler confirms absence of stream above the hepatic veins, hepatomegaly, and hypertrophy of caudate lobe, transjugular venography with "spider pattern" (Figure 2). Positive thrombophilia profile for protein S deficiency. Patient was discharged with oral anticoagulant therapy. **Conclusions.** Budd-Chiari's syndrome is a rare disorder and its diagnosis is a clinical challenge that should be considered in any patient presenting acute or chronic liver disease, a large scale of patients have at least one prothrombotic risk factor, survival rate at 5 years is close to 80% with proper treatment ranging from anticoagulation, angioplasty, TIPS and finally liver transplantation depending on the clinical presentation. Currently the TIPS have replaced surgical shunts and has become the most common invasive therapeutic method.

070

IMPACT OF NITAZOXANIDE ON SUSTAINED VIROLOGIC RESPONSE (SVR) IN EGYPTIAN PATIENTS WITH CHRONIC HEPATITIS C GENOTYPE 4: A DOUBLE BLIND PLACEBO-CONTROLLED TRIAL

MOHAMED KOHLA,* HALA EL-SAID,** ASHRAF EL-FERT,** NERMINE EHSAN,*** SAMEERA EZZAT,**** HOSSAM TAHA*
*DEPARTMENT OF HEPATOLOGY. **DEPARTMENT OF CLINICAL BIOCHEMISTRY. ***DEPARTMENT OF PATHOLOGY, ****DEPARTMENT OF EPIDEMIOLOGY, NATIONAL LIVER INSTITUTE, EGYPT.

Background and Aim. Nitazoxanide, approved for treatment of *Cryptosporidium parvum* and *Giardia lamblia,* was found to inhibit hepatitis C virus replication in replicon system. The aim of this work is to assess the impact of Nitazoxanide as an add-on therapy to pegylated interferon α 2a on sustained virologic response in a cohort of Egyptian patients with chronic hepatitis C, 24 weeks after the termination of triple therapy with pegylated interferon, ribavirin and nitazoxanide or placebo). **Material and methods.** A total of 110 patients were evaluated, 50 patients in the placebo group who received placebo orally twice daily with meals, *vs.* 60 patients in the group treated with Nitazoxanide orally at a dose 500 mg twice daily with meals, In all patients, placebo and nitazoxanide were given as an add-on therapy to pegylated interferon a 2a plus ribavirin, following a 12-week lead-in phase. Sustained virologic response (SVR) to triple therapy, defined as undetectable HCV RNA 24-weeks after termination of triple therapy with a highly sensitive assay, was evaluated in the 2 groups. Statistical analysis was done using SPSS software. This trial is registered on www.clinicaltrials.gov with a trial ID NCT01197157 (NEAR trial). **Results.** In the placebo group, 31 patients out of 50 (62%) achieved a SVR, compared to 35 patients out of 60 (58.3%) in the nitazoxanide group with a p value of (0.69), which did not show any statistically significant difference. **Conclusions.** Our data did not show any significant impact of nitazoxanide add-on therapy to pegylated interferon and ribavirin on SVR at 24 weeks from termination of triple therapy. Accordingly, it is unlikely that nitazoxanide could have a role in combination therapy for CHC genotype 4.

071

DIFFICULTIES IN ACCESS TO HEPATITIS C TREATMENT IN THE PUBLIC HEALTH SYSTEM IN BRAZIL - THE VOICE OF THE PATIENT

C.N. VARALDO,* K.M. RODRIGUES DO Ó,** A.R.P. PASCOM***
*GRUPO OTIMISMO, BRAZIL.
**HOSPITAL SÃO LUCAS, PETRÓPOLIS, RIO DE JANEIRO, BRAZIL.
***MINISTÉRIO DA SAÚDE, DEPTO DST/AIDS/HEPATITES VIRAIS, BRAZIL.

Background. The difficulties of Access to treatment of hepatitis C are known though reports in medical studies. We aimed, instead, to ascertain the situation as reported by patients. **Aim.** The objective of this study was to obtain information in order to improve care in the public and private health systems. **Material and methods.** 841 individuals infected with hepatitis C virus answered anonymously to seven questions in interviews sing the Survey Monkey System. The mean age in the group was of 53.5 years old (52 to 79 years). **Results.** 81.1% of patients were diagnosed with hepatitis C while donating blood or during routine appointments: only 18.9% of them had asked doctors to make the test. 61.1% received the diagnosis during private consultation; 21.2% in making a blood donation; 14.7% in public health system; 1.7% in testing campaigns and 1.3% in Counseling and Testing Centers. Confirmation by molecular biology was made on the average in 6.45 months (15 days to 14 years). It was made by health insurance in 58.1% of cases; 27.6% by public health system and 14.3 by the private system. The biopsy was made by health insurance in 63.3% of cases; 25.1% by the public health system and 11.6% by the private system. **Conclusion.** The treatment of 90% of cases of hepatitis C in Brazil is made by the public health system. More than 60% of patients on treatment had health insurance. In Brazil, health plans do not provide for medications. It is necessary that health insurance ensure the full treatment of hepatitis C, including medications, to allow the opening of vacancies in public hospitals for patients lacking resources.

072

PREVALENCE OF HEPATITIS B AND C VIRAL MARKERS IN BLOOD BANK DONORS AT DANIEL CARRION HOSPITAL, CALLAO, PERU. 2010-2012

L. ÁLVAREZ,*,** P. TEJADA,*,** G. MELGAREJO,*,** G. BERTO,*,** D. TICONA,*,** P. MONTES,***,**** E. MONGE*,***,****
*UNIVERSIDAD NACIONAL MAYOR DE SAN MARCOS; LIMA, PERÚ.
**ASOCIACIÓN PARA EL DESARROLLO EN CIENCIAS DE LA SALUD; LIMA, PERÚ.
***HOSPITAL NACIONAL DANIEL ALCIDES CARRIÓN; LIMA, PERÚ.
****UNIVERSIDAD PERUANA DE CIENCIAS APLICADAS; LIMA, PERÚ.

Introduction. In our country, HCV prevalence is estimated in 1-2% of the population, for HBV we have no data for Callao. The aim of our study is to know the serological prevalence of B and C virus in blood donors at Hospital Daniel Carrion.

Callao. **Material and methods.** Cross-sectional study in blood donors at Daniel Carrion Carrion Hospital's blood bank. Donors between January 2010 and December 2012 were included. Patients positive to HBV Surface antigen (HBsAg), anti core (Anti-HBc) and antibodies to HCV (Anti-HCV) were identified. Demographic data was collected and risk conducts were surveyed. Data was analyzed using EPI-Info v.7. **Results.** Included were 13 887 blood donors. Serological prevalence was 0.55% for HBsAG, 5.15% for HBcAb, and 1.25% for HCV. Those with a positive serology, had an age average of 37 years, 32% were females and 50% were from the Callao area. Only 0.22% for HBV and 3% for HCV referred a risk conduct for infectious diseases. HBV and HCV coinfection was found in 0.3% and HIV coinfection in 0.8%. Chagas disease coinfection was found in 2%, HTLV in 1.2% and Syphilis in 4.8%. **Conclusions.** Prevalence for HBsAg was 0.55%, for Anti-HBc 5.15% and for Anti-HCV 1.25%.

073

HEPATITIS C VIRUS INFECTION AND SEROPOSITIVITY ANTI-HCV IN BLOOD DONORS AT A THIRD LEVEL ATTENTION HOSPITAL IN MEXICO

N.B. GUERRA-URIBE,* M. ACOSTA-GÓMEZ,*
S.G. GONZALEZ-ZENTENO,** M.S. GONZÁLEZ-HUEZO*
*DEPARTAMENTO DE GASTROENTEROLOGÍA, **BANCO DE SANGRE, CENTRO MÉDICO ISSEMYM, METEPEC, ESTADO DE MÉXICO, MÉXICO.

Background. The hepatitis C virus (HCV) infection is one of the most important causes of chronic liver disease worldwide. With asymptomatic course and risk of progression to cirrhosis. The prevalence among low-risk subjects is consider to be minor than general population. The primary outcome of this study was to determine the prevalence HCV-seropositive and HCV infection confirmed by RIBA in blood donors at our hospital. **Material and methods.** We retrospectively analyzed the electronic database of the CMI blood bank between May 2003 and March 2014. We documented 130,460 potential donors. Once the high risk individuals were excluded by an official questionnaire performed by the (Mexican official Norm NOM-253-SSA1-2012), it was conducted the screening to determine the presence of antibodies against HCV with a third generation technique of Enzyme Immunoassay (EIA) or chemiluminescent. In the case of a positive result, the specimens were once again processed by the same method. If they were positive twice, a confirmatory test with a new sample was performed with a recombinant immunoblot assay (RIBA) (Figure). Temporal distribution of seropositivity/positive RIBA. **Results.** 130,460 interviews were conducted in accordance to the Mexican official norm NOM.253-SSA1-2012, from wich only 71,762 individuals were considered potential donors, 435 (0.60%) of them were positive to both tests and supplemental RIBA testing was performed; 64/435 (14.7%) were positive, total values 64/71,762 (0.09%). Regarding demographic data of all 64 individuals with positive HCV/RIBA, 45 (70.3%) were men and 19 (29.7%) were women, with a men age of 46 ± 11 years (25-69 years). **Conclusions.** The seroprevalence in our population is similar to the one report in the national literature of donors (0.13-2.05%). The prevalence of confirmed infection was 0.09%. It's important to mention the large proportion of subjects (44.9%) that were excluded because of high risk factors; wich might suggest an even higher prevalence in the general population. We observed a prevalence decrease in the last 5 years. This finding must be confirmed prospectively in a larger sample.

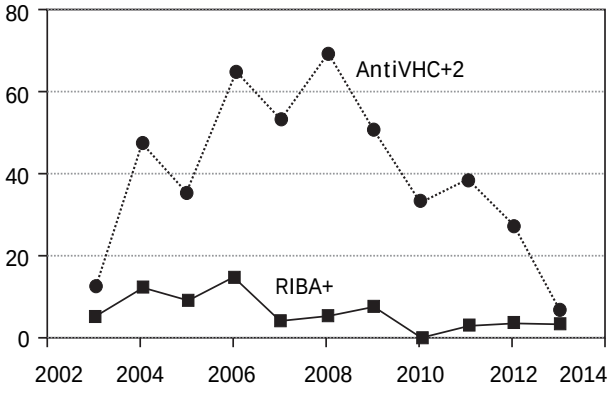

Figure. (073)

074

FREQUENCY OF INFECTION WITH HEPATITIS B AND C IN HEMODIALYSIS SERVICE, GENERAL HOSPITAL, ISSSTE TLAXCALA

PATRICIA PAZ-PEÑA-DÍAZ,* HUGO PILIADO-PAEZ,*
JUAN RAMÓN AGUILAR-RAMÍREZ**
*SERVICIO DE GASTROENTEROLOGÍA, HOSPITAL GENERAL, ISSSTE TLAXCALA, MÉXICO.
**ESCUELA MÉDICO-MILITAR, MÉXICO.

Introduction. Infection with hepatitis B and C virus (VHB, VHC) is common in patients with renal failure on hemodialysis. It is a common cause of liver disease. Studies of screening for VHB, VHC, identify the impact on survival of these. Common risk factors for infection are different in this group.Survival decreases infection and complicates the final treatment in the case of renal transplantation. It is important to identify positive patients to establish treatment. **Objective.** To determine the frequency of infection for VHB, VHC in the hemodialysis service, Hospital General, ISSSTE Tlaxcala. **Material and methods.** Thirty-five patients and 4 nurses of the hemodialysis service were screened over a period of 4 months. They made a rapid qualitative test for VHB, VHC in blood (TM Rapid Anti-VHB, Anti-VHC Test). Patients who presented "reactive test" was confirmed by PCR. **Results.** Five reagent for VHC patients (12.8%) and one for VHB (2.5%) were found; total of 17.1% of the population. The average stay in hemodialysis was 4.8 years; with range of 1-8 years. Five female patients positive (83.3%) VHC test, a patient with a renal transplant rejection; one male patient positive (16.6%) reagent for VHB with renal transplant rejection. The average age of VHC reactive patients was 40.8 years, range 31-64 years. The reagent for VHB patient age 28 years. **Conclusions.** The transmission of VHB and VHC in the hemodialysis patient often presents with permanent vascular access. One of the most important factors is the time stay in hemodialysis; was reported 13-58% of positivity, related to longer hemodialysis stay. In our population was found 17.1% positivity, with average stay in hemodialysis range of 4.8 years. It is important to identify the positive hemodialysis patients, and establish appropriate treatment to improve survive or definitive treatment for kidney transplant.

075

PREVALENCE OF VIRAL HEPATITIS IN PRENUPTIAL STUDIES IN ARGENTINA: APPROACHING TO THE PREVALENCE IN THE GENERAL POPULATION

P. ANGELERI,[*] G. VIDIELLA,[*] J. SOLARI,[*] E. CORONEL,[*] V. LEVITE,[*] D. ADASZKO,[*] A. ADASZKO,[*] C. MOYANO,[‡] D. BOUCHET,[§] H. CUELLO,[‖] M. PANDO,[†] C. FALISTOCCO[*]

[*]*DIRECCIÓN DE SIDA Y ETS, MINISTERIO DE SALUD DE LA NACIÓN, ARGENTINA.*
[†]*INSTITUTO DE INVESTIGACIONES BIOMÉDICAS EN RETROVIRUS Y SIDA, FACULTAD DE MEDICINA, UNIVERSIDAD DE BUENOS AIRES, ARGENTINA.*
[‡]*MINISTERIO DE SALUD, PROVINCIA DE SANTA FE, ARGENTINA.*
[§]*PROGRAMA PROVINCIAL DE VIH/SIDA, ITS Y HEPATITIS VIRALES. MINISTERIO DE SALUD, PROVINCIA DE CÓRDOBA, ARGENTINA.*
[‖]*HOSPITAL CENTRAL DE MENDOZA, ARGENTINA.*

Introduction. Viral hepatitis is one of the major global public health problems mostly triggered by any of the five viruses that primarily infect the liver: hepatitis A virus (HAV), hepatitis B (HBV), hepatitis C (HCV), hepatitis D (or delta) (HDV) and hepatitis E (HEV). Currently, only data from blood donors and local studies are used by policy makers. Better understanding of the epidemiological situation in general population of Argentina is needed to guide the planning of prevention and control actions. **Aim.** To estimate the prevalence of HAV, HBV and HCV infection among adults who attended prenuptial studies in selected Argentinean urban conglomerates. **Material and methods.** A cross sectional study was performed among adults who attended to do their prenuptial studies. Five conglomerates were selected according data of population and number of marriages. Until now, data from three places were analyzed. **Results.** A total of 2,086 adults individuals who attended prenuptial studies were recruited from September 2013 to January 2014 in Córdoba (n = 646), Mendoza (n = 427) and Santa Fe (n = 1,013). 50.2% were female and 49.8% male. Mean age was 31.9 years old. HAV IgG prevalence was 59.2% (95% CI: 57.1-61.3). No differences between clusters or gender were detected. Individuals over 50 years old had the highest prevalence (> 80%) of HAV IgG. HBsAg and IgG anti Hbc were used as markers of HBV infection. Ten individuals were reactive for HBsAg (prevalence: 0.48%; 95%CI: 0.18-0.78) and 21 for IgG anti Hbc (prevalence: 1.0%; 95% CI: 0.58.0-1.44). The mean age of those who had HBsAg was 33.9 years (SD 8.64) and for those who had IgG anti Hbc was 37.2 (SD 10.5). Significant differences for gender (male) were found for the latter. Eight participants were reactive for HCV reaching a prevalence of 0.38% (95% CI: 0.12-0.65). The mean age of those who were positive was 40.2 (SD 9.79) and we found no significant differences for gender. **Conclusions.** These are the preliminary results from the prevalence of viral hepatitis in prenuptial studies in Argentina in three of the five selected conglomerates of Argentina. We found high prevalence of hepatitis A with no differences by gender; IgG anti Hbc with significant differences for gender but not for HBsAg and VHC. Results from this study will be very useful for public health decisions in the viral hepatitis area.

076

LOW PREVALENCE OF HEPATITIS B AND C VIRUS MARKERS AMONG CHILDREN AND ADOLESCENTS

L.M. VILLAR,[*] L.A. AMADO,[**] A.J. DE ALMEIDA,[*] V.S. DE PAULA,[**] L.L. LEWIS-XIMENEZ,[*] E. LAMPE[*]

[*]*LABORATORY OF VIRAL HEPATITIS,* [**]*LABORATORY OF TECHNOLOGICAL DEVELOPMENT OF VIROLOGY, OSWALDO CRUZ INSTITUTE, FIOCRUZ, RIO DE JANEIRO, BRAZIL.*

Introduction. Hepatitis B and C share common transmission pathways; thus, it is possible to investigate them simultaneously. The prevalence of HBV and HCV markers in children varies by risk factors and geographic location. This study aimed to determine the prevalence of HBV and HCV among children and adolescents attending schools and daycare centres in Rio de Janeiro State, located in southern Brazil. **Material and methods.** The sample included all the children attending four primary schools and two daycare centres located in the metropolitan region of Rio de Janeiro State between 1999 and 2012. All individuals invited to participate in the study were included in this study. Schools were selected using a non-probability sampling method, and only public schools and daycare centres located in the metropolitan region of Rio de Janeiro were included. Serum samples from 1,217 individuals aged 0 to 18 years were collected and tested for HBsAg, total anti-HBc, anti-HBs, and anti-HCV by ELISA. Reactive HBsAg and anti-HBc samples were tested for HBV DNA. Reactive anti-HCV samples were tested for HCV RNA and genotyped by RFLP. **Results.** HBsAg was detected in 1.8% of individuals, and total anti-HBc was detected among 3.6% of individuals. Anti-HBs reactivity was found among 25.3% (322/1,217) of the individuals and increased from 6.28% in the years 1999-2000 to 76.2% in the years 2001-2012 ($p < 0.0001$). HBV DNA was detected in 18 of 51 individuals who presented HBsAg or isolated anti-HBc, and nine were considered occult hepatitis B cases. Three individuals were anti-HCV and HCV RNA-positive: two of them were infected with genotype 1, and the other was infected with genotype 3. **Conclusions.** Low levels of HBV and HCV markers were observed in children and adolescents. HBV immunity increased during the period of study, indicating that childhood universal HBV vaccination has been effective for controlling HBV infection in Brazil.

077

DESCRIPTION OF VIRAL LOAD ON INDIVIDUALS CHRONICALLY INFECTED WITH HEPITITIS B VIRUS

T. GARDÊNIA-LOPES, M. DE SOUZA-CAMPOS, G. PEDRAL, F. ANJOS BASTOS, E. GRACIELE A. NEVES, V. CARREIRO, R. REIS, C. LIMOEIRO, N.M.B.L. CHAGAS, R. PARANÁ, R. MEYER, M. ISABEL SCHINONI, S. MENEZES FREIRE

**UNIVERSIDADE FEDERAL DA BAHIA, SALVADOR-BRAZIL.*

Introduction. HBV infection can lead to a number of clinical conditions, ranging from asymptomatic infection to the development of hepatocellular carcinoma. About 90% of adults individuals infected do not develop symptoms; others may develop chronic hepatitis with progression to cirrhosis and hepatocellular carcinoma. The treatments of chronic hepatitis B take aim at preventing or reducing the development of liver cirrhosis and hepatocellular carcinoma. Besides, they also concentrate on viral suppression, normalization of alanine aminotransferase (ALT), decreasing liver damage and sero-

conversion (Shim, 2009). Some current guidelines focus on ALT levels, the viral load (HBV DNA) and HBeAg as predictors of response to treatment. **Material and methods.** This study was developed with 50 individuals monoinfected with HBV - men and women between 18 and 65 years old – assisted at the Outpatient Unit of Gastro-Hepatology HUPES/UFBa. The quantification of the group sample's viral load was performed by the Central Public Health Laboratory Professor Gonçalo Moniz (LACEN-BA). Real Time PCR was the method used. All the results were recorded in the patients' files. **Results.** Of all patients studied, 33 had viral load lower than 2,000 IU/mL and 17 had viral load higher than 2,000 IU/mL. No statistical differences were found in immune cell profiles among individuals with viral load below and above 2,000 IU/mL. **Discussion.** In a study with 31 patients chronically infected with HBV, in India, Mukherjee, *et al*. (2010) also found no statistical differences when comparing the lymphocyte profile of individuals who had viral load below and above 2,000 IU/mL. However, some studies have shown a strong association between the lymphocytes profile and the viral load, whereas the greater the viral load level, the lower the T lymphocytes and their subpopulations. **Conclusion.** No significant differences were found in the lymphocyte profile on subjects with viral load below and above 2,000 IU/mL.

C. NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) AND ALCOHOLIC LIVER DISEASE (ALD)

001

CLINICAL ASPECTS OF PATIENTS WITH FATTY LIVER IN BOGOTA, COLOMBIA-2 CENTERS

JHON E. PRIETO-O.,[*,**] SANTIAGO SÁNCHEZ-P.,[*] LEONARDO DÍAZ-R.,[*] LUPITA GONZALEZ[**]
[*]*CLÍNICA UNIVERSITARIA COLOMBIA, BOGOTÁ, COLOMBIA.*
[**]*CONSULTORIO DE HEPATOLOGÍA, BOGOTÁ, COLOMBIA.*

Introduction. Fatty liver, is one of the major causes of liver disease worldwide, with a prevalence of approximately 30% in adults. Fatty liver or NAFLD (nonalcoholic fatty liver disease) encompasses a histological spectrum ranging from simple steatosis, fatty liver with elevation of transaminases or NASH (nonalcoholic steatohepatitis) and culminating in cirrhosis. In Colombia there are no studies available that describe this disease and behavior. **Material and methods.** A descriptive and retrospective study, with review of medical records of patients diagnosed with fatty liver in two centers in Bogota (Colombia) from January 2009 until March 2014, describing the clinical features and association with metabolic syndrome. **Results.** 721 medical records were analyzed, 51.5% women. In relation to the metabolic syndrome 296 patients (41.1%) had dyslipidemia, 171 (23.7%) were obese , 160 (22.2%) hypertensive patients, 120 (16.6%) diabetic and 26 (3.6%) had coronary artery disease. Physical examination was normal in 51.8% of patients, the mean body mass index was 27.4. Liver biopsy was performed in 80 patients (11.1%). Mean blood glucose, insulin and resistance insulin index was 101 mgs/dL, 16 mcU/mL and 4.3. The mean cholesterol, triglycerides and TSH of 209 mg/dL, 187.4 mgs/dL and 3 uU/mL respectively, discrete transaminases elevation was showed mean AST and ALT 42 and 64 U/L. The final diagnosis of 721 patients was simple steatosis in 31.3%, non-alcoholic steatohepatitis 62.7% and cirrhosis in 6%. A multivariate analysis of parameters of metabolic syndrome was conducted and the relationship between history of diabetes and the onset of NASH with p value < 0.05 and χ^2 of 12.95 was found. **Conclusions.** Fatty liver is frequent in Colombia, with a clear association with one or more components of the metabolic syndrome and evidence of moderate insulin resistance in this population. The low percentage of patients with cirrhosis reveals the relative mildness of the disease, however 62.7% of patients showed NASH known to have a 10% risk of progression to cirrhosis.

002

NON-INVASIVE LIPIDOMICS TEST FOR IMPROVING ASSESSMENT OF NAFLD: CLINICAL PATIENTS DIAGNOSIS AND FOLLOW-UP

N.M. IRAZABAL-REMUIÑAN,[*] L.F. ERAÑA-LEDESMA,[*] P. SALVADOR,[†] S. BLANCO,[‡] F. MENÉNDEZ,[‡] P. RUIZ,[§] R. GONZÁLEZ-MONASTERIO,[§] E. DELGADO,[||] J.I. ARENAS,[¶] M. MARTOS,[¶] A. OTEGUI,[**] G. ARREGI,[**] M.C. EIZMENDI,[**] S. URQUIOLA,[**] T. PORTO,[††] A. CASTRO,[††] J. BUSTAMANTE,[†] J.I. PIJOÁN[‡‡]
[*]*UNIDAD DE GASTROENTEROLOGÍA, HOSPITAL UNIVERSITARIO DE ARABA (SANTIAGO), VITORIA-GASTEIZ, SPAIN.*
[†]*UNIDAD DE GASTROENTEROLOGÍA Y HEPATOLOGÍA, HOSPITAL UNIVERSITARIO CRUCES, BIOCRUCES HEALTH RESEARCH INSTITUTE, BARAKALDO, SPAIN.*
[‡]*UNIDAD DE GASTROENTEROLOGÍA, HOSPITAL UNIVERSITARIO BASURTO, BILBAO, SPAIN.*
[§]*UNIDAD DE GASTROENTEROLOGÍA, HOSPITAL SAN ELOY, BARAKALDO, SPAIN.*
[||]*UNIDAD DE GASTROENTEROLOGÍA, HOSPITAL UNIVERSITARIO DE ARABA (TXAGORRITXU), VITORIA-GASTEIZ, SPAIN.*
[¶]*UNIDAD DE GASTROENTEROLOGÍA, HOSPITAL UNIVERSITARIO DONOSTIA, DONOSTIA-SAN SEBASTIÁN, SPAIN.*
[**]*CENTRO DE SALUD DE ZUMARRAGA, ZUMARRAGA, SPAIN.*
[‡‡]*ONE WAY LIVER GENOMICS, S.L., PARQUE TECNOLÓGICO DE BIZKAIA, DERIO, SPAIN.*
[‡‡]*UNIDAD DE EPIDEMIOLOGÍA CLÍNICA Y SOPORTE METODOLÓGICO, HOSPITAL UNIVERSITARIO CRUCES, BIOCRUCES HEALTH RESEARCH INSTITUTE, BARAKALDO, SPAIN.*

Background and aims. The spectrum of non-alcoholic fatty liver disease (NAFLD) ranges from hepatic steatosis to non-alcoholic steatohepatitis (NASH). Developing non-invasive approaches such as a BMI-dependent lipidomic signature test could represent a diagnostic milestone. We evaluated the performance of the Owl Liver Test (OLT) to differentiate liver steatosis from NASH and determine its relation to BMI, clinical parameters and other supporting medical exams. **Material and methods.** Eighty patients with NAFLD were recruited from 7 hospitals and 1 primary care centre of the Basque Public Health System. Blood samples were taken in two separate visits in 9 months time. In first visit, patients were prescribed diet and exercise. Serum metabolic profile was performed by a LC/MS-based platform that allows the semi-quantitative analysis of 44 lipids. Clinical parameters and additional data were used to calculate NAFLD Fibrosis Score and the Clinical Model of Palekar. Other complementary tests, such as Fibroscan, were also carried out. **Results.** Forty-two females and thirty-eight males (mean age 47.4 years, range 23-65) were studied according to a specific clinical protocol profile. At baseline 12/37 patients with BMI > 30 were classified as having NASH or "borderline" NASH vs only 6/43 cases with BMI < 30. OLT staging was stable in patients with minor changes in BMI over time but discrepancies were found in 11 cases: BMI decreased or remained unchanged in six cases, although OLT diagnosis of NASH persisted or developed on follow-up. In three patients BMI increased slightly, but OLT results changed from NASH to steatosis or from steatosis to healthy liver. In another two patients a significant BMI

reduction did not modify OLT diagnosis of NASH. In all, test results were consistent with patient involvement in the control of the disease, concerning diet and exercise, for the 9 months of monitoring. They were also in accordance with biochemical and anthropometric determinations. Furthermore, a small group of lean NAFLD patients was identified. These patients with specific characteristics should be object of a closer monitoring as they fall out of common NAFLD patients profile. **Conclusions.** NAFLD is considered to become one of the most prevailing diseases of the 21th century in developed countries. Therefore, the development of a useful and non-invasive tool for NAFLD management is a matter of immediate concern. The non-invasive OLT test seems to potentially meet these requirements as it may discriminate between different stages of the disease. It might also become a valuable approach to monitor progression of patients.

003

EFFECT OF CHRONIC ALCOHOL USE ON THE LYMPHOCYTE PROFILE

J.L. PÉREZ HERNÁNDEZ,* E.G. GUTIÉRREZ REYES,**
M.F. HIGUERA DE LA TIJERA*
*LIVER CLINIC, HOSPITAL GENERAL DE MÉXICO, MEXICO CITY.
**UNIT OF EXPERIMENTAL MEDICINE, UNAM, MEXICO CITY.

Introduction. Alcoholism has deleterious effects on the immune system; there is controversy to define which are the immunity cells that are affected. **Objective.** Describing the effect of chronic alcohol use in lymphocytes: CD3+, CD4+, CD8+, CD19+, CD56+ and CD56+CD3+. **Material and methods.** Observational cross-sectional study included alcoholic men (with more than 5 years of chronic alcohol use), the following variables were obtained: AUDIT, grams of alcohol and percentage of lymphocytes in periferic blood (measured by flow cytometry using fluorescent monoclonal antibodies) to compare with healthy controls teetotalers; cirrhotic, immunocompromised, undernourished, HBV and/or HCV infected patients were excluded. The statistical analysis was carried out using Student's T considering a $p < 0.01$ as significant. **Results.** 30 individuals were included per group, age of 38.1 years in alcoholics (28-55) *vs.* 37.5 (21-53) in controls, AUDIT in alcoholics: 20 to 38 points; alcohol consumption: 150 to 350 grams per day, the result of the percentage of lymphocytes is shown in Table. **Conclusions.** The studied population were young, with great dependence of alcohol and high consumption in grams, we found no differences in the lymphocytes percentage CD3+, CD4+, CD8+ and CD19+ particularly that, in other studies were found diminished; we saw an increase in the lymphocytes percentage CD56+ and CD56+CD3+ that contrasts with previous reported literature, more studies are needed that include other factors such as polymorphisms or expression anormalities in genes of enzymes that metabolize alcohol to search an explanation of these alterations, as well as correlations with the presence of active infections.

Table. (003)

	Alcoholics %(SD)	Controls %(SD)	p
$CD3^+$	57.7 (22.73)	66 (7.56)	0.22
$CD4^+$	38.5 (13.90)	39.6 (9.88%)	0.386
$CD8^+$	22.0 (11.31)	22.2 (7.51)	0.679
$CD19^+$	15.8 (18.93)	13.6 (5.25)	0.509
$CD56^+$	17.7 (15.21)	9.7 (5.81)	0.015
$CD56^+CD3^+$	4.5 (4.47)	2 (1.30)	0.004

004

EFFECT OF THE EXTRACT OF *GERANIUM SCHIEDEANUM* ON ANTIOXIDANT ENZYMES SUPEROXIDE DISMUTASE, CATALASE, AND GLUTATHIONE PEROXIDASE DURING LIVER REGENERATION AND ALCOHOL CONSUMPTION

A. POSADAS-MONDRAGÓN,* M. BAUTISTA-AVILA,**
E. MADRIGAL-SANTILLÁN,* Á. MORALES-GONZÁLEZ,***
J.A. GAYOSSO-DE-LUCIO,** E. MADRIGAL-BUJAIDAR,****
J.A. MORALES-GONZÁLEZ*
*ESCUELA SUPERIOR DE MEDICINA, INSTITUTO POLITÉCNICO NACIONAL, MÉXICO.
**INSTITUTO DE CIENCIAS DE LA SALUD, UNIVERSIDAD AUTÓNOMA DEL ESTADO DE HIDALGO, MÉXICO.
***ESCUELA SUPERIOR DE CÓMPUTO, ****ESCUELA NACIONAL DE CIENCIAS BIOLÓGICAS, INSTITUTO POLITÉCNICO NACIONAL, MÉXICO.

Introduction. Hepatocytes exhibit a regenerative response to various stimuli, including massive destruction of hepatic tissue by toxins, viral agents, or surgical extraction. Administration of ethanol induces the increase of lipid peroxidation whether due to an increase of reactive oxygen species (ROS) or a decrease in the levels of endogenous antioxidants, inhibiting hepatic regeneration. Diverse plants and isolates of natural compounds have shown hepatoprotective activity and have been used to prevent oxidative changes in the liver during the metabolism of alcohol. Among these, we find the geranium, on which there are no studies demonstrating its antioxidative capacity. **Objective.** We evaluated the effect of the extract of *Geraninum Schiedeanum* (Gs) on the enzymatic activity of catalase, superoxide dismutase, and glutathione peroxidase of ethanol-induced toxicity in hepatic regeneration in rats with partial hepatectomy. **Material and methods.** We utilized male Wistar rats (weighing 200-230 g) and divided them into three groups: 1) Control group (Sham and rats with Hepatectomy [HP]); 2) Rats with HP and ethanol (EtOH) consumption 1.5 g/kg of body weight (BW) daily (HP-EtOH), and 3) Rats with hepatectomy treated with the same dose of ethanol and with intragastric (i.g.) doses of *Geranium Schiedeanum* 300 mg/kg (HP-EtOH-Gs). At day 7, we sacrificed the animals, obtaining serum and liver, in which we determined lipid peroxidation Thiobarbituric acid reactive substances (TBARS) in serum and liver. We evaluated total antioxidant capacity, total antioxidant status, and the enzymatic activity of catalase, superoxide dismutase, and glutathione peroxidase in liver. **Results.** We observed a significant increase in TBARS levels in the HP-EtOH group compared with the control group and the group with HP; however, in the HP-EtOH-Gs group, we observed a decrease. We observed a decrease in the antioxidant status of the HP-EtOH group and the contrary effect in the HP-EtOH-Gs group with respect to the control and HP groups. Total antioxidant capacity rose in the HP, HP-EtOH, and HP-EtOH-Gs groups with respect to the control group. Catalase, superoxide dismutase, and gluthathione peroxidase levels rose in the HP, HP-EtOH, and HP-EtOH-Gs groups; however, in the latter, the increase was less with respect to the remaining two groups. **Conclusion.** The geranium possesses a protector effect on the inhibition of liver regeneration caused by ethanol through its antioxidant property and modulation of antioxidant enzymes catalase, superoxide dismutase, and gluthathione peroxidase.

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005

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

E. MADRIGAL-SANTILLÁN,* A. POSADAS-MONDRAGÓN,* M. BAUTISTA-AVILA,† Á. MORALES-GONZÁLEZ,‡ J. ESQUIVEL-SOTO,§ E. MADRIGAL-BUJAIDAR,‖ J.A. MORALES-GONZÁLEZ*
*ESCUELA SUPERIOR DE MEDICINA, ‡ESCUELA SUPERIOR DE CÓMPUTO, ‖ESCUELA NACIONAL DE CIENCIAS BIOLÓGICAS, INSTITUTO POLITÉCNICO NACIONAL, MÉXICO.
†INSTITUTO DE CIENCIAS DE LA SALUD, UNIVERSIDAD AUTÓNOMA DEL ESTADO DE HIDALGO, MÉXICO.
§FACULTAD DE ODONTOLOGÍA, UNIVERSIDAD NACIONAL AUTÓNOMA DE MÉXICO, MÉXICO.

Introduction. Between 70 and 80% of deaths due to cirrhosis is attributable to alcohol consumption. In World Health Organization (WHO) reports, liver cirrhosis-associated mortality worldwide was 797,000 inhabitants and morbility was 14,856,000 inhabitants. But there are no reports on the damage caused by ethanol on the liver during weekend consumption, and Mexico's National Institute of Statistics and Geography (INEGI) indicates that > 20% of the population engages in chronic weekend ethanol consumption. **Objective.** To study the effect of weekend ethanol consumption on diverse biochemical parameters. **Material and methods.** We utilized male Wistar-strain rats (weighing 250 g) fed *ad libitum*. We divided the animals into a) Control group, b) Group with ethanol (1.5 g/kg, 5% concentration), and c) Ethanol group (1.5 g/kg, 40% concentration). The ethanol was adminstered intragastrically (i.g.) twice a week during 2 months. The rats were sacrificed and we obtained the sera, from which we quantified glucose, cholesterol, triglycerides, and albumin concentrations and enzymatic activity (aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) by means of spectrophotometric techniques. **Results.** AST as well as ALT activity increased significantly in both groups with ethanol in comparison with the control group, being greater in the group at 5%. Cholesterol levels decreased (30%) only in the group at 5%. Triglyceride as well as glucose levels significantly increased in the group at 5% in comparison with the control. Albumin levels did not change in any group with ethanol. The greatest biochemical alterations were observed in the group at 5%. **Conclusion.** We concluded that weekend ethanol consumption does affect diverse biochemical parameters, and that ethanol consumption at 5% extends this damage even further. Supported by Proyecto SIP 20140856, ESM-IPN.

006

HEPATOPROTECTIVE EFFECT OF THE *GERANIUM SCHIEDEANUM* EXTRACT ON DAMAGE CAUSED BY ETHANOL IN LIVER REGENERATION

Y. REYES-ROSALES,* M. BAUTISTA-ÁVILA,** E.O. MADRIGAL-SANTILLÁN,* J.D. TOSCANO-GARIBAY,*** L. AGUILAR-FAISAL,* J.A. GALLOSSO-DE-LUCIO,** J.A. MORALES-GONZÁLEZ*
*ESCUELA SUPERIOR DE MEDICINA, INSTITUTO POLITÉCNICO NACIONAL, MÉXICO.
UNIVERSIDAD AUTÓNOMA DEL ESTADO DE HIDALGO, HIDALGO. MÉXICO.*HOSPITAL JUÁREZ DE MÉXICO, MÉXICO.

Introduction. Liver regeneration is a good model for studying the protector effect that some antioxidants possess of the damage caused by some xenobiotics, and it is especially known that ethanol is especially known as an inhibitor of hepatic regeneration. **Objective.** To study the effect of the extract de *Geranium Schiedeanum* (Gs) as an antioxidant that protects the regenerating liver from free radicals formed by the metabolism of ethanol. **Material and methods.** We utilized male Wistar rats that had been submitted to partial hepatectomy according to the technique of Higgins and Anderson, with treatment with ethanol (1.5 g/kg) and/or the Gs extract (300 mg/kg) intragastrically (i.g.) during 7 days. At the end of treatment, the rats were sacrificed. We determined the following in serum: levels of glucose, cholesterol, albumin, bilirubin, aspartate aminotransferase (AST), and alanine aminotransferase (ALT); in liver, we determined AST and ALT only by means of colorimetric techniques. **Results.** Ethanol ingestion increases mortality by 20% and diminution in serum levels of glucose, cholesterol, and albumin, and increased bilirubin levels in comparison with those of the control group. On the other hand, administration of the Gs extract returns serum levels and diminution of mortality to normality. Likewise, in the group with ethanol, we found a rise in serum levels of AST and ALT, while with respect to the activity of these enzymes in liver in the same group, ALT increased and AST diminished. These values returned to normal in the group adminstered the geranium extract. **Conclusion.** These values indicate that daily administration of ethanol during 1 week caused changes in serum concentrations of metabolites and enzymes, which translates into liver damage, showing that treatment with the *Geranium Schiedeanum* extract exerted a hepatoprotective effect on interacting with the free radicals, attenuating their effect on the process of liver regeneration. Supported by Proyecto SIP 20141092, ESM-IPN.

007

EVALUATION OF LIPOPEROXIDATIVE DAMAGE IN ALCOHOLIC LIVER DISEASE

M. GALICIA-MORENO,* D. FALCON-CARRILLO,* Z. MEDINA-AVILA,* L. VERY-PINEDA,* D. ROSIQUE-ORAMAS,* T. ÁLVAREZ-TORRES,* L. RAYA-SOTO,* J.L. PÉREZ-HERNÁNDEZ,** Y. BEJAR,** J. CHÁVEZ-MAYOR,** D. KERSHENOBICH,*** G. GUTIÉRREZ-REYES*
*HIPAM LABORATORY, EXPERIMENTAL MEDICINE UNIT, SCHOOL OF MEDICINE, UNAM. MEXICO CITY, MEXICO.
**HOSPITAL GENERAL DE MÉXICO. MEXICO CITY, MEXICO.
***INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN. MEXICO CITY, MEXICO.

Background. The oxidative stress plays an important role in the pathogenesis of alcoholic liver disease (ALD). Chronic ethanol consumption induces lipid peroxidation in the liver resulting in the generation of reactive aldehydes, especially malondialdehyde (MDA), this response has been demonstrated in animal models, but little is known about this process in the human liver tissue and also in peripheral blood. **Aim.** Evaluate the role of oxidative damage in lipids through the quantification of MDA levels in subjects with ALD. **Material adn methods.** Two groups of subject were performed and included in cross-sectional study. Group 1, control group (n = 157) consisting by subjects with an ethanol consumption ≤ 10 g/day and AUDIT ≤ 8. Group 2 were patients with ALD (n = 74) according to WHO and DSM-IV criteria, at the same time this group was classified according to their Child-Pugh scores, also clinical history and informed consent was obtained. The MDA content was determined in serum by colorimetric methods (Okawa, *et al.*, 1979). **Results.** See Table. **Conclusions.** Our study shows that there is a relationship between alcohol consumption and lipoperoxidative damage generation in the severity of the ALD, which was observed by

Table. (007)

	Control	Patients with ALD Child-Pugh A	Child-Pugh B	Child-Pugh C
Gender (F/M), n (%)	40/117 (25.4/74.6%)	3/21 (12.5/87.5%)	2/25 (7.4/92.6%)	1/22 (4.3/95.7%)
Age	37.6 ± 0.7	48.1 ± 2.6[a]	49.7 ± 1.5[a]	54.4 ± 2.5[a]
Body mass index (kg/m^2)	28.0 ± 0.3	28.6 ± 0.9	28.1 ± 0.9	27.0 ± 1.0
Consumption OH (g/day)	2.0 ± 0.2	298 ± 39.1[a]	304 ± 50.2[a]	267 ± 27.5[a]
ALT (UI/L)	27.5 ± 1.4	31.4 ± 4.2	30.7 ± 2.8	36.7 ± 5.3[a]
γ-GT (UI/L)	33.0 ± 2.2	109 ± 21.9[a]	138 ± 18.2[a]	140 ± 31.3
Albumin (g/100 mL)	4.4 ± 0.02	3.8 ± 0.1[a,b,c]	3.2 ± 0.1[a,b,d]	2.5 ± 0.1[a,b,c]
MDA (nmol/mg protein)	0.09 ± 0.008	0.2 ± 0.05[a]	0.2 ± 0.04[a]	0.2 ± 0.04[a]

[a]P ≤ 0.05 *vs.* Control group. [b]P ≤ 0.05 *vs.* Child-Pug A group. [c]P ≤ 0.05 *vs.* Child-Pugh B group. [d]P ≤ 0.05 *vs.* Child-Pugh C group. Values represented as the mean ± SE.

Table. (008) Clinical and biochemical parameters of subjects included in the study.

	Control	ALD Child-Pugh A	Child-Pugh B	Child-Pugh C
Gender, n (%)				
M	19 (16)	4 (12)	2 (10)	1 (6)
H	98 (84)	30 (88)	19 (90)	15 (94)
Age (years)	36 ± 9[a,b,c,d]	50 ± 11[a,b,g]	50 ± 7[a,c,f]	57 ± 11[a,d,f,g]
BMI (kg/m^2)	28 ± 4	27 ± 4	29 ± 5	26 ± 3
Alcohol consumption (g)	2 ± 4[a,b,c,d]	273 ± 190[a,b]	304 ± 287[a,c]	239 ± 115[a,d]
GGT (U/L)	34 ± 30[a,b,c,d]	111 ± 99[a,b]	120 ± 96[a,c]	125 ± 155[a,d]
Albumin (g/dL)	4 ± 0.3[a,b,c,d]	3 ± 0.9[a,b,g]	3 ± 0.6[a,c,f]	2 ± 0.6[a,d,f,g]
IL-4 (pg/mL)	0.1 ± 0[a]	0.4 ± 0[a]	0.5 ± 0.2[a]	0.1 ± 0.2[a]
IL-8 (pg/mL)	2 ± 0.2[a,c,d]	54 ± 26[a]	23 ± 9[a,c]	50 ± 17[a,d]
TNFα (pg/mL)	0.4 ± 0[c,d]	6 ± 3.9	0.8 ± 0[c]	0.8 ± 0[d]
Lymphocytes, T (%)	67 ± 7[a,b]	59 ± 12[a,b]	64 ± 10[a]	62 ± 12[a]
NK (%)	11 ± 6[a,b,c,d]	16 ± 9[a,b]	16 ± 8[a,c]	18 ± 11[a,d]
CD8 (%)	23 ± 7[a,c]	23 ± 12[a,e]	34 ± 13[a,c,e]	26 ± 14[a]
CD4 (%)	41 ± 8[a,b,c]	31 ± 17[a,b]	23 ± 16[a,c]	34 ± 22[a]
Ratio CD4/CD8	2 ± 0.7[c]	2 ± 1[e]	1 ± 1[c,e]	2 ± 2

Data are expressed as mean ± SD. [a]P = 0.05 *vs.* CT. [b]P = 0.05 *vs.* Child-Pug. [c]P = 0.05 *vs.* Child-Pugh B. [d]P = 0.05 *vs.* Child-Pugh C. [e]P = 0.05 Child Pugh A *vs.* Child Pugh B. [f]P = 0.05 Child Pugh B *vs.* Child Pugh C. [g]P =0.05 Child Pugh A *vs.* Child Pugh C.

malondialdehyde determination. This oxidative damage is independent of to severity stage (Child-Pugh score), however evaluation of this compound could be used as a biomarker of alcohol liver damage in serum of alcoholic patients. We propose that the use of antioxidant therapy may be useful for the treatment of this disease.

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008

EVALUATION OF LYMPHOCYTIC PROFILE AND CYTOKINES IN SUBJECTS WITH ALCOHOLIC LIVER DISEASE

Z. MEDINA-ÁVILA,[*] F. ARAGÓN-VALVERDE,[*] T. ÁLVAREZ-TORRES,[*] D. ROSIQUE-ORAMAS,[*] I. ROMERO,[*] A. RAMÍREZ,[*] C. GUZMÁN,[*] J.L. PÉREZ-HERNÁNDEZ,[**] Y. BEJAR,[**] M. GALICIA-MORENO,[*] J. CHÁVEZ-MAYOR,[**] D. KERSHENOBICH,[*,***] G. GUTIÉRREZ-REYES[*]

[*]HIPAM, UNIT OF EXPERIMENTAL MEDICINE, MEDICINE SCHOOL, UNAM, MÉXICO.

[**]HOSPITAL GENERAL DE MÉXICO. MEXICO CITY, MEXICO.

[***]INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MÉXICO.

Background. The chronic alcohol consumption produces an imbalance into the immune system that induces damage to the liver. Actually the most important evidence comes from animal models and *in vitro* assays. **Aim.** Evaluate the lymphocytic profile and the cytokines in peripheral blood to alcoholic liver disease. **Material and methods.** Participants were divided in two groups. Group 1, control group consisting in subjects with an ethanol consumption < 10 g/day and AUDIT < 8. Group 2: patients with alcohol liver disease (ALD) who were classified according to Child Pugh score. The lymphocytic profile (lymphocytes T, NK, NKT, B cells, CD8 and CD4 cells) were determinate in peripheral blood by flow cytometry and the cytokines in serum by a Luminex technology (Bio-Rad). Data were analyzed using ANOVA and orthogonal analysis. **Results.** We included 188 subjects, where 71 were patients with liver injury by alcohol and 117 healthy subjects (controls) (Table). **Conclusions.** Our results showed that in subjects with alcohol liver disease increase the percentage of cytotoxic cells (NK and CD8 T) and elevated levels of pro-inflammatory cytokines, whereas that CD4 cells decrease in subjects with alcohol consumption. Therefore in alcohol liver disease the immune response was found altered and increased the risk of infection in the patients.

009

OXIDATIVE STRESS MEDIATES METABOLIC AND ENDOCRINE DYSFUNCTIONS INDUCED BY FRUCTOSE

M.C. CASTRO,* F. FRANCINI,* G. SCHINELLA,** L.F. GONZÁLES ARBELÁEZ,*** J.J. GAGLIARDINO,* M.L. MASSA*
*CENEXA (CENTRO DE ENDOCRINOLOGÍA EXPERIMENTAL Y APLICADA), UNLP-CONICET; LA PLATA, BUENOS AIRES, ARGENTINA.
**CÁTEDRA DE FARMACOLOGÍA BÁSICA, FACULTAD DE CIENCIAS MÉDICAS (UNLP); LA PLATA, BUENOS AIRES, ARGENTINA.
***CENTRO DE INVESTIGACIONES CARDIOVASCULARES, FACULTAD DE CIENCIAS MÉDICAS; LA PLATA, BUENOS AIRES, ARGENTINA.

Introduction. The prevalence of type 2 diabetes mellitus is increasing worldwide, normally associated to other risk factors: hypertension, obesity, unhealthy diets and sedentary lifestyle. Recent publications suggested that the increase in fructose consume registered in the last decades has contributed to the current obesity and diabetes epidemics. Administration of a fructose rich diet (FRD) to normal rats mimics this situation. **Objective.** To evaluate in a model of pre-diabetes the possible preventive effect of the antioxidant lipoic acid (LA) on the insulin-resistance (IR), liver steatosis, metabolic dysfunctions, oxidative stress (OS) and inflammation triggered by a FRD. **Material and methods.** Wistar rats were fed during 21 days a commercial diet and tap water (control [C]) or fructose in the drinking water 10% (F) and C and F plus LA (35 mg/kg body weight/day, i.p. during the last 5 days of the treatment) (CL and FL). After that, animals were sacrificed and measured glycemia (GOD-PAP), triglyceridemia (TG) (colorimetric) and insulinemia (RIA). Glucose tolerance test was also performed. In the liver we measured a) OS markers (GSH and carbonyls in proteins) and enzymes of the antioxidant defense system (SOD1, SOD2 and catalase), b) Liver steatosis (Oil-Red), c) Gene expression of lipogenic enzymes and the related transcription factor (GPAT, FAS, CPT-1, SREBP-1c), d) Glucokinase, fructokinase, G-6-Pase and G-6-PDH activities, e) Expression of IL-1B, TNFalfa and COX2 and f) Insulin signaling pathway mediators (IR, IRS1/2, PI3K). **Results.** Three weeks of a FRD induced: a) Hypertriglyceridemia, hyperinsulinemia and impaired glucose tolerance, b) Hepatic OS (increase in OS markers, reduction in the expression of antioxidant enzymes and enhanced p22phox and gp91phox levels –NADPH oxidase-), c) Liver steatosis related to increased FAS and GPAT expression as well as SREBP-1c and decreased in CPT-1 expression, d) Enhanced fructokinase, G-6-Pase and G-6-PDH activities and glycogen content, e) Increased glucokinase activity related to translocation to the cytosol and enhanced expression of its positive regulator in the same compartment, e) Increased in liver inflammatory markers and f) Alteration in the insulin signaling pathway. These disturbances were prevented by LA administration. **Conclusion.** OS could play a pivotal role in the development of the endocrine and metabolic alterations induced by a FRD. The protective effect on the liver glucose sensor (glucokinase) could be partially adscript to a re-localization of the enzyme in the nucleus and the cytosolic regulation by PFK-2. Interestingly LA seems to have also a corrective effect on cytosolic NADPH oxidase expression.

010

CARDIOVASCULAR RISK FACTORS IN OBESE AND NON-OBESE PATIENTS WITH NON ALCOHOLIC FATTY LIVER DISEASE

G. GARCÍA-DÍAZ, M. LIZARZÁBAL-GARCÍA
SERVICIO AUTÓNOMO, HOSPITAL UNIVERSITARIO DE MARACAIBO. VENEZUELA.

Introduction. It is well-known association between nonalcoholic fatty liver disease (NAFLD), obesity, diabetes mellitus (DM) and dyslipidemia. However, it has also been found NAFLD in patients without these risk factors. Different studies have shown an association between NAFLD and cardiovascular disease. The aim of this study was to identify and compare cardiovascular risk factors in patients obese and non-obese with NAFLD and to estimate the risk of cardiovascular disease at 10 years. Secondary aim was compare this parameters with a control group. **Material and methods.** Is a basic, descriptive and correlational, not experimental, prospective and cross sectional research. Involved a total of 102 patients, 62 with NAFLD, 31 obese and 31 non obese, and 40 controls with normal liver, 20 obese and 20 non obese. We made an interrogatory, physical exam and take blood samples to compare both groups. **Results.** Female gender prevailed in 76, 5%. There were no significant differences in personal and family history. The liver function tests did not differ greatly between patients and controls, only difference was found in platelet levels ($p = 0.0001$) and alkaline phosphatase ($p = 0.009$) without departing from the normal range. There was a significant trend on basal insulin and HOMA being higher in obese patients with NAFLD ($p = 0.02$ and 0.04 respectively) higher levels of total cholesterol and triglycerides in those with NAFLD obese and non-obese. When comparing cardiovascular risk factors among obese and non-obese with NAFLD were statistically significant differences in low HDL ($p = 0.0$ increased waist circumference ($p = 0.0001$) and metabolic syndrome ($p = 0, 03$) being higher in obese. A higher percentage of patients with NAFLD obese and non-obese with cardiovascular risk factors compared to controls without NALFD was observed. In the majority of patients in both groups according to the estimated risk Framingham score was low. **Conclusions.** The presence of NAFLD is directly related to insulin resistance, dyslipidemia and impaired fasting glycemia, which are the main cardiovascular risk factors in these patients, both obese and non-obese. Impaired fasting glycemia is a risk factor for NAFLD in obese patients and the metabolic syndrome is for both obese and non-obese patients. The risk Framingham score was low in all the groups, regardless of the presence of NASH.

011

THE USE OF SIMVASTATIN IN PREVENTING LIVER OXIDATIVE AND CELLULAR DAMAGE IN MICE WITH NON-ALCOHOLIC STEATOHEPATITIS

G. RODRIGUES,[1,**] A.J. MOREIRA,[1,**] S. BONA,[1,**] E. SCHEMITT,[1,**] C.A. MARRONI,[***] N.P. MARRONI[***,****]
[1]*UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL FEDERAL, PORTO ALEGRE-RS-BRAZIL.*
[2]*CENTER OF EXPERIMENTAL RESEARCH, HOSPITAL DE CLINICAS DE PORTO ALEGRE-RS-BRAZIL.*
[3]*UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE-RS-BRAZIL.*
[4]*UNIVERSIDADE LUTERANA DO BRASIL, CANOAS-RS-BRAZIL.*

Aim. This study aimed to evaluate the effects of use of simvastatin (SIM) in the experimental model of NASH using a me-

thionine-choline-deficient diet (MCD) on oxidative stress and cell damage. **Material and methods.** The NASH was induced in C57BL/6 male mice with 8 weeks, through a MCD for 4 weeks. The animals were divided into 4 experimental groups: CO (control), SIM4 (SIM 4mg/kg), NASH, NASH+SIM4. A 200 μL dose of SIM was administered intragastrically for 2 weeks. The oxidative stress was evaluated by thiobarbituric acid reactive substances (TBARS) and superoxide dismutase (SOD) activity in homogeneized liver. The expression of proteins HSP70 and HSF1, were evaluated in the liver tissue using the western blot method. Statistical analysis used Student Newman Keuls with $p < 0.05$. **Results.** The analyses of lipid peroxidation demonstrated significant decrease in group NASH + SIM 4 (0.19 ± 0.02) when compared to NASH (0.45 ± 0.12). SOD activity showed significant increase in NASH + SIM4 (50.80 ± 10.92) group when compared to NASH (33.72 ± 8.74) group. In NASH group decreased HSP70 expression, paralleled by similar reduction in HSF1 expression. Whereas HSP70 expression was increased in mice treated with SIM. **Conclusion.** SIM improved the stress oxidative and cellular damage. We suggest that the administration of SIM using 4mg/kg may be a possibility of antioxidant therapy in NASH.
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012

ASSOCIATION OF HYPERURICEMIA AND LIVER FIBROSIS IN PATIENTS WITH NAFLD

C. GÓMEZ-GUTIÉRREZ, W. ZAMUDIO-CORONADO, A.Y. LÓPEZ-RAMÍREZ, E. JUÁREZ-HERNÁNDEZ, N. MÉNDEZ-SÁNCHEZ, J. PÉREZ-JAUREGUI, M. URIBE, N.C. CHÁVEZ-TAPIA
OBESITY AND DIGESTIVE DISEASES UNIT. MÉDICA SUR CLINIC AND FOUNDATION. MEXICO CITY.

Background. Non-alcoholic fatty liver disease (NAFLD) is the most common form of chronic liver disease. An association between elevated levels of uric acid and the development of NAFLD has been showed, as well as a relationship between hyperuricemia and the severity degree of liver damage in patients with NAFLD. However, there is not enough evidence to link high levels of uric acid with liver fibrosis in patients with NAFLD. The objective of this study was to determine the association of high levels of uric acid and the presence of liver fibrosis in patients with NAFLD. **Material and methods.** A case-control study nested in a randomized clinical trial was conducted (NCT01874249). The sample included 386 patients attending for a routine check-up at Medica Sur Clinic and Foundation during the period comprising January 2012 to March 2013. All patients were diagnosed with hepatic steatosis by ultrasound. Non-invasive methods for diagnosing liver fibrosis were used; NAFLD score was calculated in all patients, and transient elastography was performed in only 144 patients. Patients with normal and high serum levels of uric acid were classified as controls and cases respectively. **Results.** The comparative analysis showed that the main variables associated with the presence of hyperuricemia in patients with NAFLD were high body mass index (30.92 ± 2.78 kg/m^2 *vs.* 29.36 ± 2.46 kg/m^2, $p = 0.0001$) and metabolic syndrome (62.7 *vs.* 43.3%, $p = 0.0006$). No significant association between the presence of hyperuricemia and liver fibrosis was found. **Conclusion.** In this case-control study, no association between hyperuricemia and liver fibrosis was found in patients with NAFLD.

013

RISK FACTORS ASSOCIATED WITH GREATER HEPATIC STEATOSIS DETERMINED WITH ULTRASOUND IN PATIENTS WITH NAFLD

L. VALDOVINOS-GARCIA, J. CASTRO-GÓMEZ, S. VÁZQUEZ-MANJARREZ, E. GÓMEZ-REYES, S. MARTÍNEZ-VAZQUEZ, A. DELGADILLO-TORRE, J. SÁNCHEZ-AVILA, I. GARCÍA-JUAREZ
DEPARTAMENTO DE GASTROENTEROLOGÍA, INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, CIUDAD DE MÉXICO, MÉXICO.

Background. Nonalcoholic fatty liver is recognized as a major cause of cirrhosis. The correlation between the degree of severity determined by ultrasound and the risk factors know for steatosis has not been described in the Mexican population. **Objective.** To determine the relationship between the risk factors known for nonalcoholic fatty liver and ultrasonographic severity signs of fatty liver infiltration. **Material and methods.** A retrospective analysis of 102 patients with fatty liver was made. The degree of fatty liver infiltration was estimated by ultrasound. The radiologist was blinded to the clinical characteristics of the patients. The degree of steatosis was classified into 3 categories: mild (hepatic parenchyma discretely hyperechoic relative to the renal parenchyma, diaphragm and inferior vena cava); moderate (notable increment in the hepatic parenchyma echogenicity, with difficulty in assessing the intrahepatic vessels but the suprahepatic vessel can be easily identified); severe (evident increment in the hepatic parenchyma echogenicity and impossibility to visualize the diaphragm, inferior vena cava or intrahepatic vessel). Statistical analysis, descriptive statistics, and indices of dispersion were made with the SPSS 17 program. A $p \leq 0.05$ was considered statistically significant. **Results.** Patients were classified in two groups: mild steatosis (MS) and moderate/severe steatosis (MMS). A slight majority of patients were allocated to the MS group (53 *vs.* 49 subjects). We founded that 45% (46/102) of all subjects included had normal liver biochemistry. A greater part of these patients [(78%) 36/46] had MSS. Steatohepatitis was demonstrated by liver biopsy and altered liver biochemistry in 55% (56/102) subjects. The preponderance of the cases had MMS [73% (41/56)]. The following risk factors in the MSS group were founded: hypertension 71% (35/49), DM2 71% (35/49), metabolic syndrome 20% (10/49), dyslipidemia [47% (22/46)], and hypothyroidism [40% (20/49)]. A greater proportion of the MMS subjects [72.8% (37/49)] had a least 2 comorbidities. The vast majority in the MMS group [87.5% (42/49)] had dyslipidemia plus any other comorbidity. **Conclusions.** The greater presence of risk factors correlated positively ultrasonographic severity signs of fatty liver infiltration. Hypertension and DM2 are the most prevalent comorbidities. The most important risk factor for developing moderate to severe steatosis was the combination of dyslipidemia and another risk factor.

014

ULTRASOUND AS THE FIRST TOOL IN THE EVALUATION OF LIVER STEATOSIS: DOES CENTRAL OBESITY IMPACTS THE DIAGNOSIS OF FATTY LIVER DISEASE?

R.C. BROM-VALLADARES,[*] J. GARCÍA-GÓMEZ,[*] L.F. ONATE-OCANA,[**] F. CHABLE-MONTERO,[***] I. LAVENANT,[***] L. ALVA-LÓPEZ,[*] J.F. SÁNCHEZ-ÁVILA[****]

[1]DEPARTAMENTO DE IMAGENOLOGÍA, [**]DEPARTAMENTO DE CIRUGÍA, [***]DEPARTAMENTO DE ANATOMÍA PATOLÓGICA, [****]DEPARTAMENTO DE GASTROENTEROLOGÍA. HOSPITAL Y FUNDACIÓN CLÍNICA MÉDICA SUR, MEXICO CITY.

Background. Ultrasound (US) is the first imaging modality in the detection of fatty liver changes. Mexico's population has become obese in the last decades, mainly with a central distribution. This is associated with increased number of cases of fatty liver disease. We commonly detect difuse increment of the hepatic echogenicity associated with ill-defined hepatic vessels and contour, with or without increment of the hepatic echogenicity when compared to the adjacent kidney. We wonder whether steatosis may be diagnosed under these circumstances. We analize the relationship between the classic US steatosis signs and the abdominal wall thikness, in comparison with computerized tomography (CT) and/or biopsy in the diagnosis of hepatic fat deposition. **Material and methods.** Work in progress: retrospective review of 224 patients with abdominal US and CT or liver biopsy performed simultaneously. Two separate radiologists blinded to each other's results participated. US steatosis signs (liver echogenicity equal or increased to right kidney, presence vs abscense of vessel or diaphragmatic contour bluring) were evaluated; normal liver echogenicity coexistence with blurring of vessels and contours was noted. The abdominal wall thickness was measured with US. Liver CT Hounsfield Units (below 40 HU defines liver steatosis) and/or histological evaluation of steatosis were the standards for comparison. Statistical analysis was performed. **Results.** 224 US liver studies (111 men, 113 women), ages 19 to 82 (average 50.21 years) were compared to 169 abdominal CT and 58 liver biopsies (6 patients had both). Indication of the US evaluation: checkup (N = 137), liver disease (N = 58 biopsies), other (emergency unit, intensive care unit, hospitalization) (N = 29). In 29 cases (12.94% of the sample) we found that the liver had equal echogenicity to the kidney, yet the vessels were blurry (3 cases also had blurry contours). In these cases the correlation of US to CT and biopsy was not significant for steatosis (p = 0.715) (T test) and there was a tendency, altough not significant (p = 0.062) towards a thicker wall (27.51 mm). The thickness of the abdominal wall correlated with the degree of steratosis (p < 0.000, ANOVA test) with average of 22.6mm in normal liver participants and 37.0 mm average in cases of severe steatosis. **Conclusion.** The sonographic evaluation of steatosis may not be accurate in cases of severe wall thickness due to central obesity. Increased echogenicity of the liver VS kidney is key to the diagnosis of liver fatty disease.

015

COMPLEX TREATMENT OF NAFLD PATIENTS WITHOUT HISTOLOGICAL ANSWER ON PREVIOUS THERAPY

E. SAS, V. GRINEVICH, I. KRAVCHUK

DEPARTMENT OF THERAPY POSTGRADUATE, MILITARY-MEDICAL ACADEMY, ST.-PETERSBURG, RUSSIAN FEDERATION.

Objective. The objective of this study was to assess the effectiveness of complex treatment of NAFLD patients without histological answer on previous therapy. **Material and methods.** Prospective Study of 36 NAFLD patients (38-46 years old, BMI > 30), without histological answer on previous therapy. All patients receive biguanides, thiazolidinediones, ursodeoxycholic acid drugs, have positive changes in biochemical markers, but have not any changes in histological grade of steatosis and inflammation level. All patients underwent careful physical examination, accurate collection of anamnesis findings, serum biochemistry and parenteral hepatitis markers evaluating, abdominal ultrasonography, histological evaluating baseline and 2 years later, metagenomic assessment of gut microbiota. All patients followed the basic treatment scheme included dietary, physical regimen, polyunsaturated phosphatidicholine-PUPC (Essentiale® forte N) 1,386 mg daily, Nifuroxazide 800 mg daily, and prebiotic Eubicor® (NPC BIC). **Results.** We find positive correlation between appetite and gut microbiota concentration, the most powerful correlation was with: *Lactobacillus* (r = 0.68, p = 0.0001), *Bifidobacterium* (r = 0.68, p = 0.001), *Clostridiales* (r = 0.82, p = 0.0001), *Clostridium* (r = 0.49, p = 0.013), *Faecalibacterium* (r = 0.73, p = 0,001), *Acidaminococcus* (r = 0.61, p = 0.001), *Anaerotruncus* (r = 0.59, p = 0.002), *Blautia* (r = 0.56, p = 0.003), *Collinsella* (r = 0.65, p = 0.001), *Desulfovibrio* (r = 0.62, p = 0.001), *Dorea* (r = 0.49, p = 0.012), Holdemania (r = 0.53, p = 0.005), *Ruminococcus* (r = 0.52, p = 0.01), *Subdoligranulum* (r = 0.64, p = 0.001), *Paraprevotella* (r = 0.79, p = 0.0001). People with high concentration of *Clostridiales, Faecalibacterium, Dorea, Paraprevotella* in gut microbiota were more inclined to abdominal form of obesity. Histological evaluation find positive correlation between inflammation level and gut microbiota concentration: *Alistipes* (r = 0.4, p = 0.048), *Bilophila* (r = 0.75, p = 0.0001), *Faecalibacterium* (r = 0.44, p = 0.026), *Parasutterella* (r = 0.40, p = 0.046), *Catenibacterium* (r = 0.92, p = 0.0001), *Klebsiella* (r = 0.64, p = 0.001), *Streptococcus* (r = 0.42, p = 0.036), *Peptostreptococcaceae* (r = 0.42, p = 0.036), *Enterobacteriaceae* (r = 0.42, p = 0.036). Moreover after 12 months of treatment the mean value of disease activity evaluated by Metavir scale was A1 in IG. Moreover the results of liver biopsy (histological examination) and Fibromax test showed, that in patients with NAFLD additionally treated by complex treatment, the progress of hepatic fibrosis was significantly slowly. In addition after 6 months of treatment its reduction in IG of steatosis (p < 0.02). **Conclusions.** Patients with resistant form of NAFLD requires complex treatment with PUPC, Nifuroxazide and prebiotics Protobiol. Metagenomic assessment of gut microbiota in future could explain new pathogenetic links of NAFLD.

016

THE EFFECT OF D-GALACTOSAMINE ON LEAN AND STEATOTIC RAT HEPATOCYTES IN PRIMARY CULTURE

Z. ČERVINKOVÁ, M. ČERVINKA, O. KUČERA
CHARLES UNIVERSITY IN PRAGUE, FACULTY OF MEDICINE IN HRADEC KRÁLOVÉ, HRADEC KRÁLOVÉ, CZECH REPUBLIC.

Introduction. Non-alcoholic fatty liver disease is the most common chronic liver disease in the Western world. In previous studies *in vivo* and *in vitro*, we have proved that steatotic hepatocytes are more susceptible to the toxic action of various hepatotoxins (acetaminophen, thioacetamide, tert-butylhydroperoxide) than lean hepatocytes. D-galcatosamine (GalN) is a model hepatotoxin with different mechanisms of its toxicity. GalN hepatotoxicity is primary mediated by inhibition of RNA and glycoprotein synthesis. These alterations are followed by mitochondrial dysfunction, oxidative stress, and hepatocyte apoptosis and/or necrosis. Thus, the aim of our work was to compare the hepatotoxic effect of GalN on hepatocytes isolated from lean and steatotic rat liver. **Material and methods.** Male Wistar rats were fed by standard diet (10% energy from fats) or high-fat diet (70% energy from fats) for 6 weeks. Hepatocytes were isolated by two-step collagenase perfusion and cultured in William's E medium on collagen-coated well-plates. Both lean and fatty hepatocytes were exposed to GalN (1-40 mmol/l) for 24 h. After this period, we tested lactatedehydrogenase leakage (LDH-L), activity of cellular dehydrogenases (WST-1 test), production of reactive oxygen species (ROS) using fluorescent probe DCFDA, level of lipoperoxidation (thiobarbituric acid reactive substances, TBARS), and mitochondrial membrane potential (MMP) using fluorescent probe JC-1. The statistical significance was analysed using one-way ANOVA followed by Tukey-Kramer's test or Kruskal-Wallis test followed by Dunn's test. **Results.** Control steatotic hepatocytes exerted higher LDH leakage, TBARS and ROS production, compared to intact, non-steatotic hepatocytes. In dose dependent manner, GalN induced damage to both lean and fatty hepatocytes, but the injury was more pronounced and induced by lower doses of GalN in steatotic hepatocytes. An increase in LDH-L was observed after incubation with 30 mM ($p < 0.05$) and 20 mM ($p < 0.01$) GalN in lean and steatotic hepatocytes, resp. Similarly, TBARS production was increased from 40 mM GalN in non-fatty cells ($p < 0.01$), whereas in steatotic hepatocytes, lipoperoxidation was elevated from 20 mM GalN ($p < 0.05$). ROS production exerted a dose-dependent increase in both lean and steatotic hepatocytes, but the increase was significantly higher in fatty cells. Contrary to steatotic hepatocytes, incubation with the highest tested concentration of GalN (40 mmol/l) did not lead to the loss of MMP in all lean hepatocytes; fatty hepatocytes exposed to 40 mM GalN lost MMP completely. **Conclusions.** Steatotic hepatocytes exert higher sensitivity to D-galactosamine-induced injury than lean hepatocytes.
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017

AVAILABILITY OF INTRACELLULAR cAMP REGULATES ACTIVATION OF LIVER GLYCOGEN BREAKDOWN IN HIGH-FAT DIET FED MICE

V.A. FERREIRA-DE-GODOY,* D.G. LINHARES-DE-REZENDE,* M. DE-AGUIAR-PRIMO,* M.M. DIAZ-PEDROSA,* F.P. MONTEIRO-SCHIAVON,** R. BARBOSA-BAZOTTE**
**DEPARTMENT OF PHYSIOLOGICAL SCIENCES, **DEPARTMENT OF PHARMACEUTICAL SCIENCES, STATE UNIVERSITY OF MARINGA, BRAZIL.*

Background. The quantity and quality of fat ingested in the diet exert a significant influence on the development of obesity and predisposition to type 2 diabetes and cardiovascular disease. However, little is known regarding the influence of high fat diet rich in saturated fatty acids on glycogen metabolism. Thus, liver glycogen catabolism was evaluated in male Swiss mice fed a high-fat diet rich in saturated fatty acids (HFD) or normal fat diet (NFD) during one week. **Material and methods.** Liver glycogenolysis (LG) and liver glucose production (LGP) were measured either under basal or stimulated conditions (infusion of glycogenolitic agents). Thus, isolated perfused livers from HFD and NFD mice were infused with glycogenolytic agents, i.e., glucagon, epinephrine, phenylephrine, isoproterenol, adenosine-3'-5'-cyclic monophosphate (cAMP), N6, 2'-O-dibutyryl-cAMP (DB-cAMP), 8-bromoadenosine-cAMP (8-Br-cAMP) or N6-monobutyryl-cAMP (N6-MB-cAMP). Moreover, glycemia and liver glycogen content were measured. **Results.** The HFD diet significantly increased inguinal and periepididymal fat deposits.Glycemia, liver glycogen content and basal rate of LGP and LG were not influenced by the HFD. However, LGP and LG were lower ($p < 0.05$) in HFD mice during the infusions of glucagon (1 nM), epinephrine (20 μM) or phenylephrine (20 μM). In contrast, the activation of LGP and LG during the infusion of isoproterenol (20 μM) were not different (HFD vs. NFD). Because glucagon showed the most prominent response, the effect of cAMP, its intracellular mediator, on LGP and LG was investigated. cAMP (150 μM) showed lower activation of LGP and LG in the HFD group. However, the activation of LGP and LG were not influenced by HFD whether DB-cAMP (3 μM), 8-Br-cAMP (3 μM) or N6-MB-cAMP (3 μM) were used. **Conclusions.** Considering that glucagon and cAMP, but not cAMP analogues, showed lower effects on LGP, we can suggest that the process of inactivation of cAMP overcomes its formation in livers of HFD mice. Since the activation of LGP and LG depends on the intracellular availability of cAMP, it can be concluded that cAMP played a pivotal role on the activation of LG in high-fat diet fed mice.
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018

TIBOLONE REVERSES THE STEATOSIS OF LIVER FROM OVARIECTOMIZED WISTAR RATS

L.B. CAMPOS-SHIMADA, E.L. ISHII-IWAMOTO, C.L. SALGUEIRO-PAGADIGORRIA, R.F. GARCIA
UNIVERSITY OF MARINGÁ, BRAZIL.

Introduction. The post-menopausal state is associated with profound alterations in the lipid metabolism which increases the incidence of metabolic syndrome and non-alcoholic fatty liver disease (NAFLD). Tibolone is a synthetic steroid used as an alternative form for the treatment of the symptoms of the

menopause. In this work, the effects of tibolone (0.16 mg/kg) on the liver lipid metabolism, plasma lipid profile as well as on the glycemia were assessed. **Material and methods.** Thirteen weeks after the surgical procedures of ovary removal, ovariectomized Wistar rats (OVX) were treated with daily doses of vehicle (OVX) or tibolone (TIB) over a period of 21 days. Thereafter, the overnight fasted rats were anaesthetized for the blood collection as well as for the removal of fat depots and liver. The weights of the adipose depots were matched with body weights and used to calculate the adiposity index. The liver lipid contents were assessed in these animals. Besides, the activity of liver fatty acid synthase (FAS) and the capacities of oxidizing fatty acid by the mitochondrial and peroxisomal pathways were evaluated. **Results.** At the end of the experimental period, OVX rats exhibited increased body weight gain and adiposity index as compared to control animals. The treatment of these animals with tibolone reversed these undesirable parameters. The glycemia and the plasma levels of triacylglycerol (TAG), LDL- and VLDL-cholesterol were increased in OVX animals. TIB treatment reduced the glycemia, total-, LDL- and HDL-cholesterol levels. However it was ineffective in reducing the TAG and VLDL-cholesterol levels. The liver total lipid contents and TAG levels were increased in 30% and 42%, respectively, in OVX rats. In treated animals, these values returned to levels similar to those found in control rats. The liver total cholesterol contents were unaffected in these animals. No difference was observed in the mitochondrial β-oxidation capacities between the three groups of animals. The peroxisomal β-oxidation capacities were reduced in OVX and were restored by the treatment with TIB. The FAS activity was reduced in OVX rats and further reduced by tibolone treatment. **Conclusion.** Tibolone was effective in reversing NAFLD associated with estrogen deficiency, probably by increased the peroxisomal β-oxidation and by reducing the FAS activity.

019

TIBOLONE IMPROVES THE LIVER REDOX STATE FROM OVARIECTOMIZED WISTAR RATS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

L.B. CAMPOS-SHIMADA, D.A.M. HERMOSO, R.F. GARCIA, E.L. ISHII-IWAMOTO, C.L. SALGUEIRO-PAGADIGORRIA
UNIVERSITY OF MARINGÁ, BRAZIL.

Introduction. Estrogen deficiency is associated with higher incidence of metabolic syndrome (MS) and non-alcoholic fatty liver disease (NAFLD).The fat liver accumulation is associated with oxidative stress and this is a contributing factor to the evolution of the disease to more severe forms. Tibolone is a synthetic steroid that has proven to be effective in treating many menopause symptoms. In this study, an evaluation of the effects of tibolone on the liver redox status in an animal model of estrogen deficiency with NAFLD was performed. **Material and methods.** Thirteen weeks after the surgical procedures of ovary removal, ovariectomized Wistar rats were treated with daily doses of tibolone (TIB-0.16 mg/kg) or vehicle (OVX), over a period of 21 days. The results were compared to sham-operated (control) rats. After this period, the overnight fasted rats were anaesthetized to the liver removal. The total lipid levels were measured by gravimetry to confirm the existence of NAFLD. The mitochondrial generation of reactive oxygen species (ROS) was assessed. Freeze-clamped livers or isolated mitochondria were used for evaluation of reduced glutathione (GSH) and carbonyl protein contents. Besides, the activities of the following antioxidant enzymes were assessed in the cytosol: glucose-6-phosphate dehydrogenase (G6PD), glutathione reductase (GR), glutathione peroxidase (GPX) and Cu, Zn-superoxide dismutase (Cu, Zn-SOD). Results: At the final of the experimental period, livers from OVX rats exhibited increased total lipid contents (+27%). The treatment with TIB returned these values to levels similar to control rats. TIB had a beneficial effect on the GSH and carbonyl protein contents, both in mitochondria and in liver homogenate, which were significantly reduced in OVX rats, and it was reestablished by treatment to values similar to control rats. In OVX rats, the mitochondrial ROS generation was increased in 80%. In treated animals, the ROS generation was reduced in about 30% as compared to untreated OVX rats, although it remained increased by 26%, as compared to control rats. In OVX rats, the G6PD and GPX activities were reduced, although there is no difference in the activities of GR or Cu, Zn-SOD. TIB rats presented an increased in G6PD activity as compared to OVX rats. In contrast, no differences were observed in the GPX and GR activities. The Cu, Zn-SOD activity was slightly, but significantly reduced by treatment with tibolone. Conclusion: Tibolone reduced the liver lipid accumulation and this effect was accompanied by beneficial effects on liver redox status.

020

METABOLIC ALTERATIONS IN PRE AND POSTMENOPAUSIC WOMEN WITH NONALCOHOLIC STEATOHEPATITIS

H. RODRÍGUEZ-HERNÁNDEZ, M. MACÍAS-GRANADOS, K. ACEVEDO CASTILLO, M. MORÁN YBARRA, M. SANDOVAL-RUIZ, J.M. GARCÍA-CONTRERAS, O. ALMEIDA-BORJÓN, M.A. REYES-ROMERO
FACULTAD DE MEDICINA Y NUTRICIÓN, UNIVERSIDAD JUÁREZ DEL ESTADO DE DURANGO, DURANGO, DGO., MÉXICO.

Introduction. Patients with non-alcoholic steatohepatitis (NASH) have many metabolic alterations, including hyperglycemia, hypertriglyceridemia, hypercholesterolemia and obesity. NASH has been associated with an increase in cardiovascular and liver related mortality. Many patients with NASH develop hepatocellular injury, necrosis and fibrosis; therefore, NASH is a public health problem that needs improvement in primary care. The aim of this work was to compare variables between pre and postmenopausic women with hepatic steatosis. **Material and methods.** We included 414 obese women with diagnosis of hepatic steatosis. Group I (G-I): 217 age < 45 years; group II (G-II): 197, age ≥ 45 years. We determined familiar history of diabetes, hypertension, hypertriglyceridemia, and diagnosis of obesity, diabetes, hypertension and hypertriglyceridemia. Previous diagnosis of liver disease, serum creatinine level ≥ 1.5 mg/dL, severe life-limiting medical illness, pregnancy, alcohol consumption ≥ 30 g per day were exclusion criteria. We determined in venous whole blood glucose, cholesterol, triglycerides, AST and ALT levels; measurements as body mass index (BMI) and total body fat (TBF) were done. Statistical analysis was performed by χ^2 test for qualitative variables and difference between groups with paired Student t-test or Mann-Whitney U-test. **Results.** Median age for women was 36 years in G-I and 53 in G-II. There were statistical significant differences in familiar history of obesity and triglyceridemia as well as in diagnosis of obesity, diabetes, hypertension and hypertriglyceridemia. AST and ALT levels were higher in G-II (Table). **Conclusions.** Our results show that elder obese women with NASH have a higher increase in aminotransferases as well as in other metabolic al-

Table. (020) Characteristics of the target population.

	G-I < 45 years (n = 217)	G-II > 45 years (n = 197)	p-value
Age, years, medium and CI rank	36 (30-41)	53 (50-58)	< 0.001
Family history of obesity, n (%)	184 (84)	151 (76.6)	0.037
Family history of diabetes, n (%)	167 (76.9)	140 (71)	0.180
Family history of hypertriglyceridemia, n (%)	110 (52.3)	78 (39.6)	0.027
Family history of hypertension, n (%)	159 (75.7)	146 (74.1)	0.997
Diabetes, n (%)	27 (12.8)	47 (23.8)	0.004
Hypertriglyceridemia, n (%)	47 (22.3)	71 (36)	0.002
Hypertension, n (%)	46 (21.9)	106 (53.8)	< 0.001
Weight, kg ± SD	88.6 ± 14.6	86.5 ± 13.3	0.133
Height, m	1.6 ± 0.1	1.6 ± 0.1	0.0001
BMI, kg/m^2	35.8 ± 5.4	35.9 ± 4.9	0.83
Total body fat, %	44.1 ± 6.3	44.6 ± 8.9	0.517
Glucose, mg/dL ± SD	103.6 ± 37.8	107.5± 69.7	0.491
Total cholesterol, mg/dL ± SD	216.1 ± 58.3	226.3± 54.7	0.068
Triglycerides mg/dL ± SD	217.4 ± 95.0	248.9± 83.3	0.0001
AST U/dL ± SD	43.3 ± 11.1	46.4 ± 10.9	0.005
ALT U/dL ± SD	57.48 ± 17.7	61.5 ± 11.4	0.005

Table . (021).

Comorbidity	NAFLD (n = 43) Admission	Last visit	P	NASH (n = 80) Admission	Last visit	P
Obesity	19/24	15/28	0.424	45/35	41/39	0.289
T2DM	11/34	15/28	< 0.001	31/49	39/41	0.125
HBP	9/32	15/28	0.008	36/44	49/31	0.031
Dyslipidemia	34/9	37/6	0.002	56/24	66/14	0.25
MS	11/32	15/28	< 0.001	30/50	45/37	0.125

terations, which can be related to age and hormonal status. Further studies are warranted.

021

IMPACT OF COMORBIDITIES IN LONG TERM OUTCOMES IN NAFLD. A ONE CENTER EXPERIENCE

L.A. PÉREZ-ARREDONDO,* R.F. MARTÍNEZ-MACÍAS,* G. ALARCÓN-GALVAN,** P. CORDERO-PÉREZ,* L.E. MUÑOZ-ESPINOSA*
*UNIDAD DE HÍGADO, FACULTAD DE MEDICINA, UANL, MONTERREY, NUEVO LEÓN, MÉXICO.
**DEPARTAMENTO DE ANATOMÍA PATOLÓGICA, HOSPITAL UNIVERSITARIO Y FACULTAD DE MEDICINA, UANL, MONTERREY, NUEVO LEÓN, MÉXICO.

Introduction. Non alcoholic fatty liver disease (NAFLD) is now the commonest cause of chronic liver disease. This rapid increase has been closely associated with current epidemic of metabolic syndrome (MS), composed by type 2 diabetes mellitus (T2DM), dyslipidemia, high blood pressure (HBP) and obesity. These metabolic risk factors (MRF) have been well described in NAFLD and non alcoholic steatohepatitis (NASH). Mortality in NAFLD & NASH patients is higher than overall population. The aim of this study was to determine MRF influence over NAFLD & NASH long term follow up (FU) among patients from northeast of Mexico. **Material and methods.** This is a retrospective cohort with 123 patients seen at the Liver Unit from 1994 to 2013 and with FU ≥ 12 months (mean FU of 61 ± 48 months). Group 1: NAFLD n = 43 and group 2 NASH n = 80. Diagnosis was confirmed by liver biopsy, ultrasonography and/or Fibromax®. Other etiologies were excluded. The presence of MRF were seek during FU: obesity, T2DM, High blood pressure, dyslipidemia and metabolic syndrome (MS). **Results.** There was a progression of HBP, T2DM, dyslipidemia and MS in NAFLD and NASH in spite of a decrease in obesity in both groups during the FU period. An increase in the number of comorbidities was observed in NASH but not in NAFLD. No patient with NAFLD developed cirrhosis (Table). 42/80 NASH had cirrhosis on admission and 3 developed cirrhosis in FU. There was no difference among cirrhotic patients with (cMS) or without (sMS) in regards to ascites, encephalopathy, portal hypertension (PH) and D'Amico progression. However, mortality was more common in patients with cirrhosis cMS (8/22.36%) *vs.* sMS (3/20, 15%) (p = 0.043). Most deaths were liver related (9/12). **Conclusions.** Comorbidities progression was seen in both NAFLD and NASH during 61 months FU, although the number of comorbidities was higher in NASH. 53% of NASH patients had cirrhosis on admission. No difference in cirrhosis complications were seen in patients c&sMS. Overall mortality was10%, however, it was higher in cirrhotic patients, particularly in those with cirrhosis an MS (36%).

022

DETERMINATION OF NONINVASIVE MARKERS ON THE DIAGNOSIS OF SEVERE FIBROSIS ON NAFLD

J.A. CARMONA-CASTAÑEDA, L. HERNANDEZ-FLORES, S. MEJÍA-LOZA, F. ZAMARRIPA-DORSEY
HOSPITAL JUÁREZ DE MÉXICO, MEXICO CITY.

Background. The nonalcoholic fatty liver disease (NAFLD) includes both simple fatty liver and NASH. It requires evidence of hepatic steatosis, and histological damage in hepato-

Table. (023)

	ICAM-1 x ± SD	IL-6 x ± SD	TNF-α x ± SD	VEGF x ± SD	PDGF x ± SD	VEGF-EG x ± SD
NASH	5,482 ± 613*	2,430 ± 1,506*	3,686 ± 1,409*	2,267 ± 486*	4,508 ± 1,677	2,146 ± 1,914*
CHC	2,145 ± 1,011	726 ± 735	677 ± 747	421 ± 557	4,814 ± 3,161	1,225 ± 1,388
ALD	1,830 ± 1,224**	516 ± 516 ± 603**	437 ± 70**	554 ± 619**	3,922 ± 855	799 ± 1,046**

*p < 0.05. NASH *vs.* CHC. **p < 0.05, NASH *vs.* ALD.

cytes and there are no causes for secondary hepatic fat accumulation. Generally, fibrosis It is the most important histopathological change that leads to chronic liver disease. The aim of this study was to determine the severity of liver fibrosis trough noninvasive markers on NAFLD. **Material and methods.** Retrospective study was conducted at Hospital Juarez de México from January to December 2013, based on an analysis of 73 patients with suspected of NAFLD (because of abnormal liver function tests, criteria for metabolic syndrome and ultrasound with hepatic steatosis) to which transient elastography (ET) was performed as an alternative to liver biopsy for the diagnosis of NASH. The diagnosis was based on the folllowing criteria: [elastography with presence of fat infiltration > 10% and presence of advanced fibrosis (F3-F4)]. Of the 73 patients met criteria 32 patients, scores known NAFLD score, and FIB-4 score were applied, and their comparison with ET. The cutoff values used for the diagnosis of severe fibrosis were: NAFLD score > 0.676, and FIB-4 score > 3.25. **Results.** Of 32 patients, the median age of the patients was 44 years, with a range of 11 to 82 years. There were 13 males and 19 females, where 40.65% percent of the patients had stage > F3-F4 by ET, 23.33% by NAFLD score and 23.33% FIB-4. ET was found 76.9% in male (F4) and female 23% (F3). FIB-4 score result in 77% and the age distribuition (male showed two peaks ages, the thirties and fifties), and NAFLD score in 85% in male. Transaminase levels were highest (50%) in F3. Conclusion The increased prevalence of men and elderly subjects among patients with severe fibrosis suggests aging may be risk factors for progression, and diabetes mellitus was associated in 50% with these score to severe fibrosis as is referred to in previous studies. Regarding the use of the FIB-4 score was 26.66% at F3-F4, in NAFLD score resulted on 23.33% with significant fibrosis. Whereby said association between these scales may be useful to identify NASH among NAFLD patients.

023

APLICABILITY OF PROINFLAMATORY CYTOKINES IN THE DIFFERENTIATION OF NON-ALCOHOLIC FATTY LIVER DISEASE, CHRONIC HEPATITIS C AND ALCOHOLIC LIVER DISEASE

P. CORDERO-PÉREZ,* R.F. MARTÍNEZ-MACÍAS,* L.A. PÉREZ-ARREDONDO,* I.A. CURA-ESQUIVEL,* E.G. GUTIÉRREZ-REYES,** M.C. GUTIÉRREZ-RUIZ C.,*** L.E. MUÑOZ-ESPINOSA*
**UNIDAD DE HÍGADO, HOSPITAL UNIVERSITARIO, UANL, MONTERREY, NL.*
***HIPAM, HOSPITAL GENERAL DE MÉXICO, SECRETARÍA DE SALUD, MEXICO CITY.*
****LABORATORIO DE FISIOLOGÍA CELULAR, UNIVERSIDAD AUTÓNOMA METROPOLITANA, MEXICO CITY.*

Introduction. Cytokines interactions comprise a broad number of inflammatory and immunoregulatory processes. Increased serum levels of them have been reported in persistent inflammatory conditions such as non-alcoholic steatohepatitis (NASH), chronic hepatitis C (CHC) and alcoholic liver disease (ALD). The aim of this study was to compare cytokines IL6, TNF-α, VEGF, VEGF-EG, PDGF and ICAM-1 levels in patients with NASH, CHC and ALD. **Material and methods.** Ninety patients seen in two Mexican outpatient clinics (UANL Liver Unit & HIPAM clinic) were included: NASH (30), CHC (30) and ALD (30). NASH cases were diagnosed through a liver biopsy, CHC was confirmed by molecular methods (HCV-PCR), CHC and ALD patients were diagnosed either by liver biopsy or non-invasive markers. Data regarding demographics, anthropometrics, biochemical profile, fibrosis grade and cytokine levels (ELISA) was recorded in all groups. **Results.** A statistically significant difference was found in 5/6 mediators studied among these three etiologies (Table). In NASH, correlations of TNF-α with VEGF (r= 0.515, p = 0.004) and cholesterol (r = -0.395, p = 0.034); IL-6 with VEGF-EG (r = 0.831, p < 0.001) and total bilirubin (TB) (r = -0.429, p = 0.020); ICAM-1 with cholesterol (r = -0.395, p = 0.034) and insulin (r = 0.810, p = 0.041); and PDGF with GGT (r = -0.499, p = 0.009); were found. In CHC correlations were found in VEGF with TNF-α (r = 0.447, p = 0.013) and PDGF (r = 0.411, p = 0.024); and PDGF with TB (r = -0.438, p = 0.025). Whereas, in ALD group ICAM-1 correlated with albumin (r = -0.360, p = 0.049), AST (r = 0.360, p = 0.049) and IL6 (r = -0.420, p = 0.021); TNF-α with cholesterol (r = 0.880, p = 0.037) and triglycerides (r = 0.420, p = 0.021); and PDGF with albumin (r = -0.420, p = 0.022). **Conclusions.** The inflammatory response observed was the highest in the NASH group, probably reflecting major activity in non-cirrhotic patients (79%), with most correlations between cytokines. In CHC VEGF, TNF-α and PDGF reflected an inflammatory state (73% non cirrhotics). In ALD (87% cirrhotics), TNF-α could be associated with steatosis infiltration, and PDGF could reflect major inflammation in more advanced disease. These abnormalities in cytokine profile can influence in the pathophysiology of liver injury.
This work was supported by PROMEP-SEP.

D. CIRRHOSIS OF THE LIVER AND ITS COMPLICATIONS

001

POCKET ULTRASOUND DEVICE AS A COMPLEMENT TO PHYSICAL EXAM FOR ASCITES EVALUATION AND GUIDED PARACENTESIS

D. KEIL RÍOS, H. TERRAZAS SOLÍS, I. GARCÍA JUÁREZ
INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN (INCMNSZ). CIUDAD DE MÉXICO, MÉXICO.

Introduction. The Pocket Ultrasound Device (PUD) is a new tool that can be useful for early ascites detection. Guided paracentesis with abdominal ultrasound (AUS) is superior next

to blind paracentesis, so PUD could be relevant in this scenario. The aims of this study are to assess the PUD and relevant clinical findings diagnostic usefulness for ascites detection compared to the diagnostic reference standard, study the agreement between the PUD and AUS for ascites detection ant to identify the frequency of technical difficulties and complications related to PUD guided paracentesis. **Material and methods.** This observational study included patients from the INCMNSZ with suspected ascites who were examined between March 2011 and May 2013 with the PUD to identify the presence of ascites. The examinations were performed by an internal medicine resident who received two week training in the use of PUD in the Department of Radiology. Sensitivity (sens), specificity (spec), positive and negative likelihood ratios (LR) of the PUD and relevant clinical findings for ascites detection compared to the diagnostic reference standard were calculated. The diagnostic reference standard was fluid aspiration by paracentesis or fluid visualization by AUS or computed tomography (CT). Patients who didn't have a reference standard were excluded from the study. The agreement between the PUD and AUS was assessed by using kappa coefficient. The frequency of technical difficulties and complications directly associated with PUD guided paracentesis was identified. **Results.** 89 patients were included in the study with 94 examinations performed with the PUD. The most reliable clinical findings were the fluid wave (sens 75%, spec 86.4%, +LR 5.5, -LR 0.29), the shifting dullness (sens 58.3%, spec 77.3%, +LR 2.57, -LR 0.54), an increased girth (sens 88.9%, spec 59.1%, +LR 2.17, -LR 0.18) and fluid visualization by PUD (sens 95.8%, spec 81.8%, +LR 5.27, -LR 0.05). In 51 of the examinations, the patient also had an AUS performed. The agreement between the PUD and AUS for ascites detection was good, with a kappa coefficient of 0.792 ($p < 0.001$). A PUD guided paracentesis was performed in 40 patients. Technical difficulties occurred in 5% and minor complications in 7.5% of the procedures. No severe complications or deaths were reported. **Conclusions.** The PUD is a reliable tool as a complement to physical exam for ascites detection. It has a good agreement with the AUS, one of the diagnostic reference standards. There were no severe complications or deaths related to PUD guided paracentesis.

002

DUPLEX DOPPLER ULTRASOUND OF THE HEPATIC ARTERY IN PATIENTS WITH CIRRHOSIS

M.C. ÁVILA-LANGARICA, C.I. BLANCO-VELA, A. ÁNGELES-LABRA, M.A. BARRAGÁN, F. ZAMARRIPA-DORSEY
SERVICIO DE GASTROENTEROLOGÍA. HOSPITAL JUÁREZ DE MÉXICO. CIUDAD DE MÉXICO, MÉXICO.

Background. The progression of liver cirrhosis eventually increases cardiac output, while blood pressure and systemic vascular resistance are reduced. A complex behavior of portal hemodynamic to hepatic artery and system circulation has not yet been presented. There is a lack in knowledge about the correlation of local and systemic circulation parameters to the degree of liver failure, with respect to presence of complications of portal hypertension such as ascites, variceal bleeding, and hepatic encephalopathy. **Objetive.** To determine the value of measuring quantitative parameters of portal, hepatic, and splanchnic circulation by duplex Doppler ultrasonography (DDU), to predict portal hypertension related complications. **Material and methods.** In this study, resistive indexes (RI) of hepatic artery and portal vein, patency and direction of flow in portal veins and branches, time-averaged mean blood velocity, and caliber of portal vein were calculated with DDU in 31 ambulatory cirrhotic patients. Doppler findings were compared with the presence of encephalopathy, ascites, and variceal bleeding during the year post-DDU. The frequencies are expressed as percentages, the continuous variables are expressed as median and standard deviation. Linear regression model was used to look for the variables related to complications. **Results.** The median age of the patients was 55.32 ± 9.84 and 61.3% were female. The median MELD was 12.46 ± 5.02. The main etiology of cirrhosis was alcohol in 37.5%. The median of hepatic artery RI was 0.73 ± 0.07 and portal vein RI was 0.27 ±10. The portal diameter in inspiration was 13.25 ± 2.96. The peak velocity of portal vein was 26.33 ± 8.03 mm/s, and from hepatic artery 73.54 ± 31.54 mm/s, and from portal vein 37.78 ± 20.90 mm/s. At the end of the study 6.5% of the subjects presented variceal bleeding, 3.3% hepatic encephalopathy and 38% ascites. **Conclusions.** In cirrhotic patients an elevated hepatic artery diameter or PSV measurement is suggestive of progression to upper gastrointestinal bleeding. The portal diameter was related to encephalopathy.

003

CEREBRAL ARTERIOVENOUS MALFORMATIONS IN CIRRHOTIC PATIENTS: DOES HEPATOBRAIN SYNDROME EXIST?

M. PADILLA-MACHACA, R. MAYORGA-MÁRQUEZ, F. CARRASCO-MASCARO, O. MANTILLA-CRUZATTI, C. RONDÓN-LEYVA, J.C. CHAMAN-ORTIZ
DEPARTAMENTO DE TRASPLANTES. HOSPITAL NACIONAL GUILLERMO ALMENARA I. LIMA. PERÚ.

Background or Introduction. Arterial and arteriovenous abnormalities are reported in association with advanced liver disease, those most commonly recognized are spider naevi, pulmonary arteriovenous shunts, and generalized vasodilatation. It's estimated that about one in 200-500 people may have a cerebral arteriovenous malformation (AVM). The purpose of this report is present the first cases of cerebral AVM in association with cirrhosis. **Material and methods.** Chart reviews of 256 cirrhotic patients in the pretransplant evaluation and immediately liver transplant patient (< 30 days), who developed complications of the central nervous system: seizures, cerebral hemorrhage, and persistent headache, loss of consciousness, sudden and severe headache, nausea, vomiting, and blurred vision. Diagnosis was established by neuroimaging studies CT, MRI or cerebral angiography after a complete neurologist/neurosurgeon evaluation. **Results.** We found 4 cases: 2 pretransplant (preLTx) and 2 post-transplant patients (post LTx) with cerebral AVMs. Ages: 12-50y (average: 31.2). Etiology of cirrhosis: autoimmune hepatitis (AIH): 50%, primary biliary cirrhosis (PBC): 50%, MELD score: 22-33 (average: 25.8%). Hepatopulmonary syndrome: (HPS): 75% (Table). **Conclusions.** The structural changes in cirrhotic patients, such as the cerebral AVMs as we describe have not previously reported. Our findings show an unusual frequency of Cerebral AVM that suggests the possibility of a new feature of advanced liver disease, especially in association with advanced liver disease and HPS. Preliminary data shown are too small to generalize this association; however we recommend a thorough neurological and imaging study to confirm or rule out this association in patients presenting with symptoms related or manifestations of hepatopulmonary syndrome.

Table. (003)

N	Age	Sex	Diagnosis	MELD	Cerebral AVM location	Main symptom	HPS	Treatment	Condition
1	14	F	Autoimmune hepatitis	33	Right carotid siphon	Seizures	Moderate	Stent pacement	Post LTx
2	49	F	PBC	24	Right posterior communicating aneurysm	Sub-arachnoid hemorrhage	No	Surgery	Pret LTx
3	12	M	Autoimmune hepatitis	24	Right cerebral intraventricular	Headache	Very severe	None	Pre LTx
4	50	F	PBC	22	Middle cerebral	Seizures	Mild	None	Post LTx

004

LIGANDS FROM GRAM-POSITIVE BACTERIA CONTRIBUTE TO IMMUNE REGULATION MECHANISMS IN CHRONIC LIVER DISEASE PATIENTS

V.J. BARBERO-BECERRA,[*,†] C. MALDONADO-BERNAL,[‡,§] M.C. GUTIÉRREZ-RUIZ,[||] F.I. TÉLLEZ-ÁVILA,[†] R. ALFARO-LARA,[†] JOSÉ DELGADO-DOMÍNGUEZ,[¶] MISAEL URIBE,[*] FLORENCIA VARGAS-VORÁCKOVÁ[†(†)]

[*]UNIDAD DE HÍGADO, FUNDACIÓN CLÍNICA MÉDICA SUR. MÉXICO D.F., MÉXICO.
[†]DEPARTAMENTO DE GASTROENTEROLOGÍA, INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MÉXICO D.F., MÉXICO.
[‡]UNIDAD DE INVESTIGACIÓN MÉDICA EN ENFERMEDADES INFECCIOSAS Y PARASITARIAS, HOSPITAL DE PEDIATRÍA CMN, SIGLO XXI, IMSS, MÉXICO, D.F., MÉXICO.
[§]UNIDAD DE INVESTIGACIÓN EN ENFERMEDADES ONCOLÓGICAS, HOSPITAL INFANTIL DE MÉXICO "FEDERICO GÓMEZ", MÉXICO, D.F., MÉXICO.
[||]LABORATORIO DE FISIOLOGÍA CELULAR, DIVISIÓN DE CIENCIAS DE LA SALUD, UNIVERSIDAD AUTÓNOMA METROPOLITANA-IZTAPALAPA, MÉXICO, D.F. MÉXICO.
[¶]DEPARTAMENTO DE MEDICINA EXPERIMENTAL, UNIVERSIDAD NACIONAL AUTÓNOMA DE MÉXICO. MÉXICO, D.F., MÉXICO.

Background. Chronic liver disease patients exhibit bacterial translocation which triggers bacteremia and endotoxemia episodes commonly caused by gram-negative bacteria, however, gram-positive bacteria infections also appear to influence in clinical sepsis features. Previously, we have been demonstrated that peripheral blood mononuclear cells (PBMCs) obtained from chronic liver disease patients exposed to lipopolysaccharide (LPS) or lipoteichoic acid (LTA) down-regulate CD14, TLR2 and TLR4 membrane expression and increased TNFα, IL-1β, IL-6, IL-12 and IL-10 secretion (Barbero, *et al.*, 2011). Therefore, the aim of this study was to determine if down-regulation receptor expression observed was due to a regulation at transcriptional level or an internalization receptor mechanism after LPS or LTA exposure. It also compares the ability of ligands from gram-negative and gram-positive bacteria, in promoting internalization-receptor mechanisms and gene expression of inflammatory mediators in chronic liver disease patients *vs.* healthy subjects. **Material and methods.** PBMCs obtained of 12 ambulatory patients with chronic liver disease and 12 healthy subjects were studied. PBMCs were isolated and exposed to LPS or LTA. CD14, toll-like receptor 2, 4, tumor necrosis factor (TNF) α, interleukin (IL)-1β, IL-6, IL-12 and IL-10 mRNA expression was determined by real-time PCR. Intracellular CD14, toll-like receptor 2 and 4 expression was determined using flow cytometry. The data were presented as median (minimum and maximum) values. The Mann-Whitney test was used to analyze differences between groups and the Wilcoxon sign-rank test was used to analyze differences between exposure vs. non-exposure to LPS or LTA. **Results.** Chronic liver disease was due to alcohol (3), cryptogenic (8) and NAFLD (1). Child-Pugh-Turcotte classification showed 4 stage A patients, 7 stage B patients, and 1 stage C patient. Exposure to LPS induced a significant increase in PBMC mRNA expression, primarily TLR2 ($P \leq 0.003$), IL-1β ($P \leq 0.002$), and TNF-α ($P \leq 0.01$), meanwhile LTA induced a decrease of IL-12 mRNA expression ($P \leq 0.04$) in the PBMCs of chronic liver disease patients and a decrease of TNF-α mRNA expression between chronic liver disease patients *vs.* healthy subjects ($P \leq 0.05$). Moreover, LPS induces a decrease in CD14 ($P \leq 0.02$) and an increase of TLR2 ($P \leq 0.01$) intracellular expression in the PBMCs of chronic liver disease patients vs. healthy subjects ($P \leq 0.05$). **Conclusion.** Gram positive bacteria might contribute as an immunoregulatory mediator at transcriptional level in chronic liver disease. Internalization and compensation membrane receptor mechanisms probably occurred in chronic liver disease patients, where gram negative bacteria seem to take leadership at this level.

005

PROGNOSTIC INFLUENCE OF ETIOLOGY IN PORTAL VEIN THROMBOSIS

L. ILIESCU, L. TOMA, C. ORBAN, A. TANASE
FUNDENI CLINICAL INSTITUTE, BUCHAREST, ROMANIA.

Background and aims. Portal vein thrombosis (PVT) is commonly seen in end stage liver disease but it can also occur in a variety of solid or blood tumors. This study aims to evaluate the etiology of PVT and its' impact on one year survival. **Material and methods.** We performed a prospective observational study which included 75 patients with TVP admitted to the Department of Internal Medicine of Fundeni Clinical Institute between August 2011 and August 2012. We evaluated the patients' clinical status, pro and anticoagulant status and they were followed up for one year. **Results.** The study included 75 patients: 43% male, 57% female, with a mean age of 55 years. There were 50 patients with liver cirrhosis, among which 27 had hepatocellular carcinoma. Ten patients had PVT secondary to solid cancers, while 10 patients with PVT had haematologic cancers. Five patients had idiopathic PVT. In patients with liver disease, the values of D-dimer and protein S correlated with the severity of the disease. At one year follow-up we repot the following survival rates: 48% patients with liver cirrhosis without hepatocellular carcinoma, 100% patients with liver cirrhosis without hepatocellular carcinoma, 30% patients with solid tumor underlying PVT, 100% patients with haematologic underlying PVT and 100% patients with idiopathic PVT. **Conclusion.** The etiology and coagulant status are important prognosis factors in patients with PVT.

Patients with solid cancers, including liver cancer have the lowest survival rates, while patients with hematological conditions or idiopathic PVT have the best outcomes.

006

ARTERIAL BLOOD PRESSURE IS CLOSELY RELATED TO ASCITES DEVELOPMENT IN COMPENSATED HCV-RELATED CIRRHOSIS

EDUARDO VILAR-GOMEZ, ANA TORRES-GONZALEZ, LUIS CALZADILLA-BERTOT, ALI YASELLS-GARCIA, YOAN SANCHEZ-RODRIGUEZ, YADINA MARTINEZ-PEREZ
DEPARTMENT OF HEPATOLOGY. NATIONAL INSTITUTE OF GASTROENTEROLOGY, HAVANA, CUBA.

Background. Arterial blood pressure (BP) is a reliable marker of circulatory dysfunction in cirrhotic patients. There are no prospective studies evaluating the association between different levels of arterial BP and ascites development in compensated cirrhotic patients. Therefore, we evaluated the relationship between arterial BP and ascites development in compensated cirrhotic patients. **Material and methods.** A total of 402 patients with compensated HCV-related cirrhosis were prospectively followed during 6 years to identify ascites development. At baseline, patients underwent systolic, diastolic and mean arterial pressure (MAP) measurements. Any history of arterial hypertension was also recorded. The occurrence of events such as bleeding, hepatocellular carcinoma, death and liver transplantation prior to ascites development were considered as competing risk events. **Results.** Over a median of 156 weeks, ascites occurred in 54 patients (13%). At baseline, MAP was significantly lower in patients with ascites development (75.9 mm/Hg [95%CI, 70.3-84.3]) than those without ascites (93.6 mm/Hg [95% CI: 86.6-102.3]). After adjusting for covariates, the 6-year cumulative incidence of ascites was 40% (95%CI, 34-48%) for patients with MAP < 83.32 mm/Hg. In contrast, cumulative incidences of ascites were almost similar among patients with MAP values between 83.32 mm/Hg and 93.32 mm/Hg (7% [95% CI: 4-12%]), between 93.32 mm/Hg and 100.31 mm/Hg (5% [95% CI: 4-11%]) or higher than 100.31 mm/Hg (3% [95% CI: 1-6%]). The MAP was an independent predictor of ascites development. Conclusions: The MAP is closely related to the development of ascites in compensated HCV-related cirrhosis. The risk of ascites development increases in 4.4 fold for subjects with MAP values < 83.32 mm/Hg.

007

PRONOSTIC SCORES TO DETERMINE RISK OF MORTALITY AND REEBLEDING IN PATIENTS WITH VARICEAL UPPER GASTROINTESTINAL BLEEDING

G. MARTÍNEZ-RAMÍREZ, A. LÓPEZ-LURÌA, S. MEJÍA-LOZA, E. JUÁREZ-VALDES, F. ZAMARRIPA-DORSEY
HOSPITAL JUÁREZ DE MÉXICO. MEXICO CITY, MEXICO.

Introduction. Variceal upper gastrointestinal bleeding (UGIB) in patients with hepatic failure (HF) is a common and one of the leading causes of death in these patients complication. There are several models with different variables that allow stratification based on risk of death and could be used to guide more aggressive therapeutic decisions in patients with higher risk. It has been observed that the severity of liver disease determined by scoring MELD is a significant predictor of survival after variceal bleeding, even though the MELD is not a scale described for rebleeding but for predicting terminal liver disease. As the scales designed to predict end-stage liver disease may be useful in determining the prognosis of patients with a complication of HF as variceal UGIB event, plus there are other validated scores for prediction UGIB. It is important to have a score that accurately determine the outcome of bleeding event and provide the patient efficient management. **Objective.** To comparate prognostic scores (MELD , MELD - NA, CHILD, Rockall, Blatchford , AIMS-65) to determine risk of mortality and rebleeding in patients with varicealUGIB. **Material and methods.** Patients > 18 years admitted with diagnosis of UGIB, for each patient was calculated each score. The data analysis was performed by using SPSS version 19. A descriptive analysis of quantitative variables and from qualitative variables absolute frequency distribution was performed.In order to detect the difference between the means of the scores with mortality at 8 weeks and reblending the t Student test was used for two independent samples with homogeneous variances. **Results.** 195 patients with UGIB, whom 102 were included with variceal UGIB. Seventy-seven (75%) were male, median mean age of 53.9 years (± 11.5). 74.5% required endoscopic intervention,12.3% had in-hospital rebleeding. The overall mortality to 8 weeks was 5.9%. t Student test was used to assess mortality and rebleeding. Featured Rockall statistical significance (p = 0.04), Blatchford (p = 0.01) and CHILD (0.01) for mortality, and the scale of Rockall (0.00) for rebleeding. **Conclusions.** Rockall score is the score that best predicts mortality and rebleeding in patients with variceal UGIB in cirrhotic patients, and can be routinely used.

008

EVALUATION OF RENAL FUNCTION IN DECOMPENSATED CIRRHOTIC HOSPITALIZED PATIENTS. A PROSPECTIVE STUDY

R. CONTRERAS-OMAÑA,* A. HERNÁNDEZ-HERNÁNDEZ,** J.E. LIRA-VERA,*** E. TÉLLEZ-CHÁVEZ****
**HOSPITAL GENERAL DE ZONA NÚM. 1, IMSS, PACHUCA, HIDALGO, MÉXICO.*
***MÉDICO ESPECIALISTA EN MEDICINA INTERNA, EGRESADA DEL HOSPITAL GENERAL DE PACHUCA, PACHUCA, HIDALGO, MÉXICO.*
****MÉDICO PASANTE DE SERVICIO SOCIAL, UNIVERSIDAD AUTÓNOMA DEL ESTADO DE HIDALGO, PACHUCA, HIDALGO, MÉXICO.*
*****HOSPITAL GENERAL DE PACHUCA, PACHUCA, HIDALGO, MÉXICO.*

Background. Renal failure is a common co-morbidity in cirrhotic patients. It connotes poor prognosis associated with high mortality, especially in patients who develop Hepatorenal syndrome. Establishing an appropriate evaluation of renal function is essential to diagnose renal failure in an early stage, in order to provide optimal treatment, limiting the consequences and improving the prognosis of the patient. **Objective.** To assess renal function of decompensated cirrhotic hospitalized patients based on renal dysfunction definitions and diagnostic criteria recently proposed by Wong, *et al.*, by comparing different renal function evaluation formulas and scales in order to determine their effectiveness. **Material and methods.** Observational, prospective, cross-sectional and analytic study. Realized at our center from October 2011 to October 2013, during which renal function of all decompensated cirrhotic hospitalized patients was studied. We use the definitions and diagnostic criteria proposed by Wong, *et al.*[1] renal function was measured by Cockroft-Gault and MDRD-6 formulas. Scales used to assess acute kidney injury were AKIN and RIFLE. **Results.** We studied 24 decompensated cirrhotic

hospitalized patients, both with pre-existing renal failure or with acute renal injury, of which 6 patients were in the 55-59 age group (25%) and 16 patients were male (66%). Child Pugh B was the most prevalent degree of liver failure (50%). Using the Cockroft-Gault formula, we detected 8 patients with pre-existing chronic kidney disease at admission (33.33%), while MDRD-6 detected 10 patients with this condition (41.69%). Both AKIN and RIFLE detected 8 patients with acute kidney injury during hospitalization (33.33%). Only 5 patients met the diagnostic criteria of Hepatorenal syndrome (20.83%). **Conclusions.** In our study, at the time of hospital admission, 1 of every 3 patients showed criteria of pre-existing chronic renal failure. In assessing in-hospital acute renal injury, AKIN and RIFLE scales proved to be equivalent. During hospitalization, only 1 of every 5 patients met the criteria of hepatorenal syndrome. More studies in this area are needed to validate our findings in different Centers and populations.

009

NUTRITIONAL ASSESSMENT IN AMBULATORY CIRRHOTIC PATIENTS AND ITS IMPACT ON QUALITY OF LIFE

WITHDRAWAL

010

HEPATIC ARTERY RESISTIVE INDEX IS A PREDICTOR OF GASTROINTESTINAL BLEEDING IN PATIENTS WITH CIRRHOSIS

M.C. ÁVILA-LANGARICA, C.I. BLANCO-VELA, A. ÁNGELES-LABRA, M.A. BARRAGÁN-VALAREZO, F. ZAMARRIPA-DORSEY
SERVICIO DE GASTROENTEROLOGÍA. HOSPITAL JUÁREZ DE MÉXICO. MÉXICO, DISTRITO FEDERAL.

Background. The progression of liver cirrhosis eventually increases cardiac output, while blood pressure and systemic vascular resistance are reduced. A complex behavior of portal hemodynamic to hepatic artery and system circulation has not yet been presented. There is a lack in knowledge about the correlation of local and systemic circulation parameters to the degree of liver failure, with respect to presence of complications of portal hypertension such as ascites, variceal bleeding, and hepatic encephalopathy. **Objetive.** To determine the value of measuring quantitative parameters of portal, hepatic, and splanchnic circulation by duplex Doppler ultrasonography (DDU), to predict portal hypertension related complications. **Material and methods.** In this study, resistive indexes (RI) of hepatic artery and portal vein, patency and direction of flow in portal veins and branches, time-averaged mean blood velocity, and caliber of portal vein were calculated with DDU in 31 ambulatory cirrhotic patients. Doppler findings were compared with the presence of encephalopathy, ascites, and variceal bleeding during the year post-DDU. **Results.** The median age of the patients was 55.32 ± 9.84 and 61.3% were female. The median MELD was 12.46 ± 5.02. The main etiology of cirrhosis was alcohol in 37.5%. The median of hepatic artery RI was 0.73 ± 0.07 and portal vein RI was 0.27 ±10. The portal diameter in inspiration was 13.25 ± 2.96. The peak velocity of portal vein was 26.33 ± 8.03 mm/s, and from hepatic artery 73.54 ± 31.54 mm/s, and from portal vein 37.78 ± 20.90 mm/s. At the end of the study 6.5% of the subjects presented variceal bleeding, 3.3% hepatic encephalopathy and 38% ascites. There was a significant correlation between MELD score and peak suprahepatic vein velocity (r = 0.754). Hepatic artery resistance index (HARI) was higher in cirrhotics who presented bleeding (0.78 ±.02 *vs.* 0.61 ± 0.1 p < 0.001) and splenic vein diameter was higher in patients with hepatic encephalopathy (20.9 mm *vs.* 10.3 ± 1.6 p = 0.002). **Conclusions.** There is a significant correlation between cirrhosis stage and peak vein velocity. In cirrhotic patients, an elevated hepatic artery RI is suggestive of progression to upper gastrointestinal bleeding. The splenic vein diameter was related to hepatic encephalopathy.

011

ELECTROENCEPHALOGRAPHIC FINDINGS RELATED TO INCREASED MORTALITY IN HOSPITALIZED PATIENTS WITH ACUTE HEPATIC ENCEPHALOPATHY

WITHDRAWAL

012

CIRRHOSIS: CLINICAL AND EPIDEMIOLOGY IN A COHORT OF COLOMBIAN PATIENTS. PERIOD 2010-2014

JHON E. PRIETO-O.,*,** SANTIAGO SÁNCHEZ-P.,* EVER L. ROJAS-D.,* LUPITA GONZÁLEZ**
**CLÍNICA UNIVERSITARIA COLOMBIA, BOGOTÁ COLOMBIA. **CONSULTORIO DE HEPATOLOGÍA, BOGOTÁ COLOMBIA.*

Introduction. Liver cirrhosis is the end stage of various progressive liver disease, with a variable prevalence from one country to another, currently abuse alcohol, non-alcoholic fatty liver disease (NAFLD) and chronic viral hepatitis are mentioned as the main causes. In Colombia we do not have trials in this regard. **Material and methods.** Cohort study, retrospective and descriptive, patients diagnosed with liver cirrhosis between January 1, 2010 to March 31, 2014. Chart review was performed. **Results.** The serie included 419 patients, 50.1% female with an average age of diagnosis of cirrhosis of 63 years. 73% of patients had physical findings of chronic liver disease. The main etiologies in this series were: non-alcoholic fatty liver disease (NAFLD) 25.5%, alcohol 14.8%, virus C infection 14.6%, other 14.6%, autoimmunity 10%, nonalcoholic steatohepatitis plus alcohol 6.7%, mixed causes 4.5%, primary biliary cirrhosis 3.8%, overlap 2.6%, nonalcoholic steatohepatitis and autoimmunity 1.2% B virus infection 0.5%, toxic or drug 0.5%, alcohol plus C virus infection 0.5%, alcohol plus B virus infection 0.2%. The Child-Pugh classification could be calculated for 394 patients, 59.1%, 32.4% and 8.3% were A, B and C respectively. The model for end-stage liver disease could be calculated in 341 patients having an average score of 10 with a maximum of 32. 108 patients had liv-

er biopsy of whom 12 had metavir rated F4. 40.3% of patients had at least one decompensation: 35.9% ascites, variceal bleeding 28.2%, hepatocarcinoma 15.3%, encephalopathy any grade 12.4%, encephalopathy plus ascites 4.7%, jaundice 2.4% and hepatorenal syndrome 1.2%. **Conclusions.** In Colombia the epidemiological behavior in this first cohort of patients with cirrhosis and their causes are similar to those reported in the literature. It is noteworthy that more than half of the patients showed decompensation, possibly because a quarter of patients had NASH as a cause, relatively benign in its evolution.

013

PROGNOSTIC FACTORS ASSOCIATED WITH HIGH MORTALITY IN CIRRHOTIC PATIENTES WITH VARICEAL BLEEDING: EXPERIENCE IN TWO HOSPITALS IN BOGOTA, COLOMBIA

G. HERNÁNDEZ-CELY,* J.D. MARTÍNEZ,*,** M.A. GARZÓN,*,*** J. LIZARAZU,* N. HORMAZA,* J.C. MARULANDA,* J.C. MOLANO,* M.H. REY,* A. VARÓN,*** L. SANTOS,*** E. PONCE DE LEÓN,*** J. CEBALLOS,*** R.C. BOTERO***

*GASTROENTEROLOGY, HOSPITAL UNIVERSITARIO DE LA SAMARITANA-UNIVERSIDAD EL ROSARIO.

**UNIVERSIDAD NACIONAL DE COLOMBIA.

***GASTROENTEROLOGY AND HEPATOLOGY, FUNDACIÓN CARDIOINFANTIL-BOGOTÁ, COLOMBIA.

Objective. To identify prognostic factors associated with high mortality in cirrhotic patients with variceal bleeding in two University Hospitals of Bogotá. **Material and methods.** A retrospective cohort of patients presented with variceal bleeding seen in a period of 30 months in two University Hospitals of Bogotá. **Results.** Sixty-three patients were included in the analysis (33 men and 30 women) with an average age of 56 years old. Nineteen percentage (12 cases) died. Mortality was similar in both sexes and institutions. The most frequent chief complaint was haematemesis (77.8%). The main causes of liver disease were alcoholic cirrhosis (38.1%) and cryptogenic cirrhosis (31.7%). Most patients had Child Pugh Score of B (52.4%). The average MELD Score was 12 and 3 cases required TIPS. The average period of hospitalization was 10 days. Therapy with Terlipressin was used in 61 patients (97%). History of hypovolemic shock ($p = 0.033$) and the need for red blood cell transfusion ($p = 0.05$) were the two categorical variables with statistical significance. Child Pugh Score C ($p = 0.00$) was the most statistically significant variable by Bivariate analysis. Among numerical variables, creatinine value with an average of 1.74mg/dl ($p = 0.043$) and average length of hospitalization of 10 days ($p = 0.057$) were significantly higher in patients who died. We applied a binary logistic regression. When analyzing the variables with association or statistically significant differences in the bivariate analysis, Child-Pugh C (Exp (B) = 0.068, $p = 0.002$) and creatinine (Exp (B) = 0.094, $p = 0.034$) remained statistically related to the outcome of interest (sig. Model = 0.000, percentage of patients properly classified = 85.7 %). **Conclusions.** The mortality of patients with variceal bleeding in two University Hospitals is comparable with current international standards. Advanced liver disease and impaired renal function are related to mortality in cirrhotic patients presenting with variceal bleeding. Patients with predictors of mortality during variceal bleeding require close monitoring and early interventions to prevent negative outcomes.

014

DISCRIMINANT ANALYSIS OF PROGNOSTIC SCORES FOR DETERMINING MORTALITY IN VARICEAL UPPER GASTROINTESTINAL BLEEDING

A. LÓPEZ-LURÍA, G. MARTÍNEZ-RAMÍREZ, S. MEJÍA-LOZA, E. JUÁREZ-VALDES, F. ZAMARRIPA-DORSEY

HOSPITAL JUÁREZ DE MÉXICO. MEXICO CITY, MEXICO.

Introduction. Upper gastrointestinal bleeding (UGIB) is a major complication in patients with hepatic failure (HF). Several pronostic scores have been created to stratify the risk of mortality, in-hospital rebleeding, endoscopic intervention, blood transfusion, costs and hospital length of stay. CHILD and MELD scores are used to determine mortality in patients with HF. It is important to have a tool to accurately determine a group of patients who are at increased risk of complications. Being able to predict which patients are within the group of high or low mortality, and improve medical intervention. Aim of the study was to detect the ability of AIMS-65, Rockall, Blatchford, MELD, MELD-NA and CHILD scores to predict mortality at 8 weeks in patients with variceal UGIB. **Material and methods.** Patients > 18 years admitted to the emergency room with a diagnosis of UGIB, for each patient was calculated MELD, MELD-NA, ROCKALL, Blatchford, AIMS-65 and CHILD scores. A descriptive analysis of quantitative variables was performed and from qualitative variables absolute frequency distribution was performed. In order to detect the ability of the scores as predictors of mortality at 8 weeks, a discriminant analysis was performed. The data analysis was performed by using SPSS version 19. **Results.** There were 195 patients with diagnosis of UGIB, whom 102 were included with variceal UGIB. Seventy-seven (75%) were male, median mean age of 53.9 years (± 11.5). The 74.5% required endoscopic intervention (variceal band ligation, obliteration, and/or sclerotherapy), 12.3% had in-hospital rebleeding. The overall mortality to 8 weeks was 5.9%. Discriminant analysis of the scores was performed to evaluate mortality (Rockall 0.767, CHILD 0.674, AIMS-65 0.527, MELD 0.353, MELD-NA 0.312, Blatchford 0.213) with a detection 5/6 patients died (1.51) and 83/96 alive (-0.94), with a certainty of 86% for predict mortality. **Conclusions.** The application of all scores determines correctly the risk of stayingalive or dead in 86%.

015

CYANOACRYLATE FOR ACUTE VARICEAL BLEEDING: SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CLINICAL TRIALS

S. ORNELAS-ARROYO, V. ORNELAS-ARROYO, B. SÁNCHEZ-JIMÉNEZ, M. URIBE, F. TÉLLEZ-ÁVILA, N.C. CHÁVEZ-TAPIA

OBESITY AND DIGESTIVE DISEASES UNIT. MÉDICA SUR CLINIC & FOUNDATION. MEXICO CITY.

Background. Hemostasis rates with percutaneous obliteration of gastroesophageal varices has been of > 90%, with variceal obliteration rates of 70 to 90% and rebleeding rates < 30%. The use of cyanoacrylate for acute variceal bleeding is controversial. The aim of this study is to compare hemostasis rate with cyanoacrylate compared with other endoscopic techniques in cirrhotic patients with acute variceal bleeding. **Material and Methods,** The research was made in The Cochrane Central Register of Controlled Trials (CENTRAL) and MEDLINE until 2014. Randomized clinical trials comparing the use cyanoacrylate *vs.* variceal band ligation or sclerother-

Table. (015).

Outcome	Cyanoacrylate *vs.* other endoscopic methods		Cyanoacrylate *vs.* band ligation		Cyanoacrylate *vs.* sclerotherapy	
	OR	95% CI	OR	95% CI	OR	95% CI
Hemostasis	2.22	1.36-3.60	1.75	1.00-3.07	4.71	1.66-13.32
Re-bleeding	0.52	0.33-0.81	0.45	0.26-0.78	0.70	0.30-1.61
Bleeding related mortality	0.55	0.55-1.07	0.69	0.27-1.73	0.42	0.16-1.14
All cause mortality	0.64	0.40-1.04	0.81	0.47-1.38	0.22	0.07-0.75

apy in patients with cirrhosis and acute variceal bleeding were included. The dichotomous data were analyzed using odds ratio (OR), with 95%CI. Significant heterogeneity was considered with a P value ≤ 0.10 (χ^2) or I2 > 25%. **Results.** A total of 6 randomized clinical trials with a total of 436 patients were included for analysis, 4 comparing cyanoacrylate *vs.* band ligation, 3 of them for gastric varices, and one for esophageal varices, and 2 comparing cyanoacrylate vs. sclerotherapy, both for esophageal varices. Cyanoacrylate was better for achieving hemostasis compared with other endoscopic methods, with less rate of re-bleeding compared with band ligation and less bleeding related mortality and any cause mortality compared with sclerotherapy (Table). **Conclusions.** Treatment of acute variceal bleeding with cyanoacrylate in patients with cirrhosis is better for achieving hemostasis compared with other endoscopic methods.

016

FUNCTIONAL STATUS, RESPIRATORY MUSCLE STRENGTH, AND QUALITY OF LIFE IN PATIENTS WITH CIRRHOSIS

LUCAS GALANT, JOSÉ L. FAUSTINI, CLÁUDIO A. MARRONI
UNIVERSITY OF HEALTH SCIENCES OF PORTO ALEGRE, BRAZIL.

Introduction. Liver diseases are responsible for metabolic disorders and loss of muscle mass and function that affect functional status and quality of life (QoL). **Material and methods.** To compare exercise capacity, respiratory muscle strength, and QoL in liver transplant candidates with cirrhosis of the following etiologies: hepatitis C virus (HCV), hepatitis B virus (HBV), and alcoholic cirrhosis (AC). Cross-sectional study comprising 86 patients divided into three groups: HCV (40 patients), HBV (14 patients), and AC (32 patients). Patients were evaluated using the six-minute walk test (6MWT), manometry, and the QoL questionnaire SF-36. **Results.** The AC group showed the lowest performance in the 6MWT (meters) compared to the HBV and HCV groups (373.50 ± 50.48, 464.16 ± 32, and 475.94 ± 27.84, respectively, p = 0.001). In the domains of the SF-36, the AC group had lower scores for functional capacity and physical limitations when compared to the HBV and HCV groups (p = 0.001). In the comparison of respiratory muscle strength, the AC group had lower MIP (cmH_2O) compared to the HBV and HCV groups (-65.54 ± 11.28, -71.61 ± 6.96, -82.44 ± 13.71, respectively, p = 0.001). The MEP (cmH2O) in the AC group was also lower than in the HBV and HCV groups (65.13 ± 10.74, 82.44 ± 13.87, 83.44 ± 12.20, respectively, p = 0.001). **Conclusion.** The AC group showed worse exercise capacity, respiratory muscle strength, and QoL compared to patients with HCV and HBV.

017

GASTROINTESTINAL BLEEDING IN PATIENTS WITH PORTAL HYPERTENSIVE GASTROPATHY: THE BENEFICIAL EFFECTS OF ARGON PLASMA COAGULATION

J. LLACH-VILA
SERVICIO DE ENDOSCOPIA DIGESTIVA. HOSPITAL CLINIC, BARCELONA, SPAIN.

Background. Few studies have been performed on the outcome and prognosis of patients admitted to the hospital because of portal hypertensive gastropathy (PHG) and upper gastrointestinal bleeding. There is also little knowledge on the efficacy of argon plasma coagulation (APC) in this condition. **Aim.** This study was designed to evaluate the efficacy of APC in patients admitted to the hospital with gastrointestinal bleeding because PHG. **Material and methods.** Twenty-nine patients with PHG were included and followed at 3 months and every 6 months thereafter during a mean of 31.2 months (range 26-37 months). All patients received intensive APC treatment that was repeated, depending on the endoscopic appearance or clinical evaluation. **Results.** The overall success of APC treatment was 87%, with only three recurrences of upper gastrointestinal bleeding during the follow-up period. The number of APC sessions was 2.2, with a total number of sessions of 2.1 + 1.9. The rise in hematocrit from baseline values in the overall group and in each subgroup was significant (p > 0.01). **Conclusion.** Endoscopic thermal ablation with APC is effective in managing significant upper gastrointestinal bleeding and in reducing transfusion requirements in patients with PHG.

018

ENDOSCOPIC MANAGEMENT OF GASTRIC VARICEAL BLEEDING

J. LLACH-VILA
SERVICIO DE ENDOSCOPIA DIGESTIVA. HOSPITAL CLINIC, BARCELONA, SPAIN.

Background. Gastric varices are less common than esophageal varices but may be present in up to 20% of patients with portal hypertension. Variceal ligation has performed well in esophageal varices, however results with gastric varices are not as favorable and bleeding is commonly more profound and difficult to control. **Aim.** To analyse the effect of cyanocrilate-based glue is effective in the treatment of gastric variceal bleeding. Patients and methods: thirty patients with active bleeding due to fundal varices were included and followed during a mean of 12 months (range 6-19 months). All patients had had needed higher transfusional requirements All patients were treated with cyanocrilate-based glue injection, that was repeated, depending on the endoscopic appearance or clinical evaluation. **Results.** Primary haemostasis

was obtained in all cases. During follow-up, rebleeding was present in 3 of them (10%). The mean dose of cyanocrilate-based glue injection was 4 + 2 mL. The presence of complications was observed in 3 patients (10%; asymptomatic thromboembolism in one case and fever in two cases) and one patients died due to hepatic failure. **Conclusion.** Cyanocrilate injection is effective and associated with a lower gastric varices rebleeding rate in the treatment of gastric variceal bleeding.

019

GRANULOCYTE-COLONY STIMULATING FACTOR FOR ACUTE-ON-CHRONIC LIVER FAILURE: SISTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CLINICAL TRIALS

V. ORNELAS-ARROYO,* D. VIDAÑA-PÉREZ,** G. DELGADO-SÁNCHEZ,** I. MENDIOLA-PASTRANA,** C. NOREÑA-HERRERA,** E. JUÁREZ-HERNÁNDEZ,* N. MÉNDEZ-SÁNCHEZ,* M. URIBE,* N.C. CHÁVEZ-TAPIA*
*OBESITY AND DIGESTIVE DISEASES UNIT. MÉDICA SUR CLINIC & FOUNDATION. MEXICO CITY.
**NATIONAL INSTITUTE OF PUBLIC HEALTH. MEXICO CITY.

Background. Acute-on-chronic liver failure (ACLF) is associated with increased short and long-term mortality. Currently, orthotropic liver transplantation remains the only definitive therapy for patients with ACLF. Several animal models of liver failure have demonstrated that granulocyte-colony stimulating factor (G-CSF) accelerates the liver regeneration process and improves survival. The objective of this systematic review was to assess the benefits and harms of G-CSF in patients with acute-on-chronic liver failure. **Material and methods.** The research was made in The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE and LILACS until November 2013. Additionally, the references from the identified studies were handsearched. Randomized clinical trials comparing the use of G-CSF against placebo or no intervention in patients with ACLF were selected. Three authors independently assessed the quality of the studies, evaluated the risk of bias, and extracted the data. **Results.** Two trials with a total of 102 patients were included. One trial compared the use of G-CSF against placebo. The second trial compared G-CSF against no intervention. Compared with the control group, the group that received G-CSF presented a significant reduction in short-term mortality (RR 0.56; 95% CI 0.39 to 0.80). There is not enough evidence to show an effect of G-CSF therapy on mortality secondary to gastrointestinal bleeding (RR 1.45; 95% CI 0.50 to 4.27). The adverse effects reported included: fever, rash, zoster, headache and nausea. **Conclusions.** The use of G-CSF for the treatment of patients with ACLF significantly reduced short-term mortality.

020

DISORDERS OF GLUCEMIC METABOLISM AND THE HEPATIC COMPLICATIONS IN COMPENSATED PATIENTS WITH HCV-RELATED CIRRHOSIS

YULUET MARAY SOCIAS-LÓPEZ, LUIS CALZADILLA-BERTOT, EDUARDO VILAR-GÓMEZ, ANA LUISA TORRES
INSTITUTO DE GASTROENTEROLOGÍA, CUBA.

Introduction. Disorders of glucose metabolism have been little studied in the context of the HCV-related cirrhosis. Our study determines the association between the alterations in glucose metabolism and the hepatic complications in compensated patients with HCV-related cirrhosis. **Material and methods.** We conducted a prospective longitudinal "inception cohort" study at the Institute of Gastroenterology (Havana, Cuba), tertiary care academic center between January 2011 and October 2013.Two hundred fifteen patients were continually studied every 4 months and clinical, biochemical data and the presence of clinical complications were collected. The probability of general hepatic decompensation was determined, as well as for each complication. The associated factors were determined independently from the hepatic complications. **Results.** The ascites, the hepatocellular carcinoma (HCC), the variceal bleeding and the hepatic encephalopathy were the most probable complications. The diabetes mellitus 2 (DM2) constituted the most frequent metabolic dysfunction (49%), followed by the tolerance to the altered glucose (10%) and the fasting glucose altered (4.6%). The DM2 was associated to the increase, in more than seven times, of the probability of hepatic complications and it turned out to be an independent predictor of decompensation. The factors independently associated to the clinical decompensation were the model MELD, Child-Pugh, the presence of varices, the altered glucose after 2 h, INR for prothrombin time and the platelets count. **Conclusions.** The ascites represents the most probable complication and the type 2 DM increases the risk of developing hepatic complications.

021

DIAGNOSTIC OF ASCITES DUE TO PORTAL HYPERTENSION: ACCURACY OF THE SERUM-ASCITES ALBUMIN GRADIENT AND PROTEIN ANALISES IN ASCITIC FLUID

B. RODRÍGUEZ-VARGAS,* E. MONGE-SALGADO,* P. MONTES-TEVES,* S. SALAZAR-VENTURA,* E. GUZMÁN-CALDERÓN**
*HOSPITAL DANIEL ALCIDES CARRIÓN. CALLAO, PERÚ.
**HOSPITAL EDGARDO REBAGLIATI MARTINS. LIMA, PERÚ.

Objective. To evaluate the diagnostic accuracy of the Serum-Ascites Albumin Gradient (GASA), Protein Concentration in the Ascitic Fluid (PTLA), Albumin Concentration in the ascitic fluid (CAA) and the Protein Ascites/Serum Ratio (IPAS) for the diagnosis of ascites due to portal hypertension. **Material and methods.** It was an observational and retrospective study of validation of diagnostic tests. The study population was patients from a National Public Health Hospital Daniel Alcides Carrion of Callao, Peru, during the period January to December of 2012, patients over 15 years old with a diagnosis of ascites which samples were taken for study by paracentesis with an standard technique, it was analyzed total protein and albumin, as well as study of total protein and albumin in blood. We obtained the diagnostic accuracy, sensitivity, specificity, PPV and NPV of the Serum-Ascites Albumin Gradient (GASA), Protein Concentration in the Ascitic Fluid (PTLA), Albumin Concentration in the ascitic fluid (CAA) and the Protein Ascites/Serum Ratio (IPAS) for the diagnosis of ascites due to portal hypertension. To determine ascites by HTP as diagnostic tests we took into account: GASA $\geq$ 1.1, PTLA < 2.5, CAA < 1.1 or IPAS < 0.5. **Results.** There were 126 patients diagnosed with ascites, 10 patients was excluded for having incomplete data. Of the 116 patients, the average age was 53.03 $\pm$ 15.73 years old, male 65 (56%) and female 51 (44%). 61 (52%) had ascites due to portal hypertension from liver cirrhosis, and 55 (48%) of ascites due to NO HTP. The sensitivity and specificity for GASA was 93 and 47% respectively, for PTLA was 80 and 89% respectively, for CAA was 85% and 87% respectively and for the IPAS was 83 and 80% respectively. The area under the ROC curve for GASA was

0.70, ATPL was 0.84, IPAS was 0.81 and CAA was 0.86, we found statistically significant differences between GASA compared to the other three parameters ($p < 0.01$). **Conclusion.** The diagnostic accuracy of CAA, ATPL and IPAS is higher than the GASA to discriminate between ascites due to HTP or NO HTP, so that they could be used in clinical practice alone or together to achieve a diagnostic approach more successful.

022

DIETARY INTAKE OF CIRRHOTIC PATIENTS, COMPARISON WITH THE NUTRITIONAL STATUS AND THE DISEASE STAGE

F. FEIJÓ-NUNES, S. ALVES-FERNANDES, L. BASSANI, M. EUGÊNIA DEUTRICH, D. HARTER, M. LEITE-BERTOTTO, B. PIVATO, C. AUGUSTO-MARRONI
PROGRAMA DE PÓS-GRADUAÇÃO EM MEDICINA: HEPATOLOGIA, UFCSPA, PORTO ALEGRE, BRAZIL.

Background. Patients with liver disease often have protein caloric malnutrition (PCM). The assessment of dietary intake is of great importance in the investigation of the relationship of the "health and disease". **Aim.** To assess dietary intake of cirrhotic through three-day food record, correlating with the patient's nutritional status and the disease stage. **Material and methods.** We evaluated cirrhotic patients in outpatient care at the Complexo Hospitalar da Santa Casa de Misericórdia de Porto Alegre, RS, Brazil. The methods used for nutritional assessment were anthropometry, hand-grip strength, the adductor pollicis muscle thickness, phase angle by bioelectrical impedance analysis (BIA) and Subjective Global Assessment. For analysis of food intake was performed dietary record of 3 days using scales for weighing of all foods and consumption compared to the recommendations of the literature. The statistical analysis was performed using SPSS (Statistical Package for the Social Sciences) version 17.0, and the significance level of 5%. **Results and discussion.** We evaluated 25 patients with cirrhosis prevalence of hepatitis C (68%). The arm circumference (AC), the hand-grip strength and the phase angle by BIA using cutoffs of the Brazilian population diagnosed 56% of malnourished. The phase angle by BIA and AC were associated with Child-Pugh score ($p < 0.05$). The average calorie intake was 26.4 ± 8.3 kcal/kg, carbohydrate 56.4 ± 7.1% of total energy intake (TEI), 1.05 ± 0.35 g protein/kg and lipid 29.3% of TEI, all within recommended. Sodium intake was above the recommended 106 ± 57.2 mEq. Food intake didn't varied according to the disease stage, or according to nutritional assessment by the phase angle by BIA. Sodium intake was inversely associated with Child-Pugh score ($rs = -0.410$, $p = 0.042$). There was no change in intake as the different weekdays evaluated. **Conclusion.** Dietary intake was not significantly different between the Child-Pugh scores and according to nutritional status. Patients maintained a pattern of food intake during the weekdays.

023

ROLE OF NON-INVASIVE MARKERS AND INDICES OF LIVER FIBROSIS AS PREDICTORS OF ESOPHAGEAL VARICES

M. CASTILLO-BARRADAS, A. PÉREZ-MENDOZA, M.C. BERNARDINO, H.J. RUIZ-MORALES, J. GUERRERO-ANGUIANO
HOSPITAL DE ESPECIALIDADES, CMN LA RAZA. MEXICO CITY, MEXICO.

Objectives. To determine whether the indirect markers of fibrosis and APRI, FORNS, FIB-4 and MELD, are predictors of the presence of esophageal varices in patients with liver cirrhosis. **Material and methods.** A cross-sectional, retrospective, observational and analytical study in which 151 patients with liver cirrhosis or hepatic fibrosis, regardless of etiology, treated at the Department of Gastroenterology UMAE Dr. Antonio Fraga Mouret, CMN La Raza, January 2007 to December 2011. Endoscopic findings of the first study were recorded, regardless of whether or not they had varices, plus lab results, which were calculated APRI, Forns, FIB-4 and MELD. Patients were divided into 2 groups: without varices and varices, in which the sensitivity, specificity and ROC curves mentioned indices were determined to predict the presence of esophageal varices. **Results.** Of the 151 patients, 116 were women, mean age 52.3 ± 10.8 years, the most frequent diagnosis was CBP with 29.8%, followed by chronic HCV infection. The general characteristics of the 2 groups (with and without esophageal varices) were similar, though statistically significant differences were found in the platelet level off, bilirubin and protein. The sensitivity and specificity for the APRI index cutoff fibrosis (≥ 1.50) was 56.0 and 80.3% respectively; for FORNS index (≥ 6.90) of 87.2 and 41.3%; for MELD (≥ 8) 49.3% and 89.5%; and FIB-4 index (≥ 2.67) of 88 and 50%. Using breakpoints detected for the ROC curve, sensitivity and specificity of APRI index was 57.3 and 80.3%; FORNS for 98.7 and 5.3%, FIB-4 21.3 and 94.7% respectively. **Conclusions.** FORNS FIB4 and indices can be used as good predictors of the presence of varices, however none of them can replace endoscopy.

024

DIFFERENTIAL DIAGNOSIS OF FEVER IN PATIENTS WITH CHRONIC LIVER FAILURE

M. MOROZOVA, M. MAYEVSKAYA, V. IVASHKIN
FIRST MOSCOW STATE MEDICAL UNIVERSITY, MOSCOW, RUSSIA.

Background. In most cases fever in patients with chronic liver failure is associated with infection, but sometimes it is not possible to identify site of infection and antibacterial therapy is ineffective. Early diagnosis of such cases is important for correct treatment strategy. Aim of the study was to evaluate prevalence and causes of fever and to develop the algorithm of differential diagnosis of infectious and noninfectious fever in patients with chronic liver failure. **Material and methods.** Prospective cohort observational study included 121 patients with Child-Pugh B and C liver cirrhosis. Results of clinical, laboratory, instrumental assessment and efficacy of empirical antibacterial therapy were evaluated to recognize causes of fever. Univariate and multiple regression analyses were performed to determine the risk factors of infectious and noninfectious fever. Findings were used to develop the diagnostic algorithm. **Results.** Fever was observed in 59 patients (49%). The causes of fever were recognized in 85% (n = 50) of cases. The site of infection was localized in 41 patients

(69.5%). It was pneumonia, ascitic fluid infection, pyelonephritis, soft tissue abscess and sepsis. All patients with infectious fever normalized temperature during the antibacterial therapy, but still had signs of decompensation of liver function. In 18 patients the fever was noninfectious and didn't respond to antibiotics. In 8 cases there were malignancies, in 1 case-rheumatoid arthritis. In 9 cases etiology after thorough examination was still unknown. These patients didn't respond to antibacterial therapy and normalized temperature simultaneously with compensation of liver function. Binary logistic regression indicated resistant ascites ($p = 0.025$), low serum albumin ($p = 0.035$), high total bilirubin ($p = 0.02$) as independent risk factors for the development of noninfectious fever of unknown origin. **Conclusion.** In most patients with chronic liver failure fever is caused by infection. In cases of noninfectious fever of unknown etiology there is a direct correlation between the severity of liver function impairment and development of fever. The diagnostic algorithm in patients with fever and chronic liver failure includes as follows: the first- the search for the infection site, the second- the search for other reasons of fever, the third-in case of none of the first two is applicable consider the fever with liver function impairment. Early start of antibiotic therapy in any case of fever is reasonable, because of high incidence of infectious fever.

025

LIVER CIRRHOSIS IN A HOSPITAL OF THE PERUVIAN AMAZONIA

O. PRETELL-LOVATÓN
HOSPITAL ESSALUD IQUITOS, LORETO, PERÚ.

Introduction. The Hospital EsSalud of Iquitos attends to the insured population of Loreto in the Peruvian Amazonia. The region is characterized by the high prevalence of infectious diseases and increase of chronic diseases as the Diabetes Mellitus, obesity and high blood pressure. This research is performed in order to establish the epidemiological and clinical characteristics of the liver cirrhosis in the region Loreto. **Material and methods.** Is a transverse and descriptive study of the epidemiological and clinical characteristics of the patients with diagnosis of liver cirrhosis attended from January to December, 2013. Seventy-one patients were included. **Results.** The average age was 64 years. 53.5% were male and 46.5% female. The most common associated diseases were diabetes mellitus in 33.9%, obesity 25.3%, and high blood pressure in 18.3%. The precedent of liver cirrhosis in relatives of the first and second degree of consanguinity was present in 19.7% of patients. The initial clinical manifestations were hematemesis and melena in 28.2%, hepatic encephalopathy in 18.3%, ascites in 12.7%, and 18.3% made debut with other symptoms. In 11.3% the diagnosis was for study of thrombocytopenia, hypertransaminasemia or high INR. In the 5 remaining patients was for endoscopic finding of esophageal varices, or during cholecystectomy. The causes were, chronic hepatitis B in 30.9%, alcohol in 19.7%, chronic hepatitis C in 5.6%, coinfection with hepatitis B and C virus in 5.63%, in 16.9% patients was associated with nonalcoholic steatohepatitis in patients with diabetes and/or obesity. In 18.3% it was not possible to determine the reason. The stage of disease at diagnosis was stage Child Pugh A in 33.8%, stage B in 50.7%, and stage C, 15.5%. **Conclusions.** The Liver Cirrhosis in Loreto-Peru:

- Is more frequent in men.
- The most common associated diseases were diabetes mellitus and the obesity.
- One of five patients had at least a relative of the first or second grade of consanguinity with equal diagnosis.
- Gastrointestinal bleeding is the most common initial clinical manifestation.
- Chronic infection with the hepatitis B virus is the most common cause.
- Most patients are diagnosed in stages A and B of the Child Pugh's classification.

026

FREQUENCY OF ORAL LESIONS ASSOCIATED TO LIVER CIRRHOSIS IS BASED ON THE ETIOLOGY AND DEGREE OF HEPATIC INSUFFICIENCY

M. CASTILLO-BARRADAS, H.J. RUIZ-MORALES, R.V. GARCÍA-RICO, J.J. GUERRERO-ANGUIANO, A. PÉREZ-MENDOZA, R. VARGAS-ÁNGELEZ, L.E. SOTELO-SOLÍS
HOSPITAL DE ESPECIALIDADES, CENTRO MÉDICO NACIONAL LA RAZA, INSTITUTO MEXICANO DEL SEGURO SOCIAL. MEXICO CITY, MEXICO.

Introduction. The frequency of oral lesions associated to liver cirrhosis have not been fully studied, among them the most reported are lingual varices, gingival hiperplasia, tooth mobility, parotid growth, petechiae, bruising, jaundice in mucosal tissues, gingival bleeding, disability in gestatory function, glossitis and angular cheilitis. **Material and methods.** The study was conducted with patients recruited in 2010 by the gastroenterology service at the Specialty Hospital Dr. Antonio Fraga Mouret with the diagnosis of liver cirrhosis in outpatient. **Results.** Of 100 patients evaluated the average age was 51.5 (92 women and 8 men), 34 had tongue varices, 17% had gingival hyperplasia, 27% tooth mobility and 3% parotid growth. It was observed in 54% periodontal disease, 51% xerostomia, 27% coated tongue, 17% fetor hepaticus, 13% oral ulcers, 10% halitosis and 6% salivary hyperviscosity. Based in the etiology parotid growth was associated with HCV in 27.3%, salivary hyperviscosity in 5.3% with primary biliary cirrhosis, 8.3% in autoimmune hepatitis and 9.1% in HCV associated cirrhosis. Coated tongue was associated to cryptogenic cirrhosis in 66.7%, 60% in overlap syndrome, 25% in autoimmune hepatitis, 24.6% primary biliary cirrhosis and 18.2% in HCV associated cirrhosis. Based on MELD score, red tongue was associated in 14.5% with 6-10 points, 28.6% with 11-15 points and 8.6% with 16.20 points. Halitosis in 42.9% with 16-20 points, 14.3% with 11-15 points and 4.8% with 6-10 points. Based on the degree of hepatic insufficiency the fetor hepaticus was associated to Child Pugh A patients in 8.3%, 23.5% in Child-Pugh B and 63.6% in Child-Pugh C. Oral ulcers were found in 8.3% in patients with Child-Pugh A, 35.3% in Child-Pugh B and 9.1% in Child-Pugh C patients. Conclusions. Parotid growth and coated tongue were associated in higher percentage of patients with HCV cirrhosis and salivary hyperviscosity with cryptogenic cirrhosis. Based on the degree of hepatic insufficiency through Child-Pugh score fetor hepaticus, lingual edema and halitosis were associated with Child-Pugh C. With this results there were an association between oral lesions and advanced hepatic insufficiency.

027

EPIDEMIOLOGIC AND CLINICAL FEATURES OF LIVER CIRRHOSIS IN PATIENTS OVER 65 YEARS OLD IN THE HOSPITAL GENERAL DE MÉXICO EDUARDO LICEAGA

G. ROJAS-LOUREIRO,* I. LÁZARO-PACHECO,* E. PÉREZ-REYES,* A. PEÑALOZA-POSADA,* M. GÁLVEZ-MARTÍNEZ,* P. ENRÍQUEZ-COVARRUBIAS,* A. FLORES-ARROYO,** B. MARTÍNEZ-SALDÍVAR*

*LIVER CLINIC, HOSPITAL GENERAL DE MÉXICO EDUARDO LICEAGA. MEXICO CITY, MEXICO.

**UNIVERSIDAD DEL VALLE DE ATEMAJAC. GUADALAJARA, JALISCO, MÉXICO.

Objective. A descriptive study was conducted in order to determine the epidemiological and clinical characteristics of patients with liver cirrhosis over 65 years of age at the Hospital General de México Eduardo Liceaga in the period of August 2013 to August 2014. **Material and methods.** We studied a total of 84 patients diagnosed with liver cirrhosis (54 women and 30 men) over 65 years of age, belonging to the Liver Clinic of Hospital General de México Eduardo Liceaga. The data collection was conducted by reviewing the medical record during their regular consultation of an outpatients basis. **Results.** The median age was 71 years. Etiology of alcohol (39.2%), hepatitis C virus (15.4%) and NASH were the most frequent. The average time to diagnosis of liver cirrhosis was 2 years. Most frequent grade liver failure according to Child-Pugh classifications was A (61.9%) B (30.9%) and C (7%) and the mean MELD was 10.12 points. 66.6% of patients were without descompensation in the last year prior to consultation. The most frequently associated comorbidities were type 2 diabetes (22.6%), arterial hypertension (14.2%) and cardiovascular disease (2.3%). **Conclusion.** The main cause of liver cirrhosis in patients over 65 years with predominance of women was related to alcohol and HCV infection. Therefore epidemiological knowledge of the disease in patients older than 65 years is considered relevant in establishing prevention and treatment alternatives.

028

ADHERENCE OF CIRRHOSIS PATIENT TO OUTPATIENT FOLLOW-UP IN NUTRITION

D. MIRANDA DA-SILVA,* S. ALVES-FERNANDES,* C.A. MARRONI,** C. BERTASO ANDREATTA-GOTTSCHALL***

*NUTRICIONISTA, **MÉDICO, UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE. PORTO ALEGRE, BRAZIL.

***NUTRICIONISTA, UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL. PORTO ALEGRE, BRAZIL.

Aims. To estimated the prevalence of adherence to outpatient follow-up in Nutrition in a Tertiary care Hospital and to assess its association with sociodemographic and clinical aspects in patients with cirrhosis. **Material and methods.** Retrospective cohort study based on retrospective based on the chart review of all patients who attended at least one appointment at a Nutrition ambulatory specialized in cirrhotic patients. Data were collected regarding the identification, aspects of liver disease, drug use, nutritional status, and outpatient clinical outcome. Patients were considered adherent patients when they attended the consultations for a period exceeding one year. **Results.** The study population consisted of 100 patients, with an average age of 57.6 years of whom 60% were men. The most frequent etiology was hepatitis C (37%), followed by alcohol (30%) and the association of hepatitis C virus + alcohol (13%). Disease severity at baseline was 58% Child-Pugh A, 36% B and 6% C. The rate of compliance was 25%. Gender, number of comorbidities and hypertension presented independently associated with adherence ($p = 0.002$, $p = 0.017$, $p = 0.005$, respectively). Regarding the clinical outcome after 1 year follow-up we found death rates of 13%, there was no association between death and the prognostic scores Child-Pugh and MELD. **Conclusions.** The adherence prevalence found in this study was low and concerning. The female patients, hypertensive and the ones with more comorbidities were more adherent to outpatients follow-up in Nutrition. These data contribute to alert healthcare professionals about the need to encourage patients to give continuity to the follow-up.

029

UTILITY OF GPVH AND TIPS FOR BLEEDIND OF GASTRIC VARICES.INICIAL EXPERIENCE OF A SINGLE CENTER IN SAN JUAN, ARGENTINA

R. ROMO-GONZÁLEZ

CIMAC. SAN JUAN/CAPITAL. UNIVERSIDAD CATÓLICA DE CUYO. SAN JUAN. ARGENTINA.

Background. Hepatic hemodynamics represents the most objective way to evaluate portal hypertension. Provides prognostic information of great importance and can prevent the most lethal complications mainly in regard to variceal bleeding. **Aim.** Present the clinical case of a patient with bleeding gastric varices whose treatment was defined based on the hepatic hemodynamic. **Material and methods.** Women 53 years of age with chronic hepatitis C in cirrhotic stage (Child B) no history of ascites , encephalopathy, portal thrombosis or HCC. History of multiple episodes of gastrointestinal bleeding from esophageal-gastric varices since 2008. Received medical treatment with propranolol and endoscopic ligation (banding) of esophageal varices but continued with episodes of bleeding from gastric varices (GOV 2). She underwent a surgical shunt (Warren) in 2010. In January of 2011 is referred to our center with a new episode of bleeding gastric varices (GOV 2). An early endoscopic treatment was performed plus medical treatment with terlipressin, ciprofloxacin and lactulon. It was seen the absence of flow Doppler ultrasound in surgical shunt which was confirmed by angio-MRI. At 72 h she suffer variceal re-bleeding with hemodynamic decompensation, multi-organ failure, inotropic requirements, Sengstaken-Blakemore tube and mechanical ventilation. Performing a liver hemadinamic procedure we obteined a hepatic venous pressure gradient (HPVG) of 21 mmHg so we decided the placement of a transjugular shunt intrahepatic portal-systemic (TIPS) achieving a reduction of the portal pressure to 9 mmHg. The patient improved, and fulfilled external ambulatory controls in excellent overall condition and then was referred to a transplant center for evaluation and monitoring. The patient did not require to be transplanted and still's asymptomatic with no further episodes of complications following the TIPS placement. **Discussion.** Above 20 mmHg of HVPG pressures during an episode of acute variceal bleeding can recognize patients who will have worse outcomes in terms of failure to control bleeding as well as increased risk of early rebleeding and death. In this group of patients surgical shunts and TIPS are effective preferring the latter in patients with advanced liver disease (Child B or C) as a bridge to transplantation. **Conclusions.** The use of liver hemodynamics as well as the use of alternative therapies such as TIPS

can be performed in centers within the country avoiding the need for urgent deliver to specialized institutions.

030

THERAPEUTIC OPTIONS IN LIVER ENCEPHALOPATHY: RIFAXIMIN A ALONE COMPARED TO RIFAXIMIN-A AND AN INULIN- TYPE PREBIOTIC

L. TOMA, L. ILIESCU, C. ORBAN, A. TANASE
FUNDENI CLINICAL INSTITUTE, BUCHAREST, ROMANIA.

Background. Liver encephalopathy is a frequent complication of liver failure with an important impact on quality of life. We aim to compare the efficacy of Rifaximin-a alone and Rifaximin-a and an inulin- type prebiotic (ITP) in down staging liver encephalopathy and reducing the number and length of hospital admissions. **Material and methods.** We performed a prospective study on 206 patients, with cirrhosis and liver encephalopathy. 106 patients were given 1,200 mg Rifaximin-a per day and 100 patients were given 1,200 mg Rifaximin-a and 10 g of ITP per day for 90 days. We compared the patients' results in pshychometric tests, EEG expression of liver encephalopathy and the serum levels of ammonia. **Results.** 61% of the patients included in the study were male, the mean age was 55.4 years (25-75), MELD scores were under 25 and the venous ammonia level over 50 μmol/l. 62% of the patients had significant cognitive alterations. Combined therapy lead to a faster, more important lowering in the ammonia levels that Rifaximin-a alone (p value < 0.02) and an improvement in EEG waves. Also, patients' results in the number connection, line tracing, serial dotting and digit symbol tests improved in the combined therapy group (p value < 0.001). Both the mean hospital stay and the frequency of admission were aproximately 2 times lower in the combined therapy group. **Conclusions.** Rifaximin-a and ITP have better results than Rifaximin-a alone in the management of liver encephalopathy in cirrhosis. One must also take into account the subsequent cost reduction for hospitalisation in patients with this chronic and resource- consumpting disease.

031

MONITORING THE NUTRITIONAL STATUS OF PATIENTS UNDERGOING LIVER TRANSPLANTATION OVER A YEAR

M.E. DEUTRICH-AYDOS, S. ALVES-FERNANDES, F. FEIJÓ-NUNES, L. BASSANI, L. RIGON-LEONHARDT, D. LAZAROTO-HARTER, B. PIVATO, D. MIRANDA, C.A. MARRONI
[1]*PROGRAMA DE PÓS-GRADUAÇÃO EM MEDICINA: HEPATOLOGIA, UFCSPA, PORTO ALEGRE, BRAZIL.*

Background. Nutritional assessment is crucial in the investigation of changes associated with liver diseases. Choosing the method of nutritional assessment of patients undergoing liver transplantation is essential for an accurate diagnosis, both in the pre and post-operative period, to ensure adequate monitoring of the nutritional status. To evaluate and compare the nutritional status of cirrhotic patients before and after liver transplantation over a year of monitoring by different methods of nutritional assessment. **Material and methods.** Patients undergoing liver transplantation were assessed in five phases: pre-transplant, 1, 3, 6 and 12 months after transplantation at the hospital Santa Casa de Misericordia de Porto Alegre, in Porto Alegre, RS, Brazil. The methods used for nutritional assessment were anthropometry, grip strength of the non-dominant hand (HGS) by dynamometry, thickness of the adductor pollicis muscle (APM) and phase angle (PA) by bioelectrical impedance analysis (BIA). In all evaluations, all measurements were taken according to protocol. For the statistical analysis, we considered a significance level of 5% ($p \leq 0.05$). **Results.** Evaluations were performed in a cohort of 22 patients. Methods that showed a higher prevalence of malnourished patients before transplantation were the PA by BIA (25%), arm muscle circumference (AMC) (21.9%) and arm circumference (AC) (18.8%). When comparing the nutritional status of patients during follow-up, there was a significant difference only in the evaluation methods of AC ($p = 0.009$), triceps skinfold thickness ($p = 0.044$) and PA by BIA ($p = 0.008$). At the end of follow-up, the methods of nutritional assessment were again compared. They showed a significant statistical difference ($p = 0.049$), with HGS being the method that better detected malnutrition. **Conclusion.** It is suggested that the method PA by BIA could be more widely used with this population since the results are consistent with other findings in the literature and are significant, reliable, and reproducible.

032

ASSESSMENT OF FOOD CONSUMPTION AND NUTRITIONAL STATUS IN CIRRHOTIC PATIENTS

B. COCCARO-PIVATTO, C. AUGUSTO-MARRONI, S. ALVES-FERNANDES, C. BERTASO ANDREATTA-GOTTSCHALL
UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE (UFCSPA), PORTO ALEGRE, RIO GRANDE DO SUL, BRAZIL.

Introduction. Mechanisms of malnutrition in cirrhotic patients are multifactorial and interrelated, but is often misdiagnosed because the intrinsic pathology complications such as ascites and edema affecting the results of traditional techniques for assessing nutritional status. Thus, early identification of diet modification of these patients concomitantly to assess nutritional status is an effective way to intervene in possible nutritional deficits of progressive liver failure box. **Material and methods.** We evaluated cirrhotic patients who are monitored in Nutrition in Hepatology and Liver Transplantation ambulatories from a SUS tertiary hospital in Porto Alegre, Rio Grande do Sul. The methods used for nutritional assessment were: body mass index (BMI), triceps skinfold thickness (TST), arm circumference (AC), arm muscle circumference (AMC), hand grip streng (HGS) and adductor pollicis muscle (APM). The food intake was assessed by 24-hour recall in triplicate. We used a questionnaire to assess dietary guidelines and exclusions by patients. Disease severity was assessed by the Child-Pugh classification as score. **Results.** We evaluated 59 cirrhotic patients, with an average age of 56.3 years (± 7.7 years), of whom 37 (62.7%) male subjects. The most frequent etiology was hepatitis C (45.8%), followed by alcohol (28.8%). Of the total sample, 18 (30.5%) were Child-Pugh A, 34 (57.6%) Child-Pugh B and 7 (11.9%) Child-Pugh C. The method of nutritional assessment that identified more malnourished patients was the handshake 41 (69.5%). The mean energy intake was 22.5 ± 8.0 kcal/kg, with an average intake of 0.87 ± 0.34 g protein/ kg, both below the recommended. Intake of potassium, calcium, iron, zinc and magnesium not reached the recommendation. The main source of food was the guidance of professional health care, prevailing food exclusion of foods rich in fats in the diet.

There was an association of the Child-Pugh and CB with carbohydrate intake, respectively (p = 0.004) and (p = 0.023). Child-Pugh C patients showed higher consumption of this macronutrient and normal individuals by CB properly consumed carbohydrates when compared to malnourished patients, who consumed in excess. There was a significant association with DCT lipid intake (p = 0.023), malnourished patients by DCT that consume below the recommended macronutrient. **Conclusions.** There was a high prevalence of malnutrition and inadequate caloric and protein intake in these patients, as well as guidelines of erroneous exclusions. Therefore more attention is needed concerning nutritional guidelines in cirrhotic patients, in order to correct possible nutritional deficits and contribute to a better prognosis.

033

DIETHYLNITROSAMINE INDUCED CIRRHOSIS IN WISTAR RATS: AN EXPERIMENTAL FEASIBILITY STUDY

S. BONA,[*] A.J. MOREIRA,[*] G.R. RODRIGUES,[*] M. MORAES,[*] C.T. CERSKI,[*] T.R. SILVEIRA,[*] C.A. MARRONI,[**] N.P. MARRONI[*,***]
[*]*UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL.*
[**]*UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE.*
[***]*UNIVERSIDADE LUTERANA DO BRASIL.*

Background. The experimental models that development cirrhosis in rats require long time. However, few studies have focused on the reduction of time to establish cirrhosis and evaluated the expression of heat shock protein 70 (HSP70) in cirrhotic livers of rodents. **Objective.** Adaptation of an experimental cirrhosis model using diethylnitrosamine (DEN) to evaluate lipoperoxidation (LPO), expression of stress sensitive proteins (NQO1 and HSP70), and fibrosis marker (TGF-β1). **Material and methods.** Twenty-six male Wistar rats, weighing ± 270 g, 2 groups: i) CO-Control, ii) DEN-diethylnitrosamine. The DEN group received 50 mg/kg of DEN twice a week i.p. for 7 weeks. Phenobarbital (0.3 g/L) was added to the drinking water of animals as enzymes inducer. **Results.** Levels increased in liver function tests (AST, ALT, GGT, AP) in animals with DEN compared to control. The histological examination showed changes and loss in the liver architecture, with severe ductal proliferation, cholestasis, lymphocytic infiltrate, steatosis, and nodular formations with homogeneous pattern. We also found, increased of LPO, increased expression of TGF beta and NQO1. However, the HSP70 expression was reduced in cirrhotic animals. **Conclusion.** Based on biochemical, histological, and molecular analysis this study developed cirrhosis in 7 weeks, being that the reduced expression of HSP70 associated with increased oxidative stress contributed to the worsening of the disease.

034

CIRRHOSIS INDUCES APOPTOSIS IN RENAL TISSUE THROUGH INTRACELLULAR OXIDATIVE STRESS

K.C. SIMÕES DA SILVEIRA,[*,†] C.M. VIAU,[†,‡] J.R. COLARES,[§] M.I. MORGAN-MARTINS,[§,||] J. SAFFI,[†,‡] N.P. MARRONI,[§,||] M. PORAWSKI[*,||]
[*]*DEPARTMENT OF BASIC HEALTH SCIENCES-LABORATORY OF PHYSIOLOGY AND*
[†]*LABORATORY OF GENETIC TOXICOLOGY-UFCSPA, PORTO ALEGRE, RS.*
[‡]*NATIONAL INSTITUTE FOR TRANSLATIONAL RESEARCH ON HEALTH AND ENVIRONMENT IN THE AMAZON REGION-CNPQ/INCT/INPETAM-RIO DE JANEIRO, RJ.*
[§]*LABORATORY OF OXIDATIVE STRESS-ULBRA, CANOAS, RS.*
[||]*RESEARCH CENTER OF CLINICAL HOSPITAL-UFRGS, PORTO ALEGRE, RS, BRAZIL.*

Aim. We aimed to evaluate the renal oxidative stress, cell damage and impaired cell function in animal model of cirrhosis. **Material and methods.** Secondary biliary cirrhosis was induced in male Wistar rats by ligation of the common bile duct (BDL). The animals were sacrificed after 28 days of obstruction. Animals were randomized in two groups: control (n = 6) and BDL (n = 6). All studies were in accordance with the Ethical Committee for Research Involving Animals of UFCSPA. We measured thiobarbituric acid reactive substances (TBARS), reactive oxigen species (ROS) and mitochondrial membrane potential (MMP) in kidney, and activities of the antioxidant enzymes catalase, superoxide dismutase, and glutathione peroxidase. Relative cell viability was determined by trypan blue dye-exclusion assay (TBDE). Annexin V-PE was used in conjunction with a vital dye, 7-AAD, to distinguish apoptotic from necrotic cells and comet assay was used for determined DNA integrity in single cells. **Results.** In BDL animals there was significant increase in the kidney TBARS and intracellular ROS. There was too an increase in the activity of all antioxidant enzymes evaluated. The percentage viability was above 90% in the control group and in BDL was 64.66% and the dominant cell death type was apoptosis. DNA damage was observed in the BDL. There was a decreased in the MMP from 71.40 ± 6.35% to 34.48 ± 11.40% in BDL. **Conclusion.** These results indicate that intracellular increase of ROS cause damage in the DNA and apoptosis getting worse the renal function in cirrhosis.

E. HEPATOCELLULAR CARCINOMA AND OTHER BILIARY TRACT TUMORS

001

MANAGEMENT OF PRIMITIVE LIVER TUMOURS

L. ILIESCU, L. TOMA, C. ORBAN, A. TANASE
FUNDENI CLINICAL INSTITUTE, BUCHAREST, ROMANIA.

Background and aims. Hepatocellular carcinoma (HCC) is the fifth most common cancer worldwide and the third most common cause of cancer-related death. We aim to study the diagnosis and treatment options for HCC. **Material and methods.** We used standard methods for diagnosis for HCC: radiology, determining serum alpha fetoprotein (AFP). We included 179 patients diagnosed with HCC between April 2011 and May 2013. **Results.** All patients were classified and treated according to the Barcelona Clinic Liver Cancer (BCLC) staging: resection/transplant, ablation (RAF), percutaneous ethanol injections (PEI), transarterial chemoembolization (TACE), new therapies. Our study included 45 patients with early stage HCC, 67 patients with intermediate stage HCC

Table. (001)

Early stage	Intermediate stage	Advance stage
Liver transplant (4)	TACE (46)	TACE + Sorafenib (3)
Resection (7)	TACE + RAF (9)	Sorafenib (16)
Local ablation (32)	TACE + Sorafenib (3)	Sorafenib + Bevacizumab + Erlotinib (1)
RAF (23)		Systemic therapy (48)
PEI (4)		
RAF + PEI (5)		

(Stage B) and 46 pts with advanced stage HCC (Stage C). Table presents the therapeutical options and the number of patients in each group. Most patients in the early stage underwent local ablation, while TACE was preferred in 46 patients in the intermediate stage. Systemic therapy was the most frequent treatment for patients in the advanced stage (48 patients), followed by sorafenib (16 patients). One patient with advanced stage was given sorafenib + bevacizumab + erlotinib. 21 patients with end-stage disease did not receive treatment. Survival rates depended on the HCC stage: 2-18 months in the intermediate stage and 1-12 months in the advanced stage. Survival rates after liver transplant decreased in time as expected. **Conclusion.** Early diagnosis of HCC is essential in improving the patients' outcomes, as there are several classic therapeutic options and new emerging ones addressing patients with early stage disease. The combination of molecular therapies is expected to improve the outcome benefits already obtained with Sorafenib.

002

DIAGNOSTIC YIELD OF EUS-GUIDED FNA AND EUS-GUIDED FNB IN PATIENTS WITH SUSPECTED HILAR CHOLANGIOCARCINOMA

A.R. BERNAL-MÉNDEZ,* C.G. GUERRERO VÁZQUEZ,* **A.I. RAMÍREZ POLO,*** **M.A. RAMÍREZ-LUNA,**** **F. I. TÉLLEZ-ÁVILA****
**DEPARTMENT OF GASTROENTEROLOGY, **DEPARTMENT OF ENDOSCOPY, INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MEXICO CITY.*

Background. Cholangiocarcinoma is the most common malignancy of the biliary tract. Endoscopic ultrasound (EUS) allows fine needle aspiration biopsy (FNA) or EUS-guided fine needle biopsy (FNB), with a reported sensitivity of 85% and almost 100% specificity for the diagnosis of pancreatic tumors. The aim of our study was to evaluate the diagnostic yield of EUS-FNA and EUS-FNB, as a first-line tissue-sampling acquisition approach, in patients with suspected hilar cholangiocarcinoma. **Objective.** To evaluate the diagnostic yield of EUS-FNA and EUS-FNB in patients with suspected hilar cholangiocarcinoma. **Material and methods.** We performed a retrospective analysis of electronic and paper records of patients with jaundice and suspected hilar cholangiocarcinoma diagnosed by non-invasive imaging methods (CT or MRI) and EUS-FNA/FNB. Patients were referred to the endoscopy department of the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, from January 2006 to December 2012. EUS-FNA/FNB was performed using a linear array echoendoscope GFUCT-140 (Olympus America Inc; Center Valley, Pa) by two echoendoscopists. Statistical analysis: The results were evaluated using descriptive statistics for nonparametric distribution: median and minimum-maximum, absolute and relative frequencies. Sensitivity, specificity, positive and negative predictive values were calculated based on the final result of the gold standard. All analyses were conducted using SPSS 20 for Mac. **Results.** A total of 39 patients with 50 EUS-FNA/FNB were included; 40 (80%) EUS-FNAs were performed using standard Echo-tip 22 G, the remaining 10 (20%) EUS-FNBs were performed using ProCore needles. Histological diagnosis by EUS-FNA/FNB was achieved in 32 (82.1%) patients: cholangiocarcinoma in 27 patients (69.2%), benign stricture in four (10.3%) patients, hepatocellular carcinoma in one (2.6%) patient. No differences (P = 0.55) in diagnostic yield were noted between EUS-FNA and EUS-FNB. In 30/32 (93.8%) cases the diagnosis was made in the first EUS-FNA/FNB, and in 2/32 (6.2%) patients the diagnosis was made in the second EUS-FNA. The sensitivity of EUS-FNA/FNB for cholangiocarcinoma was 79%, the positive predictive value was 100%, the negative predictive value was 41.6%, and the accuracy was 82%. No complications were observed. **Conclusions.** The diagnostic yield of EUS-FNA/FNB in patients with suspected hilar cholangiocarcinoma is high and safe. In most cases the diagnosis was made during the first procedure.

003

ANATOMIC LIVER RESECTION OF SEGMENT 6, 7 AND 8 IS AN ALTERNATIVE MODALITY FOR MAXIMAL HEPATECTOMY IN THE TREATMENT OF HEPATOCELLULAR CARCINOMA

CHANGKU JIA, QINGZHUANG YANG, JIE WENG, YOUKE CHEN, YU FU
DEPARTMENT OF HEPATOBILIARY PANCREATIC SURGERY, THE AFFILIATED HOSPITAL OF HAINAN MEDICAL COLLEGE, HAINAN, CHINA.

Introduction. Patients with huge or multifocal tumors in right liver and with small volume of left liver can not be performed right hemi hepatectomy in consideration of postoperational liver failure, thus making the overall low resection rate for hepatocellular carcinoma. To enlarge the number of resectable patients, we designed anatomic liver resection of segment 6, 7 and 8 in patients with right liver tumor(s). **Materials and methods.** Of these 6 cases report herein, multiple tumors were found in segment 6, 7 and 8 in 2 and huge tumors were found in segment 6, 7 and 8 in 4. CT volumetry analyzed that left hemihepatic volume was less than the minimal limit of safe survival in these cases. If segmentectomy of 6, 7 and 8 be performed, the percentage of future liver remnant volume (%FLR) increased by an average of 13.9%. Therefore, we planned to perform anatomic liver resection of segment 6, 7 and 8 to guarantee the maximum preservation of remaining normal liver tissue. Segment 5 was determined by two steps of Glissonean pedicle occlusion. And a "⌐¬" shaped broken resection line was marked upon the diaphragmatic surface of the liver. Then anatomic liver resection of segment 6, 7 and 8 was performed along with the broken resection line. **Results.** All hepatectomies were uneventfully completed with average operation time of 326 min (range from 260 to 470 min) and average blood loss of 758 ml (range

from 400 to 1,800 mL) in this group. Gross specimen showed that tumors were completely resected and postoperative pathology verified hepatocellular carcinoma of the tumor. There was no perioperative death. One patient dead 383 days postoperation due to obstructive suppurative cholangitis. One patient was found of intrahepatic recurrence 4 month postoperation. Lung metastasis was found in 1 post operation. No tumor recurrence was found in other patients and the parameters including liver function and AFP level were in the normal range. **Conclusions.** Anatomic liver resection of segment 6, 7 and 8 can be a conventional operation to enable maximum preservation of remaining normal liver tissue, thus improving the overall resection rate for hepatocellular carcinoma.

004

ANALYSIS ON THE OUTCOME OF CIRRHOTIC PATIENTS CARRYING HEPATOCELLULAR CARCINOMA IN WAITING LIST FOR HEPATIC TRANSPLANTATION

C.A. MARRONI, L.W. GRILLO
UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE, RS, BRAZIL.

Introduction. Patients with cirrhosis present a high risk of developing hepatocellular carcinoma (HCC). The orthotopic liver transplant (OLT) is an effective therapeutic option for treating cancer and hepatic dysfunction. This study evaluates the outcome of patients with cirrhosis with HCC in liver transplant waiting list and predictive factors for dropout. **Material and methods.** An observational, retrospective historical cohort study was conducted in a general hospital in the south of Brazil from May 2006 to December 2010 with patients up to the time of transplant or dropout. Analysis was performed using the Cox Regression model and Kaplan-Meier curves and comparison, by the Log-rank test. **Results.** Of the 148 patients evaluated, 70.9% underwent OLT and 29.1% were dropped out due to tumor progression or death; 79.1% were within the Milan criteria. Predictive factors for dropout at univariate analysis that presented statistic significance ($p < 0.05$) were alpha-fetoprotein level > 20 ng/mL [Hazard Ratio (HR), 2.4; 95% confidence interval (CI), 1.3-4.4] and tumor outside Milan criteria (HR, 3.4; 95% CI 1.8-6.2); and in multivariate analysis with statistic significance ($p < 0.05$) were Child-Pugh B and C (HR, 2.1; 95% IC 1.1-4.2). Factors independent from OLT waiting list dropout were tumor outside the Milan criteria (HR, 2.9; 95% CI 1.4-6.0) and Child-Pugh B or C (HR 2.1; 95% CI 1.1-4.2). **Conclusion.** Milan criteria, alpha-fetoprotein, and Child-Pugh classification were able to identify individuals at higher risk of dropout from liver transplant waiting list.

005

RELATIONSHIP BETWEEN APPARENT DIFFUSION COEFFICIENT AND HISTOLOGICAL TUMOR GRADING OF HEPATOCELLULAR CARCINOMA OF EXPLANTED LIVERS AND HEPATIC RESECTION IN PATIENS OF THE HOSPITAL PABLO TOBON URIBE, MEDELLIN-COLOMBIA

E. CORREA-GUTIÉRREZ,[*] L. TORO-RENDÓN,[*] G. CASTRILLÓN,[†,‡] C. CUERVO-VALENCIA,[§,||] S. HOYOS-DUQUE,[†,§] G. OSORIO-SANDOVAL,[†,||] J. RESTREPO-GUTIÉRREZ,[†,§] J. PÉREZ-CADAVID,[§,¶] C. HUERTAS-DURÁN[**]
[*]FACULTAD DE MEDICINA, [†]GRUPO DE GASTROHEPATOLOGÍA, UNIVERSIDAD DE ANTIOQUÍA. MEDELLÍN, COLOMBIA.
[‡]CEDIMED. MEDELLÍN, COLOMBIA.
[§]HOSPITAL PABLO TOBÓN URIBE. MEDELLÍN, COLOMBIA.
[||]CENTROS ESPECIALIZADOS SAN VICENTE FUNDACIÓN. RIONEGRO, COLOMBIA.
[¶]DINAMICA IPS. MEDELLÍN, COLOMBIA.
[**]INSTITUTO NEUROLÓGICO DE ANTIOQUÍA. MEDELLÍN, COLOMBIA.

Background. Histological grade in hepatocellular carcinoma (HCC) is one of the most important prognostic factors regulating recurrence and survival after surgical resection and liver transplantation in HCC patients. The aim of this study was to define the relationship between the findings in the apparent diffusion coefficient (ADC) in magnetic resonance imaging with the histopathologic grade of hepatocellular carcinoma (HCC) of explanted livers and hepatic resection. **Material and methods.** The clinical records of 17 patients (10 male and 7 female) who had undergone hepatic resection or liver transplantation for HCC between January 2010 and December 2013, were retrospectively reviewed. Evaluation of preoperative magnetic resonance imaging (MRI) sequences and histopathological findings in the explanted livers and hepatic resection was performed. The MRI sequences were reviewed by two independent radiologist blind to the histopathological results. The end points of the study were to evaluate the interobserver agreement among radiologist in measuring ADC in patients with HCC and among pathologist in histologic tumor grade. **Results.** The ADC values of the HCC evaluated in this study were 0.4 to 1.9 x 10^{-3} mm^2/s (average: 1.103 x 10^{-3} mm^2/s), the correlation of ADC for each nodules was 47%, while the agreement between radiologists was 64%. Correlation between ADC values and histopatological results given in Me (min-max) for HCC of well, moderately and poorly differentiated was 1.063 (n = 4, 1.0-1.2) 1,156 (n = 38, 0.7-1.9) and 0.940 (n = 9, 0.4-1.4) x10^{-3} mm^2/s respectively. **Conclusion.** ADC of HCC decrease as the histologic grade progresses, but we were unable to find a relationship between ADC and histopathologic grade.

006

BILIARY CYSTADENOCARCINOMA WITH ONCOCYTIC DIFFERENTIATION. CASE REPORT

E. PÉREZ-REYES,[*] M. ALEJANDRO-LÓPEZ,[**] E. PÉREZ-TORRES,[*] G. ARISTI-URISTA[**]
[*]GASTROENTEROLOGY DEPARTMENT, [**]PATHOLOGY DEPARTMENT, HOSPITAL GENERAL DE MÉXICO EDUARDO LICEAGA, MÉXICO D.F.

Introduction. Biliary cystic tumors are represented by biliary cystadenoma and cystadenocarcinoma, both are less than 5% of liver cysts. Biliary cystadenoma occurs predominantly in women while the cystadenocarcinoma occurs in both sexes. The age of presentation is 45 years for the cystadenoma and a decade later for cystadenocarcinoma. Oncocytic

degeneration occurs when some neoplasms present specific cellular features; this change is rare in liver neoplasms. **Case report.** Male, 81 years old, with history of atrial fibrillation treated with amiodarone and warfarin; and untreated obstructive prostatic hyperplasia. Presents from a month progressive jaundice and increased abdomen circumference, a liver ultrasound showed a hepatic tumor. He presented disorientation, loss of consciousness and abnormal breathing pattern and he was brought to the emergency room where he died within hours of admission because of its bad general conditions. At necropsy an ovoid tumor was found in right lobe of the liver, unencapsulated, 8cm in the major axis, solid with fibrous appearance and irregular cystic areas within the periphery. Histopathological, the lesion was composed of two components: 1) Multiple irregular-cystic tubule, of varying size, lined by epithelium with variable appearance, from flattened or cuboidal or cylindrical-single mucoproductor without atypia, to large areas with changing structures oncocytic with micropapillary hyperplasia and intraluminal projections, severe dysplasia, stromal and perineural invasion; and 2) Abundant dense and hypocellular fibrous stromal (anywhere ovarian stromal was observed type). With these findings a biliary cystadenocarcinoma with extensive oncocytic change was diagnosed. **Discussion.** Biliary cystadenocarcinoma represents 0.18% of primary liver tumors. Both, biliary cystadenoma and cystadenocarcinoma, are multicystic and they are associated with ovarian- like mesenchymal stromal, but it's not present in all neoplasms. Its clinical presentation is mild and nonspecific; some patients have right upper quadrant pain, palpable mass, or tumor complications such as jaundice, ascites, and bone pain is seen in metastatic cases. Histologically, biliary cystadenocarcinoma is a tubolopapillar or papillary neoplasm with capsular epithelium with papillae projecting into the cystic cavity. The oncocytic degeneration has been observed in neoplasms of other organs such pancreas, salivary glands, breast and ovary. In liver this change has been described in hepatic adenoma or in fibrolamellar type of hepatocellular carcinoma; its presence in biliary lesions is exceptional and its meaning is uncertain. **Conclusion.** Biliary cystadenocarcinoma is a rare cystic neoplasm of the liver; cases with oncocytic degeneration are even rarer. It has to be a differential diagnosis to another cystic liver neoplasm.

007

EFFECT OF SUSTAINED VIROLOGICAL RESPONSE ON THE INCIDENCE OF HEPATOCELLULAR CARCINOMA IN HCV CIRRHOTIC PATIENTS

H. CHEINQUER, S. COELHO-BORGES, N. CHEINQUER, A. DE ARAÚJO, J. STIFFT, F. HERZ WOLFF
HOSPITAL DE CLINICAS DE PORTO ALEGRE, PORTO ALEGRE, RS, BRAZIL.

Background. There is evidence of decreased incidence of hepatocellular carcinoma (HCC) in patients with chronic hepatitis C virus (HCV) infection who achieve a sustained virological response (SVR). The aim of this study was to compare the rate of HCC among HCV cirrhotic patients with and without SVR. **Material and methods.** In this retrospective cohort study, 357 HCV cirrhotic patients that received interferon based therapy between 2005 and 2012 in Hospital de Clinicas de Porto Alegre, Brazil, were divided in two groups: A) patients with SVR, and B) patients without SVR. At baseline, all patients were Child A with no previous history of hepatic decompensation and no evidence of HCC on abdominal ultrasound (US). SVR was defined as negative HCV-RNA 24 weeks after end of treatment using molecular amplification method with a limit of detection of 15 IU/mL. Patients were followed every 6 months with US until HCC, death, or liver transplantation. HCC was diagnosed using dynamic imaging method (computerized tomography and/or magnetic resonance) showing a liver nodule with typical vascular pattern with wash-in on arterial phase and wash-out on portal phase. The protocol was approved by the Institution Ethics Committee and all patients signed informed consent. Statistical analysis was based on Fisher's Exact Test and Kruskall-Wallis (alpha < 0.05). **Results.** Among 357 treated HCV cirrhotic patients, 125 (35%) achieved SVR (group A) and 232 (65%) did not (group B). Mean follow-up was 49.9 ± 30.0 months in those with SVR *vs.* 33.4 ± 24.0 months in those without SVR. During follow-up, HCC was diagnosed in 15 (12%) of 125 SVR patients and 48 (21%) of 232 non-SVR patients ($P=0.04$). Baseline characteristics were similar among SVR and non-SVR patients, with the exception of age (51.7 *vs.* 54.3 years; $P = 0.01$) and platelets (138,000 ± 53,000/mm^3 *vs.* 112,000 ± 54,000/mm^3; $P < 0.0001$), respectively. **Conclusions.** There was a significantly higher incidence of HCC among HCV cirrhotic patients without SVR. However it is important to notice that a fairly large proportion of patients with SVR were still able to develop HCC. These findings support the fact that cirrhotic patients need indefinite follow-up, regardless of HCV RNA eradication status.

008

EPIDEMIOLOGICAL ASPECTS OF HEPATOCELLULAR CARCINOMA IN PETRÓPOLIS, RJ, BRAZIL

K. RODRIGUES-DO-Ó,* L.H. SPIELMANN,** F.D'ALBUQUERQUE E CASTRO***
**HOSPITAL SÃO LUCAS, PETRÓPOLIS, RIO DE JANEIRO, BRAZIL.*
***HOSPITAL SANTA TERESA, PETRÓPOLIS, RIO DE JANEIRO, BRAZIL.*
****HOSPITAL GERAL DE PALMAS, TOCANTINS, BRAZIL.*

Background and aims. Hepatocellular carcinoma (HCC) is one of the most common cancers in the world. It is responsible for more than 500 000 deaths/year. In some regions of Asia and Africa, HCC is the major cause of death among cancers. Regions with the greatest incidence are those highly endemic for hepatitis B virus (HBV), including Sub-Saharan Africa and Southeast Asia. Brazil was considered to have a low prevalence of HCC. **Material and methods.** We included 38 patients diagnosed with HCC from 2008-2013. Patients were diagnosed based on imaging examinations. Only one imaging was necessary, either computed tomography or magnetic resonance imaging. A diagnosis of HCC could be confirmed with the presence of a focal hepatic lesion with typical vascularization in a patient with cirrhosis (arterial enhancement followed by wash out in late phase. **Results.** The median age was (57 years old); 65% male. All of the patients had cirrhosis. Hepatitis C virus was the main etiology (76.3%) followed by hepatitis B virus (5.26%); alcohol (7.8%) and others (10.5%). **Conclusions.** Compared with national survey published in 1977 this survey indicated a greater proportion of patient with Liver Cirrhosis that was the main risk factor for the development of HCC in Petrópolis. Efforts to increase surveillance programs in patients at risk for HCC should be stimulated because they are cost-effective in patients suitable for curative therapy.

009

COMPLETE PATHOLOGICAL RESPONSE FOR UNRESECTABLE HEPATOCELLULAR CARCINOMA WITH A FLUOROURACIL BASED REGIMEN AFTER SORAFENIB FAILURE. A CASE REPORT AND REVIEW OF THE LITERATURE

J.I. GONZÁLEZ-VILLANUEVA,[*] Y.A. LÓPEZ-CHUKEN,[*] G.A. GONZÁLEZ-CONCHAS,[*] J.L. GONZÁLEZ-VELA,[*] X. GÓMEZ-ROEL,[**] D. HERNÁNDEZ-BARAJAS,[*] O. BARBOZA-QUINTANA,[*] A. BARBOSA-QUINTANA,[*] L.C. CANALES-MARTÍNEZ,[*] J.F. GONZÁLEZ-GUERRERO[*]

[*]*HOSPITAL UNIVERSITARIO. UANL, MONTERREY, N.L. MÉXICO.*
[**]*OPCION ONCOLOGÍA, MONTERREY, N.L., MÉXICO.*

Background. Hepatocellular carcinoma (HCC) is a major health problem and represents the third most common cause of cancer death. Early stage HCC is typically silent with few symptoms until late in the disease, leading to diagnosis in advanced stages in up to 80% of patients. Therapeutic options available to these patients are limited and the prognosis is poor. At present, sorafenib is the only approved systemic treatment available for unresectable HCC. However, there is no actual consensus on a second-line systemic treatment in patients who are unresponsive or unfit to sorafenib. Recent evidence suggests that with appropriate patient selection, there may be a substantial niche for systemic chemotherapies, particularly with Fluorouracil-based schemes. **Case report.** A 51- year-old with no known history of chronic liver disease was referred to our unit by the surgery department after a complete tumor resection was attempted. During laparotomy, duodenal infiltration was found and resection was not performed. Serum alpha-phetoprotein level was found to be 3,340 ng/mL. A computed tomography (CT) scan of the abdomen showed a mass in hepatic segment V that measured 12 cm with the typical wash-in and wash-out phases seen in HCC. Oral sorafenib therapy was initiated on June 2011 with a dosage of 400 mg bid. Seven weeks after the onset of treatment, a control CT revealed a dimensional increase of the tumor and sorafenib was discontinued. Systemic chemotherapy was started on July 2011 with single-drug Oxaliplatin for one cycle and thereafter 5-Fluorouracil was added to Oxaliplatin. After 17 cycles of chemotherapy, a reduction of the neoplastic lesion was observed in a control CT scan of the abdomen and serum alpha-phetoprotein level accounted for 31.2 ng/mL. Surgical resection was performed on January 20th, 2013. Pathologic examination of the tumor reported large areas of necrosis and fibrosis compatible with a complete response. Last assessment on May 2014 with laboratory and radiological studies confirmed complete response had been maintained. **Conclusions.** To the best of our knowledge, this case represents the first example of a complete pathological remission in a patient with advanced HCC using a Fluorouracil-based chemotherapy after documented progression with sorafenib. Further investigation is required to identify clinical and molecular markers that can be correlated with prognosis in selected patients that may benefit with fluororacil based regimes, especially in those who are unfit, progress or do not have access to sorafenib.

010

MELATONIN PROLONGS OVERALL SURVIVAL IN RATS WITH HEPATOCELLULAR CARCINOMA INDUCED BY DIETHYLNITROSAMINE

A.J. MOREIRA,[†‡] G.R. RODRIGUES,[*†] S. BONA,[*†] M. MORAES,[†] C.T. CERSKI,[§] J.N. PICADA,[¶] C.A. MARRONI,[||] N.P. MARRONI[*†‡¶]

[*]*GRADUATE PROGRAM IN MEDICAL SCIENCES: MEDICINE, UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, PORTO ALEGRE - RS - BRAZIL.*
[†]*CENTER OF EXPERIMENTAL RESEARCH, HOSPITAL DE CLÍNICAS DE PORTO ALEGRE - RS - BRAZIL.*
[‡]*GRADUATE PROGRAM IN BIOLOGICAL SCIENCES: PHYSIOLOGY,* [§]*DEPARTMENT OF PATHOLOGY, SCHOOL OF MEDICINE, UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, RS - BRAZIL.*
[||]*GRADUATE PROGRAM IN LIVER DISEASES, UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE, RS - BRAZIL.*
[¶]*GRADUATE PROGRAM IN CELL AND MOLECULAR BIOLOGY APPLIED TO HEALTH, UNIVERSIDADE LUTERANA DO BRASIL - RS - BRAZIL.*

Introduction. This study developed HCC using diethylnitrosamine (DEN) in rats and proposed the treatment with melatonin (MLT). We evaluated the overall survival (OS), comet assay liver (CA), biochemical and histological analysis. **Material and methods.** 28 male Wistar rats, ± 145g were divided into: I) Control, II) HCC–DEN 50 mg/kg ip, III) MLT5-DEN 50 mg/kg ip+ melatonin at 5th week, IV) MLT12-DEN 50 mg/kg ip+melatonin at 12th week. MLT (20 mg/L) was administrated in water. Blood was collected to evaluate transaminases (AST and ALT), gamma glutamyl transferase (GGT) and alkaline phosphatase (AP) (U/L). Liver samples were removed for CA and histological analysis. Statistical analysis: Tuckey test with $p < 0.05$ and Kaplan Meier curve. **Results.** MLT prolongs OS in III and IV groups *vs.* II group ($p = 0.0001$). MLT reduced damage (DI) and frequency (DF) index in DNA (DI: I = 95 + 27; II = 339 + 56; III = 259 + 42; IV = 119 + 17; DF: I = 74 + 17; II = 99 + 2; III = 92 + 5; IV = 60 + 5). AST(I) 107 + 7 (II) 236 + 69 (III) 165 + 59 (IV) 143 + 27; ALT (I) 54 ± 15 (II) 144 + 36 (III) 102 + 36; (IV) = 95 + 18 GGT (I) 1 + 0.9 (II) 85 + 45 (III) 43 + 33 (IV) 25 + 14; AP (I) 111 + 50 (II) 279 + 91 (III) 215 + 98 (IV) 212 + 46; group II showed significant increase compared to groups I, III and IV. Liver histology of II group was characterized by pseudoacinar and trabecular growth pattern. We concluded that chronic and intermittent exposure model to carcinogenic agents develops HCC in rats. Melatonin improved hepatic function and reduced damage on DNA, resulting an increase in OS in rats with HCC. CNPq; CAPES, HCPA-FIPE, UFRGS; ULBRA/ CNPq; UFCSPA.

011

QUANTUM MECHANICAL MODEL FOR ANTI-CARCINOGENIC EFFECT OF ULTRALOW-FREQUENCY ELECTROMAGNETIC FIELDS ON EARLY CHEMICAL HEPATOCARCINOGENESIS

G.O. LÓPEZ-RIQUELME, J.J. GODINA-NAVA

DEPARTAMENTO DE FÍSICA, CINVESTAV, IPN, MEXICO CITY, MEXICO.

Introduction. Chemical carcinogenesis is a multi-step process characterized by the electrophile attack to DNA, which produces mutations, resulting in malignant transformation of normal cells. Once into the organism, most chemical carcinogens suffer a metabolic activation by the cytochrome P450 enzymes, a heme-thiolate family protein that usually detoxifies xenobiotics. Such activation produces oxidative stress (OS), which damage

the DNA. P450 are electron carrier proteins, which produce spin-correlated radical pair (RP) intermediates that can either go to non-recombination or to continue the catalytic process. Enzymes with RP intermediates exhibit electromagnetic field-dependent parameters. Previously, it was found that a treatment with extremely low frequency electromagnetic fields (ELF-EMF) inhibits more than 50%, the number and area of preneoplastic lesions in rats with chemically induced cancer through the reduction of cell proliferation. **Objective.** In this work, the effect ELF-EMF in the early stages of OS induced by chemical carcinogens was theoretically analyzed. Methods. A quantum mechanical model based on RP mechanism was developed to explain the effects of ELF-EMF on the OS produced by chemical carcinogenesis. It was assumed that the periodic stimulation with ELF-EMF modifies the RP mechanism and intermediaries generated by carcinogen activation. A system of two electrons interacting with one nucleus and the ELF-EMF was solved. Then, the recombination probability of singlet states of the RP through the magnetic influence by the hyperfine interaction was studied to assess the spin states development during singlet-triplet inter-conversions. Results. In the model, the formation of RP intermediates in the singlet state from the OS is the primary responsible for cell damage and initiated cells, which could become a preneoplastic lesion. The recombination probability is proportional to the probability of cell damage, and the ELF-EMF decreases such probability significatively, modulating OS progression. The ELF-EMF modulates charged particles through the spin state selectivity in the singlet-triplet interconversion as well as in the separation between triplet states by hyperfine interaction and permitting that 2/3 of RP participate in the enzymatic reaction. Thus, since there are less active singlet spins, the number of initiated cells diminish, and, therefore, the preneoplastic lesion formation, which is the main cytoprotective effect of the EMF found experimentally. **Conclusion.** This multidisciplinary study contributes to the understanding of chemical carcinogenic process based on the behavior of charged particles. This knowledge can be used in clinical applications for ELF-EMF as co-adjutant in cancer treatment.

012

SURGICAL TREATMENT FOR ADVANCED HEPATOCELLULAR CARCINOMAS IN JAPANESE HOSPITAL

NORIYUKI OBA,[*] HIDEYUKI KANEMOTO,[*] KYODEN YUSUKE,[*] MICHIRO TAKAHASHI,[*] MASAKAZU TAKAGI,[**] MASAYA WATANABE,[**] KO OHATA,[**] SHINSUKE SATO,[**] YUSUKE TAKI[**]

[*]*DEPARTMENT OF HEPATO-BILIARY-PANCREATIC SURGERY, SHIZUOKA GENERAL HOSPITAL, JAPAN.*

[**]*DEPARTMENT OF SURGERY, SHIZUOKA GENERAL HOSPITAL, JAPAN.*

Introduction. Hepatocellular carcinoma (HCC) is sometimes accompanied by tumor thrombus (TT) in the portal vein, from the inferior vena cava (IVC) to the right atrium and main bile duct. We report herein on the results of our surgical treatment for such cases of advanced HCC. **Material and methods.** From February 1983 to August 2012, a total of 705 HCCs were treated in our hospital. Three-, 5- and 10-year cumulative survival rates were 71.5%, 56.0%, and 39.4%, respectively, and 3-, 5- and 10-year disease-free survival rates were 44.1%, 33.3% and 33.3%, respectively. Survival > 5, > 10, and > 20 years was seen in 203, 70, and 7 cases, respectively. This study evaluated the validity of our surgical treatment for 42 cases with TT. **Results.** Twenty-five of the 42 cases had TT in the main portal vein or its first branch. The 5-year survival rate of these 25 patients was unsatisfactory at 15.4%, with the exception of 1 case that survived 19 years. In 10 cases combined with TT extending to the IVC, and right atrium in some cases, we performed hepatectomy combined with tumor thrombectomy. The 3-year survival rate of these 10 cases was 45.7%, with 1 case surviving 5 years without recurrence. We performed lobectomy or extended lobectomy with tumor thrombectomy for 7 cases with TT in the right or left hepatic or common bile duct. The 5-year survival rate of these 7 patients was 53.6%, with 1 case surviving 13 years without recurrence. **Discussion.** HCCs sometimes extend to involve the portal vein, IVC, right atrium and main bile duct. Such cases are categorized as stage C of the Barcelona-Clinical Liver Cancer classification. Sorafenib is recommended for such advanced cases; however, median survival has been reported as 11 months, which is not sufficient. Excluding cases with portal involvement, results in our series were much better. One reason is that the resection of tumors and TT, which might cause some symptoms and harmful effects for patients, improved quality of life, even some recurrences developed. We now try to perform neoadjuvant therapy by hepatic arterial infusion of fluorouracil with systemic administration of interferon for cases with portal involvement. **Conclusion.** Surgery is a valid therapeutic option for advanced HCC, even if TT is present in the major bile duct or IVC and right atrium.

013

USE OF BRIVANIB IN A PATIENT WITH ADVANCED HEPATOCELLULAR CARCINOMA

L. CISNEROS-GARZA,[*,**] H. GUZMÁN-VÁZQUEZ[**]

[*]*CENTRO DE ENFERMEDADES HEPÁTICAS, HOSPITAL SAN JOSÉ TEC DE MONTERREY, MONTERREY, NUEVO LEÓN, MÉXICO.*

[**]*INSTITUTO MEXICANO DEL SEGURO SOCIAL, MONTERREY, NUEVO LEÓN, MÉXICO.*

Background. According with the SHARP trial, the use of molecular specific targets in advanced hepatocellular carcinoma increases median survival when is compared with placebo (10.7 months *vs.* 7.9 months, HR 0.69, $p \leq 0.001$). In a study Brivanib *vs.* Sorafenib as first line they found similar ORR with both treatments. **Objective.** To report evolution and survival of a patient with hepatocellular carcinoma treated with Brivanib as part of study BRISK-FL. **Case report.** We presented the case of a male patient, 56 years-old, mechanic, married. In his background he has history of hypertension and type 2 diabetes. Addictions negative. Occasional consumption of alcohol. He has occupational exposure to solvents (Paint Thinner, Gasoline). Medical history: type 2 diabetes mellitus diagnosed in 2002, treatment with Metformin 850mg BID, arterial hypertension diagnosed in 2002, treatment with Losartan 50 mg BID. History of the present illness: On February 2010, after routine studies, we detected thrombocytopenia. First was diagnosed as idiopathic thrombocytopenic purpura and was treated with Danazol and Prednisone. After ruling out hematological disease is referred to Gastroenterology department. We performed imaging studies finding hepatic cirrhosis and a mass of 8.6cm as the longest diameter on the segment 5 with "washout feature", deciding to undertake a biopsy. The histopathology report showed hepatocellular carcinoma well differentiated. Alpha fetoprotein 4,862.4 ng/mL. We started treatment with Brivanib as part of the BRISK-FL study on May 5th, 2010 on a dose of 800 mg/day, with a posterior reduction to 600 mg/day because of adverse events (hypothyroidism, diarrhea, hypokalemia, and pruritus). We

controlled the adverse events associated to Brivanib adjusting the dose as mentioned and also adding levothyroxine at a dose of 100 mc/day first and then at 150 mcg/day. The treatment continues until present date. We continue the follow-up of the patient with laboratory and imaging studies every 6weeks finding reduction in the size of the lesion to 4.6 cm on October 14th, 2011, and a progressive reduction on the level of alpha fetoprotein reaching the level of 96.58 ng/mL on September 12nd, 2012. On October 31st, 2013 we found new elevation on the levels of alpha fetoprotein to 588.83 ng/mL and a new CT showed 2 hepatic tumors compatible with activity. The patient continues on follow-up. Results: We found a survival better that the previously published with good quality of life. **Conclusions.** Brivanib showed a survival better than expected from published data in a patient with hepatocellular carcinoma, providing a useful therapy to select cases.

014

PARANEOPLASTIC SYNDROME IN A PATIENT WITH HEPATOCELLULAR CARCINOMA

G. HERNÁNDEZ-CELY,* J.D. MARTÍNEZ,*,*** S. GIRALDO,*** M.A. GARZÓN,* J. LIZARAZU,* J.C. MARULANDA,* J. C. MOLANO,* M.H. REY*

*UNIDAD DE GASTROENTEROLOGÍA, HOSPITAL UNIVERSITARIO DE LA SAMARITANA-UNIVERSIDAD EL ROSARIO.

**UNIVERSIDAD NACIONAL DE COLOMBIA.

***UNIVERSIDAD DE LA SABANA-BOGOTÁ, COLOMBIA.

Background. The main clinical manifestations of hepatocellular carcinoma (HCC) include abdominal pain, hepatomegaly, jaundice, and coagulopathy. Uncommon presentation, due to production of substances by neoplastic activity, result in metabolic disorders directly related to tumor invasion and worse prognosis. **Material and methods.** We report a case of a 47-year-old woman, with no past medical history. She came from the Amazon region of Colombia. Twelve months before admission, she felt persistent abdominal pain and weight loss. Approximately, three months before admission, she noticed a right upper abdominal mass. Liver cirrhosis due to chronic hepatitis B was diagnosed. Abdominal images revealed a focal hepatic lesion suggestive of HCC. Metastatic involvement was ruled out. During hospital admission, she had recurrent episodes of symptomatic hypoglycemia, requiring dextrose infusions with no improvement, then she required corticosteroid therapy at high doses (Prednisone 1.5 mg/kg) with successful response. Hypercholesterolemia and hypercalcemia were found within another metabolic disorders. Complete metabolic tests ruled out metabolic diseases, therefore we considered paraneoplastic manifestations of HCC. Definitive treatment is planned with ablation interventional radiology. **Results.** Laboratory test confirmed hypoglycemia (serum glucose < 30 mg/dL) with normal serum insulin concentration. Hepatitis B surface antigen was 30,356 ng/dL. Alpha- fetoprotein serum level was 3,650 ng/mL. Serum calcium was 11.0 mg/dL and total cholesterol levels were 240 mg/dL. Abdominal ultrasound and computed tomography revealed a vascularized mass of 7.5 cm in diameter occupying most of the right lobe of the liver. Parathyroid hormone levels were normal. **Conclusions.** Hepatocellular carcinoma is a tumor with a high incidence worldwide. It is associated with metabolic manifestations nearly in one third of the cases. Limited access to health care and low clinical suspicion delays diagnosis and increases negative outcomes. We recommend screening strategies for the detection of hepatitis B in endemic areas such as The Amazon region to reduce lethal complications of the infection.

015

ALTERATIONS IN CARBOHYDRATE METABOLISM AND INDICATORS SYSTEMIC INFLAMMATION IN PATIENTS WITH CANCER HEPATOBILIOPANCREATIC UNIVERSITY HOSPITAL OF MARACAIBO

C. FOX-CUEVAS,* M. LIZARZÁBAL**

*HOSPITAL CLÍNICO DE MARACAIBO, MARACAIBO-VENEZUELA.

**SERVICIO AUTÓNOMO, HOSPITAL UNIVERSITARIO DE MARACAIBO. SERVICIO DE GASTROENTEROLOGÍA. CENTRO DE REFERENCIA REGIONAL DE GASTROENTEROLOGÍA, ENDOSCOPIA Y HEPATOLOGÍA. FACULTAD DE MEDICINE, UNIVERSIDAD DEL ZULIA. MARACAIBO-VENEZUELA.

Diabetes and altered carbohydrate metabolism represent a global health problem and are considered risk factors for developing tumors of the digestive tract, especially with hepatobiliopancreatic tumors. For this reason a translational research was conducted, descriptive field , not experimental , prospective and cross, in adult patients at the University Hospital of Maracaibo (inpatient or outpatient Gastroenterology), with hepatobiliopancreatic cancer in which metabolic parameters were measured [glycemia (fasting glucose-tolerance test), insulin (fasting, postprandial), glycosylated hemoglobin, HOMA index, lipid profile] and indicators of inflammation (white count and differential count, erythrocyte sedimentation rate, C-reactive protein, transferrin and ferritin). A total of 16 cases of cancer hepatobiliopancreatic of which 56.3 % were reported (9 cases) were females aged 58-77 years (75%) and 78 years and over (18.8 %). 62.5% were mixed ethnicity, and from the Zulia state (62.5%). Socioeconomic status was reported by 43.8% in III level (lower middle class). Depending on the type of cancer found, 37.5% (6 cases) were Hepatocarcinomas, 25% (4 cases) Pancreatic cancer, 18.3% (3 cases) tumor Klastkin, 6.3% (1 case) Cancer bladder, 6.3% (1 case) papillary tumor, 6.3% (1 case) distal extrahepatic cholangiocarcinoma. As alterations in metabolism, the presence of insulin resistance was more frequent in pancreatic cancer and hepatocellular carcinoma. The body mass index was in the range of overweight and obesity in most cases more frequently in patients with pancreatic cancer but the lipid profile was within normal limits in all types of cancer. Inflammatory markers such as ESR, C-reactive protein, fibrinogen, transferrin and ferritin were elevated more often in cases of pancreatic cancer and hepatocellular carcinoma.

016

NEGATIVE MODULATION OF THE EPIGENETIC REGULATOR BY THYROID HORMONE RECEPTORS SUPPRESSES LIVER CANCER CELL GROWTH

SHENG-MING WU, KWANG-HUEI LIN

CHANG-GUNG UNIVERSITY, TAOYUAN, TAIWAN.

Introduction. The thyroid hormone, 3,3',5-triiodo-L-thyronine (T3), mediates several physiological processes, including embryonic development, cellular differentiation, metabolism, and regulation of cell proliferation. Thyroid hormone (T3) and its receptor (TR) are involved in metabolism and growth. In addition to their developmental and metabolic functions, TRs play a tumor suppressor role, and therefore, their aberrant expression can lead to tumor transformation. Aberrant epigenetic silencing of tumor suppressor genes promotes cancer progression. The epigenetic regulator, Ubiquitin-like with PHD and ring finger domains 1 (UHRF1), is overexpressed in

various cancers. **Material and methods.** Real-time qRT-PCR or immunoblot analysis was conducted to determine the expression of UHRF1. To determine the UHRF1 promoter activity, 5'-flanking regions were cloned and reporter actitivies were assayed. The physical interaction of Sp1 with UHRF1 promoter region was determined by chromatin immunoprecipitation (ChIP). To confirm the clinical significance of UHRF1 expression in liver cancer, immunohistochemistry and tissue microarray were performed. **Results.** In the current study, we demonstrated that T3 negatively regulates UHRF1 expression, both *in vitro* and *in vivo*. Our results further indicate that UHRF1 regulation by T3 is indirect and mediated by Sp1. Sp1-binding elements of UHRF1 were identified at positions -664/-505 of the promoter region using the luciferase and chromatin immunoprecipitation assays. Notably, UHRF1 and Sp1 levels were elevated in subgroups of hepatocellular carcinoma (HCC) patients and inversely correlated with TRα1 expression. Knockdown of UHRF1 expression should therefore provide a means to inhibit hepatoma cell proliferation. Expression of UHRF1 was downregulated by TRs, in turn, relieving silencing of the UHRF1 target gene, p21. **Conclusion.** Collectively, we propose that T3/TR signaling induces hepatoma cell growth inhibition via UHRF1 repression.

017

CHARACTERIZATION OF 148 CASES OF HEPATOCELLULAR CARCINOMA IN MEXICO

LAURA ESTELA CISNEROS-GARZA,* MARÍA SARAI GONZÁLEZ-HUEZO**
**UMAE 25 IMSS, MEXICO CITY, MEXICO.*
***CENTRO MÉDICO ISSEMYM, MEXICO CITY, MEXICO.*

Background. The aim of this study is to describe the clinical features, staging, previous treatments, and survival rate of 148 patients diagnosed with HCC from two hospitals in Mexico. **Material and methods.** From January 2008 to March 2014, all HCC diagnosed patients where included, from 2 regions of the country: north (UMAE No. 25 IMSS, Monterrey, N.L., Mexico) and center (ISSEMYM Medical Center/Cancer Center, Metepec MX, Mexico). Recollected data included clinical, tumor etiology, liver disease, BCLC staging (Barcelona Clinic Liver Cancer), treatment and survival. The results where expressed in measures of central tendency. **Results.** 148 patients where included, 98 (62.2 %) were male and 50 (33.8 %) where females. The average age was 63.9 years (range 52-76). 97 patients from north, 51 from center region. 41.9 % had diabetes mellitus and 16.2 % hypertension. 130 patients (87.8 %) had chronic liver disease and its etiology in descending order of frequency was as follows: Alcohol n =38 (29.2 %), HCV n = 33 (25.4 %), cryptogenic n = 20 (15.4%), NASH n = 17 (13%), HBV n = 8 (6.15%), autoimmunitty n = 6 (4.6%) and other causes n = 8.51/130 (39.2%). Chile-Pugh score at diagnosis: (n = 82) 55% in stage A, (n = 44) 30% in stage B, (n = 12) 8% in stage C and n =10 not available (NA). BCLC Stage: A n = 42 (28.4 %), B n = 27 (18.2%), C n = 51 (34.5%), D n = 27 (18.2 %), 1 NA. Tumor characteristics: n = 56 (37.8 %) had a lesion less than 5 cm in size. In 20.9% (n = 31) the lesion was multifocal. Alpha-fetoprotein (AFP) was measured, n = 137 patients (45.9%) had an elevation of more than 100 ng/dL. Treatment: stage A: 3 cases went through liver trasplant, 28 surgical resections and 15 radiofrequency ablation (RFA). Stage B: 5 chemoembolizations, 8 ARF, 12 sorafenib (10 patients received more than one treatment modality). Stage C: 17 patients sorafenib, 6 patients systemic chemotherapy, 22 patients combined treatment approach, 6 are pending treatment. Currently 32 are alive. Survival: stage A 16.5 months, stage B 13.4 months, stage C 8.9 months and stage D 4.5 months. Conclusions. Better surveillance is required to diagnose the disease in early stages, although it is necessary to adapt the treatment to the resources of each center.

018

DIAGNOSTIC APLICABILITY OF ALPHA-FETOPROTEIN MONITORING AMONG PATIENTS WITH CHRONIC LIVER DISEASE REGARDING HEPATOCELLULAR CARCINOMA, EXPERIENCE OF A LIVER UNIT

C.A. DE-LA-GARZA-CHÁVEZ, P. CORDERO-PÉREZ, I. CURA-ESQUIVEL, **R.F. MARTÍNEZ-MACÍAS, LE. MUÑOZ-ESPINOSA**
UNIDAD DE HÍGADO, HOSPITAL UNIVERSITARIO, UANL, MONTERREY, N.L., MEXICO.

Introduction. Alpha-fetoprotein (AFP) is a serum glycoprotein proper of the embryonic life which decreases 2 months after birthday. Normal AFP serum levels in adults range from 1 to 8 ng/mL. Its increased serum levels have been reported under the context of both, established liver diseases and as a tumor marker. **Objective.** To evaluate the levels of AFP in patients with various liver diseases and to establish its utility for the diagnosis of hepatocellular carcinoma. **Material and methods.** A descriptive and retrospective study was performed at Dr. José Eleuterio González University Hospital Liver Unit at UANL, whereby 248 patients, 109 male and 139 female, with a mean age of 53 ± 13 years and seen from 2003 to 2013, were included. Patient's liver diseases diagnoses were established based upon their medical record, biochemical parameters, serological findings and imaging studies. Ultimately, patients data was also distributed and analyzed per sex and

Table. (018)

Diagnostics	Age (x)	AFP (x ± SD)	Age < 50 (x ± SD)	Age > 50 (x ± SD)
Hepatitis C virus (HCV) (63)	48	43.50 ± 134.96	14.63 ± 37.38	58.99 ± 163.68
Hepatitis B virus (HBV) (13)	51	15.45 ± 29.57	3.29 ± 0.71	19.10 ± 33.19
Liver steatosis (LS) (57)	49	10.54 ± 50.17	2.68 ± 1.41	15.12 ± 62.99
Autoimmune hepatitis (AH) (33)	51	11.16 ± 20.42	7.49 ± 6.52	11.94 ± 22.31
Nonalcoholic steatohepatitis (NASH) (32)	57	12.21 ± 35.33	13.11 ± 20.16	11.95 ± 38.86
Alcoholic cirrhosis (AC) (21)	54	6.44 ± 9.84	3.29 ± 0.84	8.01 ± 11.86
Primary biliary cirrhosis (PBC) (14)	46	3.00 ± 1.02	2.28 ± 0.44	3.48 ± 1.03
Hepatocelullar carcinoma (HCC) (13)	63	2,476.27 ± 4,341.03	0 ± 0	2,476.27 ± 4,341.03

age > or < 50 years old, strata. **Results.** AFP levels distribution per liver disease etiology and age > or < 50 years are shown in the Table. **Conclusions.** There was no statistically significant difference between the groups according to sex, however, HCV (p = 0.034) and PBC (p = 0.009) did show a statistically significant difference but according to age (< 50 *vs.* > 50 years old). HCV, HBV, LS, AH and NASH exhibited AFP values above its upper limit of normality, whereas PBC and AC AFP levels were comprehended into AFP normal range. Noteworthy, a statistically significant difference was found when comparing HCC AFP (AFP > 200 ng/mL) against the AFP levels observed in each of the other liver diseases studied here (p < 0.001).

019

THE RELATION BETWEEN POOR PROGNOSIS AND AGGRESSIVENESS OF EXPERIMENT HCC WITH HIGH LEVELS OF GGT

A.J. MOREIRA,[*,†] G.R. RODRIGUES,[*,†] S. BONA,[*,†] J.N. PICADA,[||] J. SANTOS,[*,†,‡] C.A. MARRONI,[§] N.P. MARRONI[*,†,||]

[*]UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, PORTO ALEGRE-RS-BRAZIL.
[†]CENTER OF EXPERIMENTAL RESEARCH, HOSPITAL DE CLÍNICAS DE PORTO ALEGRE-RS-BRAZIL.
[‡]SCHOOL OF MEDICINE, UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, RS-BRAZIL.
[§]UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE, RS, BRAZIL.
[||]UNIVERSIDADE LUTERANA DO BRASIL-RS-BRAZIL.

Background. Regarding the role of gamma-glutamyl transferase (GGT) overexpressed is believed to be involved with the balance proliferation/apoptosis, due to this has been associated with tumor progression and invasion. **Aim.** Our goal was to relate serum GGT levels with stages of liver carcinogenesis in animals. Also, we correlated the levels of GGT with the damage index (DI) and damage frequency (DF) of liver DNA and with the expression of proteins involved in oxidative stress and cell damage. This study evaluated the expression of iNOS, NQO1, Nrf2, HSF1, HSP70 and cytokeratin 7 (CK7). **Material and methods.** Male Wistar rats weighing 145-150 g were used for this study. Development hepatocellular carcinoma (HCC) in rats with diethylnitrosamine (DEN) 50 mg/kg i.p. (Sigma Aldrich St Louis MO, USA). The animals were divided into 3 groups according to GGT levels: I) Lower than 5 U/L; II) Between 6-39 U/L and III) High than 40 U/L. Blood was collected to evaluate transaminases (AST and ALT), gamma glutamyl transferase (GGT) and alkaline phosphatase (AP) (U/L). Liver samples were removed for histological and immunohistochemical analysis and protein expression of iNOS, NQO1, Nrf2, HSF1 and HSP70. Statistical analysis. Tuckey test with $p < 0.05$. Pearson's test (χ^2) and Spearman' test were used for correlation analysis. **Results.** This study observed strong relation between poor prognosis and aggressiveness of HCC with high levels of GGT. Histological pattern from advanced HCC and CK7 overexpression were evidenced in animals of the III group. GGT high levels were associated with overexpression of iNOS and HSF-1 protein. However, GGT levels were negatively correlated with the protein expression of NRF2 and HSP70. **Conclusions.** DEN development HCC in rats. GGT levels could be marker of HCC or predictor of prognosis by liver diseases. CNPq; CAPES, HCPA-FIPE, UFRGS; ULBRA/ CNPq; UFCSPA.

020

LAPAROSCOPIC *VS.* OPEN LIVER RESECTION FOR BENIGN AND MALIGNANT LIVER TUMORS: A SINGLE CENTER EXPERIENCE

Z. DEL-REAL-ROMO,[***] C. RODRÍGUEZ-MONTALVO,[*,**] E. FLORES-VILLALBA,[**] L. TIJERINA-GÓMEZ,[**] P. CUEVAS-ESTANDÍA,[*] F. BOSQUES-PADILLA[*]

[*]CENTRO DE ENFERMEDADES HEPÁTICAS, DIGESTIVAS Y NUTRICIÓN HOSPITAL SAN JOSÉ -TEC DE MONTERREY, MONTERREY, N.L., MÉXICO.
[**]PROFESOR, [***]RESIDENTE DEL POSGRADO DE CIRUGÍA GENERAL DEL PROGRAMA MULTICÉNTRICO DE ESPECIALIDADES MÉDICAS, ESCUELA DE MEDICINA Y CIENCIAS DE LA SALUD, TECNOLÓGICO DE MONTERREY, MONTERREY, N.L., MÉXICO.

Background or Introduction. Since first laparoscopic liver surgery in 1992 indications has grown, techniques improved and experience gained. Still minimally invasive surgery for liver resection remains controversial. This study was designed to compare open versus laparoscopic surgical approaches to liver

Table. (020)

	Total (n = 16, 100%)	Laparascopic (n = 7, 43%)	Open (n = 9, 56.3%)
Age	49.9 (17-61)	45 (17-60)	53.7 (42-61)
Gender	F: 6 (37.5%), M: 10 (62.5%)	F: 5 (71.4%), M: 2 (28.6%)	F: 1 (11.1%), M: 8 (88.9%)
Indication for liver resection			
FNH	3 (18.8%)	3 (42.9%)	0
HCC	9 (56.3%)	0	9 (100%)
Metastasis to liver	2 (12.5%)	2 (28.6%)	0
Other	2 (12.5%)	2 (28.6%)	0
Tumor			
Size (cm)	4.6 (2-9)	3.7 (2-6)	5.3 (3-9)
Location (II, III, IV, V, VI, LLS)	2 (12.5%)/2 (12.5%)/ 3 (18.5%)/4 (25.0%)/ 5 (31.3%)	1 (14.3%)/1 (14.3%)/ 1 (14.3%)/2 (28.6%)/ 2 (28.6%)	1 (11.1%)/1 (11.1%)/ 2 (22.2%)/2 (22.2%)/ 3 (33.3%)
Surgery time (min)	226 min (80-330)	165 min (80-240)	274 min (240-330)
Blood loss (m/L)	358 mL (80-700)	225 mL (80-500)	461 mL (300-700)
Hospital length stay	5 days (2-8)	4 days (2-6)	5 days (4-8)
Conversion	1 (6.2%)	1 (14.2%)	-
Complications	None	None	None

FNH: focal nodular hiperplasia. HHC: Hepatocellular carcinoma. LLS: Left lateral segmentectomy.

resection for benign and malignant disease. **Material and methods.** We performed a single-center retrospective chart review. Demographic information, operative details, and post-operative outcome data were analyzed. Results are expressed as mean ± standard deviation. A case converted from laparoscopic to open was included in the laparoscopic group. **Results.** We compared 7 laparoscopic liver resections with 9 open cases having equivalent resections based on anatomy. No one had complications. The conversion rate was 6.2%. The mean blood loss was 461 mL (300-700 mL) in open cases *vs.* 225 mL (80-500 mL) in laparoscopic cases. Measures of surgery time procedure and hospital length of stay all favored the laparoscopic group (Table). **Conclusions.** In this serie comparing laparoscopic and open liver resections, there were fewer complications, more rapid recovery, and lower morbidity in the laparoscopic group. The minimally invasive liver surgery is a safe alternative for malignant and benign pathology in our experience. Combining the proven benefits of laparoscopy approach such less blood loss, minor postoperative pain, fewer days of administration of narcotics used as analgesics and shorter hospital stay without compromising oncologic principles in properly selected patients.

F. LIVER TRANSPLANT

001

PREVALENCE OF METABOLIC SYNDROME IN LIVER TRANSPLANTATION PATIENTS IN THE INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN (INCMNSZ)

J.H. CHÁVEZ-VELÁZQUEZ, Y.I. LÓPEZ-MÉNDEZ, E. CORREA-SOLÍS, N.A. CRUZ-SANCÉN, E. GÁLVEZ-CALVO, M. VILATOBÁ-CHAPA, A. CONTRERAS SALDÍVAR, P. LEAL-VILLALPANDO, J.A. FONSECA LAZCANO, G.E. CASTRO-NARRO
INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MÉXICO, D.F.

Background. Metabolic alterations are frequently found in patients with orthotopic liver transplantation (OLT). The metabolic syndrome prevalence (MS) reported goes from 43 to 58%; There is a 40-85% systemic arterial hypertension (SAH), 13-61% diabetes mellitus (DM); 40-66% dyslipidemia (DLP), 24-40% obesity. MS is related to insulin resistance disorders and it also predisposes to DM and cardiovascular disease which contributes to a lower survival rate in this population. **Aim.** To describe the prevalence of MS in liver transplantated patients in the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ). **Material and methods.** Study retrolective, cross-sectional and descriptive study which included post (OLT) patients. All clinical charts were reviewed to obtain the demographic and clinical characteristics, and the following variables were analyzed: gender, age at the time of transplantation, body weight (kg), size (cm), 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 and post-transplantation. For MS diagnosis, the NCEP-ATPIII were used, frequencies and correlations were analyzed. The statistical analysis with a SPSS v20.0 (< 0.05) p-value was considered statistically significant. **Results.** Fifty MS diagnosed patients were included (2005-2012), 28 men (56%), 22 women (44%), median age (49y), 23 (46%) were transplanted with HCV; 7 (14%) auto immune hepatitis; 5 (10%) primary biliary cirrhosis; 4 (8%) cryptogenic cirrhosis and 11 (22%) due to other causes. 5 (21.7%) of the patients with VHC, had hepatocellular carcinoma. Nineteen (38%) post (OLT) patients, met the criteria for MS; 13 (68.4%) due to VHC ($p < 0.05$), 10 patients developed MS in a 6 month period. Basal BMI (kg/m^2) had a median of 25 kg/m^2, which was modified to 28 kg/m^2 at the time of the MS diagnose with overweight criteria ($p < 0.05$). Basal triglycerides increased from 110 to 170 ($p < 0.05$). HDL were found below the normal level (< 40 mg/dL men < 50 mg/dL women), pre-transplantation C-LDL media was 83 ± 31and 93 ± 37 post transplantation, pre-transplanted total cholesterol media was 164 ± 13 and post 168 ± 44 pre-transplantation blood pressure increased from 110/70 (85/50-140/80) to 125/ 85 (90/60-150/100) mmHg. 17 (89.4%) out of the 19 patients with MS, required pharmacological treatment; 12 (63.1%) received DM pharmacological treatment, 14 (73.6%) SAH, 5 (26.3%) DLP. **Conclusions.** MS is a frequent complication in patients with liver transplantation. Those patients transplanted due to HCV had a bigger correlation with MS. A high percentage of post-transplantation patients required AHT, DM and DLP treatment.

002

HEPATITIS E VIRUS INFECTION IN LIVER TRANSPLANT RECIPIENT, CASE REPORT

E. ROBLES,* A. RAMÍREZ-POLO,** E. NEGRETE,** L. VALDOVINOS,** A. BERNAL-MÉNDEZ,** J. AGUIRRE-VALADEZ,** M. VILATOBÁ,*** A. TORRE,**** J.M. ANTOLINEZ-MOTTA,*** I. GARCÍA-JUÁREZ***
**FACULTAD DE MEDICINA, INSTITUTO TECNOLÓGICO DE MONTERREY, MÉXICO, D.F. **DEPARTAMENTO DE GASTROENTEROLOGÍA, ***DEPARTAMENTO DE TRASPLANTES, ****DEPARTAMENTO DE HEPATOLOGÍA, INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MÉXICO, D.F.*

Background. Hepatitis E is a viral infection with a pattern of enteric transmission. This caused by the hepatitis E virus (HEV) RNA virus, the only member of the Herpesviridae family, with a worldwide distribution. Currently there are four different genotypes described. Genotypes 1 and 2 primarily affect humans and are unique to Asia, Africa and Mexico, where they produce outbreaks. Usually, the clinical presentation is an acute hepatitis yielding spontaneously. However, in recent years are being detected cases that progress to chronic liver disease. The diagnosis is made by PCR assay with DNA virus detection in serum, but the testing access is limited. Moreover, the diagnosis can be made by indirect methods too, like detection of specific anti-HEV IgG and IgM antibodies. The combination of clinical evolution and interpretation of diagnosis assays results will define the final diagnosis and the treatment. We present the case of an immunocompromised man by liver transplantation who presented an acute HEV hepatitis infection and his management. **Case report.** A 48 years-old man presented in February 2014 for a post transplant consultation with abnormalities in liver tests. The liver transplant was made in May 2013 by the diagnosis of hepatic cirrhosis and alpha 1 antitrypsin deficiency. His past medical history was significant for type 2 diabetes mellitus and several post transplant complications, including benign biliary stricture, cholangitis and late-onset acute cellular rejection. Current medication included tacrolimus, prednisone and mycophenolate mofetil. Examination only relieved conjuntival jaundice. Laboratory analyses demonstrated a mixed pattern, with hepatitic predominance. After dismiss a new post surgical complication, cholangitis and viral infection by common etiologies, the diagnosis approach was made for HEV acute in-

fection. The diagnosis by PCR assays was searched, but the test was inaccessible. The IgM and IgG antibodies determined the acute infection with positive IgG and negative IgM antibodies. Treatment with ribavirin was started. In the next consultation we observed improve in liver tests. **Discussion.** In the present case, the evolution leaded to a more extensive approach with searching for atypical infectious causes. Because we couldn't get the PCR assays and the indirect test concluded the acute infection by HEV, we decided start the antiviral treatment with following clinical improvement. The early suspect of atypical diseases after dismiss the common causes should avoid systemic disease with graft consequences.

003

TREATMENT OUTCOMES IN ORTOTOPIC LIVER TRASPLANT CAU-SED BY HEPATITIS C VIRUS IN MEXICO

E. GÁLVEZ-CALVO, Y.I. LÓPEZ-MÉNDEZ, J.H. CHÁVEZ-VELÁZQUEZ, N.A. CRUZ SANCÉN, A. CONTRERAS SALDÍVAR, M. VILATOBÁ-CHAPA, A. SÁNCHEZ-CEDILLO, P. LEAL-VILLALPANDO, A. GAMBOA, S. SIXTOS-ALONSO, G.E. CASTRO-NARRO
INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MEXICO, D.F.

Background. Cirrhosis caused by hepatitis C virus (HCV), is the most common indication for ortotopic liver trasplant (OLT) in adults. The HCV recurs immediately and universally in post-trasplant patients with detectable RNA at transplant time. 30% of patients evol-ve with severe recurrence in 5 years after transplant. The HCV treatment with interferon on the waiting list, is only indicated in compensated patients. After OLT the pegilated interfe-ron/ribavirin treatment is effective in 30%, and triple therapy adding a polimerase inhibitor (Boceprevir/Telaprevir) had reported a viral sustained response (VSR) of 65%. **Aim.** To describe the features and treatment outcomes in patients that underwent OLT caused by HCV. **Material and methods.** Retrolective and descriptive study, that included patients with HCV and OLT at Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán between 2005-January 2014. Patients files were reviewed and demographic and clinical features were obtained, there were analyzed the following: genre, age at transplant, MELD, HCV treatment before and after OLT and response, and severe HCV recurrence. The statistic analysis was executed with SPSS v17.0. There were analyzed variables and frequencies with statistic significance $p < 0.05$. **Results.** There were included 40 patients, 26 (67%) males. The most common genotype was 1b, 70%. The age median at trasplant was 47 years, 14 (38%) with hepatocellular carcinoma. 15 (38%) received pre-OLT treatment, 5 INF/Ribavirin (RBV) and 10 pegINF/RBV. From this ones, only 1 accomplished VSR. At trasplant the MELD median was 17. Post-OLT severe recurrence was reported as 2 colestatic hepatitis and 16 with F2-F4. Sixteen patients received treatment with pegINF/RBV, and 2 with pegINF/RBV and Boceprevir (BCP). From pegINF/RBV group 4 (25%) responded, from the pegINF/RBV BCP 1 accomplished VSR and 1 with end of treatment response (ETR). In the tracing, 3 patients from pegINF/RBV group, were re-treated with pe-gINF/RBV/BCP, 2 with VSR and 1 ETR. **Conclusions.** Most of the patients that under-went OLT didn´t response to previous treatment. The VSR in post-OLT patients with pe-gINF/RBV is low. Triple therapy treatment shows a greater VSR percentage.

004

FREQUENCY OF LIVER TRANSPLANTATION FOR ALPHA 1 ANTITRYPSIN DEFICIENCY RELATED CIRRHOSIS: A SINGLE CENTER EXPERIENCE

E. MUÑOZ-ANAYA, C. CÓRDOVA-GALLARDO, I. GARCÍA-JUÁREZ, A. POLO-RAMÍREZ, J.M. ANTOLIMIS-MOTTA, M. VILATOBÁ-CHAPA, A. TORRE-DELGADILLO, A. GAMBOA-DOMÍNGUEZ
INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MÉXICO, D.F.

Introduction. AAT (alpha 1 antitrypsin) deficiency is a recently discovered hereditary condition, it was first identified and an association with lung disease noted, by Laurell and Eriksson 50 years ago, Intense research over the past 40 years has led to a detailed understanding of the structural genetic abnormalities, pathophysiology of associated pulmonary emphysema and liver disease, AAT is an autosomal recessive inherited disease, it has been described that the highest prevalence is in caucasic populations, some studies have described a prevalence of 1:600 newborns in Sweden and studies in USA described a prevalence of 1 in 5,097 and 1 in 2,857 newborns. It's a consequence of a defect in a gene codified in 14q31-32.1 chromosome, there have been described more than 100 varieties, the alleles that more frequently cause the disease are PiZ an PiS, resulting in circulating levels of AAT of 15 to 60% below normal values. Liver disease may have a variety of clinical presentations. Swedish research described that 11% of PiZ phenotype develop neonatal cholestasis, from this 25%progres to early hepatic failure, 25% cirrhosis and the rest normalize HFT. **Objective.** Determine the prevalence of AAT deficiency in patients post liver transplantation on the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán with cirrhosis diagnosticated as alcoholic liver disease, cryptogenic or NAFLD. **Material and methods.** Retrospective study, PAS diastase stain was realized to explanted livers from patients from 1985 to 2014, classified as alcoholic liver disease, cryptogenic or NAFLD who had negative ASMA, AMA and ANA antibodies, viral hepatitis serology and no histologic data of hemochromatosis or other hepatic disease. **Results.** A total of 42 patients were transplanted, 13 were classified as alcoholic liver disease, 21 cryptogenic and 7 NAFLD. Patients had a median age of 47 years, two stains were positive for PAS diastase, a 47 years old male and the other was a 63 years old male, the rest of the explanted livers were negative for PAS diastase stain, discarding the diagnosis of AAT deficiency. The frequency of Alfa 1 antitrypsin in explanted livers was 4.76%. **Conclusions.** AAT deficiency is a rare disease in post liver transplantation patients in our area with a frequency of 4.76, it probably would represent a very low frequent etiology in our population, this could be due to the preponderance of mestizo population, confirming that it is more prevalent in Caucasian, However it is important to discard the diagnosis in patients with cryptogenic cirrhosis.

Table. (005)

pg/mL	PT	PR	12 h	24 h	48 h	72 h	7 d	15 d	30 d
IL-6	367 ± 132	452 ± 174	355 ± 152	343 ± 147	473 ± 181	462 ± 151	435 ± 178	370 ± 219	289 ± 68
TNF-α	42 ± 9	42 ± 7	53 ± 33	41 ± 6	41 ± 7	40 ± 6	38 ± 15	36 ± 4	41 ± 9
VEGF	110 ± 54	100 ± 58	103 ± 61	102 ± 66	102 ± 66	104 ± 68	103 ± 78	96 ± 74	82 ± 68
ICAM 1	1,481 ± 480	1,488 ± 462	1,631 ± 438	1,705 ± 528	1,705 ± 528	1,631 ± 573	1,452 ± 506	1,803 ± 265	1,361 ± 548

005

CYTOKINES PROFILE IN LIVER TRANSPLANT. PRELIMINARY REPORT

H. ZAPATA-CHAVIRA,* P. CORDERO-PÉREZ,** L.E. MUÑOZ-ESPINOSA,** O. ORTIZ-GARZA,** J.A. GONZÁLEZ-CHAPA,** M. HERNÁNDEZ-GUEDEA,* A. GUEVARA-CHARLES,* M. ESCOBEDO-VILLARREAL,* E. PÉREZ-RODIGUEZ*

**SERVICIO DE TRASPLANTES, **UNIDAD DE HÍGADO, HOSPITAL UNIVERSITARIO DR. JOSÉ E. GONZÁLEZ, UANL, MÉXICO.*

Introduction. Liver ischemia/reperfusion (LIR) injury is a complex and multifactorial process causative of poor initial function and major cause of liver graft failure. Several inflammatory mediators have been implicated, including reactive oxygen species,TNF-, IL-6, IL-1,TGF-β, interferon, endothelin-1, ICAM-I and P-selectin. **Objetive.** Investigate the systemic inflammatory response in recipents of TH during pretrasplant phase (PT), 90 min postreperfusion (PR), 12, 24, 48, 72 h (F), and 7,15 and 30 days post-transplantation (D). **Material and methods.** We included 7 patients (2F/5M) who required liver transplantation in the Trasplant Service of University Hospital. The levels of inflammatory mediators TNF-α, IL-6 VEGF and ICAM 1 were evaluated. **Results.** The results are shown in the Table. **Conclusion.** No differences in serum levels of inflammatory mediators were founded at any stages of study. However noted that IL-6, VEGF and ICAM-1 levels were lower than previous phases. Although this inflammatory mediators evaluated have been implicated in the LIR, we need to increase the simple size to draw definitive conclusions to establish whether there is a balance between pro-inflammatory and post-inflammatory post-TH cytokines.

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006

ASSESSMENT OF GLOMERULAR FILTRATION RATE BY DTPA-TC-99 BEFORE AND AFTER ORTHOTOPIC LIVER TRANSPLANTATION FOR LIVER CIRRHOSIS: A SERIES OF 4 CASES

J.M. AGUIRRE-VALADEZ,* J.M. ANTOLÍNEZ-MOTTA,* H.C. VERDUZCO AGUIRRE,* A.K. FLORES-BALBUENA,* C. CRUZ-RIVERA,** O.R. GARCÍA-FLORES,* R.U. MACÍAS-RODRÍGUEZ,* J.A. NIÑO-CRUZ,** I. GARCÍA-JUÁREZ,* A. TORRE*

**DEPARTAMENTO DE GASTROENTEROLOGÍA, **DEPARTAMENTO DE NEFROLOGÍA. INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MEXICO CITY, MEXICO.*

Objective. To determine renal function by glomerular filtration rate (GFR) before and after orthotopic liver transplantation (OLT) for liver cirrhosis. **Material and methods.** We studied prospectively four patients with liver cirrhosis of different etiologies who underwent OLT. We determined the estimated GFR by the following formulas: Cockroft-Gault (CG), MDRD-6 and CKD-EPI and compared them to the GFR obtained by DTPA-Tc-99 renal clearance as gold standard before and after OLT (mean of 106.25 days after OLT). **Results.** Patient No. 1, a 56-year-old male with alcoholic cirrhosis. GFR was assessed 73 days after OLT. Serum creatinine (SCr) was 0.89 pre-OLT and 1.12 mg/dL post-OLT. Tacrolimus levels were 4.8 ng/mL. GFR results were 37.75 mL/min/1.73 m^2 pre-OLT and 42.38 post-OLT by DTPA-Tc-99; 91.7 pre-OLT and 70.4 post-OLT by CG; 75.8 pre-OLT and 68.3 post-OLT by MDRD-6; 93.9 pre-OLT and 73 post-OLT by CKD-EPI. Patient No. 2, a 45-year-old female with primary biliary cirrhosis. GFR was assessed 115 days after OLT. SCr was 1.07 mg/dL. Tacrolimus levels were 6.7 ng/mL. GFR results were 48.79 mL/min/1.73 m^2 pre-OLT and 36.28 post-OLT by DTPA-Tc-99; 82 pre-OLT and 69.7 post-OLT by CG; 57.1 pre-OLT and 57.7 post-OLT by MDRD-6; 72.9 pre-OLT and 64 post-OLT by CKD-EPI. Patient No. 3, a 67-year-old female with hepatitis C virus infection and hepatocellular carcinoma previously treated by chemoembolization. GFR was assessed 124 days after OLT. SCr was 0.66 mg/dL. Tacrolimus levels were 8.2 ng/mL. GFR results were 101.5 mL/min/1.73 m^2 pre-OLT and 56.74 post-OLT by DTPA-Tc-99; 56.4 pre-OLT and 55.4 post-OLT by CG; 91.5 pre-OLT and 83.2 post-OLT by MDRD-6; 91.6 pre-OLT and 92.7 post-OLT by CKD-EPI. Patient No. 4, a 25-year-old female with autoimmune hepatitis. GFR was assessed 113 days after OLT. SCr was 0.77 mg/dL. Tacrolimus levels were 11 ng/mL. GFR results were 102.49 mL/min/1.73 m^2 pre-OLT and 58.48 post-OLT by DTPA-Tc-99; 210 pre-OLT and 103.1 post-OLT by CG; 188.7 pre-OLT and 95.8 post-OLT by MDRD-6; 143.2 pre-OLT and 108.8 post-OLT by CKD-EPI. **Conclusions.** Estimated GFR determined by creatinine-dependent formulas overestimated GFR obtained by DTPA-Tc-99 clearance both before and after OLT. Renal function decreased after OLT in 3 out of 4 of the patients by DTPA-Tc-99 clearance, which could be partially explained by use of calcineurin inhibitors for immunosuppression. An increased sample size is needed to obtain conclusive results. More studies are required to determine the best method to assess renal function after OLT.

007

RISK FACTORS ASSOCIATED WITH RENAL FAILURE IN POST ORTHOTOPIC LIVER TRANSPLANTATION PATIENTS

J. TOLEDO-CUQUE,* M. VILATOBÁ-CHAPA,** A. CONTRERAS-SALDÍVAR,** P. LEAL-VILLALPANDO,** E. CANTÚ-LLANOS,* A. VELASCO-ZAMORA,* I. GARCÍA-JUÁREZ*,**

**DEPARTAMENTO DE GASTROENTEROLOGÍA, **DEPARTAMENTO DE TRASPLANTES, INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MEXICO CITY, MEXICO.*

Background. Renal failure is one of the main post liver transplantation complications. Risk factors associated with increased frequency of this complication are renal failure before transplantation, the use of nephrotoxic drugs, sepsis, trans-

and postoperative hypovolemia. Also it's associated with the use of calcineurin inhibitors like tacrolimus and cyclosporine. Modification of immunosuppression either decreasing or change can improve the renal failure in some cases. **Objective.** Assess risk factors for renal failure in patients with orthotopic liver transplantation in the 2 months following transplantation. **Material and methods.** All records of patients with liver transplantation at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiran from 2007 to 2013 were reviewed retrospectively. To date 32 patients have been analyzed. The variables were pre transplant age, Child-Pugh, MELD, etiology of cirrhosis and presence of diabetes and hypertension and immunosuppression start date and immunosuppressive drug levels. Descriptive and inferential statistics were performed using index of central tendency and dispersion. For continuous variables used nonparametric tests, for independent samples and dichotomous variables and χ^2 test and Fisher's exact test were used. A multivariate logistic regression model was established. Acute renal failure was considered by the elevation 30% over baseline creatinine. **Results.** To date 32 cases have been analyzed with orthotopic liver transplantation with a median age at transplantation of 53 years (SD ± 9.6). The median age at transplantation was 46 women and men 49.5 years. 59.4% (19) females and 40.6% (13) males with a Child-Pugh grade B predominantly 50% (16) and only 34.4 % were grade C (11). With an average MELD score of 14.6 (SD ± 6.39). The etiology of cirrhosis in 37.5% (12) was predominantly HCV infection. In our cohort of 32 patients, 14 of them (43.8%) had renal failure at two months post-transplant. The variable associated with renal failure a month and two months is having Child -Pugh B or C ($p = 0.04$). Cryptogenic cirrhosis was a factor associated with renal failure at 2 months ($p = 0.03$). Patients who had renal failure at two months were aged 49. Renal failure was not associated with the initial dose immunosuppression or the start time of the same. **Conclusion.** Renal failure in this group of transplant patients ($n = 32$) is associated with Child-Pugh B and C, according to our results is not affected to the initial dose or at the time of immunosuppression. The condition of the renal function in the group of patients with Child B or C may be overestimated by what should be in the future determining renal function based on more accurate tests.

G. AUTOIMMUNE AND CHOLESTATIC LIVER DISEASE

001

PREVALENCE OF OVERLAP SYNDROME IN MEXICAN POPULATION

M. GÁLVEZ-MARTÍNEZ, E. PÉREZTORRES, J.L. PÉREZ-HERNÁNDEZ, F. HIGUERA-DE-LA-TIJERA
SERVICIO DE GASTROENTEROLOGÍA, HOSPITAL GENERAL DE MÉXICO DR. EDUARDO LICEAGA, CIUDAD DE MÉXICO, MÉXICO.

Introduction. The overlap syndrome is used to describe variant forms of autoimmune hepatitis (AIH), which has features of primary biliary cirrhosis (PBC) or primary sclerosing cholangitis (PSC). Its prevalence has been reported from 4.8% to 19% of PBC patients and 5% to 8.3% of patients with AIH. Its pathogenesis is unclear. It is diagnosed when established criteria by Chazouillères, *et al*. are met, with a sensitivity and specificity of 92 and 97%. Patients with overlap syndrome have a similar to AIH predominance of HLA B8, DR3, DR4.

Table. (001)

Clinical characteristics of patients with overlap syndrome	
Age (years)	44.3 ± 10.2
Asthenia and adynamia	90%
Arthralgias	80%
Nauseas	70%
Pruritus	50%
Jaundice	40%
Biochemical characteristics of patients with overlap syndrome	
Alanino aminotransferasa (ALT)	185 ± 73 U/L
Alkaline phosphatase (FA) U/L	383 ± 263 U/L
Glutamyltransferase (GGT) U/L	367 ± 343 U/L
Total bilirubin (BT)	3.8 ± 7.0 mg/dL
Ac. Anti mitochondrial (AMA)	69%+
Ac. Anti nuclear (ANA)	76%+
Ac. anti smooth muscle	38%+

The therapy for this syndrome includes ursodeoxycholic acid, which is combined with immunosuppressive therapy. **Objective.** To investigate the prevalence, clinical, biochemical and histological characteristics of overlap syndrome in Mexican patients attending the Liver Clinic of the Hospital General de México. **Material and methods.** Cross-sectional, retrospective case series with clinical and biochemical data, where 40 patients diagnosed with PBC and 55 patients with AIH were reviewed, of which 13 met the criteria established by Chazouillères, *et al*. for overlap syndrome. Descriptive statistics were used. **Results.** Thirteen cases of patients with diagnosis of overlap syndrome were identified, 6 cases in 40 patients with PBC and 7 cases in 55 patients diagnosed with AIH, 12 of the 13 cases (90%) were females. Seven out of 13 patients with liver biopsy had hepatitis interface, lymphoplasmacytic infiltrate, plasma cells, injury to the bile ducts and granuloma. Clinical and biochemical characteristics are shown in Table. **Conclusions.** Similar to other published series, the prevalence of overlap syndrome in our study was 13.2% with a predominance in females with a ratio of 9:1. Having as the main symptoms fatigue, weakness, nausea, pruritus and jaundice. Most of our patients had positive anti-mitochondrial antibodies and antinuclear while smooth muscle antibodies showed a low prevalence. Proper diagnose of overlap syndrome has a key role on therapeutic intervention and directly affects long term prognosis, which differs when both pathologies are presented separately.

002

PREVALENCE OF AUTOIMMUNE DISEASES ASSOCIATED WITH AUTOIMMUNE HEPATITIS DIAGNOSIS IN MEXICAN PATIENTS. RETROSPECTIVE COHORT 2001-2011

A.F. ROMANO-MUNIVE, C. GUERRERO-VELÁSQUEZ, **A. TORRE-DELGADILLO**
INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN. MEXICO CITY, MEXICO.

Background. In the international literature has been reported that autoimmune hepatitis (AIH) is associated with other autoimmune diseases in 30-50% of cases. Primary biliary cirrhosis, primary sclerosing cholangitis and ulcerative colitis are the diseases more frequently found. **Objective.** To determine the prevalence of autoimmune diseases associated with the diagnosis of AIH in Mexican population. **Material and methods.** Liver biopsies with diagnosis of AIH between Janu-

Table. (002) Autoimmune disease associated with HAI.

Autoimmune disease	Cases (n), prevalence (%)
Primary biliary cirrhosis	29 (27.1)
Sjörgren's syndrome	11 (10.28)
Rheumatoid arthritis	8 (7.47)
Systemic lupus erythematosus	8 (7.47)
Hypothyroidism	8 (7.47)
Scleroderma	6 (5.6)
Antiphospholipid syndrome	2 (1.8)
Thrombocytopenic purpura	2 (1.8)
Episcleritis	2 (1.8)
Autoimmune hemolytic anemia	2 (1.8)
Celiac disease	2 (1.8)
Ulcerative colitis	1 (0.93)
Interstitial nephritis	1 (0.93)
Diabetes mellitus type 1	1 (0.93)
Psoriasis	1 (0.93)
Mixed connective tissue disease	1 (0.93)
Pyoderma gangrenosum	1 (0.93)
Guillain-Barré syndrome	1 (0.93)
Vitiligo	1 (0.93)

ary 2001 and December 2011 were collected; clinical data were obtained from the records. **Results.** One hundred and seven patients were found with a diagnosis of HAI, 85 (79.43%) were females. Sixty patients (56.07%) had one or more associated autoimmune diseases, 39 patients with one disease, 16 with two, 4 with three and 1 with five (Table). **Conclusions.** In Mexican patients with AIH, the autoimmune disease most often associated was primary biliary cirrhosis, which is consistent with the international literature. Sjögren's syndrome, rheumatoid arthritis, systemic lupus erythematosus and hypothyroidism were frequently encountered in our population. The elevation of transaminases in this group of patients obligate to ruled out the diagnosis of AIH.

003

EVALUATION OF PATIENTS WITH PRIMARY BILIARY CIRRHOSIS ACCORDING TO DIFFERENT HISTOLOGICAL GRADING SYSTEMS

Y.K. MELCHOR-MENDOZA,* B. MARTÍNEZ-BENÍTEZ,** A. MINA-HAWAT,*** G. RODRÍGUEZ-LEAL,*** A. TORRE-DELGADILLO,** S. MORÁN-VILLOTA,*** MISAEL URIBE*

*CLINICAL FOUNDATION MÉDICA SUR. MEXICO CITY, MEXICO.

**INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MEXICO CITY, MEXICO.

***CENTRO MÉDICO NACIONAL SIGLO XXI, IMSS. MEXICO CITY, MEXICO.

Introduction. The diagnosis of primary biliary cirrhosis (PBC) is usually made by a constellation of clinical, serological, and pathological findings. There are many histological classifications of PBC according to different criteria but the information about the relationship of the different stages of the disease with biochemical parameters and survival is scared. **Material and methods.** A retrospective study was performed including patients with PBC, who were diagnosed with clinical, biochemical, histological and immunological criteria. Patients were followed for 5 years after the initial diagnosis and death related to liver disease was recorded during this time. The histological stage were determinate using Ludwing criteria, Scheuer and Japanese staging systems which pretend to describe disease progression and predict clinical out come more accurately. Exclusion criteria were other coexistent liver diseases including overlap syndrome, alcoholic liver disease, a positive serological test for hepatitis B or C virus, non-alcoholic steatohepatitis (NASH) and hepatocellular carcinoma. The relationship among biochemical parameters and histological stages was estimated using Spearman rank correlation coefficient. A p value < 0.05 was considered statistically significant. **Results.** Forty one patients were included of which 38 were women. The mean age was 45.8 ± 9.8 years. Bilirrubin levels and aspartate aminotransferanse (AST) correlated positively and significantly with Ludwig classification and with Scheuer classification. Positive and significant correlation was observed among bilirrubin and phosphatase alkaline with Nakanuma, *et. al.* classification. Table shows the probability of survival in 5 years according to the different stages of the histological classifications. **Conclusions.** All the classifications had a positive and significant correlation with bilirrubin levels. The probability of survival after 5 years of follow up was lower in stage IV in all the classifications used.

Table (003). Probability of survival after 5 years of follow up.

Stage	Ludwig	Scheuer	Nakanuma, *et al.*
I	84.4%	90.9%	100%
II	100%	87.5%	88.9%
III	80.0%	80.0%	91.7%
IV	75.0%	75.0%	66.7%

004

CLINICAL MANIFESTATIONS AT TIME OF DIAGNOSIS OF AUTOIMMUNE HEPATITIS AND FACTORS CONTRIBUTING TO INITIATION OF IMMUNOSUPPRESSIVE THERAPY

L. HERNÁNDEZ-FLORES, J.A. CARMONA-CASTAÑEDA, S. MEJÍA-LOZA, F. ZAMARRIPA-DORSEYA

GASTROENTEROLOGY DEPARTMENT, HOSPITAL JUÁREZ DE MÉXICO, SSA. MEXICO CITY, MEXICO.

Background. The clinical presentation of autoimmune hepatitis (AIH) in the 40% of the patients is as "acute hepatitis", 25% asymptomatic and 30% develop cirrhosis. Patients with AST > 5 times the upper normal limit has a high mortality (60% at 6 months) if is not treated. On the other hand patients with cirrhosis have an increased risk of side effects. **Objective.** Identify the main reasons for reference to gastroenterologist and determine stage of liver failure and the benefit in start immunosuppressive treatment. **Material and methods.** Patient's records with a diagnosis of HAI was reviewed from July 2007 to June 2012. In 30 patients who met simplified criteria of HAI was determined reason for reference, scores CHILD and MELD, and criteria for initiation of treatment according to the guidelines of AASLD 2010. Liver cirrhosis was corroborating by abdominal ultrasound or liver biopsy. **Results.** Of all patients, the main reason for shipping was altered liver function tests (43.3%), bicytopenia or pancytopenia (30%), jaundice (20%), gastrointestinal bleeding (6.7%). Of the 30 patients were in Child A (40%), B (56.7%) and C (3.3%) and 12.66 with a mean MELD, which was correlated with the progression of liver disease, presence of MELD > 12 stage B and C (11 patients, 36% of total). With indirect portal hypertension in over 50% of patients with splenomegaly and esophageal varices. Four patients accomplish absolute criteria for initiation of treatment and 3 patients receiving immunosuppressive therapy. **Conclusions.** The absolute indication for treatment only applied to 4 patients, as some

already had decompensation of their disease, leukopenia or thrombocytopenia so were not candidates for treatment with high risk of adverse effects and poor patient prognosis, so must be done more extension studies to rule out advanced liver disease even without significant clinical manifestations, since autoimmune hepatitis even when was presented acutely up to fulminant hepatic failure, mostly presented as evidence of chronic liver disease, corroborated by ultrasound or biopsy.

005

CLINICAL PROFILE OF AUTOIMMUNE LIVER DISEASES IN CUBAN PATIENTS

M. CASTELLANOS-FERNÁNDEZ, L. CALZADILLA-BERTOT, W. PALANCA, D. LA-ROSA-HERNÁNDEZ, L. GONZÁLEZ-FABIÁN, Z. DORTA-GURIDI, O. MIRIAM AGUILAR-GARCÍA
NATIONAL INSTITUTE OF GASTROENTEROLOGY. HAVANA. CUBA.

Background. Autoimmune liver diseases (AILD) comprise a set of entities whose common denominator is tissue damage as a result of the loss of self-tolerance that determines abnormal responses to own structures, in genetically susceptible individuals. There are few reports of these chronic liver diseases from Caribbean countries. The aim of this study is to show clinical, immunological and histological features of presentation of AILD in Cuban patients. **Material and methods.** A cross-sectional study was conducted at the National Institute of Gastroenterology Havana, Cuba from September 2012 to December 2013. Sixty six patients satisfied inclusion criteria. Clinical, immunologic and histologic features of autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC) and overlap syndrome AIH/PBC were determined. Estimated prevalence rate was determined for each specific disease. **Results.** Women are affected more frequently than man, sex ratio 6.3/1. The total prevalence of AILD was 2.8%. Prevalence of AIH, PBC, overlap syndrome AIH/PBC and PSC were 1.78%, 0.6%, 0.4% and 0.04% respectively. Mode of presentation in all forms of AILD was predominantly like liver cirrhosis and insidious onset. Thyroid diseases and rheumatoid arthritis were the most common concurrent autoimmune disease. Antinuclear antibody (ANA) was present in 80% of AIH and overlap syndrome AIH/PBC patients. **Conclusion.** AILD is a not a rare disease in the Cuban population. AIH type I seems to be the most prevalent one. Clinical features differ between geographical areas. More studies are needed for better understanding of the local disease prevalence among patients with chronic liver disease.

006

AUTOIMMUNE HEPATITIS-PRIMARY BILIARY CIRRHOSIS OVERLAP SYNDROME INTERNATIONAL CLASSIFICATIONS AND LONG TERM FOLLOW-UP IN MEXICAN PATIENTS

L.E. MUÑOZ-ESPINOSA,* A.B. MERCADO-MOREIRA,* G. ALARCÓN-GALVÁN,** V.H. ÁVALOS-GÓMEZ,* T.E. GUEL-PÉREZ,* Y.K. LÓPEZ-GARCÍA,* P. CORDERO-PÉREZ*
**LIVER UNIT, DEPT. INTERNAL MEDICINE, **PATHOLOGY DEPT., UNIVERSITY HOSPITAL DR. JOSÉ ELEUTERIO GONZÁLEZ. UANL. MONTERREY, N.L. MEXICO.*

Background/Aim. Autoimmune overlap syndrome (OS) represents a diagnostic and therapeutic challenge. Primary biliary cirrhosis (PBC)/autoimmune hepatitis (AIH) is the most commonly seen OS. Paris criteria (Chazouilleres-1998) have been used for diagnosis. The aim of this study was to apply international scoring systems in a group of Mexican patients with OS (AIH/PBC) and to evaluate long term follow-up. **Material and methods.** Twenty-eight patients diagnosed as OS according to Paris criteria were included at the University Hospital UANL. Revised criteria of the International Autoimmune Hepatitis Group (R-IAIHG 99) and simplified criteria 2008 (SC'08) scoring systems were applied, 35 PBC and 73 AIH patients were include as controls. Biochemical parameters, clinical complications on admission and follow up were captured. Statistics: SPSS 15.0. Patients were ungrouped according to treatment; which was Ursodeoxycholic acid (UDCA) and UDCA plus prednisone (PRED) and/or azathioprine (AZA). **Results.** Probable and definite AIH according to the R-IAIHG and SC scoring systems seen in patients with OS (Table). 78% of patients with OS were probable or definite by R-IAIHG and 60% by SC. Sensitivity for R-IAIHG was 79% for definite/probable cases, whereas, it was 60% for the SC in OS. Specificity and PPV was 100% in all instances. Patients with OS had a follow-up of 49.4 + 69 (1-356 months). Complications on admission and follow-up were: cirrhosis 17(60.7%), and 18 (64.2%); portal hypertension (PH) 7 (25%) and 11 (39%); gastrointestinal bleeding 3 (11%) and 8 (28.5%); SBP 1 (4%) and 5 (18%); encephalopathy 1 (4%) and 3 (11%), respectively. Six (22%) patients died or received a liver transplant. Survival by Kaplan Meier analysis at 356 months was 62%. Twenty-seve patients were treated with UDCA, in addition, 12 received PRED; 2 AZA. One patient received PRED + AZA. In follow-up, improvement in AST, ALT, ALP ($P < 0.05$) was seen in patients who received only UDCA, whereas in UDCA + PRED and/or AZA only GGT improved ($p < 0.05$). **Conclusions.** R-IAIHG scoring system was more accurate in diagnosing OS, specificity and PPV was 100% for both systems. Patients with UDCA treatment alone exhibited more improvement in liver enzymes. Cirrhosis and PH were not prevented by treatment. Overall long term survival was 62%.

Table. (006).

Etiology	N	R-IAIHG'99 Definite	Probable	SC'08 Definite	Probable	Non diagnosis
AIH	73	29 (39%)	44 (61%)	29 (40%)	20 (27%)	24 (32%)
PBC	35	0	0	0	0	0
AIH/PBC	28	4 (14%)	18 (64%)	2/25 (8%)	13/25 (52%)	10/25 (40%)

007

CLINICAL BEHAVIOR OF THREE DIFFERENT AUTOIMMUNE LIVER DISEASES. COHORT STUDY OF A CENTER OF EXPERIENCE IN MEXICO

F.D. BRISEÑO-GARCÍA, I. GARCÍA-JUÁREZ, A. TORRE-DELGADILLO
DEPARTMENT OF GASTROENTEROLOGY, INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MEXICO CITY, MEXICO.

Background. Coexistence of primary biliary cirrhosis (PBC) and autoimmune hepatitis (AIH) is referred to as PBC-AIH overlap. The diagnosis of PBC-AIH is challenging. The aims of the study were to investigate and to compare the clinical, biochemical and histological features, as well as responses to therapy, and overall survival in patients with PBC-AIH, CBP and AIH. **Material and methods.** Fifty three patients with simultaneous form of strictly defined PBC-AIH, 53 patients with AIH and 53 patients with PBC were included in the study. All patients with PBC-HAI were treated with ursodesoxicolic acid and steroids ± azathioprine, all patients with PBC were treated with ursodesoxicolic acid, and all AIH patients were treated with steroids ± azathioprine. **Results.** Patients with PBC-AIH were significantly younger than patients with PBC (median age: 40 *vs.* 48 years). Jaundice (69%) was the most frequent symptom in PBC-AIH and pruritus (71%) was the most frequent symptom in CBP. Patients with PBC-AIH had serum ALT, AST, and gammaglobulin levels higher than CBP but lower than de AIH group. The alkaline phosphatase and gamma-glutamyl-transpeptidase were significantly higher than the other groups. The response to therapy PBC-AIH was 64%, compared to 68% in the AIH group and 55% in the PBC group. Of the responders in the PBC-AIH group, 26% had cirrhosis at the diagnosis, and 25% and 34% of the responders in the AIH and PBC groups had cirrhosis at diagnosis, respectably. The risk of cirrhosis at 5 years of follow up was similar in PBC-AIH and PBC groups and lower in AIH ($P \leq 0.001$), and at 10 years of follow up the risk became higher in the PBC-AIH group ($P = 0.04$). The risk of developing cirrhosis at 10 years of follow up was higher in de PBC-AIH group ($P = 0.1$). The overall survival at 10 years was lower in the PBC-AIH group. The response to therapy was not associated with the development of cirrhosis in the follow up. A delay in diagnosis and early treatment is a risk factor for the development of cirrhosis. Elevated levels of GGT (> 364 UI/L) is a predictor of cirrhosis development in PBC-HAI patients. **Conclusions.** PBC-AIH patients have a different clinical, biochemical and serological characteristics than patients with PBC or HAI. The long term risk of cirrhosis appears to be higher and the overall survival is lower in PBC-HAI patients. An early diagnosis and treatment may diminish the risk of cirrhosis development.

008

DETERMINATION OF BILE ACIDS IN PATIENTS WITH LIVER DISEASES

P. CORDERO-PÉREZ, I. CURA-ESQUIVEL, M. AGUIRRE-GARZA, J.A. GONZÁLEZ-CHAPA, M.P. AGUIRRE-RODRÍGUEZ, L.E. MUÑOZ-ESPINOSA
UNIDAD DE HÍGADO, HOSPITAL UNIVERSITARIO DR. JOSÉ E. GONZÁLEZ, UANL, MÉXICO.

Introduction. The liver is the unique organ responsible for the synthesis, conjugation, transport and excretion of the bile acids (BA).The BA are produced only in the liver and good indicator of hepatobiliary function. **Aim.** To evaluate the BA concentrations in patients with liver disease with and without cholestasis. **Material and methods.** We included 49 patients, 24 with cholestasis (C) and 25 without cholestasis (WC). The concentration (umol/L) of cholic acid (CA), deoxycholic acid (DCA), chenodeoxycholic acid (CDCA) and total bile acid (TBA) were determinated basal (B) and postprandiales (P) (3-5 h) during the period January 2004-2013. The relationship between BA and liver function test was evaluated. **Results.** The results are described in the Table. A diference in the concentrations of DCA and CDCA both basal and postprandial in both groups was founded. Correlations in C: CA-B with CDCA-B ($r = 0.657$, $p = 0.000$), and TBA-B ($r = 0.853$, $p = 0.000$); DCA-B with CDCA-B ($r = 0.524$, $p = 0.006$) and TBA-B ($r = 0.561$, $p = 0.003$). CDCA-B with TBA-B ($r = 0.890$, $p = 0.000$); CA-P with DCA-P ($r = 0.638$, $p = 0.000$), CDCA-P ($r = 0.813$, $p = 0.000$), and TBA-P ($r = 0.825$, $p = 0.000$); DCA-P with CDCA-P ($r = 0.690$, $p = 0.000$) and TBA-P ($r = 0.657$, $p = 0.000$); TBA-P ($r = 0.7$, $p = 0.01$) with GGT. Correlation in WC: CA-B with CDCA-B ($r = 0.622$, $p = 0.001$), and TBA-B ($r = 0.782$, $p = 0.000$); DCA-B with TBA-B ($r = 0.395$, $p = 0.046$); the CDCA-B with TBA-B ($r = 0.917$, $p = 0.000$); CA-P with DCA-P ($r = 0.647$, $p = 0.000$), CDCA-P ($r = 0.818$, $p = 0.000$) and TBA-P ($r = 0.885$, $p = 0.000$); DCA-P with CDCA-P ($r = 0.469$, $p = 0.016$) and TBA-P ($r = 0.623$, $p = 0.001$) ; CDCA-P with TBA-P ($r = 0.88$, $p = 0.000$) and CDCA-P with GGT ($r = 0.9$, $p = 0.003$). **Conclusions.** Only DCA and CDCA were statistically different in patients with C *vs.* SC in both phases. Most bile acids correlated with GGT both period and both groups.

Table. (008)

	CA-B/CA-P	DCA-B/DCA-P	CDCA-B/CDCA-P	TBA-B/TBA-P
Cholestasis	10.8 ± 15.6/15.4 ± 19.1	4 ± 5.2/6 ± 7.3	14.1± 21.2/20.8 ± 22.4	28.1 ± 35.4/38.9 ± 39.9
No cholestasis	9.7 ± 26.2/14.3 ± 32	2.2 ± 2/2.6 ± 2.5	5.8 ± 7.9/10.4 ± 13.9	17.8 ± 31.8/27.2 ± 43.2
Value C-B *vs.* WC-B/C-P *vs.* WC-P	P = 0.877/P = 0.353	P = 0.030/P = 0.008	P = 0.001/P = 0.35	P = 0.113/P = 0.918

009

LIVER CHOLESTEROL OVERLOAD AGGRAVATES CHOLESTATIC DAMAGE INDUCED BY BILE DUCT LIGATION

N. NUÑO-LÁMBARRI,[*] A. BAULIES-DOMENECH,[**] M. DOMÍNGUEZ-PÉREZ,[*] D. CLAVIJO-CORNEJO,[*] L. MUÑOZ-ESPINOZA,[***,*****] C. GARCÍA-RUIZ,[**] M.C. GUTIÉRREZ-RUIZ,[*,*****] J.C. FERNÁNDEZ-CHECA,[**] L.E. GÓMEZ-QUIROZ[*,*****]

[*]DEPARTAMENTO DE CIENCIAS DE LA SALUD, UAM IZTAPALAPA, MÉXICO.
[**]CENTRO ESTHER KOPLOWITZ, IDIBAPS, BARCELONA, SPAIN.
[***]UNIDAD DE HÍGADO, HOSPITAL UNIVERSITARIO, UANL, NUEVO LEÓN, MÉXICO.
[****]RED PROMEP FISIOPATOLOGÍA DE LAS ENFERMEDADES HEPÁTICAS, MEXICO CITY, MEXICO.

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 and serum were evaluated. H&E and TUNEL stains were accomplished, also 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, also with H&E and TUNEL stains, suggesting an exacerbation of cholestatic damage. Examination of the main signaling pathways involved in repair process were analyzed, such as Akt, Stat3 and Erk1/2. Chow mice showed peak activation at day 2 after BDL, meanwhile HC animals show minimal activation regarding HC control. *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. In conclusion our data suggest that cholesterol overload in hepatocytes aggravates cholestasis and impairs signaling pathways involved in liver repair such as c-Met/HGF.

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H. MISCELLANEOUS

001

IMPACT OF QUALITY OF LIVER BIOPSY SAMPLES ON AGREEMENT BETWEEN PATHOLOGISTS IN LIVER FIBROSIS ASSESSMENT: WHICH IS THE MOST ADEQUATE FRAGMENT?

MARIA CHIARA-CHINDAMO, CRISTIANE ALVES VILLELA-NOGUEIRA, RENATA DE-MELLO-PEREZ, JOÃO MA. DE-ARAUJO-NETO, VERA L. NUNES-PANNAIN, HENRIQUE S. MORAES-COELHO

UNIVERSIDADE FEDERAL DO RIO DE JANEIRO. BRAZIL.

Introduction. Liver biopsy remains the golden standard for grading and staging of chronic viral hepatitis. More recently, biopsies 20 to 25 mm long and/or containing at least 11 complete portal tracts have been adopted as optimal standards. **Aim.** To evaluate the pattern of liver fragments that ensure the best coefficient of agreement between pathologists regarding fibrosis stage. **Material and methods.** A cross-sectional study in patients with chronic hepatitis C submitted to percutaneous liver biopsies was conducted at the Federal University of Rio de Janeiro, between Mar 2010 and Mar 2013. Biopsies were guided by ultrasonography using a 14 or 16 G disposable Tru Cut needle 20 mm long. Fragments were considered appropriate when presenting length ≥ 10mm and containing ≥ 6 portal tracts, considering the sum of all fragments obtained and portal tracts containing at least elements of a portal vein and hepatic artery. Biopsies were classified according to METAVIR score and reviewed by an experienced pathologist blinded to all clinical data. The agreement coefficient regarding fibrosis stage was evaluated considering fragments length 15 mm, 20 mm and 25 mm long and number of portal tracts ranging from 6 to 11. **Results.** We included 255 biopsies with median length of 24 ± 5 mm and a mean number of portal tracts of 16.1 ± 6.2. Distribution of fragment size was the following: 97.5% ≥ 15 mm, 83.3% ≥ 20 mm and 45% ≥ 25 mm. A number of portal tracts ≥ 11 was found in 82% of samples ≥ 15 mm, 85% of samples ≥ 20 mm and in 86% of samples ≥ 25 mm. The intra-observer agreement regarding liver fibrosis was 0.885 and overall agreement after review was 0.64. The smallest fragment found to demonstrate similar agreement regarding liver fibrosis comparing to the overall agreement was 20mm long (k = 0.63 *vs.* k = 0.64). No additional differences were found in agreement analyzing samples longer than 25 mm compared to 20 mm (k = 0.65 *vs.* k = 0.63). Regarding the number of portal tracts, agreement was similar when a mean number of 11 portal tracts was present in the sample in comparison to overall agreement (k = 0.64 *vs.* k = 0.64). Agreement dropped significantly to k = 0.195 after reviewing samples with a mean number of 6 portal tracts and to k = 0.56 in samples with mean number of 9 portal tracts. **Conclusion.** A liver biopsy fragment ≥ 20 mm long containing at least 11 portal tracts demonstrated the higher agreement between pathologists for fibrosis staging, confirming to represent the best pattern quality of a liver sample.

002

COULD BILIARY LITHIASIS BE A SIGN OF THE START OF A HEPATIC INJURY? CASE SERIES ANALYSIS

A. PEÑA-CHÁVEZ,[*] F.M. GONZÁLEZ-ORTIZ,[**] M. SALAMANCA-GARCÍA,[***] A. SÁNCHEZ-CEDILLO,[**] G. MEJÍA-CONSUELOS,[*] F. CARBALLO-CRUZ,[*] M. DEL C. GARCÍA-DE-LEÓN[****]

[*]*CIRUGÍA GENERAL. SECRETARÍA DE SALUD DEL DISTRITO FEDERAL. MEXICO CITY, MEXICO.*

[**]*INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN. MEXICO CITY, MEXICO.*

[***]*CENTRO MÉDICO NACIONAL 20 DE NOVIEMBRE, ISSSTE. MEXICO CITY, MEXICO.*

[****]*UNIDAD DE INVESTIGACIÓN EN MEDICINA EXPERIMENTAL, FACULTAD DE MEDICINA. UNAM/HOSPITAL GENERAL DE MÉXICO. D.F. MEXICO CITY, MEXICO.*

Background. Cholelithiasis is defined as the presence of stones in the gallbladder. The prevalence of biliary stones is different in distinct poblational groups; those differences could be represented by different genetic and environmental factors. Between the specific risk factors that predispose their formation there have been identified: age, gender, accelerated loss of weight, parenteral nutrition, pregnancy, diet, etc. similarly as non alcoholic fatty liver disease (NAFLD), cholelithiasis is associated to hypertriglyceridemia, obesity, insulin resistance and diabetes type 2, therefore, it is reasonable to expect that patients with biliary lithiasis could have a high prevalence of NAFLD. The aim of this study is to know the histological findings in liver biopsies, in a short case series of patients undergoing cholecistectomy. **Material and methods.** Descriptive study made to the trans-operative wedge biopsy of the right hepatic lobe of 12 patients with cholelithiasis that went undergo cholecystectomy. Information of the patients was taken from the medical records. Statistical analysis was made with STATA 11.0. Data was analyzed using rank sum test (Wilcoxon), and Fisher Exact-test for categorical outcomes. **Results.** Analysis by groups defined by histological findings are show in Table. All the patients had hepatic injury (Brunt classification). Inflammation 100% (41% grade 1, 58% grade 2). Steatosis 50% (66% grade 1, 34% grade 2). Fibrosis 83% (90% grade 1, 10% grade 2). 33% of the patients presented metabolic syndrome. **Conclusions.** It is known that cholelithiasis is considered of a surgical resolution without considering the hepatologist point of view. The shared risk factors of cholelithiasis, metabolic syndrome and obesity have repercussion in the liver (NAFLD). We cannot establish that all patients with metabolic syndrome have hepatic injury, but we propose other studies that verify if the frequency of hepatic inflammation, steatosis and fibrosis in patients with gallstones is real and if so, it could justify liver biopsy in all patients that undergo cholecystectomy.

003

PERCUTANEOUS ASPIRATION THROMBECTOMY AND/OR THROMBOLYSIS CATHETER-DIRECTED FOR THE TREATMENT OF ACUTE PORTAL AND SUPERIOR MESENTERIC VEIN THROMBOSIS: REPORT OF FIVE CASES

E. MÁRQUEZ-GUILLÉN, E. NEGRETE-CARBALLO, J. GUERRERO-IXTLÁHUAC, A. GONZÁLEZ-AGUIRRE, E. LÓPEZ-MÉNDEZ

INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN. MEXICO CITY, MEXICO.

Background. Acute portal-mesenteric vein thrombosis is a clinical condition that can cause portal hypertension and bowel ischemia. The prognosis is determined by early diagnosis and treatment that is crucial for the restoration of venous flow and reduction of morbidity and mortality. **Material and methods.** We analyzed retrospectively five patients (2 with liver cirrhosis) with acute portal and mesenteric vein thrombosis, all with clinical of intestinal ischemia, with severe symptoms, deteriorating clinical condition, and/or persistent symptoms despite anticoagulation. Methods. In all patients, attempt to permeabilize the porto-mesenteric system with percutaneous aspiration thrombectomy and/or thrombolysis catheter-directed. The recanalization was documented in a new angiography at 24 h post-procedure. **Results.** In the subgroup of three non-cirrhotic patients, in two of them, attempt with aspiration thrombectomy followed by thrombolysis with recombinant tissue plasminogen activator (rTPA) via catheter inserted, result in partial recanalization in one patient; however, this patient died after 6 weeks for septic shock for pneumonia. The second patient had nule response, not repermeabilization and died. The third patient received only rTPA via catheter, with partial portal-mesenteric recanalization. In the subgroup of cirrhotic patients, one patient received aspiration thrombectomy followed by thrombolysis with inmmediately repermeabilization. At 24 h post-procedure, the angiography showed rethrombosis, and received new aspiration and thrombolysis, with partial portal permeabilization. The second patient, received only aspiration thrombectomy without response, and died for acute liver failure. No major complications associated to procedure were reported. **Conclusions.** In this study, patients with acute portal-mesenteric vein thrombosis the percutaneous aspiration thrombectomy and/or thrombolysis catheter-directed, had 60% of repermeabilization, all partial, and could be considered as treatment for patients with severe disease that no respond to initial treatment. Patients with extense and symptomatic ischemia without response to thrombolysis died in this small serie.

Table. (002) Clinical and demographic data, by inflammation, steatosis and fibrosis.

Variable	Inflammation GI n = 5 (41%)	Inflammation GII n = 7 (58%)	P value	Steatosis n = 6 (50%)	Without steatosis n = 6 (50%)	P value	Fibrosis n = 10 (84%)	Without fibrosis n = 2 (16%)	P value
Age	42 ± 10	43 ± 12	0.9	40 ± 3	45 ± 16	0.4	43 ± 10	41 ± 20	0.8
Gender (fem), n (%)	5 (100)	5 (71)	0.1	5 (83)	5 (83)	-	8 (80)	2 (100)	0.4
Metabolic Sx	2 (40)	2 (28)	0.6	2 (33)	2 (33)	-	3 (30)	1 (50)	0.5
DM	0	1 (14)	0.3	0	1 (16)	0.2	1 (10)	0	0.6

004

HEPATIC CYSTIC IN 45 PATIENTS

CIRA VELASCO-ELIZALDE, ARACELI GONZÁLEZ
ENRIQUE CABRERA HOSPITAL. LAWTON POLICLINIQUE. LA HAVANA, CUBA.

Introduction. The hepatic cysts can be solitary or multiple. If they are multiple and diffusedly distributed, constitute the Polycystic Congenital of the Liver, rare entity, with dominant autosomic transmission for the most part of persons who suffer from the disease, showing hepatocellular function preserved, without portal hypertension, but at certain number of patients may develop hepatic insufficiency, and them liver transplantation may be done. The association with renal cystic can occur or at another organs. Its prevalence in autopsies comes from 0.13 to 0.6 %, and in general population is about 2 to 6%. Generally the patients are asymptomatic, but may have pain in upper right part of abdomen. The disease appears between 40-60 years. The treatment is symptomatic, except if the pain is severe or the liver insufficiency is present. **Material and methods.** Carry up prospective and longitudinal study among the patients seen in Gastroenterology's consultation of the Enrique Cabrera Hospital in Havana, Cuba, among the years 2008-2011, among the patients that assisted for dyspepsia or upper right abdominal pain during this time. The echography was performed to all this patients diagnosing hepatic cystic in 45 sick persons. Echography and liver enzymatic were performed yearly during 2 years after the diagnosis, in the above mentioned consultation to patients and theirs relatives. **Results.** The masculine sex between the 60 and 70 years predominated. Only one female patient had renal cysts too, with renal normal function. 100 % of the sick persons had hepatic normal profile, and not biliary dilatation was found. Among the 70 brothers, it was managed to go into 40 (57%). No one presented injuries echography to the start of the study, neither during two year of follow up as the 50% of the 60 studied descendants. **Conclusions.** The disease appeared more later on yielded on the worldwide bibliography reference. There was predominance of the masculine sex, with higher average of age in our study than women of the study. The multiple cysts predominated in our patients. Renal the overtaking had a minimal expression. There was no increase of the number of cysts during the year of tracking. The brothers and studied children had echography and hepatic profile normal.

005

EFFECT OF BEZAFIBRATE IN CHOLESTASIS OF PATIENTS WITH PRIMARY BILIARY CIRRHOSIS AND OVERLAP SYNDROME AUTOIMMUNE HEPATITIS WITH RESISTANT URSODEOXYCHOLIC ACID

M. CASTILLO-BARRADAS, L.E. SOTELO-SOLÍS, M.C. BERNARDINO-DEL-RÍO, R.G. VARGAS-ÁNGELES
HOSPITAL DE ESPECIALIDADES, CENTRO MÉDICO NACIONAL LA RAZA, IMSS, MEXICO CITY, MEXICO.

Backgrund. The hallmark of primary biliary cirrhosis (PBC) is cholestasis and liver damage evolving to cirrhosis, the former can also be present in PBC-autoimmune hepatitis (AIH). Ursodeoxycholic acid (UDCA) is the only accepted treatment for these entities, unfortunately biochemichal response is only achieved in a third of the patients. Acid fibric derivatives have shown to be useful in cholestatic liver disease. **Aim.** The purpose of the present study is to assess the effect of bezafibrate treatment on the biochemical profile of patients with PBC and PBC-AIH overlap resistant to UDCA. **Material and methods** A total of 23 patients were included: 17 with PBC, 6 with PBC-AIH overlap which were previously treated with UDCA for one year without biochemical response. Patients received bezafibrate 200 mg bid PO, during 16 weeks. Follow up with biochemical profile was made at 8 and 16 weeks. **Results.** Alkaline phosphatase (ALP), decreased in all patients from 484 ± 258 U/L to 272 UI ± 203 ($p = 0.001$) at 8 weeks and to 282 UI ± 294 ($p = 0.001$) after 16 weeks of treatment in UDCA-resistant PBC. Complete response to treatment using the Paris Criteria was achieved in 48% of the patients. Patients with UDCA-resistant PBC-AIH overlap achieved. **Conclusion.** Treatment with bezafibrate in UDCA-resistant PBC is useful to improve cholestasis, achieving complete response in 48% of patients with UDCA-resistant PBC.

006

BENIGN FOCAL LIVER INJURY: A FREQUENT FINDING AT THE COMPUTED TOMOGRAPHY

J. PONIACHIK, G. HORTA, M. LÓPEZ, A. DOTTE, J. CORDERO, C. CHESTA, A. CASTRO, P. PALAVECINO
HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.

Introduction. Imaging studies increasingly used today have progressively increased the detection of focal liver lesions. Multidetector computed tomography (MDCT) of the abdomen, with use of contrast medium, is able to detect and differentiate most of these lesions. **Objective.** The aim of this study was to determine the prevalence and characterization of various benign focal liver lesions detected abdominal MDCT. **Material and methods.** A retrospective, descriptive study. We reviewed the MDCT of the abdomen with contrast performed on an outpatient basis between August 2011 and July 2012. Clinical data were obtained from the application of the test and imaging findings in terms of description of the hepatic parenchyma and benign focal liver lesions. Data were statistically analyzed with comparison of proportions test, χ^2 and Fisher exact tests. **Results.** 1,184 studies were reviewed, of which 461 (38.4%) had benign focal liver lesions. The most prevalent lesions were simple cyst 290 (24%) and hemangioma 61 (5.1%), granuloma-calcification in 39 (3.2%), focal nodular hyperplasia in 19 (1.6%) and one case of adenoma. Excluding all known cases of liver disease remained similar prevalence of benign focal liver lesions with 396 (37.5%) patients. Normal livers had more cystic lesions and hemangiomas that livers with signs of liver damage (27 *vs.* 16.2%, $p = 0.014$, and 5.3 *vs.* 1.1%, $p = 0.043$). **Conclusions.** Benign focal liver lesions are a very common finding in the study by MDCT. Most of these lesions are simple cyst and hemangioma.

007

LIVER BIOPSY IN UNIVERSITY COLOMBIA CLINIC AND REINA SOFIA CLINIC DURING THE YEARS 2008 TO 2012

CRISTANCHO MIGUEL,* SANDRA HUERTAS,*,** L.C. SABBAGH,** E. PRIETO O. JHON*
**CLÍNICA UNIVERSITARIA COLOMBIA, BOGOTÁ, COLOMBIA.*
***CLINICA REINA SOFÍA, BOGOTÁ, COLOMBIA.*

Introduction. Liver biopsy is an important tool for study a large number of hepatic diseases and it is well known that the

diagnostic yield is dependent observer, based on the experience of the pathologist who interprets and characteristics of sampling, related to the number of portal tracts represented, the caliber and biopsy length. **Materials and methods.** It is a descriptive study with an analytical component- The database of the Pathology Department of Clinica Colsanitas SA was revised, identifying liver biopsies of January 1, 2008 to December 31, 2012 that corresponded to patients at Clinica Universitaria Colombia and Clinica Reina Sofia in Bogotá (Colombia). Information corresponding to demographic data of patients (age and sex), indication of liver biopsy (admission diagnosis), making technique of biopsy and histopathological outcome was obtained, discriminating the sample received in size, number of portal spaces, histopathological diagnosis, state of inflammatory activity and fibrosis in the entities concerned. Data were tabulated in a spreadsheet (EXCEL), frequencies and proportions of the data were obtained. Statistical analysis was performed with the EpiInfo program, and χ^2 test was applied, seeking to establish whether there was a conclusive relationship between outcome variables (diagnosis) and sample size and the number of portal spaces. **Results.** Records from 406 samples were included for analysis. There was 60.3% biopsies belonging to female gender patients, mean age was 53.5 years old. The techniques used for making biopsies were trucut biopsy in 87.9%, and intraoperative wedge biopsy in 12.1%. The main indications were evaluation of tumors and elevated levels of liver enzymes. The most common length of the trucut biopsies was in the range of 10 to 19 mm. The number of portal tracts had statistically significant relationship to achieve conclusive diagnoses in samples with more than 5 porta spaces. The main histopathologic diagnosis were in order: fatty liver (22.7%), tumors (21.7%), hepatitis C and B (11.6%). **Conclusions.** In this two clinics, liver biopsy keep a crucial role in the diagnosis of liver alterations, mainly fatty liver, tumors and viral hepatitis B and C, and is very important to consider that the success of a biopsy to obtain a diagnostic at this institutions depends on the number of portal tracts and the pathologist experience.

008

ACTION OF GLUTAMINE IN SEVERE ACUTE LIVER FAILURE THIOACETAMIDE-INDUCED IN RATS

ELIZÂNGELA GONÇALVES-SCHEMITT,[*,§,||] JOSIELI RASKOPF-COLARES,[†,§,||] RENATA MINUZZO-HARTMANN,[*,§,||] MARIANA DO-COUTO-SOARES,[§,||] MARIA I. MORGAN-MARTINS,[§,||] CLÁUDIO A. MARRONI,[¶] NORMA POSSA-MARRONI[*,†,‡,§,||]

[*]*PPG CIÊNCIAS MÉDICAS. UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, PORTO ALEGRE, BRAZIL.*

[†]*PPG BIOSAÚDE, UNIVERSIDADE LUTERANA DO BRASIL, CANOAS, BRAZIL.*

[‡]*PPG FISIOLOGIA, UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, PORTO ALEGRE, BRAZIL.*

[§]*LABORATÓRIO EXPERIMENTAL DE HEPATOLOGIA E GASTROENTEROLOGIA, HCPA, PORTO ALEGRE, BRAZIL.*

[||]*LABORATÓRIO DE ESTRESSE OXIDATIVO E ANTIOXIDANTES, ULBRA, CANOAS, BRAZIL.*

[¶]*PPG HEPATOLOGIA, UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE, BRAZIL.*

Severe acute liver failure is a syndrome with high mortality and morbidity and low prevalence, leading to functional impairment of the liver, with changes in their metabolism. The damage in the liver parenchyma may be due to xenobiotics such as thioacetamide, which can lead to varying degrees of liver damage according to the dose and exposure time. The production of reactive oxygen species has an important role in the pathophysiology of the disease, experiments using antioxidants may be an option for new therapies. Glutamine nucleotide is a precursor for glutathione synthesis. The objective was to evaluate the acute hepatotoxic effect of thioacetamide and the use of glutamine as an antioxidant. Project approved CEUA/HCPA:12-0116. Were used 28 rats divided into 4 groups; control (CO), glutamine (G); thioacetamide (TAA); thioacetamide with glutamine (TAA+G): Were two doses of 400 mg/kg TAA intraperitoneally (ip) with eight-hour interval was administered. G was administered at a dose of 25 mg/kg (ip) 30 min after the TAA. After 24 h of induction, the animals were anesthetized, killed, and the liver removed for analysis of the lipoperoxidation (TBARS), the activity of antioxidant enzymes SOD, CAT and GPx and histological analysis (HE). Statistical analysis was ANOVA followed by Student-Newman-Keuls (mean ± SE), which was considered significant $P < 0.05$. Increased levels of TBARS in the TAA group (0.68 ± 0.32 nmol/mgProt) relative to CO groups (0.33 ± 0.09 nmol/mgProt) and G (0.35 ± 0.08 nmol/mgProt) and a decrease in group TAA + G (0.45 ± 0.05 nmol/mgProt) relative to the TAA ($P < 0.001$). SOD significantly increased in TAA (68.93 ± 18.97 USOD/mgProt) group as compared to CO groups (24.56 ± 7.85 USOD/mgProt) and G (19.72 ± 16.04 USOD/mgProt) and a reduction in TAA + G group (30.73 ± 17.20 USOD/mgProt) relative to the TAA group ($P < 0.01$). A significant decrease was observed in the levels of CAT in the TAA group (0.28 ± 0.08 pmol/mgProt) compared to CO group (0.43 ± 0.04 pmol/mgProt) and G (0.45 ± 0.08 pmol/mgProt) and a significant increase in TAA+G group (0.38 ± 0.05 pmol/mgProt) relative to the TAA group ($P < 0.01$). In GPx activity occurred a significant decrease in TAA group (0.17 ± 0.015 nmol/mgProt) than in the CO group (0.24 ± 0.055 nmol/mgProt) and G (0.25 ± 0.034 nmol/mgProt) group ($P < 0.01$). Histological analysis TAA group showed a breakdown in the architecture of the liver parenchyma, inflammatory infiltrate and necrosis compared to CO and group G. This study suggests that Thioacetamide the time analyzed, produced a toxic effect judging by the liver. The use of glutamine was capable of alleviating the damage caused by TAA.

009

MICROBIAL ANALYSIS IN HIGH-RISK PATIENTS WITH ACUTE BACTERIAL CHOLANGITIS TREATED IN A TERTIARY CARE CENTER

J. CASTRO-GÓMEZ, C. GUERRERO-VELÁZQUEZ, E. CANTÚ-LLANOS, D. RUIZ-ROMERO, E. NEGRETE-CARBALLO, J. SÁNCHEZ-ÁVILA, I. GARCÍA-JUAREZ

DEPARTAMENTO DE GASTROENTEROLOGÍA, INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MEXICO CITY, MEXICO.

Background. Acute bacterial cholangitis (ABC) is a biliary tract infection that warrants an effective antibiotic treatment for proper resolution. In most cases, antimicrobial therapy selection is empirical. Epidemiological studies based on microbiological cultures and their resistance pattern leads us to choose the proper antibiotics. **Material and methods.** A retrospective review of 198 cases classified as acute biliary tract infection thru January 1, 2000 to August 31, 2010 was performed. Only ABC with positive bile culture and/or positive blood cultures was included. A microbial analysis including the prevalence of the bacteria cultured and its antibiotic susceptibility pattern was made. Etiology, clinical features and treatment was also reviewed. **Results.** 100 cases met our inclusion criteria. The most common etiology was iatrogenic biliary injury (29%), followed by pancreatic adenocarcinoma

(18%) and cholangiocarcinoma (16%). History of bile duct manipulation was dominant (80%) and 58 patients had experienced two or more events of ABC. Blood cultures were positive in 84 patients and bile culture in 21 cases. Five patients had a both blood and bile cultures positive. The cultures were predominantly monomicrobial (72%). A total of 139 bacteria were isolated. The most prevalent bacteria we found were: *Escherichia coli* [50.3% (70/139)], *Enterococcus* spp. 28 [20.1% (28/139)] and *Pseudomona* spp. [6.5% (9/139)]. A considerable percentage of the isolated *Escherichia coli* were resistant to ceftriaxone [30% (21/70)], but highly sensible to both meropenem and amikacin [97% (68/70)]. Almost one third of the *Enterococcus* spp. were resistant to ampicillin [29% (7/28)], but greatly susceptible to vancomycin [96% (27/28)]. Invasive treatment was merited in most of the patients (65%). Endoscopic drainage was the most frequently used [55.3% (36/65)], followed by percutaneous drainage [36.9% (24/65)] and finally surgery [30.7% (20/65]. **Conclusions.** Our hospital is a national referral center for biliary tract disease including iatrogenic injuries and biliary/pancreatic cancer. This could explain the low presence of naïve biliary tract in our population and may be associated to the high prevalence of *Enterococcus* spp. We noted a considerable proportion of *Escherichia coli* and *Enterococcus* spp. were unsusceptible to ceftriaxone and ampicillin, respectively. This study encourages the need for a well design local epidemiological study that could redefine the antibiotic selection in our center.

010

MR ELASTOGRAPHY OF THE LIVER AT 3.0T; PRELIMINARY CLINICAL RESULTS IN DIAGNOSING LIVER FIBFROSIS GRADES

K. YOSHIMITSU
FUKUOKA UNIVERSITY, FUKUOKA, JAPAN.

Background. Non-invasive assessment of liver fibrosis is definitely a recent clinical demand. The purpose of this study is to clarify the usefulness of 3.0T MR elastography (MRE) in diagnosing the histological grades of liver fibrosis using preliminary clinical data. **Material and methods.** Between October 2012 and March 2014, MRE has been applied to all patients who underwent liver MR study. Among them, those who had pathological evaluation of liver tissue within 3 months from MR examinations were retrospectively recruited. The MR equipment used was a 3.0-T clinical unit (Discovery 750W, GE, USA) along with a 32-element phased-array coil. A 19 cm diameter passive pneumatic driver was positioned over the center of the right rib cage at the level of the xiphoid process and attached to an acoustic waveform generator. A 60-Hz waveform was applied to the driver. A 2D spin-echo echo-planar MRE sequence (TR/TE = 1,000/59, 66 x 64 matrix, 10 mm slice thickness, 80-Hz magnetization encoding gradient) acquired magnitude and unwrapped phase difference wave images using 42 cm field-of-view. Four slices were obtained including the level of the hepatic hilum under 16-s breath-holding. Wave images and MRE images (stiffness map) with cross-hatching marks were automatically generated on the operating console. Liver stiffness was measured using fusion image method (Jpn J Radiol 2013; 31:336-41) and average of the 4 slices were used to represent the liver stiffness of each patient. **Results.** There were 85 patients who met the inclusion criteria, including 11, 27, and 2 patients who had chronic hepatitis B, C, and both, respectively, and 5 with alcoholic liver disease, 11 with non-alcoholic steatohepatitis, 3 with other entities of liver disease, and 25 patients without known liver disease. Liver stiffness showed significant correlation with the pathological grades of liver fibrosis (rho = 0.92, $p < 0.0001$, Spearman's rank correlation). The cutoff values and areas under the curve (Az) calculated from receiver operating characteristic analysis were 3.1 kPa and 0.97 for F0 *vs.* F1-4, 3.85 kPa and 0.97 for F0-1 *vs.* F2-4, 4.86 kPa and 0.98 for F0-2 *vs.* F3-4, and 7.50 kPa and 0.96 for F0-3 *vs.* F4. Sensitivity, specificity, and accuracy of diagnosing F0-2 *vs.* F3-4 were 94%, 92%, and 93%, respectively. **Conclusion.** The cutoff values and Az obtained at 3.0T clinical MRE were comparable to those reported in the literature obtained at 1.5T MRE. 3.0T clinical MRE may work as well as 1.5 T clinical MRE system.

011

EXTRAHEPATIC MANIFESTATIONS OF HEREDITARY HEMOCHROMATOSIS AND HEMOSIDEROSIS

C. GUERRERO-VELÁZQUEZ, J. CASTRO-GÓMEZ, E. CANTÚ-LLANOS, D. RUIZ-ROMERO, E. NEGRETE-CARBALLO, J. SÁNCHEZ-ÁVILA, I. GARCÍA-JUÁREZ
DEPARTAMENTO DE GASTROENTEROLOGÍA, INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, MEXICO CITY, MEXICO.

Background. Iron overload diseases can be a congenital disorder [hereditary hemochromatosis (HH)] or be due to iron overload [hemosiderosis (HS)]. These entities can lead to liver cirrhosis and characteristic extrahepatic manifestations. The main genetic defect in HH occurs in the HFE (C282Y) gene, leading to increased iron absorption. Hemosiderosis is characterized by hemosiderin deposits in tissues secondary to iron excess. Both diseases may present with extrahepatic manifestations affecting articular, cardiac and endocrine systems. The prevalence of extrahepatic manifestations in Mexican population is unknown. **Objective.** To determine the prevalence of extrahepatic manifestations in patients with HH and HS. **Material and methods.** We conducted a descriptive and cross-sectional study in our institute. Clinical records from January 1999 thru May 2012 were reviewed. Only cases of HH and HS that met the AASLD 2011 criteria were included. Patients with connective tissue diseases, inflammatory bowel disease, porphyria cutanea tarda and incomplete data in the clinical records were excluded. Descriptive statistics, proportions and contingency tables were used. The analysis was made with the SPSS (17 version) program. **Results.** We included 50 patients in our analysis [HH (n= 35) and HS (n= 15)]. Female sex was predominant in the HH group [63% (22/35)]. The mean age was 50.5 years *vs.* 36.2 years in the HH group and HS, respectively. Diabetes mellitus was more prevalent in [20% (7/35)] the HH group versus the HS patients [6% (1/15)] ($p = 0.243$). Cardiac involvement was found in 9/35 (26%) cases in the HH group *vs.* cero cases in HS group ($p = 0.029$). More patients with HH had hyperpigmentation [57% (20/35) *vs.* 20% (3/15)] ($p = 0.029$). Hypogonadism was present in 9/35 (26%) patients with HH. None of the patients with HS had hypogonadism ($p = 0.032$). Arthralgias were equally present in both groups [HH 46% (16/35) and HS 46% (7/15)]. Liver cirrhosis was dominant in the HH group [66% (23/35)] *vs.* the HS group [46% (7/15)] ($p = 0.345$).The mean hemoglobin level in patients with HH was higher (13.3 g/dL *vs.* 9.6 g/dL). **Conclusions.** We found that patient with HH were significantly older, had more heart disease, hyperpigmentation and hypogonadism than patients with HS. No statistical differences in diabetes mellitus, joint disease and anemia distribution were encountered.

012

AMINOTRANSFERASEMIA IN COLOMBIAN CHILDREN WITH DENGUE

C.A. VELASCO, J.L. BUITRAGO
DEPARTMENT OF PEDIATRICS. UNIVERSIDAD DEL VALLE. CALI, COLOMBIA.

Introduction. Aminotransferasemia is a biochemical alteration of dengue in children. **Objective.** To determine the prevalence of aminotransferasemia in children with dengue and identify possible associations. **Material and methos.** Prevalence study in 124 children with dengue from Hospital Universitario del Valle Evaristo García in Cali, Colombia in those considered sociodemographic, nutritional, and paraclinical variables. Statistical analysis included estimates of the prevalence of aminotransferasemia in children with dengue and its corresponding confidence interval 95%, the estimation of other descriptive measures of interest and association analysis by multiple logistic regression. **Results.** In this population of children with a mean age of 101 months, the prevalence of aminotransferasemia was 54.8%, predominantly male, being a native of Cali, Colombia and dengue with alarm signs. Aminotransferasemia was associated with the sex. There was a higher opportunity of aminotransferasemia in children originating from Valle, Colombia, with uncomplicated dengue, malnourished, with leukopenia and thrombocytopenia. There was associated factors such as gender and age. **Conclusion.** More than half of children with dengue from HUV showed elevated aminotransferases, with sex and age, associated risk factors.

013

SCREENING SERUM METABOLIC BY FLUOROMETRY IN 16 COLOMBIAN CHILDREN WITH HEPATO-SPLENIC SYNDROME

C.A. VELASCO, J.A. BELTRÁN, J.L. BUITRAGO
DEPARTMENT OF PEDIATRICS, UNIVERSIDAD DEL VALLE, CALI, COLOMBIA.

Introduction. Metabolic diseases in children with hepatosplenic syndrome (HES) from eastern Colombia is presented in 2.1%. **Objective.** To determine the presence of certain metabolic diseases in children from Hospital Universitario del Valle (HUV) Evaristo García in Cali, Colombia with a diagnosis of SHE without clear etiology. **Material and methods.** This is the report of 16 children diagnosed with SHE without clear etiology from HUV, in whom were considered sociodemographic, nutritional and paraclinical variables. Statistical analysis included measures of central tendency such as mean, standard deviation and percentages. **Results.** In this group of children with an mean age of 27 months, 10 male, 13 originating in Cali and Valle, Colombia, was ruled by fluorometry beta-glucosidase in Gaucher disease at all, and was found by fluorometry chitotriosidase 1 child, congenital enzyme deficiency and 2 children, suspicion of Niemann-Pick. Half of these patients had malnutrition and 67% delay in size, according to the WHO tables. He appeared in 89% INR altered, anemia in 71%, 60% direct hyperbilirubinemia, thrombocytopenia in 29 and 23% aminotransferasemia. **Conclusion.** In this group of children with SHE without clear etiology, by fluorometry was discarded in all Gaucher disease and 1 case of congenital deficiency of chitotriosidase and 2 suspected cases of Niemann-Pick is presented.

014

PORTAL VEIN THROMBOSIS IN NON-CIRRHOTIC PATIENTS

JHON E. PRIETO O., CARLOS GONZALEZ, L.C. SABBAGH
CLÍNICA UNIVERSITARIA COLOMBIA, BOGOTÁ, COLOMBIA.

Introduction. Portal vein thrombosis in non-cirrhotic patients (PVT-NC) is defined as blood flow obstruction of extrahepatic portal vein for blood clots inside of it, can be acute when symptoms occur within 2 months before diagnosis and without clinical or radiographical evidence of portal hypertension. Chronic with symptoms two months after diagnosis characterized by increased portal pressure and increased periportal collateral circulation (cavernoma). The aim of this review is to analyze a subset of patients with extrahepatic portal vein thrombosis presented with healthy liver. **Material and methods.** Hepatology service database at the Colombia University clinic (CUC), was reviewed and analyzed, 21 patients diagnosed with non-cirrhotic portal vein thrombosis were included during the period from January 1st 2010 to may 30 2013. It is a descriptive retrospective study. **Results.** The average age of patients was 43 years, 52.4% were men. The main reasons for patient consultation were variceal bleeding 42.9% and abdominal pain in 33%, surgical history was found in 28.6%. When analyzing the hepatic biochemical profile a normal pattern, with AST and ALT averages of 27 and 26 IU/mL was observed. Liver biopsy was performed in 7 patients (33.3%), all were normal. All patients underwent endoscopy and splenoportal Doppler and the majority had CT and/or MRI of the abdomen. At endoscopy 16 patients had varices. In splenoportal doppler old portal thrombosis evidenced in 19% of patients, cavernoma in 42.9%, cavernoma plus old thrombosis in 28.6% and splenomegaly in 9.5%. Portal hypertension was evident in 85.7% of the 21 patients. **Conclusions.** Noncirrhotic portal vein thrombosis is a condition that usually presents with signs of HTP, predominates in younger people compared to cirrhotic portal thrombosis origin and the liver has a normal profile. Its diagnosis is based on a careful history that emphasizes the presence of surgical and hematology background, associated with a series of imaging studies.

015

FACTORS INFLUENCING RELIABILITY OF TRANSIENT ELASTOGRAPHY

E. JUÁREZ-HERNÁNDEZ, M.H. URIBE-RAMOS, J.L. ROMERO-FLORES, S. ORNELAS-ARROYO, A.Y. LÓPEZ-RAMÍREZ, L.C. GONZÁLEZ-RODRÍGUEZ, M.H. RAMOS-OSTOS, N. MÉNDEZ-SÁNCHEZ, M. URIBE, N.C. CHÁVEZ-TAPIA
OBESITY AND DIGESTIVE DISEASES UNIT. MÉDICA SUR CLINIC AND FOUNDATION. MEXICO CITY, MEXICO.

Background. Transient elastography is a non-invasive method for the evaluation of fibrosis in chronic liver disease. However its reliability is variable and the factors associated with accuracy are not completely identified. The aim of this study was to determine the factors associated with transient elastography reliability. **Material and methods.** A total of 2033 transient elastography measurements were performed from 2009 until October 2013. Reliability was determined according to the interquartile range/median (IQR/M < 0.3-reliable; IQR/M < 0.1 very reliable). It was also determined the success percentage (> 60%), the procedure time and the probe size selected. The factors that could affect the reliability of the

Table. (015) Multivariate analysis for elastography reliability.

Variable	OR (95% CI)
Unsucessful studies	
Female	1.707 (1.084-2.688)
Incorrect probe	1.856 (1.164-2.959)
HCV infection	0.411 (0.17-0.973)
Non reliable studies	
Clinical trial	0.595 (0.416-0.850)
Success < 60%	1.877 (1.278-2.756)
Very reliable studies	
> 10 measurements	1.912 (1.355-2.697)
Chronic hepatic diseases	2.667 (1.109-6.415)
Success > 60%	2.809 (1.708-4.621)
Overweight	0.736 (0.564-0.961)

procedure were analyzed by multivariable logistic regression. **Results.** The sample included 872 (42.9%) women; the body mass index was 27.9 ± 4.5 kg/m^2, the prevalence of advanced fibrosis was 26%, 83% of the studies were reliable. Factors associated with an unsuccessful study were female gender incorrect probe and HCV infection; non-reliable studies are associated with the success rate and to be performed during a clinical trial; and very reliable studies were associated with > 10 measurements, chronic hepatic diseases and success rate > 60% (Table). **Conclusion.** Operator, clinical and anthropometric characteristics are factors influencing the success and reliability of transient elastography. Improving the quality of procedure is necessary in clinical practice to offer better accuracy in diagnostics.

016

LIVER GLUCOSE METABOLISM IN POST-ABSORTIVE RATS IS ALTERED BY FOOD RESTRICTION SINCE BIRTH

M.M. DIAZ-PEDROSA, L.K. RUBIRA-BABATA, A. MALTA, A. SOUZA-VITORIANO, M. VARDANEGA-PEICHER, R. FERNANDES-GARCIA, V.A. FERREIRA-DE-GODOI
STATE UNIVERSITY OF MARINGÁ, BRAZIL.

Background. Involuntary food restriction impairs growth in humans and rodents. As food supply is kept below the daily energy demands but blood glucose control remains a priority, we investigated the liver glucose production (LGP) through glycogenolysis and gluconeogenesis in rats under food restriction since birth. **Material and methods.** Male Wistar rats were raised in 6-puppies litters and were fed freely after weaning (group GC) or were subjected to food restriction (group GR) by increasing litter size (12 puppies) and decreasing food supply to 50% of the free ingestion after weaning. At 50 days of age, after overnight fasting, the animals had their liver perfused *in situ* with buffer (basal perfusion) or buffer containing alanine (ALA, 10 mM, 20 min) or lactate (LAC, 5 mM, 30 min) or glucagon (GLU, 1 nM, 20 min) or adrenaline (ADR, 1 μM, 30 min) (stimulated perfusion). Glucose concentration was determined in samples of the effluent fluid and corrected to μmol.min-1.g-1 liver. The resulting areas under the curve (AUC, in μmol glucose.g-1 liver) were compared through test t at the significance level of 5%. **Results.** The body weight of the GC was 120-230 g, while that of the age-matched GR was 100-140 g. The basal LGP was markedly greater ($p < 0.01$) in the GR (11.76 ± 3.80; n = 19) than in the GC (0.89 ± 0.25; n = 26). The LGP in the presence of ALA and GLU was significantly lower ($p < 0.05$) in the GR than in the GC (ALA 0.83 ± 0.17 in the GC; 0.45 ± 0.17 in the GR; n = 5-8) (GLU 0.27 ± 0.02 in the GC; null in the GR; n = 4-6). The LGP in the presence of ADR was exceedingly greater ($p < 0.01$) in the GR (GC 0.92 ± 0.71; GR 62.99 ± 13.09; n = 4-6), and the LGP in the presence of LAC ($p > 0.05$) did not differ between the groups (GC 4.27 ± 1.23; GR 3.83 ± 1.73; n = 5-6). Numerical data are the AUCs. **Conclusions.** Freely-fed rats show low basal LGP after overnight fasting, little response to glycogenolytic agents, and enhanced gluconeogenesis. The high basal LGP of the GR indicates intense glycogenolysis even after fasting. On the other hand, gluconeogenesis in the presence of two important natural substrates, ALA and LAC, was not enhanced. In these GR animals, liver glycogenolysis in response to GLU was absent, but it was intense in the presence of ADR. This peculiar pattern of LGP in food restriction may have important consequences to blood glucose control, especially during challenging instances, such as physical exercise and hypoglycemia.

017

MELATONIN PROTECTS LIVER DAMAGE INDUCED BY CARBON TETRACHLORIDE IN RATS

S. BONA,* A.J. MOREIRA,* G.R. RODRIGUES,* M. MORAES,* C.T. CERSKI,* T.R. SILVEIRA,* C.A. MARRONI,** N.P. MARRONI*,***
*UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, BRAZIL.
**UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE, BRAZIL.
***UNIVERSIDADE LUTERANA DO BRASIL, BRAZIL.

Introduction. The use of carbon tetrachloride (CCl4) in rats develops oxidative damage to liver tissue, triggering fibrosis and cirrhosis long term. Given the significant involvement of oxidative stress in the development of various diseases, as well as the cirrhosis, antioxidants are reported to be effective in reducing fibrosis in animal models. **Objective.** To evaluate the antioxidant effect of melatonin (MLT) in an experimental model of cirrhosis induced by CCl4 ip. **Material and methods.** Twenty males Wistar rats (± 250 g) 4 groups: I: control (CO), II: control MLT, III: (CCl4) and IV: CCl4 + MLT. The CCl4 was administered according protocol: 10 doses of 5 in 5 days, 10 doses of 4 in 4 days and 7 doses of 3 in 3 days. Animals were deaths 2 days after the last dose of CCl4 at the sixteenth week. The animals received phenobarbitone in the drinking water at the dose of 0.3 g/dL. The administration of melatonin (20 mg/kg ip) was started in 10th week and lasts until the end of the experiment. The comparison between groups was performed by ANOVA, Tukey's test, data expressed as mean ± SD. Results were considered significant when $p < 0.05$. **Results.** Biochemical analysis showed significant differences when comparing the III group *vs*. I, II and IV groups. We observed increase liver enzymes after administration of CCl4. MLT was able to reverse this increase. [AST (I: 175.4 ± 34.3; II: 161.8 ± 20:28; III: 1,016.8 ± 340.83; IV: 519.6 ± 127.46)/ALT (I: 50.2 ± 5:59, II: 43.8 ± 6.61, III: 270 ± 90.8; IV: 177 ± 42.72)/FA (I: 80.25 ± 25.41, II: 75 ± 14:26, III: 395 ± 130.83; IV: 238 ± 24.47). LPO evidenced that the animals treated with CCl4 produced a significant increase in TBARS and F2- isoprostanes. However, after treatment with melatonin were reduced significantly [TBARS (I: 0.18 ± 0.01, II: 0.15 ± 0.01, III: 0.286 ± 0.027; IV: 0.178±0.05)/F2-iso (I: 74.96 ± 3:09, II: 74.20 ± 5.85; III: 88.32 ± 2.67; IV: 77.21 ± 2.12)]. SOD activity was preserved in animals receiving MLT (I: 12.84 ± 1:09, II: 11:43 ± 0.71; III: 9.324 ± 0.288; IV: 13:18 ± 1.63). In histological analysis, CCl4 group showed changes in

the liver architecture, signs of chronics damage and lymphocytic infiltrate. We also found nodular formations with homogeneous pattern, similar to cihrrosis, confirmed by picrosirius. However, group IV showed improvement in this subject. **Conclusion.** The use of melatonin as antioxidant was effective in reducing liver damage caused by increased production of free radicals.
Apoio: ULBRA/CNPq, FIPE-HCPA, CAPES, FAPERGS. CEP/HCPA: 10-0316.

018

THE ROLE OF GLUTAMINE IN EXPERIMENTAL MODEL OF INTESTINAL ISCHEMIA AND REPERFUSION

R. MINUZZO-HARTMANN,[*] F. LICKS,[**] E. GONÇALVES-SCHEMITT,[*] J. RASKOPF-COLARES,[***] G. PANDOLFO-ZABOT,[****] H. SARUBBI-FILLMANN,[****] N. POSSA-MARRONI[*,**,***]
[*]*PPG EM MEDICINA: CIÊNCIAS MÉDICAS-UFRGS, PORTO ALEGRE, BRAZIL.* [**]*PPG EM CIÊNCIAS BIOLÓGICAS: FISIOLOGIA-UFRGS, PORTO ALEGRE, BRAZIL.* [***]*UNIVERSIDADE LUTERANA DO BRASIL-ULBRA, CANOAS, BRAZIL.* [****]*PONTIFÍCIA UNIVERSIDADE CATÓLICA DO RIO GRANDE DO SUL-PUCRS, PORTO ALEGRE, BRAZIL.*

Introduction. The intestinal ischemia-reperfusion (I/R-i) can cause cellular damage to the tissue and in distant organs such as the liver. Some aggressor agents are involved in these processes, such as: the generation of free radicals and the release of pro-inflammatory cytokines. Due to the involvement of free radicals in the lesions of I/R-i, some therapeutic antioxidants options are being studied and tested in I/R-i lesions. The aim of the study was to evaluate effects of glutamine in an animal model of I/R. **Material and methods.** Twenty male Wistar rats were divided into four experimental groups: sham operated (SO), glutamine + sham operated (G+SO), ischemia-reperfusion (I/R), glutamine+ischemia-reperfusion-i (G+I/R). The rats were subjected to occlusion of the superior mesenteric artery for 30 min followed by 15 min of reperfusion. The glutamine (25 mg/kg/day) was administered 24 and 48 h before I/R. Local and systemic injuries were determined by evaluating intestinal and liver segments for oxidative stress using lipid peroxidation (LPO), activity of superoxide dismutase (SOD) and immunohistochemical assays of interleukin-6 (IL-6) and nuclear factor kappa beta (NF-κB) in tissues. The statistical analysis used was ANOVA followed by Student-Newman-Keuls (mean ± SEM) significant at $p < 0.05$. **Results.** The animals treated with glutamine showed a significant reduced the expression of IL-6 and NF-κB and levels of LPO-Gut (SO: 0.45 ± 0.07, G + SO: 0.40 ± 0.02, I/R: 1.83 ± 0.20; G + I/R: 0.78 ± 0.04) and liver (SO: 0.16 ± 0.01, G + SO: 0.20 ± 0.02, I/R: 0.45 ± 0.03; G + I/R: 0.24 ± 0.02) compared to animals in the I/R group. The SOD activity showed a significant increase in G + I/R group compared to the I/R group - Gut (SO: 72.3 ± 6.4, G + SO: 77.9 ± 3.2, I/R: 53.18 ± 1.73; G + I/R: 74.02 ± 5.99) and liver (SO: 36.63 ± 1.52, G + SO: 33.13 ± 2.75, I/R: 26.64 ± 0.46; G + I/R: 33.21 ± 0.53). **Conclusion.** These results suggest that pretreatment with glutamine prevents mucosal injury and improves gut and liver recovery after I/R injury in rats.
Support: FIPE-HCPA/CAPES/CNPq/FAPERGS/PUCRS.

019

EXPERIMENTAL MODEL OF PORTAL HYPERTENSION POSSIBLY INDUCES HEMODYNAMIC CHANGES ON WISTAR RATS IN 1H, 3H, 6H, 24 H AND 5 DAYS AFTER SURGERY-PRELIMINARY DATA

F. LICKS,[*] C. MARQUES,[†] R. MINUZZO,[‡] M.C. SOARES,[§] M.C. IRIGOYEN,[||] N.P. MARRONI[*,‡,§]
[*]*PPG EM CIÊNCIAS BIOLÓGICAS-FISIOLOGIA.* [†]*PPG EM MEDICINA-CIÊNCIAS MÉDICAS. UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, PORTO ALEGRE, BRAZIL.* [‡]*INSTITUTO DE TECNOLOGIA DO PARANÁ, CURITIBA, BRAZIL.* [§]*UNIVERSIDADE LUTERANA DO BRASIL. CANOAS, BRAZIL.* [||]*FACULDADE DE MEDICINA. UNIVERSIDADE DE SÃO PAULO, SÃO PAULO, BRAZIL.*

Background. Portal hypertension (PH) is a clinical syndrome associated with the development of a hyperdynamic circulation. This hyperdymanic disturb is associated with hemodynamic changes on the circulatory system. The aim of the study was to evaluate these hemodynamic changes in animals submitted to an experimental model of partial portal vein ligation (PPVL), at different times after surgery. **Material and methods.** Ten male Wistar rats were divided into 2 groups: 1. Sham-operated (SO), 2. PPVL. Rats were anesthetized with ketamine hydrochloride (100 mg/kg ip) and xylazine hydrochloride (50 mg/kg ip) and the procedure of PPVL was performed. After a medium incision in the abdomen, bowels were gently withdrawn on a humidified gauze with saline and the portal vein was isolated. A 20 g needle was placed on the portal vein and both were tied up using a 3.0 silk yarn, the needle being gently withdrawn after ligation. The sham-operated group was submitted to the same procedure, although their portal veins did not undergo partial portal vein ligation. After these procedures, rats were catheterized in mesenteric vein and femoral artery in order to perform the posterior hemodynamic measures. We awaited 1 h and performed the measures. The same was done in 3 h, 6 h, 24 h and 5 days after surgery. **Results.** Systolic blood pressure showed an increase on PPVL group after 1 h (SO 122 ± 4; PPVL 132.5 ± 4: $p = 0.02$), 3 h (S 125.5 ± 5, PPVL 136.6 ±7: $p = 0.01$) and 6h after surgery (SO: 123.1 ± 4, PPVL 132.6 ± 6: $p = 0.01$). In 24 h, values of the groups tended to be equal. 5 days after surgery, an increase on SO group and a decrease on PPVL group was observed (SO 134 ± 8, PPVL 124.2 ± 9: $p < 0.001$). We also recorded simultaneously the pressure on mesenteric vein and femoral artery by 24 h and 5 days after surgery. In 24 h, portal pressure was higher in PPVL group (SO 5 ± 1, PPVL 9 ± 2: $p = 0.02$) and arterial pressure was also higher (SO 104.5 ± 4 PPVL 110 ± 7: $p = 0.04$). In 5 days, portal pressure remained higher, and we observed a tendency on arterial pressure increase. **Conclusion.** By these previous results, we come to believe that the partial portal vein ligation procedure leads to a hemodynamic disbalance on the circulatory system since the first hour after surgery, leading to probable cardiocirculatory disturbs. Further investigations are being conducted in order to understand the pathophysiology of this process.
Support: FIPE-HCPA, CAPES/CNPq/FAPERGS.

020

PREVALENCE OF LIVER FIBROSIS IN PATIENTS WITH PSORIASIS

E. JUÁREZ-HERNÁNDEZ,* B. CORRALES-ROSAS,** M. URIBE,* N.C. CHÁVEZ-TAPIA*
*OBESITY AND DIGESTIVE DISEASES UNIT. MÉDICA SUR CLINIC AND FOUNDATION. MEXICO CITY, MEXICO.
**DERMATOLOGY DEPARTMENT. CENTRO MÉDICO NACIONAL SIGLO XXI. IMSS. MEXICO CITY, MEXICO.

Background. Liver fibrosis is consider one of the major adverse effects secondary to therapeutic agents used in the treatment of psoriasis, mainly methotrexate. Currently, the prevalence of liver fibrosis in patients with psoriasis is unknown. The aim of this study was to describe the prevalence of liver fibrosis in patients diagnosed with psoriasis and its relationship with therapeutic agents for psorasis. **Material and methods.** This cross-sectional study included patients with diagnosis of psoriasis under treatment with one or more therapeutic agent. Demographic and biochemical variables were collected and liver elastography was performed in all patients in order to determine the presence of liver fibrosis. **Results.** The sample included 100 patients (Table). The age and body mass index were 54 ± 13 years and 28.8 + 4.7 kg/m^2 respectively; the average cumulative dose of methotrexate was 2,774 ± 2,953 mg. The prevalence of liver fibrosis was 16%; no significant association between the presence of liver fibrosis and the use of methotrexate or any other therapeutic agent was found (p = 0.781). **Conclusion.** The prevalence of liver fibrosis in patients diagnosed with psoriasis is high. There is no significant association between liver fibrosis and therapeutic agents for the treatment of psoriasis.

Table. (020)

Variable	n (%) SD
Male	69 (69%)
Age (years)	54.40 ± 13.1
BMI (kg/m^2)	28.79 ± 4.7
AST U/L	30.83 ± 19.9
ALT U/L	37.97 ± 33.1
BT (mg/dL)	0.78 ± 0.87
Cholesterol (mg/dL)	195.26 ± 51.48
Triglicerides (mg/dL)	181.14 ± 89.5
AST > 40 U/L	14 (14%)
ALT > 40 U/L	27 (27%)
BT > 1.0 mg/dL	13 (13%)
Topic treatment	21.1% (20)
Infliximab	18.9% (18)
Methrotexate	56.8% (54)
Cyclosporine A	4.2% (4)
Adalimumab	22.1% (21)
Etanercept	11.6 (11)
Acumulate dosis metrotexate (mg)	2,774.5 ± 2,953.4
Advanced fibrosis (>9 kPa)	16 (16%)

021

PORTAL VEIN LIGATION-INDUCED LIVER REGENERATION IS ASSOCIATED WITH AMPK PATHWAY ACTIVATION

P. ROMANQUE,* S. URIBE-ECHEVARRÍA-ARÁNGUIZ,** M. URIBE-MATURANA,** M. ZAPATA-FUENTES*
*INSTITUTO DE CIENCIAS BIOMÉDICAS, FACULTAD DE MEDICINA, UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.
**SERVICIO DE CIRUGÍA, HOSPITAL DEL SALVADOR, FACULTAD DE MEDICINA SEDE ORIENTE, UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.

Background. Complete liver metastases resection is possible only in a low percentage of the patients diagnosed. Ineligibility for complete resection may be due to metastases location, size or number, extrahepatic disease, or insufficient future liver remnant (FLR) volume. Portal vein ligation (PVL) induces enlargement of the FLR, permitting a second stage surgery for metastases resection. The mechanisms underlying PVL-induced regeneration are not completely understood, and we hypothesize metabolic signals from the portal circulation with activation of AMPK (AMP-activated protein kinase) may be involved. AMPK is a cellular energy status sensor that contributes to restoration of energy homeostasis by regulating catabolic/anabolic processes. In different systems, including liver regeneration after partial hepatectomy, AMPK is also required for cell proliferation. Material and methods: 200-220 g male Sprague Dawley rats underwent PVL under inhaled isoflurane anesthesia. Median laparotomy was performed and the portal branches feeding the median and left lateral lobes were dissected and completely ligated. 24, 72 and 120h after PVL the liver was removed, and ligated (LL) and non-ligated lobes (NL) were weighed and storage separately. Samples were fixed in 4% neutral-buffered formalin and embedded in paraffin for further histological examination or snap frozen in liquid nitrogen for qRT-PCR. **Results.** At 72h a significant increase of NL lobes weight (7.830 ± 0.6238g) and a decrease in LL weight (3.023 ± 0.3147) was observed compared to control animals ($p < 0.01$). Similar results were observed at 120h post PVL. IGF-1, as a potential signal activating AMPK pathway, S6K and mTOR RNA levels were determined in NL and LL lobes. IGF- 1 was increased significantly in the LL at all times, whereas in NL lobes the levels found were similar to sham animals. mTOR and S6K exhibit similar behavior , increasing its expression at 24, 72 and 120 h post PVL in NL lobes compared with lobes in Sham animals and ligated lobes. **Conclusion.** These results demonstrate that increased activity of AMPK pathway is observed in response to ligation of the portal vein, which has not been previously described. Metabolic signals entering NL lobes through portal circulation may induce hypertrophy.

022

ASSOCIATING LIVER PARTITION AND PORTAL VEIN LIGATION FOR STAGED HEPATECTOMY (ALPPS): SINGLE CENTER EXPERIENCE IN SANTIAGO DE CHILE

S. URIBE-ECHEVARRÍA-ARÁNGUIZ,* M. URIBE-MATURANA,*
M. ZAPATA-FUENTES,** P. ROMANQUE**
*SERVICIO DE CIRUGÍA, HOSPITAL DEL SALVADOR, FACULTAD DE MEDICINA SEDE ORIENTE, UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.
**UNIDAD DE PATOLOGÍA HEPÁTICA EXPERIMENTAL, INSTITUTO DE CIENCIAS BIOMÉDICAS, FACULTAD DE MEDICINA, UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.

Background. Liver metastases from colorectal cancer (CRC) are the first cause for malignant tumors in the liver. Complete metastasis resection is the only curative therapy; however, only 15% of the patients diagnosed are amenable for this treatment. Ineligibility for complete resection may be due to metastases location, size or number, extrahepatic disease, or insufficient future remnant liver volume (RLV). Associating liver partition and portal vein ligation for staged hepatectomy (ALPSS) procedure has been recently introduced as an alternative to PVE and PVL for liver volume augmentation in cases of right hepatectomy with small FLR and high risk of liver failure. We retrospectively analyzed our experience with ALPPS in order to evaluate the application of the procedure. **Material and methods.** Patients referred to the Hepatobiliary Surgery team at Hospital del Salvador with liver metastases from CRC from October 2011 to October 2013 were included in the study after informed consent, and according to eligibility and exclusion criteria. In a first stage, right portal vein was ligated and liver split in the limit of the left liver. Volume gain evolution was followed-up with CT-scan. The volumetric parameters evaluated include total liver volume (TLV), remnant liver volume (RLV), remnant liver volume to total liver volume ratio (RLV/TLV), remnant liver volume to body weight ratio (RLV/BWR) and median volume gain. Liver and systemic functions were evaluated through routine exams. **Results.** Between October 2011 and October 2013, we performed 9 ALPPS procedures in patients with CRC metastases. Three male and 6 female patients aged 42 to 63 years were intervened. The preoperative RLV to body weight ratio was < 0.5 with RLV range from 198-342 cc. After ALPPS the RLV increased up to 176% (66-176%). The time interval between phases 1 and 2 was 8 to 16 days. All patients presented transient transaminases elevations and low prothrombin time, which normalized in the first month control. Surgical complications included one case of bile collection, one hematoma of the abdominal wall and one case of pleural effusion. **Conclusion.** A significant volume increased was achieved with ALPPS in 8 to 16. This period is shorter than the time required to achieve similar liver augmentation with PVL/PVE, which decrease the risk of recanalization and the chances of increasing the size of metastases. Selection of candidates and morbidity/mortality rates are parameters that will require a careful interdisciplinary assessment from hepatologists, oncologists, radiologists and surgeons.

023

INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN 1 EXPRESSION DURING LIVER FIBROSIS IN THE RAT

O. SÁNCHEZ-JERÓNIMO,* I.I. ROMERO-BELLO,*
A. RAMÍREZ-MENDOZA,* E. IBARRA-CORONADO,**
G. GUTIÉRREZ-REYES,*** C. GUZMÁN*
*LABORATORIO DE HÍGADO, PÁNCREAS Y MOTILIDAD, UNIDAD DE MEDICINA EXPERIMENTAL, FACULTAD DE MEDICINA, UNAM/HOSPITAL GENERAL DE MÉXICO, MÉXICO.
**DEPARTAMENTO DE EMBRIOLOGÍA, FACULTAD DE MEDICINA, UNAM, MÉXICO.

Introduction. Insulin-like growth factor binding proteins (Igfbp) are mainly produced in the liver. IGFBP-1 has been shown to be significantly increased in the blood of chronically infected patients of Hepatitis C. After an acute insult of carbon tetrachloride (CCl4), Igfbp-1 changes its pattern of expression in the rat liver and it has been related to hepatocyte proliferation and liver regeneration. However, this protein has not been studied during the chronic CCl4 treatment or related to fibrosis in the liver. **Objective.** To evaluate the mRNA expression of Igfbp-1 in the liver of rats with different levels of fibrosis induced by CCl4. **Material and methods.** Male Wistar rats weighing 250 ± 20 g were included in groups of 10 to receive 8, 12, 20 and 40 intraperitoneal doses of CCl4 (250 μL; 33% V/V in olive oil) to induce different degrees of liver fibrosis. A control group (C) without liver fibrosis was included as well as a group that received 20 CCl4 doses and a 4 week period of recovery (20d-R). Liver samples from every group were obtained and total RNA was isolated. Specific oligonucleotide sequences were used to assess the expression of Igfbp-1 by RT-PCR. 18S was used as an internal control. Negative controls were included in all trials. Images were captured with a digital camera and quantified by densitometry using image J software (NIH, USA). Igfbp-1 expression levels were normalized to that of 18S. Histological assessment of the liver tissue was performed by Hematoxylin-Eosin as well as Masson's thrichrome staining. Data was analyzed by One-way ANOVA and stundent's t test. $P<0.05$ was considered significant. **Resultados.** Liver fibrosis increased as the number of CCl4 doses was administered. Igfbp-1 expression was lower in the group that received 12 doses (moderate fibrosis) compared to C and 8d (C= 0.46 ± 0.03; 8 d = 0.47 ± 0.02; 12 d = 0.38 ± 0.03; 20 d = 0.41±0.03; 40 d = 0.46 ± 0.11 relative units). Igfbp-1 expression was significantly lower in the 20d-R group compared to the 20d group (20 d = 0.41 ± 0.03; 20 d-R = 0.13 ± 0.01 relative units). **Conclusions.** The expression of Igfbp-1 in the liver has the potential to differentiate the moderate and the mild stages of fibrosis in the rat. Recovery of liver fibrosis diminished Igfbp-1 expression. Igfbp-1 expression and function could be associated to de progression and reversal of liver fibrosis induced by CCl4.

024

GENISTEIN MODIFY THE EXPRESSION OF EGFR, TYROSINE PHOSPHORYLATION AND SIGNALING PATHWAYS IN ACUTE LIVER DAMAGE

E. ÁLVAREZ-AYALA,* J.A. REYES-ESPARZA,* F.J. GARCÍA-VÁZQUEZ,**
L. RODRÍGUEZ-FRAGOSO L.*
*FACULTAD DE FARMACIA, UNIVERSIDAD AUTONOMA DEL ESTADO DE MORELOS, MÉXICO.
**INSTITUTO NACIONAL DE PEDIATRÍA, MEXICO CITY, MEXICO.

Background. The epidermal growth factor receptor (EGFR) is highly expressed in the adult liver and has been proposed to

play an important role during liver development. Evidence indicates that the EGFR system plays an important role in liver regeneration and hepatocyte protection in acute and chronic liver injury. The primary active component of soy is an isoflavone called genistein (4,5,7-trihydroxyisoflavone), has a wide spectrum of biological effects, which include: induction of cell differentiation and apoptosis, inhibition of cell growth, and abrogation of signal transduction pathways. Genistein, thus, has attracted a considerable amount of attention in cancer research especially for its inhibitory action on protein tyrosine kinase (PTK) activities that are important in cell survival and proliferation. Our aim was to evaluate the role of genistein on EGFR expression, phosphorylation and signaling pathways in acute liver injury caused by carbon tetrachloride (CCl4). **Material and methods.** For this study, we used male Wistar rats which were randomly divided into four groups: control, genistein 5 mg/kg oral (2 weeks), acute damage CCl4 4 mg/kg intraperitoneally (4 weeks) and acute damage treated with genistein a dose mentioned. Rats were sacrificed and liver were collected for determinate EGFR expression and phosphorylation on Y845, Y992, y1045 and Y1068, and pathways like STAT5, Gab1, Plc-γ1 and Akt by Western blot and immunoprecipitation. **Results.** EGFR expression was elevated in groups with acute liver damage and acute damage treated with genistein. On the other hand when we analyzed EGFR phosphorylation we founded a reduction on Tyr845 EGFR phosphorylation in group with liver damage, nevertheless the genistein increased this phosphorylation 5 fold compared with CCl4 group, on Tyr1045 the phosphorylation was to decrease in acute damage and acute damage treated with genistein group. On Tyr992 and Tyr1068 EGFR phosphorylation genistein and acute damage not showed modification. In addition when analyzing the different pathway we founded increase on phosphorylation STAT5 but not in your expression. **Conclusion.** The genistein can be involved in process like proliferation, apoptosis and EGFR degradation in the liver during acute damage, because it modifies specific tyrosine phosphorylation on EGFR and phosphorylation on STAT5, these proteins are associated with proliferation.

I. DILI

001

DRUG INDUCED LIVER DISEASE ASSOCIATED WITH HERBAL SUPPLEMENTS AND THE RISK OF ACUTE LIVER FAILURE

E. ROBLES ROVELO, D. KERSHENOBICH, A. LOAEZA DEL CASTILLO.
DEPARTMENT OF MEDICINE. INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN. MEXICO CITY, MEXICO.

Introduction. Drug induced liver injury (DILI) is an entity rising in frequency whose prognosis may be severe and associated to acute liver failure. **Objective.** To investigate which are the drugs and dietary or herbal supplements most frequently related with hepatotoxicity and the risk of developing acute live failure. **Material and methods.** Medical records of patients with clinical or histological diagnosis of DILI attending the institute during a six year period (2008-2013) were reviewed. Clinical, biochemical and histological data were collected and analyzed. Acute liver failure (ALF) was defined as the presence of encephalopathy and INR > 1.5. **Results.** Thirty-seven cases of DILI were identified. Mean age of the patients was 48.4 ± 15.6 years. Twenty-two (59.5%) women and 15 (40.5%) men. The scoring system of the Council for International Organizations of Medical Sciences Roussel Uclaf Causality Assessment Method (CIOMS/RUCAM) scale allowed the identification of 4 highly probable, 16 probable and 17 possible cases. The most common route of drug or supplement administration was oral in 94.6 % (n = 35), the median time of exposure was 17 days (6-30). Jaundice was present in 33 patients (89.2%), followed by fever (29.7%), arthralgia (16.2%) and rash (13.5%). Thirty-five patients were hospitalized (94.6%), for a mean hospital length of 13.4 ± 10.1 days. Hepatotoxicity was related to herbal supplements in 14 cases (37.8 %), anti-tuberculosis drugs in 6 (16.2%), antibiotics in 4 (10.8%), anti-neoplastic agents in 3 (8.1%) and anti-fungals in 3 cases (8.1%). Ten patients (27%) developed ALF and 3 patients died (8.1%). Factors significantly associated with ALF were albumin (p = 0.03, IC 95%: -1.19-0.06), INR (p = 0.001, IC 95%: 1.03-1.93). In 6/10 patients ALF was associated with the use of herbal supplements (60%). Liver biopsy was performed in 18 patients (48.6%). The most frequent histological findings were hepatic necrosis and intra-cytoplasmic cholestasis. **Conclusions.** DILI was most commonly associated to oral administration of drugs or dietary supplements. Herbal dietary supplements are a common alternative in suspected DILI, including ALF. These findings further support the need of regulatory and educational measures directed to reduce the risk among the general population.

002

SPANISH AND LATIN AMERICAN PROSPECTIVE DILI NETWORKS: DIFFERENCES ACROSS REGISTRIES

F. BESSONE,[*] N. HERNÁNDEZ,[†] A. SÁNCHEZ,[†] M. DI PACE,[†] M. ARRESE,[‡] A. RUÍZ,[‡] J.R. BRAHM,[§] J. ARANCIBIA,[§] D. KERSHENOBICH,[||] A. LOAEZA,[||] M. GIRALA,[¶] M. LIZARZABAL,[**] E. MENGUAL,[**] N. MÉNDEZ SÁNCHEZ,[††] M. DÁVALOS,[‡‡] R. PARANÁ,[§§] M.I. SHINONI,[§§] I. MEDINA CÁLIZ,[||||] M. ROBLES DÍAZ,[||||] **C. STEPHENS,[||||] A. GONZÁLEZ JIMÉNEZ,[||||] B. GARCÍA MUÑOZ,[||||]** M.I. LUCENA,[||||] R.J. ANDRADE[||||]

[*]HOSPITAL PROVINCIAL DEL CENTENARIO. ROSARIO, ARGENTINA.
[†]HOSPITAL DE CLÍNICAS. MONTEVIDEO, URUGUAY.
[‡]PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE. SANTIAGO, CHILE.
[§]HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE. SANTIAGO, CHILE.
[||]INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN SALVADOR ZUBIRÁN, HOSPITAL GENERAL DE MÉXICO. MEXICO CITY. MEXICO.
[¶]HOSPITAL DE CLÍNICAS. ASUNCIÓN, PARAGUAY.
[**]HOSPITAL UNIVERSITARIO DE MARACAIBO, VENEZUELA.
[††]FUNDACIÓN CLÍNICA MÉDICA SUR, MEXICO CITY, MEXICO.
[‡‡]HOSPITAL REBAGLIATI, FACULTAD DE MEDICINA, UNIVERSIDAD SAN MARTIN DE PORRES. LIMA. PERU.
[§§]HOSPITAL UNIVERSITARIO PROF. EDGARD SANTOS, UNIVERSIDAD FEDERAL DA BAHÍA, SALVADOR DE BAHÍA, BRAZIL.
[||||]INSTITUTO DE INVESTIGACIÓN BIOMÉDICA DE MÁLAGA (IBIMA), HOSPITAL UNIVERSITARIO VIRGEN DE LA VICTORIA, UNIVERSIDAD DE MÁLAGA, CIBEREHD, MÁLAGA, SPAIN.

Background. Drug-induced liver injury (DILI) differs across geographical areas due to differential drug polices, prescription habits, drug consumption, and genetic factors. In this study, we aimed to compare DILI cases included in the Latin American DILI Network with those in the Spanish DILI Registry to identify differences in phenotypic presentations and causative agents. **Material and methods.** Demographic, clinical parameters and causative agents were compared between 148 Latin American and 858 Spanish DILI cases. **Results.** The mean age of DILI development was similar between the two registries with 51 years in Latin America and 54 years in Spain. However, females predominated among the Lain American cases (58%)

compared to the Spanish cases (48%). Although hepatocellular damage was the most frequent type of injury in both registries, the percentage of hepatocellular cases was higher in the Spanish Registry (65 *vs.* 54%). Jaundice was present in 72 and 67% of the Latin American and Spanish cases, respectively. Hospitalization was required in 47% of the Latin American cases, compared to 53% in the Spanish cases. Severe cases predominated in Latin America (11 *vs.* 8%) while fatal cases (liver-related death or liver transplantation) were similar, 3.4 and 4% of the Latin American and Spanish cases, respectively. Considering therapeutic classes, antiinfectives and musculo-skeletal system drugs were the most frequently imputed groups in both registries. However, when compared the main causative agents we found differences. Amoxicillin-clavulanate, nimesulide, diclofenac and nitrofurantoin were more common in Latin America, while in Spain amoxicillin-clavulanate predominated followed by antituberculosis treatments, ibuprofen and atorvastatin. A variety of drugs, such as cyproterone, nevirapine, nitrofurantoin, propylthiouracil, agomelatine and albendazole, were found to cause DILI more frequently in Latin America. **Conclusions.** Latin American DILI cases show differences when compared to Spanish with a predominance of females and higher rate of cholestatic/mixed cases. This could be the result of variations in prescription patterns between the different geographical areas and distinct drug signatures.

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003

HERBAL RISKS: REPORT OF A CASE OF MEXICAN POPPY HEPATITIS *(ARGEMONE MEXICANA L.)*

CARLOS A. MELÉNDEZ-GONZÁLEZ
HOSPITAL GENERAL DE ZONA, INSTITUTO MEXICANO DEL SEGURO SOCIAL, TUXTLA GUTIÉRREZ, CHIAPAS, MÉXICO.

Background and introduction. The Mexican Poppy *(Argemone Mexicana L.)* belongs to the Papaveraceae family, of American origin. Distribution is worldwide in tropical and subtropical climates. It is responsible for ascites epidemic. However, its role as a cause of liver damage in humans is not associated with epidemic ascites is not documented in the medical literature. Proposed mechanisms of toxicity include cell membrane damage by reactive oxygen species and lipid peroxoidation, inhibition of DNA polymerase and the accumulation of pyruvate because of an increase in glycogenolysis. Sanguinarine (13-methyl [1.3] benzodioxol [5,6 - c] -1,3-dioxol [4,5-i] phenanthridine) one its alkaloids, is postulated as the principal toxic constituent. **Material and methods.** The following scales were used to assess drug-induced liver injury; Maria and Victorino score, the scale of the Council for International Organizations of Medical Sciences (Council for International Organizations of Medical Sciences/Roussel Uclaf Causality Assessment Method/CIOMS/RUCAM) and Naranjo Scale Adverse Drug Reactions Probability Scale (NADRPS).The patient consents in writing grant. Clinical case. Female 55 years old, who refused to be consuming alcohol or using complementary and alternative medicine such as herbal medicine, homeopathy, acupuncture and products multilevel company in their initial consultations, refused transfusions and viral hepatitis. Attended in 2 different periods –2012 and 2013– the symptoms in both were, loss of stool consistency in number 8-10 in 24 h without blood or mucus, abdominal pain and tenesmus, nausea without vomiting, headache and fatigue, denied the presence of fever in 2012 and feeling fever in 2013, without quantifying temperature. Physical examination showed vital signs within normal parameters and the presence of yellowing of the sclera of the eyes, mild pain on palpation of the right upper quadrant without hepatomegaly. Viral serology was performed for determination of antibodies to hepatitis A (anti HVA-IgM) antigen and antibody to hepatitis B (HBsAg, anti-HBc) , antibodys to hepatitis C (anti-VHC) and to hepatitis E (anti-VHE-IgM) was resulting negative. The determination of serum copper (161.4 mcg/dL. Vn = 70-175 mcg/dL) and ceruloplasmin (0.29 g/L vn = 0.20 to 0.60). Abdominal ultrasound was normal in 2012, but in 2013Abdominal ultrasound reported hepatomegaly of the right lobe, without change in echogenicity. Finally patient admitted having consumed in 2012 as in 2013 Mexican argemona until the appearance of symptoms and aid digestive disorders. Currently the patient is without clinical manifestations with normal examinations. **Results.** Mary and Victorino score obtained was 19 which places as defined. The CIOMS/RUCAM scale, was 11, as highly probable. While the scale of Naranjo score was 8, giving probable result. **Conclusions.** The elevated aminotransferases has been associated with the induction of alterations in the biotransformation both in phase I and II. Sanguinarine to interact with proteins of p-450 system and its activity decreases glutathione and increases sorbitol dehydrogenase and alanine aminotransferase.

004

FULMINANT HEPATIC FAILURE INDUCED, ALLOPATHIC DRUGS, HERBAL MEDICINES, AND ALIMENTARY SUPPLEMENTS IN REFERENCE CENTRES IN BRAZIL: INTERIM ANALYSIS

G. OLIVEIRA JR.,[*] I. BOIN,[†] CAMPOS JR.,[†] R. SILVA,[‡] L. FARIA,[§] C. VIANA,[||] P. BITTENCOURT,[*] R. PARANÁ[*]
[*]*HOSPITAL UNIVERSITARIO PROF. EDGARD SANTOS-UFBA, BRAZIL.*
[†]*UNIDADE DE TRASPLANTE DE FIGADO DO HOSPITAL DAS CLÍNICAS DA UNICAMP, BRAZIL.*
[‡]*HOSPITAL DE BASE DE SÃO JOSÉ DO RIO PRETO-FUMARM /FUMERP, BRAZIL.*
[§]*INSTITUTO ALFA DE GASTROENTEROLOGÍA DO HOSPITAL DAS CLÍNICAS DA UFMG, BRAZIL.*
[||]*HOSPITAL UNIVERSITARIO WALTER CANTÍDIO-UFC, BRAZIL.*

Introduction. Acute liver failure is characterized by rapid loss of liver function. It has different etiologies, especially viral hepatitis and drug-induced liver disease (DILI). According to WHO, in the period of 35 years, fulminant hepatic failure cases related to DILI has been reported mainly by the use of medications, such as acetaminophen, flutamina, herbal medications and halothane. Although the case reports of severe DILI are frequent in the literature, there are few data on the epidemiology of severe DILI in Brazil. **Objective.** To determine the frequency of cases of fulminant hepatitis drugs in Brazil. **Material and methods.** Retrospective multicenter study. The data collection instrument was a questionnaire sent by email to get information from each involved center, The Name Center Coordinator of the liver transplant center, the number of transplants performed/year, the number of fulminant hepatitis cases and their causes. Subsequently, each center was visited to review the medical records and validation of causality using HUCAN methods. **Results.** Data from a total of five liver transplant centers were collected. Medical filies for five years of suspected all suspected cases were revised. We could Identify 49 cases of fulminant Hepatic cases, of which 31% (15/49) were secondary to DILI. The non-steroidal antiinflammatory drugs were the most frequent cause of fulminant hepatitis, however other medicines and Herbal Medicines were

reported. Unlike what happens in the United States, England and Denmark acetaminophen was not a frequent cause of Fulminant Hepatitis in these Brazilian Centers. **Conclusion.** Fulminant hepatitis cases due to DILI are frequent in Brazil, but seems to have a different profile compared to USA. In our Brazilian centers, the anti-inflammatory drugs was the main cause of fulminant hepatitis. However, this is an interin analysis with only five Brazilian transplant centers.

005

ACUTE LIVER FAILURE AFTER THE INTAKE OF HERBALIFE PRODUCTS

G. ROJAS-LOUREIRO, I. LÁZARO-PACHECO, B. MARTÍNEZ-SALDÍVAR, E. PÉREZ-TORRES
HOSPITAL GENERAL DE MÉXICO, MEXICO CITY, MEXICO.

Background. The intake of Herbalife products such as medical treatment, weight loss and food supplement has been controversial around the world in the last 10 years. About 70 cases, specially women, has been reported in differents hospitals with acute hepatic failure and some of them died in weeks. One of the implicate substances is the *Camellia sinensis* used in Herbalife's tea drink in association with ethanolic extracts and result o liver injury. Other cause of hepatotoxicity linked to Herbalife products is the probably contamination with *Bacillus subtilis* in some batches and the possible, though still unproven, contamination of the substrates from which raw herbs are extracted. The majority of liver biopsies reported steatosis, spotty necrosis and extensive inflammation with Kupffer cell hypertrophy and hyperplasia. **Case report.** Female of 25 years old without pathological history, suddenly after a month of herbalife's drink tea intake started with nausea, vomiting, weakness, jaundice and rash. Then with itching, coluria, acholia, severe abdominal pain in the right upper quadrant and encephalopaty. Laboratory results creatinine 0.6, albumin 3.8, TB 23.1, DB 2.4, AST 2269, ALT 1237, GGT 39, DHL 1626, TP 23.2, INR 3.4, TP% 34%. HBsAg, anti-HBs, anti HBcIgM, HBeAg, AntiHbE, anti HA IgM, anti HC, CMV-IgM, EB-IgM, Tox-IgM, VHS all of them negative. Serum ceruloplasmin, beta-2 microglobulin, anti-mitococondrial antibodies, anti-smooth antibodies, and the complete test for LES were negative; alpha 1-antitrypsin and serum ferritin levels were normal. The liver ultrasonid Doppler with heterogenic echogenicity slightly enlarged, without evidence of thrombosis. Abdominal tomography with changes that suggest steatosis. Magnetic cholangioresonance without evidence of pathology. Liver biopsy demostrated steatosis, cholestasis with inflamatory necrosis, and hepatitis with necrosis. **Conclusion.** The relationship between the intake of herbalife products and the liver injury still been a complex issue for understanding completely. The cases reported around the world are people who has no other liver disease. The reason of hepatic failure remains unclear, however, exists many importat points to study in the future like time of intake, genre, and the process of liver injury before present acute liver failure, the dose and type of the product.

006

CASE REPORT: PATIENT WITH TWO DIFFERENT EPISODES OF DILI WITH EVOLUTION TO AUTOIMMUNE HEPATITIS AND ADVANCED FIBROSIS

M. ISABEL SCHINONI, M. PORTO-MAGALHÃES, T. REQUIÃO-ROCHA, V. SOUZA-VILANOVA, V. L. MENEZES-JESUS, S. CARVALHO-CUNHA, R. PARANÁ
HOSPITAL UNIVERSITÁRIO PROFESSOR EDGARD SANTOS, UFBA, SALVADOR-BAHIA, BRAZIL.

Introduction. Drug induced liver injury (DILI), mostly, is idiosyncratic. However, preexisting liver diseases may have synergistic factors, also trigger autoimmune reactions in the liver.This is a case report of a patient with metabolic syndrome and dyslipidemia without prior hepatic manifestations which featured two episodes of DILI by different drugs, developing after one year autoimmune hepatitis, and histological manifestations ofs teatohepatitis. **Objective.** Report a case of DILI. **Results.** 64 years-old woman, BMI: 29.6 kg/m^3, waist circumference 92 cm, alcohol consumption 20 g/week. History of ciprofloxacin allergic diverticulitis, metabolic syndrome and dyslipidemia. Regular use: simvastatin 20 mg/day for 6 years and acetylsalicylic acid 100 mg/day for 3 months, developed an acute hepatitis presented with asthenia, adynamia, pain in HD with mild hepatomegaly, dark urine without jaundice, presenting: AST 871U/L (31), ALT 1207U/L (31), GGT 239 U/L (12-43), FA 129 U/L (27-100), albumina 3.4 g/dL, TP 100%, BT 1.1 mg/dL, normal upper abdomen ultrasonography (USG), negative anti-HCV, anti-HBc, IgM anti-EHV, anti-CMV, anti-EBV, anti-herpes virus 1 and 2 and autoantibodies. The reaction was resolved 2 months later with suspension of drug and without other treatment. A year later, after using nimesulide 4 x 20 mg and omega 3 syrup with methyl paraben for a month, the patient developed a new acute hepatitis presenting asthenia, adynamia, painful hepatomegaly with increased consistency, with no splenomegaly; AST 523 U/L, ALT 559 U/L, GGT 125 U/L, FA 128 U/L, albumina 3.7 g/dL, TP 89%; BT: 0.56 mg/dL, BD: 0.33 mg/dL, anti-M. Liso: 1/160, negative anti-DNA, FAN, ANTI-LKM and ANCA. One month after onset, an USG showed signals of chronic liver disease. Biospy: portal spaces enlarged by fibrosis with septa and issuing draft parenchymal nodules with moderate mononuclear inflammatory infiltrate with multiple foci of aggression of peri-portal hepatocytes (interface activity), sometimes formation of rosettes; parenchyma with macro and microvacuolar steatosis, with component between 10-20% of hepatocytes, followed by mild to moderate ballooning of hepatocytes; foci of mononuclear infiltration, hepatocytes with nuclear pseudoinclusion of glycogen, mild peri-sinusoidal fibrosis; and absence of iron overload. **Conclusion.** Chronic hepatitis, moderate activity, stage 3, progression to fibrosis. Treatment was initiated: azathioprine 75 mg and prednisone 40 mg, with dose reduction of prednisone. After 3 months of treatment with azathioprine 75 mg and prednisone 10 mg, aminotransferases reached normal levels. Case of development of autoimmunity after second episode of DILI and histological findings of steatohepatitis. It's remarkable in this case that the liver presented with advanced liver fibrosis a year after the first event, which could be related to a pre-existing condition of steatohepatitis.

Table 1. (007)

AST	243 IU	Anti-HAV	Negative
ALT	346 IU	Anti-HCV	Negative
Alkaline phosphatase	372 IU	HBsAg	Negative
Γ-GTP	293 IU	Anti-HBc Total	Negative
Total bilirubin	12.2 mg/dL	AMA	Negative
D. bilirubin	10.1 mg/dL	ASMA	Negative
Albumin	3.6 g/dL	Anti-LKM 1	Negative
INR	1.04	p-ANCA	Negative

007

VANISHING BILE DUCT SYNDROME INDUCED BY CLAVULANATE

E. SILVA-PEREIRA, B. MEDRANO-OSSIO, P. POLLO-FLORES, T. GUARANÁ, P. GAVA, R. DANTAS, A. GOUVEA, E. BORDALO
HOSPITAL UNIVERSITÁRIO ANTÔNIO PEDRO-UNIVERSIDADE FEDERAL FLUMINENSE, BRAZIL.

Introduction. The Vanishing bile duct syndrome is characterized by destruction of intra-hepatic bile ducts and progressive cholestasis, may progress to liver cirrhosis. The pathophysiology is unknown, however it is noted association with drugs, cancer, infections, autoimmune diseases, transplantation, ischemic disorders and genetic. **Objectives.** Case report of amoxicillin/clavulanate hepatotoxicity characterized by vanishing bile duct syndrome. **Material and methods.** Pubmed's bibliographic review of articles by clavulanate hepatotoxicity. Case report. A 35 year old female, presented with progressive jaundice, acholic stools, choluria and pruritus preceded by nonspecific symptoms. She denied co-morbidities, but claimed that three weeks ago was admitted for treatment of pneumonia whit amoxicillin and clavulanate for 14 days. On physical examination revealed jaundice 3+/4+, no rash and no signs of hepatic encephalopathy. Abdominal ultrasonography was normal. Laboratory tests in Table 1. Needle biopsy of the liver showed important intra-hepatic cholestasis in addition to areas of hepatic necrosis associated with lymphocytic infiltrate and pericellular fibrosis. The portal tracts include porto-portal fibrosis sometimes sketching nodules, lymphocytic infiltrate with some plasma cells around the small and medium-sized bile ducts with exocytosis, destruction and disappearance of ducts. Interlobular bile ducts were absent in some portal tracts, finding compatible with Vanishing bile duct syndrome. Elastography was performed one year later (Table 2). **Conclusions.** Literature describes cholestasis induced by amoxicillin/clavulanate. Histopathologic findings include cholestatic hepatitis, ductopenia and rarely cirrhosis. Therefore there was rapid progress (31 days) to advanced fibrosis in a patient with vanishing bile duct syndrome induced by amoxicillin/clavulanate. Subsequently elastography showed reversion of fibrosis after one year preceded by blood tests within normal parameters.

Table 2. (007)

Success rate	100%
Median	3.3
IQR	0.3
IQR/Med	9%

008

HEPATOTOXICITY AFTER HAART IN COLOMBIAN CHILDREN WITH VERTICAL HIV INFECTION

A. SIERRA, P. LÓPEZ, C.A. VELASCO
DEPARTMENT OF PEDIATRICS. UNIVERSIDAD DEL VALLE. CALI, COLOMBIA.

Introduction. Hepatotoxicity in HIV-infected adults after HAART has been described in 2.6%. **Objective.** To determine the prevalence of hepatotoxicity after HAART through minimum three times elevated serum aminotransferases in Colombian children with HIV and identify possible associations. **Material and methods.** Prevalence study in 99 children with vertical HIV from Clínica Pediátrica VIH/SIDA of Cali, Colombia. Were considered clinical, paraclinical and sociodemographic variables. Statistical analysis included estimation of the prevalence of hepatotoxicity in children and its corresponding confidence interval 95%, the estimation of other descriptive measures of interest and association analysis by multiple logistic regression. **Results.** In this population of children with a mean age of 42.2 months the prevalence of hepatotoxicity was 14.1%, with female, being a native of Cali, Colombia and with stage C predominance. Hepatotoxicity not associated with viral load or %CD4. Greater opportunity of hepatotoxicity was found in children with previous hospitalizations. There was no associated factors. Hepatotoxicity after HAART was introduced to an mean of 756 days. The mean elevation of AST and ALT was 1,497 and 450 IU/L, respectively. **Conclusion.** Less than 15% of patients had hepatotoxicity and without association with any of the studied variables.