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POSTER PRESENTATIONS

A. VIRAL HEPATITIS

01

PHYLOGENETIC ANALYSIS OF GENOTYPES OF HEPATITIS B VIRUS CIRCULATING IN AN ENDEMIC AREA OF PERU

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Background. Although hepatitis B virus (HBV) infection is still endemic in Abancay-Peru two decades after vaccination against hepatitis B started in the area, little is known about the diversity and circulation of genotypes and subgenotypes of the virus.

Objective. Identify the diversity of HBV genotypes and subtypes circulating in the endemic area of Abancay, Peru two decades after the start of vaccination in the area.

Material and methods. Study design: Complete genomes of eleven treatment-naïve HBV-infected patients were sequenced and HBV genotypes and subgenotypes were determined. A phylogenetic tree was constructed based on complete genome sequences along with GenBank reference sequences of American countries. The sequences were aligned with Clustal-X and phylogenetic analysis was carried out using the maximum likelihood method with RAxML.

Results. HBV genotyping revealed the presence of genotype F in all samples from Abancay. Subgenotype F1b was dominant (n = 10) and only one isolate belonged to subgenotype F4. The phylogenetic analysis revealed 2 clusters, distinct from any known F1b subgenotypes for Peru, and one sample grouped within this subgenotype. Similarly, the subgenotype F4 sequence does not seem to be closely related to isolates characterized as F4 subgenotypes from Latin American countries.

Conclusions. After two decades post-vaccination hepatitis B, only genotype F of HBV seems to be circulating in Abancay, with predominance of subgenotype F1b. The sequences of these subgenotype are not closely related to each other, suggesting that diverse lineages of this subgenotype may be circulating within this population. Similarly, we identified a subgenotype F4 strain that might represent a novel subgenotype for Peru.

02

GENETIC DIVERSITY OF THE HEPATITIS B VIRUS IN CUBA

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Introduction. Cuba is an HBsAg low-prevalence country with a high coverage of anti-hepatitis B vaccine. Its population is essentially the result of the population mix of Spanish descendants and former African slaves. Information about genetic characteristics of hepatitis B virus (HBV) strains circulating in the country is scarce.

Objectives. To know the genetic diversity of the HBV circulating in Cuba and its relationship with worldwide strains.

Material and methods. The HBV genotypes/subgenotypes, serotypes, mixed infections and S gene mutations of 172 Cuban HBsAg and HBV-DNA positive patients were determined by direct sequencing and phylogenetic analysis.

Results. Phylogenetic analysis of HBV S gene sequences showed a predominance of genotype A (92.4%), subgenotype A2 (84.9%) and A1 (7.6%). Genotype D (7.0%) and subgenotype C1 (0.6%) were also detected but typical (sub)genotypes of contemporary West-Africa (E, A3) were conspicuously absent. All genotype A, D and C strains exhibited sequence characteristics of the adw2, ayw2 and adr_q serotypes, respectively. Thirty-three (19.1%) patients showed single, double or multiple point mutations inside the Major Hydrophilic domain associated with vaccine escape and eighteen (10.5%) patients had mutations in the T-cell epitope. One patient had an HBV A1/A2 mixed infection.

Conclusions. This genetic study of Cuban HBV viruses revealed only strains that were interspersed with strains from particularly Europe, America and Asia. The absence of genotype E supports previous hypotheses about an only recent introduction of this genotype into the general population in Africa. The presence of well-known vaccine escape (3.5%) and viral resistance mutants (2.9%) warrants strain surveillance to guide vaccination and treatment strategies.

03

ANDROID APPLICATIONS FOR VIRAL HEPATITIS DIAGNOSIS, RESEARCH AND TEACHING

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Introduction. Informatics and Communications Technology (ICTs) are valuable tools for information exchange. ICTs can contribute to the technological and scientific development, teaching, and learning and in general to all aspect of modern society. Amongst ICTs, cell phone technology has the necessary qualities that allow its use in laboratories to facilitate the daily work.

Objectives. To design and develop simple, didactic, dynamic, interactive and flexible Android applications for viral hepatitis diagnosis, research and teaching.

Material and methods. For the development of the applications a flexible methodology with the aim to adapt to new platform changes was use. The Android Studio Programming tool was used for the design and development of the applications. Applications can be executed in devices using Android 4.0 platform or superiors.

Results. The application LabCalc was successfully designed and developed. It allows calculation of Polymerase Chain Reaction (PCR) Mix, reagents dilutions (primers) and evaluation of diagnosis assays (sensitivity, specificity, concordance and predictive values). In addition, the text application HepText was also successfully designed and developed. It includes relevant information in regard to the etiology, diagnosis, clinical and epidemiological aspects of viral hepatitis. It also contains the more frequent laboratory techniques used.

Conclusions. The applications LabCalc and HepText were successfully designed and developed and are available for its use. These applications facilitate reagents calculation; the assessment of the analytical performance of in house diagnosis assays standardized in the laboratory and improves the teaching and learning of viral hepatitis.

04

HEPATITIS E: AN UNDERESTIMATED ROLE IN LIVER TRANSPLANTATION?

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Background. HEV infection was not considered a major clinical problem in developed countries until its description of chronic courses in solid organ transplant recipients increasing the awareness for an underestimated disease.

Material and methods. Case report.

Results. Case 1. 37 years-old women, no past medical history, complaints of 2 weeks of jaundice, malaise and nausea. Consumption of pork and green tea over a couple of months. After 24 h of admission developed encephalopathy. LFTs: elevated aminotransferases (> 10 times), cholestasis and elevated INR. HAV, HBV, HCV, CMV, EBV, HIV and leptospirosis were ruled out. ANAS 1/180, AMA/ASMA negative and protein electrophoresis (slightly increase in gamma region). Liver biopsy: Severe panlobular hepatitis, ballooning and ex-

tensive necrosis compatible with autoimmune origin. Right after LT, HEV IgM came back positive. She has been on Ribavirin for 3 months with proper clinical course. Case 2. 60 years-old women, history of LT 3.5 yrs ago due to NASH. 6 months after LT a twist of the graft was documented and surgically corrected. However, persistent elevation of aminotransferases was documented. Acute rejection, biliary and vascular complications were ruled out. Autoimmune markers, HBV, HCV, CMV, EBV and HIV were negative. HEV IgM came back positive. Liver biopsy: chronic hepatitis with mild activity and fibrosis 4/6. MRI confirmed cirrhosis and portal hypertension. Immunosuppressive regimen included MMF 1,500/day, prednisone 10 mg PO, mTOR 2.5 mg PO. Ribavirin was started following the diagnosis.

Conclusions. An increase in the seroprevalence of HEV in patients with autoimmune hepatitis indicates a possible role of the virus in the development of the disease and a more severe clinical course. At the same time, HVE is an underestimated cause of cirrhosis and graft loss following LT.

05

PATIENTS WITH HCV SEEKING CARE IN ARGENTINA AND URUGUAY. PHYSICIAN AND PATIENT'S PERSPECTIVE ACCORDING TO DATA FROM THE MOSAIC STUDY

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Introduction. Chronic hepatitis C virus (HCV) infection negatively impacts patient quality of life (HQL). In contrast with interferon (IFN)-containing regimens, antiviral therapy with direct acting antivirals (DAA) free of IFN have been associated with significantly higher rates of sustained virological response, shorter treatment durations and improved tolerability.

Aim. To describe the demographic, clinical and virological characteristics of HCV patients seeking care among Argentinean and Uruguayan patients included in the Mosaic Study, an international prospective multicenter observational study.

Material and methods. The study had 2 phases: 1) Patients seeking HCV care. 2) Patients initiating IFN-therapy within 12 weeks. Demographics, clinical, virological and histological variables were analyzed at phase 1, and impact of IFN-therapy on HQL, work productivity, activities of daily living, health care use at phase 2.

Results. Forty-one patients were included in Phase 1 and 4 continued to phase 2. Mean age was 56.5 yrs and men accounted for 51% of patients. Eighteen pts (44%) were treatment naïve, and 23(56%) experienced of which 12 were relapsers (52%). Genotype 1 accounted for 73% (30/41) of infection with 1b as the most common sub genotype (16/26, 61%). Portal/septal fibrosis was found in 16 patients (16/36, 44%) with 25% of them having cirrhosis (9/36). Physicians did not recommended IFN-based treatment in 66,6% of patients while 11% of patients declined treatment, mainly due to the expectation for IFN-free treatment options. Four patients received treatment, all 4 with pegylated interferon plus ribavirin. **Conclusions.** Deferral of treatment was frequent, reflecting the evolving paradigm of HCV treatment in the DAA era. The fact that 25% of patients have cirrhosis highlights the medical need for access to novel IFN-free therapies in these Latin-American countries.

06

ADH1B, ADH1C AND CYP2E1 GENOTYPES IN PATIENTS WITH DIAGNOSIS OF CIRRHOSIS AND/OR HEPATOCELLULAR CARCINOMA IN A HOSPITAL OF MEDELLIN CITY, COLOMBIA

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Introduction. A study carried out in a hepatology unit in Medellin city showed that chronic alcohol consumption was the main risk factor for cirrhosis and/or hepatocellular carcinoma (HCC). Studies in some populations around the world suggest a relation between the genetic variants of alcohol dehydrogenase (ADH1) and cytochrome p450 (CYP2E1) and the risk of development of liver disease.

Aim. To characterize the genetic variants of ADH1B, ADH1C and CYP2E1 in a population of patients diagnosed with cirrhosis and/or HCC in a hospital of Medellin city.

Material and methods. Patients with diagnosis of cirrhosis and/or HCC who attended a hospital in Medellin voluntarily agreed to participate in the study. A blood sample was obtained from the patients and DNA extraction was performed using a commercial kit. PCR - RFLP was carried out to determine the polymorphism of ADH1B, ADH1C and CYP2E1 genes. The allelic frequencies were compared with the data available in the 1000 Genomes database for populations from Medellin, Peru and Mexico.

Results. Forty-six samples were collected, 80.4% from patients with cirrhosis, 17.4% with cirrhosis and HCC and 2.2% with HCC. A predominance of females (56.5%) was observed, and the main risk factor were autoimmune diseases (28.9%), followed by chronic alcohol consumption (22.2%). The most common genotypes were ADH1B*1/1 (84%), ADH1C*1/1 (69%) and CYP2E1*C/C (89%). The ADH1B allele frequency between the study population and Peru population showed significant difference.

Conclusion. This study is the first description of ADH1B, ADH1C and CYP2E1 genotypes in patients with cirrhosis and/or HCC from Colombia. The most frequent genotypes in the study population are the same described in Caucasian population. This study establishes a baseline for the development of further investigations in Colombia.

07

RISK FACTORS FOR THE INFECTION WITH THE HEPATITIS C VIRUS IN THE COLOMBIAN CARIBBEAN COAST: A CASE-CONTROL STUDY

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Introduction. It is estimated that 6.8-8.9 million people are infected with the hepatitis C virus in Latin America, from which less than 1% gets antiviral treatment. Until now, studies in Colombia have tried to determine the prevalence of the disease in some risk groups, which has prevented the identification of other factors potentially implied in the infection.

Objectives. To identify risk factors for the chronic infection with the Hepatitis C virus in the Colombian Caribbean coast.

Material and methods. Case-control study (1:3) paired up by Health Company, age (\pm 10 years), done in the first attention level in the gastroenterology and hepatology consult. All patients with a positive ELISA had a confirmatory viral load test done. A multivariate logistic regression analysis identified the independent predictors of infection.

Results. Blood transfusion (OR 159.2; 95% CI 35.4 - 715; $p < 0.001$) and a hospitalization record before 1994 (OR 4.7; 95% CI 1.3 - 17.1; $p = 0.018$) were identified as the only two independent predictors of infection.

Conclusion. It is necessary to confirm the reproducibility of these results and carry out cost-effectiveness studies before recommending its use in the design of new screening strategies.

08

QUALITY OF LIFE (HRQoL) IN PATIENTS WITH CHRONIC HEPATITIS C IN COLOMBIA

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Introduction. Data on the quality of life in Hepatitis C patients are scarce in our context. Up to date, there are no studies that have determined the load of the disease in this population in Colombia.

Objective. To determine the quality of life in chronic Hepatitis C patients and to identify its determinant factors using the SF36V2 questionnaire.

Material and methods. This was an analytic transversal study carried out between 06/01/2015 and 08/31/2015. A trained survey researcher applied the Spanish version SF-36 V2 questionnaire (Qualitometric Inc.) to each one of the patients and collected their epidemiological, clinical and analytical information updated to their date of inclusion in the study. Patients with hepatic encephalopathy or physical or mental limitations to fill out the SF-36V2 were excluded. All patients signed an informed consent before their inclusion in the study. The multivariate linear regression identified the factors related to health related quality of life (HRQoL). Charlson index estimated the weight of comorbidities in the sample.

Results. The sample (41 patients) was made up by a similar number of men and women and the mean for age was 57 years (DE 12.6). In all, 50% of the subjects presented advanced cirrhosis/fibrosis. RCF and RCM were 48.2 and 45.6, respectively. Univariate linear regression analysis identified gender, age, Charlson index and the presence of hepatic cirrhosis as the main determinants of quality of life. Charlson index expressed as a 10-year survival probability was the only independent predictor of the utility index in this study.

Conclusion. Age, gender, and hepatic cirrhosis were identified as the determinants of the health related quality of life. Charlson index was the only independent predictor of SFD6. The implementation of multidisciplinary programs is necessary for the integral treatment of infected patients.

09

FAMILY PHYSICIAN PERSPECTIVES ON HEPATITIS B AND C SCREENING AND DIAGNOSIS IN A MEDIUM-SIZED MUNICIPALITY IN THE CENTRAL AREA OF SÃO PAULO STATE, BRAZIL

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Introduction. Strategies to increase early hepatitis B and C diagnosis and treatment have often been discussed worldwide. There is general agreement regarding the role of primary care providers in identifying hepatitis B and C infected patients in the early stages of disease. However, many issues remain regarding primary care provider's motivations and their knowledge basis for carry out the high-risk populations screening.

Objective. To evaluate family physician's knowledge basis regarding hepatitis B and C screening and diagnosis.

Material and methods. The proposal was to interview all practicing family physicians working in Family Health Teams in São Carlos municipality, using a structured, objective questionnaire containing issues related knowledge about hepatitis B and C screening and diagnosis. This project was approved by the Federal University Research Ethics Committee (number 1.503.883/2016).

Results. Ten family physicians were interviewed, half (five) were man, aged 26-59 (mean: 41). One hundred percent reported open access to rapid test kits for hepatitis B and C diagnosis. According to the international screening recommendations: 90% correctly identified as high risk population man who have sex with man, 80% agreed with screening among intravenous drug users and 60% would among inhaled drugs users. Only 20% correctly identified the HCV and HBV transmission risk through blood transfusions, while 100% failed to identify baby boomers. Concerning the serological interpretation of the following: HBV prior contact, chronic hepatitis B, HBV vaccination and HCV infection, the number of corrected answers were 30%, 40%, 60% and 70%, respectively.

Conclusion. Most family physicians are not up to date with hepatitis B e C screening and diagnosis recommendations. Specific training into primary care settings are needed expand early diagnosis and refer these infected population for treatment.

10

FIVE YEARS REAL-LIFE EXPERIENCE WITH ANTIVIRAL ADHERENCE IN CHRONIC HEPATITIS B INFECTION: A BRAZILIAN COHORT STUDY IN A TERTIARY HOSPITAL

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Background and aims. Chronic hepatitis B (CHB) real-life treatment adherence has been poorly studied worldwide. In this study, we evaluate the causes of non-response to antiviral treatment in CHB subjects.

Material and methods. A prospective cohort study with CHB patients (n=183) treated with adefovir-dipivoxil, entecavir or lamivudine and/or tenofovir-DF was performed in a Brazilian reference tertiary hospital. Treatment adherence was evaluated by a validate questionnaire named CEAT-HBV within three year-periods (2010/2011, 2013/2014 and 2014/2015). Single-dose pharmacokinetics was determined by LC-MS. HBV drug resistance were determined by using standard direct PCR sequencing and ultra-deep pyrosequencing (UDPS). IRB approved the study.

Results. CEAT-HBV identified 104/183 (57%) on HBV treatment adherence. Among 79/183 (43%) subjects with non-adherence to antiviral treatment, 53/79 (67%) were more frequently viral load positive. However, 38% (70/183) had positive viral loads suggesting treatment non-response. Most frequent drug resistance mutations were M204I/V (78%), L180M (59%), L80I (15%), V173L (7%) and Q215H (6%) by the standard direct PCR sequencing method. UDPS showed HBV resistance mutations in 10/54 (19%) that were not detected by the standard method. The main causes associated with nonresponse to antiviral treatment were drug resistance mutations (51%), non-adherence without drug resistance mutations (37%), short treatment duration (8%), and undetermined (4%). Single-dose pharmacokinetics indicated 35% (23/65) antiviral non-adherence. Two years after the first evaluation, the CEAT-HBV indicated that 101/143 (71%) subjects were adhered treatment. However, 21% (40/183) of the subjects could not be evaluated and were excluded. The main reasons for exclusion were death (20/183). All persons received at that time one treatment booklet for guidance. The third (2014/2015) CEAT-HBV evaluation showed that 112/135 (83%) patients were on treatment adherence and 6% (8/143) were excluded.

Conclusions. In the first year-period, non-adherence was high among CHB subjects receiving antiviral treatment. However, the knowledge about drug resistance mutations and non-adherence to anti-HBV therapy promoted antiviral replacement and new interventions to improve antiviral adherence. UDPS was more sensitive than standard direct PCR sequencing method in showing HBV resistance mutations.

11

ESTIMATION OF PREVALENCE OF HEPATITIS E VIRUS ANTIBODIES AMONG BLOOD DONORS IN WORLD

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Introduction. Hepatitis E virus (HEV) is normally transmitted by fecal-oral route. Several studies in Europe and Asia reported potentially HEV transmission associated to blood transfusion, however, this route is still uncertain.

Objective. This systematic review aimed to estimate anti-HEV IgG seroprevalence among blood donors in world using Bayesian-based methods.

Material and methods. This systematic review was conducted through Pubmed/Medline, Scopus, Web of Science and Cochrane Library databases using the terms "prevalence", "hepatitis E" and "blood donors". It was included studies with a timeframe from inception to march 2016, in roman characters and that had outcomes of interest such as prevalence of

IgG antibodies. The estimation of anti-HEV IgG (presented as event rate and 95% credible intervals - CrI) was calculated by Bayesian-based random effect model using Comprehensive Meta-Analysis version 2. χ^2 was used to test significant differences between sex and age.

Results. 68 studies with a total 113316 patients were included for analysis. Anti-HEV IgG was positive in 19,745 patients, prevalence was statistically significant in male and over 40 years old donors ($p < 0.05$). Overall estimation of anti-HEV IgG was 0.059 (CrI 95%: 0.039-0.090). Subgrouping by continent, estimation was higher in Asia and Middle East, respectively: 0.103 (CrI 95%: 0.043-0.225) and 0.110 (CrI 95%: 0.047-0.234). Europe, Africa, Oceania and America had estimated prevalence between 0.004-0.006.

Conclusion. These findings demonstrate a significant prevalence of anti-HEV IgG among blood donors suggesting the screening of HEV before blood donation to avoid transfusion complications, particularly in males and over 40 years old donors.

12 SAFETY NETWORK META-ANALYSIS OF INTERFERON-FREE TREATMENTS FOR CHRONIC HEPATITIS C

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Introduction. Interferon-free (IFN-free) therapies for hepatitis C virus (HCV) had been developed to provide more effective, tolerable and safer therapeutic strategies. To date no network meta-analysis (NMA) evaluating the safety profile of these regimes was performed.

Objective. To evaluate the safety outcomes of IFN-free therapies for hepatitis C using NMA and Bayesian-based methods.

Material and methods. A systematic review followed by NMA was performed following PRISMA and Cochrane recommendations. Randomized controlled trials (RCTs) comparing the use of second generation direct acting antiviral were included (IFN-free schemes). The electronic search was conducted in Pubmed, Scopus, Cochrane Library, International Pharmaceutical Abstracts and Web of Science. Safety outcomes of interest were collected. NMA allowed estimating probability for the interventions to be more or less safe.

Results. Twenty clinical trials were included (6,323 patients, mean age 53 years), mostly with HCV genotype 1 patients and treated during 12 weeks. Two NMA were built: (i) any adverse events (AE) and (ii) serious AE, comparing respectively 13 and 10 IFN-free therapies. Elbasvir associated to grazoprevir with or without ribavirin (RBV) and placebo exhibited a better safety profile in both NMA. On the other hand, asunaprevir with daclatasvir; ledispavir associated to sofosbuvir with placebo leaded to more serious AE. Ombitasvir combined to paritaprevir, ritonavir and RBV with or without dasabuvir; sofosbuvir combined to velpatasvir with RBV caused more AE (worst position in the rank), explained probably by the presence of RBV.

Conclusion. Schemes presented similar profiles and slight statistical differences concerning serious AE and any AE. Further well-design clinical trials and pharmacoeconomic studies are needed to enhance evidence and support decision-making.

13 LEDIPASVIR/SOFOSFUBIR WITH OR WITHOUT RIBAVARIN FOR HEPATITIS C: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Introduction. Ledipasvir combined with sofosbuvir (LED/SOF), an interferon-free therapy suggested by international protocols to patients infected with hepatitis C virus (HCV), can be used concomitantly with or without ribavirin (RBV). Although collaborate to treatment success in some patients, RBV is well known to promote adverse events (AE) that can lead to treatment discontinuation, such as anaemia and rash.

Objective. To conduct a pairwise meta-analysis to compare efficacy and safety between LED/SOF with or without RBV in patients infected with HCV.

Material and methods. It was performed a systematic review though Pubmed, Scopus, Cochrane Library, International Pharmaceutical Abstracts and Web of Science electronic databases followed by pairwise meta-analysis, that included randomized controlled trials (RCTs) comparing the use of LED/SOF with RBV *vs.* the same therapy but without RBV. RCTs must have provided efficacy (SVR4 and SVR12) and safety outcomes (any AE, discontinuation owing to AE, anemia and rash). Results were reported as odds ratio (OR) and mean differences with 95% credible interval (95 % CrI).

Results. Seven randomized controlled trials with 2567 patients were analyzed. LED/SOF with RBV showed a worst safety profile compared to LED/SOF without RBV on following outcomes: any AE (OR 0.56 [95% CrI 0.46-0.69]), anaemia (OR 0.08 [95% CrI 0.04-0.17]) and rash (OR 0.35 [95% CrI 0.19-0.65]). No significant differences were observed regarding SVR4, SVR12 and discontinuation owing to AE.

Conclusion. LED/SOF with or without RBV presented a similar efficacy profile. On the other hand, the treatment without RBV presented a better safety profile. Risk-benefits to use LED/SOF combined with RBV should be considered for patients infected with HCV.

14 INUSUAL VIROLOGICAL FINDINGS IN ACUTE HEPATITIS C

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Introduction. Acute Hepatitis C (HCVa), is a diagnostic challenge because it is asymptomatic or nonspecific in more than 80% of cases. Spontaneous clearance is observed only in 20% of cases, and its predictive factors are high level of ALT, female sex, hiperbillirrubin, age less than 40 y and IL28B-CC polymorphism. International treatment guidelines, recommend to wait at least 12-16 weeks before considering antiviral treatment. Due to its low frequency, the information about evolution and management is limited.

Material and methods. Two case report of HCVa are discussed, both were evaluated in our clinical consultation during May 2015.

Results. Patient 1: 64 year old female, NAFLD, overweight. Upper endoscopy in the previous 6 months. Nausea and icterus at consultation. Acs HCV (+) PR = 2, AST x31, TP 100%,

Table 1 (014). Biochemical and virologic controls of patient 1.

	AST (UI/L)	Bilirubin	CV HCV (logI)
Week 1	x 31	7.4	7.4
Week 4	x 7.3	2.5	4
Week 6	x 1	1.4	1.2
Week 8	x 1	1	< 1.2
Week 12	x 1	1.2	< 1.2
Week 24	x 1	0.8	3.3
Week 28	x 1	0.9	< 1.2
Week 32	x 2	0.9	< 1.2
Week 36	x 1	0.3	< 1.2
Week 40	x 1.5	0.5	2.8
Week 44	x 2	0.6	3.1

Table 2 (014). Biochemical and virologic controls of patient 2.

	AST (UI/L)	Bilirubin	CV HCV (logI)
Week 1	x 24	10.6	5.7
Week 4	x 4.7	1.4	2.4
Week 8	x 1	0.9	1.6
Week 12	x 9.5	0.8	2.4
Week 18	x 1	0.9	< 1.2
Week 28	x 1.5	0.9	< 1.2
Week 30	x 17	2	6
Week 36	x 3	1	2
Week 40	x 1	0.5	< 1.2
Week 44	x 2	0.5	Detectable
Week 48	x 1	0.5	< 1.2

Bi 7.4/6.9, HCV Viral Load (VL) 23.900,000 UI/ml (7.4), GEN 1b, IL28B-CC. Patient 2: 62 year old female. Odontologic treatments for the previous 6 months and acupuncture. Icterus at consultation. Acs HCV(+) PR = 6, AST x24, TP 89%, Bi 10.6/8.7, HCV VL 476.000 UI/mL (5.7), GEN 1b, IL28B-CC. At week 30 of follow up she had a biochemical, virologic and clinical relapse (pruritus and asthenia) (Tables 1 and 2).

Conclusion. Both patients had good predictors for spontaneous clearance: female sex, icterus, IL28B CC. In these cases the importance of virologic follow up once a negative VL control is achieved, because there is a possibility of later rebound. The patient 1 was asymptomatic all along and she experienced a rapid decline of VL at week 4, with a later relapse of viremia at week 24. This rapid decline of viremia at week 4, is described in the medical literature as a possible predictor of viral clearance. In the second case, although there were some predictive factors for a spontaneous clearance, high and persistent viremias are observed and the patient experienced a clinical, biochemical and virologic relapse at week 24. In our patients, the long term follow up allowed to detect the clinical and virological relapse. More studies in HCVa are needed to make recommendations regarding optimal time of follow up.

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

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Introduction. Chronic hepatitis C (CHC) is a public health problem throughout the world. There is limited current data on the disease characteristics of patients with CHC in Latin America (LATAM). This information is relevant now that interferon-free regimens with direct antiviral regimens are becoming available in LATAM countries.

Objectives. The HEPLA study evaluated demographic, viral and disease characteristics of patients with CHC in Latin America. This report describes the results from patients enrolled in Chile.

Material and methods. HEPLA is an epidemiological study conducted in Argentina, Chile, Colombia, Mexico, and Brazil. This report describes the demographic, disease, and comorbidities information collected from chart data of consented adults with CHC attending a routine clinical visit in Chile.

Results. Fifty-nine patients were enrolled in 3 centers in Chile. 66% were female (39/59). Mean age 56.9 y \pm 11.08 y. Genotype 1 accounted for 88.2% (52 of 59) of infections most due to GT1b (84%; 44/52). Previous history of HCV treatment was found in 52% of patients. Blood transfusion was the most common source of infection (16/30). 56% (33/59) of patients had cirrhosis or transition to cirrhosis. 78% (46/59) had non liver comorbidities being cardiovascular disease (37.3%), psychiatric disorders (27.1%), immunological disease (8.5%) and CKD (6.8%) the most frequent. Liver comorbidities were observed in 27.1% (16/59), non-alcoholic steatosis (11.9%) was the most common.

Conclusions. The results from the HEPLA study AID in better describing the medical profile of patients with CHC in LATAM. In Chile, HCV GT1 accounted for the majority of infection and GT1b was the most frequent. These data should help medical communities and government agencies when developing strategies for managing the disease burden as new therapies including interferon-free regimens emerge.

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**TOPAZ-III, A PHASE 3B TRIAL EVALUATING
 THE EFFICACY AND SAFETY OF
 OMBITASVIR/PARITAPREVR/RITONAVIR
 AND DASABUVIR ± RIBAVIRIN IN
 TREATMENT-NAIVE OR - EXPERIENCED ADULTS
 IN BRAZIL WITH HCV GENOTYPE 1 INFECTION:
 STUDY DESIGN AND PATIENT CHARACTERISTICS**

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Introduction. The 3 direct-acting antiviral (3-DAA) regimen of ombitasvir/paritaprevir/ritonavir (paritaprevir identified by AbbVie and Enanta, co-dosed with ritonavir) and dasabuvir with or without ribavirin (RBV), was approved in Brazil for patients infected with HCV genotype 1 (GT1). However, Brazilian patients have not been enrolled in Phase 3 clinical trials of this regimen to date.

Objective. This report summarizes the study design and baseline characteristics of HCV GT1-infected Brazilian patients enrolled in a trial conducted to evaluate the 3-DAA regimen ± RBV.

Material and methods. TOPAZ-III (NCT02442271) was a phase 3b, open-label trial conducted at 16 Brazilian sites to assess efficacy and safety of 3-DAA ± RBV in GT1-infected patients, treatment-naive or interferon (IFN) regimen-experienced, with advanced fibrosis or compensated cirrhosis. GT1a-infected patients received 3-DAA + RBV for 12 weeks (n = 91), except null responders to pegIFN + RBV with cirrhosis, who were treated for 24 weeks (n = 19). GT1b-infected patients with or without cirrhosis received 3-DAA + RBV (n = 69) or 3-DAA (n = 43), respectively, for 12 weeks. Patients were monitored for 24 weeks post-final dose. The primary efficacy measure was the percentage of patients with SVR12. Safety and tolerability were assessed by monitoring adverse events (AEs), vital signs, and laboratory values.

Results. In the safety population (n = 222; median age, 57 years), 55% participants were men, 82% were white, 76% had BMI < 30 kg/m², 77% were IL28B non-CC, 50% were GT1a-infected, and 54% were treatment-experienced. At baseline, 40% of subjects had advanced fibrosis (F3) and 60% had cirrhosis (F4). Baseline estimated glomerular filtration rate was

> 60 mL/min/1.73 m² in 97% of participants; baseline albumin was ≥ 35 g/L in 96% of patients, and platelet count was ≥ 90 x 10⁹/L in 79%.

Conclusion. TOPAZ-III represents the first large-scale evaluation of 3-DAA ± RBV in Brazilian patients advanced fibrosis or compensated cirrhosis.

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**LEDIPASVIR/SOFOSBUVIR (LDV/SOF) FOR
 8 WKS IN GENOTYPE 1 (GT1) TREATMENT-NAIVE
 (TN) NONCIRRHOTIC (NC) PATIENTS WITH HCV
 VIRAL LOAD (VL) < 6 MILLION IU/ML (6M); A
 COMPARATIVE ANALYSIS OF THE PHASE-3 ION-3
 DATA TO REAL WORLD EFFECTIVENESS (RWE)**

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Background and aims. Optimal duration of therapy to achieve SVR depends on multiple factors. Patients treated with LDV/SOF with 8-24 weeks achieved SVR12 from 94-100% in the ION phase 3 studies. A decision to shorten therapy to 8 weeks is based on treatment history, cirrhosis status and baseline VL. In a post-hoc analysis of the ION-3 (TN, NC patients) 8 week data, a VL < 6M was the best predictor of SVR. RWE is often different from Phase III trials and there is a need to understand real-world 8 week regimens in a broader spectrum of patients.

Material and methods. RWE 8 week LDV/SOF data is emerging from multiple single-center and multicenter retrospective and prospective cohorts. In this analysis, the phase-3 ION-3 data is compared with data from several diverse real world populations and one post-marketing investigator sponsored HIV/HCV trial. Patient demographics, characteristics, SVR12 and discontinuation data has been collated and compared.

Results. The ION-3 post-hoc analysis reported 123 patients who were TN, NC and VL < 6M and treated with 8 weeks of LDV/SOF. Mean age was 52, 22% black, 72% GT1a; the SVR12 was 97% (119/123). The overall SVR12 rate from six diverse real world and post marketing cohorts was also 98% (1726/1767). There was no significant impact of HCV genotypes or subtypes (GT1a, 1b vs. GT4), prior treatment history, presence or absence of cirrhosis, high viral load (HCV VL > 6M), or HIV/HCV co-infection.

Conclusions. LDV/SOF for 8 weeks yielded high SVR rates in ION-3. Analysis of RWE data from several cohorts shows SVR outcomes that were consistent with the Phase-3 ION-3 results and supports the use of 8 weeks LDV/SOF in TN, NC GT1 patients with a baseline HCV VL < 6M and possibly in other populations including HIV/HCV co-infected patients. Discontinuation rates were low despite diverse patients and clinical settings. Data from the TARGET and TRIO cohorts also suggests that the 8-week regimen is underutilized.

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EAL WORLD EFFECTIVENESS OF LEDIPASVIR/ SOFOSBUVIR (LDV/SOF) IN TREATMENT EXPERIENCED CIRRHOTIC GENOTYPE 1 PATIENTS WITH CHRONIC HEPATITIS C (CHC): A COMPARATIVE ANALYSIS OF GILEAD SPONSORED TRIALS WITH 4 REAL-WORLD COHORTS (RWC)

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Background and aims. Treatment-experienced (TE) cirrhotic HCV-infected patients are among the most difficult to treat. Several single and multicenter cohorts have described treatment in this population. EASL and AASLD/IDSA treatment recommendations for the use of LDV/SOF in this population are based on several Phase 2/3 Gilead sponsored clinical trials (GST). SVR12 results in these TE cirrhotic patients are described by Reddy, *et al.* and range from 90-100%. In addition, ION-4 and study 1,118 (NCT01987453) describe LDV/SOF ± RBV in a number of TE cirrhotic patients and are included in the analysis. Our aim is to describe and compare GST to 4 RWC (one large multi-center - TRIO, two smaller multi-center and one single center).

Material and methods. In this comparative analysis, data from 7 Phase-2 and Phase-3 LDV/SOF studies in TE cirrhotic subjects is compared to 4 RWC. SVR12, safety, and baseline characteristics has been collated and compared. A multivariate regression analysis was used to determine if any baseline factors have an impact on SVR, within the on-label treatment regimens.

Results. SVR results from the Phase 2/3 GST, are 118/132 (89%) with LDV/SOF for 12 weeks, 153/160 (96%) with LDV/SOF + RBV for 12 weeks, 97/99 (98%) with LDV/SOF for 24 weeks, and 26/30 (87%) with LDV/SOF + RBV for 24 weeks. In the RWC, HCV-TRIO, Pungpapong, *et al.*, Kohli, *et al.*, and Modi reported combined SVR of 98/116 (85%) with LDV/SOF for 12 weeks, 45/45 (100%) with LDV/SOF+RBV for 12 weeks, 311/334 (93%) with LDV/SOF for 24 weeks, 8/8 (100%)

with LDV/SOF+RBV for 24 weeks. There were no baseline predictors of SVR.

Conclusions. Real-world data in TE cirrhotics correlates closely with data seen in the GST. SVR rates were highest with the on-label treatments of LDV/SOF+RBV for 12 weeks and LDV/SOF±RBV for 24 weeks. Discontinuations rates were low and the highest relapse rates were seen in those receiving LDV/SOF for 12 weeks. Likelihood of achieving SVR in the RWC was not affected by prior SMV and/or SOF exposure. This data supports current treatment recommendations.

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EPIDEMIOLOGICAL PROFILE OF HEPATITIS A, B AND C IN THREE AFRO-BRAZILIAN COMMUNITIES

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Introduction. The Brazilian population is descendant mainly from European colonizers, African and Ameridians. Africans were introduced to Brazil by the slave descendants stayed in culturally isolated communities called quilombos.

Material and methods. 389 samples from Tapera quilombo (Petrópolis, RJ), Rasa quilombo (Búzios, RJ) and Abaetetuba quilombo (Belém, Pará) were collected. All serum samples were tested by Elisa for the presence of anti-HAV antibodies (total anti-HAV). All serum samples were screened by enzyme-linked immunosorbent assay for the presence of hepatitis B surface antigen (HBsAg). HBsAg positive samples were submitted to DNA extraction and a fragment of 1306 bp partially comprising HBsAg and polymerase coding regions (S/Pol) was amplified by nested PCR and its nucleotide sequence was determined.

Results. Among 442 individuals studied, the overall prevalence of anti-hepatitis A virus antibodies was 33% between the fourth and fifth decade of life. Of the 442 individuals

Table 1 (08).

Studies	Regimen (duration in weeks)	N	SVR, n (%)	Relapse, n (%)	LTFU/Other, n (%)
Gilead phase 2/3	LDV/SOF (12)	118	110 (93)	7 (6)	0 (0)
Data from Reddy, <i>et al.</i>	LDV/SOF + RBV (12)	173	166 (96)	7 (4)	0 (0)
+ Study 1,118 + ION-4	LDV/SOF (24)	100	98 (98)	2 (2)	0 (0)
	LDV/SOF + RBV (24)	22	22 (100)	0 (0)	0 (0)
Real world cohorts	LDV/SOF (12)	131	110 (84)	14 (11)	2 (2)
	LDV/SOF + RBV (12)	45	44 (98)	0 (0)	1 (2)
	LDV/SOF (24)	359	331 (92)	7 (2)	17 (5)
	LDV/SOF + RBV (24)	20	19 (95)	0 (0)	0 (0)

33(7.46%) were positive for HBsAg ; anti-HBc and anti-HBs markers, 9 (2.03%). An occult HBV infection rate of 1.13% (5/442) was found among anti-HBc positive individuals. Only 2 of 442 individuals (0.45%) were positive for anti-hepatitis C virus (HCV). HCVRNA was detected in two of them, who were infected with genotype 1.

Conclusion. Our findings point out, intermediate, high and low endemicity for hepatitis A, hepatitis B and hepatitis C respectively. Further studies in remnants of quilombos from different geographical regions of Brazil are needed to design effective prevention and control strategies for this target population.

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PHYLOGENETIC ANALYSIS OF HEPATITIS B VIRUS ISOLATES FROM A QUILOMBO COMMUNITY IN THE STATE OF RIO DE JANEIRO, BRAZIL

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Background. Hepatitis B virus (HBV) genotypes (A-J) and subgenotypes have distinct geographical and ethnic distribution. Brazil is a mestizo country with its population made up of individuals of European, African and Indian origins. During the slavery period, some Afro-descendants lived in small isolated communities named Quilombos, some of which have been maintained until today. We evaluate the different HBV genotypes circulating in an Afro-descendant community and characterize them molecularly by phylogenetic analysis.

Material and methods. Fifty individuals (31 male, 19 female) living in Rasa quilombo, Búzios, RJ were evaluated. Occurrence of hepatitis B surface antigen (HBsAg) was evaluated by means of rapid tests. HBsAg positive samples were submitted to HBeAg and anti-HBe serological tests. All samples (positive and negative by rapid tests) were subjected to DNA extraction to detect eventual occult infection. HBVDNA of the pre-S/S genome region was amplified by a semi-nested PCR assay and the amplicons were directly sequenced. HBV genotyping was performed by phylogenetic analyses of the sequences compared with representative sequences of all subgenotypes of HBV.

Results. 20/50 (40%) samples were HBsAg positive. Among them, four genotypes A1 (8%) and ten D4 (20%) were found. Phylogenetic analysis revealed that HBV/A1 and HBV/D4 samples formed monophyletic groups. HBV/A1 isolates were closely related (mean genetic distance, 1.3-1.7%) to samples circulating in the Northern and Northeastern regions of Brazil and Somalia. Our A1 samples clustered within the Asian-American clade, together with samples from Asia and East Africa. Alignment of deduced amino acid sequences of 134 HBV/A1 isolates revealed a specific variation (Q275H) in the pre S/S region, found exclusively in the HBV isolates (molecular signature). A 33bp deletion in pre S2 region, previously observed in relatively young patients with development of Hepatocellular Carcinoma, was detected in one sample. Isolated D4 samples share the same origin with Brazilian and Indian sequences.

Conclusion. These data corroborated a previous study that showed that Brazilian HBV/A1 samples originated from countries of the eastern coast of Africa, through the slave trade

during the late XVIII century. This is first phylogenetic analysis of HBV (A1 and D4) isolates from a quilombo community in the state of Rio de Janeiro, Brazil.

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DESCRIPTIVE ANALYSIS OF PATIENT CLINICAL CHARACTERISTICS AND EPIDEMIOLOGY ASSOCIATED WITH THE HEPATITIS DELTA DIAGNOSTICS OF PATIENTS IN A REFERRAL CENTER IN THE AMAZON REGION

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Introduction. The hepatitis Delta Virus (HDV) is a defective RNA virus that requires the presence of the hepatitis B virus (HBV) to complete its life cycle. The HDV is an important cause of morbidity and mortality in endemic regions for the presence of this virus.

Aim. To describe the clinical and epidemiological characteristics of patients diagnosed with HDV at a reference center in the Brazilian Amazon.

Material and methods. Retrospective study involving a cohort of patients with serologic diagnosis of the HDV infection at a referral service in the State of Rondônia, Brazilian Amazon in the period 1993 to 2015. The diagnosis of HDV was performed using serology (ELISA). The clinical data was obtained through the analysis of medical records.

Results. After analyzing the data, 208 patients had confirmed serologic diagnosis of HDV. The follow-up procedure has a mean of 4.5 years (averaging 9 consultations). The mean age at the first visit was 35 years (6-71 years), 64.4% were male and 16.3% were indigenous people. Ninety-one patients (43.7%) reported contact with family members infected with HBV and 11% reported contact with at least two relatives with this diagnosis. Two patients were co-infected with HDV/HCV and two with HDV/HIV. Of the 208 patients, 89 (42.8%) had cirrhosis features and 82 displayed signs of portal hypertension. The presence of hepatocellular carcinoma was detected in 9 patients (4.3%). Ten patients underwent liver transplantation (mean age 41 years).

Conclusion. 1) The presence of family members infected with HBV was frequent. 2) The presence of infection with HDV was associated with a significant number of liver complications and was a frequent cause of death in the population studied. 3) The occurrence of death was common among young adults.

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PREVALENCE OF PRE-EXISTING HEPATITIS C VIRUS (HCV) VARIANTS RESISTANT TO PROTEASE INHIBITORS IN PATIENTS INFECTED WITH HCV GENOTYPE 1 IN ARGENTINA

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Introduction. The incorporation of direct acting antivirals (DAA) in the treatment of HCV significantly increases the sustained virologic response rates. However, despite the greater potency offered by these antivirals, drug resistance plays a key role in patients with failure to DAA. Nevertheless, there is no information about the prevalence of resistant variant in Argentina.

Objective. The aim of this study was to analyze HCV variants resistant to NS3 inhibitors in naïve patients infected with HCV genotype 1 from the hepatology Unit of a tertiary care center in Buenos Aires, Argentina.

Material and methods. In this retrospective cross-sectional study, 30 patients infected with HCV-1a and 30 with HCV-1b were included. In particular, 16 positions related with resistance to treatment were analyzed in this work: V36, Q41, F43, T54, V55, Y56, Q80, V107, R109, P131, I132, S138, R155, A156, D168 and V170.

Results. In the HCV-1a sequences, amino acid substitutions conferring resistance to NS3 inhibitors were detected as follows: V36L 1 (3.3%), V36M 1 (3.3%), I132V 2 (6.6%), R155S 1 (3.3%) e IV170G 1 (3.3%). For HCV-1b sequences, resistance mutations in the NS3 region were: V36L 4 (10.2%), Y56F 10 (25.6%), I132V 36 (92.3%) e IV170A 1 (2.6%). Surprisingly, Q80K was not found in HCV-1a even when 60% of the samples belonged to cluster 1, which is associated with a high frequency of Q80K.

Conclusion. Mutations conferring resistance to HCV NS3 inhibitors were more frequent in treatment-naïve Argentinean patients infected with HCV-1b than HCV-1a. The high prevalence of Y56F and I132V might be characteristic of a particular lineage of this population.

This study supports the need for surveillance of resistance in patients who will be treated with DAA in each particular country.

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SAFETY AND EFFECTIVENESS OF PARITAPREXIR/R/OMBITASVIR/DASABUVIR ± RIBAVIRIN IN GENOTYPE 1 AND 4 HCV INFECTED PATIENTS TREATED IN REAL LIFE SETTINGS: A SOUTH AMERICAN COHORT EXPERIENCE

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Background. The combination paritaprevir/r/ombitasvir and dasabuvir ± ribavirin (3D ± RBV) was reported to be safe and highly efficacious achieving high-sustained virologic response at follow-up week 12 (SVR12).

Aims. To evaluate safety and effectiveness of 3D ± RBV regimen in a real-world (RW) setting.

Material and methods. Patients with Gt1 or Gt4 infection treated with 3D ± RBV regimen were retrospectively included. Data on demographics, clinical features, safety and virological response were collected from 19 centers in South America. Effectiveness was assessed by SVR12 and safety was reported in all patients that received at least one dose of study drug.

Results. Eighty-three patients received 3D treatment associated with RBV in 77% of the cases; 65 patients reached end of treatment (EOT). Patients included 15 (18%) with Gt1a, 64 with Gt1b (77%), 3 (4%) with unspecified Gt1 and 1 with Gt4 infection. Cirrhosis was present in 49 (59%) patients and 44 (53%) have prior HCV treatment experience. Adverse events (AEs) occurred in 64% of patients. The most common AEs were hyperbilirubinemia (31%), headache (19%) and pruritus (19%). Five patients discontinued therapy prematurely due to hepatic decompensation, four of them were Child B at baseline and one patient died due to multi-organ failure. Modified ITT analysis showed undetectable HCV-RNA at the EOT in 65 of 65 patients (100%) and SVR12 in 56 of 56 patients

(100%). In 51% of those patients who achieved SVR12, MELD score decreased at least 1 point when compared to baseline.

Conclusions. Treatment with 3D ± RBV regimen in RW setting is safe and highly effective in Gt1 patients, including those with Child A cirrhosis. Treatment in Child B cirrhosis has higher incidence of hepatic decompensation. Updated data will be presented at the meeting.

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OBSERVATIONAL DESCRIPTIVE STUDY OF 10 YEARS OF MONITORING OF PATIENTS WITH CHRONIC HEPATITIS C IN A PUBLIC HOSPITAL IN SANTIAGO, CHILE

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Introduction. Chronic infection by hepatitis C virus is an endemic disease worldwide. The overall prevalence is around 2%. In Chile it is considered a disease of low endemicity with an estimated prevalence 0.01-0.3%.

Objective. To describe the population of patients with chronic hepatitis C treated as an outpatient in our institution between 2005 and 2015, and analyze the response to treatment according to genotype.

Material and methods. A cohort analysis of 120 patients with chronic hepatitis C virus by reviewing medical records. Data collected included; age, sex, comorbidities, date of diagnosis, genotype, presence of cirrhosis, type of treatment, sustained viral response (SVR) and co-infection. Univariate analysis was performed using Chi square test. Data were analyzed using SPSS version 24.

Results. 58% of patients were women. At the time of diagnosis, the average age was 54 years and 24.4% had cirrhosis. The most common genotypes were type 1b with 60.6% and type 3 with 8.7%. 76% of patients received treatment, of which 76% corresponded to peginterferon/ribavirin; 10% used first generation protease inhibitors associated with peginterferon and 14% only oral direct-acting antivirals. Most adverse effects were reported with the use of peginterferon/ribavirin, corresponding to hematological disorders in 58%. SVR was achieved in 58% of patients with genotype 1 and 92% in genotype 3.

Conclusion. Our results do not differ significantly with respect to that described in the international literature. Clinical features and treatment results are comparable to those of other countries. A good knowledge of the characteristics of our patients will allow us to better planning in relation to new antiviral therapies.

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TWO INTERFERON-FREE REGIMENS FOR GENOTYPE 1 HEPATITIS C. REPORT OF TREATMENT "REAL LIFE" IN PATIENTS IN CHILE

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Introduction. New interferon-free treatments with direct-acting antivirals (DAA) are nowadays the standard of care in the treatment of hepatitis C virus (HCV). They represent a paradigm shift, achieving a radical increase in sustained viral response (SVR) of 50-85% to 85-100%. To date, in Chile there is no published experience with these treatments, due to recent approval.

Objective. Report response of two different interferon-free regimens in Chilean patients with HCV infection.

Material and methods. Treatment response and tolerance to it was analyzed in patients infected with HCV who were receiving compassionate therapy with Ombitasvir / Paritaprevir / Ritonavir / Dasabuvir + Ribavirin (3D) or Daclatasvir / Asunaprevir (DA).

Results. Twenty-five patients were treated with DAA, 15 with 3D and 10 with DA. Median age was 59 years (36-80); 56% were men; genotype 1b 84% (21); viral load > 800,000 IU/mL in 68% (17); 84% cirrhotic patients; MELD score average of 9 (7-13). At the time of submission of this abstract, 20 patients had 12 weeks post-treatment viral loads, 18 (90%) with SVR12 and 2 (10%) without SVR12; both received therapy with DA. The most common side effects reported were fatigue (40%), nausea (28%) and headache (24%), mostly mild and transient. Only one patient had significant anemia, which required ribavirin dose adjustment. No patient required treatment suspension.

Conclusion. This report represents one of the first experiences with interferon-free therapies in South America. Both combinations of DAA are effective, safe and well tolerated.

*Results of this report will be updated at the Congress.

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CORRELATION BETWEEN HEPATITIS C VIRUS (HCV) CHRONIC INFECTION WITH FATTY LIVER DISEASE (FLD) AND FIBROSIS

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Introduction. Chronic infection with HCV is associated with hepatic steatosis and metabolic syndrome. It was reported that 48% of HCV-infected patients show steatosis; with a relationship with genotype 3. Transient elastography (TE) is noninvasive technique that estimates the degree of hepatic fibrosis and fat by Controlled Attenuation Parameter (CAP).

Objectives. Evaluate the correlation between fibrosis and FLD in HCV chronic infected patients by TE and CAP.

Material and methods. We performed a cross-sectional study on HCV infected patients (pts); all the subjects were evaluated with clinical assessment, blood test, TE and CAP; Statistical analysis was performed with SPSS software version 22; median and confidence interval for continuous variables description, categorical variables with percentages and spearman correlation between kPa and CAP results.

Results. 105 pts were analyzed, median age 59 (CI 95% 57 - 61), 58 females (55.2%). Genotype frequency was: 74 pts (70.5%) type 1, 16 pts (15.2%) type 2 and 9 pts (8.6%) type 3; 4 pts (5.7%) without genotype determination. Median kPa obtained was 9.1 (CI 95% 7.8 - 10.9) and median CAP was 206 (CI 95% 196 - 217). 44 pts (41.9%) had steatosis, 88 pts (83.8%) with fibrosis and 37 pts (35.2%) with cirrhosis. Steatosis in genotype 1 was 22% (17 pts), 45% (5 pts) in genotype 2 and 12% (1 pt) in genotype 3; fibrosis in genotype 1 was 83% (62 pts), 81% (13 pts) in genotype 2 and 88% (8 pts) in geno-

type 3. There wasn't correlation between kPa, CAP, steatosis, fibrosis and cirrhosis.

Conclusions. Our study shows a higher steatosis frequency in genotype 2 with low frequency in genotype 3; the liver stiffness isn't related with the CAP score.

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REAL LIFE EXPERIENCE WITH INTERFERON FREE DIRECT-ACTING ANTIVIRALS (IFDAA) IN MEXICAN PATIENTS WITH CHRONIC HEPATITIS C INFECTION

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Introduction. Treatment of HCV patients with IFDAA have demonstrated better outcomes (sustained viral response (SVR) and liver fibrosis regression) and more adherence to treatment with less adverse effects compared with IFN regimens.

Objective. To evaluate IFDAA efficacy in Mexican patients with chronic HCV infection.

Material and methods. We performed a prospective cohort study, on chronic HCV infected patients treated with IFDAA; all patients had clinical assessment, blood test follow-up and radiological studies to determine the therapy response; viral load, SVR 12, adherence to treatment, fibrosis and adverse effects (AEs) were recorded. SPSS software version 22 was used; continuous variables were described with median or mean (depending in the central tendency distribution), categorical variables with percentages and confidence interval. We utilized 8 different IFDAA regimens, they were chosen accordingly to clinical criteria and availability.

Results. Fifty patients (pts) were analyzed (mean age, 59 \pm 12.6 SD, 28 females (56 %)). Genotype frequency was: 38% (19 pts) type 1a, 38% (19pts) type 1b, 20% (10 pts) type 2 and 4% (2 pts) type 3; 16% had liver transplant before therapy and 54% were treatment naïve. 72% had transient elastography (TE) before treatment and 58% with a result compatible with liver cirrhosis. 44 pts had completed treatment and 3 pts presented therapy withdrawal (only one because side effects). Among pts with completed therapy, 42 (95%) presented SVR: among the patients with unfinished therapy (3 pts), all their viral loads are negative (8 weeks of follow-up). Side effects frequency was 68% (any side effect), the most common was malaise (82%).

Conclusion. IFDAA is an effective therapy in Mexican population with results in accordance with the literature.

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WHOLE-EXOME SEQUENCING IN PATIENTS WITH CHRONIC HEPATITIS C AND HEPATOCELLULAR CARCINOMA

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Introduction. Genetic alterations in liver carcinogenesis are important events in the development and progression of hepatocellular carcinoma (HCC). Emerging technologies to

perform genomic analyses have been important tools to improve tumor characterization.

Material and methods. We evaluated the whole-exome sequencing in six patients with hepatocellular carcinoma (HCC) and cirrhosis due to chronic hepatitis C (CHC), and in two subjects with CHC, but without liver cancer (one with mild fibrosis and other with cirrhosis). The exome capture was performed using the Nextera Exome Rapid Capture kit (Illumina Inc., San Diego, CA, USA). Then, the captured DNA was sequenced on Illumina Genome Analyzer IIx (GAIIx), based on the Solexa or SBS technology (Sequencing-by-Synthesis) using the TruSeq SBS kit v5 (Illumina Inc.), configured to 2x75bp paired-end. The reads were analyzed for quality, and those with phred-score higher than 30 were aligned to the human reference genome (GRCh37) using the Burrows-Wheeler Aligner (BWA, version 0.7.12). The variants were called with the Genome Analysis Toolkit (GATK, version 3.5) and annotated with Spneff (version 4.2).

Results. The whole-exome sequencing of all samples generated 135,699 variants (one variant for each 22,388 bases). We found 15,449 somatic mutations, of which 6,806 were in the 3'UTR; 2,929 were missense mutations; 2,803 silent mutations; and 1,128 were in the 5'UTR. The most mutated genes were MUC4 (n = 76); ZNF717 (n = 65); HLA-DRB1 (n = 38); and PDE4DIP (n = 36). When evaluating the HCC samples, the most mutated genes were RSPH3 (n = 3; one missense mutation and 2 silent); and NOTCH4 (n = 3; one missense mutation and 2 silent). The variants MORN1 (intron), DUSP28 (5'UTR) and TP63 (3'UTR) were observed only in HCC patients.

Conclusion. These are the preliminary results of a pilot study evolving whole-exome sequencing in Brazilian HCC patients. At this point, we could identify some genes of interest in this group of subjects, but more studies are needed to confirm these findings.

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HEPATITIS B COMPREHENSIVE RESPONSE IN BRAZIL AND THE PAHO PLAN OF ACTION FOR THE PREVENTION AND CONTROL OF VIRAL HEPATITIS 2016-2019

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Introduction. More than one third of the world's population has been infected with hepatitis B virus (HBV). Around 0.37% of population between 10-69 years of age in Brazil lives with chronic hepatitis B. In order to improve its comprehensive response to viral hepatitis initiated in 1989, the country has taken additional steps and recently committed to the Plan of Action for the Prevention and Control of Viral Hepatitis developed by PAHO member states.

Objective. Development of public policies towards elimination of hepatitis B as a public health issue.

Material and methods. Review of epidemiologic data and cases reported to the official notification system, mathematical modelling, evaluation of vaccine coverage, and scale-up of prevention, diagnosis and treatment services have been continuously conducted with support of the Strategic and Technical Advisory Group (STAG) for viral hepatitis and civil society. These are initiatives supported by the PAHO Plan of Action.

Results. Historical records of notified cases of the disease and mathematical modelling display that hepatitis B cases in Brazil are concentrated in young adults, with steep increase at ages 10-15, same groups in which annual vaccine coverage numbers decrease significantly and sexual initiation takes place. Reviews displayed important differences in prevalence rates for different population groups, especially those living in the Amazon Basin, and STAG inputs promoted updates for the National Guidelines.

Conclusion. Rising prevalence rates in teenagers and young adults raises concerns about the focus and extent of current public health policies, requiring improvements in our response to the epidemic. Universal immunization, important updates in treatment and prevention of mother-to-child transmission and the development of appropriate campaign material and media options to relate to younger audiences are essential steps to strengthen systems and achieve success.

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BRAZILIAN RESPONSE TO HIV AND HEPATITIS C COINFECTION THROUGH NEW FREE OF CHARGE INTERFERON FREE TREATMENT

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Introduction. Hepatitis C has emerged as one of the leading causes of death among people living with HIV/AIDS (PLWH) after the advent of highly active antiretroviral therapy (ART). Differently from HIV/AIDS, benefited from the major scientific advances since 1996, hepatitis C has been sidelined for a long time. It is known for its poor treatment options and high rates of adverse events, also unlikely to be taken along with ART or not recommended for PLWH. In Brazil approximately 10.7% of chronic hepatitis C patients are coinfecting with HIV. Although hepatitis C virus (HCV) kinetics little interferes with HIV cycles, the chronic liver infection is known to be related to poor clinical outcomes in HIV. Besides liver damages by HCV is highly accelerated in the presence of HIV.

Objective. To improve treatment for hepatitis C and coinfections, counting HIV, through the new national guidelines.

Material and methods. The Brazilian Ministry of Health (MoH) proceeded with careful evaluation and negotiations of new treatments and elaborated new National Clinical Guidelines for treatment of hepatitis C and coinfections. The new guidelines included HIV/HCV as criteria for immediate treatment and suitable regimens for PLWH being under ART.

Results. From October 2015 to June 2016, 32,000 treatments composed of daclatasvir, simeprevir, sofosbuvir, ribavirin and pegylated interferon were made available in the Unified Health System (SUS). Less than 4% of patients reported adverse events. Moreover, regional reports identified recent improvements in patient adherence to treatment, which benefits HIV care.

Conclusion. Considering the harmful synergy between HIV and hepatitis C, Brazilian MoH was able to improve the treatment for hepatitis C and coinfections in SUS and, by the end of 2016, will have provided approximately 60,000 treatments for hepatitis C and coinfections.

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EPIDEMIOLOGIC AND CLINICAL COMPARISON OF PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV) AND HEPATITIS C VIRUS (HCV) CO-INFECTION AND INFECTED BY HCV WITHOUT COINFECTION TREATED IN THE SAN BORJA-ARRIARAN CLINICAL HOSPITAL

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Introduction. HIV and HCV infections have a high prevalence. The prevalence of coinfection in Chile in patients with HCV is unknown.

Objective. To describe the prevalence of HIV co-infection in patients with HCV and their clinical characteristics.

Material and methods. review of clinical records of patients with chronic HCV infection controlled at the San Borja Arriarán Clinical Hospital since 2005 to date, and comparison of the coinfecting patients with a control group with HCV matched according to age and gender.

Results. 150 patients with HCV infection were recorded, 14 cases (9.3%) presented coinfection. Mean age was 52.2 and 50.2 years, and male:female ratio was 0.8: 1 and 1.33: 1 respectively. The average of CD4 lymphocytes of the coinfecting patients was 469 cells/mL; 12/14 patients showed HIV viral load below the detectable value. The route of transmission of HCV was intravenous drug use in 3/14 (21.4%) and 2/28 (7.1%)* patients, and transfusion of blood products in 0/14 and 9/28 (15.5%)* patients. Extensive fibrosis (F3) and cirrhosis (F4) was observed in 63% of coinfecting patients and in 43% of control patients (p = 0.07). Frequent genotypes were 1a and 1b (28.6% each) in the group of coinfecting patients and 1b (60.7%) in the control group. Coinfecting (8/14) and control (14/28) patients received therapy for HCV, with SVR in 50% in each group. 77.7% and 47.3% of coinfecting and controls had viral load > 800,000 IU/mL*. *P < 0.01.

Conclusion. A significant number of patients with HCV is co-infected with HIV. Its most common mode of transmission is intravenous drug use and coinfecting patients have higher viral load than controls. The SVR rate was similar in both groups.

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PROFILE OF CHEMOKINES, CIRCULATING MICROPARTICLES AND BIOLOGICAL SYSTEMS APPROACH IN PATIENTS WITH CHRONIC HCV INFECTION BEFORE AND DURING TRIPLE THERAPY

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Introduction. Is necessary understanding of the kinetics of immunological biomarkers over triple therapy.

Aims. To characterize the immunological profile related to HCV treatment.

Material and methods. Twenty patients with chronic HCV infection GT1 treated with PR and telaprevir (TVR) or boceprevir (BOC) were included. The MCP-1/CCL2, RANTES/CCL5, IL-8/CXCL8, MIG/CXCL9 and IP10/CXCL10 chemok-

ines and microparticles (MPs) were analyzed by flow cytometry before (BT) and during treatment (AT) at weeks 2 (n = 20), 4 (n = 20), 8 (n = 19), 12 (n = 18), 24 (n = 16) and 48 (n = 12). The protocol was approved by Ethical Board of UFMG/Brazil.

Results. 12/14 (86%) achieved SVR. CCL2 and CXCL8 were increased at week 12 AT compared to BT. CXCL9 and CXCL10 decreased at week 24 compared to week 12 AT. The MPs from lymphocytes TCD3+ decreased at weeks 12, 24 and 48 AT compared to BT and decreased at weeks 24 and 48 compared to week 4 AT. The MPs from lymphocytes TCD4+ decreased at the weeks 12 and 24 compared to BT and decreased at week 12 compared to week 4 AT. MPs from monocytes decreased at weeks 2, 12 and 24 AT compared to BT and increased at week 48 compared to week 24. The MPs from neutrophil decreased at the weeks 2 and 24 AT compared to BT decreased at week 24 compared to week 8 AT and increased at week 8 compared to week 2 AT. Of note, there was a progressive decrease in liver enzymes and microparticles after treatment and peak of chemokines at week 12 of treatment. Most biomarkers reduced at week 24 post-treatment, except for CCL2 and CCL5.

Conclusions. CCL2, CXCL8 are associated with recruitment of immune cells involved in mechanisms against viral infection. In contrast, the chemokines CXCL9 e CXCL10 exhibit reduction throughout treatment. The reduction of microparticles during the treatment suggests that it promotes a favorable environment for more effective immune response against the HCV virus. This immune scenario suggests an immunomodulatory modulation during HCV treatment.

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EPIDEMIOLOGY OF PORTAL THROMBOSIS DIAGNOSED BY SCREENING OF HEPATOCARCINOMA IN PATIENTS WITH CHRONIC LIVER DISEASE

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Introduction. Portal thrombosis is a common complication in cirrhotic patients of any etiology. The prevalence in such population varies from 4-15%, reaching 25% in decompensated cirrhotic ones. Its diagnosis depends on the clinical presentation according to time of establishment and of complementary images supporting, being the chronic asymptomatic form the most frequent one. The importance of diagnosis is to avoid complications of secondary portal hypertension and anticoagulation in patients with eventual need of liver transplantation.

Objective. To describe the epidemiological characteristics of patients with chronic portal thrombosis diagnosed by ultrasound screening of hepatocellular carcinoma (CCH) in patients with Chronic Liver Disease (CLD).

Material and methods. Abdominal ultrasound screening of HCC was performed in 193 patients with CLD, from June 2015 to June 2016 in the Japanese Chilean Institute of Digestive Diseases at Hospital San Borja Arriarán.

Results. Six out of 193 (3%) patients were found portal thrombosis. All of them were confirmed by CT. 67% were men, average age 60 years old (range of 52-72). 50% of CLD resulted alcoholic etiology, predominating Child B (4/6). Two

patients presented a MELD score more than 15 and none of them was on transplant list. Compromised of splenic vein was found in 2 patients, 1 with cavernomatosis and 5 with signs of recanalization. 2 patients received anticoagulant therapy. All had small esophageal varices and 1 patient also presented gastric varices. Only 1 of these patients concomitantly had one focal liver lesion.

Conclusion. In our study the prevalence of chronic portal vein thrombosis in CLD patients was similar to with CLD similar to the description in the literature. All of the patients were asymptomatic and most of them with signs of recanalization.

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SEROLOGICAL AND MOLECULAR RETROSPECTIVE ANALYSIS OF HEPATITIS E VIRUS INFECTION AMONG SUSPECTED CASES FROM BRAZILIAN AMAZON, 1993-2014

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Introduction. Hepatitis E virus (HEV) is a pathogen worldwide distributed that is recognized as an etiological agent of acute and chronic hepatitis in humans. Occurrence and geographical distribution of HEV are still poorly understood in Latin America. There are only five cases of HEV infection confirmed by HEV-RNA detection in Brazil and, particularly the HEV prevalence remains unknown in Brazilian Amazon region.

Objectives. The aim was determination of seroprevalence and molecular investigation of HEV infection in serum samples of hepatitis E suspected cases attended in a viral hepatitis reference unit of Eastern Brazilian Amazon from 1993 to 2014.

Material and methods. Serum samples (n = 318) of hepatitis E suspected cases (stored at -20°C) were analyzed for research of anti-HEV IgM and IgG antibodies by ELISA and confirmatory recombinant immunoblot test (RIBT). HEV-RNA was investigated in each sample by RT-qPCR.

Results. Fifty-one percent (162/318) of individuals were female and the average age was 30,5 years (range \pm SD; 0-84 \pm 20,21). Seroprevalence were 5.0% (16/318) for anti-HEV IgM and 9.1% (29/318) for IgG by ELISA; and 3.4% (11/318) for anti-HEV IgM and 5.9% (19/318) for anti-HEV IgG by RIBT. Higher occurrence for IgM anti-HEV was observed in individuals among 16-30 years old. No samples were positive for HEV-RNA by RT-qPCR.

Conclusion. This is the first molecular and serological evaluation of HEV infection using hepatitis E suspected samples from Brazilian Amazon region. Our results showed only serologic evidence of acute and past HEV infection among evaluated samples and a low circulation of HEV among patients with clinical and/or laboratory suspicion of HEV infection. In addition, we emphasize that it is interesting to develop additional serological and molecular studies covering healthy individuals and patients with acute or chronic liver disease for better characterization of public health impact of HEV in Brazilian Amazon region.

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NEW ANTIVIRALS FOR HEPATITIS C IN BRAZIL: PRELIMINARY EFFECTIVENESS ANALYSIS WITH CURRENT NATIONAL DATABASES

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Introduction. Seventeen states of Brazil have successfully implemented the HORUS and GAL public platforms. These are systems dedicated, respectively, to the management of over eighty different high-cost medicines and registry of laboratory data. Both registries could be used together to provide information about patient laboratory status according to treatment and evaluate effectiveness of new direct antiviral agents provided by Unified Health System (SUS).

Objectives. Analyze new hepatitis C treatments effectiveness provided by SUS.

Material and methods. We searched HORUS for treatments distributed in the last quarter of 2015 with patient, genotype and treatment information and GAL for HCV-RNA quantitative results from March 1st to June 20th, 2016. We consolidated the resulting registries with simple spreadsheet software and evaluated the sustained virologic response at week 12 (RVS12) for sofosbuvir + daclatasvir and sofosbuvir + simeprevir 12 weeks regimens.

Results. 2.851 of hepatitis C treatments (24%) distributed in the last quarter of 2015 in SUS have been registered in HORUS. Nearly 72% of them had additional data on HCV genotype and 960 treatments were initiated between October 26 and December 31, 2015. Database consolidation identified two hundred and fifty seven records in both HORUS and GAL that were suitable for SVR12 analysis - Genotype 1: 96% (195/202), genotype 1A: 98% (83/85), genotype 1B: 95% (93/98), genotype 2: 100% (6/6), genotype 3: 86% (42/49).

Conclusion. This experience displays that the consolidation of HORUS and GAL databases is a practical alternative for quick evaluation of treatments. It presents an optimistic first glance at the successful results of the new National Guidelines for Hepatitis C and Co-infections and secures opportunities for further analysis of other treatments distributed through HORUS. A nationwide databases consolidation for hepatitis C treatment is in development.

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ALPHA-FETOPROTEIN BASED CLINICAL SCORE PREDICT BETTER SMALL HEPATOCELLULAR CARCINOMA IN HEPATITIS C VIRUS CIRRHOSIS

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Introduction. Hepatitis C virus (HCV) infection is considered one of the main causes of liver cirrhosis and hepatocellular

carcinoma (HCC). Early diagnosis allows use of curative treatments with impact on patient survival.

Aims. The aim of this study was to identify possible prediction factors of HCC by analyzing a set of patients with HCV related cirrhosis with and without small diameter HCC (≤ 3 cm).

Material and methods. We conducted a case control transversal study between 1998 and 2003 involving a total of 93 patients with hepatitis C cirrhosis, among these, 31 patients with small diameter HCCs and 62 without HCC. Groups were matched by age and gender. Clinical and biochemical parameters were studied. Univariate analysis followed by multiple logistic regression using Akaike Information criteria to estimate the probability of HCC were performed. A model score was generated. Bootstrap analysis was also performed for internal validation.

Results. Three significant laboratorial variables for HCC prediction were found: alanine aminotransferase > 37 U/L [(OR: 7.43 (1.61-34.19), $p = 0.01$], alpha-fetoprotein > 20 ng/mL [OR: 16.2 (4.17 -63.01), $p < 0.001$] and platelet count $< 100,000$ [OR: 3.62 (1.43 -9.14), $p = 0.007$]. A model score with a sensitivity of 0.79 (IC 0.7 - 0.89) and a specificity of 0.66 (IC 0.53 -0.58) was built based on these variables.

Conclusion. This study presents an easy and practical model score, which can be applied in routine clinical practice. It may help identify potential subjects at higher risk of HCC. Further studies in other populations, including non-HCV related cirrhosis are needed to address its role in HCC prediction.

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CONCORDANCE OF NON-INVASIVE TESTS (MECHANICAL AND SERUM MARKER) FOR LIVER STIFFNESS IN A REAL LIFE STUDY OF OUTPATIENTS WITH CHRONIC HEPATITIS C

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Introduction. Non-invasive tests such as liver stiffness measurement (LSM) and serum markers (SM) are well documented methods for assessment of fibrosis in hepatitis C virus (HCV) patients.

Aims. To analyze the concordance of LSM and SM with the METAVIR score in order to identify the best test to apply in routine care.

Material and methods. Between 2012 and 2014, 81 consecutive patients with HCV were assessed at the Department of Gastroenterology, of Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Brazil. They were submitted to concurrent LSM (FibroScanTM/ARFI SIE-MENS) and SM (FIB4/APRI) exams and liver biopsy (LB), in order to compare the data with METAVIR score. The diagnostic performance of these tests was assessed using ROC curves. The best cut-off levels of each test was chosen to define fibrosis stages $F \geq 2$, $F \geq 3$, and $F=4$. The Kappa index set the concordance analysis.

Results. Baseline characteristics: 41/81 (50.6%) female; median age 51 years, (30-78); 52/81 (64.2%) ethnicity white; BMI median 26.9 (48.5-18.8), and 70% were treatment-naïve. The best cut-off values for predicting $F \geq 2$ stage fibrosis with Transient Elastography (TE) was 6.6 kPa, for ARFI 1.22 m/s, for APRI 0.75 and for FIB4 1.47. For $F \geq 3$, TE was 8.9 kPa, ARFI was 1.48 m/s, APRI was 0.75, and FIB4 was 2. For $F = 4$, TE was 12.2kPa, ARFI was 1.77 m/s, APRI was 1.46, and

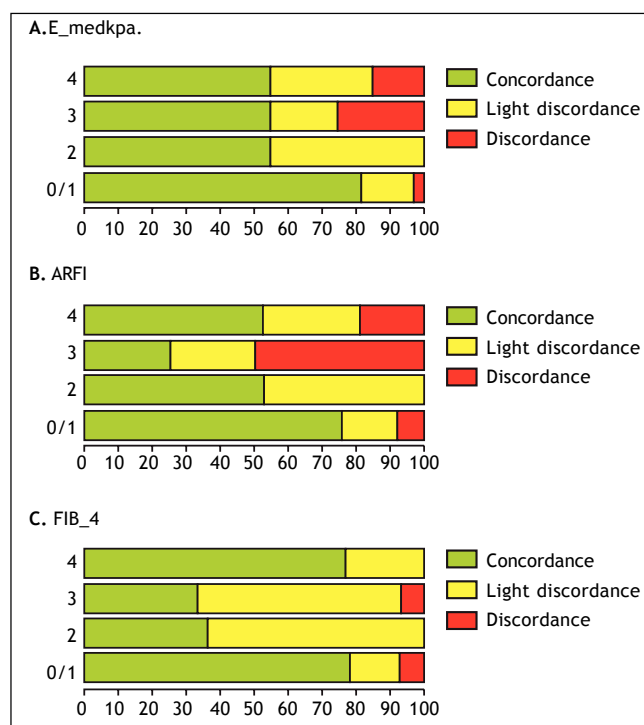


Figure 1 (037).

FIB4 was 3.91. The APRI could not distinguish between F2 and F3, $p = 0.92$. The NPV for $F \geq 3$ METAVIR score for TE, ARFI and FIB4 were 0.687, 0.606 and 0.654, respectively. This demonstrates strong concordance between all three methods, but moderate to APRI (Kappa index = 0.507) (Figure 1).

Conclusion. Given the higher cost and reduced accessibility of LSM methods, and the similarity with the outcomes of SM, we suggest that FIB4 as well as TE and ARFI may be good tools for prediction of the degree of fibrosis and cirrhosis. This may be of particular importance to developing countries.

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EFFECTIVENESS OF ASUNAPREVIR PLUS DACLATASVIR IN PATIENTS WITH HEPATITIS C VIRUS AND ADVANCED FIBROSIS: REAL-WORLD EXPERIENCE FROM THE LALREAN NETWORK

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Background. Despite the approval and widespread use of several direct acting antivirals (DAA) against hepatitis C virus (HCV) in developed countries, access to these drugs is limited in many areas of the World. The combination of asunaprevir

(ASV) plus daclatasvir (DCV) has been already approved in several Asian and Latin American countries for HCV genotype 1b, but information regarding its effectiveness and safety in patients with HCV related cirrhosis is scanty.

Aim. To confirm safety and efficacy of this study regimen in real-life settings.

Material and methods. Data of patients enrolled in a compassionate use program of ASV + DCV for 24 weeks were obtained through the Latin American Liver Research Education and Awareness Network (LALREAN) platform. Patients were treated mainly in academic centers in Chile, Argentina and Colombia. Cirrhosis was determined by either liver biopsy, clinical or non-invasive methods. Adverse events were retrospectively collected from the medical charts.

Results. From October 2014 to June 2016, 44 patients have started treatment. Mean age was 62 years old. All patients were HCV genotype 1b and most had compensated cirrhosis (97%). Ribavirin was not used in any patient. Baseline characteristics of the patients and virologic results are summarized in table 1. Adverse events were generally mild, but 8 severe adverse events, which felt not to be related to treatment, occurred. One patient had grade 3 aminotransferase elevation which resolved spontaneously without treatment discontinuation. EOT response was 89% (31/35) and SVR12 was 86% (24/28), with two virologic breakthrough and two relapses.

Conclusion. ASV + DCV were well tolerated in a cohort of mainly cirrhotic patients with a satisfactory preliminary response. Addition of ribavirin should be explored in this particular group of patients.

Funding. BMS provided ASV and DCV in a compassionate program use. Data was collected and analyzed by LALREAN without the intervention of BMS. As was partially funded by grant # 1130357 from FONDECYT.

Table 1 (38).

Variable	Result
N	44
Age, years, mean \pm SD	62 \pm 11
Female gender, n (%)	19 (43%)
Ethnicity, Hispanic / Amerindian	43 / 1
BMI, mean \pm SD	26 \pm 3.6
Cirrhosis (F4), n (%)	38 (86%)
F3, n (%)	4 (9%)
F0-F2, n (%)	2 (5%)
MELD (in cirrhotic patients), mean \pm SD	9 \pm 8
Presence of esophageal varices, n (%)	25(57%)
Platelet count cells/mm ³ , mean \pm SD	124000 \pm 79000
Albumin g/dL, mean \pm SD	3,8 \pm 0,8
Total bilirubin mg/dL, mean \pm SD	1,33 \pm 1,3
Basal HCV viral load, mean log IU/mL \pm SD	6.2 \pm 0.6
End of treatment response, n/N (%)	31/35 (89%)
SVR12, n/N (%)	24/28 (86%)

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THE ANTIBODY RESPONSE TO HEPATITIS B VIRUS VACCINATION IS NOT INFLUENCED BY THE HEPATITIS C VIRUS VIRAL LOAD IN PATIENTS WITH CHRONIC HEPATITIS C

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Background. Some immunogenicity studies of anti-HBV vaccine in patients with chronic HCV infection have demonstrated a diminished response ranging from 63.6% to 72.9% on seroconversion rate, compared to 90.9% in healthy controls. One possible explanation is the high HCV viral load in some patients.

Aim. To evaluate the impact HCV viral load on anti-HBV vaccination response in treatment naïve chronic HCV patients without cirrhosis.

Material and methods. 110 chronic HCV adult patients without cirrhosis were randomized to receive anti-HBV vaccination regimen at standard 3 doses (0, 1 and 6 months) of 20ug or higher dose of 40ug. Response to vaccination was measured by titers of anti-HBs 1 and 6 month after the last dose of anti-HBV vaccine. Healthy controls were negative to anti-HCV, anti-HBc, HBsAg and anti-HBs antibodies, and received standard 3 doses of 20ug at intervals of 0, 1 and 6 months, and were also evaluated for anti-HBs titers.

Results. Of the 110 HCV vaccinated patients the seroconversion rate (anti-HBs \geq 10 IU/mL) was 74.5% (82/110). Out of the 45 healthy controls vaccinated with standard dose, we observed seroconversion rate of 93,3% (42/45). Variables included in the logistic regression model were: Age, Gender, HCV-RNA and Liver Fibrosis by Metavir (F0/F1 vs. F2/F3). Age was the only variable that negatively influenced anti-HBs titers ($p = 0.003$).

Conclusions. Our study had demonstrated that chronic HCV patients without cirrhosis presented impaired anti-HBV vaccine response compared to healthy controls, similar to data previously demonstrated in the literature. This impairment is apparently not influenced by HCV viral load.

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CHRONIC HEPATITIS C TREATMENT WITH DIRECT ANTIVIRAL AGENTS IN A REAL LIFE SETTING

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Introduction. In clinical trials, new oral direct acting antiviral agent (DAA) therapies have demonstrated a high-sustained viral response (SVR) rate in patients with hepatitis C virus (HCV) infection.

Material and methods. We aimed to analyze the efficacy and safety data from DAA interferon-free therapy in HCV infection in a study performed in 6 different clinical settings in Mexico City in a real-world scenario.

Results. Eighty-four patients were treated with 7 different DAA regimens, in which the end of treatment (EOT), SVR12 and adverse effects were evaluated. At their discretion, the attending physicians selected the treatment regimens and durations. A total of 69.1% of the patients were female, and 72.6% had blood transfusion as a risk factor. The mean age was 61 years. The most common genotype was 1b (GT1b) (70.3%). The fibrosis score was F3 and F4 for 55.9% of the patients; liver cirrhosis was present in 45.2% of the patients; the overall EOT response was 98.8%; and the SVR12 rate was 96.05%, independent of the regimen. Three patients did not achieve SVR12; they were cirrhotic, treatment-experienced patients, and two had hepatocarcinoma. Minor non-significant adverse effects that did not interfere with treatment were documented in 36.9% of the patients.

Conclusion. Real-life data shows that in Mexico as probably in Latin America patients access DAA treatment at an advanced age. Treating such population currently challenges us; an SVR12 rate of 96% to DAAs is achieved. This study provides data that may be useful in guiding health professionals and health authorities in the development of health policies.

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IMMUNOLOGICAL BIOMARKERS OF VIROLOGICAL RESPONSE IN PATIENTS WITH CHRONIC HEPATITIS C TREATED WITH PEGYLATED INTERFERON AND RIBAVIRIN

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Introduction. Treatment of chronic hepatitis C have evolved in the last five years from the use of IFN- α + ribavirin towards IFN-free regimens. However studies have shown that cytokines have clinical potential in different therapies of infectious diseases.

Objectives. We sought to investigate the immunological biomarkers related to the treatment of patients with chronic hepatitis C with pegylated interferon alpha (PegIFN- α) and ribavirin (RBV) by correlating serum cytokines/chemokines levels at distinct time points of therapy with patterns of virological response.

Material and methods. Fifty-four naïve monoinfected patients with chronic hepatitis C infected with G1 who were treated with PegIFN- α and RBV for 48 weeks (w) were included. Virological response were 24/54 (44,4%) SVR, 16/54 (29.6%) non responders (NR) and 14/54 (25.9%) relapsers (R). Chemokines (CCL2, CCL5, CXCL8, CXCL9, CXCL10 and IFN- α) were quantified (Cytometric Beads Array CBATM BD) at baseline (16 NR, 14 REL and 24 SVR), 12th w (16 NR, 11 REL and 17 SVR) and 48th w (6 NR, 12 REL and 18 SVR) of treatment and compared among patients with distinct virological response. The control group (CG, n = 19) consisted of healthy blood donors.

Results. At baseline: Higher levels of CCL2, CCL5, CXCL8 CXCL9, CXCL10 and IFN- α were observed in HCV patients compared to CG. SVR patients presented significant lower levels of CXCL8 versus NR. IFN- α levels were lower in SVR patients as compared to NR and REL. SVR and REL patients had similar CCL2 levels. CCL2 and CXCL9 were higher in SVR patients vs. NR. At 12nd week of treatment: SVR patients had up-regulated levels of CXCL8 and IFN- α when compared to NR. CCL5 levels were higher in REL vs. NR.

Conclusion. Patients with chronic hepatitis C have upregulated levels of serum chemokines/cytokines, which can be explained by the HCV-induced pro-inflammatory/regulatory status. The serum levels of CXCL8 and IFN- α might be used as surrogate biomarkers to predict virological response to therapy.

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SEROEPIDEMIOLOGY OF HEPATITIS B IN VOLUNTEERS AGED BETWEEN 30 TO 70 YEARS RESIDENTS IN SALVADOR- BAHIA, BRAZIL

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Introduction. Immune response to hepatitis B can result in chronic liver injury that may progress to cirrhosis or hepatocellular carcinoma. Despite the existence of effective immunoprophylaxis, HBV infection remains a serious public health problem. Sexual and social habits or health conditions situation can interfere with the epidemiology of this infection. In Brazil, the economic development between the 1950s and 1980s have led to behavioral, social and economic changes that could justify changes on the epidemiology of some diseases that are parenterally and sexually transmissible.

Objectives. Evaluate the seroprevalence of hepatitis B virus infection or vaccinating markers in volunteers born between 1945 and 1985 undergoing laboratory tests at Labimuno/UFBA; Associate the results with demographic and socioeconomic covariates and characterize B hepatitis in the studied population.

Material and methods. A Transversal study composed by a sample of 650 randomly selected patients undergoing laboratory tests at Labimuno/UFBA between 2015 and 2016. The serologies (Anti-HBs, Total Anti-HBc/Anti-HBc IgM and HBsAg) were performed by immunochemiluminescence. The data are currently undergoing evaluation.

Results. The following percentage of markers for hepatitis B were found: 2.15% of HBsAg, 17.08% Anti-HBcTotal, 27.38% of anti-HBs. From the reagents for Anti-HBc Total, 2.7% were reagents for IgM anti-HBc, suggesting acute infection. According to the sociodemographic questionnaire, 15.2% reported having tattoos, 95.7% reported sexual intercourse without condom use and 6.3% reported being drug users in the past. Only 28.8% reported being vaccinated for hepatitis B (without comprobation), of which 42.8% were seropositive for anti-HBs.

Conclusion. Preliminary results suggest that behavioral changes could be associated with the spread of hepatitis B, among 30-70 year age population which could indicate that this population need more attention from the public health services.

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RESULTS OF ALL-ORAL THERAPY FOR CHRONIC HEPATITIS C IN A SINGLE CENTER

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Background. All-oral therapy for hepatitis C has changed the perspectives of patients and health providers in the couple

of years, but its availability and experience in Latin America is just starting.

Aims. To report the clinical characteristics and preliminary virological response of patients starting all-oral therapies for chronic hepatitis C in an academic center in Chile.

Material and methods. From June 2013 to June 2016, all patients starting on oral therapies for chronic hepatitis C have been followed. Treatments include compassionate use programs (31%), clinical trials (26%), therapies paid by the patients or reimbursed by the patient's health system (16%) and generic therapies acquired from India (27%). Cirrhosis was determined by either liver biopsy, clinical or non-invasive methods. Adverse events were retrospectively collected from the medical charts. Treatments included asunaprevir (ASV) + daclatasvir (DCV), paritaprevir/ritonavir/ombitasvir + dasabuvir (PrOD), sofosbuvir (SOF) + DCV, and SOF + ledipasvir (LDV). Intention to treat analysis was used.

Results. In total, 71 patients started treatment. Mean age was 62 years old and 64% of patients were male. Most patients had HCV genotype 1b (97%). Cirrhosis was present in 64% of patients. Adverse events were generally mild. Overall SVR12 was 89% (39/44). SVR12 for ASV + DCV was 69% (11/16), whereas for other regimens SVR12 was 100% (28/28).

Conclusion. All-oral therapies are very effective and safe in this group of patients in our country.

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MOLECULAR EPIDEMIOLOGY OF HEPATITIS B VIRUS IN THE STATE OF ACRE, BRAZIL

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Introduction. Hepatitis B virus (HBV) is an important cause of infectious disease of the liver, and its transmission has been partially reduced by antiviral treatment programs and by immune prophylaxis. However, mutations in the coding sequence of the reverse transcriptase (rt) domain of the P gene and that overlaps the S gene region can result both in resistance to the nucleos(t)ide analogs (NAs) drugs available and in vaccine escape.

Objective. To identify NAs resistance and vaccine escape mutations in patients with chronic hepatitis B.

Material and methods. Blood samples were collected from 156 patients with chronic HBV who attended the University Hospital at Rio Branco-AC, a northern region of Brazil, between 2012 and 2014 HBV-DNA from each sample was amplified and direct sequenced for HBV genotyping and screening the mutants.

Results. Circulating genotypes were A (57%), F (23,1%) and D (19,9%), subtypes A1, D1, D2, D3, D4, F1 and F2, respectively. Overall NAs resistance mutation rate of 1.2% was determined, mostly due to the presence of the primary mutations rtA181E and rtT184S/T. Secondary rt mutations were also found (rtN246S, rtH248N and rtI233V). Vaccine escape mutations rate was 7.1%.

Conclusion. Since Brazil has provided treatment for HBV infection for more than a decade, it is important to track for HBV mutations and evaluate its clinical implications.

Table 1 (46). Demographics and baseline characteristics.

Patient	Age	Cirrhosis	Varices	Treatment experience	Basal HCV-RNA UI/mL (logs)	MELD at baseline	Treatment duration	Reason for D/C treatment
1	70	Yes	Gastric varices	NR to PR	2.160.000 (6.3)	7	11 weeks	Health insurance
2	62	Yes	No	NR to PR	755.000 (5.9)	6	8 weeks	Health insurance
3	62	Yes	No	Naïve	464.000 (5.6)	12	12 weeks	Liver transplantation

D/C: discontinued. NR: non-response. PR: pegylated interferon plus ribavirin.

45 TREATMENT OF HEPATITIS C-ACUTE AUTOIMMUNE HEPATITIS OVERLAP SYNDROME WITH BUDESONIDE AND DIRECT ACTING ANTIVIRAL THERAPY

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Introduction. The management in patients with Hepatitis C-Autoimmune hepatitis (HCV-AIH) overlap syndrome has been facilitated with the development of direct acting antiviral (DAA) therapy. Use of budesonide in these patients seems an attractive alternative, because of its lower incidence of corticosteroid-related adverse reactions. We present the treatment of a patient with chronic hepatitis C who developed autoimmune hepatitis years after diagnosis.

Objective. To describe the management of VHC-AIH overlap syndrome with budesonide and DAA.

Material and method. A 42-year old woman with known HCV G1b infection acquired after blood transfusion at birth, was diagnosed in 2006 after giving birth. Her evaluation, including a liver biopsy (F0A0) revealed mild aminotransferase elevation and negative serological markers of AIH. She was lost to follow up until 2013. Her LFT, albumin, total protein and platelet count were unchanged, however her biopsy at that time had progressed to F1A2. She refused treatment at that time. Again she was lost to follow up until she presented with jaundice in 2015. Her blood work, serology and biopsy (F3) was diagnostic of acute autoimmune hepatitis. She began treatment with budesonide 9 mg QD and Azathioprine 1.5 mg/kg with prompt marked improvement in her LFT and synthetic function. Fourteen weeks after beginning therapy with budesonide, treatment with simeprevir 100 mg QD and sofosbuvir 400 mg QD was begun and was given for 20 weeks. The budesonide was tapered 3 mg every 8 weeks, until it was discontinued 6 months after beginning therapy.

Results. Aminotransferase levels promptly normalized, HCV RNA was undetectable by week 4 and week 12 and SVR24 was achieved. The patient developed no significant side effects to the treatment during the entire therapy.

Conclusion. The combination of budesonide and DAA appears to be an effective, safe and well tolerated treatment modality for HCV/AIH overlap syndrome.

46 DACLATASVIR PLUS ASUNAPREVIR TREATMENT FOR HEPATITIS C GENOTYPE 1B INFECTED PATIENTS WITH COMPENSATED CIRRHOSIS: DO WE NEED TO TREAT ALL THE PATIENTS FOR 24 WEEKS?

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Background. All-oral combination of direct-acting antivirals could lead to higher sustained virologic response (SVR) in hepatitis C virus (HCV)-infected patients. Dual oral treatment with a NS5A inhibitor, daclatasvir (DCV) plus NS3/4A protease inhibitor, asunaprevir (ASV), for 24-weeks has been proven to be safe and effective in genotype 1b-infected patients. In South America, this regimen has been approved in Chile, Colombia, Peru and Mexico.

Aims. To describe effectiveness in three patients who received DCV-ASV for less than 12 weeks.

Material and methods. Data of patients was obtained from the Latin American Liver Research Education and Awareness Network (LALREAN). Patients were followed at one academic center. Cirrhosis was determined either by liver biopsy, non-invasive methods or clinical findings. Medical information was obtained retrospectively from medical charts.

Results. Three patients with HCV Gt1b infection and compensated cirrhosis discontinued DCV-ASV therapy before achieving 24 weeks. Table 1 describes baseline demographics and clinical characteristics of the 3 patients. Treatment was safe and well tolerated in all patients. Therapy was discontinued in two patients because the health insurance ceased DCV supply at week 8 and 11; respectively. The third patient developed hepatocellular carcinoma and underwent liver transplantation after completing 12 weeks of treatment. The three patients presented undetectable HCV-RNA at week 4 and achieved SVR12.

Conclusions. These cases suggest that some patients might achieve SVR with shorter course of DCV-ASV treatment. Real world evidence cohorts from countries where this regimen is approved can help us to identify those patients that might benefit with a shorter regimen.

B. COMPLICATIONS OF CIRRHOSIS

01

FIRST THREE CASES OF ALFA PUMP IN LATIN AMERICA FOR THE MANAGEMENT OF REFRACTORY ASCITES IN WAITING LIST FOR LIVER TRANSPLANTATION

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Background and aims. The management of refractory ascites remains a challenge. In our waiting list for Liver Transplantation, the highest mortality rate is among patients with refractory ascites. Our institution was the first in Latin America to implant ALFA PUMP for the management of this entity.

Material and methods. Case report.

Results. Case 1. 58 years-old female with autoimmune cirrhosis. She underwent large-volume paracentesis (LVP) weekly in a period of 6 months. Child C-11 MELD 14. Follow up after 4 months of ALFA PUMP implantation, she required just 1 LVP and underwent LT. Case 2. 54 years-old male with cirrhosis due to alcohol. He required LVP every other week during 6 months. He underwent laparotomy and umbilical hernia repair with the use of synthetic mesh due to incarceration. Child B-9 MELD 10. Follow up after 8 months of implantation, he required 4 LVP and underwent LT. Case 3. 48 years-old female with autoimmune cirrhosis. LVP every week with weight loss and severe hypoalbuminemia as consequence. Child C-11 MELD 14. After 10 months of implantation, she is still in waiting list, she has required 5 LVP, her nutritional status improved considerably and therefore her quality of life.

Conclusions. ALFA PUMP is a novel therapy in America for refractory ascites. It constitutes an excellent choice for LT candidates improving survival rates in waiting list as well as providing excellent quality of life and reducing health care expenditures.

02

HEPATOPULMONARY SYNDROME IN PATIENTS WITH CIRRHOSIS WHO ATTENDED THE GASTROENTEROLOGY OUTPATIENT CONSULTATION AT HOSPITAL EUGENIO ESPEJO, QUITO 2015

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Introduction. Hepatopulmonary Syndrome (HPS) is a complication observed in patients with chronic liver disease and/or portal hypertension imputable to intrapulmonary vascular dilatation, which may include severe hypoxemia. Its presence weakens the prognosis and the quality of life of the patients; therefore, screening is essential since its diagnosis is an exception in the MELD score as a priority indication to enter the waiting list for a liver transplant.

Goals. To determine the prevalence of the Hepatopulmonary Syndrome diagnosed through saline contrast echocardiogram and its relation with the level of liver dysfunction in patients suffering from cirrhosis who attended the Gastroenterology outpatient consultation at Hospital Eugenio Espejo in the city of Quito during February – April 2015.

Methodology and instruments. A descriptive and prospective study was performed based on a cross-section design with 66 patients diagnosed with cirrhosis from multi-factorial origins who met the inclusion criteria and who initially underwent oxygen saturation with pulse oximeter, sitting and in decubitus position, arterial gas analyses, and pulmonary dilatation confirmed through saline contrast transthoracic echocardiography.

Results. The study showed that the sample included 39.39 % men and 60.61 % women, and the HPS prevalence was 13.64% (IC95% 5.36 – 21.92). The Pearson Chi-squared test showed there is no statistically significant relation between HPS and the liver dysfunction degree ($p = 0.12$). The HPS average presentation altitude was 1553 masl (IC 95% 714.76 – 2391.46).

Conclusions. Although there are no prior studies on this syndrome's prevalence in Ecuador, the results show moderately relevant values that deserve performing studies with larger regional and national target population.

03

DETECTION OF INFECTION AFTER CYANOACRYLATE INJECTION USING F-18 FDG PET/CT SCAN IN A PATIENT WITH ENDOSCOPIC MANAGEMENT OF MASSIVE GASTRIC VARICEAL BLEEDING

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Introduction. CA glue obturation for GV bleeding has excellent rates of acute hemostasis, prevent rebleeding with well-known but rare complication.

Aim. We are reporting a very uncommon infection case after N-butyl-2-cyanoacrylate (CA) injection for management of acute gastric variceal (GV) bleeding detected and followed using F-18 FDG PET/CT Scan.

Material and methods. A 63 year-old woman with hepatitis C cirrhosis was admitted to emergency room for fever, chills, and nausea. One previous month she was in our hospital for massive GV bleeding with hemodynamic instability, hemoglobin 4 g/dL and needed CA obturation endoscopy. Patient was initially treated in other institution with antibiotics without clinical improvement. At arrive our hospital hemocultures (6) were made with negatives results and exhaustive fever protocol study discarding other pathologies. Presepsin and procalcitonin levels were higher suggesting bacterial infection. Abdominal CT showed CA plugs in gastric fundus. Patient had fever peak 40 degrees Celsius, chills, and meropenem plus vancomycin was started empirically during three

weeks with clinical improvement and normalizing infections biomarkers.

Results. Due antecedent of cyanoacrylate (CA) injection a F-18 FDG PET/CT Scan was performed on a Phillips Ingenuity TF PET/CT scanner 60 minutes after intravenous injection of 185 MBq of FDG and showed focal hyperdense FDG uptake (maximum SUV 12.8) on a 12 thoracic vertebrae level around CA plug and discrete hyperdense material (maximum SUV 4.9) in gastric fundus corresponding CA plug. The attenuation correction images with hyperglycolitic metabolism experimented marked reduction in both areas (SUV 3.6 and undetectable respectively) during follow up FDG PET/CT performed two week after antibiotics.

Conclusion. We are reporting one of the first uncommon CA plug infection case in the recent literature detected and followed using F-18 FDG PET/CT Scan

04

BALLON-OCCLUDED ENDOSCOPIC INJECTION SCLEROTHERAPY AS A TREATMENT FOR HIGH-RISK CARDIOFUNDAL GASTRIC VARICES: REPORT OF TWO CASES

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Introduction. Gastric varices bleed less frequently than esophageal varices, but when they bleed, is much more severe. Effective management of such bleeding is particularly difficult. Their treatment options are cyanoacrylate endoscopic injection, the Transjugular Intrahepatic Portosystemic Shunt (TIPS) and the Balloon-occluded Retrograde Transvenous Obliteration (BRTO). Cyanoacrylate endoscopic injection has embolic risk and frequent partial occlusion. It has proven to be inferior in reducing the risk of rebleeding in relation to TIPS and BRTO. On the other hand, TIPS has the risk of hepatic encephalopathy and BRTO produces increased portal pressure, which implies volume retention and development of esophageal varices. Therefore, the optimal treatment of cardiofundal gastric varices is a matter of ongoing research.

Clinical cases. We present two cases of recurrent gastrointestinal bleeding from cardiofundal gastric varices treated by Balloon-Occluded Endoscopic Injection Sclerotherapy (BO-EIS). In this technique, by upper digestive endoscopy 7 and 8 vials of cyanoacrylate are directly injected within gastric varices. Excluded outflow through one or two occlusive balls installed by venous catheter, either systemic through femoral catheter or through the portal by percutaneous transhepatic catheter reduces the embolic risk. When controlled by x-ray, sclerosing material was not observed passing through the portal or systemic system. One patient is doing well after 8 months without a new bleeding. The other patient had a new bleeding, which was stopped with 14 vials of cyanoacrylate injected by another BO-EIS procedure. He died because multifocal hepatocellular carcinoma.

Conclusions. BO-EIS has the advantages over other treatment options of lower risk of embolism, not producing increased portal pressure, not producing hepatic encephalopathy and using less volume of sclerosant than

BRTO, being equivalent to BRTO in preventing rebleeding by cardiofundal gastric varices.

05

APPLICATION OF CLIF-C ACLF SCORE AND CLIF-C AD SCORE IN HOSPITALIZED PATIENT WITH CIRRHOSIS

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Introduction. Acute decompensation (AD) is a frequent cause of hospitalization. The scores developed by the European foundation for the study of chronic liver failure (EF-Clif) for patient with AD without acute on chronic liver failure (ACLF) and for patient with ACLF allow to assess the survival of these patients.

Objective. Evaluate the predictive value of mortality scores CLIF-C-AD and CLIF ACLF in cirrhotic patients hospitalized for DA.

Material and methods. The scores were applied in cirrhotic patients hospitalized with DA between 2010 and 2012 at the Clinical Hospital San Borja Arriarán. We evaluated their correlation with mortality at 30 and 90 days.

Results. 109 patients were hospitalized with a diagnosis of cirrhosis between 2010 and 2012. 59 were hospitalized with AD. 18 and 41 patients respectively had ACLF and AD. In patients with DA without ACLF the median survival was 23 months. CLIF-C AD score correlation with mortality at 3 months was 0.35 ($p < 0.05$). The CLIF AD AUROC curves to predict mortality at 3 months was 0.76 ± 0.07 , with a sensitivity of 100%, specificity of 58%. The mortality was significantly different in patients with and without ACLF, 33% vs. 7.4% at 30 days ($p = 0.02$) and 55.6 vs 11.5% ($p = 0.0004$) at 90 days respectively. In patients with ACLF the observed mortality at 30 days was 33% ($p < 0.02$) and 56% at 90 days ($p < 0.0004$).

Conclusion. In our patients the use CLIF-C AD and CLIF-C ACLF scores was significantly correlated with the observed mortality in the short term.

06

CLINICAL PROFILE OF PATIENTS WITH ACUTE ON CHRONIC LIVER FAILURE: EXPERIENCE IN A REFERENCE LIVER TRANSPLANT CENTER IN COLOMBIA

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Introduction. Acute-on-chronic liver failure (ACLF) is an entity characterized by an acute deterioration in liver function in an individual with pre-existing chronic liver disease. Epidemiological data in our environment are needed for a better understanding.

Objective. To determine the underlying etiology, precipitating causes, clinical features and natural course of ACLF in

patients at the waiting list for liver transplantation (LT) between January 2012 to December 2015, in Fundación Cardioinfantil, Bogotá, Colombia.

Material and methods. Retrospective observational study.

Results. Out of 214 patients, 38 (17.7%) fulfilled the ACLF criteria according to the definition EASL CLIF-C. The four main etiologies of cirrhosis were alcohol (26.3%), cryptogenic (18.4%), autoimmune hepatitis (15.8%) and hepatitis C (13.2%). The triggering factors were infection (63%), unknown (23.7%), gastrointestinal bleeding (10.5%) and alcoholism (2.6%). Out of the infections, 80% were Healthcare-associated infections (HAIs). 40% Multidrug resistant bacteria (MDR bacteria) and 7.9% fungal infections. 25% had a second infection [Hospital-acquired infection (HAI)]. Out of the total, 44.7% had renal failure from the beginning and 13% over the course of 3 to 7 days. Overall mortality was 50% at 28 days and 60.5% at 90 days. The 28-day mortality rate was correlated with the degree of ACLF: ACLF-1 33.3%, ACLF-2 53.8% and ACLF-3 69.2%. A total of 11 patients (29%) underwent LT [7 (18.5%) during the episode of ACLF and 4 (10.5%) afterwards.

Conclusions. Our patients with ACLF have similar clinical outcomes to that described in the western population, although with low frequency of alcoholism as trigger and high frequency of infection, perhaps resulting in a worse prognosis. Prospective studies are required to confirm these observations.

07

MINIMAL HEPATIC ENCEPHALOPATHY DIAGNOSIS THROUGH A PSYCHOMETRIC HEPATIC ENCEPHALOPATHY SCORE TEST (PHES) IN PATIENTS WITH CIRRHOSIS

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Introduction. Minimal hepatic encephalopathy (MHE) is a neuropsychiatric disease this affects patients with hepatic cirrhosis and foresees the development of episodes of clinical hepatic encephalopathy, is associated with a deterioration of the quality of life and lower survival rates.

Objetive. Determine the prevalence of MHE by applying the PHES psychometric test.

Material and methods. This is a transversal descriptive epidemiological study; it was used PHES adjusted to the average tables of the Spanish population (< -5 as a diagnostic) to cirrhotic patients at the Hospital Eugenio Espejo in Quito in 2015. The analyses were performed using the statistical packet Stata v 13. The data was expressed in frequencies, percentages, means and standard deviations. The distribution differences were carried out using one-way ANOVA. The relations the variables were evaluated using the Pearson correlation coefficient and were represented through dispersion graphs. The relationship the variables was summarized with odds ratios (OR) and their confidence intervals CI of 95%, obtained through logistic regression. The value of $p < 0.05$ was considered statistically significant.

Results. Obtained from 90 subjects with complete information. The prevalence of MEH was determined to be 35%, using PHES, the degree of correlation with the clinical values presented and inverse correlation with INR -0.30, Ascites -0.44, Child Pugh -0.445 and Meld -0.366. The variables that are associated with the risk of developing MEH are severe ascites, prolonged INR, Child Pugh C and 14% increase in risk with each increase in the Meld scores.

Conclusions. The prevalence of MHE in cirrhotic patients was determined to be 35%, using PHES. Its increase is directly proportional to the deterioration of liver functioning, with significant statistical differences in Child Pugh and Meld.

08

STROOPTEST VALIDATION FOR DIAGNOSIS OF MINIMAL HEPATIC ENCEPHALOPATHY IN AMBULATORY CIRRHOTIC PATIENTS

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Introduction. Minimal hepatic encephalopathy (MHE) is a neuropsychiatric syndrome with mild manifestation, underdiagnosed and its treatment could be beneficial. Detection is based on specific psychometrical tests, being PHES (Psychometric Hepatic Encephalopathy Score) the gold standard test. The smartphone application, Strooptest, may be an alternative diagnostic modality.

Objetives. To validate Strooptest as a diagnostic method of MHE in cirrhotic ambulatory patients from our hospital.

Material and methods. Transversal study of 45 patients, 62.2% male, mean age 60.6 years old (IC 95% 58.1-63.2). Psychometric PHES and Strooptest were used. The diagnosis of MHE was made with a PHES <-4 and Strooptest OffTime + OnTime on >145 seconds in <45 years old, and >190 seconds in ≥ 45 years old. Sensitivity and specificity of alternative test and PHES concordance was calculated.

Results. We report a MHE frequency for PHES test of 37.8% and 55.6% for Strooptest. The mean score was -3.18 for PHES and 220,260 seconds for OffTime + OnTime for Strooptest. Sensitivity and specificity was 94 and 68% respectively when compared with PHES. Negative predictive value was 0.95 and concordance of 77.8% with ($p < 0.001$).

Conclusion. Strooptest demonstrated a high sensitivity and concordance with the gold standard. Its high predictive value supports its use as screening, allowing a practical and accessible evaluation for MHE.

09

ASSOCIATION BETWEEN HEPATIC SIDEROSIS AND HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS

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Introduction. Hepatic siderosis is a form of iron overload disorder, is found in 35 to 78% of patients with end-stage liver disease, irrespective of the cause of cirrhosis. Liver biopsies provide a direct measure of liver iron concentration. Iron overload is also frequently present in the liver of patient with hepatocellular carcinoma (HCC).

Objetives. To investigate the influence of hepatic iron overload on the occurrence of HCC in cirrhotic patients and to assess the association of hepatic siderosis with different causes of cirrhosis.

Material and methods. A retrospective study of 82 patients who underwent an orthotopic liver transplant between 2005 and 2016, searching for iron stores with Prussian blue on tissue of the explanted livers. Was considered siderosis when

staining was positive. Binary variables were compared by χ^2 analysis.

Results. Eighty-two patients were studied, 40 of them had HCC, with an average of 55 ± 10 years, 62% were male. 41/82 (50%) patients had hepatic siderosis and of these 48.7% were NASH. From the 40 HCC patients, 57% had NASH, 14.2% were alcoholic, 7.1% had HCV and 21.7% other causes. Data analyzed showed a statistically significance between HCC and NASH ($p < 0.05$). However, it was not possible to demonstrate an association of hepatic siderosis and HCC and no association could also be demonstrated between NASH and siderosis.

Conclusions. This study showed that hepatic siderosis was very frequent in cirrhotics, present in 50% of our patients, unrelated to the presence of HCC. However, patients with NASH had higher frequency of HCC.

10 HEPATOCELLULAR CARCINOMA MORTALITY, ETIOLOGY AND CHARACTERISTICS DURING A 8 YEAR REVIEW IN A TERTIARY CARE HOSPITAL IN CHILE

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Introduction. Hepatocellular carcinoma (HCC) is a common complication of liver cirrhosis and is the third cause of cancer death worldwide. The incidence and mortality is growing in western countries, but the Statistical data of HCC in Chile is lacking.

Objectives. Describe the clinical characteristics, etiology of cirrhosis and survival rates in a group of Chilean patients that have being diagnosed with HCC from 2008 and 2015 in a Tertiary care Hospital of Chile.

Material and methods. This is a retrospective study and were reviewed the clinical records of every patient that was diagnosed with HCC, checking their clinical findings, images, diagnostic criteria, etiology of cirrhosis, laboratory tests and staging (classified by the Milano criteria). An univariate statistical analysis using χ^2 test was made.

Results. A total of 117 patients with HCC and followed for at least 12 months were included. Overall, 58.97% were men, the median age was 64.79 years (range 53-76). The most prevalent etiology of cirrhosis was alcohol 26.5%, HCV infection 21.37% and NASH with 16.24%. At diagnosis 44.4% of the patients met Milano criteria. Global mortality rate at 12, 24 and 36 months were 45.3%, 67.37% and 77.42%. An univariate analysis for mortality at 12, 24 and 36 months were statistically significant higher between patients that exceeded Milano criteria [60%, 82.14%, and 89.09% vs. 26.92%, 46.15% and 60.53% respectively ($p < 0.01$)].

Conclusions. As in international series most patients were male. The three leading causes of HCC were cirrhosis due to alcohol, HCV and NASH, which correlates with the national epidemiology of cirrhosis. Mortality rates are high, especially in patients that exceeded Milano criteria. This finding shows the importance of having adequate health policies for achieve diagnosis in early stages.

11 IMPACT OF SOCIO-DEMOGRAPHIC CHARACTERISTICS IN HEPATOCELLULAR CARCINOMA SURVEILLANCE

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Introduction. Hepatocellular carcinoma (HCC) is the most common primary liver cancer and the 3rd cause of cancer-related death in the world. The main risk factors for HCC are cirrhosis, hepatitis B (HBV) and C (HCV). Although surveillance in high-risk patients can be highly efficacious for detecting early HCC, it has being underutilized in clinical practice. There are few studies analyzing the impact of demographic characteristics in adherence to HCC screening and tumor diagnosis.

Aim. To assess the socio-demographic characteristics of patients with hepatocellular carcinoma and their impact on HCC surveillance.

Material and methods. We conducted a prospective study from March-2013 to December-2014, which included 173 patients with HCC, referred for treatment in our service. We applied a questionnaire with demographic data, knowledge of the disease, habits, addictions, adherence of HCC screening and tumor characteristics at diagnosis.

Results. Of the 173 patients, median age was 60y, 66% were male and 95.4% Caucasian. Most patients were married and 50% attended only the fundamental education. Etiology of cirrhosis was HCV in 51%, alcohol in 18%, HBV in 14% and NASH in 3.5%. Previous or current history of smoking or alcoholism was present in 62% and 32%, respectively. The majority of patients had prior knowledge of their disease (73%) and 70% was performing regular medical follow-up. Regular screening was performed in 67%, and of these 55.2% was performing USG every 3-6 months. At diagnoses, most patients had early HCC (84% BCLC 0/A). Married patients ($p = 0.006$) and patients who had prior knowledge of their disease ($p < 0.001$) performed more surveillance and it was done more frequently ($\leq 6m$). Patients submitted to regular screening had HCC diagnosis in earlier stage - BCLC 0/A ($p = 0.001$).

Conclusion. Utilization rates of HCC screening were high in our study. The realization of regular medical follow-up and surveillance allowed early diagnosis of HCC in most of our patients.

12 USEFULNESS OF TRANSYUGULAR INTRAHEPATIC PORTO-SYSTEMIC SHUNT (TIPSS) PLUS COLLATERAL EMBOLIZATION IN THE TREATMENT OF SEVERE VARICEAL BLEEDING

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Introduction. TIPSS is widely use in treatment of portal hipertensión (PHT) mainly control of acute variceal bleeding (AVB). Therapeutic goal is to reduce portal pressure gradient (PPG) ≤ 12 mmHg. It could increase liver failure and enceph-

alopathy (EH). Polytetrafluoroethylene (ePTFE) stent has been used due to less stent dysfunction than bare stent. It is unknown the effectiveness of TIPSS with a less strict PPG therapeutic goal plus collateral embolization (CE).

Objective. To determine the effectiveness of TIPSS plus CE in severe AVB patients who did not lowered PPG ≤ 12 mmHg and to determine its outcome.

Material and methods. Between Jan 2014 and Jan 2016, 34 patients received TIPSS as AVB treatment (n = 25) and recurrent rebleeding (AVR; n = 9). 16 had severe AVB defined as uncontrollable (n = 11) and AVB from gastric varices (n = 5). All patients receive ePTFE TIPSS plus main gastric vein embolization with Vascular Plug (VP). Therapeutic goal was 20% decrease of PPG. Follow-up included Doppler ultrasound 7, 30 days and every 3 months. Patients underwent hepatic hemodynamic before stent dysfunction or when presenting clinical manifestation of PHT. Dysfunction was defined as a reduction greater than 50% of the shunt or PPG greater than 12 mmHg. Endpoints were initial control of bleeding and 6/12 months survival. In addition, clinical outcome was evaluated.

Results. Initial PPG was 19.5 ± 2.6 mmHg. The initial dilatation of the liver path was 7 mm and further dilatation was applied as required. In all patients PPG decreased 20% or more. 3/16 patients had PPG ≤ 12 mmHg after TIPSS. All patients received main gastric vein embolization with AVP. The initial control of bleeding was 100%. Follow up was 14.2 months (6.3 – 24.4 months). Two patients (8 %) showed TIPSS dysfunction. Recurrence occurred in only 1 patient (6.3%) with TIPSS dysfunction. Probability of EH was 22% (4 pts) and overall survival was 100% at 6-12 months.

Conclusion. This study shows that in patients with severe AVB, decreased PPG by TIPSS could be less than that standard goal when associated with collateral embolization. This procedure offers high rate of control of bleeding. These severely ill patients shows high survival and low clinical complications of portal hypertension.

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MICROBIOLOGICAL FINDINGS IN CULTURE CIRRHOTIC PATIENTS

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Introduction. Infections are a common cause of decompensation in cirrhotic patients. Therefore, it is important to know the local bacteriology in order to choose the right antibiotics.

Aim. To evaluate the microbiology of cirrhotic patients (CP) at the University of Chile Hospital.

Material and methods. Retrospective descriptive study, 1511 cultures of 200 CP were included. 324 corresponded to ascites fluid (AF), 597 urine cultures (UC), 475 blood cultures (BC) and 115 to other cultures (OC). 359 (24%) were positive, 28 AF, 203 UC, 86 BC and 43 OC. Demographic and clinical variables were recorded.

Results. Positive cultures: 58% was GRAM (-), 32% was GRAM (+) and 8.6% fungi. 47% were resistant to first-line antibiotics, 63% of *Staphylococcus* was methicillin-resistant (MRS), 38% were vancomycin-resistant enterococci (VRE), 54% producing extended-spectrum beta-lactamase (ESBL), 2 cases of producing bacteria carbapenemases and 54% resistant to ciprofloxacin. The use of rifaximin as prophylaxis encephalopathy was associated with increased risk of infections by Gram (+) (OR 2.3, 95% CI: 1.4-3.7, p = 0.0006). There was no

relationship between the presence of antibiotic resistance and prophylaxis with Ciprofloxacin, hospitalization greater than 3 days or the presence of 6 months prior hospitalization. The use of ciprofloxacin was not associated with increased risk of bacteria resistant to ciprofloxacin.

Conclusions. The bacteriology indicates that frequency of infections by GRAM (-) remain predominant. There is a high antibiotic resistance, finding ESBL producing bacteria, MRS, VRE in 47% of cases. The use of Rifaximin as prophylaxis for encephalopathy was associated with increased risk of infections by Gram (+).

14

CONTRAST-ENHANCED ULTRASOUND IMPROVES THE DIAGNOSIS OF LIVER NODULES IN PATIENTS WITH CHRONIC LIVER DISEASES

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Introduction. The etiological diagnosis of solid liver nodules in patients with chronic liver disease by ultrasound is challenging because images characteristics are not specific. Contrast-enhanced ultrasound (CEUS) is a promising tool with the advantage of avoiding exposure to radiation and being fast, safe and well tolerated by the patient.

Aim. To report our initial experience with CEUS.

Material and methods. Thirty-four consecutive patients with liver nodules were assessed. Male n = 17, median of age 59 years (range 30-88), BMI 27.5 (range 21-40). All patients had chronic liver disease of different etiologies (HCV n = 9, alcohol n = 6, HBV n = 3, NASH n = 8, NAFLD n = 5, PBC n = 1, cryptogenic n = 4), 63.6% of them with cirrhosis.

Results. The median nodule size was 28.5 mm (8 - 63). CEUS correctly classified the nodules in 88.2% (n = 30) of the cases as follow: adenoma (n = 3; 8.8%); focal nodular hyperplasia (n = 6; 17.6%); HCC (n = 13; 38.2%); hemangioma (n = 3; 8.8%); macro regenerative nodule (n = 4; 11.8%) and 2.9% (1/34) ruled out HCC relapse.

Conclusion. CEUS is a useful tool to classify liver nodules in patients with chronic liver disease.

015

TERLIPRESSIN AND HEPATORENAL SYNDROME (HSR) - PRELIMINARY ANALYSIS

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Introduction. HRS is a functional acute renal failure (AKI) potentially reversible, in cirrhosis with high mortality: for HSR-1, rapid course and lower survival and SHR-2, slower and progressive frame.

Objective. To evaluate safety and effectiveness of terlipressin in cirrhotics with HRS-1.

Material and methods. Cirrhotics with ascites and AKI (creat > 1.5mg/dL or increase of 0.3 mg/dL in 48 h) with HRS-

1 were included. Prospective study of 18m is part of a research project for the Brazilian Public Health (PPSUS/FAPESP) in two school hospital. Inclusion criteria: age 18-75y, liver cirrhosis, HRS-1, no advanced HCC, possibility for liver transplant or TIPS, signing Informed Consent.

Results. 122 patients had AKI and 9 completed criteria for HRS-1. Median age 60, 4 years, 5 (56%) men, cirrhosis etiology: 2 (22%) HCV, 5 (56%) alcoholic, 1 (11%) alcohol and Nash, 1 (11%) Nash. 78% Child C and MELD 21 (17-34). Infection: 7 (78%), 2 (22%) urinary tract infection; 4 (44%) SBP; 1 (25%) blood infection. Mean creat. at HRS-1: 2, 68 (\pm 0.62). FE: Na 0.20 \pm 0.09, urea 21 \pm 7. Treatment was: terlipressin and IV albumin; average time 5.1 d (2-10). Four patients had adverse event: 2-diarrhea, 2-hypertension; 8-congestion. Complete response (CR < 1.5 mg/dL) 7 (78%) and no response 2 (22%); 1 had TIPS and 2 liver transplant. Two patients had HRS-1 recurrence. Hospital mortality: 8 (89%), 6 (67%) sepsis and 2 (22%) hypovolemic shock.

Conclusions. Terlipressin was well tolerated and no patient had suspension for adverse events. There were response in most patients, but 89% mortality, confirming high morbidity and mortality of type 1 HRS.

16

MINIMAL HEPATIC ENCEPHALOPATHY: FREQUENCY, CHARACTERIZATION AND ASSOCIATION WITH DRIVING HABITS IN AMBULATORY CIRRHOTIC PATIENTS

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Introduction. Minimal hepatic encephalopathy (MHE) is a neuropsychiatric syndrome with a wide range of manifestations which cannot be detected during a regular physical examination. The diagnosis is based on established psychometric tests and the importance of its treatment is currently being discussed.

Aim. To evaluate the frequency of MHE, clinical characterization, associated factors and driving habits in ambulatory cirrhotic patients.

Material and methods. A Cross-sectional study of 45 patients. 62.2% males, average age of 60.6 years (CI 95%: 11.6-14.2). Psychometric Hepatic Encephalopathy Score (PHES) test was applied to diagnosis of MHE. A driving habits survey was applied and medical records were reviewed. Percentage and average were used with confidence intervals for characterization and logistic regression to assess risk.

Results. The most common etiologies of cirrhosis were NASH 33.3%, 20.0% alcohol and 15.6% autoimmune hepatitis. 40% were Child A, 46.7% B and 13.3% C. Average MELD was 12.9 (95% CI 11.6-14.2) and body mass index 27.9 (95% CI 26.6-29.2). 31.1% had porto-systemic shunt. We reported MHE frequency of 37.8%. 55.6% (25) of cirrhotic patients reported driving and 11.1% (5) do it professionally. 52.9% (9) of MHE patients drive, and 17.6% (3) do it professionally. 16% (4) of cirrhotic patients reported accidents, all of them were minor. Only the education level was associated with MHE, as a protective factor with OD 0.94 (95% CI 0.89-0.99, p = 0.04).

Conclusion. We demonstrated a high frequency of MHE in our series associated with a high percentage of driving. Only education level determined increased risk of MHE.

17

HEPATOCARCINOMA PREVALENCE IN EUGENIO ESPEJO HOSPITAL FROM 2000 TO 2015

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Introduction. Hepatocarcinoma incidence has been increasing worldwide in recent decades. In Ecuador there is limited information about this pathology, survival and treatment instituted. It is the fifth leading cause of cancer in men and eighth in women in our country. The aim of this study is to analyze the number of patients with hepatocarcinoma in Eugenio Espejo Hospital in the last 15 years.

Objective. To know hepatocarcinoma prevalence, risk factors, diagnostic methods, survival and treatment instituted from January 2000 to December 2015 in HEE.

Material and methods. Type of study: Retrospective. Period: January 2000-December 2015. Inclusion criteria: Hepatocarcinoma diagnosed in patients over 16 years old. Were reviewed hospital records, ultrasound, pathologic and outpatient. Variables such as age, sex, risk factors were examined (hepatitis B and C virus infection, cirrhosis, NASH), laboratory values, survival time, diagnostic and therapeutic methods.

Results. The average age is the sixth decade, and the female/male ratio appears to be the same. This pathology is often associated with underlying liver diseases such as hepatic cirrhosis (67%) and NASH (9%). Diagnostic methods have been: imaging studies (tomography most used), Alpha-fetoprotein determination (20% of patients had > 400 mg/dL), and focal liver lesions biopsy. Because it is a poor prognosis disease, 70.2% of patients died, a figure that is in relation to the HCC worldwide mortality rate.

Conclusions. Hepatocarcinoma is increasing in our country with similar epidemiological characteristics to other populations; however in this study draws attention the high percentage of NASH as the causative agent in relation to other HCC studies, possibly to the high number of obesity and diabetes mellitus patients. The main aspects of epidemiology, etiology, treatment and survival was addressed; and, shows the HCC prevalence in Gastroenterology service of Eugenio Espejo Hospital, to achieve its most aggressive and adequate early detection and therapeutic to get a better result in survival.

018

CIRRHOTIC PATIENTS: OUTCOME AFTER SURGERY

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Introduction. Cirrhotic patients undergoing surgery have higher morbimortality risk. Severity of cirrhosis, comorbidities, portal hypertension and ascites are some of factors related to worse outcomes.

Aim. To measure adverse surgery-related outcomes and their predictors in Chilean cirrhotic patients.

Material and methods. Pre-surgery features and adverse outcomes after surgery were evaluated in a historical cohort of 102 cirrhotic patients operated between 2010 and 2016 at the University of Chile Clinical Hospital.

Results. 52% were male, mean age 58.63 \pm 10.8 years. 71% of

the patients had a MELD score > 10 and 29% had MELD score \geq 15. 51% of patients were Child Pugh A, 28%, Child Pugh B and 21%, Child Pugh C. Emergency surgery was 27% of cases. Most common surgeries were cholecystectomy (32%) and hernia repair (25%). At least one adverse outcome was observed in 37% of patients, being the most frequent renal failure (27%), respiratory failure (17%), major bleeding (13%), and sepsis (10%). 90-days mortality after surgery was 6%. After adjustment by age and sex, variables associated with worse outcomes were: emergency surgery (OR 6.04; 95%CI: 1.70 - 21.50), encephalopathy (OR 6.17; 95%IC: 1.18 - 32.36), bilirubin > 1.5 mg/dL (OR 5.82; 95%IC: 1.53 - 22.19), ASA score (OR 3.37; 95%IC 1.35 - 8.413) and MELD score > 15 (OR 4.15; 95%IC 1.12 - 15.34). Multivariable analysis showed that age, sex, emergency surgery, high bilirubin and encephalopathy were statistically significant to predict adverse outcomes (AUC = 0.801, Sensitivity of 47.62%, Specificity of 88.24%). **Conclusions.** The most frequent complications after surgery in cirrhotic patient were renal failure, respiratory failure, major bleeding and sepsis. Emergency surgery, encephalopathy, high bilirubin, ASA score and MELD score > 15 are associated to worse outcome.

19 MANAGEMENT OF ACUTE BLEEDING IN ESOPHAGEAL VARICES IN PATIENTS WITH CIRRHOSIS. FIVE YEARS EXPERIENCE WITH LIGATURES

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Introduction. This work was done retrospectively from November 2011 to January 2016 at the Digestive Endoscopy Unit of the General Hospital Enrique Garcés of Quito - Ecuador. The hospital receives a lot of cirrhotic decompensated patients with or without active bleeding from esophageal varices, the technique of the bands was implemented, since mortality in the first 48 h was more than 40% with the technique of injection sclerotherapy. The results with ligation were very encouraging. **Aim.** To evaluate the effectiveness of the bonds in the treatment of esophageal varices in cirrhotic patients with liver disease exogenous origin was admitted for emergency service. Endoscopic treatment in the acute phase and follow-up in our unit was the reason for this work. The questions posed were: a) Assess the efficacy of treatment in the acute phase, b) Long-term follow-up, c) Assess the mortality rate with the method in the acute phase.

Material and methods. The methodology includes: a) Emergency patients evaluated had alcoholic liver disease in which it was found on physical examination jaundice, ascites and different degrees of encephalopathy. b) Patients were evaluated with additional tests such as complete blood count, TP, bilirubin. It is noteworthy that patients were diagnosed with ascites by physical examination. c) All patients underwent an upper endoscopy with Fuji 4500 gastroscope and ligatures in the number of 1 to 6 were placed. The number of patients was 61, 35 men representing 57.3% and accounted for 26 women 42%. Various age group between 28 and 88 years. d) Varicose veins.

Results. The results of the study were: a) Standard methodology was used in all patients was the only method ligatures. b) Esophageal varices were classified according Paquet and placement of bonds was done in type II - III and IV. The sta-

tistical evidence that 30% were grade II, 50% were grade III and 20% were grade IV. Patients with active bleeding and bleeding stigmata were 40%, the rest 60% had positive predictive signs of bleeding (red dots - cherry). c) 100% of patients were referred to the Emergency Service and stable hospital without active bleeding.

Conclusions. The implementation of the placement of ligatures in esophageal varices in our unit decreased the mortality rate as a whole, showing the cost - benefit of this technique. The long-term monitoring was not demonstrative as patients because of their social condition could not be monitored and not returned to the track mostly. The continuous collaboration and social work monitoring program looks to improve.

C. AUTOIMMUNE LIVER DISEASE

01 AUTOIMMUNE LIVER DISEASES ARE THE MOST COMMON CAUSE OF EVALUATION FOR LIVER TRANSPLANTATION (LT) IN A HISPANIC ADULT POPULATION: 10 YEARS OF EXPERIENCE AT A REFERENCE CENTER IN LATIN AMERICA

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Background and aims. Most data describing evaluation for LT have been collected from adult populations in Europe, North America and Asia. Information in Hispanic patients has not been assessed. The aim of this study is to characterize the patient population served by Fundación Cardioinfantil's LT Program over the first 10-years of service in Bogotá-Colombia.

Material and methods. Retrospective review of all medical records and institutional database of patients assessed for LT between 2005 and 2015.

Results. In the 10-year period, the program assessed 678 patients for LT. For this group, 351 were women (52%) and 327 men (48%). The median age at referral was 53 years for women and 56 for men. Of all evaluations 50% underwent LT, 25% remained stable, 14% died, 6% are at the waiting list, 3% are in the evaluation process and 3% were not suitable transplant recipients. The 3 leading causes of liver diseases indicating evaluation were autoimmune liver diseases (24%), alcohol-related liver disease (21%) and viral hepatitis (19%). The median MELD score was 11, 16 and 23 for patients that remained stable, that underwent LT and died before LT, respectively. The most common blood type was O (61%), follow by A (27.5%), B (8.5%) and AB (2.5%).

Conclusions. Autoimmune Liver Diseases are considered rare worldwide, but in Colombia is the most common indication of Evaluation for LT especially among women. Therefore, additional research is needed in this particular area in Adult Hispanics to develop targeted interventions at early stages to prevent progression to end-stage liver disease and LT.

02

LIVER BIOPSY REPORTS REVEAL MALIGNANCIES, AUTOIMMUNE LIVER DISEASES, VIRAL HEPATITIS C AND NON-ALCOHOLIC FATTY LIVER DISEASE AS A PUBLIC HEALTH PROBLEM IN LATIN AMERICA: 20 YEARS OF EXPERIENCE AT A REFERENCE CENTER FOR LIVER DISEASES

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Background and aims. Liver diseases are considered a public health problem worldwide as they affect the general population. Despite technological advances, liver biopsy remains the “gold standard” to establish a diagnosis and assess the prognosis of most liver diseases.

Material and methods. We retrospectively reviewed all liver biopsy reports from 1995 to 2015 at the Fundación Cardioinfantil, Bogotá-Colombia. Only liver biopsies and liver explants from adults (older than 18 years) were included.

Results. A total of 109,075 biopsies were processed in 20 years. Out of the total, 3032 were liver biopsies and liver explants. Age ranged from 18 to 89 years old. Median age in women was 51 years old and among men 50 years old. The majority were women accounting for 58%. From 1995 to 2005, the indication for liver biopsy was abnormal LFTs or abnormal images. From 2005 to 2015, there was a shift toward liver explants and post LT related diagnosis. Among diagnosis the top five were malignancies (primary and secondary), autoimmune liver diseases (AILD), Hepatitis C, Non-alcoholic fatty liver disease (NAFLD) and chronic hepatitis of unknown etiology.

Conclusions. Findings in liver biopsies have been described in Europe, USA and Asia. In Hispanic populations the information is limited and in Colombia only one study in pediatric population has been published. Our study is pioneer, since it describes liver diseases in Adult Hispanics. It revealed chronic conditions as the leading cause of liver diseases as in many developed countries, therefore more research is needed to identify factors related to these entities in Latin America and to develop targeted interventions addressed to Adult Hispanics.

03

AUTOIMMUNE HEPATITIS IN ASSOCIATION WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION. REPORT OF TWO CASES AND REVIEW OF LITERATURE

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Introduction. The association of Human Immunodeficiency virus infection (HIV) and autoimmune hepatitis (AIH) is rare. There are few reports in the literature and there are no reported cases in Chile.

Objectives. We present two cases of the association of HIV with AIH.

Results. Case 1: 38 year old woman diagnosed with HIV in 2011. He started antiretroviral therapy with good response. 2014 has elevated transaminases (10-15 times baseline). Coinfection and viral drug hepatotoxicity was discarded. Examinations highlighted: antinuclear antibodies (ANA) (+) 1/80 Anti Smooth Muscle Antibodies (ASMA) (+) 1/40, 1,782 mg/dL. Liver biopsy showed chronic inflammatory lymphoplasmocytic infiltrate and some eosinophils, focal alteration of the limiting plate and bridging fibrosis. Score of the International Autoimmune Hepatitis Group (IAHG) was concordant with definitive diagnosis of AIH. Treatment was started with prednisone and azathioprine, with normalization of liver tests. Case 2: 24 year old man with a history of diabetes mellitus 1. Diagnosis of HIV by 2013, with good response to therapy. In January 2014, he presented elevated transaminases (10-40 times baseline). Viral coinfection and drug hepatotoxicity was discarded. Examinations highlighted: ANA: (-), ASMA: (+) 1/80, IgG 3426 mg/dL, IgM: 319 mg/dL. Liver biopsy showed portal tracts expanded by chronic inflammation of lymphocyte predominance, with plasma cells, eosinophils and some alteration of the limiting plate with porto-portal bridging. Score IAHG was concordant with AIH definitive diagnosis. Treatment was initiated with prednisone and azathioprine, showing gradual decline in liver function tests.

Conclusion. The association between AIH and HIV is uncommon. We report for the first time the association of these diseases in Chile.

Table 1 (04).

Patients	Pre T	1-2 W of HD St alone	2 W of CyA+St	2-3 M CyA+St	6-12 M CyA+St	1-2 Y CyA+St	3-5 Y CyA+St	5-10 Y CyA+St
n	7	7	7	6	6	6	5	3
ALT (UI/L)	956 + 487	433 + 242*	241 + 112*	106 + 64*	46 + 24	36 + 6.5	31 + 10	31 + 26
Bili (mg/dL)	23.3 + 9.4	24.9 + 10.3	19.8 + 7.3*	3.8 + 3*	1 + 0.4	0.7 + 0.3	0.7 + 0.2	0.6 + 0.4
INR	2.7 + 0.6	3 + 1.1	1.6 + 0.25*	1.2 + 0.2*	1.2 + 0.3	1.1 + 0.09	1 + 0.05	1.1 + 0.2
MELD	28.7 + 3.4	29.8 + 3.7	22 + 1*	12.8 + 3.9*	8.3 + 3.2*	7.3 + 1	6.6 + 0.9	7.7 + 1.5

T: treatment. Bili: bilirubin. ALT: alanine aminotransferase. INR: International Normalized Ratio. HD: high dose. 2W: 2 weeks. St: steroids. M: months. Y: years. Results expressed as Mean ± Standard deviation. MELD score: Model for End Stage Liver Disease (points). Comparison through paired *t*-test with previous measurements (**p* < 0.05).

04 NOVEL RESCUE THERAPY WITH CYCLOSPORINE IN ACUTE SEVERE AND FULMINANT AUTOIMMUNE HEPATITIS: A CASE SERIES REPORT WITH A LONG-TERM FOLLOW-UP

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Introduction. Patients (Pt) with an acute severe autoimmune hepatitis (S-AIH), often progress to acute liver failure (ALF), liver transplantation (LT) or death, if an effective therapy is not initiated promptly. High dose steroids (St) act slowly in this setting. Cyclosporine (CyA), has been used in St resistant chronic AIH, but rarely in the acute setting. We have previously reported favorable short-term results in 2 Pt with autoimmune ALF (Zapata R, Ann Hepatol 2004, Abs).

Aims. Evaluate the short and long-term response to rescue therapy to CyA in acute S-AIH and autoimmune ALF, not responding to initial high dose St.

Material and methods. Between 2002-2013 we included Pt with acute S-AIH (INR > 1.5) or autoimmune ALF not improving after 7-14 days of high dose St (prednisone > 60 mg). All were inpatients, ALT > 600 U/L, reasonable liver size, creatinine < 1 mg/dL, < grade II encephalopathy and no evidence of infection. They received standard management in ICU. CyA was added (3 mg/kg/day) if no improvement after 7-14 days of St. CyA was then maintained for > 12 months, and then switching to St/azathioprine was attempted. In case of a flare, CyA was reintroduced. Results are compared by means/SD with paired samples t-test analysis before and after treatment.

Results. Seven adult Pt (6 Women), age 38 ± 13 years old. The table 1 shows laboratory data before/after treatment. At 2 weeks of St, no change in LFT/MELD was seen. After 2 of CyA a significant improvement of all LFT/MELD was observed (P<0.01), which then continued improving for up to 1 year of CyA. 5/7 Pt had ALF, but none required LT. One Pt died at day 35 of CyA (pneumonia), after an initial favorable response. In only one Pt, it was possible to switch to St/azathioprine successfully.

Conclusions. This novel experience with the use of CyA in Pt with S-AIH and autoimmune ALF not responding to St, shows a favorable, and significant rapid clinical response in

most cases. Early infectious complications should be considered. In a long term follow-up we have not seen significant complications and most cases need to maintain CyA due to the frequent reactivations of AIH.

05 AUTOIMMUNE HEPATITIS WITH ACUTE PRESENTATION IS MAINLY ASSOCIATED WITH HISTOLOGICAL FINDINGS OF CHRONIC LIVER DAMAGE

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Introduction. Autoimmune hepatitis (AIH) is known as a chronic disease, but its initial presentation can be as acute hepatitis, as shown in around 30% of patients. In these cases, histological findings can also vary from acute to chronic hepatitis and even cirrhosis.

Objective. To analyze histological findings of patients with AIH of acute presentation.

Material and methods. Retrospective revision of AIH of acute presentation cases in patients hospitalized in three centers between years 2000 and 2015. Patients were classified in three groups. a) Acute AIH: total bilirubin greater than 10 mg/dL and/or ALT more than 15 times, b) Severe AIH: same as a), plus Prothrombin lower than 50%; and c) Fulminant AIH: same as b), plus presence of encephalopathy. Severity of necrosis and fibrosis were compared between groups A, B y C.

Results. In our study were included 108 patients, 96 with complete data, 60 in group A, 26 in group B and 10 in group C. Age 48 ± 15 years, 79% female patients. 64 (68%) had elevated IgG and 69 (71%) had positive ANA. Liver biopsy exposed 69 (72%) patients had characteristics of chronic liver disease, 62% had necrosis, being severe necrosis in 43% patients. 60% had fibrosis and 3% had cirrhosis. 72% of group B (p = 0.001) and 80% of group C (p = 0.019) had severe necrosis, which was statistically significant compared to group A. However, there was not significant differences in fibrosis.

Conclusions. Most patients with AIH of acute presentation had a corresponding liver biopsy with features of chronic liver disease and fibrosis. Findings of necrosis were significantly higher on groups with severe and fulminant AIH, while fibrosis showed no statistical differences between the 3 groups, according to severity.

Table 1 (06).

Patients	Pre CyA, on St/Aza	2 W of CyA	2-3 M CyA	6-12 M CyA	1-2 Y CyA	3-5 Y CyA	5-10 Y CyA
n	5	5	5	5	5	4	1
ALT (UI/L)	299 ± 208	125 ± 72	67 ± 41*	61 ± 9*	72 ± 25*	119 ± 102	120
Bili (mg/dL)	4.7 ± 4.4	2.7 ± 1.9	2.4 ± 2	2 ± 2.1*	1.3 ± 0.6*	2.6 ± 2.5	0.9
INR	1.7 ± 0.4	1.4 ± 0.3	1.2 ± 0	1.2 ± 0.2	1.2 ± 0.3	1.4 ± 0.5	1.2
MELD	17 ± 4	14 ± 2	12 ± 4	11 ± 5	10 ± 4	12 ± 7	8

Bili: bilirubin. ALT: alanine aminotransferase. INR: International Normalized Ratio. 2W: 2 weeks. St: steroids. M: months. Y: years. Results expressed as mean ± standard deviation. MELD score: Model for End Stage Liver Disease (Points). Comparison through paired t-test with previous measurements (* p < 0.05).

06

LONG TERM RESULTS OF CONSECUTIVE PATIENTS WITH STEROID RESISTANT CHRONIC AUTOIMMUNE HEPATITIS TREATED WITH CYCLOSPORINE

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Introduction: Current international guidelines recommend treating chronic autoimmune hepatitis (AIH) with an induction phase [high-dose steroids (St), adding Azathioprine (AZA)] with a progressive taper to decrease dose in St (maintenance phase). Although this strategy has a good overall success rate (> 80%), some patients (Pt) may not respond or present flares, requiring continued high dose of St, which is referred to as St resistant AIH (StR-AIH). Second line treatment strategies for these Pt, include immunosuppressant's like calcineurine inhibitors [Cyclosporine A (CyA) or Tacrolimus] or Mycophenolate mofetil. Case reports with small or medium number of Pt, have shown beneficial effects on pediatric and adults with the use of CyA in StR-AIH.

Aim. To evaluate the short and long-term response to CyA in a group of consecutive StR-AIH Pt.

Material and methods. Between 2007-2013 we included Pts with StR-AIH (recurrent autoimmune flares or persistently elevated liver function tests (LFT) despite standard treatment with optimal doses and adequate adherence to St + AZA). CyA was initiated at a dose of 2-5 mg/kg/d (q 12 h P.O) and adjusted to obtain through levels of 100-250 ug/mL. Clinical data and LFT were regularly registered. Results are compared by means/SD with paired samples *t*-test analysis before and after treatment.

Results. Five adult Pt (4 Women), mean age 33±12 years old. 3 with celiac disease. At the moment of beginning CyA, 4 out of 5 Pt (80%) had clinical evidence of Cirrhosis (MELD of 17 + 4 points). Table shows laboratory data before and after treatment. A favorable response was observed as early as 2 weeks of CyA, with a progressive trend towards improvement on follow-up. Because of a small number of Pt, it resulted in a few statistically significant results. Two patients were initially listed for liver Transplantation (LT), and were delisted during CyA due to improvement in MELD score, nevertheless one of them had sudden death. Another Pt has had recurrent urinary tract infections, but otherwise has improved LFT (follow up of 35 months). One patient had frequent flares despite CyA and is currently on the LT waiting list. One patient died with massive hematemesis, being Child Pugh A (after 7.4 years of successful treatment).

Conclusions. This case series report shows a favorable experience on the use of CyA in StR-AIH, and supports its use as a successful second line treatment in this setting. We report on a long term follow up of 5 Pt obtaining a reasonable response and avoiding or delaying LT in most cases.

07

AUTOIMMUNE HEPATITIS: A SINGLE CENTER EXPERIENCE IN COLOMBIA

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Introduction. Autoimmune hepatitis (AIH) is an inflammatory liver disease which can affect all populations and age groups.

Objective. Our objective was to determine the clinical profile of patients diagnosed with AIH between 2010 and 2013 at the Hospital Universitario San Ignacio in Bogotá, Colombia.

Material and methods. This is a retrospective and descriptive study.

Results. We included 50 patients who had been diagnosed with AIH according to the International Autoimmune Hepatitis Group (IAIHG) Criteria. Forty three (86%) were female. The average age at onset was 48.2 years with a range of 18 to 84 years with no observable bimodal peaks. Clinical presentation was acute in 24.3% of the patients, subacute in 31.7%, and chronic in 43.9%. Cirrhosis was diagnosed in 34% of the patients. A large number, nineteen (38%), were diagnosed with overlap syndrome of AIH and primary biliary cirrhosis (PBC). Significant numbers had associated autoimmune thyroiditis (10%), scleroderma (10%), systemic lupus erythematosus (8%), Sjogren syndrome (6%), and rheumatoid arthritis (6%). Men showed higher serum levels of ALT (592.4 IU/L vs. 317.9 IU/L) and total bilirubin (5.5 mg/dL vs. 2.9 mg/dL). Therapeutic responses were achieved in 46 of 50 patients with remission in 80.43%. Several second-line treatments were used for patients without clinical remission: mycophenolate mofetil (4 patients), high-dose steroids (2 patients), cyclosporine (1 patient) and tacrolimus (1 patient).

Conclusions. The clinical characteristics of our patients were similar to those described in the literature. There were more diagnoses of overlap syndrome of AIH and PBC (38%) than reported (7% to 13%). The lack of a scoring system to define the limits of AIH and PBC could explain these different prevalences which are important because of their prognostic and therapeutic implications.

08

AUTOIMMUNE HEPATITIS WITH GIANT-CELL TRANSFORMATION IN HISPANIC ADULTS

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Background and aims. Giant cell hepatitis is common in infants but rare in adults where it is known as postinfantile giant cell hepatitis (PIGCH). It is characterized by large multinucleated hepatocytes and unusual response of hepatocytes to several stimuli.

Material and methods. Case report.

Results. Case 1-2: 52 yrs-old woman, Liver Transplantation (LT) in 2009 for autoimmune hepatitis (AIH) and 57 yrs-old woman, LT in 2012 for cryptogenic cirrhosis. Both presented with aminotransferases > 1,000 U/L. Viral hepatitis (A, B, C, D, E, CMV, Epstein Barr, HIV), biliary tract obstruction, vascular occlusion and acute graft rejection were ruled out. Liver biopsy showed GCH, severe necroinflammation (Score 15/18) and no fibrosis (Score 0/6). ANA, AMA, ASMA came back negative. IgG and IgM levels were high and serum protein electrophoresis showed Gammapeak. Case 3: 37 yrs-old woman, complains of 2 weeks of jaundice, fatigue, aminotrans-

ferases > 1,000 U/L, negative viral markers (A, B, C, D, Leptospira, Dengue, CMV, Epstein Bar, HIV). ANAS 1/180, AMA/ASMA negative, normal IgG and IgM and gamma region over the limit. Progressed to fulminant liver failure. Received prednisolone 60 mg QD and underwent LT the following day. Liver explant showed panlobular hepatitis, GCH and extensive necrosis. HEV IgM reported positive and ribavirin was started. Case 4: 57 yrs-old man diagnosed with GCH in 1998, ANA, AMA/ASMA positive. Received steroids for long time. When off medication he relapsed (jaundice and transaminases > 1,000 U/L, ANA +, AMA + and IgG high) developing cirrhosis.

Conclusions. The PIGCH is rare in Adult Hispanics. We report 4 cases of AIH and GCH, two after LT, one acute liver failure in association with hepatitis E that underwent LT and one autoimmune cirrhosis and GCH.

D. FULMINANT HEPATITIS AND LIVER TRANSPLANTATION

01

ACUTE LIVER FAILURE: AN EXPERIENCE IN COLOMBIA

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Introduction. Acute liver failure (ALF) is defined as a severe and sudden liver dysfunction in patients without previous liver disease and result in very different clinical courses. Often affects young persons and carries a high morbidity and mortality.

Objective. This paper presents the outcomes of patients with ALF at the Pablo Tobón Uribe Hospital (HPTU)- Medellín, Colombia.

Material and methods. Medical records of patients who had ALF were analyzed using the database of the University of Antioquia to obtain retrospective information between 2004 and 2014. The statistical analysis was based on the descriptions of the various clinical and sociodemographic variables. Clinical outcomes (death, OLT, or hepatic recovery) and associated morbidities (renal failure, bleeding, and sepsis) also were noted.

Results. 51 patients who had ALF were studied. 59% were female and 66% were between 15 and 45 years old. The majority of patients enrolled comprised 3 etiologies: indeterminate cause (21.6%), Hepatitis B (19.6%) and autoimmune hepatitis (15.7%). They were classified as hyperacute, acute and subacute; 33.3%, 35.3 % and 31.4 % respectively. 70% of patients were admitted with encephalopathy G I - II and 80% progress to severe encephalopathy. In 43% of cases sepsis was found, but 84% of patients received antibiotics. Monitoring of intracranial pressure (ICP) was used in 47% of patients and intracranial hypertension was documented in 37%. Liver transplant

was performed in 23 patients (45%). Overall survival was 67% and post liver transplant survival was 78%. The main causes of death were multiple organ failure, sepsis and intracranial hypertension.

Conclusion. Acute liver failure is a serious disease with a high mortality. Because there is no proven therapy for ALF in general, management consists of intensive care support. As patients may deteriorate rapidly, receiving treatment in a center with experience will secure the best possible outcomes.

02

ACUTE LIVER FAILURE DUE TO WILSON DISEASE IN THE URUGUAYAN'S LIVER TRANSPLANT PROGRAM

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Background. Wilson disease (WD) is an uncommon cause of acute liver failure (ALF), so clinical data are limited.

Objective. To describe clinical features, diagnostic findings, treatments and outcomes of patients with ALF due to WD in the Uruguayan's Liver Transplant Program.

Material and methods. Medical records of patients with ALF due to WD between 2009-2015 were reviewed retrospectively.

Results. Six patients were included, all women. Mean age: 18. Mean time to referral to the program: 8.5 days. Jaundice was the chief complaint of all patients. Four were hyperacute and 2 acute. Mean laboratory values: total bilirubin (TB) 27.5 (5.2-44), alkaline phosphatase (AP) 45.5 (11-102), AST 156 (83-250), ALT 51 (15-119). Four patients had AP/TB < 4 and AST/ALT > 2.2. All had Coombs-negative hemolytic anemia and acute kidney injury. Five had a prognostic index WD > 11. Mean MELD score: 36. Serum ceruloplasmin was decreased in 4/6, urinary copper elevated in 4/5. Kayser-Fleischer rings present in 2/4, characteristics abnormalities in brain magnetic resonance in 1/2. All had histochemically identifiable copper and advance fibrosis on liver histology. ATP7B mutations were detected in 1/1. All patients were treated with d-penicillamine and listed for urgent liver transplantation. The patient with a prognostic index WD < 11 survive without transplantation. Two died before transplantation, with waiting times > 7 days. Three underwent transplantation: 2 from deceased donor in < 7 days, 1 died post-surgery; 1 from living related donor in > 7 days, Prometheus® was performed, with good outcome. The mean time to referral to the program was superior in dead patients: 14 days *vs.* 3. Mean follow up of survival patients: 44 months.

Conclusion. All cases had typical clinical and analytical features. Histopathology was characteristic. Early referral was determinant of prognosis.

03

LIVER INSUFFICIENCY, RISK OF LIVER FAILURE AND ACUTE RENAL FAILURE IN A INFANT WITH SEVERE DENGUE

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Introduction. Hepatitis is a common complication of dengue, however, few cases progress to necrosis of liver tissue.

Objective. To describe an infant with severe dengue who surviving liver failure (LF), risk of fulminant hepatic failure (FHF) and acute renal failure (ARF).

Case report. Female infant of 11 months from the Pediatric ICU of the University Hospital Rafael Uribe Uribe in Cali, Colombia, who four days before with fever and cough; aminotransferase and LDH elevated, chest X-ray normal and IgM positive for dengue. Later signs of tissue hypoperfusion and progressive respiratory distress, shock index 1.5, underactive, somnolent, oral enanthem, edema and gingival erythema and scaly sores, and generalized rash; hepatomegaly; paraclinical with prolonged bleeding, chest X-ray with bilateral pleural effusion, leptospira IgM, antibodies to hepatitis A, B and C, and HIV-negative; NS1 positive to dengue, maximum ALT/AST 3,850/15,700 IU/L, low platelet count, anemia, hypoalbuminemia severe; and diagnosis of severe dengue with hypovolemic shock, LF and risk of FHF, start crystalloid, vasoactive support, fresh frozen plasma, vitamin K, oxygen therapy and noninvasive mechanical ventilation. It is complicated by pericardial effusion, myocardial dysfunction, electrolyte imbalance, FRA according P-RIFLE scale, abdominal hypertension multifactorial syndrome for which it is handled with peritoneal dialysis and renal replacement therapy. For clinical and paraclinical improvement liver transplantation is discarded.

Conclusion. Female infant with clinical, epidemiological and serological diagnosis of severe dengue, who survives LF, risk of FHF and ARF.

04

REVERSIBILITY OF ACQUIRED HEPATOCEREBRAL DEGENERATION AFTER LIVER TRANSPLANTATION. REPORT OF THREE CASES

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Introduction. Acquired hepatocerebral degeneration (AHD) is a neurological condition that occurs in cirrhotic patients and is characterized by neurocognitive and extrapyramidal symptoms, especially Parkinsonism and ataxia. It is produced by portosystemic shunts to allow the passage of manganese into the systemic circulation. Magnetic resonance imaging (MRI) of the brain shows hyperintensity on T1 of the basal nuclei, especially the Globus pallidus, which represent the accumulation of manganese. AHD evolution is usually progressive and long time considered irreversible. Orthotopic liver transplantation (OLT) arises as a treatment.

Clinical case. We have three cases of AHD with almost total improvement post OLT. Case 1: Female patient, 51 years old, cirrhosis by hepatitis C virus. She presented qualitative awareness commitment, Parkinsonism, hemidystonia and

dysarthria, which prevented her from wandering and communicate verbally. Partial clinical improvement with splenorenal shunt embolization and prolopa therapy. Brain MRI showed hyperintensity on T1 of the Globus pallidus, suggestive of manganese deposits. Decrease of hyperintensity on T1 in MRI was observed one month after OLT. She had slowly clinical improvement, to only have dysarthria. Case 2: Female patient, 58 years old, cirrhosis by alcohol. She presented qualitative conscientious commitment, Parkinsonism, ataxia and dysarthria. Brain MRI revealed hyperintensity on T1 of the Globus pallidus, suggestive of manganese deposits. Four months after the OLT, there was a decrease of hyperintensity to the MRI, with partial clinical improvement. Case 3: Female patient of 40 years old, with cirrhosis by NASH. She presented awareness commitment, ataxia and dysarthria. MRI showed hyperintensity on T1 of the Globus pallidus. One year after OLT, she had progressive clinical improvement.

Conclusions. AHD is a neurological complication of cirrhosis that could be treated with OLT.

05

EVALUATION OF REMOTE ISCHEMIC PRECONDITIONING EFFECT TO IMPROVE THE VIABILITY OF THE GRAFT IN LIVER TRANSPLANTATION. PILOT STUDY

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Background. The effect of remote ischemic preconditioning (RIP) in liver transplantation (LT) has been suggested experimentally as a strategy to reduce ischemia-reperfusion injury (IRI), however, has been little studied clinically.

Objective. The aim of this pilot study was to evaluate the effect of RIP on liver graft in cadaveric donors and the impact of various inflammatory mediators in this process.

Material and methods. Ten LT recipients, 5 controls and 5 PIR, were made in the cadaver donors by applying a pneumatic tourniquet in the upper third of both thighs for a period of 10 min. followed by 10 min reperfusion. The determination of IL-1, IL-6, TNF- α , VEGF and ICAM-1 was performed as well as hematological and biochemical parameters at various stages of LT.

Results. A significant increase of AST, ALT and FA enzymes in the early stages of post LT is observed, however after 72 h subjects who received LT subjected to RIP they showed a better response, which was also evident in recovery platelets, which persisted until phase 3 months in this group. IL-6

Table 1 (06).

Form of presentation	n = 18	Mean age	Sex	Etiologies	MELD score at LT	WT for LT (days)	LH (days)	Deaths
ALF	4 (22%)	21.5+4	2M	4 WD	34.2+ 2.8	8.5+2	12.7+ 3.9	1 (6 years of LT, rejection)
Cirrhosis	14 (77%)	46+17*	13M	5 HH, 3 GTD 3 A1AT def, 1 Tyr 2 chronic WD	19.5+ 7.3*	251+ 202*	21.5+ 10.3*	2 (at day 45, infection; and at 2.3 years, HCC recurrence)

M: men. WT: waiting time. LH: length hospitalization. * p < 0.05.

Table 1 (07).

	Crypto	Autoimmune	DILI	Virus	Acet	Others
Number (n = 168)	43 (25%)	35 (20%)	32 (19%)	23 (13%)	13 (7%)	22 (13%)
Age (years)	35.8 ± 15.5	46.1 ± 15.7	39.5 ± 16.5	37.1 ± 14.5	27 ± 10.6	34.7 ± 14.4
Female (%)	58%	88%	93%	44%	88%	86%
HE Grade III-IV	69.7%	48.2%	34.3%	56.5%	30.7%	31.8%
ALT (U/L)	1,144 ± 1,054	534 ± 438	1,081 ± 1,095	2,374 ± 2,261	5,947 ± 4,677	1,017 ± 1,476
Bili (mg/dL)	26.4 ± 11.3	24.4 ± 5.8	22.1 ± 10.6	19.3 ± 13.3	3.8 ± 2.8	11.9 ± 9.4
MELD ≥ 32 (%)	90.7*	57.1	71.9	78.3	46.1	64.6
KCC + (%)	95.3	100	90.6	65.2	53.8	40.9
LT+M (%)	93*	68.6	62.5	60.9	15.4	36.4

HE: hepatic encephalopathy. Bili: bilirubin. ALT: alanine aminotransferase. *p < 0.05.

appears to participate in the early stages of the IRI, contrary to FNT- α that increases until day 7, while ICAM-1 was increased in all phases.

Conclusion. In this pilot study the PIR decreased the damage by IRI, although the greatest effect was observed after 72 h.

06

LIVER TRANSPLANTATION FOR ADULTS WITH INHERITED METABOLIC LIVER DISEASES: NA EXPERIENCE FROM TWO LIVER TRANSPLANT CENTERS IN CHILE (1993-2016)

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Introduction. There are many inherited metabolic liver diseases (IMLD) which result in the accumulation of metabolic products, leading to acute liver failure (ALF), progressive cirrhosis (Cirr) or hepatocarcinoma (HCC). The defect may lie in the hepatocytes [e.g., Wilson's disease (WD), glycogen storage diseases (GSD), alpha1-antitrypsin deficiency (A1AT def)], or they may be affected secondary to increased intestinal absorption [e.g., hereditary hemochromatosis (HH)]. For IMLD, liver transplantation (LT) does not only replace the diseased organ, but also can correct the defect. Although individually rare, when considered together, they represent approximately 10% of pediatric patients (Pt) undergoing LT. In adults there is very poor data and it is very possible an underestimation of this problem.

Aims. To evaluate the frequency and etiologies of IMLD in adults in whom LT was performed; and their results and outcomes.

Material and methods. Between 1993 - 2016 we evaluated all LT performed in adult Pt (> 15 years old) in 2 liver Centers. We grouped Pt for different etiologies, with clinical and laboratory data. In all cases the explant was evaluated in detail. We also evaluated the outcomes after LT.

Results. A total of 289 LT, were performed in 270 adult Pt. 140 men (52%), mean age at LT: 47.8 years old (16-72 years). The cause for LT was Cirr (83.5%) and ALF (16.5%). We found 18 Pt with IMLD (18/270: 6.7%). Mean age at LT: 40.7 ± 19 years old. 15 were men (83%). Table summarizes data for Pt with IMLD with acute or chronic presentation (Table 1). For Pt with ALF (n = 4), 3 of them are alive at a mean follow-up of 5.5 years (75% survival rate/5 years). For Pt with Cirr (n = 14), 71% Child C, 3 also had HCC, 12 are alive at a

mean follow-up of 5.9 years (85.7% survival rate/5 years). Overall, in LT for IMLD < 30 years (n = 7), 6 were WD and for those IMLD > 50 years old (n = 7), 5 were HH.

Conclusions. IMLD should be considered in the differential diagnosis of acute and chronic liver diseases, even in adults, and especially in those cases of "unknown" etiology. In our experience 6.7% of Pt who have received LT as adults, had IMLD as the underlying cause for liver disease. The main cause for LT due to IMLD in > 50 years was HH, and in < 30 years old WD. The complication rate, waiting time, LH and cumulative survival rates of Pt with LT due to IMLD at 1 and 5 years is similar to those of other etiologies.

07

CRYPTOGENIC ACUTE LIVER FAILURE HAS THE WORSE OUTCOME WHEN COMPARED TO OTHER ETIOLOGIES IN CHILE

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Introduction. Acute liver failure (ALF) is an infrequent acute severe disease with high mortality (50-80%). Its prognosis has improved due to the access to liver transplantation (LT). Cryptogenic, drug-induced (DILI) and autoimmune etiologies have been traditionally associated with a worse prognosis when compared to other etiologies. On a previous study on 129 consecutive ALF Patients (Pt) seen up to 2012 (Zapata R, et al. Ann Hepatol 2014), we have showed that MELD score, Kings College criteria (KCC) and the degree of hepatic encephalopathy (HE), were independent predictors of worse outcome. There is poor information on Latin America on the impact of the etiology on the prognosis of ALF.

Aim. To determine the impact of etiology on the overall prognosis among Pt with ALF.

Material and methods. Observational study of all consecutive Pt with ALF evaluated between 2001-2014 in 2 LT Centers. Clinical and laboratory data were collected prospectively. The cohort was divided into 5 groups: Acetaminophen (Acet), drug-induced non acetaminophen (DILI), viral, autoimmune, cryptogenic (Crypto) and others. We compared clinical and laboratory data, and the need for LT and mortality (LT + M) as a marker of severity of disease and prognosis. Univariate statistical analysis using the χ^2 test.

Results. 168 Pt with ALF, 15-83 years, 75% female. MELD score was 35.7 ± 6.8 points. 80% of cases fulfilled KCC for LT.

Table 1 (10). Liver inflammatory activity

Inflammatory activity preOLTx	Recurrence, n: 11	Non recurrence, n:25	P value
Non activity	2	7	0.58
Mild	2	4	0.88
Moderate	6	11	0.67
Severe	1	3	0.81

Table 2 (10). HLA and recurrence.

HLA II	Recurrence n: 11	Non recurrence n: 21	Total	P value
DR4	5	7	12	0.48
DR8, DR13	2	5	7	0.83
DR17, DR13	1	1	2	0.59
DR1, DR14	1	1	2	0.59
DR7, DR11	1	2	3	0.96
DR9	0	2	2	0.3
DR16	0	2	2	0.3
DR13	1	1	1	0.4
DR3	0	0	0	0

60.7% of Pt (102/168) were activated for LT, and of this group, only 42% finally received LT (44% died awaiting LT and 13.7% recovered with medical support). Of Pt not activated for LT (less severe ALF or contraindication), 70% recovered with medical support. Table 1 shows clinical, laboratory data, and outcomes between groups. HE, Bilirubin and MELD score in Crypto Pt, tends to be higher than in the other groups. The comparison of need of LT + M between Crypto *vs.* all other groups has significant statistical difference (*p-value < 0.01).

Discussion. Crypto ALF has the worst outcome when compared to other etiologies in Chile (only 7% survived with medical support). Acet ALF has the best outcome when compared to other etiologies in Chile (84.7% survival with medical support). The etiology of ALF has clearly an impact on the final prognosis of these Pt and in the decision of whom to consider for LT. It is possible that some Pt labeled as Crypto are probably autoimmune or drug-induced ALF, due to similarities in biodemographic characteristics.

08 PROFILE OF ALCOHOL CONSUMPTION IN PATIENTS SUBMITTED TO LIVER TRANSPLANTATION

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Introduction. Liver transplantation is an effective treatment for end-stage liver diseases related or not related to alcohol intake. Alcohol recidivism is frequent after liver transplantation and its characteristics should be determined.

Aims. To verify the alcohol intake in these patients, to analyze the transplanted patients profiles according to their alcohol intake, and analyze the alcohol intake predictors. **Material and methods.** Cross-sectional, observational and descriptive study from January of 1998 to march of 2014 including 124 adult patients who underwent to liver transplantation. All the trans-

planted patients for more than six months were included and those who were inaccessible or who were under treatment for hepatitis C (6) were excluded. Two instruments were used for the data collection: 1- questionnaire about the perception of the patient regard to the post-transplant overall health, 2- AUDIT-C questionnaire for substance intake.

Results. The 124 studied patients were divided according to AUDIT-C classification, in which 29 had alcoholic consumption and 95 were abstainer. From the 29 alcohol consumers, there was 2 groups: 22 were excessive alcohol consumers and 7 were acceptable. Among the 29 alcohol consumer patients, 14 had recidivism (had alcoholic liver disease as a cause of cirrhosis) and 15 had no recidivism (*de novo*). From the 14 patients with recidivism, 11 had excessive alcohol intake and 3 had acceptable alcohol intake. Among the 15 patients with no recidivism, 11 had excessive alcohol intake and 4 had acceptable alcohol intake. Patients with acceptable alcohol consumption were 100% male (p value = 0.015). Patients subgroups were compared as follows: 1) Excessive *vs.* acceptable consumption of alcohol post transplantation and the time after liver transplantation was significantly higher in the excessive consumption sub-group (105 month versus 53 month respectively) p-value = 0.03. 2) Recidivism *vs.* *De novo* alcohol intake post-transplantation: the time from liver transplantation was higher among patients with recidivism (120 month *vs.* 62 month respectively) p-value = 0.009; and de age was higher among the same patients (57 *vs.* 51 respectively) p-value = 0.04. Factor associated to post transplantation alcohol recidivism were: pre transplant smoking (p value = 0.042) and pre transplant alcohol consumption (p = 0.023).

Conclusion. We identify different patterns of post-transplant alcohol consumption: excessive or acceptable consumption, recidivism or de-novo alcohol consumption. It was observed significant and excessive alcohol consumption in liver transplanted patients with or without previous alcoholic cirrhosis. The analysis of alcohol consumption should be done among all the transplanted patients and not only in the patients with previous alcoholic cirrhosis.

09 ECONOMICAL EVALUATION OF LIVER TRANSPLANTATION IN A REFERENCE CENTER IN THE SOUTHERN REGION OF BRAZIL

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Introduction. Liver transplantation (LTx) is the main treatment for acute liver disease or chronic, irreversible and progressive, with a complex and costly procedure. With the growing increase in costs in the health sector, brought the need for knowledge acquisition costs which seeks to rationalize resource allocation and the balance of costs and financial resources with the results of optimization aimed quality, efficiency and effectiveness. The first evaluations of liver transplantation, began in 1990 and should have been estimated above in relation to costs.

Objectives. To determine the perspective of a reference center in southern Brazil the cost of liver transplantation, and the steps that compose it.

Material and methods. A retrospective cohort study evaluated 109 patients who underwent liver transplantation, since

the admission pre transplant immediately to discharge hospital, including clinical outcomes, discharge, death or retransplantation.

Results. Most patients were male with 62.4%, the average age was 57.5 ± 9.1 years. The main cause was cirrhosis due to chronic infection C virus complicated with hepatocellular carcinoma (HCC) with 34.9% and the most prevalent liver functional class was Child-Turcotte-Pugh A in 67 patients (62%) and the score closest MELD the LTx was between 20-25 points, and the hospital stay was 25.1 ± 19 days. The cost resulting from the current policy generated an average spending of US \$16,332.25, the average was US \$18,644.10 and US \$88,757.40 maximum cost, flat fee for transplantation team was 22.1%, the value surgical center (DC) and the daily Intensive Care Unit (ICU) and the hospital ward were 20.9%, 18.2% and 11.7% respectively. The cost of immunosuppressant medication encumbered 1.2%, and laboratory tests, and specialized image borne by 7%, the Renal Replacement Therapy in 3.2%.

Conclusion. The cost of liver transplantation, is related to the severity of liver disease, so with the complications of the underlying liver disease related to MELD and CTP scores.

10 AUTOIMMUNE HEPATITIS RECURRENCE AFTER LIVER TRANSPLANTATION IN PERU: 15 YEARS OF EXPERIENCE

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Introduction. Autoimmune hepatitis (AIH) is an unknown chronic inflammatory disease of unknown etiology may require liver transplantation. Recurrence occurs between 8-68%, related risk factors are postulated.

Aim. To determine the recurrence of autoimmune hepatitis and evaluate the risk factors associated with recurrence of HAI.

Materials and methods. A retrospective, descriptive and cross-sectional study. From March 2000 to December 2015; 200 transplants were performed in 190 liver transplant patients. The medical records of 36 patients transplanted liver cirrhosis diagnosed with autoimmune hepatitis who underwent liver biopsy to confirm the histologic diagnosis of autoimmune hepatitis recurrence after liver transplantation were reviewed.

Results. The indication for liver transplantation for autoimmune hepatitis was 19%. The average age was 35 years, the ratio female/male gender was 2.2, the type most common of HAI is HAI type 1 (89%). The histologic recurrence rate was 31% (11/36), the mean follow-up was 54 months. (range 8 - 169 months). 63% of recurrences appeared 36 months after liver transplantation (Tables 1 and 2).

Conclusions. Autoimmune hepatitis is a frequent indication for transplantation in our experience. HAI recurrence after liver transplantation was 31%, being more common in women. No significant differences in the degree of histological activity in the cirrhotic liver or HLA type in the patient was found.

11 HEPATITIS B AND LIVER TRANSPLANTATION: RESULTS IN PERU

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Introduction. Liver transplantation is the treatment of choice in patients with end stage liver disease for HVB cirrhosis using control strategies to prevent reactivation of the virus B post transplantation.

Aim. To describe the results obtained in patients diagnosed with cirrhosis for HVB virus and post-transplant follow up.

Material and methods. A descriptive, retrospective cross-sectional study. We recorded the medical records of liver transplant patients with diagnosis of cirrhosis by virus B. data of HBs Ag, HBeAg, viral load HBV, as well as the immunosuppressive regimen and the use of antiviral HVB treatment pre and post-transplant to avoid recurrence.

Results. From March 2000 to December 2015; 200 transplants were performed in 190 liver transplant patients, identifying 7 patients transplanted for HVB cirrhosis (3.5%), male/female ratio 6/1, 6 patients with mono-infection HBV and 1 patient was coinfected HBV + HCV virus. HBeAg was negative in 6/7 (85.7%). HVB viral load was not detectable at the time of transplantation 6/7 (85.7%). Patients received treatment with entecavir 1 mg/day V.O. in 13.2 months before transplant (range 4-24 months), follow-up time was 61 months (range 9-107 months). Only 3/7 patients (42.8%) received HBIG (10,000 IU intraoperatively and according to fixed schedule until 12 months' post-transplant to maintain HBsAg levels > 100 IU/mL). All patients continued treatment with entecavir 1 mg VO/day. Immunosuppressant schedule: Induction with monoclonal antibodies (basiliximab 20 mg IV 2 doses for renal dysfunction) 2/7 patients (28.6%): All of them received steroid-free scheme. Tacrolimus and MMF were used in 100% patients. Loss of HBsAg was observed in 4/7 patients (57.1%) around 8.6 months (range 8- 12 months). No cases of reactivation of hepatitis B virus in the post-transplant occurred. No episodes of cellular rejection or ductopenic in our series were presented.

Conclusions. The indication of transplantation for cirrhosis B virus is low in our center (3.5%). Control strategies B HBIG post transplantation and the use of antiviral drugs (entecavir) virus are safe to prevent long-term post-transplant recovery. The loss of the surface antigen was observed in 57.1% within the first year post-transplant and it could be related to the use of potent antiviral agents against hepatitis B before and post-transplant.

E. MISCELLANEOUS

01

HEPATOCYTE GROWTH FACTOR: A GRAVITY MARKER IN CHRONIC LIVER DISEASE

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Introduction. In the liver, the hepatocyte growth factor (HGF) is known for being a potent mitogenic agent, both in vivo and in vitro. However, the role of HGF in cirrhosis are not completely clear and some studies show it as a severity marker in cirrhosis, acute liver failure and chronic hepatitis.

Objective. To determine the relation between HGF and the stadium of liver cirrhosis and to identify the factors associated to the levels of HGF in this population.

Material and methods. All patients with liver cirrhosis attended from January to March 2014 were evaluated. Transient elastography, the collection of clinical information and the extraction of the sample for determining the HGF were performed simultaneously at the moment of inclusion.

Results. No relation between the levels of HGF and the Child-Pugh classification was found. However, more elevated levels were observed in patients with decompensated cirrhosis. A positive linear association between HGF and liver stiffness estimated by elastography ($b = 0.53$; $r^2 = 0.26$; $p = 0.002$) and a negative linear association with albumin ($b = -0.62$; $r^2 = 0.39$; $p < 0.001$) were determined. Only albumin kept this association during the multivariate analysis.

Conclusion. HGF is a severity marker in liver cirrhosis. Albumin and the degree of fibrosis determined by transient elastography were associated with HGF levels.

02

LIVER FIBROSIS IN PACIENTS WITH DIABETES MELLITUS II IN ESSALUD HOSPITAL IQUITOS - PERU

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Introduction. The diabetes mellitus II (DMII) is a high prevalence disease in Peru, is an important risk factor of the non-alcoholic fatty liver disease, than can progress to fibrosis and liver cirrhosis, being necessary to know the risk factors and the percentage of diabetic patients of this hospital that are likely to evolve to liver disease with high morbidity and mortality.

Objetives. To determine the prevalence of advanced liver fibrosis and the risk factors of advanced fibrosis in patients with DM II of the EsSalud Hospital Iquitos.

Material and methods. Is an observational descriptive study in 341 outpatients with DM II from April 2015 to March 2016 in whom other causes of liver fibrosis was discharged. Ultrasound scan and analysis of hematology, biochemistry and immunology were performed. Assessment of liver fibrosis: NAFL score (1.455 low risk, > 0.676 high risk of advanced fibrosis). Statistical analysis: Data were filled in Excel spreadsheet and analyzed using SPSS 23 program where the χ^2 test of Pearson was used for comparison of variables and for age and sex variables was used the mean value and percentage.

Results. The age mean for patients of low risk was 51.7 years

and 65 years for the high risk ones advanced fibrosis. The 25.6% of patients with low risk and the 30.1% of patients at high risk were obese. The 16.7% of patients had advanced fibrosis. Age and obesity were associated with advanced liver fibrosis ($p = 0.001$, 5% significance).

Conclusion. 16.7 % of patients with diabetes mellitus II of EsSalud Hospital Iquitos have advanced liver fibrosis and high risk of complications or death from liver disease. Age and obesity were risk factors for advanced liver fibrosis.

03

ACOUSTIC RADIATION FORCE IMPULSE (ARFI) FOR FIBROSIS STAGING IN PATIENTS WITH CHRONIC AUTOIMMUNE LIVER DISEASES: A PRELIMINARY STUDY

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Introduction. Acoustic radiation force impulse (ARFI) is a new technique that evaluates liver stiffness during B-mode ultrasonography. It has shown promising results for the staging of liver fibrosis. However, its performance has not been well studied in autoimmune liver diseases. **Objective.** To evaluate the diagnostic accuracy of ARFI imaging for the assessment of liver fibrosis in patients with chronic autoimmune liver diseases.

Material and methods. Prospective study. Included adult patients with autoimmune hepatitis (AIH), primary sclerosing cholangitis and overlap syndrome who underwent a liver biopsy. All AIH patients undergone for liver biopsy (LB) after at least two years of biochemical remission period. Liver stiffness was performed using a Siemens Acuson S2000 ultrasound system. Liver fibrosis was staged according to the METAVIR.

Results. Included 10 patients, 9 (90%) women. 1 patient with primary sclerosing cholangitis, 7 patients with AIH and 2 patients with overlap syndrome. On LB 4 (40%) patients had F1, 3 (30%) had F2, 2 (20%) had F3, and 1 (10%) had F4. A significant correlation was found between ARFI measurements and fibrosis ($p < 0.001$). For predicting significant fibrosis ($F \geq 2$), for a cut-off of 1.3 m/s, ARFI had 83.3% sensitivity (Se) and 75% specificity (Sp) [area under the receiver operating characteristic curve (AUROC) 0.70]. For predicting severe fibrosis ($F \geq 3$), for a cut-off of 1.64 m/s, ARFI had 100% Se and 89.5% Sp (AUROC 0.93).

Conclusions. ARFI elastography is able to differentiate severe from non severe liver fibrosis in patients with autoimmune hepatitis and primary sclerosing cholangitis; however, it appears to be modestly accurate in detecting significant fibrosis in this group of patients.

04

BARD SCORING SYSTEM FOR DETECTION OF FIBROSIS IN NONALCOHOLIC FATTY LIVER DISEASE

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Introduction. Nonalcoholic fatty liver disease (NAFLD) includes a wide spectrum of liver diseases, ranging from pure steatosis to nonalcoholic steatohepatitis (NASH), and to liver cirrhosis with its complications. Identifying significant fibrosis in patients is crucial to evaluating prognosis and possible therapeutic intervention. BARD score is one of the many non-invasive scoring systems proposed in the evaluation of the fibrosis in patients with NAFLD biochemically.

Objective. To evaluate the diagnostic accuracy of BARD score for the assessment of significant fibrosis in patients with morbid obesity and NAFLD before bariatric surgery.

Material and methods. Prospective study. Forty-four patients with morbid obesity were included in this study. They were evaluated with routine laboratory before bariatric surgery. Fibrosis in liver biopsies, during surgery, was evaluated according to Brunt. The BARD scoring system was assessed according to Harrison, *et al.*: BMI > or = 28 = 1 point, AST/ALT ratio (AAR) > or = 0.8 = 2 points, type 2 diabetes mellitus = 1 point.

Results. Liver biopsy revealed 38 (86,3%) patients with NAFLD, 18 (40,9%) patients with NASH and 4 (0,9%) patients with fibrosis \geq F2. A significant correlation was found between BARD score and significant fibrosis ($p < 0.001$). For predicting significant fibrosis ($F \geq 2$), a BARD score of 2-4 points had 75% sensitivity, 70,6% specificity and an area under the receiver operating characteristic curve (AUROC) of 0.78.

Conclusions. There was a positive correlation between BARD score of 2-4 points and severity of liver fibrosis in patients with NAFLD. The BARD scoring system appears to be modestly accurate in detecting significant fibrosis in morbid obesity patients with NAFLD.

05

CLINICAL PHENOTYPE AND OUTCOME OF AMOXICILLIN-CLAVULANATE HEPATOTOXICITY IN LATIN-AMERICA: AN ANALYSIS OF THE SLATINDILI REGISTRY

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Introduction: Amoxicillin-clavulanate (AC) is one of the most prescribed antibiotics worldwide. Its liver toxicity potential is well recognized and it ranks first in the different prospective drug-induced liver injury (DILI) registries in Spain, USA and Iceland.

Aim. To describe the phenotype and outcome of the patients with AC hepatotoxicity included in the Latin America DILI Network.

Material and methods. Demographics, clinical and biochemical parameters of AC-induced DILI cases included in the SLATINDILI registry were studied. Causality was assessed by applying the CIOMS scale.

Results. From November 2011 to December 2015, 27 (11%) cases of AC-DILI were retrieved from a total of 237 patients. Amoxicillin clavulanate was the drug with the highest number of cases. There were 17 men (63%), with a mean age of 60 years (range 27-88 y). Cholestasis pattern was seen in 17 (63%) patients, mixed in 6 (22%), and hepatocellular in 4 (15%). The median duration of treatment was 11 days (range 1-22 days). In 22 (81%) cases, symptoms appeared after drug cessation, with a mean time lapse between therapy cessation and abnormal liver test of 15 days (3-39 days). Jaundice was present in 25 patients, but no patients developed hepatic failure or death. Fifteen patients were hospitalized, and there was complete recovery in 19 cases, with a mean follow up of 64 days (14-270 days). The remaining 8 patients are still on follow-up (mean 74 days; 26-120 days).

Conclusion. AC is the most common cause of idiosyncratic hepatotoxicity in SLATINDILI registry. The most common phenotype is cholestatic damage, presenting once treatment is over with recovery in an average time of 3 months. This information helps to identify AC-induced liver injury and to prevent re-exposure.

06

ALAGILLE SYNDROME IN AN INFANT FROM HOSPITAL UNIVERSITARIO DEL VALLE IN CALI, COLOMBIA

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Introduction. The neonatal cholestasis is an urgency in pediatric hepatology. Its main causes are biliary atresia and choledochal cyst. Bile duct hypoplasia rarely occurs.

Objective. To describe the case of an infant with neonatal cholestasis who finally meets criteria for Alagille syndrome.

Case report. Infant female than 2 months old, from Hospital Universitario del Valle in Cali, Colombia, with jaundice in the first week of life, hipocolia, direct hyperbilirubinemia, elevated aminotransferases and normal abdominal ultrasound. Eutrophic, with systolic murmur in pockets of the base and hepatomegaly. With diagnosis of neonatal cholestasis has negative studies for syphilis, rubella, CMV, toxoplasma, HBV, HCV and HIV. For hepatobiliary scintigraphy and magnetic cholangioresonance, biliary atresia is diagnosed. Intraoperative cholangiography with biliary tract permeable. Liver biopsy with biliary hypoplasia. Urinary screening rule out galactosemia. Cerebral CT, blood ammonia and Rx long bones are normal. Ophthalmology described posterior embryotoxon. Rx thoracolumbar with butterfly vertebrae. Echocardiography with mild pulmonary stenosis. Diagnosed with Alagille syndrome nutritional support is decided with special infant formula semielemental, macrodosis of fat-soluble vitamins and ursodeoxycholic acid.

Conclusion. In an infant with neonatal cholestasis, biliary hypoplasia, posterior embryotoxon, pulmonary stenosis and butterfly vertebrae, clinical suspicion should be directed to Alagille syndrome.

07

SIMULTANEOUS LIVER AND CARDIAC INVOLVEMENT IN A MALE TEENAGER WITH SEVERE "ATYPICAL" DENGUE

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Introduction. The severe "atypical" dengue, more common in adults, is a rare entity in pediatrics, which involves primarily liver and nervous system, and less kidney, heart, lung and pancreas, among others.

Objective. To report the case of a male teenager from Hospital Universitario del Valle in Cali, Colombia, who presented simultaneous liver and cardiac involvement as severe presentation of "atypical" dengue.

Case report. White male teenager with 4-day history of fever, malaise, bleeding gums, vomiting and abdominal tenderness, who has leukopenia, thrombocytopenia, aminotransferasemia > 1,000 IU/L and positive for dengue Acs; who two days later manifest chest pain without heart failure, EKG variable RR, bradycardia, T peaked DII and DIII, high creatin phosphokinase, troponin negative and echocardiography with myocardial dysfunction and bradycardia (48% ejection fraction and 24% fractional shortening).

Conclusion. Male teen with clinical, epidemiological and serological diagnosis of dengue grade D according to Souza et al, who presented "atypical" with severe simultaneous liver and cardiac involvement, who not progressed to insufficiency or liver failure or dilated cardiomyopathy or cardiac failure, or death.

08

CHRONIC NONCIRRHOTIC, NONMALIGNANT PORTAL VEIN THROMBOSIS: A PROSPECTIVE COHORT STUDY INCLUDING 17 CASES IN A LIVER REFERENCE CENTER IN COLOMBIA

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Introduction. Chronic non cirrhotic, non-malignant portal vein thrombosis or portal cavernoma (PC) is a rare condition with extrahepatic portal vein obstruction. AIM: We are present a 4 years prospective cohort study in reference liver center of Barranquilla, Colombia.

Material and methods. From august of 2012 to December 2015 all patients with PC suspect were include in a prospective protocol that included: clinical history about manifestations and local risk factors, liver functions test, thrombophilic conditions (antithrombin, protein C/S, factor V Leiden mutation, prothrombin gen variant, antiphospholipid syndrome, fibrinogen, homocysteine, MTHFR gen, hemoglobin electrophoresis,

JAK 2 gen mutation), Doppler ultrasound, CT or MR dynamic images, MRC, fibrotest, Fibroscan, biopsy and upper endoscopy.

Results. Seventeen patients mean age 41 years-old, 65% female, with PC confirmed diagnostic using Doppler ultrasound or CT/MR dynamic images. Cirrhosis was reliably discarded with non-invasive methods such as Fibrotest, Fibroscan in 82% or biopsy in 47% and initial manifestation were variceal bleeding in 70%, abdominal pain 18%. Local risk factors were evident in 40% (pancreatitis, splenectomy, partial gastrectomy, cholecystectomy, omphalitis, sickle cell anemia). One patient had relative with pulmonary vein thrombosis. Nine patients (53%) had thrombophilic conditions (severe deficits of protein C, protein S, antithrombin, antiphospholipid syndrome, factor V Leyden mutation, JAK 2 gen mutation and MTHFR gen mutation) and three patients (18%) with local and systemic conditions together. 82% patients hypersplenism with mild liver dysfunction, but one with cholestasis showed changes of portal cholangiopathy in MRC. Variceal banding was made in all patients with bleeding plus propranolol. All patients with thrombophilic conditions start long term anticoagulation.

Conclusion. PC is a rare condition to be reliably diagnosed and treated in young patients with variceal bleeding and portal hypertension in our countries.

09

ASSOCIATION OF COELIAC DISEASE WITH PRIMARY BILIARY CIRRHOSIS IN URUGUAY

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Introduction. Although an association between primary biliary cirrhosis and coeliac disease has been reported, there are still conflicting data concerning about this issue.

Objective. The aim of this study was to evaluate the prevalence of coeliac disease among uruguayan patients with primary biliary cirrhosis.

Material and methods. In patients with primary biliary cirrhosis assisted in a liver unit in Montevideo between 2002 and 2016, immunoglobulin A (IgA) human antibodies against tissue transglutaminase (tTGA) and IgA levels were determined. In those with IgA-tTGA antibodies positivity, upper endoscopy with duodenum biopsies was performed. The criteria for primary biliary cirrhosis was the presence of at least 2 of the following: positive antimitochondrial antibody, cholestatic biochemistry, and liver biopsy consistent with the diagnosis. The diagnostic criteria for coeliac disease were IgA-tTGA positive and duodenal villous atrophy with or without evidence of malabsorption.

Results. Sixty four patients with primary biliary cirrhosis (95% female, mean age 55 years), diagnosed during the mentioned period were studied. Five patients (7.8%), all women, with a mean age of 48 years were positive for IgA-tTGA and had atrophy in duodenal biopsies. In one of them the diagnosis of coeliac disease was made first. Immunoglobulin A deficiency was not detected. Pruritus was the most common symptom, followed by asthenia and jaundice. Three of them had diarrhea.

Conclusion. this study revealed a high prevalence of coeliac disease (7.8%) between Uruguayan patients with primary biliary cirrhosis and screening for coeliac disease in this population should be recommended.

10

CLINICAL MANIFESTATIONS AND OUTCOMES OF BUDD CHIARI SYNDROME

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Introduction. Budd-Chiari syndrome (BCS) is a rare disorder characterized by a hepatic venous outflow obstruction. The obstruction may be thrombotic or non-thrombotic. It can occur anywhere along the venous course from the hepatic venules to the inferior vena cava (IVC).

Objective. We present 4 cases in which the causes, clinical presentation and outcomes vary from resolution with treatment to requirement of liver transplantation (LT).

Material and methods. Descriptive observational study. The population was taken from patients admitted to the Fundación Cardio infantil, Bogotá, Colombia between 2015 and 2016.

Results. Case 1: 33 yrs old woman with 6 weeks of ascites and abdominal pain. Thrombosis of the 3 hepatic veins was documented. Antiphospholipid syndrome (APS) was confirmed and anticoagulation was started. TIPS failed. She had an adequate clinical outcome with anticoagulation and diuretics. Case 2: 52 yrs old man with 5 days of abdominal pain, jaundice and fever. Images were not conclusive. Liver biopsy confirmed BCS. He received anticoagulation and presented normal LFTs after seven days. Case 3: 53 yrs old woman with variceal bleeding and ascites. MRI showed thrombosis of middle and left hepatic veins. She developed acute liver failure and underwent LT. Case 4: 30 yrs old woman with liver mass at the left hepatic lobe with compressive effect over the IVC blocking its flow. Liver biopsy of the mass showed caseification necrosis suggestive of tuberculosis (TB). Stent in IVC was implanted and anti-TB treatment was started. Thrombosis extended to the superior mesenteric vein despite of anticoagulation. Currently, she is at the waiting list for LT.

Conclusions. BCS exhibits a variety of etiologies, clinical manifestations and outcomes ranging from acute and reversible courses to chronic conditions requiring LT.

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USEFULNESS OF TRANSIENT ELASTOGRAPHY (FIBROSCAN R) IN CHRONIC LIVER DISEASES: INITIAL EXPERIENCE IN PERU

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Introduction. The transient elastography (ET) has been extensively validated as a non-invasive assessment method of liver fibrosis stage in the most chronic liver diseases.

Objective. To describe the initial experience of measuring liver fibrosis using transient elastography in Peru.

Material and methods. Retrospective evaluation of a cohort of patients with liver disease who underwent Transient elastography (Fibroscan R) from October 2015 to May 2016 at Delgado Private Hospital. Lima Peru. We included adult patients with different etiology of liver disease; validated internationally, including liver transplant patients in follow-up. They were performed at least 10 measurements by three trained physicians and certified by Echoscans using the same equipment of Transitory elastography (probe M model 402 and newly calibrated). Those studies that did not meet minimum

standards of measurement were not included in the study.

Results. There were 160 patients, women 47.5%, 52.5% men; average age 55.9 years (range 16-87 years). The average body mass index (BMI) was 25.1 (range: 17.9- 39.5). Indications for more frequent evaluation by transient elastography were: Nonalcoholic Fat Liver Disease (NAFLD): 56.9%, hepatitis C: 16.3%, hepatitis B: 5.9%, cryptogenic cirrhosis 5.9%, Primary biliary Cirrhosis 4.6%, Alcohol 3.9% and others 6.5%. The results found by transient elastography identified according to its etiology were: Average median 13.2 kPa (range: 2.3- 75 kPa) (Table 1). The success rate of the measurements was 96%.

Conclusion. Transient elastography is a new tool in Peru which determines reliably and safely the stage of fibrosis.

Table 1 (11).

Fibrosis stage	N (%)
F0	48 (30)
F0-F1	23 (14.4)
F1	16 (10)
F1-F2	8 (5)
F2	12 (7.5)
F3	12 (7.5)
F3-F4	5 (3.1)
F4	36 (22.5)
Total	160 (100)

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SHORT TERM MORTALITY IN ALCOHOLIC HEPATITIS: COMPARISON OF PROGNOSTIC MODELS IN A HOSPITALIZED COHORT

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Introduction. Maddrey discriminant function (MDF) is considered as the standard score for the prognostic assessment of alcoholic hepatitis, although it may overestimate mortality. Other prognostic models have shown improved accuracy, but they lack validation in our population.

Objectives. To validate the MDF, Mayo End-Stage Liver Disease (MELD), Glasgow Alcoholic Hepatitis Score (GAHS) and age, bilirubin, INR, creatinine (ABIC) scores in a group of patients with alcoholic hepatitis and to identify clinical and humoral parameters predictive of short term mortality.

Material and methods. Retrospective analysis of 92 alcoholic hepatitis episodes (78 patients) admitted between May 2007-May 2016. MDF, GAHS, MELD and ABIC were calculated at admission and at day 7. The relationship between death and clinical-humoral variables was determined by the χ^2 test, Pearson's or Fisher's exact test. Mortality was estimated by Kaplan Meier method. The utility of each model to predict mortality was evaluated using receiver operating characteristic (ROC) curves and the area under the curve (AUC) was calculated.

Results. 87% of patients were male (51 ± 10 years). Overall mortality was 14% at 30 days and 29% at 6 months. MDF ≥ 32 overestimated 30-day mortality (predicted mortality 35-45%, observed mortality 14%, AUC 0.56) whereas MELD and GAHS performed well with no significant difference (AUC 0.71 and 0.70 respectively). Similar performance was obtained

to estimate 90-day mortality (AUC GAHS 0.69, ABIC 0.73). Recalculating scores at day 7 increased their accuracy (AUC MDF 0.70, MELD 0.75, GAHS 0.79) except for ABIC (AUC 0.64). Age, renal failure and hyponatremia at hospital admission were independent predictors of short term mortality.

Conclusion. MDF ≥ 32 was inadequate to predict 30 day mortality whereas MELD, GAHS and ABIC had a good performance. Score recalculation at day 7 increased their accuracy.

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PREDICTIVE CAPACITY OF FIBROSIS ACCORDING TO CLINICAL AND LABORATORY FACTORS ON PRIMARY BILIARY CHOLANGITIS: VALIDATION OF THE ASSOCIATION BETWEEN ALBUMINEMIA AND CHOLESTEROLEMIA

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Introduction. Primary Biliary Cholangitis (PBC) causes chronic cholestasis and eventually liver fibrosis (LF). The liver biopsy is the best diagnostic tool, but it has potential associated complications.

Aims. To evaluate clinical and laboratory variables as risk and predictor factors of LF in PBC.

Material and methods. Retrospective analysis of 67 PBC biopsied patients, seen from 2005-2014. Evaluation included clinical variables (age, sex, body mass index, symptoms related to PBC, drugs in use and associated pathologies), laboratory variables (liver profile, coagulation, full blood count, cholesterol, albuminemia, immunoglobulins and autoantibodies). Also, fibrosis score ALT/AST, APRI, FIB4 and FORNS were searched. The association and risk of LF was evaluated by Pearson's test and logistic regression.

Results. 64 (95%) patients were women, with a mean age of 53 ± 9.5 years. There was an association between presence of fatigue ($p = 0.01$), coexistence of autoimmune hepatitis ($p = 0.03$), increased bilirubin ($p = 0.009$), alkaline phosphatase ($p = 0.003$), total cholesterol ($p = 0.03$) and low platelets ($p = 0.03$) with advanced stages of PBC (III-IV). APRI < 0.5 ($p < 0.001$) and FIB4 < 1.45 ($p = 0.014$) were associated with early stage of PBC (I-II). Hypoalbuminemia (OR = 1.35, 95% CI, 1.18-1.66; $p = 0.01$) and thrombocytopenia (OR = 1.29, 95% CI, 1.16-1.52; $p < 0.01$), proved to be risk factors for advanced stages. APRI < 0.5 (OR = 0.03, 95% CI, 0.01-0.21; $p = 0.001$) and FIB4 < 1.45 (OR = 0.09, 95% CI, 0.02-0.37; $p = 0.01$), proved to be protective factors. Predictive model was constructed by adding albuminemia and cholesterolemia within variables, finding statistical significance ($p=0.001$) with AUC of 0.73.

Conclusion. We validated albuminemia and cholesterolemia as predictor factors of LF in PBC, which are noninvasive tools and can be used as an alternative to liver biopsy. In addition, APRI and FIB4 showed to be predictor factors in early stages of PBC.

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THERAPY RESPONSE FOR NON ALCOHOLIC STEATOHEPATITIS (NASH) ASSESSED WITH LIVER STIFFNESS (LS) AND CONTROLLED ATTENUATION PARAMETER (CAP) BY TRANSIENT ELASTOGRAPHY (TE)

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Introduction. Pharmacological therapy may be used in NASH. There're two categories: drugs that improve the underlying metabolic conditions and hepato-protectants. Fibrosis progression or improvement after treatment could be evaluated by liver biopsy or different noninvasive tests including transient elastography (TE).

Objectives. Describe Liver stiffness changes after medical treatment in NASH patients measured by TE.

Material and methods. We performed a retrospective cohort study, on NASH patients (pts) treated with several pharmacological therapies (ursodeoxycholic acid and vitamin E, Vitamin E alone) and changes in lifestyle (diet recommendations and exercise); all had clinical assessment, blood test follow-up and TE to determine therapy response; depending in their clinical status, patients received co-interventions with statins and/or metformin. SPSS software version 22 was used; continuous variables were described depending on the central tendency distribution, categorical variables with percentages; we compared continuous variables with nonparametric Wilcoxon test.

Results. 26 pts were analyzed (mean age, 55 ± 10.95 SD, 10 females (38.5%); 6 (23%) were in steatosis stage 1, 8 (30.8%) in stage 2 and 12 (46%) stage 3; cirrhosis was present in 26.9% (CI 95% 13% - 46%). The most common treatment was ursodeoxycholic acid, vitamin E and co-interventions (38.4%), ursodeoxycholic acid and vitamin E without co-interventions (26.9%) and vitamin E alone or with co-interventions (23%), the rest with other treatments. After therapy there were no change in body weight; ALT and GGT presented statistical significant reduction (p -value, 0.031 and 0.040); 9 pts (34.6% CI 95% 19% - 53%) presented fibrosis regression and 10 pts (38.5% CI 95% 22% - 63%) steatosis regression.

Conclusions. Our patients presented improvement in the fibrosis, steatosis and liver enzymes profile with pharmacological therapy

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STUDY FINDINGS HFE (C282Y / H63D) AT A REFERENCE LABORATORY IN SANTIAGO OF CHILE

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Introduction. Hereditary hemochromatosis (HH) is an inherited disorder characterized by excess of iron deposited in liver and other tissues secondary to an abnormal iron metabolism. High serum Ferritin (SF) and transferrin saturation (%TS) lead us to suspect this disease, but they can also be elevated in other conditions. Mutations C282Y/H63D in HFE gene account for 90% of HH phenotypes in European population, but in Latin American population this is poorly described.

Aims. Describe the findings of HFE gene mutations (C282Y/H63D) and its relationship with SF, %TS and subjacent pathology in Chilean patients referred to our center.

Material and methods. From 2004 to 2016, 166/486 patients (34%) were positive for mutation C282Y and/or H63D. 155(93%) were men and the average age was 52 years [14-79]. Clinical data such as SF levels, % ST and subjacent diseases was obtained from medical records.

Results. Of the 166 patients with HFE mutation, 47(28%) had C282Y mutation, 14(30%) homozygotes and 33(70%) heterozygotes. The H63D mutation was found in 131(79%) patients, 119 (91%) heterozygotes and 12 (9%) homozygotes. We found 12(7%) C282Y/H63D compound heterozygotes. SF was 4,570 + 8,549 in C282Y homozygotes and 375 + 364 in heterozygotes and TS% 79 and 50 respectively, in H63D homozygotes SF was 3,524 + 4,099 and 960 + 801 in heterozygotes with TS% 63 and 60 respectively and in compound heterozygotes SF was 712 + 660. 17% of patients had a family history or diagnosis of HH, 16% NAFLD and 5% Virus C infection.

Conclusion. 34% of patients referred for study of HH presented some mutation of the HFE gene, being associated with higher levels of SF and % ST especially in homozygous mutation. Only 17% of the patients were associated with HH and the rest to other pathologies.

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MALIGNANT PRIMARY LIVER TUMOR OTHER THAN HEPATOCELLULAR CARCINOMA AND CHOLANGIOCARCINOMA

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Background. Hepatic malignant neoplasms include malignant primary hepatic tumors (MPHT) other than hepatocellular carcinoma (HCC) and cholangiocarcinoma (CC). These are very rare tumors and little is known about them. Imaging allows to characterize the tumor and could help in their diagnosis. Though the definitive MPHT diagnosis it is made by histopathological study.

Aim. To compare clinical and imaging data with pathological study of patients diagnosed with malignant hepatic tumor others than HCC and CC.

Material and methods. Retrospective study of patients with MPHT others than to HCC and CC, between 1999 and 2016. Clinical data, imaging studies (tomography and/or magnetic resonance) and pathology was considered.

Results. Twenty-five patients presented this type of cancer. Mean age 57 ± 17 years old, 60% male. Pathology diagnosis was made during surgery or percutaneous liver biopsy. Patients with MPHT others than HCC and CC resulted in neuroendocrine 10/25 (40%), lymphoma 6/25 (24%), hemangioendothelioma 4/25 (16%) and sarcoma 3/25 (12%). Angiosarcoma (4%) and sarcomatoid carcinoma (4%) was diagnosed in one patient each one. There was a high number of clinical and imaging unsuspected diagnosis 22/25 (88%). 4/25 (16%) patients presented chronic liver disease. Most frequent symptoms were weight loss 7/25 (28%) and abdominal pain 6/25 (24%).

Conclusions. Most frequent MPHT other than HCC and CC were neuroendocrine, lymphoma, hemangioendothelioma and sarcoma. There is very low clinical suspicious index, only in 12% the prior diagnosis was right. There was a high prevalence of chronic liver disease, probably because of the regular imaging studies in this group of patients.