ANNALS of Hepatology

ABSTRACT SECTION

November-December, Vol. 15 No.6, 2016: 953-982

XXIV Annual Meeting of the Latin American Association for the Study of the Liver

September 28 - October 1, 2016. Santiago de Chile.

ORAL PRESENTATIONS

A. THE 6 BEST ORAL PRESENTATIONS

01
GENETIC PROFILES OF KILLER-CELL IMMUNOGLOBULIN-LIKE RECEPTORS AND HLA LIGANDS IN AMOXICILLIN-CLAVULANATE HEPATOTOXICITY

STEPHENS C.,[1] MORENO-CASARES M.,[2] LÓPEZ-NEVOT M.A.,[2] GARCÍA-CORTÉS M.,[1] MEDINA-CÁLIZ I.,[1] HALLAL H.,[3] SORIANO G.,[4] RUIZ-CABELLO F.,[2] ROMERO-GÓMEZ M.,[5] LUCENA M.I.,[1] ANDRADE R.J.[1]

[1]UGC APARATO DIGESTIVO Y SERVICIO DE FARMACOLOGÍA CLÍNICA, INSTITUTO DE INVESTIGACIÓN BIOMÉDICA DE MÁLAGA (IBIMA), SPAIN.
[2]HOSPITAL UNIVERSITARIO VIRGEN DE LA VICTORIA, UNIVERSIDAD DE MÁLAGA, CIBEREHD, MÁLAGA, SPAIN.
[3]HOSPITAL MORALES MESEGUER, MURCIA, SPAIN.
[4]SERVICIO DE GASTROENTEROLOGÍA, HOSPITAL DE LA SANTA CREU I SANT PAU.
[5]UCM DIGESTIVE DISEASES, HOSPITAL VIRGEN DEL ROCIO, CIBEREHD, SEVILLE, SPAIN.

Introduction. Natural killer cells are an integral part of the immune system and their activity is partly regulated by the binding of activating and inhibiting killer-cell Ig-like receptors (KIR) to HLA class I ligands on target cells.
Objectives. We aimed to examine KIR gene and HLA class I allele profiles in amoxicillin-clavulanate (AC) DILI patients in search for potential risk associations.
Material and methods. Presence and absence of 16 KIR genes were examined using sequence-specific oligonucleotide probes. HLA class I alleles were similarly determined in 102 Spanish AC DILI patients and 227 controls.
Results. The four framework loci KIR3DL2, 3DL3, 3DP1 and 2DL4 were present in all tested subjects. 2DL1, 3DL1, 2DS4 and 2DP1 were found in > 90% of patients and controls, while 2DS1, 2DS3, 2DS5 and 3DS1 where only present ≤ 45%. The A and B haplotypes were present in 49.5% and 50.5% (DILI) and 50.4% and 49.6% (controls), respectively. The genotypes translated into 28 (DILI) and 44 (controls) different gene profiles, with 18 being present in both groups. The most frequent gene profile 2DS2/2DL2/2DL3/2DP1/2DL1/3DL1/2DS4/3DL2/3DL3/2DL4/3PD1 was present in 16% of the DILI patients and 14% of the controls. Distribution of HLA ligands C1 (HLA-C, 80N), C2 (80K), Bw4 (HLA-B, 80I or T and HLA-A*2301, 2402 and 3201) and HLA-A3/A11 did not differ between DILI patients and controls. The most frequent DILI receptor-ligand combinations were 2DL3 + C1 (67%) and 3DL1 + Bw4 (67%), while 2DL1 + C2 (69%) and 3DL1 + Bw4 (69%) predominated in the controls. In contrast, 3DS1+Bw4 was the least frequent combination in DILI (9%) and controls (11%).
Conclusions. Our AC DILI cohort presented KIR gene distributions similar to the controls, which were comparable to previously reported KIR data from ethnically similar cohorts. The analyzed KIR receptor–HLA ligand combinations do not appear to play a major role in AC DILI development.
Funding: FEDER: PI-0239-2012, PI12-00378, AC-0073-2013. CIBERehd-ISCIII.

02
EVALUATION OF SOMATOTROPIC AXIS DYSFUNCTION AND SARCOPENIA IN NAFLD ANIMAL MODELS

BARRERA F., IRIGOYEN B., CABRERA D., SOLÍS N., PIZARRO M., COFRE C., FRÍAS C., HERNÁNDEZ A.A., CABELLO-VERRUGIO C., ARRESE M.

GASTROENTEROLOGY DEPARTMENT, PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE, SANTIAGO, CHILE.

Background. Somatotropic axis dysfunction has been previously described in subjects with NAFLD. This event has been postulated to be a major driver in NAFLD induced sarcopenia.
Aim. To analyze somatotropic axis dysfunction and its relation to sarcopenia in high fat diet (HFD) and Choline-deficient L-amino-defined (CDAA) diet induced NAFLD animal models.
Material and methods. C57/BL6 mice were fed in three different groups: Chow diet, HFD (12 weeks) and CDAA diet (20 weeks). Growth hormone (GH) serum levels were assessed at baseline and 5 min after intraperitoneal GH release hormone injection (1 ug) on each group. Insulin Growth Factor-1 (IGF-1) expression were assessed at baseline and 2 h after subcutaneous GH injection (1.6 ug/g) on each group. Muscle strength was estimated by in vivo functional assessment and by tibialis anterior electromyography *ex vivo*. Muscle fiber cross-sectional area (CSA) was determined estimating the minimal Feret's diameter. Myosin protein levels were evaluated by western blot as a marker of muscle atrophy.
Results. HFD group presented significantly lower GH levels at baseline (P = 0.01) and 5 minutes after GHRH (P= 0.02) compared to Chow and CDAA group. CDAA and Chow group presented a significant increase in IGF- -1 liver expression (P = 0.05 and P = 0.02 respectively), were as no significant response was observed in HFD group (P = 0.68). CDAA and HFD presented a significant decrease in muscle strength assessed by in vivo assay and ex vivo electromyography studies compared to chow diet. Muscle fiber CSA and myosin protein levels were similar in the three groups.
Conclusion. Only obesity associated NAFLD model is associated to a significant somatotropic axis dysregulation at hypophysis and liver level. Both NAFLD evaluated models (HFD and CDAA) exhibit a similar muscle strength reduction without evidence of muscle atrophy. These findings suggest that muscle strength loss (dynapenia) is an early event in NAFLD pathogenesis and is independent of somatotropic axis dysfunction.

DOI:10.5604/16652681.1222122.

03
COMPARATIVE EFFICACY OF AN INTENSIFIED RE-VACCINATION SCHEME FOR HEPATITIS B VIRUS INFECTION AMONG PATIENTS INFECTED WITH HIV (CORE-HIV): A RANDOMIZED CONTROLLED TRIAL. INTERIM ANALYSIS

VARGAS J.I.,[1-4] JENSEN D.,[2] MARTÍNEZ F.,[3] SARMIENTO V.,[4] ACUÑA P.,[5] PEIRANO F.,[6] FUSTER F.[4]
[1]DEPARTAMENTO DE GASTROENTEROLOGÍA, AND
[2]ENDOCRINOLOGÍA, FACULTAD DE MEDICINA, PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE, CHILE.
[3] DEPARTAMENTO DE SALUD PÚBLICA, ESCUELA DE MEDICINA, UNIVERSIDAD DE VALPARAÍSO. CHILE.
[4]UNIDAD DE HEPATOLOGÍA, HOSPITAL GUSTAVO FRICKE, VIÑA DEL MAR, CHILE.
[5]ESCUELA DE MEDICINA. UNIVERSIDAD DE VALPARAÍSO. CHILE.
[6]ESCUELA DE MEDICINA. UNIVERSIDAD ANDRÉS BELLO. VIÑA DEL MAR. CHILE.

Background and aims. HIV patients are at risk of acquiring HBV infection, therefore active immunization against HBV is mandatory. Scarce evidence is available about most appropriate scheme of HBV vaccination to achieve positive serological response among those who have not responded to initial vaccination. Our purpose is to determine the effectiveness of standard dose immunization schedule compared to an intensified high-dose one.
Material and methods. Randomized controlled trial, double blinded. Primary outcome was serologic response, 4-8 weeks after exposure, defined as anti-HBs titres > 10 UI/mL. Experimental arm: High dose: Patients received three doses of 40 mcg each of recombinant hepatitis B vaccine, administered at 0-1-2 months. Active comparator: Standard Dose, considering three doses of 20mcg, at 0-1-2 months. Main inclusion criteria: Adults infected with HIV with failed previous HBV vaccination. Interim analysis comparing serological response to HBV vaccination in the two arms. ClinicalTrials.gov Identifier: NCT02003703.
Results. From 130 patients considered for the study, results are available in 50. Twenty-seven patients were allocated to standard dose and 23 to high dose vaccination scheme. Baseline characteristics showed 76% male gender, mean age 48.9 years. Mean CD4 count 425 cell/mm3, mean CD4/CD8 ratio 0.54 and 90% undetectable HIV viral load. 98% using HAART at the time of randomization. No differences in baseline characteristics were observed between groups. Younger age was the only variable associated to positive seroconversion in overall results (46.7 *vs.* 52.9, p = 0.047). Serological response in the standard dose arm were 55.5% (CI95% 35.3-74.5) and 78% (CI95% 56.2-92.5) in the high dose group (p = 0.091). Mean anti-HBs titres were 332.3 UI/mL in the standard dose group and 554.5 UI/mL in the high dose group (p = 0.071). 72% of patients in the high dose group had anti-HBs titres > 100 UI/mL, compared to 47% in the standard dose group (p = 0.135).
Conclusion. In interim analysis, high dose arm showed a tendency to better serological response compared to standard dose arm. Results needs to be confirmed once calculated sample size is obtained. An intensified scheme of HBV vaccination could be effective in achieving seroconversion in HIV patients.

04
TREATMENT WITH OMBITASVIR/PARITAPREVIR/R PLUS DASABUVIR WITH RIBAVIRIN IS NOT ASSOCIATED WITH ADVERSE CHANGES IN RENAL FUNCTION: AN ANALYSIS OF 4 PHASE 2/3 TRIALS

JACOBSON I.M.,[1] POCKROS P.J.,[2] SULKOWSKI M.S.,[3] BERNSTEIN D.E.,[4] KOWDLEY K.V.,[5] BOURLIÈRE M.,[6] WANG D.,[7] MENON R.,[7] ABUNIMEH M.,[7] RENJIFO B.,[7] REINDEL R.,[7] COHEN D.E.,[7] MARTIN P.[8]
[1]ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI, NEW YORK, NY, USA.
[2]DIVISION OF GASTROENTEROLOGY/HEPATOLOGY, SCRIPPS CLINIC, LA JOLLA, CA, USA.
[3]VIRAL HEPATITIS CENTER, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MD, USA.
[4] DIVISION OF GASTROENTEROLOGY, NORTH SHORE-LIJ HOFSTRA SCHOOL OF MEDICINE, MANHASSET, NY, USA.
[5]SWEDISH MEDICAL CENTER, SEATTLE, WASHINGTON.
[6]HÔPITAL SAINT JOSEPH, MARSEILLES, FRANCE.
[7]ABBVIE INC., NORTH CHICAGO, IL, USA.
[8]DIVISION OF HEPATOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF MIAMI, MIAMI, FL, USA.

Introduction. HCV and HIV infection are associated with renal disease. Worsening renal function has been reported with use of DAAs. We analyzed data from four phase 2/3 trials of the 3-DAA (3D) regimen of ombitasvir, paritaprevir (boosted with ritonavir [r] and dasabuvir, with ribavirin (RBV) among patients with HCV GT1 infection or patients co-infected with HIV and HCV GT1. 3D does not undergo significant excretion through the kidney.
Material and methods. *Post-hoc* analysis. Baseline (BL) and end of treatment (EOT) serum creatinine levels and MDRD estimated glomerular filtration rate (eGFR) in trials of 3D + RBV in non-cirrhotic naive (SAPPHIRE-I) or experience (SAPPHIRE-II), cirrhotic patients (TURQUOISE-II) and HIV/HCV co-infected patients trials (TURQUOISE-I). Changes in renal function compared at BL and over time.
Results. BL eGFR was lower in HIV/HCV co-infected pts (80.3-81.7 mL/min/1.73 m^2) *vs.* HCV mono-infected pts receiving 3D + RBV or placebo (88.2-91.2 mL/min/1.73 m^2). NS mean change from BL to EOT observed in 3D + RBV *vs.* placebo (-0.5 *vs.* +0.1, p = 0.798 [SAPPHIRE-I and –II]), or 12 *vs.* 24 weeks of 3D + RBV for cirrhotic (-3.3 *vs.* -1.6, p = 0.356 [TURQUOISE-II]) or HCV/HIV co-infected (+ 0.1 *vs.* -0.1, p = 0.970 [TURQUOISE-I]). No differences in changes in serum creatinine levels over time between groups. A pooled analysis of all HCV mono-infected patients on 3D + RBV indicated that patients with BL eGFR ≤ 60 mL/min/1.73 m^2 or 60 - ≤ 90 mL/min/1.73 m^2 had mean increases in eGFR from baseline to treatment week 12 (+6.0 and +1.3) greater than in patients with a BL eGFR > 90 mL/min/1.73 m^2 (-5.6; P = 0.009, and 0.011, respectively).
Conclusion. Treatment with 3D + RBV was not associated with deterioration in renal function for either 12- or 24-week 3D + RBV in HCV mono- and HIV/HCV co-infected patients and increases in eGFR were observed among HCV mono-infected subjects with baseline eGFR < 90 mL/min. Baseline eGFR was slightly lower in HCV/HIV co-infected patients than in HCV mono-infected patients.
Acknowledgements. AbbVie sponsored the studies, contributed to their designs, participated in the collection, analysis, and interpretation of the data, and in the writing, reviewing, and approval of the publication. Medical writing support was provided by Sian Deeves of Medical Expressions, funded by AbbVie.

05
URINARY NGAL BIOMARKER PREDICTS NON RESPONSE TO THERAPY WITH ALBUMIN AND TERLIPRESSIN IN PATIENTS WITH HEPATORENAL SYNDROME

XIMENES R.,[1] HELOU C.,[2,3] BARBEIRO D.,[4] SOUZA H.,[4] MIGITA B.,[1] D'ALBUQUERQUE L.,[1] CARRILHO F.,[1] FARIAS A.[1]
[1]GASTROENTEROLOGY DEPARTMENT,
[2]NEPHROLOGY DEPARTMENT,
[3]LIM 12,
[4]EMERGENCY DEPARTMENT, UNIVERSITY OF SAO PAULO SCHOOL OF MEDICINE, SAO PAULO - SP, BRAZIL.

Introduction. The response rate to the standard treatment of hepatorenal syndrome (HRS) with vasoconstrictors and albumin infusion is 50% and side effects are severe in up to 10% of patients. Current clinical and laboratorial predictors of response have limited accuracy, leading to the administration of ineffective treatment and substantial costs. Urinary neutrophil gelatinase-associated lipocalin (uNGAL) is an early appearing biomarker of renal tubular injury.
Aim. Evaluate the utility of uNGAL as a predictor of non-response to albumin and terlipressin treatment in patients with HRS.
Material and methods. A prospective study was conducted at a tertiary care unit between June 2013 and November 2015. Inclusion criteria: a) Cirrhosis; b) Age > 18 years; c) HRS diagnosis according to International Club of Ascites criteria; d) Informed consent. Exclusion criteria: a) Severe systemic comorbidities; b) Shock; c) Chronic kidney disease; d) Intrinsic nephropathy; e) Nephrotoxic drug use; f) Previous dialysis; g) Liver transplantation recipient. uNGAL, serum catecholamines and renin plasmatic activity were determined in the first day of treatment. Patients received standard treatment with albumin and terlipressin for up to 14 days.
Results. Forty-nine patients (75% male, median age 59 years, 41% alcoholic cirrhosis, 73.5% Child C) were included, of which 24 (49%) did not respond to treatment. Median uNGAL levels were 728.8 μg/L in non-responders, and 182.9 μg/L in responders ($p = 0.020$). uNGAL had an AUC of 0.69 to predict non response to combined treatment, with the optimal cutoff value of 214.4 μg/L. With this cutoff, sensitivity was 0.83, specificity 0.56, positive predictive value 0.65 and negative predictive value 0.78. Other variables associated with non-response were albumin, INR, MELD and fractional excretion of urea ($p < 0.05$).
Conclusion. uNGAL is a useful predictor of unresponsiveness to combined treatment with albumin and terlipressin in patients who fulfill HRS diagnosis criteria.

06
LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA: RESULTS FROM A MULTICENTER COHORT FROM LATIN AMERICA

PIÑERO F.,[1] COSTA P.,[2] DE ATAIDE E.C.,[3] HOYOS DUQUE S.,[4] MARCIANO S.,[5] ANDERS M.,[6] VARÓN A.,[7] ZEREGA A.,[8] PONIACHIK P.,[9] SOZA A.,[10] PADILLA MACHACA M.,[11] MENÉNDEZ J.M.,[12] ZAPATA R.,[13,14] VILATOBA M.,[15] MUÑOZ L.,[16] MARASCHIO M.,[17] PODESTÁ L.G.,[1] MCCORMACK L.,[6] GADANO A.,[5] FATIMA BOIN I.S.F.,[3] HUYGENS J. PARENTE GARCÍA,[2] SILVA M.[1]
[1]HOSPITAL UNIVERSITARIO AUSTRAL, ARGENTINA.
[2]HOSPITAL FEDERAL UNIVERSITY OF CAERÁ, BRAZIL.
[3]HOSPITAL DE CLINICAS, STATE UNIVERSITY OF CAMPINAS, BRAZIL.
[4]HOSPITAL PABLO TOBÓN URIBE AND GASTROENTEROLOGY UNIVERSIDAD DE ANTIOQUÍA, MEDELLÍN, COLOMBIA.
[5]HOSPITAL ITALIANO FROM BUENOS AIRES, ARGENTINA.
[6]HOSPITAL ALEMÁN, ARGENTINA.
[7]FUNDACIÓN CARDIOINFANTIL, INSTITUTO DE CARDIOLOGÍA, BOGOTÁ, COLOMBIA.
[8]SANATORIO ALLENDE FROM CÓRDOBA, ARGENTINA.
[9]HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE, CHILE.
[10]HOSPITAL UNIVERSIDAD CATÓLICA DE CHILE, CHILE.
[11]HOSPITAL GUILLERMO ALMENARA, PERU.
[12]HOSPITAL MILITAR-CLÍNICAS, URUGUAY.
[13]CLÍNICA ALEMANA DE SANTIAGO, FACULTAD DE MEDICINA, UNIVERSIDAD DEL DESARROLLO, CHILE.
[14]HOSPITAL DEL SALVADOR, FACULTAD DE MEDICINA, UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.
[15]INSTITUTO DE CIENCIAS MÉDICAS, MEXICO.
[16]HOSPITAL UNIVERSITARIO DE MONTERREY, MEXICO.
[17]HOSPITAL PRIVADO FROM CÓRDOBA, ARGENTINA.

Background and aims. Limited data has been reported related to liver transplantation (LT) for hepatocellular carcinoma (HCC) in Latin America.
Aim. To describe results and recurrence rates of LT for HCC from a Latin-American cohort.
Material and methods. Consecutively transplanted adult patients with HCC in 17 LT centers (2005-2011) were included. Cox regression multivariate models for pre LT and explant variables were assessed. Kaplan Meier survival curves (log-rank test).
Results. From 2761 transplanted patients, 527 had HCC (17% incidental HCC). Contribution per country was as follows: 42% Brazil, 26% Argentina, 15% Colombia, 10% Chile, 3% Peru, and 2% each from Mexico and Uruguay. Study population: age 57 ± 9 years, 82% males, 33% hepatitis C, median waiting list time 2 months, 59% with MELD supplementary points. At listing, 81%, 91% and 81% of the patients were within Milan, UCSF and AFP model ≤ 2, respectively. Five-year recurrence and survival rates were 13% and 64%; post-LT mortality rate of 11% (HCC related and non-related deaths of 36% and 64%, respectively). Independent factors related to 5-year recurrence were: 1) Pre-LT model: AFP >2 points HR 2.4 ($P = 0.004$) and UCSF criteria HR 0.4 ($P = 0.03$); 2) Explant model: Up-to 7 criteria HR 0.4 ($P = 0.02$), microvascular invasion HR 4.0 ($P = 0.0001$) and poor differentiation HR 1.8 ($P = 0.03$).
Conclusions. Most Latin American centers transplanted within Milan criteria. However, the AFP model could be prospectively implemented. Although survival rates were similar when compared to European and US populations, a high number of non-HCC related deaths were observed.

B. VIRAL HEPATITIS + DILI

01
GENOTYPING OF HBV AND TRACKING OF RESISTANCE MUTATIONS IN TREATMENT-NAIVE PATIENTS WITH CHRONIC HEPATITIS B IN THE NORTHEASTERN AND NORTH REGIONS OF BRAZIL

PACHECO S.R.,[1] SANTOS M.I.M.A.,[1] STOCKER A.,[2] ZARIFE M.A.S.,[3] SCHINONI M.I.,[2] PARANÁ R.,[2] REIS M.G.,[1] SILVA L.K.[1]
[1]CENTRO DE PESQUISA GONÇALO MONIZ- FUNDAÇÃO OSWALDO CRUZ - LABORATÓRIO DE PATOLOGIA E BIOLOGIA MOLECULAR, SALVADOR, BAHIA-BRAZIL.
[2]UNIVERSIDADE FEDERAL DA BAHIA, SALVADOR, BAHIA-BRAZIL.
[3]LABORATÓRIO CENTRAL DE SAÚDE PÚBLICA DO ESTADO DA BAHIA- LACEN, SALVADOR, BAHIA-BRAZIL.

Introduction. Resistance mutations analogues to nucleos(t)ides have been described in naïve patients treated for chronic hepatitis B, with clinical implications.
Aim. The aim of this study is to investigate resistance mutations of primary and secondary and genotypes circulating in

naive patients to chronic hepatitis B (CHB), in the Northern and Northeastern regions of Brazil.
Material and methods. HBV DNA samples isolated from 189 patients (105) Northern and (84) Northeastern, were sequenced and the RT region subjected to mutational analysis.
Results. We conducted a study of resistance mutations and genotypic characterization naive patients chronically infected with HBV. Only 5 treatment-naive patients of the Northeastern region (n = 84) had mutations RT gene P at positions that may be associated with viral resistance, with a rate of 6 %. The mutations were rtA194T, rtL180M + M204V, rtS202I, rtM204I and rtA181S. No patient had the resistance mutation in the Northern region. In the gene S region, the frequency of vaccine escape mutations were in the Northeast 2.4% region and the Northern region 8.6%.
Conclusion. This information before the start of treatment may contribute to clinical decision making, reducing treatment failure and the risk of progression to cirrhosis and hepatocellular carcinoma for CHB.

02
CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF A PEDIATRIC POPULATION WITH HEPATITIS DELTA VIRUS INFECTION IN A ENDEMIC AREA, IN BRAZIL

VASCONCELOS M.,[1,3] DE OLIVEIRA L.,[2] BORZACOV L.,[3] DE CASTRO SILVA E.,[3] VILLALOBOS SALCEDO J.,[3] CÁSSIA MENDES-CORRÊA M.[1]
[1]UNIVERSITY OF SÃO PAULO MEDICAL SCHOOL, SÃO PAULO, BRAZIL.
[2]APARICIO CARVALHO INTEGRATED COLLEGE, PORTO VELHO, BRAZIL.
[3]CENTER FOR RESEARCH IN TROPICAL MEDICINE IN RONDÔNIA, PORTO VELHO, BRAZIL.

Introduction. Hepatitis Delta virus (HDV) is a defective RNA virus that requires hepatitis B virus (HBV) to complete its life cycle. Hepatitis Delta is an important cause of morbidity and mortality in endemic areas for this infection. Nevertheless, there is few data regarding this infection among the pediatric population.
Aim. Analyze the clinical and demographic characteristics of patients ≤ 18 years-old (at the time of enrollment) at a Viral Hepatitis Outpatient Clinic from an endemic area for this infection.
Material and methods. A retrospective analyzes of all patients referred for consultation at the Viral Hepatitis Outpatient Clinic at the State of Rondônia, from 1993 to May 2015, was developed. Patients aged ≤ 18 years with positive serology for HDV, were included and a descriptive analysis of clinical and demographic characteristics of this population was performed.
Results. Among 208 patients with hepatitis delta serologic diagnosis at the time of registration, 22 (10.5%) were aged ≤ 18 years, 59% male, 10 Amerindians (45.4%). The most important epidemiological aspect was the history of family members infected either by HBV (59,1%) or HBV/HDV (27.3%). Among 22 patients HDV infected patients, 7 (31.8%) had signs of liver cirrhosis and portal hypertension (clinical, imaging, or liver biopsy). Out of the 22 patients, 2 were hospitalized at diagnosis, dying due to clinical complications of liver disease.
Conclusion. In the population of patients younger than 18 years: 1- delta hepatitis was associated with significant morbidity and mortality 2- In this population, about 32% of patients had signs and symptoms of advanced liver disease and its complications.

03
RE-EVALUATION OF SEROPREVALENCE OF HEPATITIS E VIRUS IN AUTOIMMUNE HEPATITIS

HURTADO C., MAC-VICAR M., COVARRUBIAS N., MIRANDA J., VENEGAS M., PONIACHIK J., BRAHM J.
GASTROENTEROLOGY SECTION, DEPARTMENT OF INTERNAL MEDICINE, CLINICAL HOSPITAL UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.

Introduction. In 2002, we communicated a prevalence of IgG antibodies to hepatitis E virus (Anti-HEV) of 36% in patients with autoimmune hepatitis (AIH), significantly higher than in blood donors (BD) 4%, which could indicate that HEV had a potential pathogenic role. In 2013, with the development of new and better diagnostic kits, the prevalence of Anti-HEV in BD was reevaluated, being 30.2%.
Aim. To re-evaluate seroprevalence of Anti-HEV and the presence of hepatitis E virus antigen (HEV-Ag) in patients with AIH.
Material and methods. 45 patients with clinical, serological and histological characteristics compatible of AIH were included, mean age 56.3 ± 16 years, 37 (82%) women. Anti-HEV and HEV-Ag were measured in serum by a two commercial enzyme-linked immunosorbent assay, ELISA, with AccuDiag™ HEV IgG (USA) and kit Wantai HEV Ag, Beijing (China), respectively. We considered as control group the samples of 186 blood donors (BD) studied in 2013. The statistical analysis used was chi-square test. This study was approved by ethics committee, and the patients signed informed consent to participate.
Results. 17 of 45 cases (38%) with AIH were positive for Anti-HEV. No significant differences were found compared to control group (30.2%) or the results found in the first study in 2002. HEV-Ag was not detected in any of patients.
Conclusions. The group of patients with AIH had a high relative prevalence of Anti-HEV, which was higher but not significantly different to that found in control group recently evaluated. No patient with AIH showed active presence of HEV, measured by HEV-Ag.

04
THE PREVALENCE OF HEPATITIS E VIRUS AMONG GROUPS AT HIGH A LOW RISK IS SIMILAR IN THE MEXICAN POPULATION

AGUILAR-OLIVOS N.E.,[1] TRUEBA-GÓMEZ R.,[2] ROSENFELD-MANN F.,[2] ROQUE-ÁLVAREZ E.,[1] NOFFAL-NUÑO V.M.,[1] BAPTISTA-GONZÁLEZ H.,[2] URIBE M.,[1] MÉNDEZ-SÁNCHEZ N.[1]
[1]LIVER RESEARCH UNIT. MÉDICA SUR CLINIC & FOUNDATION. MEXICO CITY. MEXICO.
[2]HEMATOLOGÍA PERINATAL. INSTITUTO NACIONAL DE PERINATOLOGÍA. MEXICO.

Introduction. Several studies have reported greater prevalence of hepatitis E virus (HEV) among pregnancy women and, hepatitis C virus (HCV) or hepatitis B virus (HBV) infection. Mexico is considered an endemic area for HEV. However, this status has been stablished on small serological studies during outbreaks. Therefore, it is required to re-evaluate the prevalence of HEV in the Mexican population.
Objetives. The aim of this study was to compare the HEV seroprevalence among high-risk and average- risk groups in the Mexican population.
Material and methods. We evaluated patients with HCV or HBV, pregnancy women and dentist as high-risk group. Blood donors were considered as the average-risk group. We compared the results with a group with suspected HEV infection. Clinical symptoms of suspected HEV infection were diarrhea, jaundice, fever, pain and hepatomegaly without evidence of

HAV, HCV or HBV infection. We determined serological IgG antibodies against HEV recombinant antigens by ELISA method in all patients. Local ethics committee approved the protocol and, all patients were asked for written consent. The prevalence of HEV in each group was obtained.

Results. We did not find any case of positive HEV IgG in the blood donors considered as average-risk group. Between the 88 patients with reactivity to HBV surface antigen (n = 9) or antibodies against HCV (n = 79) we found a HEV prevalence of 1.1%. Prevalence values of HEV in the other high-risk groups were similar between them (Table 1).

Discussion and conclussion. In this study we found that the prevalence of HEV was similar between pregnancy women, HCV or HBV infected patients and dentists. We did not find any evidence of HEV infection in an average group of blood donor. The frequency of HEV IgG detection was higher in patients with symptoms suggesting the infection. We concluded that prevalence of HEV in Mexican population, even between high-risk groups seem be lower than the previously reported.

Table 1 (04). Prevalence of HEV by group of subjects.

Group	Total (n)	Positive HEV IgG (n)	Prevalence (%)
Average-risk	110	0	-
High risk			
HCV or HBV infection	88	1	1.1
Dentists	159	3	1.9
Pregnancy	127	1	0.8
Suspected HEV infection	94	7	7.4

HCV: hepatitis C virus. HBV: hepatitis B virus. HEV: hepatitis E virus. IgG: immunoglobulin G.

05
FREQUENCY OF THE HEPATITIS C AND HTLV IN THE BABY BOOMER POPULATION IN BAHIA-BRAZIL: PRELIMINARY RESULTS

BASTOS F.A.,[1] SOUZA B.S.,[1] SIMÕES J.M.,[2,4] SCHAER R.E.,[2,3,4] CAMPOS M.S.,[1,4] TRINDADE S.C.,[2,4] PIMENTEL R.A.,[2] MEYER R.,[2,3,8] PARANÁ R.,[5,6] FREIRE S.M.,[2,3,7,8] SCHINONI M.I.[6,9]

[1]FACULDADE DE MEDICINA DA BAHIA, UNIVERSIDADE FEDERAL DA BAHIA, SALVADOR, BRAZIL. [2]LABORATÓRIO DE IMUNOLOGIA E BIOLOGIA MOLECULAR, INSTITUTO DE CIÊNCIAS DA SAÚDE, UNIVERSIDADE FEDERAL DA BAHIA, SALVADOR, BRAZIL. [3]DEPARTAMENTO DE CIÊNCIAS DE BIOINTERAÇÃO, INSTITUTO DE CIÊNCIAS DA SAÚDE, UNIVERSIDADE FEDERAL DA BAHIA, SALVADOR, BRAZIL. [4]PÓS GRADUAÇÃO EM IMUNOLOGIA, INSTITUTO DE CIÊNCIAS DA SAÚDE, UNIVERSIDADE FEDERAL DA BAHIA, SALVADOR, BRAZIL. [5]DEPARTAMENTO DE MEDICINA E SUPORTE DIAGNÓSTICO, UNIVERSIDADE FEDERAL DA BAHIA, SALVADOR, BRAZIL. [6]SERVIÇO DE GASTROHEPATOLOGIA, HOSPITAL UNIVERSITÁRIO PROFESSOR EDGAR SANTOS, SALVADOR, BRAZIL. [7]CURSO DE ODONTOLOGIA, ESCOLA BAHIANA DE MEDICINA E SAÚDE PÚBLICA, SALVADOR, BRAZIL. [8]MEMBRO DO INCT-DT/CNPQ/MCT. [9]DEPARTAMENTO DE BIOFUNÇÃO, INSTITUTO DE CIÊNCIAS DA SAÚDE, UNIVERSIDADE FEDERAL DA BAHIA, SALVADOR, BRAZIL.

Introduction. The hepatitis C prevalence is 1.7% in Bahia State and HTLV prevalence is 1.5% in Salvador, in previous studies of general population. The CDC announced higher hepatitis C prevalence in baby boomer generation. There were no found data with these informations from Brazilian population.

Objectives. To study the frequency of infection and coinfection VHC and HTLV infections in baby boomer in Bahia.

Material and methods. Cross-sectional study. The randomly patients statewide at Clinical Laboratory answered to a socio-cultural questionnaire. They were tested for hepatitis C with Alere quick test and they were tested for HTLV with chemiluminescence test. Those with serum reactivity were taken to the medical specialist for infectious disease clinical care volunteer.

Results. 650 participants. The majority were women (2:1). Hepatitis C frequency was 3.7%, 79% belongs to the baby boomer. 45.8% referred had used illicit drugs: cocaine 33.3%, crack 25%, heroin 4%. The 27% of those who used some kind of illicit drugs had hepatitis C (χ^2 = 65.754 Pearson), when we consider those who injected drugs the prevalence of hepatitis C was 67% (χ^2 Pearson = 136.346). The HTLV frequency was 1.7%. 18.2% had used illicit drugs 9%, crack 9%. 81.2% had used glass syringe. 54.5% had shared personal items. The most of patients (69.1%) didn't know about hepatitis and HTLV infection. Coinfection (HCV-HTLV) was 0.3%.

Conclusion. The frequency of HTLV agrees with other published in the state. The hepatitis C infection was highest frequency than national previous statistics. The frequency of infection by hepatitis was largest among the baby boom population and these state of use of illicit drugs was high. More public medical attention need to be offered to these population.

06
A COMPARATIVE ANALYSIS OF CLINICAL PRESENTATION AND OUTCOME IN NONSTEROIDAL ANTI-INFLAMMATORY-INDUCED LIVER INJURY CASES IN THE SPANISH AND LATINAMERICAN DILI REGISTRIES

DÍAZ-JIMENEZ P,[1] ZOUBEK M.E.,[1] GONZALEZ-JIMENEZ G.,[1] MEDINA-CÁLIZ I.,[1] ROBLES-DÍAZ M.,[1] BESSONE F.,[2] HERNÁNDEZ N.,[3] ARRESE M.,[4] PARANÁ R.,[5] SHINONI M.I.,[5] NUNES V.,[5] GARASSINI M.,[6] ORTEGA-ALONSO A.,[1] GARCÍA-CORTES M.,[1] GARCÍA-MUÑOZ B.,[1] CABELLO M.R.,[1] SLIM M.,[1] SANABRIA-CABRERA J.A.,[1] SANJUAN-JIMENEZ R.,[1] FERNANDEZ M.C.,[7] ROMERO-GÓMEZ M.,[8] MONTANE E.,[9] HALLAL H.,[10] LUCENA M.I.,[1] ANDRADE R.J.[1]

[1]UGC APARATO DIGESTIVO Y SERVICIO DE FARMACOLOGÍA CLÍNICA, INSTITUTO DE INVESTIGACIÓN BIOMÉDICA DE MÁLAGA (IBIMA), HOSPITAL UNIVERSITARIO VIRGEN DE LA VICTORIA, UNIVERSIDAD DE MÁLAGA, CIBEREHD, MÁLAGA, SPAIN. [2]HOSPITAL PROVINCIAL DEL CENTENARIO, ROSARIO, ARGENTINA. [3]HOSPITAL DE CLÍNICAS, MONTEVIDEO, URUGUAY. [4]PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE, SANTIAGO DE CHILE, CHILE. [5]HOSPITAL UNIVERSITARIO PROF. EDGARD SANTOS, UNIVERSIDAD FEDERAL DA SALVADOR DE BAHÍA, SALVADOR DE BAHÍA, BRASIL. [6]HOSPITAL UNIVERSITARIO DE CARACAS, CARACAS, VENEZUELA. [7]HOSPITAL TORRECÁRDENAS, ALMERIA, SPAIN. [8] UCM DIGESTIVE DISEASES, HOSPITAL VIRGEN DEL ROCIO, CIBEREHD, SEVILLE, SPAIN. [9]HOSPITAL GERMANS TRIAS I PUJOL, BADALONA, SPAIN. [10]HOSPITAL MORALES MESEGUER, MURCIA, SPAIN.

Introduction. Nonsteroidal anti-inflammatory drugs (NSAIDs) is the second most frequent therapeutic class associated with drug-induced liver injury (DILI) in the Spanish and Latin-American DILI Registries.

Objective. To analyze differences in NSAID DILI clinical presentation and outcome.

Materiaal and methods. Demographic, clinical and biochemical parameters in single causative NSAID cases included in the Spanish and Latin-American DILI Registries were analyzed.

Results. 91 (10.7%, 91/852) cases from both registries were attributed to NSAIDs, with 25% caused by ibuprofen, 25% diclofenac, 19% nimesulide and 31% others (piroxicam, naproxen, ketoprofen). Females predominated in nimesulide cases

(88%) compared with diclofenac (48%), ibuprofen (52%) and others (46%) (p = 0.03). Positive autoantibody titers were detected in diclofenac, ibuprofen and nimesulide cases (30%, 26%, 29%, respectively) compared with 25% in others. Hepatocellular damage predominated in all groups: 87% (diclofenac), 65% (ibuprofen), 65% (nimesulide) and 57% (others). Total bilirubin mean values were significantly higher in nimesulide cases (14 mg/dL) compared with ibuprofen (4.9 mg/dL), diclofenac (4.1 mg/dL) and others (5.8 mg/dL) (p = 0.001). Similarly, ALP mean values were significantly different between the groups with nimesulide (2.5 x ULN) and ibuprofen (2.5 x ULN) case presenting higher ALP than diclofenac (1.7 x ULN) and others (2.1 x ULN) (p = 0.047). Severity differed significantly between groups, with 35% fatal/severe nimesulide cases, 14% fatal/severe ibuprofen cases, 11% fatal/severe in others and neither fatal nor severe diclofenac cases (p = 0.01).
Conclusions. NSAID-induced liver injury offers a wide range of clinical phenotypes and severity. Nimesulide showed highest severity among NSAID cases. Ibuprofen-induced liver injury was most prevalent with a hepatotoxicity potential that could lead to acute liver failure.
Funding: AEMPS, FEDER:PI12-00620, AC-0073-2013, CIBERehd-ISCIII.

07
DRUG-INDUCED AUTOIMMUNE HEPATITIS, IDIOPATHIC AUTOIMMUNE HEPATITIS AND DILI WITH AUTOANTIBODIES: DIFFERENCES AND SIMILARITIES

ORTEGA-ALONSO A.,[1] CASTIELLA A.,[2] ROBLES-DIAZ M.,[1] MEDINA-CALIZ I.,[1] ZAPATA E.M.,[2] OTAZUA P.,[3] BESSONE F.,[4] HERNÁNDEZ N.,[5] ARRESE M.,[6] GIRALA M.,[7] STEPHENS C.,[1] SANABRIA-CABRERA J.A.,[1] GONZALEZ-JIMENEZ A.,[1] GARCIA-MUÑOZ B.,[1] GARCIA-CORTES M.,[1] BLANCO S.,[8] PRIETO M.,[9] CONDE I.,[9] FERNANDEZ M.C.,[10] HALLAL H.,[11] PRIMO J.,[12] MORENO-PLANAS J.M.,[13] LUCENA M.I.,[1] ANDRADE R.J.[1]
[1]UGC APARATO DIGESTIVO Y SERVICIO DE FARMACOLOGÍA CLÍNICA, INSTITUTO DE INVESTIGACIÓN BIOMÉDICA DE MÁLAGA (IBIMA), HOSPITAL UNIVERSITARIO VIRGEN DE LA VICTORIA, UNIVERSIDAD DE MÁLAGA, CIBEREHD, MÁLAGA, SPAIN.
[2]HOSPITAL DE MENDARO, GIPUZKOA, SPAIN.
[3]HOSPITAL DE MONDRAGÓN, GIPUZKOA, SPAIN.
[4]HOSPITAL PROVINCIAL DEL CENTENARIO, ROSARIO, ARGENTINA.
[5]HOSPITAL DE CLÍNICAS, CLÍNICA DE GASTROENTEROLOGÍA, MONTEVIDEO, URUGUAY.
[6]ESCUELA DE MEDICINA, PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE, SANTIAGO DE CHILE, CHILE.
[7]HOSPITAL DE CLÍNICAS, ASUNCIÓN, PARAGUAY.
[8]HOSPITAL UNIVERSITARIO DE BASURTO, BILBAO, SPAIN.
[9]HOSPITAL LA FE, CIBEREHD, VALENCIA, SPAIN.
[10]HOSPITAL TORRECÁRDENAS, ALMERÍA, SPAIN.
[11]HOSPITAL MORALES MESEGUER, MURCIA, SPAIN.
[12]HOSPITAL DE SAGUNTO, VALENCIA, SPAIN.
[13]COMPLEJO HOSPITALARIO UNIVERSITARIO DE ALBACETE, ALBACETE, SPAIN.

Introduction. Drug-induced liver injury (DILI) may be associated with an autoimmune phenotype (DILI-AIH).
Objectives. We aimed to characterize phenotypes, outcomes and culprit drugs in idiopathic autoimmune hepatitis (AIH), DI-AIH and DILI with/without autoantibodies (AAB) in a large cohort of DILI patients.
Material and methods. Demographic variables in 21 of 1013 (2.1%) patients from the Spanish-Latin DILI Registries diagnosed with DI-AIH (detectable ANA/ASMA titres and high gammaglobulin levels) were compared with 51 idiopathic AIH patients and 129 (12.7%) DILI AAB+ and 371 (36.6%) DILI AAB-.
Results. DILI-AIH and AIH patients had similar age and gender distribution, 38% males (mean 58 y) in DILI-AIH. DILI AAB+ patients were older (mean 53 years *vs.* 49, p = 0.025) and female predominated (57% *vs.* 52%, p = 0.306) than DILI AAB- patients. Among drugs triggering DILI-AIH and concomitant drugs in AIH patients, statins (19% *vs.* 12%) and antibiotics (24% *vs.* 2%) featured more frequently in DILI-AIH. Statins were also more frequent in DILI AAB+ than in AAB- (4.6% *vs.* 3.6%). Compared to AIH, DILI-AIH patients were more frequently jaundiced (62% *vs.* 31%) and had higher AST (23 xULN *vs.* 11 xULN, p = 0.001) and ALT values (27 x ULN *vs.* 14 x ULN, p = 0.001) at presentation. DILI-AIH patients required immunosuppressant treatment less often than AIH patients (81% *vs.* 93%), but more frequently than DILI AAB+ (81% *vs.* 24%, p = 0.00). DILI with autoimmune features responded better to treatment than AIH patients (100% *vs.* 92%).
Conclusions. DILI-AIH and DILI AAB+ typically affects older females and require steroid therapy less often than AIH cases, despite exhibiting a more severe phenotype at onset. Statins are likely to unmask DILI-AIH and DILI AAB+ and could be the unidentified trigger in cases of "idiopathic" AIH, suggesting a role for this drug group across the spectrum of drug-induced autoimmune liver disease.
Funding: AEMPS, FEDER: PI12-00620, P10-CTS-6470, PI12/00378, AC-0073-2013. CIBERehd-ISCIII.

08
CHARACTERISTICS OF A GROUP OF PATIENTS WITH IDIOSYNCRATIC DRUG INDUCED LIVER INJURY (DILI) AND IDENTIFICATION OF RISK AND PROTECTIVE FACTORS FOR DEVELOP ACUTE LIVER FAILURE AND DEATH

HIGUERA-DE LA TIJERA F.,[1] SERVÍN-CAAMAÑO A.I.,[2] GÁLVEZ-MARTÍNEZ M.,[1] CÓRDOBA-REYES M.,[1] CAMACHO-AGUILERA J.,[2] CRUZ-ESTRADA A.,[2] PEREZ-HERNANDEZ J.L.[1]
[1]GASTROENTEROLOGY DEPARTMENT, [2]INTERNAL MEDICINE DEPARTMENT, HOSPITAL GENERAL DE MÉXICO, MEXICO CITY, MEXICO.

Background and aims. Idiosyncratic drug induced liver injury (DILI) can lead to liver failure or death. DILI is a diagnosis of exclusion. On the basis of R-value it can be classified into hepatocellular, cholestasis, or mixed types. The hallmark of treatment is withdrawal of the causal agent. No definitive therapy is available. Our aim was to describe the main characteristics of patients diagnosed with DILI, and to identify risk and protective factors for develop acute liver failure (ALF) and death.
Material and methods. We collected data retrospectively from medical records of 69 patients diagnosed with DILI, treated between January 2006 and June 2014 at Hospital General de México. Univariate and multivariate regression models were performed to identify risk and protective factors associated with ALF and death.
Results. The following drugs were identified as causal agent of DILI: Herbal 28 cases (40.6%); quinolones 9 (13%); ceftriaxone, amoxicillin/clavulanate, ketoconazole 6 (8.7%) each one; antituberculosis drugs, carbamazepine 3 (4.3%) each one; diclofenac, oral contraceptives 2 (2.9%) each one; valproic acid, dapsone, tamoxifen 1 (1.4%) each one. The mean age was 38.8 ± 11.3 years; 52 (75.4%) were female; according to R-value 34 (49.3%) had hepatocellular injury, 24 (34.8%) mixed, 11 (15.9%) cholestasis; 27 (39.1%) were obese; ALF occurred in 32 (46.4%) cases, and 10 (14.5%) died; 26 (37.7%) patients were treated with metadoxine 500 mg b.i.d. or t.i.d., median duration of therapy 35 (range 15-60) days. Risk factors for develop ALF were obesity (66.7% *vs.* 33.3%, P = 0.01; OR 4.0, 95%CI = 1.4-11.1); hepatocellular injury (61.8% *vs.* 31.4%,

Table 1 (08). Comparison between liver function tests of patients with drug induced liver injury who received therapy with metadoxine and those who did not receive it.

LFT	CM, n = 43	MTD, n = 26	P	CM, n = 40	MTD, n = 24	P	CM, n = 35	MTD, n = 24	P
TB	16.1 (13.3-19.0)	17.7 (14.4-22.6)	0.2	10.2 (8.2-13.8)	3.6 (2.3-7.0)	< 0.0001	1.6 (1.1-3.1)	1.0 (0.9-1.2)	0.001
ALT	398 (218-718)	226 (147-540)	0.1	175 (67-312)	86 (51-132)	0.01	60 (41-82)	41 (40-53)	0.005
AST	326 (192-318)	179 (123-445)	0.07	123 (45-245)	56 (38-114)	0.02	40 (28-56)	31 (23-35)	0.05
AP	254 (192-318)	215 (147-312)	0.4	122 (67-174)	125 (110-242)	0.1	56 (35-115)	56 (44-98)	0.9
GGT	198 (131-233)	181 (121-276)	0.6	111 (65-156)	124 (86-191)	0.4	50 (35-80)	47 (39-66)	0.8

P = 0.01; OR 3.5, 95%CI = 1.3-9.5); and herbal (64.3% *vs.* 34.1%, P = 0.01; OR 3.4, 95%CI = 1.3-9.5). Risk factors for death were obesity (37% *vs.* 0%, P < 0.0001; OR 51.0, 95%CI = 2.8-918.7); hepatocellular injury (29.4% *vs.* 0%; P = 0.003; OR 30.4, 95%CI = 1.7-543.9); herbal (32.1% *vs.* 2.5%, P = 0.003; OR 13.2, 95%CI = 2.2-79.9); female gender (19.2% *vs.* 0%, P = 0.003; OR 30.4, 95%CI = 1.7-543.9). Metadoxine was protective factor against the development of ALF (30.8% *vs.* 55.8%, P = 0.05; OR 0.3, 95%CI = 0.1-0.9). Those treated with metadoxine showed a faster recovery and normalization of bilirubin and transaminases (Table 1), but there was not difference regard to mortality.

Conclusions. Obesity, herbal, hepatocellular injury are risk factors for ALF, besides them, female gender is a risk factor for death. Metadoxine, a potent antioxidant, which prevents glutathione depletion and has a multifactorial mechanism of action, favors a faster recovery and was identified as a protective agent against ALF.

09
HERBALS AND DIETARY SUPPLEMENTS INDUCED LIVER INJURY: A CAUSE FOR CONCERN

MEDINA-CÁLIZ I.,[1] ROBLES-DÍAZ M.,[1] GARCÍA-CORTÉS M.,[1] STEPHENS C.,[1] GONZÁLEZ-JIMÉNEZ A.,[1] SANABRIA-CABRERA J.,[1] ORTEGA-ALONSO A.,[1] GARCÍA-MUÑOZ B.,[1] SLIM M.,[1] SANJUÁN-JIMÉNEZ R.,[1] BESSONE F.,[2] HERNÁNDEZ N.,[3] SÁNCHEZ A.,[3] CARRERA E.,[4] LIZÁRZABAL M.I.,[5] MENGUAL E.,[5] KERSHENOBICH D.,[6] LOAEZA DEL CASTILLO A.,[6] BRAHM J.R.,[7] PARANÁ R.,[8] SCHINONI M.I.,[8] DÁVALOS M.,[9] MÉNDEZ-SÁNCHEZ N.,[10] JIMÉNEZ-PÉREZ M.,[11] FERNÁNDEZ M.C.,[12] NAVARRO J.M.,[13] MONTANÉ E.,[14] BARRIOCANAL A.M.,[14] PRIETO M.,[15] CONDE I.,[15] CABELLO M.R.,[1] LUCENA M.I.,[1] ANDRADE R.J.[1]

[1]INSTITUTO DE INVESTIGACIÓN BIOMÉDICA DE MÁLAGA (IBIMA), HOSPITAL UNIVERSITARIO VIRGEN DE LA VICTORIA, UNIVERSIDAD DE MÁLAGA, CIBEREHD, MÁLAGA, SPAIN. [2]HOSPITAL PROVINCIAL DEL CENTENARIO, ROSARIO, ARGENTINA. [3]HOSPITAL DE CLÍNICAS, MONTEVIDEO, URUGUAY. [4]HOSPITAL DE ESPECIALIDADES EUGENIO ESPEJO, QUITO, ECUADOR. [5]HOSPITAL UNIVERSITARIO DE MARACAIBO, VENEZUELA. [6]HOSPITAL GENERAL DE MÉXICO. INSTITUTO NACIONAL CIENCIAS MÉDICAS Y NUTRICIÓN "SALVADOR ZUBIRÁN", MÉXICO. [7]HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE, SANTIAGO, CHILE. [8]HOSPITAL UNIVERSITARIO PROF. EDGARD SANTOS, UNIVERSIDAD FEDERAL DA BAHÍA, SALVADOR DE BAHÍA, BRAZIL. [9]HOSPITAL REBAGLIATI, FACULTAD DE MEDICINA, UNIVERSIDAD SAN MARTIN DE PORRES, LIMA, PERÚ. [10]FUNDACIÓN CLÍNICA MÉDICA SUR, CIUDAD DE MÉXICO, MÉXICO. [11]HOSPITAL REGIONAL UNIVERSITARIO DE MÁLAGA, MÁLAGA, SPAIN. [12]HOSPITAL DE TORRECÁRDENAS, ALMERÍA, SPAIN. [13]HOSPITAL COSTA DEL SOL, MÁLAGA, SPAIN. [14]HOSPITAL GERMANS TRIAS I PUJOL, BARCELONA, SPAIN. [15]HOSPITAL LA FE DE VALENCIA, CIBEREHD, VALENCIA; SPAIN.

Background. Heterogeneous regulatory framework of herbals and dietary supplements (HDS), their widespread use and unawareness of health risks, particularly liver injury, are main causes for concern.

Aims. We aim to evaluate clinical phenotype and outcome associated with HDS hepatotoxicity (DILI).

Material and methods. Demographics and clinical-biochemical parameters were compared between HDS and conventional medication DILI cases included in the Spanish and Latin-American DILI registries.

Results. Out of 1025 DILI cases included, 26 were induced by anabolic steroid (AAS) and 44 by herbals and other dietary supplements (HDS). Women (60%) predominated among the Spanish HDS-DILI cases. The HDS-DILI mean age was significantly higher than that of AAS-DILI cases, but lower for conventional drugs (48 *vs.* 33 and 54) (p < 0.001) among the Spanish and similarly the Latin-American cases. The Spanish HDS cases presented higher ALT mean value (39 x ULN) compared to AAS (15 x ULN) and conventional medications (20 x ULN) (p < 0.001) respectively, but lower total bilirubin values than AAS-DILI cases (9 *vs.* 17 x ULN) (p < 0.001). Similar results were found among the Latin-American cases. In total, HDS-DILI patients developed acute liver failure (ALF) more frequently than DILI patients associated with conventional drugs (9% *vs.* 5%) (p = 0.03). No AAS cases developed ALF. Rechallenge was more atélites with HDS than with conventional medication in both registries (14% *vs.* 6%) (p = 0.02).

Conclusions. In comparison to conventional drugs, HDS-DILI is more common in atél women, presenting with hepatocellular injury, higher transaminase values, higher risk of ALF and inadvertent re-exposition. Greater awareness and stricter regulation are required to prevent HDS-related severe adverse effects to the liver.

Funding: Research grants from the Agencia Española del Medicamento and Fondo de Investigación Sanitaria (PI15-01440, AC-0073-2013). Fondo Europeo de Desarrollo Regional (FEDER). CIBERehd is funded by Instituto de Salud Carlos III.

10
THE INFLUENCE OF DRUG PHYSICOCHEMICAL PROPERTIES AND HOST CHARACTERISTICS ON DELAYED ONSET IN DRUG-INDUCED LIVER INJURY

GONZALEZ-JIMENEZ A.,[1] SUZUKI A.,[2] STEPHENS C.,[1] CHEN M.,[3] MEDINA-CALIZ I.,[1] ROBLES DIAZ M.,[1] PRIETO M.,[4] SORIANO G.,[5] MONTANE E.,[6] ALDEA A.,[7] LUCENA M.I.,[1] ANDRADE R.J.[1]

[1]IBIMA. HOSPITAL VIRGEN DE LA VICTORIA, UNIVERSITY OF MÁLAGA, MÁLAGA, SPAIN;(CIBEREHD), MÁLAGA,SPAIN. [2]DEPARTMENT OF MEDICINE, UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES, LITTLE ROCK, AR. [3]DIVISION OF BIOINFORMATICS AND BIOSTATISTICS, NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH, US FOOD AND DRUG ADMINISTRATION, JEFFERSON, AR. [4]HEPATOGASTROENTEROLOGY SERVICE, UNIVERSITY HOSPITAL LA FE, VALENCIA, SPAIN. [5]GASTROENTEROLOGY ATÉLITE, HOSPITAL DE LA SANTA CREU I SANT PAU, UNIVERSITY OF BARCELONA, BARCELONA, SPAIN. [6]CLINICAL PHARMACOLOGY, HOSPITAL GERMANS TRIAS I PUJOL, BADALONA, SPAIN. [7]DEPARTMENT OF CLINICAL PHARMACOLOGY, UNIVERSITY HOSPITAL OF CANARIAS, CANARIAS, SPAIN.

Background. Most patients with drug-induced liver injury (DILI) manifest liver injury while they are still on the drug treatments; however, some manifest after the treatment is

completed (i.e., delayed onset). Mechanism underlying the delayed onset is unknown. We aimed to identify drug properties and host factors which are associated with delayed onset.
Material and methods. 680 Spanish DILI cases were classified into delayed onset (DO) *vs.* No delayed onset (NDO) according to the temporal relationship of the first DILI manifestation to the time of treatment cessation.
Result. Among the 654 cases, 146 cases (22%) manifested DILI 2 to 82 days after treatment cessation (DO), while 508 (77%) developed symptoms during the drug treatment (NDO). Amoxicillin-clavulanate (AC) was responsible for 62% of the DO and 14% of the NDO cases. Excluding the AC cases, DO cases had higher daily dosage (mean: 300 *vs.* 200 mg, p = 0.0143). Regarding host manifestations, eosinophilia was more atélites in DO cases (31% *vs.* 20%, p = 0.0450), while positive autoantibody titers were more common in NDO cases (25% *vs.* 12%, p = 0.0463). NDO cases were more associated with chronic underlying diseases (81% *vs.* 64%, p < 0.0034). In a multivariate analysis, the absence of underlying diseases (OR: 2.7, 95% CI: 1.4-5.0, p = 0.0022) and daily dose (OR: 0.066, 95% CI: 0.009-0.50, p = 0.0104) were found to be independent predictors for DO. In the second part the analyses, we compared 34 drugs responsible for DO and 65 drugs not associated with DO. A significantly higher proportion of the DO drugs were excreted without metabolize compared to the NDO drugs (21% *vs.* 7%, p = 0.0064).
Conclusions. Delayed onset was found to be associated with higher drug dose and less underlying chronic diseases. In addition, DO cases more frequently manifested eosinophilia, but less commonly developed positive autoantibodies. The association of drugs with low hepatic atélitess with DO suggests na additional mechanism outside hepatic metabolism.
Funding: AEMPS,P10-CTS-6470,PI12/00378 PI12-00620,AC-0073-2013,CIBERehd-ISCIII.

C. LIVER TRANSPLANTATION, CIRRHOSIS, AND HEPATOCELLULAR CARCINOMA

01
HEPATOCELLULAR CARCINOMA IN NON-ALCOHOLIC STEATOHEPATITIS (NASH) – HISTOPATHOLOGICAL ASPECTS

BRIZOLLA DE CAMPOS P.,[1] OLIVEIRA C.,[1] KIKUCHI L.,[1] TADEU STEFANO J.,[1] LOPES CHAGAS A.,[1] HERMAN P.,[2] CARNEIRO D'ALBUQUERQUE L.,[2] ALVARES DA SILVA R.,[4] CARRILHO. F.J.,[1] FERREIRA ALVES V.A.[3]
[1]DEPARTMENT OF GASTROENTEROLOGY (LIM-07). [2]DIVISION OF LIVER AND GASTROINTESTINAL TRANSPLANT (LIM-37) AND [3]DEPARTMENT OF PATHOLOGY (LIM-14), UNIVERSITY OF SÃO PAULO SCHOOL OF MEDICINE, SÃO PAULO, BRAZIL, SÃO PAULO, BRAZIL UNIVERSITY OF SÃO PAULO SCHOOL OF MEDICINE, SÃO PAULO, BRAZIL. [4]DIVISION OF GASTROENTEROLOGY, HOSPITAL DE CLINICAS DE PORTO ALEGRE, UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, PORTO ALEGRE, BRAZIL.

Background. Hepatocellular carcinoma (HCC) is the most common primary malignancy of the liver. The raise in incidence has been ascribed to the increase in obesity, diabetes and non-alcoholic fat liver disease (NAFLD).
Aim. The aim of this study is to evaluate the pathological and clinical aspects in patients with HCC secondary to NAFLD.
Material and methods. We evaluated 28 HCC specimens from 18 patients diagnosed with NAFLD undergoing liver resection (10 patients) or liver transplantation (8 patients) from 2005 to 2015. We compared histological features, clinical aspects, imaging findings, demographic and biochemical data, as well as their survival.
Results. We analyzed 11 patients with cirrhosis and 7 patients without cirrhosis, and from them, 28 HCC nodules, 8 (28%) were developed in patients without cirrhosis (NASH staging: F2: 5pts, F3 = 2 pts), while 20 (72%) nodules were developed in patients with cirrhosis (8 F4A x 11 F4B, x 1F4C according Laennec Stage). Ages ranged from 58 to 77 years and 13 patients were male (72%). Thirteen patients (72%) had diabetes mellitus, 13 patients (72%) had arterial hypertension, and 14 patients (77%) had BMI above 25. Only 6 patients (33%) had dyslipidemia. HCC occurred in 7 patients Child A, 4 Child B and in 7 patients without cirrhosis. As the performance status, 16 patients had a good performance status (NA) with Eastern Cooperative Oncology Group (ECOG) = 0. Alpha-fetoprotein level was normal in 12 patients. The dimensions of the HCC nodules ranged from 0.8 cm (single nodule) to 15 cm in diameter and the predominant macroscopic pattern was nodular (93%). The predominant microscopic pattern was trabecular (46%). Major histological features of HCC are depicted at table 1. Of all the patients, 11 evolved to death, 8 cases in patients who underwent resection and 3 cases that underwent liver transplantation. The causes of death were primary non function, infection, acute rejection and palliative care caused by the evolution of HCC.
Conclusion. HCC secondary to NAFLD can arise in patients without cirrhosis with normal level of alpha-fetoprotein. Histological markers of "steato-hepatitic HC" and high architectural and nuclear degrees (g.3) were atélites. The survival rate was low, especially in patients who underwent resection, despite the good performance status.

Table 1 (01). Histological variables x assigned degree in the analysis of 28 samples of HCC.

	0	1	2	3	4
Architectural degree (1-4)	x	7	8	12	1
Nuclear degree (1-4)	x	4	9	13	2
Intratumoral steatosis (0-3)	4	15	5	4	x
Intratumoral balooning (0-2)	1	8	19	x	x
Intratumoral inflammation (0-4)	4	11	9	4	0
Intratumoral fibrosis (0-4)	0	13	8	7	0
Vascular invasion (0-2)	13	4	11	x	x

02
EXERCISE CAPACITY AND SURVIVAL AFTER LIVER TRANSPLANT IN CIRRHOTIC PATIENTS WITH HEPATOPULMONARY SYNDROME

PEREIRA F.J.L., GALANT H. L., GARCIA E., TELLES DA ROSA L.H., DE MELLO BRANDÃO A. B., MARRONI C. A.
GRADUATE PROGRAM IN HEPATOLOGY, FEDERAL UNIVERSITY OF HEALTH SCIENCES OF PORTO ALEGRE – RIO GRANDE DO SUL STATE – BRAZIL.

Introduction. Hepatopulmonary syndrome (HPS) is a complication associated with cirrhosis which may contribute to the worsening of execise capacity and poor survival after liver transplant (LTx).
Aims. Compare survival 2 years after LTx between cirrhotic patients diagnosed with HPS and cirrhotic patients without HPS, and identify atélitess predictors for this outcome.
Material and methods. A prospective cohort of four years, consisting of 178 patients (92 with and 86 without SHP) diagnosed with cirrhosis and potential candidates to LTx. All patients underwent a atélites assessment made by the six-minute

walk test (6MWT), ergometric test and manovacuometry. For the statistical analysis we used the Kolmogorov-Smirnov test, Student's *t* test, the linear association square test, the Kaplan Meier survival curves and Cox regression.

Results. Patients with cirrhosis without HPS diagnosis had higher survival in a period of 2 years after transplantation (p = 0.01). There was a 17% higher survival rate with increasing distance in the 6MWT (HR = 0.83, CI95% = 0.73-0.94, p = 0.003), as well as improved oxygen consumption peak (VO_2peak) increased by 30% survival (HR=0.70 CI95% 0.57-0.82, p = 0.001) and a higher maximum inspiratory pressure (MIP) increased by 15% survival (HR = 0.85 IC95% 0.75-0.92, p = 0,002).

Conclusion. Patients with cirrhosis without HPS diagnosis have a higher survival within 2 years after LTx. The HPS, 6MWT, VO_2peak and MIP were considered atélitess predictors for this outcome.

03
REAL-LIFE ADHERENCE TO BCLC THERAPEUTIC ALGORITHM OF HEPATOCELLULAR CARCINOMA IN A MULTICENTER COHORT FROM ARGENTINA

PIÑERO F.,[1,11,12] MARCIANO S.,[2] FERNÁNDEZ N.,[5] SILVA J.,[10] ZAMBELO Y.,[8] COBOS M.,[4] ZEREGA A.,[9] RIDRUEJO E.,[3] MIGUEZ C.,[6] AMEIGEIRAS B.,[14] D'AMICO C.,[13] GAITE L.,[7] CORONEL M.,[1] BERMÚDEZ C.,[2] ROSALES C.,[10] ROMERO G.,[6] MCCORMACK L.,[4] REGGIARDO V.,[8] COLOMBATO L.,[5] GADANO A.,[2] SILVA M.[1]

[1]HOSPITAL UNIVERSITARIO AUSTRAL, BUENOS AIRES, ARGENTINA.
[2]HOSPITAL ITALIANO FROM BUENOS AIRES, ARGENTINA.
[3]CENTRO DE EDUCACIÓN MÉDICA E INVESTIGACIONES CLÍNICAS NORBERTO QUIRNO (CEMIC), BUENOS AIRES, ARGENTINA.
[4]HOSPITAL ALEMÁN FROM BUENOS AIRES, ARGENTINA.
[5]HOSPITAL BRITÁNICO FROM BUENOS AIRES, ARGENTINA.
[6]HOSPITAL UDAONDO, BUENOS AIRES, ARGENTINA.
[7]HOSPITAL CULLEN FROM SANTA FE, ARGENTINA.
[8]HOSPITAL DEL CENTENARIO, ROSARIO, SANTA FE, ARGENTINA.
[9]HOSPITAL PRIVADO FROM CÓRDOBA, ARGENTINA.
[10]HOSPITAL G RAWSON, SAN JUAN, ARGENTINA.
[11]SANATORIO TRINIDAD SAN ISIDRO. BUENOS AIRES, ARGENTINA.
[12]CLÍNICA PRIVADA SAN FERNANDO. BUENOS AIRES, ARGENTINA.
[13]CENTRO ESPECIALIDADES MÉDICAS AMBULATORIAS (CEMA), MAR DEL PLATA, BUENOS AIRES, ARGENTINA.
[14]HOSPITAL RAMOS MEJÍA, CIUDAD DE BUENOS AIRES, ARGENTINA.

Background & Aims. The Barcelona Clinic Liver Cancer (BCLC) algorithm has been accepted for staging and management of hepatocellular carcinoma (HCC). However, adherence to BCLC in the daily practice is still challenging. We aimed to analyze adherence to BCLC recommendation and its atélites patient survival.

Material and methods. A cohort study was conducted between 2009 and 2016 in 14 different regional hospitals from Argentina including adult patients with newly diagnosed HCC. Study data was registered into a web-based electronic system.

Results. Between 2009 and 2016, 720 consecutive patients were included (non-cirrhotic n = 73). Hepatitis C atél was the main cause of liver disease (37%). Overall, 58% of the cohort was under screening. At diagnosis, BCLC stages were as follows: stage 0 4%, A 43%, B 22%, C 9% and D 22%. Overall analysis of treatments performed according to BCLC recommendation showed that 45% of the patients were first treated according to BCLC, 24% under-treated, 29% over-treated and 2% not treated until last day of follow-up. BCLC adherence increased to 55.3% for atélitess treatments. Corresponding 5-year survival rates were as follows: stage 0 77%, stage A 74%, stage B 62%, stage C 33% and stage D 19%. Significantly lower survival was observed among patients who were not screened (43% *vs.* 70%; HR 3.27, P < 0.0001). Non-transplant centers (n = 8) had lower proportion of patients who were under screening compared to LT centers (31.6% *vs.* 65.7%; P = 0.0001), and less patients diagnosed at early BCLC stages 0-1 (34.2% *vs.* 52.9%; P = 0.0001).

Conclusion. Adherence to BCLC is still needs to be improved, with only half of the patients being treated accordingly. Screening for HCC atélitess a major goal to improve survival.

04
LIVER TRANSPLANTATION IN LATIN AMERICA: ACHIEVEMENTS AND CHALLENGES

NOCETI O.,[1] GADANO A.,[2] RUF A.,[3] D'ALBUQUERQUE C.,[4] PESSOA M.G.,[5] SEDA NETO J.,[6] BRAHM J.,[7] HOYOS S.,[8] CASTRO E.,[9] BENALCÁZAR G.,[10] VILATOBÁ M.,[11] CHAMÁN J.C.,[12] VALVERDE M.,[1] GERONA S.[1]

[1]NATIONAL CENTER FOR LIVER TRANSPLANTATION, MONTEVIDEO, URUGUAY.
[2]LIVER TRANSPLANT CENTER HOSPITAL ITALIANO, BUENOS AIRES, ARGENTINA.
[3]LIVER TRANSPLANT CENTER HOSPITAL BRITÁNICO, BUENOS AIRES, ARGENTINA.
[4]DEPARTMENT OF SURGERY, SCHOOL OF MEDICINE, UNIVERSITY OF NA PAULO, SÃO PAULO, BRAZIL.
[5]DIVISION OF GASTROENTEROLOGY AND HEPATOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF SÃO PAULO, SÃO PAULO, BRAZIL.
[6]LIVER TRANSPLANT CENTER, HOSPITAL SÍRIO-LIBANÉS AND AC. CAMARGO CENTER, SÃO PAULO, BRAZIL.
[7]DEPARTMENT OF MEDICINE, HOSPITAL CLÍNICO UNIVERSITY OF CHILE, SANTIAGO, CHILE.
[8]LIVER TRANSPLANT CENTER HOSPITAL PABLO TOBÓN URIBE, UNIVERSITY OF ANTIOQUIA, MEDELLÍN, COLOMBIA.
[9]LIVER TRANSPLANT CENTER, SAN JOSÉ, COSTA RICA.
[10]LIVER TRANSPLANT CENTER HOSPITAL LUIS VERNAZA, GUAYAQUIL, ECUADOR.
[11]LIVER TRANSPLANT CENTER NATIONAL INSTITUTE OF MEDICAL SCIENCES AND NUTRITION SALVADOR ZUBIRÁN, MEXICO CITY, MEXICO.
[12]LIVER TRANSPLANT CENTER HOSPITAL NACIONAL GUILLERMO ALMENARA IRIGOYEN ESSALUD, LIMA, PERU.

Background. Latin America (LA) is a continent of disparities and the same occurs with liver transplantation (LTx) programs. The lack of continental policies is one of the causes to such heterogeneity. Argentine and Brazil lead by far the number of Tx pmh sustained by regulation and financial resources. On the contrary several centers face the risk of closure due to legal gaps and sustainable economic resources attempting against universal accessibility.

Objective. To review the state of the art of LTx programs in LA to identify the actions required to upgrade centers towards to those of most expertise.

Material and methods. Na e-mail survey was sent to all LTx and ESLD representatives in LA covering different issues. Data of 9 countries were conciliated to publish: Argentine, Brazil, Chile, Colombia, Costa Rica, Equator, Mexico, Peru, Uruguay. Results obtained by Excel® are expressed as mean, range and percentage.

Results. 1-78 LTx centers exist per country; 40% have financial government and 60% public-private funds. 80% count on organ allocation policies and all of them use MELD score for prioritizing. Donation rates are: 0.7-20 pmh. Donor type: up to 10 living related and 90% cadaveric. Waiting list time: 2.6-45 months. MELD at Tx: 15-29. Pediatric programs are working in 80% of the countries. 90% use MELD way exemptions. Generics/originals immunosuppressant drugs use atélites health care system characteristics. Adherence to ESLD guidelines reported: 57 (25-75%); pitfalls are due to resource scarcity.

Conclusion. Different maturity and expertise of the centers was evidenced. Since last review in 2010 no significant grow up was achieved. We state that programs should be exclusively conceived inside the atélite of regional or national reference

centers, supported with sustainable funds; their conception must satisfy country characteristics to ensure universal accessibility, rational organ allocation and quality of the results. Urgency for continental policies is desirable.

05
SUBLINGUAL ADMINISTRATION OF TACROLIMUS IS A FEASIBLE ROUTE AND REQUIRES A LOWER DOSE TO ACHIVE SIMILAR DRUG EXPOSITION IN ADULT LIVER TRANSPLANT RECIPIENTS

SOLARI S., CANCINO C., NORERO B., WOLFF R., VARGAS J.I., SOZA A., ARRESE M., GUERRA J.F., JARUFE N., MARTÍNEZ J.M., BENÍTEZ C.
HOSPITAL CLÍNICO PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE, LIVER TRANSPLANT UNIT, CHILE.

Background and aims. Oral administration of immunosuppressive drugs is not always feasible after liver transplantation specially in immediate post-transplant period. Parenteral administration of tacrolimus (TAC) implies a significantly higher expense of resources. The aim of this study was to evaluate the feasibility of sublingual (SL) administration of TAC and compare drug exposition expressed as AUC on liver recipients to receiving conventional per oral (PO) administration.
Material and methods. In patients on PO administration serum TAC levels were determined at differents time points (0, 1, 2, 4, 6, 8, 12 h). Then patients were switched to SL administration. For this purpose, TAC dose was tapered (starting with 20-30% reduction of PO dose) to obtain a similar trough level that in PO administration. Then TAC levels were determined at same time points. Exposition to TAC (AUC) was estimated and compared for SL and PO administration.
Results. Thirty-two patients were included. There were no differences on trough levels between PO and SL administration (6.76 ± 2.09 *vs.* 6.55 ± 1.93 ng/mL, p = 0.4732). When AUC was evaluated, no differences were found between groups (118.5 ± 36.28 *vs.* 110.3 ± 39.29 ng/mL/h, p = 0.07). The maximum concentration achieved after TAC administration (Cmax) was differences in both groups (18.3 ± 8.89 *vs.* 14.15 ± 6.63 ng/mL, p = 0.0085). The dose required to achieve a similar trough level (and AUC) was higher when TAC was administered PO *vs.* SL route (4.22 ± 2.04 *vs.* 2.61 ± 1.48 mg/d, p < 0.0001), meaning a 38% reduction. There was good correlation between through levels and AUC either in SL and PO administration.
Conclusion. SL administration of tacrolimus is a feasible alternative to oral administration and similar drug exposition can be reached employing the same objective trough levels as in PO administration. SL TAC administration requires lower dose to achieve same drug exposition. Trough levels seems to be na appropriate tool to monitor liver seems on SL TAC administration.

06
MULTICENTRIC STUDY OF LIVER TRANSPLANTATION IN PATIENTS WITH HEPATOCELULLAR CARCINOMA IN BRAZIL

CHAGAS A.,[1,2] FELGA G.,[3] MATTOS A.A.,[4] SILVA R.F.,[5] DE CÁSSIA DA SILVA R.,[5] BRANCO F.,[6] D. ALMEIDA M.,[3] BOIN I.F.,[7] GARCIA J.H.,[8] D'ALBUQUERQUE L.C.,[1,2] CARRILHO F.J.,[1,2] AND THE BRAZILIAN HCC STUDY GROUP[9]
[1]DEPARTMENT OF GASTROENTEROLOGY, UNIVERSITY OF SÃO PAULO SCHOOL OF MEDICINE, SÃO PAULO, BRAZIL.
[2]SÃO PAULO CLINICAS LIVER CANCER GROUP, SÃO PAULO, BRAZIL.
[3]LIVER TRANSPLANT , HOSPITAL ISRAELITA ALBERT EINSTEIN, SÃO PAULO, BRAZIL.
[4]DEPARTMENT OF GASTROENTEROLOGY, FUNDAÇÃO UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE, PORTO ALEGRE, BRAZIL.
[5]SERVIÇO DE GASTROENTEROLOGIA E UNIDADE DE TRANSPLANTE DE FÍGADO, HOSPITAL DE BASE – FUNFARME, FACULDADE DE MEDICINA DE SÃO JOSÉ DO RIO PRETO, SÃO JOSÉ DO RIO PRETO, BRAZIL.
[6]DEPARTMENT OF GASTROENTEROLOGY, SANTA CASA DE MISERICÓRDIA DE PORTO ALEGRE, PORTO ALEGRE, BRAZIL.
[7]DIGESTIVE SURGERY DEPARTMENT, STATE UNIVERSITY OF CAMPINAS, CAMPINAS, BRAZIL.
[8]CENTRO DE TRANSPLANTE DE FÍGADO DO CEARÁ, DEPARTMENT OF SURGERY AND LIVER TRANSPLANTATION, FEDERAL UNIVERSITY OF CEARÁ, FORTALEZA, BRAZIL.
[9]BRAZILIAN HCC STUDY GROUP, BRAZIL.

Introduction. Liver transplantation (LT) is the treatment of choice for patients with cirrhosis and unresectable early hepatocellular carcinoma (HCC).
Aim. To analyze the demographic characteristics, clinical features and outcomes of patients submitted to liver transplantation with HCC in Brazil.
Material and methods. We conducted a multicentric study to evaluate the results of LT in HCC patients. Medical records of 668 HCC transplanted patients, between 2006 and 2014, from 10 transplant centers in Brazil, were retrospectively analyzed. Patient and tumor characteristics, pathologic data and rate of tumor recurrence were collected.
Results. Of the 668 patients, median age was 57y and 81% were male. Etiology of cirrhosis was HCV in 63%. At diagnosis, most patients had uninodular HCC (68.5%), median tumor burden was 30 mm and 86% were within Milan criteria (MC). Pre-transplant HCC treatment was performed in 72% and chemoembolization was used in 80%. In explant tumor was uninodular in 46% and moderately differentiated in 69.5%. Median size was 29 mm and 81% were within MC. Vascular invasion and satellite nodules were observed in 29% and 26% of patients, respectively. Excluding patients who died in the immediate post-transplant period, overall survival was 69% in 5 years. Tumor recurrence occurred in 8%, at a mean time of 16 m. Sites of recurrence were 38% liver, 48% extrahepatic and 14% both hepatic and extrahepatic. Alpha-fetoprotein (AFP), MC at diagnosis, vascular invasion (VI) and satellite nodules (SN) were risk factors for recurrence. Age, etiology, MELD, AFP, CHC outside MC, SN and VI were predictors of poor survival.
Conclusion. HCC recurrence occurred in 8% of patients. Pre-transplant tumor staging, evaluated by Milan Criteria, AFP levels and explant factors, such as vascular invasion and atélites nodules, were associated with increased risk of post-transplant tumor recurrence and worse survival.

07
CONVERSION TO MYCOPHENOLATE MOFETIL MONOTHERAPY IN LIVER RECIPIENTS: CALCINEURIN INHIBITOR LEVELS ARE KEY

NORERO B.,[1] SERRANO C.,[2] SANCHEZ-FUEYO A.,[5] DUARTE I.,[3] TORRES J.,[3] OCQUETAU M.,[4] VARGAS J.I.,[1] BARRERA F.,[1] ARRESE M.,[1] SOZA A.,[1] BENÍTEZ C.[1]
DEPARTAMENTOS DE [1]GASTROENTEROLOGÍA, [2]GASTROENTEROLOGÍA Y NUTRICIÓN PEDIÁTRICA, [3]PATOLOGÍA Y [4]HEMATO-ONCOLOGÍA, ESCUELA DE MEDICINA, PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE.
[5]INSTITUTE OF LIVER STUDIES, MRC CENTRE FOR TRANSPLANTATION, KING'S COLLEGE LONDON, LONDON SE5 9RS, UNITED KINGDOM.

Background and aims. The use of calcineurin inhibitors (CNI) after liver transplantation is associated with post-transplant nephrotoxicity. Conversion to mycophenolate mofetil (MMF) monotherapy improves renal function, but is related

to graft rejection in some recipients. Our aim was to identify variables associated with rejection after conversion to MMF monotherapy.

Material and methods. Conversion was attempted in 40 liver transplant recipients. Clinical variables were determined and peripheral mononuclear blood cells were immunophenotyped during a 12-month follow-up. Conversion was classified as successful (SC) if rejection did not occur during the follow-up.

Results. MMF conversion was successful with 28 patients (70%) and was associated with higher glomerular filtration rates at the end of study. It also correlated with increased time elapsed since transplantation, low baseline CNI levels (Tacrolimus ≤ 6.5 ng/mL or Cyclosporine ≤ 635 ng/mL) and lower frequency of tacrolimus use. The only clinical variable independently related to SC in multivariate analysis was low baseline CNI levels (p = 0.02, OR: 6.93, 95%, CI: 1.3-29.7). Mean baseline fluorescent intensity of FOXP3+ T cells was significantly higher among recipients with SC.

Conclusion. This study suggests that baseline CNI levels can be used to identify recipients with higher probability of SC to MMF monotherapy.

Clinicaltrials.gov identification: NCT01321112.

08
SEVERE HYPONATREMIA IN CIRRHOSIS: BOON OR BANE?

KESAVARAPU K., ROTHSTEIN K., MUNOZ S.
DEPARTMENT OF MEDICINE, DREXEL COLLEGE OF MEDICINE, HAHNEMANN UNIVERSITY HOSPITAL, PHILADELPHIA, PENNSYLVANIA, USA.

Introduction. Severe hyponatremia (LowNa) is increasingly observed in decompensated cirrhotics. The mechanism of low-Na are complex and management is heterogeneous. There is renewed interest in lowNa due to its recent inclusion in liver allocation by incorporation into the MELD score.

Aim. To characterize severe hyponatremia in patients with decompensated cirrhosis and analyze management strategies including mortality, outcomes, and impact on liver transplantation.

Material and methods. We identified 40 cirrhotic patients who developed severe LowNa (defined as erum Na < 125 meq/L) and 41 control cirrhotics without LowNa, matched for bilirubin, creatinine, and INR. We analyzed the diuretic regimens up to 1 week prior to severe LowNa episode, treatment modalities for the hyponatremia, number of days to correction of sodium, and mortality at index admission. The endpoint of hyponatremia correction was set when native MELD was within three points of sodium adjusted MELD (MELD-Na).

Results. Demographics in lowNa patients and control cirrhotics were similar. Serum Na was 122±3.1 mEq/L (113-125) and 134 ± 3.8 (129-147) in lowNa and controls respectively. On the week preceding the lowNa episode, 26/40 patients (65%) and 24/41 (58%) of controls were on diuretics respectively. Within the lowNa group, 6/26 (23%), 5/26 (19%), and 13/26 (50%) were on loop diuretic only, spironolactone only, and combination of spironolactone and loop diuretic combination respectively. However, in the LowNa patients, 9/13 (69%) were on inappropriate dosing (more loop diuretic or 1:1 ratio relative to spironolactone). LowNa was corrected in X% of patients. Multiple treatment modalities were required to correct the LowNa in 55% (22/40) and included water restriction, cessation of diuretics, volume repletion, salt tablets, and vasopressin receptor antagonists (vaptans). Inpatient mortality in LowNa groups was high at 35%. Low Na listed patients were not eligible for liver transplantation for the duration of the severe LowNa episode.

Conclusions. Severe hyponatremia is often related to inadequate diuretic therapy in patients with cirrhotic ascites and require multiple modalities of treatment in most cases. Severe LowNa is associated with high mortality admissions and although MELD-Na increases during LowNa episodes, patients are often placed on hold until severe LowNa is corrected. Our data suggest that further education is necessary on diuretic therapy in advanced cirrhotics.

09
PRELIMINAR REPORT: LIVER TRANSPLANT SURVEY IN LATIN AMERICA AND THE CARIBBEAN

RESTREPO J.C.,[1] ZAPATA R.,[2] HERNÁNDEZ H.,[3] PADILLA M.,[4] GERONA S.,[5] BENALCÁZAR G.,[6] SERPA F.,[6] CARRERA E.,[6] SUÁREZ J.J.[6]
[1]COLOMBIA. [2]CHILE. [3]CUBA. [4]PERU. [5]URUGUAY. [6]ECUADOR.

Introduction. The Latin American Association for the Study of the Liver (LAASL), in the meeting held in Valparaiso-Chile, resolve to create the Permanent Council and appoint a coordinator in charge of all issues regarding liver transplant (LT). The Council's approved work plan included a LT survey. On February 2016, LAASL's Secretary sent this survey, in digital version, to opinion leaders or competent authorities in liver transplant matters, aiming to gather this information from each country.

Materials and methods. The survey encompassed 30 questions, 27 of those questions required answers wit precise and objective information and three were open opinion questions. To the date, only seven countries of Latin America have answered the survey. Among them, five of South America: Colombia, Chile, Peru, Uruguay and Ecuador; one of Central America: Guatemala and one of the Caribbean: Cuba. The preliminary report hereby, presents the compilation and analysis of the information delivered by the representatives of each country.

Results. The number of medical centers that perform LT varies form one in Uruguay to seven in Colombia. The principal centers operate in the capital of each country; however, country such as Colombia, Chile, Peru and Ecuador (until 2014) had other centers in different cities. Guatemala does not have a LT program. The LT programs started in the region started in 1985 in Chile and the most recent one in 2011 in Guayaquil-Ecuador. All of them based on a previous Liver Transplant Law, which to the date, in every case provides for presumed consent, although, permission and consultation is still requested from the donor's relatives, with the exception of Ecuador, where since 2011 such practice is no longer in force. Some LT programs have had temporary suspensions. In Uruguay from 2002 to 2009, in Chile, in one of its centers in 2014, and in Quito-Ecuador the program has been suspended since April 2014. LT programs are financed by the State or social security together with private institutions, except from Cuba and Peru, where there is no participation of private institutions. Organ donation rates vary from 2.3/million inhabitants in Peru to 23/million in Colombia (this last country with a regional donation rate up to 64/million). The LT that predominates in adult is from cadaveric donors, with a cumulative number from 103 in Ecuador to 1,700 in Colombia. The living donor LT in children varies from six in Ecuador to 120 in Chile. The cadaveric donor LT global survival rate varies from 71% in Ecuador to 86.4% in Peru. It has improved with time, since in 2015 the reported survival rates go from 80% in Chile to 95.4% in Peru. The number of patients in waiting lists varies widely in the different countries, from 24 in Uru-

Table 1 (09).

Country	No. Cent	Year CDT	Year LDT	Don. Rate/ million	No. LT	Surviv. rate	No. wait list	Tim. wait. list	Tim. WL F H	MELD Code 0	Milan P.	Time ICU	Tim Hosp	Medi	Finan.	Costs US
JC Restrepo Colombia	7	1983	2004	23-64	1.7	82-95%	50-70	3 m.	3 d.	Yes Yes	Yes 22 p.	3d.	14d	All	State Priv.	100.000
R. Zapata Chile	7	1985	1999	5.2-6.7	980	75-80%	110 15	12-16 m.	5.6 d.	Yes Yes	Yes 21 p.	7d	16d	All	State Priv.	45.000
H. Hernandez Cuba	3	1986-1990 1999	2009	14.3	310	N/A	27	6 m.	5-7 d.	N/A Yes	Yes N/A	7d.	30d	All	State	N/A
J. Suárez Ecuador	2 (1)	2009-2011	2012	5.1	103	71-83%	29	3-6 m.	N/A	Yes Yes	Yes 17-18p	5-6d.	12-15d	All	State Social Securt	38
M. Padilla Perú	2	2000	2001	2.3	202	86.40%	40 5	4 m.	7 d.	Yes Yes	Yes 22p	3d.	10d	All	Social Securt	35
S. Gerona Uruguay	1	1998	N/A	20	119	77-85%	24	6 m.	15 d.	N/A Yes	Yes 22p	3-4d.	12d	All	State	N/A

guay to 110 in Chile. The waiting period for cirrhotic patients in order to get a LT fluctuates between three months in Colombia and 12 to 16 months in Chile. In cases of fulminant hepatitis the waiting period varies form 3 days in Colombia to seven days in Peru. The death rate in waiting list LT candidates varies from 9% in Uruguay to 44% in Chile. The mentioned rate increases up to 50% in cases of fulminant hepatitis (only reported by Peru and Ecuador). Every country, with the exception of Cuba, which provided no report, use the MELD system in order to prioritize patients in the waiting list for LT and assign the code 0 as the highest priority for fulminant hepatitis cases. Also, the countries assign additional points to MELD score to patients with hepatocarcinoma, 17 points in Ecuador, 21 points in Chile and 22 points in the rest of the countries. The average reported time spend in the intensive care unit (ICU) varies from three days in Colombia and Peru to seven days in Chile and Cuba. The average hospitalization time reported varies from 12 days in Uruguay to 30 days in Cuba. Every country has complete immunosuppressive medication to treat LT. This medication in most of the countries is covered by the State or the social security. Only Chile and Colombia report private insurance coverage for this medication. The countries have original medication, also copies and generics medication, without a clear specification. The average cost for the LT differs between US 34,000 in Peru and US 100,000 in Colombia (Uruguay and Cuba did not report this information) (Table 1). All the countries agree that the LT programs should be improved, through governmental support, with the objective of increasing the donation rate, improve the reference mechanisms for patients with LT indication, as well as the procurement of potential donors. Also, they consider that prompt and efficient payment of costs is required in order to guarantee the sustainability of LT programs. Likewise, the countries agree that up to the present date, there has been no support from the LAASL to the LT area. They suggest a permanent capacitation, exchange of knowledge and support through counsel and guide ship in order to: implement LT programs in countries that do not have them, improve the current LT programs in some countries, and extend LT program to new areas (living donor) in other countries. All the countries, except form Cuba that did not answered, offer to share experience and help other countries without or with a smaller LT program.

Comments. This survey has shown that is important to promote a more fluent exchange of information, which should be complete, accurate and updated. The use of tools such as this survey or other similar in the future should accomplish the gathering of statistical data that may be shared between the LAASL, STALYC and other LT international associations.

10
CORRECTION OF COAGULOPATHY PRIOR TO PARACENTESIS IS ASSOCIATED WITH EXCESSIVE ALBUMIN ADMINISTRATION AND NO CLINICAL BENEFIT

MANICKAVASAGAN H., BIANCO B., TREBELEV A., ROTHSTEIN K., MUNOZ S.
DEPARTMENT OF MEDICINE, DREXEL COLLEGE OF MEDICINE, HAHNEMANN UNIVERSITY HOSPITAL, PHILADELPHIA, PENNSYLVANIA, USA.

Background. Large volume paracentesis (LVP) is a common procedure performed to effectively relieve symptoms of tense ascites in advanced cirrhosis. Following LVP, plasma volume expansion with albumin replacement is recommended by AASLD and other professional societies to prevent post-paracentesis circulatory disturbance, mainly expressed as impairment of renal function. However, cirrhotic patients frequently have marked coagulopathy that is often treated with fresh frozen plasma (FFP) prior to LVP in order to reduce bleeding risk, in accordance with recommendations of the Society of Interventional Radiology.

Aim. To determine if the amounts of albumin contained in FFP administered prior to LVP is clinically significant, and effective in preventing post-LVP renal dysfunction.

Material and methods. For each patient who received FFP

prior to LVP over a 6 month period in 2015 at our university tertiary center for liver disease, we determined the following: number of FFP units received prior to LVP, volume of ascitic fluid removed, amount of albumin received after the procedure (according to 2012 AASLD guidelines), and serum creatinine before and after the LVP. Albumin content in FFP units was determined by direct assay of albumin level in FFP samples.

Results. 243 large volume paracentesis were performed in 107 patients between April and September 2015. FFP was administered prior to LVP in 112 (46%) instances to correct INR (30 females, 95 males, age 55 ± 1.7 yrs). Causes of cirrhosis included NASH, HCV, alcohol, autoimmune, and other miscellaneous liver disorders; MELD score was 26±1.5 points (10-40). Mean volume of ascites removed was 6.8 ± 0.5 liters (range: 2.0-13.1 L; more than 5 L were removed in X% of the paracenteses). Prior to LVP, patients received 4±0.5units of FFP (range: 1-11) per patient. After LVP, patients received 51.7 ± 7.9 g of intravenous albumin (range: 0-200). Albumin content of FFP was 3.6 ± 0.1 g/dL. Total amount of albumin administered was 96.9 ± 9 g/patient, including albumin in FFP prior to LVP and albumin administered after LVP. The amount of albumin administered in excess of guidelines recommendation (i.e., 6-8 g of i.v. albumin per liter of ascites removed) was 51.9 ± 8 g/patient. Serum creatinine increased minimally (0.07 ± 0.1 mg/dL) after LVP.

Conclusions. Almost half of cirrhotic patients receive FFP prior to large volume paracentesis. The FFP administered in preparation for paracentesis contains a significant amount of albumin (near 40 g) and leads to substantial excess albumin infusion when i.v. albumin is also given following the paracentesis (following standard of care guidelines). The excess albumin from FFP and post-LVP did not appear to cause clinically significant improvement or worsening of renal function following paracentesis. Our results suggest that significantly less albumin should be given after LVP when patients receive FFP prior to the procedure.

D. VIRAL HEPATITIS C

01
EFFICACY AND SAFETY AMONG PATIENTS TREATED WITH OMBITASVIR/PARITAPREVIR/R + DASABUVIR ± RIBAVIRIN ACCORDING TO BASELINE RENAL FUNCTION: ANALYSIS OF SIX PHASE 3 TRIALS

SULKOWSKI M.S.,[1] POCKROS P.J.,[2] JACOBSON I.M.,[3] BERNSTEIN D.E.,[4] TATSCH F.,[5] RENJIFO B.,[5] WANG D.,[5] COHEN D.,[5] MARTIN P.[6]
[1]VIRAL HEPATITIS CENTER, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MD, USA.
[2]DIVISION OF GASTROENTEROLOGY/HEPATOLOGY, SCRIPPS CLINIC, LA JOLLA, CA, USA.
[3]ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI, NEW YORK, NY, USA.
[4]DIVISION OF HEPATOLOGY, NORTH SHORE-LIJ HOFSTRA SCHOOL OF MEDICINE, MANHASSET, NY, USA.
[5]ABBVIE INC., NORTH CHICAGO, IL, USA.
[6]DIVISION OF HEPATOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF MIAMI, MIAMI, FL, USA.

Introduction. HCV infection is common in patients with chronic kidney disease (CKD). DAA regimens have not been adequately studied in patients with CKD. This *post-hoc*, pooled analysis from 6 phase 3 trials investigated the efficacy and safety of the 3 DAA (3D) regimen of ombitasvir, paritaprevir/ritonavir, and dasabuvir, ± ribavirin (RBV) among HCV GT1-infected patients with CKD.

Material and methods. Patient-level data were pooled and patients were categorized by baseline estimated glomerular filtration rate (eGFR; mL/min/1.73 m^2): 60-90; > 90; ptes with < 60 mL/min/1.73 m^2 were excluded due to small number. pegIFN/RBV naive and experienced patients, with or without cirrhosis, were included. Efficacy and safety were assessed in all patients.

Results. 2,005 patients included. Characteristics: 51% GT1a, 91% white race, 79% were IL28B non-CC, 66% treatment-naïve, 82% baseline HCV RNA ≥ 800,000 IU/mL. During therapy, 1511 patients received 3D + RBV and 494 3D regimen alone. Overall, SVR12 rates for 3D + RBV were 97% (eGFR 60-90; n = 862) and 96% (eGFR > 90; n = 649), and for 3D were 97% (eGFR 60-90; n = 300) and 94% (eGFR > 90; n = 194). Among patients with cirrhosis who received 3D + RBV, SVR12 rates were 95% (eGFR 60-90; n = 199) and 93% (eGFR > 90; n = 166). Among the patients who received 3D + RBV, 3.4% of patients with eGFR 60-90 and 2.5% of patients with eGFR > 90 experienced a serious adverse event (SAE) or adverse event (AE) leading to study drug discontinuation. Overall 1.3% and 3.4% of patients with eGFR 60-90 and 1.5% and 2.5% of patients with eGFR > 90 experienced a SAE or AE leading to study drug discontinuation among patients receiving 3D alone and 3D + RBV, respectively.

Conclusion. SVR12 rates among patients with eGFR 60-90 mL/min/1.73 m^2 treated with 3D ± RBV were comparable to those in patients with eGFR > 90 mL/min/1.73 m^2. The proportion of patients who reported at least one SAE or discontinued treatment due to an AE was low and similar across both eGFR categories.

Acknowledgements: We thank the study participants, investigators, and coordinators who made this study possible. AbbVie sponsored the studies, contributed to their designs, participated in the collection, analysis, and interpretation of the data, and in the writing, reviewing, and approval of the publication. Medical writing support was provided by Nazneen Siddiqui of Medical Expressions, funded by AbbVie.

02
TREATMENT OF CHRONIC HCV INFECTION WITH THE NEW DIRECT ACTING ANTIVIRALS (DAA): A REAL WORLD EXPERIENCE IN BRAZIL

SETTE JR. H.,[1] CHEINQUER H.,[2,3] WOLFF F.H.,[2,3] BARROS M.F.A.,[1] SOARES S.R.P.,[1] DE ARAUJO A.[2,3]
[1]PRÓ-FÍGADO, SÃO PAULO.
[2]HOSPITAL DE CLÍNICAS DE PORTO ALEGRE E PROGRAMA DE PÓS-GRADUAÇÃO EM GASTROENTEROLOGIA E HEPATOLOGIA DA UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL.
[3]HOSPITAL MOINHOS DE VENTO, PORTO ALEGRE, BRAZIL.

Introduction. There is a paucity of data with DAA therapy in Latin America.

Objective. Describe safety and efficacy of DAA therapy among DAA treatment naïve Brazilian chronic hepatitis C patients.

Material and methods. Historical cohort analysis of consecutive chronic HCV patients treated since February 2014 with DAAs in three hepatology centers from Brazil, one in São Paulo and two in Porto Alegre. Only patients with HCV RNA result twelve weeks after end of therapy were included.

Results. 273 patients started DAA treatment. Of those, 141 had an HCV RNA result twelve weeks after the end of therapy and were analyzed: mean age was 58.4 ± 10.9 years (range: 29-85) and 86/141 (61%) were male. Genotype 1 was present in 112 (79.5%; 1a 29.5%, 1b 70.5%); Genotypes 2, 3 and 4 were detected in 3 (2.1%), 24 (17%) and 2 (1.4%), respectively. Cirrhosis was present in 62 (44%) patients. 81 patients (57.4%) were treatment experienced. DAA therapies were: sofosbuvir

(SOF) + ribavirin (RBV) in 6 patients; SOF + simeprevir (SMV)±RBV in 67; SOF+pegylated interferon (PEG-IFN)+RBV in 3; SOF+daclatasvir (DCV) in 23, SOF+ledipasvir (LDV) in 41, and ombitasvir+paritaprevir/ritonavir+dasabuvir (3D) in one patient. SVR-12 was achieved in 132/141 (93.6%). Nine patients failed therapy: 6 were cirrhotics, 5 were treatment experienced, and 4 were either genotype 3 or 1a. Three patients died during treatment, all because of liver decompensation. No adverse event was attributed to the DAA therapy.

Conclusion. Real world experience with DAA therapy in Brazil showed a high rate of SVR and excellent tolerability. Failure to achieve SVR was only observed among patients with at least one of the known predictors of non-response: cirrhosis, previous failure to PEG-IFN therapy, and either genotype 3 or 1a.

03
MALACHITE-I: PHASE 3B TRIAL OF OMBITASVIR/PARITAPREVIR/RITONAVIR AND DASABUVIR ± RIBAVIRIN OR TELAPREVIR + PEGINTERFERON/RIBAVIRIN IN TREATMENT-NAIVE ADULTS WITH HCV GENOTYPE 1 IN CHILEAN PATIENTS

CONTRERAS J.,[1] FUSTER F.,[2] SOZA A.,[3] OYANEDER C.,[4] YAN LUO.,[5] RENJIFO B.,[5] ARAVENA E[6]

[1]CLÍNICA ALEMANA. FACULTAD DE MEDICINA, UNIVERSIDAD DEL DESARROLLO, SANTIAGO, CHILE.
[2]CENTRO DE INVESTIGACIONES CLÍNICAS VIÑA DEL MAR. CLÍNICA REÑACA, VIÑA DEL MAR, CHILE.
[3]DEPARTAMENTO DE GASTROENTEROLOGÍA. PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE.
[4]ABBVIE LTDA., HUECHURABA, SANTIAGO, CHILE.
[5]ABBVIE INC. NORTH, CHICAGO, ILLINOIS, ESTADOS UNIDOS.
[6]HOSPITAL CLÍNICO SAN BORJA ARRIARÁN, UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.

Introduction. MALACHITE-I was a multicenter head to head study comparing the efficacy and safety of ombitasvir/paritaprevir/r with dasabuvir ± ribavirin (3D +/-RBV) versus telaprevir (TPV) + pegIFN/RBV in treatment-naive HCV GT1-infected patients without cirrhosis. MALACHITE-I study showed both superior efficacy and better safety profile of 3D ± RBV compared to TPV + pegIFN/RBV.

Objectives. To describe the baseline demographics, sustained virological response and safety results of 3D ± RBV and TPV + pegIFN/RBV in the Chilean patients enrolled in MALACHITE-I.

Material and methods. This multicenter, open-label trial enrolled 29 HCV GT1 non-cirrhotic treatment-naive patients from Chile. Patients were randomized to receive 3D ± RBV for 12 weeks, or TPV + pegIFN/RBV for 12 weeks followed by pegIFN/RBV for an additional 12-36 weeks. The primary endpoint was SVR12. Patients were evaluated for AEs.

Results. 18/29 patients were women (62.1%), 24 (82.8%) were < 55 years of age, and 23 (79.3%) had a BMI (kg/m^2) of ≥ 25. 24 (82.8%) patients received 3D ± RBV, and 5 patients (17.2%) received TPV + pegIFN/RBV. SVR12 rates were 100% in both groups. Any adverse event (AE) was reported in 19/29 pts (65.5%) with 14/24 (58.3%) in the3D ± RBV and 5/5 (100%) in the TPV + pegIFN/RBV group. Most frequent AEs were pruritus and rash in the 3D ± RBV vs anemia, nausea, rash, erythema and depression in the TPV + pegIFN/RBV group, respectively.

Conclusions. In the group of Chilean patients enrolled in the MALACHITE-I study the regimen of 3D ± RBV showed better safety outcomes than TPV + pegIFN / RBV, but the small numbers of patients in Chile limited our ability to draw conclusions regarding efficacy. The inclusion of clinical research sites in Chile allowed local investigators to evaluate safety and efficacy 3D ± RBV, a new complete interferon free therapy.

Acknoowledgements: AbbVie Inc. was involved in the study design; collection, analysis and interpretation of data; and the preparation and approval of this manuscript.

04
HEPLA: A MULTICENTER, OBSERVATIONAL STUDY ON DEMOGRAPHIC AND DISEASE CHARACTERISTICS OF PATIENTS SEEKING CARE FOR CHRONIC HEPATITIS C IN LATIN AMERICA

MORAES COELHO H.S.,[1] VARON PUERTA A.,[2] VIOLA L.,[3] CARVALHO-FILHO R.J.,[4] PÉREZ-RIOS A.M.,[5] RESTREPO J.C.,[6] MARCIANO S.,[7] CONTRERAS J.,[8] FUSTER F.,[9] KING J.,[10] RENJIFO B.,[10] MÉNDEZ-SÁNCHEZ N.[11]

[1]HOSPITAL UNIVERSITÁRIO CLEMENTINO FRAGA FILHO - UERJ; RIO DE JANEIRO, BRAZIL. [2]FUNDACIÓN CARDIO INFANTIL, BOGOTÁ, COLOMBIA.
[3]CENTRO INTEGRAL DE GASTROENTEROLOGÍA, CIUDAD AUTÓNOMA DE BUENOS AIRES, ARGENTINA.
[4]ESCOLA PAULISTA DE MEDICINA, UNIFESP - UNIVERSIDADE FEDERAL DE SÃO PAULO; SAO PAULO, BRAZIL.
[5]CENTRO DE INVESTIGACIÓN FARMACEÚTICA ESPECIALIZADA, GUADALAJARA, JALISCO, MEXICO.
[6]HOSPITAL PABLO TOBÓN URIBE AND UNIVERSITY OF ANTIOQUIA GASTROHEPATOLOGY, MEDELLÍN, COLOMBIA.
[7]HOSPITAL ITALIANO DE BUENOS AIRES; BUENOS AIRES, ARGENTINA.
[8]HOSPITAL PADRE HURTADO, SANTIAGO, CHILE.
[9]CENTRO DE INVESTIGACIONES CLINICAS VIÑA DEL MAR; VIÑA DEL MAR, CHILE.
[10] ABBVIE INC., NORTH CHICAGO, ILLINOIS, U.S.
[11]MEDICA SUR CLINIC & FOUNDATION, MEXICO CITY, MEXICO.

Introduction. Epidemiologic information on HCV in Latin America is not widely reported. A better understanding of these data may help optimize emerging Direct Acting Antiviral (DAA) treatment strategies.

Objective. The aim of the HepLa study was to describe patient demographics, comorbidities, and HCV disease characteristics in patients seeking care for chronic hepatitis in Latin America (HepLa).

Material and methods. HepLa was a prospective, observational study. Between August 2014 and December 2015 we enrolled treatment-naive, treatment-experienced, or currently treated HCV-infected patients in Argentina, Brazil, Chile, Colombia, and Mexico. Demographics, HCV disease characteristics, comorbidities, concomitant medications, and laboratory results were collected during a clinical visit.

Results. A total of 817 patients from 30 sites were enrolled; 54% female, 42% Mestizo, and median age 58 years. Overall, 80% of patients had HCV genotype (GT) 1 infection; GT1b accounted for 41.6% of all infections. In total, 41% of patients had a METAVIR score of F3–F4; 40% had cirrhosis; 41% were treatment naive; 50% were treatment experienced; and 9% were currently being treated at the time of enrollment. All treatment-experienced patients had received an IFN-containing regimen (67% pegylated IFN + ribavirin (pegIFN/RBV), 9% pegIFN/RBV + telaprevir, 13% pegIFN/RBV + boceprevir). Overall, 26% of patients had liver-related comorbidities; 5.8% had a liver transplant; 5.6% had chronic kidney disease; 3.9% were HIV/HCV co-infected; and 72% were taking co-medications for conditions other than HCV infection.

Conclusion. HCV GT1b was most prevalent and 40% of all patients had cirrhosis. One-half of patients were treatment experienced; all previously received IFN-based therapy. The HepLa study should help medical communities optimize screening, diagnosis, and treatment strategies and help gov-

ernment agencies to integrate novel therapies as part of their strategic planning for HCV treatment. (Acknowledgments: The design, study conduct, analysis, and financial support of the HepLa study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of the content. All authors had access to all relevant data and participated in writing, review, and approval of this presentation. Medical writing support was provided by Andrew Kerr of Medical Expressions, funded by AbbVie).

05
IMPLEMENTATION OF THE ECHO® TELEMENTORING MODEL FOR THE TREATMENT OF PATIENTS WITH HEPATITIS C IN ARGENTINA

MARCIANO S.,[1] HADDAD L,[1] PLAZZOTTA F.,[1] MAURO E.,[1] TERRAZA S.,[1] ARORA S.,[2] THORNTON K.,[2] RÍOS B.,[3] CARLOS DANS G.,[4] RATUSNU N.,[5] CALANNI L.,[6] ALLEVATO J.,[7] SIROTINSKY M.E.,[8] PEDROSA M.,[9] GADANO A.[1]

[1]HOSPITAL ITALIANO DE BUENOS AIRES, BUENOS AIRES, ARGENTINA. [2]PROJECT ECHO, SCHOOL OF MEDICINE, UNIVERSITY OF NEW MEXICO, ALBUQUERQUE, USA. [3]CENTRO DE INVESTIGACIÓN (CEIN), NEUQUÉN, ARGENTINA. [4]HOSPITAL ZONAL RAMÓN CARRILLO, RIO NEGRO, ARGENTINA. [5]HOSPITAL REGIONAL DE USHUAIA, TIERRA DEL FUEGO, ARGENTINA. [6]HOSPITAL DR. CASTRO RENDÓN, NEUQUÉN, ARGENTINA. [7]INSTITUTO NORPATAGÓNICO DE GASTROENTEROLOGÍA Y ENDOSCOPÍA DIGESTIVA DE NEUQUÉN, ARGENTINA. [8]CENTRO DE ESTUDIOS DIGESTIVOS (CEDIG), COMODORO RIVADAVIA, ARGENTINA. [9]ABBVIE INC, USA.

Aim. To implement the ECHO model for hepatitis C in Argentina and to evaluate the provider outcomes.

Material and methods. Following the ECHO model, an hepatitis C teleECHO clinic was established at the Hospital Italiano in Buenos Aires (Argentina). The teleECHO clinic provides support and training to physicians from Patagonia who are treating patients with hepatitis C. In order to evaluate the teleECHO clinic outcomes, participants completed a survey focused on skills and competence in hepatitis C before and after six months of participation in the project. The survey consisted of 10 questions, which participants rated from 1 to 7 (1 no ability; 7 highest ability). To analyze the difference before and after participation in the project, Wilcoxon signed-rank test was used. Significance was declared for $p < 0.05$.

Results. During the first six months of implementation of the model, a total of 14 physicians from 12 sites in Patagonia agreed to participate in the survey. The median age of the participants was 42 years. Participants' primary specialties were Hepatology (55%), Infectious Diseases (25%), General Practice (10%), and other (10%). A significant improvement was observed in all the evaluated fields after six month of the participation in the teleECHO clinic. The hepatitis C teleECHO clinic participants significantly improved in the following areas: fibrosis staging, determining appropriate candidates for treatment, and selecting appropriate HCV treatment. In addition, their general interest in hepatitis C increased.

Conclusion. We successfully replicated and implemented the first teleECHO clinic in Argentina and participants have improved their ability to provide best practice care for patients with Hepatitis C.

06
TREATMENT PATTERNS AMONG HCV PATIENTS IN FOUR SOUTH AMERICAN COUNTRIES

GADANO A.,[1] SILVA M.,[2] BRAHM J.,[3] RESTREPO J.C.,[4] DAVALOS M.,[5] OLIVERA M. DEL R.,[6] BAIGUN M.,[7]

FOR THE TREATMENT PATTERNS AMONG HCV PATIENTS IN FOUR SOUTH AMERICAN COUNTRIES STUDY INVESTIGATORS

[1]LIVER UNIT, DEPARTMENT OF MEDICINE, HOSPITAL ITALIANO, BUENOS AIRES, ARGENTINA.

[2]HEPATOLOGY AND LIVER TRANSPLANT UNITS, HOSPITAL AUSTRAL, BUENOS AIRES, ARGENTINA.

[3]GASTROENTEROLOGY SECTION, HOSPITAL CLINICO DE LA UNIVERSIDAD DE CHILE, SANTIAGO DE CHILE, CHILE.

[4]HEPATOLOGY DEPARTMENT, HOSPITAL PABLO TOBON URIBE, MEDELLIN, COLOMBIA.

[5]GASTROENTEROLOGY AND HEPATOLOGY DEPARTMENT, HOSPITAL EDGARDO REBAGLIATI MARTINS, LIMA, PERU.

[6]BRISTOL-MYERS SQUIBB, BOGOTA, COLOMBIA. [7]BRISTOL-MYERS SQUIBB, BUENOS AIRES, ARGENTINA.

Introduction. Burden on health and clinical management of patients with hepatitis C virus (HCV) infection in Latin-America have been insufficiently studied so far.

Objectives. To describe the profile and management of patients with HCV infection in Argentina, Chile, Colombia, and Peru prior to new generation DAA era.

Material and methods. Observational, multi-center, cross-sectional and retrospective medical chart review study. Main inclusion criteria were age ≥ 18 years, confirmed HCV infection, no spontaneous HCV eradication. Consecutive medical charts from patients fulfilling inclusion criteria were selected on the basis of clinical visits to selected specialized centers between Sept 2013 - Mar 2015, most recent charts being reviewed first. Data was summarized descriptively. Differences between countries were analyzed by ANOVA or χ^2.

Results. 492 patients were recruited for this study (Argentina = 156, 32%; Chile = 60, 12%; Colombia = 168, 34%, Peru = 108, 22%). 78% percent of patients had genotype determination, whereas only 18% had IL28 genotypification. Most frequent HCV type was 1, predominately 1b (40%), with the exception of Peru where the most frequent genotype was 1a (34%). Most frequent IL28 polymorphism was CT. Overall frequency of

Table 1 (05). Survey. Results are presented in median and interquartile range. N = 14.

	Prior to participation	After 6 months of participation	Paired difference	p
Ability to identify patients who should be treated	5 (3-6)	7 (6-7)	2 (1-3)	0.0002
Ability to stage liver fibrosis	6 (5-6)	7 (6-7)	1 (1-2)	0.0005
Ability to identify different DDAs*	4 (2-5)	6 (6-7)	2 (2-4)	0.0003
Ability to identify DDAs* combinations	3 (2-4)	6 (6-7)	3 (2-4)	0.0003
Ability to identify available DDAs*	5 (3-5)	7 (7-7)	2 (2-4)	0.0003
Ability to share with patients treatment options	4 (3-5)	7 (6-7)	2 (2-3)	0.0003
Ability to share with colleagues treatment options	4 (3-5)	6 (6-7)	2 (2-3)	0.0002
Ability to access to a second opinion	3 (3-5)	7 (7-7)	3 (2-4)	0.0003
Ability to rapidly access to a second opinion	3 (3-5)	7 (6-7)	3 (2-4)	0.0003
General interest in hepatitis C	6 (5-7)	7 (7-7)	1 (0-2)	0.0032

cirrhosis was 44%, 33% in Argentina to 55% in Colombia ($p < 0.001$). Decompensated cirrhosis was observed in 9.3% (3.3% in Chile to 18.5% in Colombia, $p < 0.001$). Fibroscan® was performed in 22% of patients (2% in Peru *vs.* 54% in Argentina, $p < 0.001$). Mean score and standard deviation was 10.8 ± 6.6. Biopsy was available in 53% of cases, with Metavir staging in 80% of cases. Hepatocellular carcinoma was observed in 7% of patients (2.7% in Peru to 11% in Colombia, $p < 0.001$). Most frequent transmission route was blood transfusion (37%). Co-infection with HIV was present in 1.4% of cases, with HBV in 4.5% and with both in 0.2%. 63% of subjects received drug treatments, with most frequent reasons for lack of treatment being wanting to wait for new options and patients' comorbidities. Most frequent treatment was peg-IFNa 2a/RBV (48%). Protease inhibitors were used in 28% of patients. SVR was observed in only 22% of patients, 25 % of patients were relapsers and 20% non-responders.

Conclusion. This is one of the largest epidemiological studies about patients' characteristics and clinical management of HCV infection in Latin-America. HCV treatment patterns varies and relevant differences could be noticed across countries. Understanding epidemiological patterns is critical for developing adequate strategies to manage or eliminate HCV infection.

07
NATURALLY OCCURRING NS3 RESISTANCE-ASSOCIATED VARIANTS IN HEPATITIS C VIRUS GENOTYPE 1 IN URUGUAYAN HCV INFECTED PATIENTS

ECHEVERRÍA N.,[1] BETANCOUR G.,[1] GÁMBARO F.,[1] HERNÁNDEZ N.,[2] LÓPEZ P.,[2] CHIODI D.,[2] SÁNCHEZ A.,[2] BOSCHI S.,[3] FAJARDO A.,[1] SÓÑORA M.,[1] MORATORIO G.,[1] CRISTINA J.,[1] MORENO P.[1]

[1]LABORATORIO DE VIROLOGÍA MOLECULAR, CENTRO DE INVESTIGACIONES NUCLEARES, FACULTAD DE CIENCIAS, UNIVERSIDAD DE LA REPÚBLICA,
[2]CLÍNICA DE GASTROENTEROLOGÍA Y DEPARTAMENTO DE LABORATORIO CLÍNICO, HOSPITAL DE CLÍNICAS, FACULTAD DE MEDICINA, UNIVERSIDAD DE LA REPÚBLICA.
[3]LABORATORIO DE BIOLOGÍA MOLECULAR, ASOCIACIÓN ESPAÑOLA PRIMERA DE SOCORROS MUTUOS; MONTEVIDEO, URUGUAY.

Introduction. Although the direct-acting antiviral agents (DAAs) increase HCV response rates and allow shortened and simplified regimens of treatment, the emergence of genetic variants is worrisome since they generate resistant phenotypes that might jeopardize their effectiveness. The circulation of resistance-associated variants (RAVs) in treatment-naïve patients has not been reported in South America, with few exceptions.

Aim. To investigate the presence of RAVs in the NS3 serine protease region in a cohort of Uruguayan patients with chronic hepatitis C who had not been treated with any DAAs.

Material and methods. After written informed consent was signed, serum samples from 20 patients, DAA treatment-naïve, infected with HCV genotype 1 were obtained. Viral RNA was extracted, retrotranscribed and used for PCR amplification of the complete NS3 genome region. The amplicons were sequenced in order to analyse the presence of mutations.

Results. 15 serum samples with genotype 1a and 5 with genotype 1b were studied. RAVs to protease inhibitors (PI) were identified in HCV isolates from 5 patients (25%). The mutation Q80K conferring resistance to simeprevir (SMV), paritaprevir (PTV), asunaprevir y faldaprevir (FDV) was found in two patients, and one had the mutation Q80L associated to PTV and FDV intermediate resistance. Three patients had substitutions at position 122 (S122R/G), RAVs associated to SMV resistance, and only one showed the V55A substitution which confers resistance to both boceprevir and telaprevir. Three patients also exhibited the substitutions P334S and S342P which were reported to emerge in some relapsers and non-responder patients to therapy including PTV.

Conclusion. Naturally occurring mutations conferring resistance to NS3 inhibitors exist in a substantial proportion of Uruguayan treatment-naïve patients infected with HCV genotype 1.

08
COMPARISON BETWEEN THE ACCURACY OF NON-INVASIVE METHODS FOR EVALUATION OF FIBROSIS AND LIVER BIOPSY IN PATIENTS WITH CHRONIC HEPATITIS C

RAGAZZO T.G.,[1] VEZOZZO D.C.P.,[1] MAZO D.F.,[1] PESSOA M.G.,[1] OLIVEIRA C.P.,[1] LIMA F.R.,[2] ALVES V.A.F.,[2] CARRILHO F.J.[1]

[1]DEPARTMENT OF GASTROENTEROLOGY, UNIVERSITY OF SÃO PAULO, BRAZIL.
[2]DEPARTAMENT OF PATHOLOGY, UNIVERSITY OF SÃO PAULO, BRAZIL.

Introduction. Chronic hepatitis C affects approximately 130 to 150 million people worldwide and about 300 to 500 000 deaths occur annually related to its complications. Liver biopsy is considered the gold standard method for evaluation of the degrees of hepatic fibrosis, however, non-invasive methods are becoming more popular due to their convenience, efficiency and absence of risks.

Objectives. To compare the accuracy of non-invasive methods for evaluation of liver fibrosis: Fibroscan, ARFI, ELF, APRI, FIB4 in relation to liver biopsy in METAVIR classification.

Material and methods. Liver biopsies, Fibroscan, APRI and FIB4 were performed in 107 patients, ELF in 68 patients, ARFI in 51 patients. Based on the area under the ROC curve, the AUROC, it was possible to identify the accuracy of each method significant fibrosis (≥ F2), severe fibrosis (≥ F3) and cirrhosis (≥ F4).

Results. Aurocs: ≥ F2 Fibroscan: 0.83; FIB4: 0.76; ELF: 0.70; APRI: 0.69; ARFI: 0.67; ≥ F3: Fibroscan: 0.85; ELF: 0.82; FIB4: 0.77; ARFI: 0.74; APRI: 0.71, ≥ F4 APRI: 1; FIB4: 1; Fibroscan: 0.99; ARFI: 0.96; ELF: 0.94.

Conclusion. Fibroscan has better accuracy in the evaluation of varying degrees of liver fibrosis. All methods have the same efficiency in ≥ F4.

09
DISTRIBUTION AND CHARACTERIZATION OF POLYMORPHISMS IN THE IL28B GENE (rs12979860 and RS8099917) IN A URUGUAYAN POPULATION WITH AND WITHOUT HCV INFECTION

CHIODI D.,[1] LÓPEZ P.,[2] ECHEVERRÍA N.,[3] SÁNCHEZ A.,[1] ANGULO J.,[4] LÓPEZ-LASTRA M.,[4] SILVERA P.,[2] LÓPEZ L.,[5] CANAVESI A.,[1] BIANCHI C.,[6] MORENO P.,[3] HERNÁNDEZ N[1]

[1]CLÍNICA DE GASTROENTEROLOGÍA Y
[2]DEPARTAMENTO DE LABORATORIO CLÍNICO, HOSPITAL DE CLÍNICAS, FACULTAD DE MEDICINA, UNIVERSIDAD DE LA REPÚBLICA, MONTEVIDEO, URUGUAY.
[3]LABORATORIO DE VIROLOGÍA MOLECULAR, CENTRO DE INVESTIGACIONES NUCLEARES, FACULTAD DE CIENCIAS, UNIVERSIDAD DE LA REPÚBLICA, MONTEVIDEO, URUGUAY.
[4]LABORATORIO DE VIROLOGÍA MOLECULAR, INSTITUTO MILENIO DE INMUNOLOGÍA E INMUNOTERAPIA, CENTRO DE INVESTIGACIONES MÉDICAS, PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE, SANTIAGO, CHILE.
[5]DEPARTAMENTO DE BANCO DE SANGRE, SERVICIO NACIONAL DE SANGRE, MONTEVIDEO, URUGUAY.
[6]SANATORIO SEMM-MAUTONE, MALDONADO, URUGUAY.

Introduction. Host single nucleotide polymorphisms (SNPs) near the interleukin 28B (IL28B) locus on chromosome 19

have been associated with sustained virological response (SVR) to anti-viral therapy and spontaneous HCV clearance. The genetic prevalence of these SNPs varies depending on ethnicity. This data has not been addressed in Uruguay so far.
Objective. To determine and compare the distribution of polymorphisms in the IL28B gene (rs12979860 and rs8099917) in infected and uninfected individuals in Uruguay.
Material and methods. DNA recovered from blood samples collected from non-infected control individuals (National Blood Service) or HCV infected patients were genotyped by two different techniques: restriction fragment length polymorphism (RFLP) and allelic discrimination by real-time PCR.
Results. 78 patients with chronic HCV infection were included (61.5% were male and the average age was 46 years). Cirrhosis was observed in 29 out of 49 patients (59%). The control group was represented by 92 cases (73% male, average age 40 years). The distribution of rs12979860 genotypes for the infected population was 29.5 (CC), 47.4 (CT) and 23.1% (TT) while for the control group it was 45.6, 42.4 and 11.9%, respectively. The distribution for rs8099917 was 57.7 (TT), 28.2 (TG) and 14.1% (GG) and for the control group 60.8, 33.7 and 5.4%, respectively. The comparison of the distribution of CC and TT genotypes (rs12979860) between the two populations evidenced a higher prevalence of the favorable genotype (CC) in the control group ($p < 0.05$).
Conclusion. As expected, patients with HCV infection have a lower prevalence of CC genotype when compared to uninfected population. The prevalence in both populations is similar to those reported in other Latin American countries.

10
DECREASING PREVALENCE OF HEPATITIS C VIRUS INFECTION IN PEOPLE BORN FROM 1905 TO 2015 IN ARGENTINA

MARTINEZ A.P.,[1] FERNANDO F.,[1] RIDRUEJO E.,[1] PEREZ P.,[2] MANDO O.,[1] CAMPOS R.H.,[2,3] DI LELLO F.A.[2,3]

[1]CENTRO DE EDUCACIÓN MÉDICA E INVESTIGACIONES CLÍNICAS NORBERTO QUIRNO "CEMIC", CIUDAD AUTÓNOMA DE BUENOS AIRES, C1425ASG BUENOS AIRES, ARGENTINA.
[2]CÁTEDRA DE VIROLOGÍA, FACULTAD DE FARMACIA Y BIOQUÍMICA, UNIVERSIDAD DE BUENOS AIRES, BUENOS AIRES, ARGENTINA.
[3]CONSEJO NACIONAL DE INVESTIGACIONES CIENTÍFICAS Y TÉCNICAS (CONICET), BUENOS AIRES, ARGENTINA.

Introduction. Hepatitis C virus (HCV) infection is a major public health issue of concern in Argentina. It is the leading cause of chronic hepatitis, hepatocellular carcinoma, as well as the most common condition for liver transplantation in Argentina. Recommendations to test HCV are based on risk factors for transmission. In this sense, the CDC recommended to screen individuals born during 1945-1965, based on data from population prevalence of infection. However, these recommendations cannot be used in Argentina since the age distribution of infected individuals is unknown.
Objective. The aim of this study was to analyze HCV prevalence among people born during 1905-2015 in Argentina.
Material and methods. In this study, 22043 patients attending a tertiary-care hospital in Buenos Aires, Argentina, from January 2001 until December 2015, were tested against anti-HCV. The patients reactive for antibodies to HCV by EIA were confirmed by PCR for HCV RNA.
Results. Out of these 22,043 patients (media age: 40.38 years), 8,724 (39.6%) were male and 13,319 (60.4%) were female. HCV prevalence in the general cohort was 5.1%. The prevalence was significantly higher in men than in women (7% *vs.* 3.8%, respectively, $p < 0.001$) and substantially higher among older adults. In this sense, within the cohort, anti-HCV prevalence was 9.3% (range 18.2% to 5.5%) for individuals born during 1905-1974 *vs.* 1.1% for individuals born during 1975-2015 ($p < 0.001$).
Conclusion. Although regional differences could exist, our data suggest that the incidence of HCV infection in our population is higher than what was previously estimated for Argentina. These data highlight the importance of testing people born before 1975 in order to identify those who remain infected and to link them to appropriate care and treatment.

E. COMPLICATIONS OF CIRRHOSIS

01
ACUTE TUBULAR NECROSIS IN CIRRHOTIC PATIENTS WITH HEPATORENAL SYNDROME

HAURYLENKA D.,[1] SILIVONTCHIK N.[2]

[1]EMERGENCY DEPARTMENT, STATE INSTITUTION "REPUBLICAN RESEARCH CENTRE FOR RADIATION MEDICINE AND HUMAN ECOLOGY", GOMEL, BELARUS.
[2]DEPARTMENT OF GENERAL MEDICINE, BELORUSSIAN MEDICAL ACADEMY OF POSTGRADUATE EDUCATION, MINSK; BELARUS.

Introduction. In decompensated cirrhosis increase in serum creatinine may be caused structural or functional of kidney injury.
Ojectives. We aimed to investigate the frequency of acute tubular necrosis (ATN) in hospitalized patients with decompensated cirrhosis who died with hepatorenal syndrome.
Material and methods. This was a retrospective study of 142 hospitalized cirrhotic patients (City Hospital's medical records). All of them had died of cirrhosis complications from 2008 to 2010. In hospitalized patients AKI was defined according to AKIN criteria (2011).
Results. Total 142 patients with histologically confirmed cirrhosis were included (male 68%). Median age was 53 year (range 28-75). Mostly alcohol induced cirrhosis. ATN at autopsy among 142 patients was found in 70 patients (49.3%; 95%CI: 40.8-57.8). Among 142 hospitalized patients antemortem conditions were follow: 53 meet criteria of type 1 HRS (37.3%; 95%CI: 29.4-45.3) and 11 meet criteria of type 2 HRS (7.8%; 95%CI: 3.9-13.4). In group with ATN 46 patients meet criteria HRS (65.7%, 95% CI: 53.4-76.7). In fact, it is interpretation of serum creatinine increase in the absence of morphological examination of kidneys. Frequency of variceal bleeding was higher in patients without ATN compared to patients with ATN (41.4% *vs.* 58.3%, $p = 0.044$). Median length of stay of the ATN group was higher than in the group without ATN: 7 (IQR 2-12) *vs.* 4 (1-10) days, respectively ($p = 0.044$). Infectious complications associated with ATN among hospitalized patients – OR = 5.3 (95%CI: 2.5-10.9; $p < 0.001$).
Conclusion. ATN as a form of acute kidney injury is common in critically ill cirrhotic patients. In or study 65.7% (95% CI: 53.4-76.7) patients with cirrhosis who meet criteria of HRS, was found ATN.

02
A SURVEY AMONG INDIVIDUALS BEARING HEPATIC DISEASES AIMING TO ASSESS DOCTOR/PATIENT RELATIONSHIP - THE PATIENT'S VOICE

VARALDO C.N.,[1] PARANÁ R.[2]
[1]PRESIDENT OF GRUPO OTIMISMO - AN ORGANIZATION THAT PROVIDES SUPPORT TO HEPATITIS BEARERS - RIO DE JANEIRO; BRAZIL.
[2]PROFESSOR OF GASTRO-HEPATOLOGY AT UNIVERSIDADE FEDERAL DA BAHIA – SALVADOR, BRAZIL.

Introduction. Learning how hepatitis patients perceive the way they are tented to by SUS (Brazilian Public Health System), private health plan and private doctors.
Objective. The objective of this study is to obtain information in order to improve services and care in public and private health systems.
Material and methods. 1,152 individuals with hepatic problems answered anonymously to 15 questions in interviews using Survey Monkey system. 535 participants assisted by SUS (Brazilian Public Health System); 245 assisted by private doctors and; 372 assisted by private health plans; 92.35% infected with hepatitis C; 10.75 with cirrhosis/cancer; 9.6% with NASH; 3.52% co-infected with HIV/HCV and 2.89% infected with hepatitis B. The research was released to Brazilian associates on web pages www.hepato.com and www.facebook.com/hepatocom and shared on social media.
Discussion. Assistance to patients is given by hepatologists in 41.62% of the cases, 31.63% by infectologists, 24.56 by gastroenterologists and 4.99% by Clinical Doctors. 59% of SUS doctors, 70% of private health plan doctors and 83% of private doctors talk about the disease. 76% of doctors are optimistic in relation to the disease. 52% of doctors inquire their patients about their jobs and family relations, 88% inquire their patients about the use of medicines. Although doctors are treating liver problems only 38% ask their patients if they take dietary supplements, only 30% ask if they take any kind of herbal tea, 57% if they use drugs, 82% about alcoholic beverages intake and 52% about their diets. Only 56% explain the purpose of the exams required and 66% explain the objective of medicines prescribed. 57% of doctors have legible handwriting and 12% print on a computer. 69% give detailed answers to patient's questions. Chairs where doctors sit are higher than those of patients in 7% in SUS, 9% in private health plans and 15% in private offices. 58% of consultations last less than 20 min in SUS and private health plans. 80% of consultations with private doctors last 25 to 45 min. In SUS and in private health plans doctors do not stand from their chairs and do not touch patients. Should a patient need assistance on holidays or weekends, 26% of doctors in SUS give a telephone number, 31% in private health plans and 43% in private care do.
Conclusion. The results show that nearly half of the patients with hepatic problems are not being assisted adequately. There is a lack of protocol and consensus about treatments that may guide doctors to treat patients with hepatic problems appropriately.

03
FUNCTIONAL CAPACITY, RESPIRATORY MUSCLE STRENGTH, AND OXYGEN CONSUMPTION PREDICTS MORTALITY IN PATIENTS WITH CIRRHOSIS

FAUSTINI PEREIRA J.L., HOMERCHER GALANT L., ROSSI D., GARCIA E., TELLES DA ROSA L.H., DE MELLO BRANDÃO A.B., MARRONI C.A.
GRADUATE PROGRAM IN HEPATOLOGY, FEDERAL UNIVERSITY OF HEALTH SCIENCES OF PORTO ALEGRE - RIO GRANDE DO SUL STATE – BRAZIL.

Introduction. Liver diseases influence musculoskeletal functions and may negatively affect the exercise capacity of patients with cirrhosis.
Aim. To test the relationship between the Six-Minute Walk Test (6MWT), maximal inspiratory pressure (MIP), and exercise capacity (VO_2peak) measures and the survival rate of patients with cirrhosis.
Material and methods. This prospective cohort study consisted of 86 patients diagnosed with cirrhosis with the following aetiology: hepatitis C virus (HCV), hepatitis B virus (HBV), and/or alcoholic cirrhosis (AC). All patients were followed for three years and submitted to the 6MWT, pressure measurements with a compound gauge, and an exercise test (VO_2peak).
Results. The study included 66 males and 20 females, with 40 patients in the HCV group, 30 patients in the AC group, and 16 patients in the HBV group. The survival rate analysis showed that the individuals who covered a distance shorter than 410 m during the 6MWT had a survival rate of 55% compared with a rate of 97% for the individuals who walked more than 410 m ($p = 0.0001$). Individuals with MIPs below -70 cm H_2O had a survival rate of 62% compared with a rate of 93% for those with MIPs above -70 cm H_2O ($p = 0.0001$). The patients with VO_2peak values below 17 mL/kg had a survival rate of 55% compared with a rate of 94% for those with VO_2peak values above 17 mL/kg ($p = 0.0001$).
Conclusion. The 6MWT distance, MIP, and oxygen consumption are predictors of mortality in patients with cirrhosis.

04
ANTHROPOMETRIC AND BIOCHEMICAL NUTRITIONAL STATUS IN 69 CHILDREN WITH HEPATOSPLENIC SYNDROME FROM THE HOSPITAL UNIVERSITARIO DEL VALLE OF CALI, COLOMBIA

VELASCO-BENÍTEZ C.A., ORTIZ-RIVERA C.J., LOZANO-ÁLVAREZ S.L.
UNIVERSIDAD DEL VALLE. CALI, COLOMBIA.

Introduction. Hepatosplenic syndrome (HES) in pediatrics may be secondary to infectious, metabolic, oncohematologic and liver causes, among others. The assessment of nutritional status of these children by anthropometry and biochemistry, allow their comprehensive overall assessment.
Objective. To determine through body mass index (BMI), height for age (HE) and paraclinical the anthropometric and biochemical nutritional status of children at the Hospital Universitario del Valle of Cali, Colombia with HES.
Material and methods. This is an observational cross-sectional study in children with HES (2 with krabbe disease, 2 with mucopolysaccharidosis type I, 3 with Niemann pick disease, 2 with congenital deficit chitotriosidase and 59 with indetermiate HES) who were taking socio-demographic data, weight (kg), height (cm) and laboratory (blood count and liver function tests); data were analyzed with Anthro and Anthroplus WHO, being classified by BMI: obesity, overweight, severe malnutrition, malnutrition, eutrophic; according to the HE in: tall stature, short stature, severely stunted, eutrophic and as reference standards as altered paraclinical for age and sex.
Results. There were 69 children aged 3.5 ± 4.6 years; 65.2% male; 34.8% with malnutrition; 37.7% by age altered size; 95.0% with altered coagulation tests; 78.6% with anemia; 54.6% with hyponatremia; 40.0% with hypoglycemia; 35.0% with direct hyperbilirubinemia, and 28.0% with altered aminotransferases.
Conclusion. The anthropometric nutritional status of these children with HES was committed by 23.2% severely stunted

at 14.5% for severe malnutrition and stunting, respectively, and 8.7% by malnutrition; biochemical mainly being compromised by altered coagulation tests, anemia and hyponatremia.

05
SERUM LEVELS OF GP73 AND OSTEOPONTIN AS SEROLOGICAL MARKERS FOR SCREENING OF LIVER DAMAGE IN CIRRHOTIC PATIENTS WITH AND WITHOUT HEPATOCARCINOMA. PRELIMINARY REPORT

GONZÁLEZ K.,[1] URZÚA A.,[1] COVARRUBIAS N.,[3] BELTRÁN C.,[2] MAC-VICAR M.,[1] MIRANDA J.,[3] PÉREZ-LUCO T.,[4] NAVEA C.,[1] PONIACHIK J.,[1] VENEGAS M.[3]

[1]SECTION OF GASTROENTEROLOGY, [2]LABORATORY OF INMUNO-GASTROENTEROLOGY, [3]LABORATORY OF GASTROENTEROLOGY, SECTION OF GASTROENTEROLOGY, HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE. [4]FACULTY OF MEDICINE, UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.

Background and aim. Cirrhosis is a major health problem worldwide and frequently leads to hepatocellular carcinoma (HCC). Alpha-fetoprotein (AFP) is a well-known serological marker for HCC detection, but there are some controversies on its use. Novel serum screening markers have been described, such as Golgi Protein-73 (GP73) and Osteopontin (OPN). We determined serum levels of AFP, GP73 and OPN in a group of Chilean cirrhotic patients (CP) and subject controls (SC).
Material and methods. Serum samples were collected from SC (n = 15), CP with HCC (CP-HCC, n = 24) and CP without HCC (CP no-HCC, n = 20) to measure AFP (normal value = 8.8 ng/mL), GP73 and OPN levels, using ELISA test. Statistical analysis was performed using Mann-Whitney *U* test.
Results. Higher levels of GP73 were observed in both CP-HCC (median: 114 ng/mL, range 50-336, $p < 0.0001$) and CP no-HCC (median: 150 ng/mL, range 84-262, $p < 0.0001$) groups than SC (median: 64 ng/mL, range 35-153). No significant difference between CP-HCC and CP no-HCC groups was found. Elevated levels of OPN were observed in both CP-HCC (median: 53 ng/mL, range 21-935, $p = 0.0066$) and CP no-HCC (median: 51 ng/mL, range 16-102) ($p = 0.047$) groups than SC (median: 64 ng/mL, range 35-153), with no significant difference between both cirrhotic groups. Higher levels of AFP were observed in CP-HCC (median: 13.9 ng/mL, range 2-3507) compared to CP no-HCC group (median: 3.3 ng/mL, range 2-30, $p = 0.0012$) and SC (median: 2 ng/mL, range 2-4.4, $p < 0.0001$).
Conclusion. OPN and GP73 are not better serological markers than AFP for HCC screening in Chilean cirrhotic patients. Interestingly, we found that GP73 and OPN may be useful as a marker of liver damage. In this group, AFP confirms the evidence reported in the literature.

06
P300 POTENTIALS EVOKED BY VISUAL STIMULATION FOR DIAGNOSIS OF MINIMAL HEPATIC ENCEPHALOPATHY

PÉREZ HERNÁNDEZ J.L.,[1] HIGUERA DE LA TIJERA M.F.,[1] LUPIAN SÁNCHEZ A.,[1] GARCÍA FORONDA C.G.,[2] DURAN MEZA H.,[2] JIMÉNEZ CORREA U.,[2] SERVÍN-CAAMAÑO A.I.,[3] SANTANA VARGAS D[2]

[1]GASTROENTEROLOGY DEPARTMENT, [2]SLEEP DISORDERS CLINIC, [3]INTERNAL MEDICINE DEPARTMENT. HOSPITAL GENERAL DE MÉXICO "DR. EDUARDO LICEAGA". MEXICO.

Introduction. Minimal hepatic encephalopathy (MHE) diagnosis is complex. P300 potentials evoked by visual stimulation (P300v) have not been explored in this setting; they are an objective tool, capable of detecting minimal changes in cerebral function when it is tested to process information. They are obtained from pairing stimulus with the electroencephalographic register.
Aim. To evaluate P300v for diagnosis MHE, and to compare them with other diagnostic tools.
Material and methods. We included cirrhotic patients, and also a group of healthy-controls. We excluded patients with overt hepatic encephalopathy, taking medications as: antidepressants, anxiolytics, anti-ammonia; also infected patients, or with previous diagnosis of any neurological disease. The same day we applied to patients PHES, CFF, P300v and P300 potentials evoked by auditory stimulation (P300a), this last one was taking as the gold standard.
Results. Twenty-six healthy-controls were included, 17 women, age 39.69 ± 8.7; and 40 cirrhotics, 24 women, age 56.10 ± 9.23. Child-Pugh A-B-C 24-14-02, the frequency of detection of MHE was: PHES 21 (52.50%) patients, CFF 29 (72.50%), P300a 27 (67.50%), P300v 30 (75%). The sensitivity and specificity were 51.7%, 45.5% for FCC; 66.7%, 76.9%, for P300a; 60%, 70%, for P300v. The positive and negative predictive values were: 76.9%, 51.2% for P300v. The cut-off value on the ROC curve was 38.2 Hz for CFF and 383 miliseconds for P300v.
Conclusions. Nowadays there's no exist an ideal diagnostic tool for MHE. P300v have never been evaluated in this setting. Same as P300a, P300v shown better sensitivity and specificity than CFF; also predictive values were better for P300v, than the other diagnostic tools.

07
BODY COMPOSITION ASSESSMENT BY ANALYSIS OF ELECTRIC BIOIMPEDANCE VECTOR (BIVA) AND PHASE ANGLE BIOMARKER CIRRHOTIC PATIENT

MARRONI C.A., LEONHARDT L.R., ALVES F. S.

UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE - HEPATOLOGY. BRAZIL.

Introduction. The choice of method for nutritional assessment and body composition of patients with liver cirrhosis is still a challenge due to several factors such as hydration (edema and ascites), and there is yet a golden standard. The bioelectrical impedance vector analysis (BIVA) and phase angle (AF), measured by bioelectrical impedance (BIA), are capable of diagnosing more accurate body composition, enabling earlier and more specific nutritional performance.
Objective. To evaluate the body composition and hydration and cellularity of cirrhotic patients by BIVA method.
Material and methods. Cross-sectional study with cirrhosis of different etiologies in attendance in the Complexo Hospitalar da Santa Casa de Porto Alegre, RS, Brazil. The methods used for nutritional assessment were AF and BIVA through the BIA. For statistical analysis , it was considered a significance level of 5 % ($p \leq 0.05$).
Results and discussion. We evaluated 189 patients with a mean age of 56.9 (± 11.0 years), 62% male. Of these, 55% had score Child- Pugh A and the most prevalent etiology was hepatitis C virus (HCV) (46%). Patients with poor prognosis ranked from PA are significantly older ($p < 0.001$) , more often women ($p = 0.039$) , a higher proportion of Child C ($p < 0.001$) and the most common etiology was HCV ($p = 0.031$). There was statistically association between the child and the etiology ($p < 0.001$), and patients with alcohol etiology had a higher proportion of the Child A and Alcohol + HCV had

a higher prevalence of Child C. Patients were classified as BIVA in: Normal (33.3%), good condition (12.2%), dehydrated (14.8%), edema (36.5%) and malnourished (3.2%). Patients in good condition has a significantly lower average age than those with normal and edema classification. Patients in good condition AF have significantly higher than all other groups. In addition, with edema and Malnourished present significantly lower PA than all other groups. Patients with edema showed greater proportion of Child C. Patients with normal BIVA rating have a higher prevalence of alcohol, in good condition and Dehydrated have a higher prevalence of other etiologies and more edema prevalence of HCV. There was statistically association between BIVA ratings and PA ($p < 0.001$), and the poor prognosis was more prevalent in patients with edema and malnourished. Also patients in good condition had a higher prevalence of good prognosis.

Conclusion. This study was able to set BIVA of measurement points as cirrhotic characteristics. Also determine the real state of hydration and cellularity of these patients compared to their clinical condition through the Child-Pugh score. The BIVA results are very important because it provides information of body composition, assisting in nutritional management and improving the clinical condition of cirrhotic.

08
ACUTE KIDNEY INJURY (AKI) IN CIRRHOSIS-PRELIMINARY ANALYSIS

VALE E.P.B.M.,[2,5] FUCUTA P.S.,[2,5] LIMA E.Q.,[3,5] RAMALHO R.J.,[3,5] LOBO S.M.A.,[4,5] SEVÁ-PEREIRA T.,[6] SILVA R.C.M.A.[1,5]

[1]UNID.TRANSPLANTE FÍGADO,
[2]SERV.GASTRO-HEPATOLOGIA, [3]DEPART. NEFROLOGIA,
[4]UNID.TERAPIA INTENSIVA,
[5]HOSPITAL BASE/FACULDADE MEDICINA FUNFARME/FAMERP, SAO JOSE DO RIO PRETO-SÃO PAULO, BRAZIL,
[6]SERV. GASTROENTEROLOGIA UNID. TRANSPLANTE HEPÁTICO, FAC. CIÊNCIAS MÉDICAS, CAMPINAS, SÃO PAULO, BRAZIL.

Introduction. Acute kidney injury (AKI) in hospitalized cirrhotic patients is about 20% prevalence and a mortality rate of 55-91%.

Objective. Analyze the AKI etiology and mortality in hospitalized cirrhotic patients.

Material and methods. Multicentre prospective study; included all hospitalized patients with cirrhosis and AKI (creat > 1.5 mg/dL or increase of 0.3 mg/dL at baseline creat in 48 h). Types of AKI: volume-responsive (VR); intrinsic (I) and hepatorenal syndrome (HRS). Statistical analysis: with *t* Student, χ^2 or Fisher's exact test.

Results. Included 122 patients, age 58(28-75 y), 77% men. Main causes of cirrhosis: 49,5% alcohol; HCV 18,7%; HCV + alcohol 16,5%; NASH 5,5%. Child-Pugh score: B-35.8% and C-58%. MELD 21.8 ± 8.7 (9-48). Decompensated cirrhosis: 95%-ascites, encephalopathy-46,3% and 13,6%-bleeding. Infection: 66.7% (urinary-35.7%; 21.4%-SBP; erysipelas/cellulitis-8.9%). HCC 8.4%, AST-53 (21-380), ALT-27 (7-135) and creat-2.3 mg/dL (1.1-5.5). FE: Na-0.25 (0.03-6.2), urea-29 ± 14. Treatment: albumin 1 g/kg on Day-1 and 20 g/day from day 2; AKI were categorized: normalized creatinine - AKI VR:59,8%; among non-responders, AKI I: 30.5% and HRS 8.5%; type HRS-1, 9 patients. HRS-1 was treated with terlipressin plus albumin. Complete response: 5 of 9 patients. Other treatments: 14.7%-dialysis, 6.1%-TIPS and 15.1%-liver transplantation. Mortality in-hospital: AKI VR-36.2%, AKI I-80%, and SHR-83.3%.

Conclusion. AKI in cirrhosis has high mortality. Infection was common factor associated with AKI. The majority of patients had volume responsive AKI with good response to volume expansion with albumin and only a minority of patients had HRS. Mortality was high in significant association with HRS and infection.

09
GENETIC FACTORS RELATED A VITAMIN D PATHWAY HAD ASSOCIATION WITH CIRRHOSIS AND HEPATOCELLULAR CARCINOMA – PRELIMINARY RESULTS

DA SILVA R.C.M.A., MORETI B.O., LIMA S. P. S., BAITELLO M. E.L., TENANI G. D., OLIVEIRA-BRANCATI C. I. F., FERNANDES-FERREIRA R., BRAIT B. DE J., PINHEL M. A. S., SILVA R. F., PINHEIRO JÚNIOR S., SOUZA D. R. S.

MEDICALR SCHOOL OF SÃO JOSÉ DO RIO PRETO – NPBIM/FAMERP. BRAZIL.

Introduction. Studies have shown that progression to fibrosis, cirrhosis and hepatocellular carcinoma (HCC) are associated with vitamin D receptor (VDR).

Objective. To evaluate the association of VDR (rs731236-T> C and rs7975232-T> G) polymorphisms with cirrhosis (with or without HCC), as well as to characterize the clinical profile and lifestyle habits in patients and controls.

Material and methods. A total of 370 subjects were selected, regardless of gender, ethnicity and age, where 91 patients had cirrhosis (G1), 59 patients had cirrhosis and HCC (G2) and 220 were healthy individuals (G3). All subjects filled in a questionnaire to assess comorbidities and lifestyle habits. In addition, peripheral blood samples were collected from all subjects for analysis of VDR using PCR/RFLP. Alpha level was set at 5%.

Results. Males, advanced age, alcohol consumption, smoking and diabetes mellitus (DM) prevailed among patients, compared with controls ($P < 0.0001$). G1 showed increased frequency of genotypes with mutant allele (G/G and _/G) for *VDR-rs7975232*, compared with controls ($P = 0.0216$ and $P = 0.0006$, respectively). In the logistic regression analysis, smoking, alcohol consumption and DM were identified as independent risk factors as well mutant G allele of *VDR- rs7975232* for cirrhosis and/or HCC ($P = 0.0002$; $P < 0.000$; $P < 0.0001$ and $P = 0.0189$, respectively).

Conclusion. *VDR-rs7975232* polymorphism, as well lifestyle habits and DM, are independent factors for cirrhosis and/or HCC, highlighting the association of genetic factors with the carcinogenesis process.

10
FATIGUE IS COMMON SYMPTOM IN MILD CIRRHOTIC PATIENTS

OROSCO J.,[1,3] MORENO P.,[2] GAUNA F.,[2] PONIACHIK J.[1]

[1]GASTROENTEROLOGY SECTION.
[2]STUDENTS OF MEDICINE, UNIVERSITY OF CHILE CLINICAL HOSPITAL. SANTIAGO, CHILE.
[3]GASTROENTEROLOGY FELLOW.

Background. Fatigue is an unspecific symptom in cirrhosis which may interfere with daily life activity and disturb quality of life.

Aims. To evaluate the presence and magnitude of fatigue in cirrhotic patients and the relationship to the liver disease severity.

Material and methods. Between June and September 2015 Demographic and clinical variables were obtained from cirrhotic patients (age, gender, etiology, Child-Pugh, MELD score). Validated surveys were applied to fatigue study (the brief fatigue inventory, from University of Texas) classifying

them according to score in mild, moderate, severe. Goldberg's tests were applied to discriminate depression.
Results. Fifty-five cirrhotic patients were interviewed, mean age 59.2 (29-84) years old; 28 (51%) women. Most common cause was NASH 27%. Child-A 33 (60%); Child-B 12 (22%) Child-C 10 (18%). MELD 11.8 ± 5.9. Fatigue and depression was present in 58.1% and 10.9% respectively. Eliminating depression patients from the analysis, cirrhotic patients with moderate and severe fatigue was 71.8%, more frequent in women (83% *vs.* 17% p < 0.0001). Child-A 65.2%; Child-B 22%; Child-C 13%. 48% had MELD score < 10; 35% MELD 11-15; 17% MELD > 15.
Conclusions. Cirrhotic patients have a high prevalence of moderate to severe fatigue, being more significant among women. Patients with lower clinical severity (Child-Pugh A and MELD score < 10) have a higher prevalence and fatigue degree, meaning that this symptom is not related to severity of liver dysfunction.

F. BASIC SCIENCES

01
GLUTAMINE REDUCES OXIDATIVE DAMAGE TO THE LIVER AND INTESTINE PATHWAY ACTIVATION OF NRF2 IN A MODEL OF INTESTINAL ISCHEMIA AND REPERFUSION IN RATS

HARTMANN R.,[1] LICKS F.,[1] SCHEMITT E.,[1] COLARES J.,[2] SOARES M.,[1] ZABOT G.,[3] FILLMANN H.,[3] MARRONI N.[1,2]
[1]UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL (UFRGS), PORTO ALEGRE, BRAZIL. [2]UNIVERSIDADE LUTERANA DO BRASIL (ULBRA), PORTO ALEGRE, BRAZIL. [3]PONTIFÍCIA UNIVERSIDADE CATÓLICA DO RIO GRANDE DO SUL (PUCRS), PORTO ALEGRE, BRAZIL.

Introduction. Intestinal ischemia-reperfusion (I/R) can cause tissue and oxidative damage in the injured tissue and also distant organs, such as the liver. Some aggressive agents are involved in these processes, such as the generation of free radical and release of pro-inflammatory cytokines.
Aim. To evaluate the effects of pre-treatment with glutamine in the animal model of intestinal I/R.
Material and methods. Twenty male Wistar rats were divided into four groups: sham operated (SO), glutamine+ sham operated (G + SO), intestinal ischemia-reperfusion (I/R) and glutamine + intestinal ischemia-reperfusion (G + I/R). The animals underwent occlusion of the superior mesenteric artery for 30 min, followed by 15 min of reperfusion. Glutamine (25 mg kg/day) was administered via intraperitoneal 24 and 48 h before I/R. Damage to the intestine and liver were determined by the expression of Nrf2 (nuclear factor erythroid 2), NADPH quinone oxidoreductase enzyme 1 (NQO1) and superoxide dismutase (SOD) by Western blot. The statistical analysis used was ANOVA followed by Student-Newman-Keuls test (mean ± SE) significant when p < 0.05.
Results. In animals pretreated with glutamine (G + I/R), there was a significant increase in the expression of Nrf2, NQO1 and SOD, compared to I/R group (Nrf2 - Intestine: SO: 3.1 ± 0.3; G + SO: 2.9 ± 0.6; I/R: 2.2 ± 0.1; G + I/R: 2.8 ± 0.2; Liver: SO: 3.1 ± 0.1; G+SO: 2.7 ± 0.2; I/R: 1.4 ± 0.2; G + I/R: 2.8 ± 0.2); (NQO1 - Intestine: SO: 2.2 ± 0.1, G+SO: 2.3 ± 0.1, I/R: 0.8 ± 0.1, G + I/R: 1.9 ± 0.1; Liver: SO: 1.2 ± 0.1, G + SO: 1.4 ± 0.2, I/R: 0.6 ± 0.1; G+I/R: 1.5 ± 0.2) (SOD - Intestine: SO: 2.1 ± 0.2, G + SO: 2.1 ± 0.3, I/R: 0.5 ± 0.1, G + I/R: 1.4 ± 0.3; Liver: SO: 3.3 ± 0.1, G+SO: 3.2 ± 0.4, I/R: 1.3 ± 0.1; G + I/R: 2.3 ± 0.1).
Conclusion. We suggest that pretreatment with glutamine contributed to the regulation against oxidative damage protection system in the gut and liver in an experimental model of ischemia and reperfusion in rats.

02
IMPROVEMENT IN COGNITION AND MOTOR SKILLS IN CHIRROTIC RATS TREATED WITH MELATONIN

BOUCHET A,[1] OSSANDON C,[1] HAEGER P,[2] BRESKY G.[2]
[1] MEDICAL STUDENTS, [2] PROFESSOR
DEPARTMENT OF BIOMEDICAL SCIENCES. FACULTY OF MEDICINE. UNIVERSIDAD CATÓLICA DEL NORTE. COQUIMBO. CHILE.

Introduction. Patients diagnosed with liver cirrhosis (LC) and also minimal hepatic encephalopathy (MHE) are associated with a higher degree of accidentability. LC carries an impairment in the normal sleep-awake cycle, disturbances in behavior, cognition and motor skills. The physiopathology of this events remains uncertain but some studies describe an astrocyte swelling process due to high level of reactive oxygen species (ROS). Abnormal plasma melatonin (MT) levels have also been identified. MT act as "internal synchronizer" for circadian rhythms and also works as a free radicals scavenger which additionally modulates the neuroinflammatory response. Exogenous administration of MT may regulate circadian rhythms and prevent the oxidative damage responsible of astrocyte edema and the further impairment of motor and cognition skills.
Objectives. Study the possible effects of MT in spatial memory acquisition (SMA) and motor skills in Sprague-Dawley rats with carbon tetrachloride (CT) induced LC.
Material and methods. The study included 45 Sprague Dawley rats, divided in 4 groups [G1: LC; G2: LC + MT; G3:MT; G4:Healthy control (HC)]. LC was induced by intraperitoneal injections of CT (0.2 mL/kg). MT was administered during 4 weeks (0.4 mg/kg/day). The SMA process was according the Morris Water Maze protocol. Data were registered by SMART® for a further statistical analysis.
Results. Mean speed: G1: 13.60 ± 1.1 cm/s G2: 18.87 ± 1.1 cm/s; G3: 22.91 ± 0.7 cm/s; G4: 23.43 ± 0.5 cm/s. Whereas CS > MT > CH + MT > CH (p < 0.0001: CS *vs.* CH) (p < 0.01: CH *vs.* CH + MT; CH + MT *vs.* MT) (NS: CS *vs.* MT). Escape Latency: G1: 50.26 ± 3.4 s. G2: 35.37 ± 3.1 s. G3: 20.88 ± 2.9 s. G4: 15.18 ± 6.5 s. Whereas CS < MT < CH + MT < CH (p < 0.001: CS *vs.* CH) (p < 0.01: CH *vs.* CH + MT; CH + MT *vs.* MT) (NS: C *vs.* MT).
Conclusion. Results show a significant improvement Escape Latency and Mean Speed in rats with LC treated with MT in an antioxidant dose. According to the MWM protocol applied, we can establish that MT effect over the Mean Speed is independent from the effect in the Escape Latency. This findings suggests that MT improves cognition and motor skills in rats with LC. MT could be used to manage the neurologic impairments in cirrhotic patients.

03
EFFECTS OF MELATONIN ON CIRRHOSIS SECONDARY BILIARY INDUCED BILIAR DUCT LIGATION IN RATS WISTAR

COLARES J.R.,[1,5,6] SCHEMITT E.G.,[1,5,6] HARTMANN R.M.,[1,5,6] LICKS F.,[3,5,6] SOARES M.C.,[5,6] DAL BOSCO A.,[1,5] FERNANDES S.,[4,5] MARRONI N.P.[1,2,3,5,6]

[1]*PPG EM MEDICINA: CIÊNCIAS MÉDICAS – UFRGS, PORTO ALEGRE, BRAZIL.*
[2]*PPG EM BIOLOGIA CELULAR E MOLECULAR APLICADA À SAÚDE – ULBRA CANOAS, BRAZIL.*
[3]*PPG EM CIÊNCIAS BIOLÓGICAS: FISIOLOGIA - UFRGS, PORTO ALEGRE, BRAZIL.*
[4]*PPG EM MEDICINA: HEPATOLOGIA - UFCSPA, PORTO ALEGRE, BRAZIL.*
[5]*LABORATÓRIO DE HEPATOLOGIA E GASTROENTEROLOGIA EXPERIMENTAL – HCPA, PORTO ALEGRE, BRAZIL.*
[6]*LABORATÓRIO DE ESTRESSE OXIDATIVO E ANTIOXIDANTES – ULBRA, CANOAS, BRAZIL.*

Introduction. Liver cirrhosis is characterized by the appearance of septa and fibrotic nodules. The bile duct ligation (BDL) in rats is an effective experimental model of secondary biliary cirrhosis induction. The melatonin (Mel) has proven to be a potent antioxidant in different experimental models.
Objectives. To investigate the effects of Mel on cirrhosis induced by BDL.
Material and methods. Thirty-two Wistar rats were used (± 300 g), divided into four groups: CO, CO + Mel, BDL and BLD + Mel. Mel (20 mg/kg) was administered from the 15th day after the BDL. On day 29th, blood, liver and spleen were collected for different analyzes.
Results. ALT, AST and ALP are presented increased in BDL group when compared to the control groups ($p < 0.001$) and we observed a significant decrease in BDL + Mel group. The hepatosomatic relation and splenosomatic relation (RHS and RES) showed an increase in the BDL group when compared to CO and CO + Mel groups ($p > 0.001$) and a decrease in the BDL + Mel group ($p < 0.001$). When assessing the lipoperoxidation (LPO), we observed an increase in the BDL group when compared to the control groups ($p < 0.001$) and a reduction in BDL + Mel group ($p < 0.001$). The enzymes SOD and CAT were decreased in BDL group when compared to the control and when administered Mel they increased significantly ($p < 0.01$) in the BDL + Mel group. The GPx, GST and GSH enzyme showed an increase in BDL group when compared to controls ($p < 0.001$) and decreased BDL + Mel group ($p < 0.001$). In the histological analysis of liver tissue (HE and sirius red), we observed a normal and no collagen deposition hepatic parenchyma in control groups, whereas in the BDL group we observed tissue disorganization, presence of inflammatory infiltrate and fibrosis and when administered MeI (BDL + Mel) we observed a reorganization of parenchymal and decreased of fibrosis.
Conclusion. The results suggest a protective effect of melatonin when administered in rats with secondary biliary cirrhosis induced by ligation of the bile duct.

04
EFFECTS OF HIGH AND LOW SODIUM INTAKE ON NAFLD DEVELOPMENT IN MICE

ARAB J.P.,[1] SOLIS N.,[1] PIZARRO,[1] CABRERA D.,[1] ASPICHUETA P.,[3] RIQUELME A.,[1] BAUDRAND R.,[2] BARRERA F.,[1] ARRESE M.[1]

[1]*GASTROENTEROLOGY & HEPATOLOGY, SCHOOL OF MEDICINE, PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE, SANTIAGO, CHILE.*
[2]*ENDOCRINOLOGY, SCHOOL OF MEDICINE PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE, SANTIAGO, CHILE.*
[3]*DEPARTMENT OF PHYSIOLOGY, UNIVERSITY OF THE BASQUE COUNTRY UPV/EHU, LEIOA, SPAIN.*

Background. Nonalcoholic fatty liver disease (NAFLD) is considered the hepatic manifestation of metabolic syndrome (MetS). It is known that a high intake of carbohydrates and sodium is associated with a higher risk of MetS but few studies have assessed the role of sodium intake on NAFLD development.
Aim. To evaluate the effects of high (high-Na^+) and low sodium (low- Na^+) intake on liver injury in experimental models of NAFLD.
Material and methods. C57BL6J mice were fed with high fat diet (HFD) or choline and methionine deficient diet (MCD) with different concentrations of dietary sodium (low-Na^+: 0.03%, high-Na^+: 3%). Hepatic triglyceride and other lipid species content, serum levels of aldosterone, liver histology and hepatic mRNA levels of mineralocorticoid receptor (MR), selected lipogenic enzymes [acetyl-CoA carboxylase (ACC), fatty acid synthase (FAS) and stearoil-CoA desaturase 1 (SCD1)] as well as of pro-inflammatory and pro-fibrotic markers were assessed.
Results. Mice fed a HFD with high-Na+ exhibited a lower HOMA-IR ($p < 0.05$), higher levels of aldosterone ($p = 0.028$), lower percentage of steatosis ($p = 0.04$), lower hepatic triglyceride ($p = 0.008$), diacylglycerol ($p = 0.005$), and non-sterified fatty acid ($p = 0.005$) content as well as lower hepatic MR mRNA levels ($p = 0.01$) compared with mice fed a HFD with low-Na^+. Also, mRNA expression of proinflammatory (tumor necrosis fator-α and monocyte chemoattractant protein-1) and tissue inhibitor of metalloproteinase (TIMP) 1 were also lower than those observed in mice fed a HFD with low-Na^+. In addition, the expression of ACC, FAS and SCD1 was lower in animals fed HFD with high-Na^+. Similar results were observed with the MCD diet model.
Conclusion. High-sodium intake determines a phenotype of less steatosis and reduced expression of proinflammatory and profibrotic markers in HFD and MCD fed mice likely due to reduced lipogenesis. Reduced levels of MR in the liver could play a role in the observed protective effects of high-Na^+ against steatosis development in experimental NAFLD.
Supported by grants from Fondo Nacional de Desarrollo Científico y Tecnológico (FONDECYT) #1150311 to F.B. and #1150327 and CONICYT PIA/Basal PFB12 to M.A.

05
PROTECTIVE EFFECT OF MELATONIN ON CARBON TETRACHLORIDE-INDUCED CHRONIC HEPATOTOXICITY

BONA S.,[1,2,3] MOREIRA A. J.,[2,4] RODRIGUES G.,[2] NODA J.,[2,4] SOARES M.C.,[2] DI NASO F.C.,[2] SILVEIRA T.R.,[2] MARRONI C.A.,[5] MARRONI N.P.[2,3,4,6]

[1]*BOLSISTA DE PÓS-DOUTORADO JÚNIOR – CNPQ.*
[2]*CENTER OF EXPERIMENTAL RESEARCH, HOSPITAL DE CLÍNICAS DE PORTO ALEGRE, PORTO ALEGRE-RS, BRAZIL.*
[3]*POSTGRADUATE PROGRAM IN MEDICAL SCIENCES: MEDICINE, UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, PORTO ALEGRE- RS, BRAZIL.*
[4]*POSTGRADUATE PROGRAM IN BIOLOGICAL SCIENCES: PHYSIOLOGY, UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, PORTO ALEGRE- RS, BRAZIL.*
[5]*POSTGRADUATE PROGRAM IN LIVER DISEASES, UNIVERSIDADE FEDERAL DE CIÊNCIAS DA SAÚDE DE PORTO ALEGRE, PORTO ALEGRE-RS, BRAZIL.*
[6]*POSTGRADUATE PROGRAM IN CELL AND MOLECULAR BIOLOGY APPLIED TO HEALTH, UNIVERSIDADE LUTERANA DO BRASIL, CANOAS- RS, BRAZIL.*

Introduction. Melatonin (MLT) is a antioxidant molecule that is shown to have a beneficial effect in various pathological situations, due to its action against free radicals.
Objectives. To evaluate the effect of MLT on carbon tetrachloride (CCl_4) induced liver injury in rats in terms of oxidative stress, reticular stress, and cell damage.
Material and methods. Twenty male Wistar rats (230 - 250 g) four groups: I: control (CO), II: CO + MLT, III: CCl_4, and IV: CCl_4 + MLT. CCl_4 was administered as follows: ten doses every

five days, ten every four days, and seven every three days. MLT was administered intraperitoneally at a dose of 20 mg/kg from the 10th week to the end of the experiment (16th week). Means and standard deviations (SD) were calculated for all data. Significant differences between means were evaluated by one-way analysis of variance (ANOVA) – Tukey's test. P-values < 0.05 were deemed significant.

Results. MLT was able to reduce the release of liver enzymes in the bloodstream and to decrease oxidative stress in the CCl_4 + MLT group by the decreasing level of thiobarbituric acid reactive substances and increasing superoxide dismutase activity; additionally, it increased the expression of nuclear factor (erythroid-derived 2)-like 2 (Nrf2) and decreased the expression of Kelch-like ECH-associated protein 1 (Keap1). MLT also decreased the expression of the proteins that endoplasmic reticulum stress, i.e., glucose-regulated protein 78 (GRP78) and activating transcription factor 6 (ATF6), as well as of heat shock factor 1 and heat shock protein 70 (HSP 70).

Conclusion. MLT had a hepatoprotective effect in an experimental model of CCl_4-induced liver injury, since it modulated oxidative stress, endoplasmic reticulum stress, and HSP70 expression.

06
ACTION OF GLUTAMINE IN EXPERIMENTAL SEVERE ACUTE LIVER FAILURE

SCHEMITT E.G.,[1] COLARES J.R.,[2] HARTMANN R.M.,[1] SOARES M.C.[1] LICKS F.,[3] SALVI J.O.,[3] MARRONI C.A.,[4] MARRONI N.P.[1,2,3]

[1]POST-GRADUATE PROGRAM IN MEDICAL SCIENCES, MEDICAL SCHOOL, FEDERAL UNIVERSITY OF RIO GRANDE DO SUL, PORTO ALEGRE, BRAZIL.

[2]POST-GRADUATE PROGRAM IN CELLULAR AND MOLECULAR BIOLOGY APPLIED TO HEALTH OF LUTHERAN UNIVERSITY OF BRAZIL, CANOAS, BRAZIL.

[3]POST-GRADUATE PROGRAM OF PHYSIOLOGY AT THE FEDERAL UNIVERSITY OF RIO GRANDE DO SUL, PORTO ALEGRE, BRAZIL.

[4]POST-GRADUATE PROGRAM IN HEPATOLOGY, FEDERAL UNIVERSITY OF HEALTH SCIENCES OF PORTO ALEGRE, BRAZIL.

Introduction. Severe acute liver failure is a syndrome which leads to functional impairment of the liver. The thioacetamide is a xenobiotic that causes liver damage. Glutamine is an amino acid involved in the synthesis of glutathione.

Objectives. To assess the hepatotoxic effect of thioacetamide and anti-inflammatory action of glutamine.

Material and methods. CEUA project/HCPA: 12-0116. 28 rats were divided into 4 groups: control (CO), glutamine (G), thioacetamide (TAA), glutamine + thioacetamide (TAA + G). TAA doses were administered (400 mg/kg ip) with an interval of 8 h. The glutamine (25 mg/kg ip) was administered 30 min after the last dose of TAA. 24 h after the beginning of the experiment, the animals were anesthetized and killed. Blood samples were collected to assess the levels of AST, ALT and AP. The liver was removed for analysis interleukins (Assay kits using Luminex®technology by Invitrogen™) and immunohistochemical evaluation of NF-κB, TNF-α and iNOS. Statistical analysis was ANOVA + Student-Newman-Keuls (mean ± SE) being significant $P < 0.05$.

Results. There was an increase in AST, ALT and AP levels in TAA group (598.89 ± 39.45, 298.47 ± 9.12 and 58.78 ± 2.69 U/L) relative to groups CO and G and a decrease in the TAA + G group ($P < 0.001$). IL-1β increased in TAA group relative to groups CO and G and decreased in the group TAA + G ($P < 0.001$). IL-6 increased in TAA group relative to groups CO and G and decreased in the group TAA + G ($P < 0.01$). A increase IL-10 was observed in the TAA group in relation to the CO group and G and an decrease in TAA + G group ($P < 0.01$). Immunohistochemical expression of NF-κB, TNF-α and iNOS in animals exposed to TAA showed the highest staining for all proteins compared to the control groups. Glutamine treatment led to decreased expression of the protein in the significantly TAA + G group.

Conclusion. Glutamine has been shown to have anti-inflammatory effects against liver damage generated by this experimental model thioacetamide.

07
EFFECTS OF ROSEHIP OIL (ROSA RUBIGINOSA) SUPPLEMENTATION ON TRANSIENT STEATOSIS IN LIVER REGENERATION AFTER PARTIAL HEPATECTOMY IN RATS

GUINEZ D.,[2] ROMANQUE P.,[2] TAPIA G.,[1] ZAPATA M.,[2] MANDIOLA C.[3]

[1]CLINICAL PHARMACOLOGY, UNIVERSITY OF CHILE, SANTIAGO, CHILE.

[2]PHYSIOPATHOLOGY, UNIVERSITY OF CHILE, SANTIAGO, CHILE.

[3]SURGERY, CLINICAL HOSPITAL, UNIVERSITY OF CHILE, SANTIAGO, CHILE.

Introduction. Liver regeneration is a complex and tightly regulated process of liver growth in response to liver mass loss. transient steatosis occurs during the process, and its meaning is not completely understood. There is limited and contradictory evidence about the effect of long chain polyunsaturated fatty acids (lcpufa) ω-3 on liver regeneration. Rosehip oil (ro) is a rich source of α-linolenic acid (ala), precursor of lcpufa ω-3 and antioxidants.

Objective. We proposed that rosehip supplementation, prior partial hepatectomy (ph) change the lipid profile on transient steatosis seen in liver regeneration with an impact on liver growth.

Material and methods. Sprague-dawley rats received ro (1 gr/kg/day ala) or saline solution (control group) for 21 days prior 70% ph or sham surgery. 3, 6, 24 and 120 h after surgery, animals were sacrificed, and liver tissues harvested (n = 6, per group and time). Analysis of liver regeneration included liver to body weight ratio, mitotic index and cyclin d1 mrna expression. Transient steatosis analysis included qualitative estimation of steatosis in histological sections and liver lipid profile by chromatography. all experiments were conducted in accordance to the "guide for care and use of laboratory animal". Data are reported as mean ± sem. comparisons between groups were conducted using a Mann-Whitney test. Significance $p < 0.05$.

Results. Proliferative response to ph was not impaired in animals supplemented with ro compared with control group at 120 h post ph, although animals supplemented with ro exhibited a modest but significant delay on recovering ratio of liver weight to body weight at 24 h post ph (1.77 ± 0.02% *vs.* 2.18 ± 0.07%, $p < 0.01$). At this time after ph no mitotic figures were found on the supplemented group compared with control group (0.73 ± 0.26 *vs.* 0.00 ± 0.003 mitosis/ high-power field, $p < 0.05$), but exhibited augmented hepatic cyclin d1 expression (3.02 ± 0.6 *vs.* 49.76 ± 4.09 relative mrna expression, $p < 0.05$). Liver transient steatosis, was present on ro and saline groups at 24 h post hpx. higher levels of ala and eicosapentaenoic acid (epa) in the supplemented ro sham group compared to saline sham group. Similar trend was observed when comparing levels of ala, epa on groups under hpx.

Conclusion. The rosehip oil supplementation previous a two-thirds ph delays liver proliferation without impairment of reaching an optimal ratio of liver to body weight. This findings are not associated with changes on lipid liver profile and might be explained by the antioxidant components of rosehip oil. The biological significance of these results require further studies.

08
MELATONIN DECREASED OXIDATIVE DAMAGE AND ACTIVATES APOPTOSIS IN LIVER CARCINOGENESIS INDUCED BY DIETHYLNITROSAMINE IN RATS

MOREIRA A.J.,[1] RODRIGUES G.R.,[1] BONA S.,[1,2] NODA J.M.,[1] CERSKI C.T.,[1] PICADA J.N.,[3] MARRONI C.A.,[4] MARRONI N.P.[1,3]
[1]CENTER OF EXPERIMENTAL RESEARCH, HOSPITAL DE CLÍNICAS DE PORTO ALEGRE, PORTO ALEGRE, RS, BRAZIL.
[2]POSTDOCTORAL JUNIOR - CNPQ.
[3]POS GRADUATE PROGRAM IN CELL AND MOLECULAR BIOLOGY APPLIED TO HEALTH, UNIVERSIDADE LUTERANA DO BRASIL (ULBRA), CANOAS, RS, BRAZIL.
[4]UNIVERSIDADE FEDERAL DA CIÊNCIAS DA SAÚDE DE PORTO ALEGRE (UFCSPA), PORTO ALEGRE, RS, BRAZIL.

Introduction. Hepatocellular carcinoma (HCC) is the fourth most frequent cause of cancer death.
Aim. To evaluate the effects of melatonin (Mel) on oxidative stress, endoplasmic reticulum (ER) stress and apoptosis during hepatocarcinogenesis.
Material and methods. For the experimental protocol, Wistar male rats (145-150 g) received diethylnitrosamine (DEN) (50 mg/kg) intraperitoneally (i.p) and a single dose of 2-acetylaminofluorene (100 mg/kg). The animals were divided into three groups: Control (CO): just received the vehicle; DEN50: 50 mg/kg DEN i.p. twice a week for the first six weeks and once a week from weeks 11 to 13; DEN+Mel: received 50 mg/kg DEN and Mel (20 mg/L) from the 12th to the 19th week. After 19 weeks liver samples were removed for analysis.
Results. Animals of the group DEN50 developed advance HCC and an increase in expression of pro-inflammatory proteins (iNOS, COX-2 e NFκB). When the animals were treated with Mel histological samples showed cirrhotic pattern and a decrease in these pro-inflammatory proteins. As for the oxidative stress, DEN50 group showed low lipid peroxidation, more protein oxidation, reduced activity of superoxide dismutase (SOD) and higher rate of DNA damage. Mel treatment resulted in a significant reduced in a protein oxidation and DNA damage and increased activity of SOD. Finally, referring to the ER stress and apoptosis, animals DEN50 showed no activation of reticulum stress proteins (BiP, ATF6 and CHOP) as well as no triggered apoptotic routes. However, animals treated with Mel were significantly increased in the expression of proteins BiP, CHOP and ATF6, as much as pro-apoptotic proteins.
Conclusion. Our results suggest that Mel, during the process of experimental hepatocarcinogenesis, acts an anti-inflammatory, antioxidant and pro-apoptotic. These actions contributed to prevent the progression of HCC.

09
THE HYPOXIA-MIMETIC AGENT COCL2 INDUCES PROINFLAMMATORY AND PROFIBROTIC SIGNALS AS WELL AS INFLAMMASOME ACTIVATION IN LIVER CELLS

HERNÁNDEZ A., CABRERA D., BARRERA F., ARRESE M.
DEPARTMENT OF GASTROENTEROLOGY, SCHOOL OF MEDICINE, CATHOLIC UNIVERSITY OF CHILE, SANTIAGO, CHILE.

Background. Clinical observations made in patients with syndrome obstructive sleep apnea (OSA) suggest that intermittent hypoxia may contribute to nonalcoholic steatohepatitis (NASH) development through induction of the hypoxia inducible factor 1α (HIF1α). In addition, sterile inflammation and activation of the inflammasome seem to play a role in NASH.
Aim. To explore whether hypoxia modulates inflammatory and fibrogenic responses in an *in vitro* model of NASH.
Material and methods. Huh-7 cells were incubated with 250 μM palmitic acid and 500 μM oleic acid for 24 h. Then, chemical hypoxia was induced by incubation with 200 mM Cobalt (II) Chloride (CoCl2) for 24 h. We assessed the expression of selected proinflammatory cytokines [interleukin 1β, interleukin 18, tumor necrosis factor-α and interferon-γ] and profibrotic markers [transforming growth factor (TGF) β1, Collagen A1 (ColA1), Tissue inhibitor of metalloproteinase (TIMP) 1, Connective tissue growth factor (CTGF) and α-smooth muscle actin] as well as inflammasome components by RT-qPCR and Western Blot.
Results. In all exposed cells CoCl2 treatment was associated with a significant (about 5-fold) increase in protein levels of HIF1α. Also, CoCl2 increased the number but decreased the size of intracellular lipid droplets in lipid loaded cells as assessed by Nile Red technique. Combined treatment of palmitic acid/oleic acid and CoCl2 resulted in a significantly increased expression of IL1β (8 fold) and TNFα (10-fold) as well as in upregulation of the profibrogenic cytokine CTGF and the metalloproteinase inhibitor TIMP1. In addition, CoCl2 treatment was associated with an increased expression of both ASC and NRLP3 ($p < 0.05$) and with a significant increase in caspase 1 protein levels (1,5 fold, $p < 0.01$).
Conclusion. Chemical hypoxia promotes inflammatory and fibrogenic responses in hepatic cells, as well as inflammasome activation in na *in vitro* model of NASH. The latter may be involved in liver injury observed in OSA.
Supported by grants from Fondo Nacional de Desarrollo Científico y Tecnológico (FONDECYT) #1150311 to F.B. and #1150327 and CONICYT PIA/Basal PFB12 to M.A.

10
N-ACETYLCYSTEINE PROTECTS THE INTESTINAL MUCOSA OF INFLAMMATORY AND OXIDATIVE DAMAGE IN AN ANIMAL MODEL OF PORTAL HYPERTENSION

LICKS F.,[1] HARTMANN R.M.,[2] SCHEMITT E.,[2] COLARES J.R.,[2] FILLMANN H.,[3] MARRONI N.P.[1,2,4]
[1]UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, PROGRAMA DE PÓS GRADUAÇÃO EM CIÊNCIAS BIOLÓGICAS: FISIOLOGIA, PORTO ALEGRE, BRAZIL.
[2]UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, PROGRAMA DE PÓS GRADUAÇÃO EM MEDICINA: CIÊNCIAS MÉDICAS, PORTO ALEGRE, BRAZIL.
[3]PONTIFÍCIA UNIVERSIDADE CATÓLICA DO RIO GRANDE DO SUL, PORTO ALEGRE, BRASIL.
[4]UNIVERSIDADE LUTERANA DO BRAZIL, PROGRAMA DE PÓS GRADUAÇÃO EM BIOSAÚDE, CANOAS, BRAZIL.

Introduction. Portal hypertension (PH) is a disease caused by an obstruction in the portal system and progressively increased portal pressure, characterized by a portal vasodilation. The gut is one of the severely affected organs in this syndrome. N-acetylcysteine (NAC) is an antioxidant and anti-inflammatory molecule, widely used in clinic, and a good candidate for the treatment of portal hypertension.
Objective. To investigate the effects of NAC on portal hypertensive rats.
Material and methods. Eighteen rats Wistar were divided into three groups (n = 6): sham - operated (SO), partial portal vein ligature (PPVL), PPVL + NAC. On the 8th day after surgery, N-acetylcysteine (10 mg /kg,ip) was administered daily for 7 days. On the 15th day we collected the intestines for oxidative stress analysis, immunohistochemistry and Western blot. Intestinal lipid peroxidation was evaluated by TBARS technique, and the activities of antioxidant enzymes superox-

ide dismutase (SOD) and glutathione peroxidase (GPx) were assessed. We also evaluated NF-κB and TNF-α expression by immunohistochemistry and iNOS expression by Western blot.
Results. We observed an increase in oxidative stress in the intestinal tissue of rats of PPVL group when compared to SO, being NAC effective in reducing this parameter in PPVL + NAC group. We also observed a reduction in the activity of SOD and GPx enzymes in the PPVL group, and in the PPVL + NAC group the activity of both were restored. We observed an increased expression of NF-κB and TNF-α in PPVL group as well as an increase in iNOS expression assessed by Western blot. NAC was able to reduce the expression of all proteins evaluated.
Conclusion. With these results we suggest the anti-inflammatory action and antioxidant NAC in the intestine of animals submitted to the experimental model of portal hypertension.
This study received financial support from the Incentive Fund for Research and Events (FIPE Project No. 11-0293) of Hospital de Clínicas de Porto Alegre (HCPA).

G. FATTY LIVER, ALCOHOLIC HEPATITIS, NON-INVASIVE DIAGNOSIS OF LIVER FIBROSIS

01
MULTI-PARAMETRIC ULTRASOUND (mp-US) PARADIGM IN THE CHRONIC DIFFUSE LIVER DISEASE DIAGNOSIS

DYNNYK O.,[1] FEDUSENKO O.,[2] KOBYLIAK N.[3]
[1]BOGOMOLETS INSTITUTE OF PHYSIOLOGY OF THE UKRAINIAN NATIONAL ACADEMY OF SCIENCES, KYIV, UKRAINE.
[2]NATIONAL MEDICAL POSTGRADUATE ACADEMY, KYIV, UKRAINE.
[3]BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE.

Introduction. Numerous ultrasound (US) technology are based on different physical principles for evaluation of acoustic, mechanical and hydrodynamic properties of the liver and it circulation.
Aims. To investigate in real time, for one moment and in one patient the basic principles of multi-parametric ultrasound (mp-US) assessment complex for chronic diffuse liver diseases (CDLD) diagnosis.
Materials and methods. The study was conducted from 2015 to 2016 and totally 2,352 patients of both sexes with CDLD were included. For all these patients mp-US measurement were performed on SoneusP7 device (Ultrasign, Ukraine) and Angiodin-Sono/P-Ultra (Bioss, Russia), with a 1-6 MHz convex transducer in the right and left lobes. Each measurement divided on 4 sets of parameter assessment. The first include: biometrics of liver and related organs in B-mode; second – liver and splanchnic vessels Doppler architectonics and blood flow velocity assessment; third – liver stiffness measurement by Shear-Wave Elastography (kPa); forth – hepatic steatosis assessment using original algorithm for US attenuation coefficient measurement – ACM (patent UA N° 2014 111234).
Results. A valid mp-US measurement in one patient examination is possible to apply with evaluation of involving organs and splanchnic blood flow. Difficulties have arisen in 22 "difficult" for US assessment patients. Using this approach the following syndromes were evaluated: hepato- and splenomegaly, portal hypertension, fibrosis and steatosis staging, changes of liver parenchyma structure.
Conclusion. Liver mp-US is available and economically viable, provides clinicians with a complete pattern of the disease in the one patient simultaneously, eliminating the numerous of visits and should become routine for the diagnosis CDLD.

02
ATTENUATION COEFFICIENT MEASUREMENT (ACM) AS NOVEL REAL TIME ULTRASOUND APPROACH FOR HEPATIC STEATOSIS: FROM ACCURACY TO COMPARISON WITH OTHER TECHNIQUE

DYNNYK O.,[1] KOBYLIAK N.,[2] FEDUSENKO O.[3]
[1]BOGOMOLETS INSTITUTE OF PHYSIOLOGY OF THE UKRAINIAN NATIONAL ACADEMY OF SCIENCES, KYIV, UKRAINE.
[2]BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE.
[3]SHUPYK NATIONAL MEDICAL ACADEMY OF POSTGRADUATE EDUCATION, KYIV, UKRAINE.

Introduction. The presence of fat droplets in the hepatocytes (micro- or macrovesicular hepatic steatosis) under condition of chronic diffuse liver disease (CDLD) increases the attenuation of ultrasound (US). A group of Ukrainian scientists proposed an original algorithm for real-time US attenuation measurement (attenuation coefficient measurement – ACM – patent UA N° 2014 111234).
Materials and methods. From total of 3274 patients who underwent to comprehensive abdominal US (2015-2016) in our clinic, 949 have been diagnosed with fatty liver according to Hamaguchi criteria. All these patient we provide ACM (dB/cm) measurement on SoneusP7 device (Ultrasign, Ukraine), with a 1-6 MHz convex transducer in the right and left lobes. For diagnostic accuracy assessment (used CT as standard) and comparison with CAP measured by Fibroscan (Echosens, France) we included 142 patients for subanalysis. Evaluation of diagnostic accuracy of ACM performed using ROC-analysis.
Results. Depending on the stage of steatosis according to B-mode median, 25 and 75 quartiles for ACM were as follows: control group 1.57 (1.32-1.85); S1 – 1.86 (1.78 – 2.11); S2 – 2.26 (2.20-2.49) and respectively for S3 - 2,7 (2.40-2.82) dB/cm. ACM value increase parallel the hepatic steatosis progression ($p < 0.001$), which was also accompanied with presence of very strong correlation between these parameters ($r = 0.814$, $p < 0.001$). The AUROC of ACM for steatosis diagnosis was 0.919 (95% CI 0.854-0.985). The optimal cutoff point was > 1.99 dB/cm, with sensitivity, specificity, PPV and NPV respectively 74.4%, 96.3%, 72.2% and 96.6%. ACM value also significantly correlated with CAP ($r = 0.630$, $p < 0.001$).
Conclusion. The ACM as novel real time ultrasound approach can be used for noninvasive hepatic steatosis diagnosis, allows clinicians to monitor disease progression and response to treatment.

03
ASSOCIATION BETWEEN *TM6SF2 rs58542926* POLYMORPHISM AND RISK OF FATTY LIVER AND HEPATIC FIBROSIS IN CHILEAN PATIENTS WITH CHRONIC HEPATITIS C

VENEGAS M.,[1] URZÚA A.,[1] MEZZANO G.,[1] BRAHM J.,[1] PONIACHIK J.,[1] MIRANDA J.,[1] CÁCERES D.D.,[2] ARANCIBIA J.P.,[1] GONZÁLEZ K.,[1] CARREÑO L.[3]

[1]*SECCIÓN DE GASTROENTEROLOGÍA, DEPARTAMENTO DE MEDICINA, HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE.*

[2]*PROGRAMA DE SALUD AMBIENTAL, ESCUELA DE SALUD PÚBLICA, FACULTAD DE MEDICINA, UNIVERSIDAD DE CHILE AND*

[3]*DEPARTAMENTO DE ANATOMÍA PATOLÓGICA, HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.*

Background and aim. Recently, the rs58542926 C>T genetic variant of the transmembrane 6 superfamily member 2 (TM6SF2) gene, which encodes E167K amino acidic substitution, has been identified as a determinant of hepatic fat content and fibrosis progression in patients with non-alcoholic fatty liver disease. Only a few data have been published to date on this topic in chronic hepatitis C. We studied the impact of *TM6SF2 rs58542926* polymorphism on risk of liver steatosis and fibrosis in Chilean patients with chronic hepatitis C (CHC) infection.

Materials and methods. A total of 153 biopsied CHC patients were genotyped for *TM6SF2 rs58542926* using PCR-RFLP methodology. The risk on fatty liver was assessed comparing absence (< 5 %, n = 73) with presence (≥ 5 % = 80) of steatosis. The association with fibrosis was assessed according to METAVIR score, comparing patients with either no fibrosis, mild fibrosis, or intermediate fibrosis (F0-F1-F2, n = 98), with patients with severe fibrosis or cirrhosis (F3-F4, n = 55).

Results. The *rs58542926* genotype CC was found in 64 (87.7%) patients without steatosis, whereas genotypes CT was found in 9 (12.3%). In patients with steatosis, the distribution of *rs58542926* genotype was 74 CC (92.5%) and 6 CT (7.5%). No statistical association was observed (OR 0.58, 95% CI 0.19-1.71, p = 0.32). In patients with METAVIR score F0-F1-F2, *rs58542926* genotype CC was found in 88 (89.8%) and genotype CT in 10 (10.2%), whereas in patients F3-F4, genotype CC and CT were determinated in 50 (90.9%) and 5 (9.1%) patients, respectively. There was no statistical association (OR 0.88, 95% CI 0.28-2.72, p = 0.824).

Conclusions. *TM6SF2 rs58542926* polymorphism is not associated with risk of liver steatosis or fibrosis stage in Chilean patients with CHC.

Grant support: OAIC 747/15 to M.V.

04
ASSOCIATION BETWEEN *PNPLA3 rs738409* POLYMORPHISM AND RISK OF FATTY LIVER AND HEPATIC FIBROSIS IN CHILEAN PATIENTS WITH CHRONIC HEPATITIS C

VENEGAS M.,[1] MEZZANO G.,[1] URZÚA A.,[1] BRAHM J.,[1] PONIACHIK J.,[1] MIRANDA J.,[1] CÁCERES D.,[2] ARANCIBIA J.P.,[1] GONZÁLEZ K.,[1] CARREÑO L.[3]

[1]*SECCIÓN DE GASTROENTEROLOGÍA, DEPARTAMENTO DE MEDICINA, HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE.*

[2]*PROGRAMA DE SALUD AMBIENTAL, ESCUELA DE SALUD PÚBLICA, FACULTAD DE MEDICINA, UNIVERSIDAD DE CHILE AND*

[3]*DEPARTAMENTO DE ANATOMÍA PATOLÓGICA, HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.*

Background and aim. The patatin-like phospholipase-3 *(PNPLA3)* gene polymorphism rs738409 C>G encoding for the I148M protein variant, is associated with steatosis and severity of fibrosis in nonalcoholic fatty liver disease. The association of *PNPLA3* rs738409 polymorphism with HCV related liver disease severity is controversial. We studied the impact of this polymorphism on risk of liver fat and fibrosis in Chilean patients with chronic hepatitis C (CHC).

Materials and methods. A total of 144 biopsied CHC patients were genotyped for *PNPLA3* rs738409 using PCR-RFLP methodology. The effect on risk of fatty liver was assessed comparing absence (< 5%, n = 67) with presence (≥ 5%, n = 77) of steatosis. The risk association with fibrosis was assessed according to METAVIR score, comparing patients with either no fibrosis, mild fibrosis, or intermediate fibrosis (F0-F1-F2, n = 90), with patients with severe fibrosis or cirrhosis (F3-F4, n = 54).

Results. The *rs738409* genotype GG was found in 30 (44.8%) patients without steatosis, whereas genotypes GC and CC were found in 14 (20.9 %) and 23 (34.3%), respectively. In patients with steatosis, the distribution was 49 GG (63.6%), 14 GC (18.2%) and CC (18.2%). There was statistical association between CC v/s GG PNPLA3 variants and steatosis (OR 2.62, 95% CI 1.13-6.05; p = 0.021). In patients with METAVIR score F0-F1-F2, *rs738409* genotype GG was found in 47 (52.2%), GC in 18 (20%) and CC in 25 (27.8%), whereas in patients F3-F4, genotype GG, GC and CC were determinated in 32 (59.3%), 10 (18.5%) and 12 (22.2%) patients, respectively. There was no statistical association between PNPLA3 genotype and fibrosis stage.

Conclusions. The *rs738409 PNPLA3* genotype influences the risk of steatosis in CHC but it is not associated with risk of liver fibrosis in Chilean patients.

05
ASSOCIATION BETWEEN INTERFERON-λ*4 rs12979860* POLYMORPHISM AND RISK OF LIVER FIBROSIS IN CHILEAN PATIENTS WITH CHRONIC HEPATITIS C

ARANEDA G.,[1] BRAHM J.,[1] PONIACHIK J.,[1] MIRANDA J.,[1] CÁCERES D.D.,[2] ARANCIBIA J.P.,[1] GONZÁLEZ K.,[1] CARREÑO L.,[3] VENEGAS M.[1]

[1]*SECCIÓN DE GASTROENTEROLOGÍA, DEPARTAMENTO DE MEDICINA, HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE.*

[2]*PROGRAMA DE SALUD AMBIENTAL, ESCUELA DE SALUD PÚBLICA, FACULTAD DE MEDICINA, UNIVERSIDAD DE CHILE, AND*

[3]*DEPARTAMENTO DE ANATOMÍA PATOLÓGICA, HOSPITAL CLÍNICO UNIVERSIDAD DE CHILE, SANTIAGO, CHILE.*

Background and aim. Several factors have been recognized as being associated with the progression of liver fibrosis in patients with chronic hepatitis C (CHC). As liver fibrosis progression remains variable between individuals with similar environmental or virological risks, host genetic predispositions have been suggested as another critical determinant. Contradictory data exist on the association between Interferon-λ 4 (IFNL4) *rs12979860* polymorphism (formerly named IL28B) and liver fibrosis in CHC. The aim of this study was to assess the impact of *IFNL4 rs12979860* polymorphism on risk of fibrosis in Chilean patients with CHC.

Material and methods. A total of 150 biopsied CHC patients were genotyped for *IFNL4 rs12979860* using real time PCR methodology. The risk association between *IFNL4 rs12979860* genotype with fibrosis was assessed according to METAVIR score, comparing patients with either no fibrosis, mild fibrosis, or intermediate fibrosis (Group 1 = F0 + F1 + F2, n = 96), with patients with severe fibrosis or cirrhosis (Group 2 = F3 + F4, n = 54).

Results. In group 1, *rs12979860* genotype CC was found in 22 (22.9%), whereas genotypes CT and TT were found in 57 (59.4 %) and 17 (17.7%), respectively. In group 2, the distribution of rs12979860 genotypes was 10 CC (18.5%), 29 CT (53.7%) and 15 TT (27.8%). There was not statistical association between *IFNL4 rs12979860* polymorphism and fibrosis (CC v/s CT OR 1.12, 95% CI 0.47-2.68, p = 0.81; CC v/s TT OR 1.94, 95% CI 0.68-5.5, p = 0.2).
Conclusions. The *IFNL4 rs12979860* genotype is not associated with risk of liver fibrosis in Chilean patients with CHC.

06
VALIDATION OF FOUR SCORING MODELS FOR SHORT-TERM MORTALITY IN ALCOHOLIC HEPATITIS

ARAUJO R.C., ALMEIDA P.H., OLIVEIRA B.B.M., MARTINELLI A.L.C.
GASTROENTEROLOGY DEPARTMENT - HOSPITAL DAS CLINICAS, FACULTY OF MEDICINE, UNIVERSITY OF SÃO PAULO, RIBEIRÃO PRETO, SÃO PAULO, BRAZIL.

Introduction. Several prognostic models have emerged in alcoholic hepatitis (AH), but lack of external validation precludes their universal use.
Objective. To analyze the applicability of model for end-stage liver disease (MELD), age-bilirubin-INR-creatinine(ABIC), Glasgow alcoholic hepatitis score(GAHS) and Maddrey's discrimination function index as prognostic scores and to compare their accuracy to predict mortality during hospitalization in patients with AH.
Material and methods. Data from 89 AH patients was retrospectively assessed. Prognostic scores were calculated on the 1st day of hospital admission (1st Day) and after seven days (7th Day). Short-term mortality was assessed at the end of hospitalization. Receiver operation characteristic curve(ROC) was performed and the area under the ROC curve(AUC) was calculated on the 1st and 7th Day.
Results. Seventy-nine patients (87.8%) were male, and mean age was 44.5 ± 11 years. Mortality rate during hospitalization was 23.3%. At admission, all scores were associated with mortality, in the univariate analysis (P < 0.05). At the 7th Day, only Maddrey (P = 0.006) and MELD (P < 0.001) were associated with mortality. The AUC for mortality rate on the 1st Day, was 0.70(95%CI: 0.56-0.84) for MELD; 0.69(95%CI: 0.55-0.82) for Maddrey, 0.69 (95%CI: 0.55-0.82) for GAHS and 0.67(95%CI: 0.54-0.80) for ABIC. The AUC for mortality on the 7th Day was 0.804 (95%CI: 0.68-0.92) for MELD; 0.73 (95%CI: 0.58-0.88) for Maddrey; 0.67(95%CI: 0.50-0.83) for ABIC and 0.64(95%CI: 0.47-0.81) for GAHS. In the multivariable analyses, GAHS on the 1st Day was the only score that was an independent predictor of mortality.
Conclusion. All four scores models proved to be valid in predicting AH mortality during hospitalization. GAHS on the 1st Day was the only independent predictor. Higher accuracy was observed on the 7th Day of hospitalization. These scores represent valuable tools to stratify patients by mortality risk at hospitalization and they should be used to manage AH patients.

07
NON-ALCOHOLIC FATTY LIVER DISEASE IS ASSOCIATED TO SARCOPENIA AND DECREASED SERUM IGF-1 LEVELS

CABRERA D.,[1,2,3] RUIZ A.,[4] CABELLO-VERRUGIO C.,[5,6] BRANDAN E.,[3,7] ESTRADA L.,[2] PIZARRO M.,[1] SOLIS N.,[1] TORRES N.,[8] BARRERA F.,[1] ARRESE M.[1]
[1]DEPARTAMENTO DE GASTROENTEROLOGÍA, FACULTAD DE MEDICINA, PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE, CHILE.
[2]DEPARTAMENTO DE CIENCIAS QUÍMICAS Y BIOLÓGICAS, FACULTAD DE SALUD, UNIVERSIDAD BERNARDO O´HIGGINS, CHILE.
[3]CENTRO DE REGENERACIÓN Y ENVEJECIMIENTO (CARE), PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE.
[4]INSTITUTO DE MEDICINA, FACULTAD DE MEDICINA, UNIVERSIDAD AUSTRAL DE CHILE.
[5]DEPARTAMENTO DE CIENCIAS BIOLÓGICAS, FACULTAD DE CIENCIAS BIOLÓGICAS & FACULTAD DE MEDICINA, UNIVERSIDAD ANDRÉS BELLO, CHILE.
[6]MILLENNIUM INSTITUTE ON IMMUNOLOGY AND IMMUNOTHERAPY. SANTIAGO, CHILE.
[7]LABORATORIO DE DIFERENCIACIÓN CELULAR Y PATOLOGÍA, DEPARTAMENTO DE BIOLOGÍA CELULAR Y MOLECULAR, MIFAB, PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE. SANTIAGO, CHILE. [8]DEPARTAMENTO DE PATOLOGÍA, FACULTAD DE MEDICINA, PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE, CHILE.

Background. Decreased muscle mass or sarcopenia has been associated to nonalcoholic fatty liver disease (NAFLD). However, the functional consequences of this association and its pathogenesis remain ill-defined.
Aim. To evaluate muscle mass and function in a diet-induced NAFLD mouse model and explore its association to changes in serum insulin growth factor-1 (IGF-1).
Material and methods. Weight gain, visceral fat, serum biochemical parameters, liver histology and hepatic triglyceride content (HTC) were assessed in C57/Bl6 mice fed a westernized diet (ALIOS-diet) and fructose-enriched water during 16 weeks. In addition, we determined muscle fiber size and strength of limb skeletal muscle, myosin heavy chain (MHC) protein levels and IGF-1 serum levels.
Results. ALIOS diet was associated with weight gain, increased visceral fat mass (epydidimal pad: 0.76 g ± 0.13 *vs.* 0.33 ± 0.27 g; p = 0.0023), hepatic steatosis (HTC: 118.2 ± 6.88 mg/g liver *vs.* 43.26 ± 5.63 mg/g<, p < 0.05) and a higher NAS score (1.29 ± 0.42 *vs.* 4.00 ± 0.53<, p < 0.05). Compared with control animals ALIOS diet-fed mice had an increased proportion of low-diameter muscle fibers (0-30 ìm) and a decreased proportion of high-diameter muscle fibers (60-90 ìm), which correlated with decreased MHC protein levels, consistent with significant muscle atrophy. Functional studies showed that ALIOS diet-fed mice had reduced muscle strength and lower serum levels of IGF-1 (284.2 ± 20.04 pg/mL) compared with chow-fed mice (366.0 ± 12.42 pg/mL, p < 0.05).
Conclusion. Experimental NAFLD is associated with sarcopenia, decreased muscle strength and reduced IGF-1 serum levels. IGF-1 reduction may be involved in pathogenesis of NAFLD-associated sarcopenia.

08
ROLE OF FCGAMMA RECEPTORS IN EXPERIMENTAL NON-ALCOHOLIC STEATOHEPATITIS

CABRERA D.,[1,3] JARA E.,[2] CRUZ R.,[1] MUÑOZ N.,[2] ROJAS DE SANTIAGO P.,[1] KALERGIS A.,[2] ARRESE M.[1]
[1]DEPARTAMENTO DE GASTROENTEROLOGÍA, FACULTAD DE MEDICINA, PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE, SANTIAGO, CHILE.
[2]DEPARTAMENTO DE GENÉTICA MOLECULAR Y MICROBIOLOGÍA, FACULTAD DE CIENCIAS BIOLÓGICAS, PONTIFICIA UNIVERSIDAD CATÓLICA DE CHILE, SANTIAGO, CHILE.
[3]DEPARTAMENTO DE CIENCIAS QUÍMICO-BIOLÓGICAS, UNIVERSIDAD BERNARDO O HIGGINS, SANTIAGO, CHILE.

Background. The role of innate immunity in Non-alcoholic steatohepatitis (NASH) development is emergent. Different populations of innate immune cells are present in the liver controlling tissue cytokine production through Fc gamma receptors (FcγRs), which are receptors for the Fc region of IgG antibodies. FcγRs cell-type specifically interact with various other receptors for selective amplification or inhibition of particular cytokines.

Aim. To evaluate the role of the inhibitory (FcγRIIB) and activatory (FcgRIII) receptors in NASH pathogenesis.

Material and methods. Wild Type, FcγRIIb (-/-) and FcγRIII (-/-) mice were fed a methionine-choline deficient (MCD) diet for 5 weeks. Liver injury was assessed by measuring serum levels of alanine aminotransferase (ALT) and histologically. Hepatic triglyceride content (HTC) and hepatic mRNA levels of selected pro-inflammatory (TNF-α, IFN-γ, IL-1β, etc.), profibrotic (TGF-β, CTGF, Collagen-1, etc.) and inflammasome (ASC, NLRP3, Caspase-1, etc.) genes were also assessed. Serum pro-inflammatory cytokine levels (TNF-α, IFN-γ, etc.) were determined by cromatographic bead assay (CBA). By flow cytometry was evaluated different populations of inflammatory cells infiltrated in the liver such as dendritic, neutrophils, macrophages and lymphocytes.

Results. FcγRIIb (-/-) MCD-fed mice developed a more robust hepatic inflammatory (decreased hepatic expression of TNFα and other cytokines) and fibrotic response (decreased hepatic expression of collagen I) in comparison with WT MCD-fed mice with no differences in HTC. No differences were found in liver cell populations of lymphoid and myeloid lineages. The main finding in FcγRIII (-/-) MCD-fed mice was a significant reduction in histological steatosis and HTC likely related to reduced interleukin-10 production. Liver lymphoid and myeloid cell populations remained unchanged in these mice.

Conclusion. Our results suggest and important role of the FcγRs in NASH development. While the absence of FcγRIIb seems to promote NASH induction, the absence of FcγRIII strongly reduces liver steatosis. This is the first report that shows a direct role of FcγRs in the pathogenesis of NASH.

Grant support: FONDECYT 1150327 to M.A., PD3140396 to D.A. and CONICYT PIA/Basal PFB12 to M.A.

09
HIGH RATE OF LIVER FIBROSIS IN RELATIVES OF NON-ALCOHOLIC FATTY LIVER DISEASE CIRRHOTIC CHILEAN PATIENTS, A PRELIMINARY COMPARATIVE STUDY

NAVEA C.,[1] FUENTES L.,[1] CHESTA C.,[2] CABELLO N.,[3] GAJARDO A.,[2] GONZALEZ K.,[1] PONIACHIK J.[1]
[1]GASTROENTEROLOGY SECTION.
[2]DEPARTMENT OF INTERNAL MEDICINE.
[3]FACULTY OF MEDICINE, UNIVERSIDAD DE CHILE, HOSPITAL CLÍNICO DE LA UNIVERSIDAD CHILE, SANTIAGO, CHILE.

Introduction. Non-alcoholic fatty liver disease (NAFLD) is a common condition affecting 5 to 20 % of people worldwide and may lead to cirrhosis in up to 5%. Transient elastography (TE) is a non-invasive test used as an alternative to liver biopsy for the assessment of the different degrees of liver fibrosis. Relatives of NAFLD patients are under similar environmental conditions and share genetic heritance, so the risk of developing NAFLD could be higher.

Aim. To measure TE to NAFLD cirrhotic relatives and compare them with other etiologies cirrhotic relatives.

Material and methods. The presence of liver fibrosis through TE in relatives of NAFLD cirrhotic patients (NAFLD group) compared to relatives of other causes cirrhotic patients (control group) was measured. Relatives without known liver disease or history of alcohol consumption were included and demographic data and metabolic risk factors (diabetes mellitus, smoking or others) were recorded. Coefficient of attenuation (CAP), which indirectly suggest liver fatty when is higher than 250 UH, also was measured.

Results. Thirty-two subjects were evaluated. Each group included 16 patients. No differences were observed in demographic data, comorbidities or metabolic risk factors. In the NAFLD group 50% had F1 or higher ranges but in the control group only 12.5% had values for F1 or higher ($p < 0.05$). The NAFLD group showed an O.R = 7 (95% IC: 1.185 - 41.359) to have some degree of liver fibrosis compared with control group. The 90% of subjects with F1 or higher had CAP > 250 *vs*. only 36% in those with F0.

Conclusion. Relatives to NAFLD cirrhotic patients have higher TE values and fatty infiltration than relatives of other causes of cirrhosis patients.

Table 1 (10). Fibrosis, activity, steatosis severity, age and gender according to country and tests.

Country (FT only or FT-ST)	n (% Fibrosis stages F0/F1/F2/F3/F4.1/F4.2/F4.3)	n (% Activity grade A0/A1/A2/A3)	n (Steatosis stage S0/S1/S2/S3)	Age median	% women
Mexico (FT)	12,989 (32/22/9/13/9/11/4)	12,989 (50/24/8/19)	NA	53.8	49.7
Mexico (FT-ST)	5,611 (37/24/8/12/7/9/3)	5,611 (58/22/6/14)	5,611 (22/28/21/29)	54.0	44.7
USA CHC (FT)	252,688 (35/22/10/15/9/8/1)	252,688 (46/24/8/22)	NA	53.0	38.4
USA NAFLD (FT-ST)	37,315 (62/18/6/7/4/3/1)	37,315 (58/23/7/12)	37,315 (15/17/15/53)	53.9	55.9
France (FT)	470,762 (40/23/9/13/7/6/2)	470,762 (54/23/7/16)	NA	50.7	42.6
France (FT-ST)	31,154 (47/24/8/11/5/4/1)	31,154 (62/22/6/10)	31,154 (36/24/16/24)	53.5	38.0

10
SEVERITY OF FIBROSIS, ACTIVITY AND STEATOSIS ASSESSED USING SOFTWARE-COMBINED BIOMARKERS OF LIVER FIBROSIS, NECROINFLAMMATORY ACTIVITY AND STEATOSIS. A PROOF OF CONCEPT COMPARING MEXICAN, USA, AND FRENCH AWARENESS

POO J.L.,[1,2] KERSHENOBICH D.,[1] CORONA C.,[3] DECKMYN O.,[4] MUNTEANU M.,[4] RATZIU V.,[5,6,7] POYNARD T.,[*,5,6, 7,] ON BEHALF OF "FIBRO-MEXICO" GROUP AND "FIBRO-FRANCE" GROUP*

*[1]INSTITUTO TECNOLÓGICO DE ESTUDIOS SUPERIORES DE MONTERREY, [2]INSTITUTO NACIONAL DE CIENCIAS MÉDICAS Y NUTRICIÓN, SALVADOR ZUBIRÁN, [3]BIOMÉDICA DE REFERENCIA, MEXICO, [4]BIOPREDICTIVE, PARIS, FRANCE, [5]GROUPE HOSPITALIER PITIÉ SALPÊTRIÈRE APHP, [6]SORBONNE UNIVERSITÉS, [7]UPMC UNIV PARIS 06, UMR-S 938& INSTITUTE OF CARDIOMETABOLISM AND NUTRITION (ICAN), PARIS, FRANCE. *INSERM. FRANCE.*

Background. The burden of chronic liver diseases could be dramatically reduced given the emergence of highly effective antivirals (DAA) in chronic hepatitis C (CHC) and B (CHB), and promising drugs in NAFLD, together with the availability of liver injury biomarkers. Large-scale screening studies are therefore possible now, but with heterogeneous context among countries.

Aims. We aimed to compare between 3 countries (Mexico, USA and France) the awareness of liver fibrosis (F), activity (A), and steatosis (S), using as estimates the prescription rates of FibroTest (FT), ActiTest (AT), and SteatoTest (ST), respectively.

Material and methods. We constructed a global centralized database of 1,016,557 FT-AT consecutive samples, including 134,148 ST, performed between 2002 and 2014. We compared age, gender, F, A and S spectra from Mexico samples (n = 12,657) to those from USA (n = 252,688) and France (n = 470,762). In USA the indications were separated between CHC investigated by FT-only and NAFLD investigated by FT and ST (FT-ST). In France the indications were wider and mixed, but mostly related to CHC (40%) and CHB (20%). In Mexico the indications were mainly related to CHC, alcoholic liver disease or NAFLD.

Results. See table 1. In Mexico, the investigated subjects either using FT or FT-ST, had higher severity of liver disease *vs.* USA or France subjects, both for the cirrhosis prevalence (FT/FT-ST: 24%/, 19%; 18%, /8%; 15%, /10% respectively), and the severity of cirrhosis with more F4.3; despite this overall increase of severity in Mexico the subjects investigated using FT-only were more often women (50%) than in USA subjects investigated for CHC (38%), suggesting different causes or selection bias. Mexico subject's profiles investigated using FT-ST had less severe profiles (both F stages and cirrhosis severity) than those investigated using FT-only, differences persisting after adjustment on age and gender by multiple regression analysis as observed in USA and France samples. In USA, subjects with CHC (all investigated by FT-AT) had 10% more cirrhosis and 11% more significant activity (A2A3) than NAFLD (All $P < 0.0001$). We were able to show that in the USA, 82.4% (208,174 out of 252,688, [95% CI, 82.2-82.5]) of investigated CHC subjects could be classified according to consensual recommendations, either as the highest priority F3 or F4 (n = 83,058; 32.9% [32.7-33.1]) or the lowest priority F0F1 and A0A1 (n = 125,116; 49.5% [49.3-49.7]). In Mexico similar spectrum was observed 85.4% consensual, including 37.2% highest priority (4,829 out of 12,989) and 48.2% lowest priority (6,255 out of 12,989).

Conclusions. This proof of concept study suggested that it is possible to simply compare the awareness of liver Fibrosis, Activity and Steatosis in different countries using centralized validated biomarkers. In Mexico, patients investigated were more severe than in USA and France. As in USA and France there was less severe Fibrosis and Activity in patients investigated for steatosis than those investigated for fibrosis only. Finally the proportion of Mexico subjects consensually classified as highest priority or lowest priority for expensive treatments (85%) was similar to USA and France proportions.


Annals
of
Hepatology