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Incidental finding of fatty liver in necropsies

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Background and aim: Non alcoholic fatty liver disease (NAFLD) and alcoholic fatty liver disease (ALD) are the most common emerging causes of chronic liver disease. By knowing the factors involved in their development and screening could improve the prognosis of these patients. To determine prevalence of NAFLD as incidental finding at autopsies performed for all causes of mortality and to analyze the main characteristics of these patients.

Methods: Type and design of the study: Observational, descriptive, transversal study. Last 10 years-death causes reports of Department of Pathology were analyzed (January 2010 – December 2019). Descriptive and analytical statistics: X 2, exact Fisher's test, univariate and multivariate logistic regression models were used.

Results: 4557 autopsies were registered. Fatty liver was found in 6.4% of the cases. 53.3% were women; 51 ± 15 years-old, otherwise 53.6% and 46.4% of the cases were diagnosed with simple steatosis and steatohepatitis with necroinflammatory activity respectively. A 49.8% presented liver fibrosis (F1 = 13.1%; F2 = 16.5%; F3 = 5.2%; F4 = 15.1%. The etiology through clinical history and histological findings compatible with alcoholic liver injury occurred in 23% of cases, NAFLD 33.7%, mixed type 6.5%, and 36.8% with unidentified etiology. The multivariate analysis showed alcohol intake as the major risk factor for necroinflammation (OR = 1.97). History of alcohol intake (OR = 2.52;) and presence of necroinflammatory activity (OR = 6.53; p<0.0001) were predictive factors of fibrosis F2-F4. (Table 1).

Conclusions: Steatosis, steatohepatitis, and fibrosis / cirrhosis were found in a high proportion. Alcohol consumption is significantly associated with liver injury in Mexico.

Conflicts of interest: The authors have no conflicts of interest to declare.

Table 1
Multivariate predictive models.

A. Multivariate predictive model to evaluate factors associated with the presence of steatohepatitis with hepatic necroinflammatory activity at autopsy.

Variables	*p* Value	OR	95% CI	
			Lower	Higher
Atherosclerosis	0.008	.405	.208	.789
Obesity	0.948	1.025	.490	2.144
Alcohol consumption	0.044	1.974	1.018	3.827
Diabetes	0.142	.603	.307	1.184
Arterial hipertension	0.185	1.607	.797	3.238
Constant	0.351	1.385		

B. Multivariate predictive model to evaluate factors associated with the presence of significant or greater liver fibrosis (F2-F4) at autopsy.

Variables	*p* Value	OR	IC 95% CI	
			Lower	Higher
Atherosclerosis	0.067	.573	.316	1.041
Obesity	0.934	1.032	.489	2.178
Alcohol	0.002	2.529	1.407	4.546
Diabetes	0.955	1.020	.517	2.011
Arterial hipertension	0.077	1.811	.938	3.498
Necroinflammatory activity	<0.0001	6.533	3.720	11.471
Constant	<0.0001	.176		

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Obesity and diabetes as a risk factor of chronic disease of the liver in the regional hospital

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Background and aim: Obesity and diabetes 2 are health problems in western countries. And Mexico is probably the main cause

of chronic liver disease. To assess the relationship of obesity and DM 2 as risk for chronic liver disease.

Material and methods: 200 patients with a diagnosis of chronic liver disease for 5 years in Gastroenterology were evaluated. 177 with a diagnosis of chronic liver disease. With support: ultrasound, fibroScan, biopsy, endoscopy; HbA1c, BH, PFH INR, ALBUMINE,), (HVC, HVB, AML, AMA, ANA and Ant-LKM-1 antibodies); Quantitative PCR; BMI.

Results: Patients with steatohepatitis and cirrhosis secondary to obesity and DM 68%, alcohol liver disease 14%, VHB and VHC liver disease 13%, autoimmune hepatitis 4%. The average age in steatohepatitis was 53.5 and in cirrhosis 63.4 years. The metabolic syndrome appeared in 47% of the patients with obesity and diabetes; the mean obesity was BMI> 35. The average glycated hemoglobin was 7.9% in patients with steatohepatitis and in patients with cirrhosis it was 7.6%. Cirrhosis secondary to obesity and diabetes accounted for 50% of all causes of cirrhosis in this study; steatohepatitis was also the leading cause of chronic liver damage.

Conclusions: Obesity and diabetes represent the first cause of chronic liver disease at the ISSSTE Dr. Valentin Gómez Farias Regional Hospital, both diseases are highly prevalent problems in Mexico and require preventive programs to avoid the high costs and income of third-level care for effect of its complications.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Normal values and diagnostic errors of psychometric tests and critical flicker frequency in vulnerable Mexican population

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Background and aim: Gold standard for diagnosis of minimal encephalopathy is psychometric tests (PHES) and critical flicker frequency (Flicker) is an adjunct method. The aim of this study is to determine the normal values of PHES and Flicker in a population without chronic liver disease and to identify risk factors to obtain abnormal values.

Material and methods: Study carried out in Tlapa, Guerrero between 2017 and 2018. Subjects older than 18 years were included. Liver disease was ruled out by fibroscan®, examination and screening for hepatitis C. Illiterate patients, visual or motor impairment, dementia, cognitive impairment or liver diseases were excluded. Sociodemographic data were collected; PHES and Flicker were applied to participants.

Student's *T*-test was used for continuous variables and Fisher's exact test for categorical variables. Results are expressed with measures of central tendency and dispersion. A univariate and multivariate analysis was performed to identify risk factors for presenting abnormal values. A value of $P < 0.05$ was considered.

Results: 96 subjects were included, 63% female, BMI of $28.3 \pm 4.6\ kg/m^2$, aged 42 ± 12 years and schooling of 10 ± 3 years, 73% worked outside the office. Fibroscan® was performed in 43 participants, none presented fibrosis.

26 abnormal values were obtained with PHES and 11 with Flicker; Identifying 3 false positives for MHE. Occupation and schooling were associated with abnormal values in the PHES; No independent risk factors were identified in the multivariate analysis. No risk factors were identified for the Flicker.

Conclusions: Performing a single test leads to diagnostic errors, which is reduced by using both tests.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Main clinical characteristics of hospitalized cirrhotic patients with acute on chronic liver failure

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Background and aim: ACLF is a dynamic syndrome. It may improve, follow a steady course or worsen during hospitalization. Although there is considerable variability between patients, some broad principles regarding the course of the condition can be put forward. ACLF in cirrhosis frequently develops in the setting of an acute event that acts as a precipitating factor. The aim was to describe the main characteristics of hospitalized cirrhotic patients who met acute on chronic liver failure (ACLF) criteria.

Material and methods: Study design. Observational, descriptive, transversal study. A case series. Procedure: The clinical data of hospitalized cirrhotic patients, from October 2019 to February 2020, who met criteria for ACLF, were collected. Descriptive statistics were used to summarize the main characteristics of the series of patients.

Results: A total of 24 admissions of cirrhotic patients who met criteria of ACLF were registered in the study period, 20 (83.3%) were men, mean age 52.2 ± 13.3 years, the most common cause of liver disease was heavy alcohol intake in 19 (79.2%) cases, followed by 3 (12.5%) with NASH, 1 (4.2%) autoimmune hepatitis, and 1 (4.2%) cryptogenic origin. Mean MELD-Na was $30.2 \pm 6,7$. The most important cause of acute decompensation was gastro-intestinal bleeding 13 (54.2%), followed by hepatic encephalopathy 4 (16.7%), recent in-crease on alcohol intake 3 (12.5%), bacterial infections 2 (8.4%), ascites 1 (4.2%), development of jaundice 1 (4.2%). The distribution according to the ACLF category is shown on Table 1.

Table 1
Distribution of studied patients through the different ACLF categories.

ACLF	Number of patients	%
0	4	16.7
1	3	12.5
2	8	33.3
3	9	37.5
Total	24	100.0

Conclusions: Alcohol intake remains as an important cause of chronic liver disease in México. Gastrointestinal bleeding is the most important cause of acute decompensation in our cirrhotic patients.

Conflicts of interest: The authors have no conflicts of interest to declare.

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The fructose enhances the HCC progression in mice under a high intake of fructose in dieT

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Background and aim: Hepatocellular carcinoma (HCC) is the fourth cause of cancer-related death and its incidence has been increasing in both men and women. One of the main concerns has been the consumption of hypercaloric diets mainly rich in carbohydrates such as fructose. High fructose diet is related to the development of Non-Alcoholic Fatty Liver Disease (NAFLD) and the progression of HCC since it potentiates the lipogenic pathway and the accumulation of lipids. The aim of the study is to determine the effect of a high fructose diet on the progression of HCC, induced by DEN, in C57Bl/6J mice strain.

Materials and methods: We used C57Bl/6J mice strain (both sex) with a high Fructose diet (Fru)(33% of Fructose in the drinking water, *ad libitum*). Fru supplementation started with 15 days old mice, two days after DEN was injected (10 μg/Kg, i.p) and the treatment was ended 8 months later to evaluate the role of fructose in tumor progression by histological and biochemical tests. The protocol was approved by the UAM ethics commission.

Results: The major number of tumors were found in the Fructose + DEN (FD) mice group *vs*. only DEN (CWD) mice group. Triglyceride levels (TG) was evaluated in the serum with no detectable values; however, in the liver tissue the FD group showed significantly higher TG content. On the contrary, the Cholesterol (CHO) levels were significantly higher in the serum of dietary fructose group and had no differences in the tissue. The protein content in tissue followed the same observed pattern, since significance was only found in Fatty acid synthase (Fasn) with a higher protein content in the groups with dietary Fructose. Curiously, we noticed tumors in the lungs. Conclusion. The data strongly suggests that the high consumption of Fru in the diet induces effects in liver tumor promotion, in a mechanism dependent on FASN and independent of CHO. High consumption of Fru should be considered as a liver toxic factor.

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Gallbladder adenomyomatosis

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Background and aim: Adenomatous hyperplasia of the gallbladder or adenomyomatosis is a benign neoplasia characterized by epithelium hyperplasia with invaginations into the subserose forming intramural diverticula (Rokitansky-Aschoff sinuses). It is reported in 1 to 8.5% of cholecystectomies and 7% of autopsies. It has been associated with cholelithiasis in 80% of cases and may have an asymptomatic course or present with biliary cholic. According to its site it can be localized, annular, diffuse or segmental; the later associated with cancer in 3.2%.

Material and methods: Retrospective review of medical records of patients with pathology study diagnosis of adenomyomatosis from January 1st, 2015 through December 31st, 2019.

Results: Twenty-four cases were found, with 58.3% of women and mean age of 51 years. Elective cholecystectomy was found in 26% of cases. Most frequent symptoms were abdominal pain, nausea and, vomit with 75%, 41.7%, and 33.3%, respectively. Duration of symptoms was less than 24 hours in 21.1%, and 7 days to 3 months in 57.9% of cases. Smoking was reported in 58.3%, alcohol consumption in 12.5% and dyslipidemia in 20.8% of cases. Murphy's sign was reported in 37.5% and the most frequent clinical diagnosis was acute cholecystitis in 66.7% of cases. Mean alkaline phosphatase was 105.6 ± 76.0 UI/L and mean gamma-glutamyl transpeptidase was 113.2 ± 161.3 UI/L. In abdominal ultrasound, the gallbladder had a thin wall in 50%, thick wall in 8.3%, polyps in 20.8% and stones in 54.2% of cases. In pathology studies, mean thickness of adenomyomatosis was 90.5 mm and the location were localized (fundus) in 58.3%, diffuse in 20.8% and annular in 4.2% of cases.

Conclusions: Female sex (estrogens), chronic inflammation (cholecystitis) and cholelithiasis are the few associated factors for the development of adenomyomatosis. Most ultrasound findings are non-specific and, therefore, presurgical diagnosis is difficult. In most of the cases, the diagnosis of adenomyomatosis was an incidental finding associated with acute cholecystitis.

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HGF induces a protective response in a preclinical model of nephropathy induced by acute cholestasis

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Background and aim: The relationship between the liver and the kidneys in some hepatic diseases is well known. Hepatorenal syndrome usually occurs in chronic damage but has also been observed in the acute one. Therapeutic approaches remain limited and poorly optimized, especially to address the commitment of both organs. HGF induces protection in various organs, but its effects are unknown in a scenario of multi-organ compromise, as in the case of hepatorenal syndrome or colemic nephropathy. The aim of this investigation was to determine the mechanism induced by HGF to counteract liver and kidney damage in a preclinical model of systemic damage induced by intrahepatic cholestasis in a setting of colemic nephropathy.

Material and methods: CD-1 mice were treated with α-naphthyl isothiocyanate (ANIT, 60 μg / kg, i.g.) for 48 h. After 24 h of ANIT treatment, HGF (10 μg / kg, i.v.) was administered. Mice were throughout treatment in metabolic cages. Urine samples were collected from the last 12 h of treatment. After 48 h, mice were sacrificed, blood and tissue were obtained. Liver function tests (ALP, GGT and bile salts), analysis of bile transporter expression by qRT-PCR, serum and urine creatinine content, albuminuria and HSP27 in urine, and H-E staining were performed, ROS content was addressed in kidney tissue.

Results: Cholestasis induced by ANIT was corroborated by the increase of bile salts in the liver and serum, and the increase in GGT and ALP. Interestingly, we found renal dysfunction determined by the increase in serum creatinine, and decrease in its clearance, as well as proteinuria and the increase in urine HSP72. Treatment with HGF reduced to control values the markers of liver and kidney damage, significantly improving renal histology. The protection mechanism was closely associated with the control of oxidative damage. In conclusion, HGF is presented as a therapeutic intervention point in cholestasis-mediated renal damage, counteracting the oxidative damage.

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Prevalence of acute kidney injury in hospitalized patients with cirrhosis and their transition to chronic kidney disease

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Background and aim: Acute Kidney Injury (AKI) is frequent in patients with cirrhosis and is associated with a poor prognosis. LRA can lead to Chronic Kidney Disease (CKD). The objective of the study was to determine the prevalence of AKI in hospitalized patients with decompensated cirrhosis, as well as the frequency of CKD after an episode of AKI.

Material and methods: Retrospective, descriptive and observational study. Information was obtained from 146 patients hospitalized in the Gastroenterology department of the Centro Medico Nacional La Raza in the period from January-December 2019. They included patients who met the LRA criteria. Information on the evolution of patients after hospital progress will be collected from the electronic medical system. The results were analyzed with recommended and central frequency measures to obtain percentages, means and average. 3-month survival was estimated using the Kaplan-Meier method and compared using the log-rank test. The odds ratio (OR) of the different factors related to the development of CKD was determined.

Results: Forty patients were excluded, of the remaining 106, 46 (43%) presented with AKI, with a median age of 58 years (19-75 years), 27 (58.6%) women and 19 (41.3%) men. 14 patients (30.4%) present some comorbidity, of which arterial hypertension and diabetes stand out. During hospitalization, all were treated with isotonic solutions and 12 received albumin for 2 days. 15 (32.6%) obtained a total response to treatment and 9 (19.5%) a partial response. 10 patients (21.7%) developed CKD. The severity of liver disease from high MELD predicted an increased risk of developing CKD. Grade 2 or 3 ascites, hypoalbuminemia, comorbidities, and the degree of AKI are associated with an increased risk of CKD.

Conclusions: The prevalence of both AKI and CKD is high in patients with decompensated cirrhosis. Most of the AKI episodes in patients with cirrhosis are reversible, however, it constitutes a risk factor for the transition to CKD, influencing the evolution of the disease.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Correlation of serum ferritin concentrations with laboratory and demographic paramters and its alteraration by different clinical conditions in patients with liver disease

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Background and aim: Ferritin is a protein whose main function is to store iron. It is documented that in liver diseases, proinflammatory states and metabolic syndrome (MS) its serum levels increase. This study's objective was to describe serum ferritin levels in a population with liver disease; evaluated at a hepatology center in northeast Mexico and its correlation with biochemical markers and comorbidities.

Material and methods: A retrospective study was carried out on patients from the Hepatology Center of the University Hospital "Dr. José Eleuterio González" from 2015 to January 2020, including 165 subjects (80 men and 85 women) aged 17-80 years. The following laboratory test results were analyzed: Serum ferritin, blood chemistry, blood count, lipid profile, liver function tests, coagulation

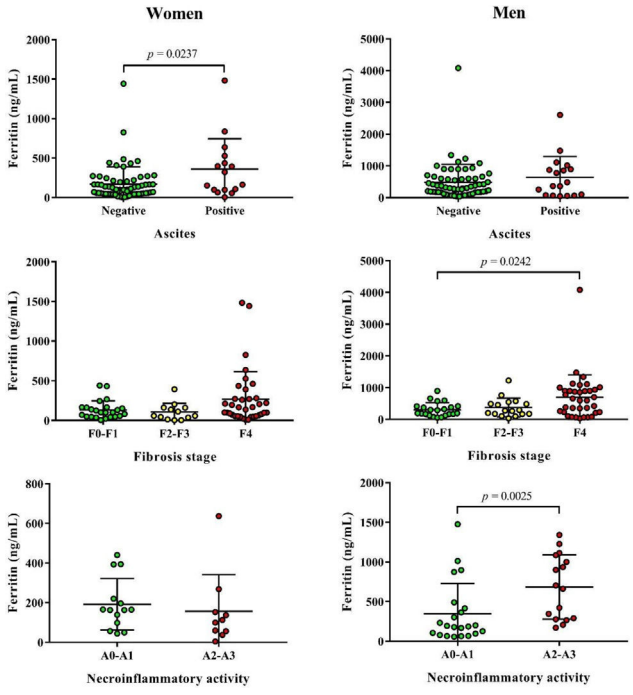

Figure 1. Ferritin levels between women and men with and without ascites, with different fibrosis stage and necroinflammatory activity.

times, serology for Hepatitis B, C and autoimmune and Fibromax. Clinical parameters such as body mass index (BMI), type II diabetes mellitus (DMII), systemic arterial hypertension (SAH), presence of ascites, alcohol consumption (gr / week) and endoscopic findings (esophageal varices) were also analyzed.

Results: Significative difference was observed in serum ferritin levels between men and women [353.0 ng/mL (170.5–747.5 ng/mL) vs 108.3 ng/mL (55.8–253.5 ng/mL), $p < 0.0001$], as well as in serum ferritin levels between women with and without ascites, in men with different fibrosis stage (FibroTest) and necroinflammatory activity (ActiTest) (Figure 1). A poor but significant correlation was observed between serum ferritin and age, erythrocytes, MCV, MCH, uric acid, direct bilirubin, albumin and HDL cholesterol in women and alcohol consumption, uric acid, ALT and AST in men. All other evaluated clinical parameters and biomarkers showed no significant difference.

Conclusions: An association was observed between the degree of fibrosis and serum ferritin and necroinflammatory activity in men, as well as between ferritin and ascites in women. A poor correlation was observed between serum ferritin levels and the analyzed chemical biomarkers.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Moringa oleífera decreases insulin resistance, novo lipogenesis and modifies the expression of mirnas in a non-alcoholic esteatohepatitis model

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Background and aim: In Mexico there is a high prevalence of non-alcoholic steatohepatitis (NASH) and liver diseases are the fourth leading cause of death. NASH is characterized by hepatocyte ballooning, inflammation, and steatosis. Moringa Oleifera (MO) extracts have been shown to have hypoglycemic, anti-inflammatory and antioxidant effects. The aim was to evaluate in a NASH model the effect of the aqueous extract of MO the gene and protein expression of molecules involved in steatosis and liver inflammation and on miRNAs involved in the development of NASH.

Material and methods: Male C57BL / 6J mice were fed a high fat diet (HF, 60% lipid, 42gr / L sugar in water) for 16 weeks. The administered dose of the MO extract was 300 and 500 mg / Kg / day from week 9 to 16. The serum levels of adipokines were measured, the HOMA-IR was calculated; In the liver miR-21a-5p, miR-103-3p, miR-34a-5p and IL1β, IL-6, TNFα, SREBP1, FASN and DAGT2 were evaluated by qRT-PCR and SREBP1 by Western Blot. The transcriptome was evaluated by microarrays. Inflammation, reactivity to αSMA and fibrosis were analyzed in histological sections. Quantitative variables were analyzed with ANOVA, Tukey for parametric data, Mann-Whitney U for non-parametric data. Approved by the CUCS Ethics, Research and Biosafety Committees: 1937.

Results: Moringa treatment reduced serum insulin, PAI-1, leptin, and resistin levels. In liver: IL1β, IL6, TNFα, SREBP1c, FAS, and DAGT2 mRNAs decreased; SREBP1 protein decreased. Expression of mir-21a, mir-103, and mir-34a were reduced. In the transcriptome, the mRNAs involved in the response to DNA damage and stress of the endoplasmic reticulum, lipid biosynthesis, and extracellular matrix synthesis were underexpressed. In liver histologies, the number of inflammatory nodules and the presence of αSMA and fibrosis decreased.

Conclusions: MO supplementation decreased serum adipokine levels; as well as the mRNAs of proinflammatory cytokines and lipogenic genes in liver. The histological quantification of MEC, collagen, inflammatory nodules and αSMA decreased; miRNAs evaluated were modified. Moringa extract showed anti-inflammatory, antifibrogenic and antilipogenic effect in a NASH model.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Prolonged-release pirfenidone decreases hepatic miRNAs expression in a NAFLD/NASH experimental model

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Background and aim: Nonalcoholic steatohepatitis (NASH) is featured by lipid accumulation, inflammation, and fibrosis. miRNAs are small non-coding RNAs that participate in post-transcriptional genetic regulations and are involved in various pathologies such as NASH. The drug pirfenidone is an antifibrotic, anti-inflammatory and antioxidant agent. Aim: To evaluate the effect of prolonged-release pirfenidone on histological parameters, activation of hepatic stellar cells, expression of hepatic miRNAs and target genes in an experimental model of NAFLD/NASH.

Material and methods: Male C57BL/6J mice were fed a high fat diet (HFD, 60% lipids, 42gr/L sugar in water) for 16 weeks. Prolonged-release pirfenidone (∼300 mg/kg/d, PR-PFD) was administered in food from the eighth week to the end of the protocol. α-SMA immunohistochemistry and hematoxylin-eosin, Masson's trichrome and Sirius red staining were made. Hepatic expression of miR-21a-5p, miR-103-3p, miR-34a-5p and IL-1β, TNFα, COL1A1, and SREBP1 genes was determined by qRT-PCR and the transcriptome by microarrays. Statistical significance was determined for parametric data with one-way analysis of variance and Tukey's or Bonferroni post hoc test, and Kruskal-Wallis and Mann-Whitney *U* test for nonparametric data (Graph Prism 6.0). Ethics Committee registration number: CI00518.

Results: Animals treated with PR-PFD have a decrease in inflammatory nodules, macrosteatosis, fibrosis, collagen and activation of hepatic stellar cells. PR-PFD reduced hepatic expression of miR-21a-5p, miR-34a-5p and miR-103-3p expression showed a tendency of decrease compared to HFD group. PR-PFD decreased IL-1β, TNFα, COL1A1, and SREBP1 expression. Transcriptome analysis showed that 36 genes that participate in lipid transport and antiox-

idant activity were overexpressed in the treated group compared to HFD group. On the contrary, 52 genes involved in lipid and collagen biosynthesis and inflammatory response were downregulated.

Conclusions: Prolonged-release pirfenidone decreased miR-21a-5p expression, miR-34a-5p and miR-103-3p expression showed a tendency to decrease. PR-PFD exhibited an anti-steatogenic, anti-inflammatory and anti-fibrotic effect in the experimental model of NAFLD/NASH.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Clinical and epidemiological characteristics of patients with autoimmune hepatitis in a center of Northeast Mexico

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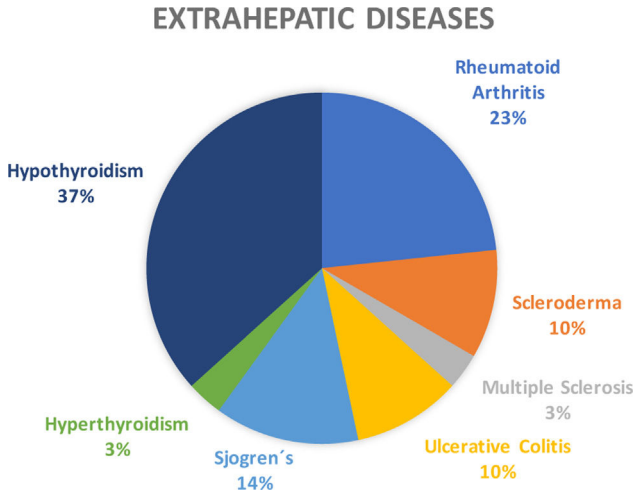
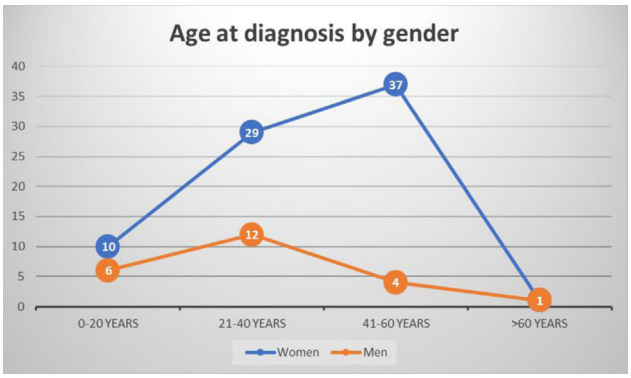
Background and aim: Autoimmune hepatitis (AIH) is a very heterogeneous disease with an impact on the morbidity and mortality of patients, which affects all ages, genders, and ethnic groups. It can present either asymptomatically, such as acute hepatitis, cirrhosis, or acute liver failure. Aim: To describe the demographic, biochemical and clinical characteristics of patients with HAI, due to the few epidemiological data that exists in Latin America.

Material and methods: A retrospective cohort study was conducted that included patients with HAI attended at the Northeast National Medical Center of the IMSS (Monterrey, Nuevo León). The information was collected from the digital file between March 01, 2019 to April 01, 2020.

Results: A total of 100 patients, 77% female, with an average age at diagnosis of 37 years were included (Graph 1). In the presentation form, 38% were cirrhotic at diagnosis, 2% debuted with acute liver failure, 16% with acute hepatitis, and 44% with asymptomatic abnormal liver tests. Regarding autoantibodies, 75% had positive antinuclear antibodies (ANAs) or smooth muscle antibodies (ASMA). 25% associated autoimmune extrahepatic diseases (Graph 2), and 46% fulfilled criteria for Overlap Syndrome, mostly primary biliary cholangitis (CBP). Regarding treatment, 40% were considered refractory to conventional therapy, meriting the use of other immunosuppressors (mycophenolic acid and tacrolimus). Of the total of patients, 32% had received Orthotopic Liver Transplantation (THO).



Graph 1. Age at diagnosis by gender ($N = 100$).



Graph 2. Associated extrahepatic diseases.

Conclusions: Autoimmune hepatitis in our population behaves similarly to that described in the world literature, with a greater association to overlap syndrome and refractory treatment, perhaps because it is a reference center.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Pirfenidone induces epigenetic changes modulating the activity of the ppargamma-SIRT1-DNMT1 axis in hepatic stellate cells

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Background and aim: The role of epigenetic changes in liver diseases has been described through abundant experimental evidence, highlighting the de-acetylation in residue lysine 9 of histone H3 (H3K9) regulated by SIRT1 (NAD-dependent deacetylase), and methylation of promoters of genes involved in fibrogenic response regulated by DNA-Methyl transferase 1 (DNMT1). Our research group characterized the regulation of pirfenidone (PFD) on PPARalpha/gamma-SIRT1 axis in two experimental animal models: (1) NASH and (2) hepatocarcinoma. The objective of this work was to characterize the changes in the acetylation/de-acetylation of H3K9 induced by PFD treatment in hepatic stellate cells (HSCs), in addition to analyzing the global methylation patterns

Material and methods: HSCs were treated with PFD (500 μM), SIRT172 activator (20 μM) and inhibitor EX527 (80 μM) of SIRT1 for 24 hrs. Subsequently, changes in the expression of SIRT1 and DNMT1 were analyzed by western blot. Immunofluorescence was carried out using markers that detect H3K9 acetylation and global methylation (5MeC; 5Metyl-Cytosine), images were captured with a confocal microscope in order to visualize the cellular co-location of proteins.

Results: The western blot shows that the treatments with PFD and SIRT1720 treatments increase the expression of SIRT1 and DNMT1 proteins, while EX527 reduces them. Immunofluorescence demonstrated that PFD and SIRT1720 decrease the acetylation of H3K9, but increase overall methylation; contrarily, treatment with

EX527 induces an increase in acetylation of H3K9 but decrease overall methylation.

Conclusions: The results of our work indicate for the first time that PFD can regulate epigenetic marks possibly through modulation of the PPARγ-SIRT1-DNMT1 axis. Acetylation in H3K9 decreases with PFD treatment, however overall methylation increases. The perspectives of this work will be to analyze the methylation of specific genes (PPARalpha, IL-6, TNFalpha) involved in the development of liver diseases.

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Conflicts of interest: The authors have no conflicts of interest to declare.

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14

Molecular, histological and biochemical changes in a NASH murine model whit a diet high in fats and sugars

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Background and aim: The increase in NASH prevalence coincides with the current obesity pandemic. Obesity is characterized by a state of chronic inflammation with oxidative stress in adipose tissue and liver. A high fat/sugar diet can induce non-alcoholic steatohepatitis, which is characterized by inflammation, hepatocyte swelling, and steatosis. To assess molecular, histological, and biochemical changes in a murine NASH model subjected to a high-fat diet for 16 weeks.

Material and methods: Male mice 4-5 weeks old, C57BL / 6J were fed a high-fat diet (HF, 60% fat, 42gr / L sugars in water) for 16 weeks. Every 4 weeks 4 mice were sacrificed for a follow-up of the model at 4, 8, 12 and 16 weeks. Serum glucose was measured after 4 hours of fasting, animal weight and caloric intake. The liver was removed and weighed, as was the epididymal adipose tissue. AST, ALT, TAG, Chol and VLDL were measured. Immunohistochemistry was performed for α-SMA and hematoxylin-eosin staining, Masson's trichrome and Syrian red. The hepatic expression of IL-6, TNFα, COL1A1 and TGF-β mRNAs was determined by qRT-PCR. Quantitative variables were analyzed with ANOVA, Tukey for parametric data and Kruskal-Wallis for non-parametric data. Opinion CI00518 of ethics and investigation committee.

Results: Animals at week 16 showed high body weight compared to animals with standard diet, presence of steatosis and liver inflammation ($p < 0.05$). Serum glucose increased at week 12 and 16 ($p < 0.05$). The weight of the liver and epididymal fat increases as the model is established, without achieving statistical significance. The histological parameters coincide with the establishment of a steatohepatitis, while the values of the biochemical parameters increase remarkably compared to the control group. Inflammatory and fibrotic genes increase at 16 weeks compared to the control group.

Conclusions: Exposure to a diet high in fat and simple sugars induced increased body weight, steatohepatitis, inflammation, hyperglycemia, and increased expression of liver enzymes and genes involved in inflammation and fibrosis.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Development of a defatting strategy to reduce lipid accumulation and improve the viability of steatotic grafts in liver transplantation

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Background and aim: In order to reduce mortality on waiting list, therapeutic strategies are required to increase the use of steatotic liver grafts in transplantation. However, steatotic grafts tolerate poorly ischemia-reperfusion (I/R) injury, and therefore they show a very high risk to early allograft dysfunction or primary nonfunction after transplantation. The aim of the present research was to evaluate the potential of 3 pharmacological modulators of lipid metabolism to induce defatting and protection against hepatic damage during cold preservation period in steatotic liver grafts.

Material and methods: Wistar rats were fed with a high-fat diet to induce steatosis. Then, steatotic livers were preserved at 4° C for 6 hours, either in Custodiol preservation solution, or in Custodiol solution enriched with caffeine, choline, or L-carnitine. At the end of this period, grafts were washed-out and transaminases and triglycerides in liver tissue were determined. This study was approved by the institutional Research Ethics Committee.

Results: Addition of caffeine to Custodiol solution decreased hepatic triglycerides content by 56% in steatotic grafts when compared with grafts preserved only in Custodiol. Triglycerides content was similar in steatotic grafts preserved in Custodiol enriched with choline or L-carnitine, and in those grafts preserved in Custodiol without additives. Regarding liver injury, preservation in Custodiol supplemented with caffeine, choline or L-carnitine resulted in a decrease in transaminases, compared to the levels observed in preservation with solely Custodiol.

Conclusions: Addition of caffeine to preservation solution trigger defatting in steatotic liver grafts, which is associated with protection against I/R injury. The enrichment of preservation solution with choline or L-carnitine decrease I/R injury in steatotic grafts, but this effect was not related to reduction in triglyceride content.

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Conflicts of interest: The authors have no conflicts of interest to declare.

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Hepatoprotective effect of sodium (*S*)-2-hydroxyglutarate against ischemia-reperfusion injury in Wistar rats

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Background and aim: Ischemia-reperfusion (IR) injury is one of the leading causes of early graft dysfunction in liver transplantation. Techniques such as ischemic preconditioning protect the graft through the activation of the hypoxia-inducible factors, which are the main regulators of oxygen homeostasis and are downregulated by the EGLN prolyl-hydroxylases. The inhibition of EGLN has a therapeutic effect against IR injury. Our aim was to evaluate the effect of the EGLN inhibitor sodium (*S*)-2-hydroxyglutarate [(*S*)-2HG] against liver IR injury in Wistar rats.

Material and methods: (*S*)-2HG was synthesized from L-glutamic acid by diazotization/alkaline hydrolysis, and its structure was confirmed by nuclear magnetic resonance. Thirty-one female Wistar rats were used, weighing 250 – 300 g, randomly divided in the following groups, following the specifications of the NOM-062-ZOO-1999: IR (n = 7, ischemia: 20 minutes, reperfusion: 60 minutes), sham (SH, n = 7, laparotomy without IR), non-toxicity (HGTox, n = 6, 25 mg/kg, *p.o.*, twice per day for two days, laparotomy without IR), and (*S*)-2HG + IR (HGIR, n = 7, same dose as HGTox group + IR induction). Serum levels of ALT, AST, LDH, ALP, glucose, and total bilirubin, were assessed. Tissue levels of IL-1β, IL-6, TNF-α, malondialdehyde, SOD, and glutathione peroxidase were also evaluated. This project was approved by the Ethics and Research Committee of our institution (Registration number: HI19-00003).

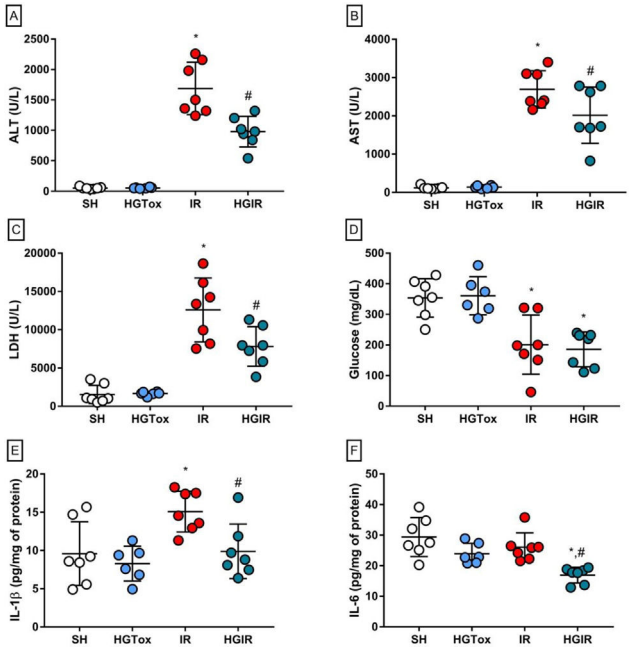

Figure. Liver injury and inflammatory biomarkers. (A) Serum alanine aminotransferase; (B) Serum aspartate aminotransferase; (C) Serum lactate dehydrogenase; (D) Serum glucose; (E) Tissue interleukin 1β; (F) Tissue interleukin 6. One-way ANOVA with Tukey *post hoc* test, $^{*}p < 0.05$ versus SH; $\#p < 0.05$ versus IR.

Results: A difference in the levels of ALT, AST, LDH, glucose, IL-1β, and IL-6 was observed among the groups (Figure). No hepatotoxic effect was observed when comparing the HGTox group versus the SH group. There were also no differences in the other biomarkers assessed.

Conclusions: (*S*)-2HG showed a hepatoprotective effect, decreasing the levels of liver injury and inflammation biomarkers. No hepatotoxic effect was observed at the tested dose.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Cellular and molecular characterization of the pirfenidone effects on an hepatocarcinogésis experimental model

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Background and aim: Hepatocellular carcinoma (HCC) is a primary neoplasm of the liver with high recurrence and high mortality rate. The etiological factors are hepatitis B and/or C virus infections, non-alcoholic steatohepatitis, alcohol consumption, and aflatoxin b1 exposition. These factors promote inflammation, fibrosis, and cirrhosis, and alter the expression of genes and molecular mechanisms, initiating hepatocarcinogenesis. The modified resistant hepatocyte model (MRHM) has been established which simulates the stages of carcinogenesis. Pirfenidone (PFD) has shown antifibrotic, anti-inflammatory and antioxidant effects in liver damage models, so the aim was to evaluate the administration of PFD on histopathological alterations and the expression of key proteins in the development of hepatocarcinogenesis in MHRM.

Material and methods: Longitudinal experimental study. 30 Wistar rats were divided into 3 groups: control group, carcinogenic damage group, and carcinogenic damage group plus daily administration of PFD. The physical and clinical data of the animals were analyzed at 30 days. All tissues were subjected to H&E, and Masson trichrome histological assays, and analysis of proteins involved in liver fibrosis, acute and chronic inflammation, apoptosis, cell division, tumor promotion/suppression, and cell metabolism using Western-Blot tests and microscopy confocal. Experiments for triplicate were performed; data were analyzed and plotted in GraphPad Prism 7.

Results: Morphological analysis: damage group shows dense, pale brown and inflamed livers compared to control and PFD groups. PFD administration prevents damage in the hepatocyte architecture, reduces periportal fibrosis and prevents inflammation overexpression markers (NFkB, IL-6, and TNFalpha) and cell

division activation. PFD increases apoptotic markers expression (Cas-3), tumor suppressors (p53) and re-establishes proteins in cellular metabolism regulation (PPARalpha/PPARgamma).

Conclusions: PFD administration prevents chemical-induced carcinogenic damage in MMRH. PFD decreases fibrotic and proinflammatory markers; likewise, PFD regulates tumor suppressor and mitogenic markers.

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Conflicts of interest: The authors have no conflicts of interest to declare.

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Analysis of the molecular interaction of pirfenidone with PPAR-gamma and effects on the beta-catenine pathway in HEPG2 line

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Background and aim: PPARgamma is a nuclear receptor that regulates genes involved in energy metabolism. It consists of a transactivation domain at the N-terminus, two zinc fingers required for DNA binding, and a ligand-binding domain at the C-terminus that facilitates RXR-alpha binding and activation. The interaction of PPARgamma/beta-catenin has recently been established in type 2 diabetes and the development of colon cancer. On the other hand, Pirfenidone (PFD) has shown antifibrotic, anti-inflammatory, and antioxidant effects in various models of liver damage. The objective of our work was to demonstrate by *in silico* analysis that PFD is a ligand/agonist of PPARgamma and subsequently analyze the activity of beta-Catenin in the HepG2 hepatocarcinoma cell line.

Material and methods: Molecular interaction analysis was performed using the SwissDock platform, the images were made with the 3D UCSF CHIMERA processor. For in vitro analysis, the HepG2 cell line was used. The cells were treated with 500 μM PFD, the non-selective agonist (GW7647; 100 nM) and the selective antagonist (GW9662; 100 nM) of PPARgamma for 24 hrs. Immunofluorescence and Western-Blot of PPAR gamma and beta-Catenin were performed. The experiments were carried out in triplicate, GraphPadPrism 7 was used to prepare the graphs and statistical analysis.

Results: *In silico* analysis shows that Pirfenidone binds to the Serine342 residue of PPARgamma, the same site that Rosiglitazone binds to. Immunofluorescence shows increased PPARgamma placement and lower beta-Catenin in the nucleus for cells treated with PFD and GW7647. The opposite is observed in control and GW9662-treated cells. There is a differential expression of PPARgamma and beta-Catenin in cells treated with PFD and GW7647.

Conclusions: PFD is a ligand /agonist of PPARgamma because it binds to the Serine342 residue, just as Rosiglitazone does (a pharmacological agonist used in the treatment of type 2 diabetes mellitus). Additionally, treatment with PFD in HepG2 cells decreases the translocation of beta-Catenin to the nucleus, which could contribute to slow the progression of HCC.

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Conflicts of interest: The authors have no conflicts of interest to declare.

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Prolonged-release pirfenidone prevents myocardial fibrosis in a mouse nonalcoholic steatohepatitis model

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Background and aim: Obesity is associated with insulin resistance, nonalcoholic steatohepatitis (NASH) and myocardial fibrosis. Peroxisome proliferator-activated receptors (PPARs) regulate carbohydrate and lipid metabolism; improving insulin sensitivity, triglyceride levels, inflammation and oxidative stress. Pirfenidone has anti-inflammatory, antioxidant and antifibrotic effects. Aim, we investigated the molecular effects of prolonged-release pirfenidone (PR-PFD) in ventricular tissue of male C57BL/6J mice with NASH.

Material and methods: All experiments were performed in compliance with the guidelines of the bioterium-CUCS Research Committee at the University of Guadalajara and National Institutes of Health (NIH). Five-week-old mice were fed with normal diet (ND, 18% kcal from fat, $n = 5$) and high-fat/high-carbohydrate (HFHC, 60% kcal from fat, plus 42 g/L: 55% fructose y 45% sucrose in water, $n = 10$) diet for 16 weeks of feeding. At 8 week, five mice with HFHC diet were administered PR-PFD (350 mg/kg/day). We assessed insulin resistance, oil red o, hematoxylin-eosin, Masson's trichrome and picrosirius staining, western blot, immunohistochemistry, RT-qPCR and data by SPSS.

Results: Mice showed NASH with insulin resistance, myocardial steatosis and fibrosis, which were prevented by PR-PFD. Ventricular tissue of HFHC mice showed increased TNF-α, Nrf2, Desmin, Tgfβ1, Timp1, Collagen-I, Collagen-III, mRNA levels, including NF-kB, Nrf2, α-SMA, Troponin-I, Acox1, Cpt1A and Lxrα protein levels compared to the ND ventricular tissues ($P \leq 0.05$). PR-PFD treatment decreased these genes overexpressed by HFHC diet ($P \leq 0.05$). PR-PFD overexpressed the Pgc1a mRNA levels and Pparα, Pparγ, Acox1 and Cpt1A protein levels ($P \leq 0.05$).

Conclusions: PR-PFD prevents the cardiac steatosis and fibrosis by sobreexpressing Pparα, Pparγ, Acox1 y Cpt1A proteins. PR-PFD is a promising drug for the treatment of cardiac fibrosis induced by NASH.

This work was supported by "Fondo de Desarrollo Científico de Jalisco (FODECIJAL, 8149-2019 and 7941-2019)" and by "Consejo Nacional de Ciencia y Tecnología (CONACYT, 259096)".

Conflicts of interest: The authors have no conflicts of interest to declare.

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Hepatoprotective effect of nifedipine against ischemia-reperfusion injury in rats

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Background and aim: Ischemia-reperfusion (IR) injury is the leading cause of early graft dysfunction. Many mechanisms are involved in IR injury; activation of apoptosis is one of the most important. The blockade of the Ca^{2+} channels inhibits apoptosis and has a potential protector effect against IR injury. Calcium channel blockers, like nifedipine, have potential therapeutic activity against this process in organs such as brain, testicle and intestine. In this project, we aimed to assess the hepatoprotective effect of nifedipine in our IR model.

Material and methods: A total of 18 female Wistar rats were divided into three groups: Sham (SH), IR, and nifedipine + IR (NIR, 10 mg/kg, p.o., twice a day for three days). A midline laparotomy was performed, exposing the liver hilum and inducing IR injury to the IR and NIR groups, by using an atraumatic vascular clamp (ischemia: 20 min; reperfusion: 1 hour). Serum activities of ALT, AST, LDH, and ALP, and serum concentrations of total bilirubin and glucose were measured. Proinflammatory cytokines (IL-1β, IL-6, and TNF-α) were determined, and oxidative stress biomarkers (superoxide dismutase, malondialdehyde, and glutathione peroxidase) were assessed. Histological parameters, such as congestion, vacuolization, and necrosis, were evaluated in tissue samples stained with hematoxylin and eosin. All rats were handled according to the Official Mexican Norm NOM-062-ZOO-1999. This project was approved by the Ethics and Research Committee of our Institution with registry: HI19-00003.

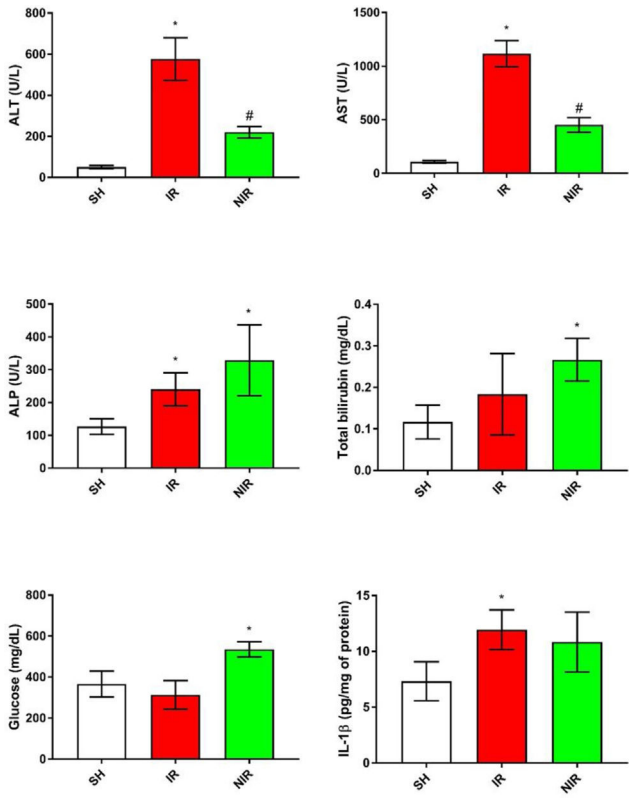

Figure. Biochemical and inflammation markers. *$p < 0.05$ against SH. #$p < 0.05$ against IR.

Results: The administration of nifedipine caused a decrease in the serum activities of ALT and AST compared against the IR group. Also, it caused an increase in the activity of ALP probably caused by osteoclastic induction due to nifedipine. The concentration of glucose and total bilirubin compared with the SH group showed an elevation (Figure). There were no significant differences in the other parameters analyzed.

Conclusions: Nifedipine presents a hepatoprotective effect against IR injury, evidenced by the decrease of liver enzymes. This compound does not show an immunomodulator or antioxidant effect.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Reported resistance to different antibiotics in cirrhotic patients with spontaneous bacterial peritonitis

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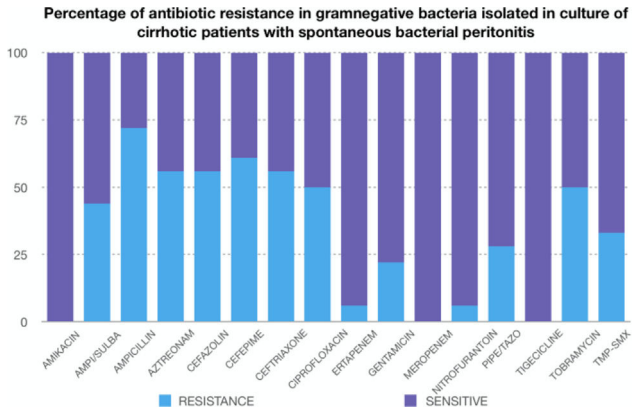
Background and aim: Spontaneous bacterial peritonitis (SBP) is one of the most frequent bacterial infections in cirrhotic patients, its mortality without specific treatment is high. Within the first choice of empirical therapy, cephalosporins and quinolones are recommended. However recent studies have shown an increase in the prevalence of infections caused by multiresistant bacteria, especially in nosocomial episodes, which has caused a change in practice. The national literature present only a few data regard this subject, thus its study is important. Aim: To describe the reported resistance to different antibiotics in cirrhotic patients with SBP.

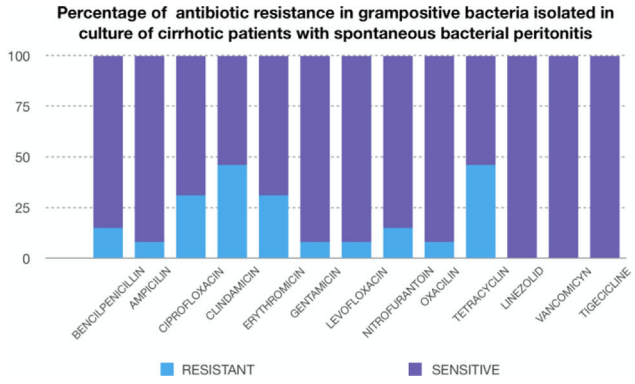
Material and methods: Observational, descriptive, transversal, retrolective study. Procedure: We reviewed the clinical records of patients admitted to the Gastroenterology Department in hospitalization area with diagnosis of SBP from March 2018 to December 2019, taking in count the bacterial culture result and the reported sensitivity or resistance to different antibiotics included in the antibiogram. The qualitative variables were expressed as frequencies and percentages. The numerical variables were expressed as mean and standard deviation.

Results: The study included 70 patients of whom 61.4% were men. The main age was 52.2 ± 12.2 years-old. About 20% of patients were Child Pugh B, and 80% Child Pugh C. Of all patients, 55.7% corresponded to neutrocytic ascites, a gram-negative microorganism was isolated in 25.7% of the cultures, and a gram-positive microorganism was isolated in 18.6%. The most frequently isolated bacterium was *Escherichia coli*. Acquisition of SBP: 56% of infections were acquired in the community, 33% related to health care and 11% nosocomial. The sensitivity and resistance to different antibiotics obtained in the cultures are shown in the following graphs.

Conclusions: There is increasing resistance to different antibiotics, especially in hospital-acquired infections. In the case of spontaneous bacterial peritonitis, resistance to cehalo-sporins and quinolones is observed in more than half of the cases, so we must be careful with its prescription.

Conflicts of interest: The authors have no conflicts of interest to declare.





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Sustained viral response in patients with hepatitis C and chronic kidney disease in hemodialysis and treatment with direct acting antivirals in the UMAE 71

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Background and aim: In Mexico, there is a high prevalence of patients with hepatitis C virus (HCV) with chronic kidney disease on hemodialysis (CKD-H); since the appearance of new direct-acting antivirals (DAAs), 95-99% of patients have been documented to be cured worldwide, however, in a mexican population with these characteristics, there are no studies that support the response to treatment. The objective was to determine the sustained viral response (SVR) and drug safety in patients with HCV and CKD-HD treated with DAAs free of sofosbuvir in patients at UMAE 71.

Material and methods: Observational and retrospective study that including patients over 18 years old with HCV diagnosed by positive RNA test using CRP technique, who also had permanent CKD-HD received at UMAE 71. Twenty-eight patients were included, of whom 25 received glecaprevir/pibrentasvir for 8 weeks and 3 received ombitasvir/paritaprevir/ritonavir/dasabuvir for 12 weeks; all completed treatment. SVR was considered negative CRP 12 weeks after treatment was completed; in addition, treatment-related adverse effects were documented. Statistical analysis was based on frequencies and percentages, means and standard deviation.

Table 1
Baseline Characteristics of the Patients.

Characteristics	Glecaprevir/ Pibrentasvir Total ($n = 25$)	Ombitasvir/ paritaprevir/ ritonavir/ dasabuvir Total ($n = 3$)
Sex: Women-Men (%)	52%-48%	100% (M)
Age (years)	57.8 ± 16.4	52.6 ± 17.6
Diabetes mellitus (%)	40%	33.3%
Systemic arterial hypertension (%)	96%	100%
Genotype 1B (%)	96%	100%
Non-significant fibrosis (FIB4 F1-F2) (%)	68%	66.6%
Significant fibrosis (FIB4 F3-F4)	32%	33.3%

Results: The patients were analyzed from February 2019 to January 2020. The baseline characteristics of the patients are shown in Table 1. SVR was documented at 12 weeks of 100% and they presented minimal side effects.

Conclusions: Using sofosbuvir-free DAAs demonstrated SVR in all patients with frequent but not serious side effects, guaranteeing its efficacy and safety in the population studied with HCV and CKD-H.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Total cholesterol/high-density lipoprotein cholesterol ratio, high-density lipoprotein triglycerides/colesterol with hepatic fat infiltration grade in non-alcoholic fat liver

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Background and aim: Nonalcoholic Fatty Liver Disease (NAFLD) is a de worldwide public healthproblem, has a relationship with insulin resistance and, hyperglycemia, related to type 2 diabetes. Total cholesterol (TC)/ High density lipoprotein cholesterol (HDL) and ultrasensitive reactive C protein has been a biomarker of CVD risk, the Framingham Cardiovascular Institute suggested that TC/HDL should be <4. Because optimal cut-off values of TC/HDL and Triglycerides (TG)/HDL are already known to predict NAFLD, however, it has not been correlated with the degree of hepatic fat infiltration using abdominal ultrasound mode B (AUMB) study, with a sensitivity of 79.7% and specificity 86.2%. AIM: Describe the TC/HDL, TG/HDL ratio with degree of hepatic fat infiltration in patients diagnosed with Non-Alcoholic Fatty Liver.

Material and methods: Retrospective study of patients registered with NAFLD in external gastroenterology consultation at hospital Juárez in Mexico, froml January 1, 2017 to January 31, 2020, who complied with the following: 1. No history of alcohol consumption or quantity < 30 grams/day men and < 20 grams/day women, 2. Exclusion of a history of specific diseases that may cause NAFLD, 3. AUMB with 3.5 MHz (Toshiba) soda according to the diagnostic criteria of NAFLD by the Chinese society of Hepatology 2010

that shows excessive accumulation of liver fat interpreted by the same radiologist doctor. 4. Full fasting lipid. Data was obtained from the clinical dossier and processed in the statistical program Jamovi 1.1.9, for obtaining means, medians and percentages. Chi squared test was used for categorical variable analysis and one-way variance analysis (ANOVA) for continuous variables, setting a p-0.05 to significant.

Results: In total 102, mean age 52 years (20-79), female 80 (78.4%), nos previous history 63 (61.8%) metabolic syndrome 90 (88.2%) diabetics 46 (45.1%) obesity 64 (62.7%).

AUMB for fat infiltration: Grade I, 8 (7.8%) grade II 48 (47.1%) and grade III 46 (45.1%) being by FIB4 scale (Ishak 2-3) and NAFLD score for indeterminate fibrosis.

The median TC/HDL was correlated with the degree of hepatic fat infiltration by AUMB, grade I: 3.65 (2.81- 4.10) II, 4.06 (2.04-6.83) III, 4.81 (1.95-10.3), $p < 0.001$ value.

TG/HDL was also correlated with degree of hepatic fat infiltration being: grade I, 2.27 (1.31-3.05), II, 4.32 (0.887- 12.5) III, 6.05 (1.80-16.9) with p value <0.0011 III, 6.05 (1.80-16.9) p value < 0.0011 III, 6.05 (1.80-16.9) with p value $p < 0.0011$.High triglyceride levels and metabolic syndrome correlate with the degree of hepatic fat infiltration value of <0.001.

Conclusions: The TC/HDL and TG/HDL ratio correlates with the degree of hepatic fat infiltration by AUMB, however, it should be considered that in patients with high body mass index this study lowers its sensitivity and specificity so it should be performed in addition to other imaging modalities.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Incidence and impact of bacterial infection on the forecast of patients with acute liver failure on chronic "ACLF", hospital juárez de México

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Background and aim: Cirrhosis is associated with the deterioration of the immune system and the altered systemic inflammatory response, which predisposes to bacterial infections and a four-fold increase in mortality. Regarding ACLF, a study published by EF-Clif reported a 33% infection at diagnosis. Another study by Shalimar et al. He reported 10.8% of infections at diagnosis, with a 30-day survival of 24.0%; Infections were associated with ACLF-3 50%. Therefore, we consider it relevant to recognize this condition, since it confers a worse prognosis. Aim: To determine the incidence and impact of bacterial infection on the prognosis of patients with ACLF.

Material and methods: Retrospective descriptive observational study of patients diagnosed with ACLF according to the criteria of the European and American associations, bacterial infections were identified on admission, the records were reviewed, survival curves were evaluated using the Kaplan-Meier method, and the Cox regression with the SPSS statistical program.

Results: In our study, we identified 58 patients who met the ACLF criteria during 2019, of these 53.44% (n31) presented infection on admission. Most frequently, 41.9% (n13) presented urinary tract infection (UTI) followed by 22.5% (n7) spontaneous bacterial peritonitis (SBP), and more than one focused UTI/ SBP 25.8% (n8). Survival at 30 days was compared between patients without infection and with infection, using the Kaplan-Meier method reported a survival of 20% and 19% respectively ($p = 0.71$). A Cox regression was performed to assess whether the type of infection affects mortality, reporting HR = 1.14 ($p = 0.22$). In relation to the ACLF degree in patients with G1 infection 29.04% (n9) G2 45.16% (n14) G3 25.8% (n8) without significant difference in relation to mortality HR 1.06 ($p = 0.83$) With a 30-day survival 12.5% Y 30.7 for G1 and G2 ($p = 0.38$ 95% CI).

Conclusions: In our population, unlike previous studies, infections were higher, occurring in more than half, with a more frequent UTI followed by SBP, although this does not have an impact on prognosis, giving a survival similar to those patients without infection. Nor was a worse prognosis identified in relation to the types of infection. Grade 2 ACLF was the most frequent but with no significant impact on mortality.

Conflicts of interest: The authors have no conflicts of interest to declare.

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"CLIF-C ACLF mortality predictive utility in patients with acute liver failure in chronic "ACLF" in the hospital Juarez de Mexico population

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Background and aim: ACLF is a condition associated with high mortality. The CANONIC trial developed a score that classifies the ACLF grade according to the number of extrahepatic organic failures. Useful to determine prognosis of mortality with 33% ACLF-1, 35% ACLF-2 and 74% ACLF-3. Furthermore, it was identified that a score >70 at admission is associated with a 90% mortality in 90 days. That is why we consider it relevant to objectify the risk of mortality associated with the degree of complication in our population. Aim: To determine ACLF grade and CLIF-C score that predicts 28-day mortality in patients with chronic acute liver failure at the Juárez hospital in Mexico.

Material and methods: Retrospective descriptive observational study of patients diagnosed with ACLF according to the criteria of European and American associations, 2019 records were reviewed, severity was classified according to CLIF-C, survival curves were assessed using the Kaplan-Meier method and Cox Regression with the SPSS statistical program.

Results: In our study, 58 patients who met ACLF criteria were collected, of these 36.2% (n 21) ACLF-1, 39.7% (n 23) ACLF-2, 24.1% (n 14) ACLF-3. Survival curves were performed using the Kaplan-Meier method, reporting a 28-day survival of 25%, 18%, and 7.7%, respectively. It was compared between these without showing statistical significance ($p = 0.25$). It was decided to carry out a multivariate analysis using the Cox regression method, analyzing the degree of ACLF, CLIF-C score, age, sex, infection, gastrointestinal bleeding, acute kidney injury (AKI), resulting among these that AKI is the only variable with significant association in survival ($p = 0.017$).

Conclusions: In our population, it was identified that there is no significant statistical impact on survival between ACLF grades, nor the number of organic failures (Clif-C score). The presence of LRA proved to be a better independent predictor of mortality.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Precipitating factors and epidemiological characteristics in acute on chronic liver failure of a unity medical of high speciality

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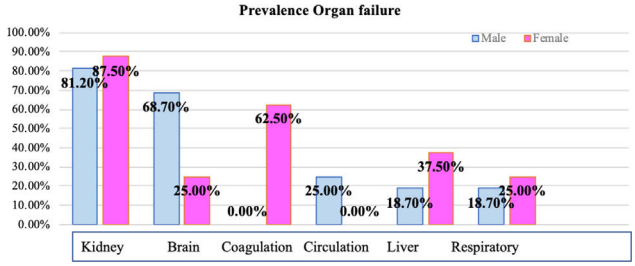
Background and aim: Acute on chronic liver failure (ACLF) is an acute decompensation in a patient with chronic liver disease associated with organ failure. The precipitating factors described most prevalent in the West are alcohol and bacterial infections, in a considerable proportion it is not possible to identify a factor. Aim. Identify the precipitating factors of ACLF and determine the epidemiological characteristics in patients of a Unity Medical of High Speciality.

Material and methods: Descriptive, retrospective and observational study, with analysis of 24 patients diagnosed with ACLF from January 01, 2019 to February 01, 2020 of Unity Medical of High Speciality Manuel Ávila Camacho Puebla. The data collected was from clinical files and digitized in Excel, analyzed in the IBM SPSS version 24 program.

Results: From the 24 patients, (M: 16 and F: 8) the precipitating factors of ACLF were determined in 16 patients (66.7%). The most prevalent etiology of cirrhosis by sex found (M: alcoholic 43.7%, cryptogenic 25%, Hepatitis C Virus (HCV) 18.7% and NASH 12.5%). (F: cryptogenic 37.5%, HCV 25.5%, NASH 12.5% and Autoimmune 15.6%). Previous recorded decompensations M: 68.7% and F: 62.5%. By CLIF score (F: 62.5% with grade 3, 25% grade 2 and 12.5% grade 1), (M: 75% with grade 2 and 25% grade 3). In both sexes, the most affected organ was the kidney.

Conclusions: The ACLF represents a big challenge in clinical practice, the early identification of precipitating factors will allow the timely diagnosis and treatment for decrease in their morbimortality.

Conflicts of interest: The authors have no conflicts of interest to declare.



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The clinical expression of lysosomal acid lipase severity in patients with cryptogenic cirrhosis

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Background and aim: The liver cirrhosis is a global public health problem with an estimated prevalence of 0.27%, and a prevalence of chronic liver disease in the Latin American population of 61.1%. The lysosomal acid lipase (LAL) is an enzyme involved in the last steps of lipid metabolism to hydrolyzeesters of cholesterol and triacylglyceride, therefore its deficiency generates a disease by lysosomal deposit. The patients with cryptogenic cirrhosis (CC) presents a clear LAL deficiency without a mechanism yet established.

Material and methods: The present study has a retrospective and analytical design of a sample of 55 patients diagnosed with CC. It was determined the degree of association of LAL with the results of the ALT and ALP enzymes, likewise with the clinical manifestation of portal hypertension (PH). Next the sensibility and specificity of the test for the diagnosis of PH manifestation was determined.

Results: The most frequent complication of PH was the variceal bleeding with a 40% ($n = 22$), followed by ascites with 32.7% ($n = 18$) and lastly hepatic encephalopathy with 18.2% ($n = 10$). The association by test of x^2 with Fisher's test did not present a statistically significant association with values of 0.177, 0.299 and 0.184 for encephalopathy, variceal bleeding and ascites respectively. Through ROC curves it was obtain results of area under the curve (AUROC) near to 0.5.

Conclusions: It is established that there was no tendency or statistical significance of the correlation between LAL with the enzymes alanine aminotransferase and alkaline phosphatase, as well as the complications of portal hypertension. In our population the complication of portal hypertension most frequent was the variceal bleeding, unlike other studies in patients with cryptogenic cirrhosis, so it would be important to recognize which are the risk factors that increases the bleeding rate in our population, since this complication is consider the one with the highest mortality in patients with liver cirrhosis.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Hepatocelullar carcinoma is a major risk factor for the development of portal ven thrombosis in cirrhotic patients

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Background and aim: Portal vein thrombosis (PVT) is a rare complication in cirrhotic patients specially in advanced

stages, multiple series demonstrated 5-20% prevalence in cirrhotic patients.

Aim: To identify risk factors for the development of PVT in cirrhotic patients.

Material and methods: Research Design: Case-control study. Procedure: We searched medical records from inpatients during 2019 with the diagnosis of PVT; cirrhotic patients with PVT were used as cases and paired in a 1:2 ratio with cirrhotic patients without PVT. Qualitative variables were depicted as frequencies and percentage, numeric variables as mean and standard deviation. X2, fisher's exact, student's t and Mann-Whitney's U were used to compare groups accordingly. Logistic regression was used to examine risk factors. *P* value <0.05 was considered statistically significant.

Results: Out of 1371 records, 40 patients with PVT were found (2.92%); 30 of them with cirrhosis were paired with 60 non-PVT cirrhotic patients. 53 (58.9%) were male; mean age: 56,2 ± 13,9 years. According to Child-Pugh: 49 (54,4%) A, 22 (24,4%) B and 19 (21,1%) C. Fifteen (16,7%) had hepatocellular carcinoma (HCC). PVT was more prevalent in women than men (17/37 vs. 13/53 [45.9 vs. 24.5%]; OR = 2.6, IC95%: 1.1-6.4; *P* = 0.03). Patients with HCC had a higher prevalence of PVT against those without HCC (11/15 vs. 19/75 [73.3 vs. 25.3%]; OR = 8.1, IC95%: 2.3-28.5; *P* = 0.001). Decompensated cirrhosis patients had a higher rate of PVT than compensated patients (19/41 vs. 11/49 [46.3 vs. 22.4%]; OR = 2.9, IC95%: 1.2-7.4; *P* = 0.02). Adjusted multivariate logistic regression model is shown in Table 1.

Table 1
Adjusted multivariate logistic regression model exploring risk factors for PVT in patients with cirrhosis.

Variables	*P*	OR	95%CI	
			Lower	Upper
Female	0.06	2.690	0.951	7.606
Hepatocellular carcinoma	0.005	7.722	1.876	31.783
Child-Pugh B	0.86	1.114	0.325	3.820
Child-Pugh C	0.07	3.184	0.889	11.400
Constant	0.000	0.165		

Conclusions: PVT is more frequent in women and decompensated cirrhosis, the presence of HCC in cirrhotic patients is the main prothrombotic factor.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Prevalence and characteristics of cirrhotic patients with portal vein thrombosis admited in the Gastroenterology Department of the Hospital General de Mexico

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Background and aim: Portal vein thrombosis (PVT) is a complication in the natural history of liver disease, a "rebalanced" coagulation system can promote bleeding or thrombotic tendency. The prevalence of PVT in cirrhosis is 1% among compensated patients and 8-25% in decompensated patients. Aim. To determine the prevalence and characteristics of cirrhotic patients with PVT.

Material and methods: Research design: Descriptive, cross-sectional / prevalence. Procedure: We analyzed medical records of patients admitted during 2019, all cirrhotics subjects with PVT were included. Qualitative variables were expressed in frequencies and percentages and numerical variables in mean and standard deviation.

Results: Of 491 cirrhotic patients hospitalized to the Gastroenterology department in 2019, we found 24 patients with PVT (4.89%), 15 (62.5%) were women, mean age was 58.13 ± 13.51 year. 6 (25.0%) with malignancy, of those latter 6/6 (100.0%) with hepatocellular carcinoma. Regarding of cirrhosis etiology: 9 (37.5%) were of unknown cause, 6 (25.0%) ASH, 3 (12.5%) from NASH, 1 (4.2%) from hepatitis-C, 1 (4.2%) autoimmune hepatitis and 1 (4.2%) CBP. Regarding Child-Pugh: 11 (45.8%) B, and 13 (54.2%) C. Mean MELD was 21.58 ± 9.74. Upper gastrointestinal bleeding was present in 17 (70.8%) subjects, of those 15 (88.2%) due to esophageal varices and 11 (64.7%) for esophageal-gastric varices. 5 (41.7%) presented spontaneous bacterial peritonitis (SBP). 9 (37.5%) admitted with hepatic encephalopathy. 21 (87.5%) with ascites, of those: 6 (28.6%) grade I, 12 (57.1%) grade II, only 3 (14.3%) grade III. Complementary studies in patients without acute infection: leukocytes: 8,058 ± 4.41, creatinine 1.54 ± 0.86, albumin: 2.5gr/dl ± 0.62, AST: 127 U/L ± 224.83, ALT: 70 U/L ± 107.44, ALP: 155.75 U/L ± 74.51, GGT: 62.58 U/L ± 52.04, total bilirubin: 5.41 mg/dl ± 7.34, PT: 18.20 ± 4.32, INR: 1.57 ± 0.40. Regarding the location of the thrombus: 14 (58.3%) presented in the portal vein trunk, 6 (25.0%) in the trunk and its branches, and 4 (16.7%) only in one branch.

Conclusions: PVT is more frequent in cirrhotic women, decompensated cirrhosis, alcohol related and the presence of hepatocarcinoma. The most frequent location was in the portal vein trunk.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Prevalence and characteristics of non-cirrhotic patients with thrombosis of the portal system

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Background and aim: Portal vein thrombosis (PVT) is the blood clot formation within the trunk of the portal vein or its main branches. PVT prevalence is ~1% in the general population. Aim: To determine the prevalence and characteristics of non-cirrhotic patients with PVT.

Material and methods: Research design: Descriptive, cross-sectional/prevalence. Procedure: We reviewed the medical records of all the patients admitted in 2019 with diagnosis of PVT. Of those we included only non-cirrhotic patients with a diagnosis of PVT. Qualitative variables were expressed as frequencies and percentages, numerical variables as mean and standard deviation.

Results: From 1371 patients admitted in the Gastroenterology Department in 2019, we found 40 patients with PVT (2.92%), of those only 10 non-cirrhotic patients were included. The prevalence was 0.76%; eight (80%) were men, mean age was 48.38 ± 12.4 years-old. 1 patient had autoimmune hepatitis (10.0%) and 2 (20.0%)

acute pancreatitis. 4 (40.0%) neoplasia, of them 1 (25.0%) with hepatocellular-carcinoma, 1 (25.0%) with cholangiocarcinoma, 1 (25.0%) with colon cancer and 1 (25.0%) with pancreatic cancer. Upper gastrointestinal bleeding was found in up to 5/10 (50.0%), of them: 2 (40.0%) had isolated gastric varices. 3 (30.0%) presented infection, of those 100.0% presented liver abscess. 9 (90.0%) had ascites, of them 7 (77.8%) grade I and 2 (22.2%) grade II. The results of complementary studies in patients without acute infection: leukocytes: 13,657 ± 7.87, neutrophils: 12,314 ± 8.12, albumin: 2.8gr/dl ± 0.64, AST: 54.55 U/L ± 40.96, ALT: 38.57 U/L ± 22.08, ALP: 212.57 U/L ± 171.27, GGT: 233.43 U/L ± 155.98, total-bilirubin: 1.37 mg/dl ± 0.70, PT%: 74.71 ± 20.87, DHL: 396.80 U/L ± 270.17. Regarding thrombus localization: 6 (60.0%) were in the portal vein and its branches, 3 (30.0%) in the portal vein trunk and 1 (10.0%) in a single branch. The mean flow of the portal vein was 20.70 cm/s ± 15.52.

Conclusions: PVT in non-cirrhotic patients is more frequent in men, with protrombotic entities such as neoplasms, autoimmune diseases, pancreatitis and liver infections. The main pattern found in the liver function tests was cholestasic predominance and the most frequent localization was the portal vein trunk.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Characteristics of ascitic fluid and flow of the portal system in cirrotic patients with diagnosis of portal vein thrombosis

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Background and aim: Portal vein thrombosis (PVT) in cirrhotic patients is most commonly detected incidentally on routine ultrasound (US), but should be suspected in any patient with worsening or liver decompensation and in patients with a portal vein flow <15 cm/s. Patients with acute PVT may develop or worsen ascites. The detection of multiple small vessels flow at the usual portal vein site is considered cavernous (chronic) transformation that can form in as little as 6 days. Aim. To determine the characteristics of the ascitic fluid and the portal vein flow of cirrhotic patients with PVT.

Material and methods: Research design: Descriptive, cross-sectional / prevalence. Procedure: Ascitic fluid cytology and Doppler ultrasound (DUS) results of patients admitted during 2019 were reviewed, from these all the cirrhotics with PVT were selected. The qualitative variables were expressed in frequencies and percentages and numerical variables in mean and standard deviation.

Results: Of 491 cirrhotic patients admitted to the Gastroenterology department in 2019, we found 24 cirrhotic patients with PVT (4.89%), of them regarding the composition of the ascitic fluid: the mean protein value was 1.71 gr/dl ± 1.37, DHL: 88.00 ± 5.56, and glucose was 165.67 ± 66.52. On the other hand, the mean cell count in the cytological exam of patients with PVT was 144.67 ± 191.44. Regarding the flow characteristics in the DUS, 14 (58.3%) presented chronic characteristics reported as cavernomatosis of the portal vein. The mean flow of the portal vein was 19.04 cm/s ± 4.71, lastly, 13 (54.2%) cirrhotic patients diagnosed with PVT 4 (16.7%) had flow less than 15 cm/s.

Conclusions: In our hospital, according to the laboratory normal ranges, most patients diagnosed with PVT presented an increase in LDH and had an increase in the number of cells in the ascites fluid, and more than half were diagnosed in the late stage with recanalization and more than ten percent of these patients were at high risk for new thrombosis due to a reduced flow of the portal vein.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Most commonly liver function test alterations on adult patients with septic shock

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Background and aim: Liver function test (LFT) alterations in critically ill patients are frequent. The objective of the following investigation is: to describe the prevalence, patterns and clinical implications of liver function test alterations in adult patients with septic shock in ISSEMyM Medical Center.

Material and methods: Observational, retrospective study, realized from January 2016 to February 2020. Inclusion criteria: adult patients admitted in Internal Medicine and Surgery services with septic shock diagnosis, with no evidence of preexistent chronic liver disease and complete medical records. Analyzed variables: age, sex, shock etiology, LFT, concomitant diseases and outcome of the hospitalization. The "*R*" factor (*R*) was calculated to classify patients in three groups; cholestatic (*R* = <2), hepatocellular (*R* = >5), mixed pattern (*R* = 2 to 5), an analysis per subgroup was performed.

Results: 550 clinical records were reviewed, 360 met inclusion criteria. 48.3% (*n* = 174/360) presented LFT alterations. According to R, cholestatic pattern was predominant in 81% (*n* = 141/174), followed by the mixed pattern with 10.3% (*n* = 18/174) and the hepatocellular with 8.6% (*n* = 15/174). The main etiology of septic shock was pneumonia in all three groups. On the comorbid diseases, the highest prevalence in the cholestatic group was diabetes mellitus (57.4%) and hypertension in the mixed and hepatocellular group with 72.2% (13/18) and 66.7% (10/15) respectively. Mortality rate in the group without LFT alterations was 30% (55/186), and 38% (66/174) in LFT group with alterations. In subgroup analysis, the group with the highest mortality was the mixed pattern with 11/18 deaths (61.1%), followed by the hepatocellular group with 9/15 (60%) and lastly the cholestatic with *n* = 46/141 (42.6%).

Conclusions: LFT alterations in patients with septic shock are common; in our study, the general prevalence and predominant pattern was the cholestatic group, similar to international literature. The group with the highest mortality reported in the international literature is the hepatocellular (57%), however, in our study, hepatocellular and mixed pattern presented a similar mortality rate (60% and 61.1%, respectively).

Conflicts of interest: The authors have no conflicts of interest to declare.

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Mexican experience with direct-acting antivirals in the treatment of hepatitis C

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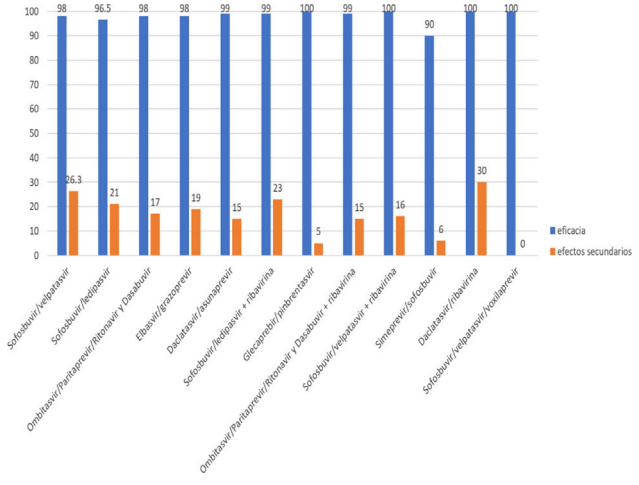
Background and aim: Chronic hepatitis C infection, develops cirrhosis with all its complications, the arrival in our country of direct-acting antivirals (DAAs), gave the opportunity to have safer and more effective drugs.

Material and methods: Retrospective, cross-sectional study of patients who received AAD in hospitals in the Mexican Republic. 20 hospital centers. Variables analyzed: gender, age, genotype, degree of fibrosis, initial and final viral load of ADA treatment. SVR and side effects were documented. Descriptive statistics were performed.

Results: Were included 813 patients, 529 women and 284 men, age 58.88 ± 12.10 years were included. Genotype 1: 647 patients (1A: 316, 1B: 318, 1A / B: 11 and 1 A / C: 2), genotype 2: 145, genotype 3:19 and genotype 4: 2. By degree of fibrosis: F0: 93 F1: 88, F2; 86, F3: 95 and F4; 451. Patients with F4 (451), Child Pugh were classified as A: 363 and B: 88. From the Child Pugh group A 7 (1.9%) did not respond and from the group B 1 (1.1%). There were 561 näive and 252 no näive, the percentage that presented SVR was from 90 to 100%. The most frequent side effects: headache 16% and fatigue 22%, nausea (3%), muscle pain (1%), abdominal pain (1%), with ribavirin, anemia was documented in 22%.

Conclusions: Direct Action Antivirals is an effective and safe option in the Mexican population studied. Adverse events were not significant.

Conflicts of interest: The authors have no conflicts of interest to declare.



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Characterization of patients with primary sclerosing cholangitis in a third level hospital

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Background and aim: Primary sclerosing cholangitis (CEP) is a syndrome of unknown cause, but it may be the result of an environmental insult that occurs in patients genetically susceptible to the disease, which would indicate an autoimmune component. Aim: To describe the clinical characteristics, treatment and complications of patients with Primary Sclerosing Cholangitis

Material and methods: Design: retrospective, cross-sectional study. It was held at INNSZ during 2009-2019. 40 patients were included with the diagnosis of Primary Sclerosing Cholangitis, Both genders, ages 18-69 years. Statistic analysis: Percentages, means, medians with standard deviation were used. The X^2 test was used. A value of $p \leq 0.05$ was considered statistically significant with a 95% confidence interval. The analysis was carried out using the statistical package SPSS® v. 25

Results: The number of patients was 40, male predominance in 52.5%, with a median age of 53 years and body mass index of 22.9. 22.7% of the patients had arterial hypertension and Type 2 Diabetes Mellitus as comorbidity. Cholecystectomy was the surgical antecedent in 29.5%. The predominant symptom at the time of diagnosis was jaundice in 57.5%. Primary large duct sclerosing cholangitis was observed in 92.5%, cirrhosis in 83%. and association with ulcerative colitis in 67.6%. 77% of the patients received ursodeoxycholic acid. Recurrent cholangitis presented in 37.5%. Liver transplant 30%, mortality was 12.5%, identifying as cause of death: $n = 2$ due to complications from liver cirrhosis, $n = 1$ due to infection, $n = 1$ due to liver transplant complications and $n = 1$ due to cholangiocarcinoma.

Conclusions: 1. Primary Sclerosing Cholangitis was presented predominantly in men, with a median of aged 53 years and associated with UC, 77% of the patients received medical treatment with AUDC. 2. Complications: recurrent cholangitis and dominant stenosis. 3. Liver transplant in 30%. 4. Main cause of death was due to complications associated with liver cirrhosis.

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Clinical, demographic, radiological and histological features of a series of liver adenomas in a reference hospital

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Background and aim: Liver adenomas are benign tumors of epithelial origin, infrequent, predominantly in women of childbearing age, and associated with the use of oral contraceptives

(ACO), and comorbidities such as metabolic syndrome, obesity, diabetes, etc. They are usually asymptomatic, of incidental diagnosis, associated with complications such as bleeding and malignant transformation to hepatocarcinoma, which has been related to their histological characteristics. Aim: To determine the clinical, demographic, radiological and histological characteristics of a series of liver adenomas in a reference hospital.

Material and methods: Observational, cross-sectional, retrolective study, carried out in the period 2009-2019.

Results: In this study female sex predominated in 61.1% and an average age of 34.3 years. The most frequent comorbidities were overweight and dyslipidemia with 38.9% and 27.8% respectively. Most were single lesions, in the right liver lobe, less than 5 cm in 55.6%. They were associated with ACO consumption in 27.8%. Adenoma subtypes were identified in 54% of cases, with inflammatory adenomas found in 66.6%, beta-catenin adenomas activated in 16.6% and inactivated adenomas in 16.6%, with evidence of complications such as hepatocarcinoma foci, hemorrhages and abscess.

Conclusions: Liver adenomas are rare tumors. They occurred predominantly in women, as single lesions smaller than 5 cm, associated with comorbidities and use of OAC. Complications such as hemorrhages, abscesses, and transformation to hepatocellular carcinoma were evident, which were associated with the histological subtype of adenomas.

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Characteristics of the overlap syndrome (HAI / CBP, HAI / CEP): a cohort type study in a reference center in Mexico during the period 2008–2018

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Background and aim: There is a clinical subgroup of patients with a combination of autoimmune liver disease, an "overlap", with features of cholestasis (CBP or CEP) in combination with HAI. Its management is relevant since, without an adequate treatment, these patients are in increased risk for developing cirrhosis and liver failure, have lower therapeutic response and their prognosis is worse than those with isolated autoimmune hepatitis, their behavior tends to be more aggressive with higher rates of cirrhosis and need for liver transplantation. Aim: To describe the clinical and biochemical characteristics and the natural history of a cohort of patients with overlap syndrome at Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán in the period January 2008 - December 2018.

Material and methods: Clinical, radiologic and histopathological records of patients with overlap syndrome were reviewed. Variables included; diagnosis (CBP / HAI or CEP / HAI), date of diagnosis, symptoms, laboratory values, metabolic comorbidities, other autoimmune diseases, characteristics of liver biopsy, time-associated variables: development of cirrhosis, decompensation, death, liver transplantation, biochemical response and relapse.

Results: Fifty patients were included in the study, 90% were women, mean age was 43.2 years (SD 11.0). The predominant comorbidity was arterial hypertension; fatigue and pruritus were the main symptoms; an important association with thyroid disease was evident, antinuclear antibodies were serologically observed in 100% of cases and mitochondrial antibodies in 57%. According to International's group criteria 14 were definitive cases and 32 were probable, with Paris criteria 33 were diagnosed. The most common outcomes were cirrhosis (50%) and disease relapse (60%). The median progression to cirrhosis was 73 months, survival and decompensation medians were not available. The percentage of biochemical response for CBP was 35.4% and for HAI 47%.

Conclusions: Overlap Syndrome at Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán predominantly affects middle-aged women with autoimmune comorbidities, the most common outcomes were cirrhosis and disease relapse.

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Correlation between the index platelet/ spleen diameter with the presence of esophageal varices by endoscopy in cirrhotic patients from the State of Mexico

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Background and aim: Endoscopy is the method of choice to determine the presence of esophageal varices (EV) in cirrhosis, however, it is invasive and expensive. Having a simple and non-invasive method would allow optimizing endoscopic procedures, minimizing costs and complications. The platelet / spleen diameter ratio (P / DB) has shown utility in predicting the presence of EV. The objective of this study is compare the P / DB index with endoscopic findings to predict the presence of EV in cirrhotic patients and to determine the best cut-off point in our population.

Material and methods: Retrospective study conducted from January 2015 to January 2019. Inclusion criteria: adults with a diagnosis of cirrhosis, sent for screening endoscopy of VE for the first time in our hospital and with complete clinic files. Patients with a history of non-cirrhotic portal hypertension, history of variceal hemorrhage and under treatment for primary or secondary prophylaxis were excluded. Variables analyzed: sex, age, etiology, Child Pugh score (CP), endoscopic findings. The P / DB index was determined by dividing the number of platelets by the maximum bipolar diameter of the spleen in millimeters. Statistical analysis was performed using Excel and SPSS.

Results: Of 455 files, 155 met inclusion criteria, 84/155 (54.1%) women and 71/155 (45.8%) men. Mean age: 60 years + 29 years. Etiology: alcohol was the most frequent in 45/155 (29.0%) followed by HCV in 33/155 (21.2%). 131/155 (84.5%) had VE, of these 82 (62.5%) were CP A, 36 (27.4%) CP B, and 13 (9.9%) CP C. The P / DB index with cutoff point on 1101 (n / mm3) / mm obtained a sensitivity of 73%, specificity of 61.9%, and AUC of 73%.

Conclusions: Previous studies suggest a cut-off point of the P / DB index of <909 (n / mm3) / mm, in our study the cut-off point identified with the best sensitivity and specificity was <1101 (n / mm3) / mm, undoubtedly it is not ideal. The results could change or be confirmed with a larger study population, in order to have a simple tool that allows optimization of the screening endoscopy.

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Spontaneous bacterial peritonitis and bacterioascitis. Microbiological and resistance profile in a third level hospital

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Background and aim: Spontaneous bacterial peritonitis (PBE) and bacterioascitis are frequent complications in cirrhotic patients with ascites. Treatment guidelines recommend third-generation cephalosporins (C3G) as the first choice, however, antimicrobial resistance in our setting is unknown. The objective of the study was to know the microbiological and resistance profile associated with PBE and bacterioascitis in our population.

Material and methods: Retrospective study, which included results from ascites fluid culture between May 2017 to May 2020. Adults with a diagnosis of PBE (> 250 PMN cel / ml^3 and a positive culture) or with a diagnosis of bacterioascitis (positive culture with <250 PMN cel / ml^3) were included. Incomplete records or non-cirrhotic ascites were excluded. Variables: sex, age, etiology, treatment, and bacteriology results. The analysis was descriptive.

Results: Of 242 files, 214 (88.4%) were included. 84 women (39.2%) and 130 men (60.7%); average age 61 years (range 26-91). 26/214 (12.1%) with PBE and 16/214 (7.4%) bacterioascitis. 42/214 (19.6%) cultures were positive, of these 26/42 (61.9%) had PBE and 16/42 (38.0%) bacterioascitis. The pathogens isolated in descending order were: E. Coli 21 (50%, 11/21 BLEE), S maltophila 5 (11.9%), Staphylococcus 4 (9.5%), Sphingomonas 2 (4.7%), Klebsiella 2 (4.7%), Candida 2 (4.7%), Enterococcus 2 (4.7%), Streptococcus 2 (4.7%), L. inocua 1 (2.3%), C. neoformans 1 (2.3%). The results of the antibiogram highlighted: resistance to Cs3G in 30.9% (13/42), to quinolones in 33.3% (14/42), carbapenems in 3/42 (7.1%) and to piperacillin / tazobactam in 1/42 (2.3%).

Conclusions: The positivity of the culture was low. The most frequent causal agent was E. Coli, similar to that reported in the literature. Rare isolated pathogens such as S. Maltophila and fungi can translate intense immunosuppression and multiple previous antibiotic exposures in this population. We found high resistance to antimicrobial groups commonly used in hospital such as cephalosporins and quinolones. Undoubtedly, the antimicrobial scheme must be adapted locally and dynamically according to microbiology results, in order to optimize the outcome in these cases.

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Frequency and characteristics of alterations in liver function tests (LFT) in adult patients with COVID-19 (preliminary report)

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Background and aim: Daily evidence arises from of other organs involvement in this new viral disease called COVID-19, several publications describe variable liver involvement, characterized by cholestasis and mild hyperbilirubinemia. The objective of the present work was to describe the frequency and characteristics of alterations in liver function tests (LFT) in patients diagnosed with SARS-COV2 in our hospital.

Material and methods: Descriptive study type. Data obtained from database in COVID-19 unit. Hospitalized adult patients confirmed with SARS-COV2 diagnosis by using RNA through PCR were included, from April 7 to May 12, 2020. Demographic, biochemical variables were analyzed upon admission, as well as comorbidities and outcome.

Results: 27 out of 113 patients, including those with suspicious diagnosis, were confirmed with SARS-COV2 which at the time of the cutoff were also included in the analysis. Average age 50.7 years (range 25-91 years). Male sex 74% ($N = 20/27$). 13 patients (48.1%) presented Liver Functions Tests (LFT) alterations, the cholestatic pattern predominated in 84.6% ($N = 11$). Ferritin value $\geq$ 1000 ng / mL and severe Acute Respiratory Distress Syndrome (ARDS) had a Predictive Positive Value (PPV) = 0.7%, Predictive Negative Value (PNV) 0.7%, $S = 0.7\%$, $E = 0.6\%$ as a diagnostic marker. 20 patients have been discharged at the time of the cutoff, 4 remain hospitalized, and 3 deaths. 3/3 deaths had Liver Functions Tests (LFT) alterations. 55% (N = 11/20) of discharged patients had LFT alterations. None presented liver failure.

Conclusions: Half of the patients affected with SARS-COV2 present LFT alteration, with predominance of cholestatic pattern in our sample. All deaths showed alteration at admission time, while 55% of discharged patients presented said alteration. The cause can be multifactorial, and involve hepatotoxicity due to drugs, deficient blood circulation, the effect of assisted ventilatory mechanics, among others, and not necessarily attributed exclusively to viral infection. Therefore, there is no evidence that suggests SARS-COV2 virus is directly hepatotropic. Serum ferritin could be useful in (ARDS) diagnosis secondary to SARS-COV2.

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Evaluación de marcadores fibroticos en células estelares expuestas al extracto metanolico de *Turnera diffusa*

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Background and aim: Activation of stellar liver cells is the cellular basis for the establishment of liver fibrosis. In search of drugs that reverse and/or inhibit the fibrogenic process, plants are important sources of bioactive compounds. *Turnera diffusa* methanol extract (METD) shows "hepatoprotective" activity. Aim: To explore the effect of METD on the expression of fibrotic markers, modulators of extracellular matrix proteins (ECM), underlying mitochondrial mechanisms and epithelial-mesenchymal transition (EMT) in an *in vitro* model of human liver stellar cells (LX-2).

Material and methods: The IC50 of the METD in the LX-2 cells was evaluated by the MTT assay. LX-2 cells were exposed to METD (100-200 ng/mL) with TGF-β (10 ng/mL) at 24, 48 and 72 h. RNA and proteins were extracted, RT-PCR, qPCR and WB were performed, the relative expression of tumor growth factor beta (TGF-β), collagen 1α 1 (COL1α-1), smooth muscle alpha actin (α-SMA), inhibitor of metalloproteinase 1 (TIMP1), metalloproteinase 2 (MMP2), SNAIL1 an EMT marker and mitofusin 2 (MNF2) of mitochondrial function. Endogenous β-actin gene and GAPDH. ANOVA analysis ($p < 0.05$).

Results: The METD has a concentration of 150 ng/mL mantain over 80% viability in LX-2 cells. The presence of METD in cells treated with TGF-β modifies fibrogenic markers, decreasing COL1α-1 and increasing α-SMA RNA expression at all times, but increase the translational expression of α-SMA at 48 and 72 h. We find TIMP1 and MMP2 RNA overexpression, and decreased TIMP1 translational expression was found at all times. It was found Snail1 and MFN2 RNA overexpression, controversially found decreased the translation of MNF2 at all times.

Conclusions: The METD modulates the expression of profibrogenic markers, ECM modulators and some pathways related to EMT and mitochondrial morphology and function, attenuating the expression of profibrogen markers in human LX-2 stellar cells. This work was partially subsidized by PAICYT SA669-18. Registration number of the ethics committee HI11-003.

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Prevalence of spontaneous bacterial peritonitis in patients with hepatic cirrhosis in the military central hospital

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Background and aim: Spontaneous bacterial peritonitis (SBP) is one of the main complications of cirrhotic patients with ascites and is of great importance due to the high mortality rate and even in asymptomatic patients, a high prevalence of SBP has been documented. The objective of the present study was: To calculate the prevalence of SBP in decompensated cirrhotic patients who were hospitalized in the HCM, as well as to identify which is the main agent that appears in the SBP.

Material and methods: A retrospective study was performed in cirrhotic patients with SBP who were hospitalized in the Gastroenterology Section of the Central Military Hospital from the period of January 2017 to January 2018. Patients with CH with data on SBP were included, those patients with HCC were excluded, secondary or cirrhotic peritonitis with tumor-caused peritoneal carcinomatosis.

Results: A review of the records was carried out and there were 134 patients, 68 (50.7%) male, with an average age of 56.42 ± 15.27 years, the etiology of cirrhosis had alcoholic cirrhosis with 80 (40%), autoimmune etiology 72 (36%) patients, CBP 12 (6%), cirrhosis due to NASH 12 (6%), cirrhosis due to HBV 16 (8%) and cirrhosis due to HCV 8 (4%). According to the reports of the cultures and antibiograms, there was a higher frequency of E. Coli 84 (42%) and a lower frequency of S. aureus 15 (8%) (See Table 1). AKI type SHR was diagnosed in 188 (94%) of patients.

Conclusions: The most common etiology found was E. Coli ESBL with sensitivity to carbapenems (Meropenem), so in our hospital, the use of this type of antibiotics should be considered as first-line treatment to avoid progression to RHS and thus decrease the day of hospital stay and recurrence of hospitalization for SBP

Conflicts of interest: The authors have no conflicts of interest to declare.

Ascites fluid culture report and antibiogram	
Enterococcus sp	Ceftriaxona
Escherichia coli BLEE	Meropenem
Klebsiella pneumoniae	Piperacilina-Tazobactam
Staphylococcus aureus	Ceftriaxona

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Comparison of two ROC curve-based methods for determining the cross-point critting frequency in the diagnosis of EHM

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Background and aim: Minimal hepatic encephalopathy (MHE) is characterized by time of reaction, executive function, as well as high disability and mortality. There is an absence of a Gold Standard for its prognosis; the application of psychometric tests combined with neurophysiological tests to identify the presence of MHE is worldwide accepted. Critical flicker frequency (CFF)test is commonly used; however, there exist discrepancies with respect to the determination of the cutoff value.

Material and methods: While analyzing CFF's continuous scale, the application of Logistic Regression Analysis proved to be suitable to define the appropriate cutoff point. A set of 59 patients with hepatic cirrhosis were studied. The ROC curve showed ambiguities in the determination of the cutoff point when using "Youden's index" as well as the closest point on the graph to the upper left

corner point. It was decided to apply Regression Analysis, Algebra, Analytic Geometry and Differential Calculus to determine the cutoff point. MINITAB software was used for computations.

Results: Regression allowed two different ways to reach the same conclusion: CFF's cutoff point is 38.0 Hz to identify patients with MHE. CFF test is a promising tool but to be of help, it needs a valid cutoff point in the scale.

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Impact of liver enzymes on SARSCoV-2 infection and on the severity of clinical disease

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Background and aim: SARSCov-2 infection, currently responsible virus for the pandemic, can have a multi-organic impact, recent studies show that liver injury could be a manifestation of the disease, and liver disease could also be related to a worst prognosis. AIM**:** To compare the characteristics of patients with severe COVID-19 due to SARSCov-2 disease requiring intubation versus stable patients.

Methods. Type of study: Observational, a case-control, nested in a cohort study. Procedure: Complete medical records of patients admitted for COVID-19 at a third level center were reviewed. Clinical and biochemical data were collected and then characteristics between seriously ill patients who required intubation were compared versus stable patients without mechanical ventilation.

Results: We included 166 patients with COVID-19 due to SARSCov-2 infection, 114(68.7%) were men, mean age was 50.6 ± 13.3 years old, 27(16.3%) were assessed as seriously ill patients requiring intubation for SARS. The comparative analysis between those who required intubation versus those who remained without requiring intubation showed significant elevation of ALT, AST, LDH and D-dimer, also older age, see Table.

Conclusions: This is the first study in a Mexican cohort, which demonstrate that

seriously ill patients have significant raises of liver enzymes (AST, ALT) with prognostic implications in the SARSCov-2 disease course.

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Table
which compares characteristics between patients who developed SARS and required intubation, versus those with COVID-19 pneumonia without severity criteria for intubation.

Variable	SARS requiring intubation *n* = 27	COVID-19 pneumonia without severity criteria and without mechanical ventilation *n* = 139	*P* (*<0.01)
Male gender, n(%)	20 (74.1)	94 (67.6)	0.51
Albumin, g/dL	3.27 ± 0.52	3.48 ± 0.50	0.09
ALT, UI/L	225.4 ± 341.2	41.3 ± 41.1	0.003*
AST, UI/L	325.3 ± 382.4	52.8 ± 47.1	0.001*
Alkaline Phosphatase, UI/L	109.1 ± 74.8	96.8 ± 54.4	0.39
GGT, UI/L	205.6 ± 360.4	125.4 ± 163.3	0.35
Age, years-old	58.6 ± 12.7	49.1 ± 12.8	0.001*
Glucose, mg/dL	168.2 ± 95.0	149.8 ± 97.8	0.54
Urea, mg/dL	54.7 ± 37.0	42.1 ± 37.7	0.14
Creatinine, mg/dL	1.1 ± 0.7	0.9 ± 0.7	0.29
Cholesterol, mg/dL	102.9 ± 33.8	123.0 ± 27.0	0.03
Triglycerids, mg/dL	142.4 ± 45.8	145.7 ± 49.4	0.83
Direct Bilirubin, mg/dL	0.8 ± 1.7	0.3 ± 0.3	0.23
Indirect Bilirubin, mg/dL	0.8 ± 1.1	0.5 ± 0.3	0.31
Total proteins, g/dL	6.5 ± 0.7	6.3 ± 1.0	0.60
LDH, UI/L	764.6 ± 401.9	461.0 ± 185.6	0.001*
Sodium, mEq/L	128.8 ± ± 26.8	135.8 ± 3.5	0.38
Potasium, mEq/L	4.2 ± 0.4	4.0 ± 0.5	0.19
Chlorine, mEq/L	102.2 ± 5.04	100.6 ± 4.35	0.25
Calcium, mg/dL	7.8 ± 0.47	8.0 ± 0.44	0.77
Phosphorus, mg/dL	3.2 ± 1.0	3.1 ± 0.8	0.75
Magnesium, mg/dL	2.3 ± 0.3	2.2 ± 0.4	0.27
Leukocytes, cel/mm^3	10.3 ± 5.1	8.7 ± 4.5	0.23
Neutrophils, cel/mm^3	8.9 ± 4.6	7.1 ± 4.2	0.09
Limphocytes, cel/mm^3	1.0 ± 0.4	1.0 ± 0.6	0.99
Hemoglobin, g/dL	14.7 ± 1.7	14.5 ± 2.3	0.82
Red cells Wide Distribution	14.8 ± 1.4	14.2 ± 1.4	0.15
Platelets, cel/mcL	219.7 ± 73.1	226.4 ± 86.2	0.77
Mean Platelet Volume, fL	8.9 ± 0.9	8.4 ± 0.9	0.11
Fibrinógeno, mg/dL	640.7 ± 207.5	608.6 ± 168.9	0.54
D Dimer, ng/mL	7765 ± 9109	1871 ± 4146	0.003*
Reactive C Protein, mg/L	210.3 ± 157.4	142.7 ± 121.2	0.17
Ferritin, ng/mL	782 ± 518	786 ± 1011	0.98
CPK, UI/L	169 ± 188	300 ± 462	0.36
CPK-MB, ng/dL	34 ± 42	25 ± 17	0.29
Troponine I, ng/L	49.4 ± 136.7	26.1 ± 96.3	0.45
Mioglobin, ng/mL	151 ± 151	110 ± 192	0.47
Brain Natriuretic Peptid, pg/mL	56.9 ± 80.5	136.1 ± 342.2	0.49

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Development of the analytical method for the quantification of 3-nitrotirosin and 3-chlorothyrosin in human plasma as potential biomarkers to evaluate minimal liver encephalopathy (MHE)

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Background and aim: Minimal hepatic encephalopathy (MHE) is the earliest form of hepatic encephalopathy (HE) and can affect up to 80% of patients with liver cirrhosis. It is characterized by impaired cognitive function; mainly in the domains of attention, memory, speed of response, surveillance and integrative function. Patients with MHE show reduced performance in selective and which has a negative impact on the patients' health-related quality of life. Currently, there is no gold standard for diagnosis of EHM. Reports Montoluiu et al. evaluated the serum levels of different nitro-oxidative stress metabolites, cyclic guanosine monophosphate (cGMP), nitrites + nitrates and 3-nitrotyrosine (3-NO-Tyr); For each metabolite, its diagnostic precision was evaluated as an indicator of MHE, correlating it with the level of performance in psychometric tests for the diagnosis of HE as a comparison, finding high sensitivity and specificity for 3-nitrotyrosine. Despite the fact that 3-NO-Tyr has been evaluated in EHM, there is a wide variation of results that support its clinical utility, mainly due to the quantification methods used. AIM. To develop an analytical method to quantify the products of nitro-oxidative stress 3-NO-Tyr and 3-chloro-Tyrosine (3-Cl-Tyr) of high sensitivity and specificity to quantify the levels of these metabolites in samples from participating subjects with liver damage and MHE and comparing against the levels of subjects with liver damage without MHE, as well as the baseline level in healthy control subjects.

Material and methods: This study was approved by the Institute's Ethics and Research Committee. An analytical method was developed for the quantification of 3-NO-Tyr as 3-Cl-Tyr by means of triple quadrupole mass spectrometry coupled to an ultra high efficiency liquid chromatography system (UPLC-MS / MS XEVO TqD Waters). The spectrometer was programmed using the molecular transitions of NO-Tyr (227.2> 181.1), Cl-Tyr (216.2> 170.1) and the internal standard (EI) (132.2 > 86.2) for the internal standard respectively. The samples were hydrolyzed prior to processing and analysis to quantify free and protein-derived metabolites.

Results: The method was linear in the range of 0.5 - 2500 nM for both metabolites, it met the validation tests of the analytical methods. The results show that, by means of the developed method, it is possible to perform the simultaneous quantification of free 3-NO-Tyr and Cl-Tyr and protein derivatives, so it can be used to quantify them in samples of MHE, non-MHE and control subjects.

Conclusions: With the developed method, it is possible to accurately and precisely quantify the concentrations of both metabolites in the proposed biological matrix, so if they show differences between study groups, they could be used to determine them in the early diagnosis of MHE.

Financing: Project supported by the SS / IMSS / ISSSTE-CONACYT Fondo sectorial de investigación en salud 1-2017. 289979. Project supported by Program E015 Research and Technological Development in Health of the Instituto de Seguridad y Servicios Sociales de los trabajadores del Estado.

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Experience of Yttrium-90 radioembolization in patients with hepatocellular carcinoma

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Background and aim: Nowadays there are several treatments for hepatocellular carcinoma BCLC B, among them is radioembolization with Itrio-90 (RE-Y90) which is a form of locoregional intra-arterial brachytherapy towards HCC, among its advantages is prolonging the HCC progression time and improve the quality of life of patients. Adverse effects could be extrahepatic (radiation pneumonitis) and intrahepatic (radiation-induced liver disease), among others. Objective of our work is to assess the time free of progression, response to treatment and adverse effects that occur with the administration of RE-Y90.

Material and methods: All HCC BCLC B patients who were candidates for RE-Y90 were analyzed.

Inclusion criteria: cirrhotic patients of any etiology, with a diagnosis of HCC stage B, Child Pugh A and B with 7 points, who had previously undergone a morphological study (CT / MRI) and arteriography to characterize the lesion, to know the irrigation of the tumor and rule out extrahepatic shunts that contraindicate the application of RE-Y90. Subsequently, the procedure was simulated with MAA-Tc99m in order to record its distribution, perform dosimetry, and on the day of RE-Y90, an image study was performed with PET / CT in order to verify the distribution. Exclusion criteria. Patients with liver cirrhosis of any etiology with BCLC Stage B of the Child Pugh B plus 7 points or those with Child Pugh A or B 7 points with extrahepatic shunts. Do not accept this type of therapy. Patients who were not candidates for this therapy were sessioned at the Gastrointestinal and Liver Tumor Meeting to decide their treatment. Response to treatment at 3 and 6 months was analyzed using the mRECIST criteria, progression-free time at 6 months, and adverse effects were recorded.

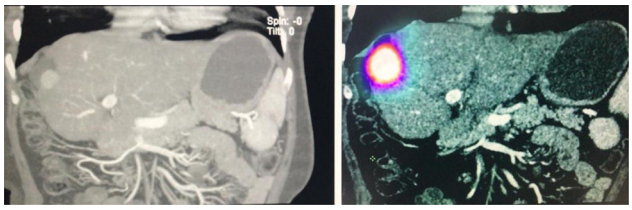
Results: Two patients with HCC BCLC B, a 70-year-old woman with HCC from AIH and a 67-year-old man with HCC of alcohol etiology, both Child Pugh at 6 points, with no data on arterial thrombosis, were performed.

After RE-Y90, there were no complications and the patients were discharged after 24 hours.

Control Computed Axial Tomography was performed with good response, without disease progression at 3 and 6 months, asymptomatic.

Conclusions: RE-Y90 for the treatment of BCLC stage B HCC is a good therapeutic option in well selected patient.

Conflicts of interest: The authors have no conflicts of interest to declare.



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Aspartate aminotransferase as predictor of severity in SARSCoV-2 infection: linear regression model

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Background and aim: Some patients with SARSCov-2 infection develop severe disease (SARS); however, the factors associated with severity are not yet fully understood. Some reports indicate that liver injury may be a poor prognostic factor. AIM**:** To identify the biochemical factors related to the development of SARS with mechanical ventilation (MV) requirement in patients with SARSCov-2 and COVID-19.

Methods. Type of study: Observational. Cohort study. Procedure: Data from COVID-19 patients were collected at admission time to a tertiary care center. Differential factors were identified between seriously ill SARS + MV patients versus stable patients without MV. Transformation to the natural logarithm of significant variables was performed and multiple linear regression was applied, then a predictive model of severity called AAD (*Age-AST-D dimer*) was constructed.

Results: 166 patients were included, 114(68.7%) men, mean age 50.6 ± 13.3 years-old, 27(16.3%) developed SARS + MV. In the comparative analysis between those with SARS + MV versus stable patients without MV we found significant raises of ALT (225.4 ± 341.2 vs. 41.3 ± 41.1; *P* = 0.003), AST 325.3 ± 382.4 vs. 52.8 ± 47.1; *P* = 0.001), LDH (764.6 ± 401.9 vs. 461.0 ± 185.6; *P* = 0.001), D dimer (7765 ± 9109 vs. 1871 ± 4146; *P* = 0.003), age (58.6 ± 12.7 vs. 49.1 ± 12.8; *P* = 0-001). The results of the regression are shown in the Table, where model 3 was the one that best explained the development of SARS + MV; with these variables was constructed the model called AAD, where: [AAD = 3.896 + ln(age)x-0.218 + ln(AST)x-0.185 + ln(DD)x0.070], where a value ≤ 2.75 had sensitivity = 0.797 and 1-specificity = 0.391, AUROC = 0.74 (95%CI: 0.62-0.86; *P* < 0.0001), to predict the risk of developing SARS + MV (OR = 5.8, 95%CI: 2.2-15.4; *P* = 0.001).

Conclusions: Elevation of AST (probable marker of liver damage) is an important predictor of progression to SARS, together with elevation of D-dimer and age early (at admission) and efficiently predict which patients will potentially require MV.

Conflicts of interest: The authors have no conflicts of interest to declare.

Multiple linear regression models predictive of SARS development in patients with COVID-19 and requirement for intubation

Model		Non-standarized Coeficients	Standarized Coeficients		P	95% Confidence Interval for B		Colinearity statistics	
	B	Error Desv.	Beta			Inferior limit	Superior limit	Tolerance	VIF
1	C	2.721	.131		.000	2.462	2.980		
	AST	−.229	.033	−.512	.000	−.293	−.164	1.000	1.000
2	C	3.161	.198		.000	2.770	3.551		
	AST	−.194	.034	−.435	.000	−.261	−.127	.878	1.139
	DD	−.081	.028	−.221	.004	−.135	−.026	.878	1.139
3	C	3.896	.414		.000	3.077	4.714		
	AST	−.185	.034	−.413	.000	−.252	−.118	.860	1.163
	DD	−.070	.028	−.190	.014	−.125	−.014	.844	1.185
	Age	−.218	.108	−.148	.046	−.433	−.004	.915	1.093

AST, aspartate aminotransferase; C, constant; DD, D dimer; VIF, variance inflation factors.

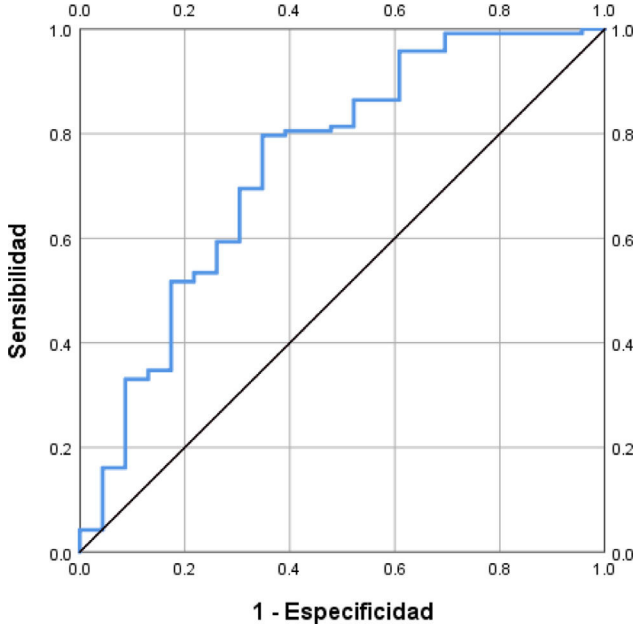
Resume of the model:

R = 0.512, r^2 = 0.262, r^2 adjusted = 0.256, standard error = 0.331.

R = 0.552, r^2 = 0.305, r^2 adjusted = 0.294, standard error = 0.322.

R = 0.570, r^2 = 0.325, r^2 adjusted = 0.310, standard error = 0.318. Durbin-Watson = 1.53.

AAD MODEL TO PREDICT SEVERE FORM (SARS) + INTUBATION



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Classification of alcohol consumption pattern in the Mexican population

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Background and aim: The evaluation of alcohol consumption is estimate by the evaluation of frequency and the concentration of

alcohol ingest. Until now has been accepted the use of several methods to determine the prejudicial and risk consumption. Also, it is possible to evaluate the control and abuse of the ingestion. Nevertheless, the broad spectrum of classification sometimes causes controversy to classify the alcohol consumption in the clinical. Aim: To design a guide to classify the pattern of alcohol consumption using social, clinical and biochemical information from a Mexican population.

Material and methods: Observational study. The subjects were classified according to alcohol consumption, using AUDIT test (Alcohol Use Disorders Identification Test), and the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). The pattern of consumption was determined via the amount of alcohol in grams of alcohol per day and its equivalent in cups, frequency, as well as type of alcohol. Finally, the evaluation of liver damage considers the clinical and biochemical data referred in consultation. Protocol approved by the General Hospital of Mexico (HG/DI/16/107/03/082) and UNAM (FMD/DI /15/2019).

Results: Table. Classification of according to the pattern of alcohol consumption.

Conclusions: The pattern of alcohol consumption guide is a quick tool for the identification of prejudicial ingest of alcohol without evidence of any disease, this provides a first line to the proper diagnosis and management of patients with alcohol consumption and their future prognosis and treatment of liver alcohol diseases, which is prevalent in our country.

Conflict of interests: This work has been partially funded by CONACYT: SALUD-2016-272579 and none of the authors has a conflict of interest.

	CONTROL	RISK	ABUSE	ALCOHOLISM	ALCOHOL LIVER DISEASE CIRRHOSIS BY ALCOHOL
AUDIT DSM-IV	<8 Without abuse and dependence criteria	>8 Without abuse and dependence criteria	>8 With abuse criteria but not alcohol dependence (1 positive answer)	>8 With criteria of alcohol dependence (3 or more positive answers)	>8 With criteria of alcohol dependence (3 or more positive answers)
FRECUENCY	Occasionally	Consuetudinary Weekend	Consuetudinary Weekend 1 to 4 times per week	Daily, almost daily or Consuetudinary	Daily or almost daily
AMOUNT	1 cup <10 g	2-4♂ y 1-3♀ cups 40-60g y 20-40g	≥4-5♂ y ≥3-4♀ Cups +60g y +40g	≥5♂ y ≥4 ♀ cups per 5 years +70g y +50g	≥5♂ y ≥4 ♀ cups per 5 years +70g y +50g
MAIN TYPE OF ALCOHOL		Ferment	Ferment, and distilled	Ferment, and distilled	Ferment, distilled, 96° alcohol
LIVER DAMAGE	Without evidence of clinical and biochemical liver damage	Without evidence of clinical and biochemical liver damage	Without evidence of clinical and biochemical liver damage	Without evidence of clinical and biochemical of liver damage	Clinical evidence: (Anorexia, weight loss, asthenia, adynamia, hepatojugular reflux) and positive for biochemical changes typical of liver cirrhosis

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Cell death in patients with different alcohol consumption and alcoholic liver disease

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Background and aim: Cell death maintains homeostasis and eliminates damaged cells. The role of this cellular process in alcohol consumption and in pathogenesis of alcoholic liver disease (ALD) has not been fully established. Objective: Characterize the cell death of T-CD4, T-CD8, NK and NKT lymphocytes in peripheral blood of patients with different patterns of alcohol consumption and ALD.

Material and methods: Cross-sectional study. Control subjects with alcohol consumption <10 g/day (CT); risk alcohol consumption (AUDIT > 8) (R); alcohol abuse (A); alcoholism without clinical or biochemical stigmas of liver damage (OH); cirrhosis by alcohol (CiOH) and alcoholic hepatitis (AH). Determination of T-CD4, T-CD8, NK and NKT was performed in peripheral mononuclear fraction. The expression of Fas receptor and ligand (Fas R, Fas L), active caspase 3, early and late apoptosis, necrosis, and cell viability was evaluated by flow cytometry. Statistical analysis: Kruskall-Wallis and U-Mann Whitney, ($p < 0.05$). Protocol approved by the General Hospital of Mexico (HG/DI/16/107/03/082) and UNAM (FMD/DI /15/2019)

Results: 48 participants were included, 14CT, 5R, 5A, 7OH, 6 CiOH y 11AH; the average age was 29 ± 9, 29 ± 10, 26 ± 4, 32 ± 6, 52 ± 11 and 40 ± 10 ($p < 0.05$), respectively. Alcohol consumption per day was higher in ALD groups (292 ± 150, 336 ± 180) ($p < 0.05$). Determination of lymphocyte showed that T-CD8 + cells decrease in AH vs CT (12 ± 1.4 vs $19 \pm 2.3\%$) ($p < 0.04$), while the expression of Fas R, Active Caspase increased. Whereas early Apoptosis and Necrosis increases in AH ($p < 0.02$, $p < 0.01$; $p < 0.02$, $p < 0.01$). The percentage of NK and NKT cells as well as the expression of Fas R and active Caspase 3 increased in HA vs CT ($p < 0.03$, $p < 0.04$; $p < 0.01$, $p < 0.02$).

Conclusions: The results show that according to consumption pattern, expressions of the cell death markers were not high in risk consumption, abuse and alcoholism because these events are still subclinical. While in patients with ALD, T-CD8, NK and NKT cells express a higher percentage of death markers, especially in the alcoholic hepatitis due to the elimination of damaged cells.

Conflict of interests: The authors have no conflicts of interest to declare. This work was partially financed by CONACyT SALUD-2016-272579 and PAPIIT- UNAM TA200515.

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Evaluation of TLR-4 in peripheral M1 monocytes and IL-6 and CXCL-8 in alcoholic liver disease

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Background and aim: Intestinal permeability increases in alcoholics allowing the passage of lipopolysaccharide (LPS) to liver, promoting TLR-4 activation in Kupffer cells and the production of pro-inflammatory cytokines. At the present, the modulation of LPS in alcoholics at systemic level, is not fully understood. Aim. To evaluate TLR-4 in M1 monocytes and the production of IL-6 and CXCL-8 in alcoholic liver disease.

Material and methods: Cross-sectional study, that include Alcoholic patients (according WHO) from the Liver clinic of the General Hospital of Mexico were included. They were classified by absence (OH) or presence (CiOH) of liver damage and patients with active alcoholic hepatitis (HOH). Control group (CT): AUDIT <8 and intake of <10gOH / day. Blood samples were taken on one occasion (10 ml) to obtain mononuclear cells by density gradient. To which cell marking was performed by flow cytometry (M1 and TLR-4) and in serum was performed the determination of cytokines (IL-6 and CXCL-8) by arrangement in multiple suspension. Mann Whitney U statistical analysis. All patients signed informed consent. Protocol approved by the General Hospital of Mexico (HG/DI/16/107/03/082) and UNAM (FMD/DI/15/2019).

Results: 24 CT, 12 OH, 10 CiOH and 10 HOH were included. The percentage of Monocytes was: CT = 8%, OH = 19%, CiOH = 22% and HOH = 35% (OHvsCT $p = 0.003$, CiOHvsCT $p = 0.05$, HOHvsCT $p < 0.0019$). The significant differences in M1 monocytes were found in CiOHvsCT $p = 0.05$, HOHvsCT $p = 0.019$, CiOHvsOH$p = 0.009$ and HOHvsOH $p = 0.01$. Interestingly, TLR4 expression showed differences in OHvsCT $p = 0.002$, CiOHvsCT $p = 0.007$ and HOHvsCT $p < 0.001$. On the other hand, the concentration of IL-6 and IL-8 (pg/mL) presented significant differences according with liver damage (CiOHvsCT $p < 0.05$, HOHvsCT $p < 0.001$, OHvs.HOH $p = 0.001$ and CiOHvsHOH $p = 0.01$).

Conclusions: Alcohol has an effect at a systemic level promoting the increase of monocytes/M1 and the expression of TLR-4, supporting the fact that the receptor is activated in the periphery, being higher in patients with active Alcoholic Hepatitis, favoring a state of continuous inflammation and promoting susceptibility to infections and mortality.

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Conflicts of interest: The authors have no conflicts of interest to declare.

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Evaluation of IL-1RA, IL-1β IFN-γ and CXCL-10 as mediators of damage and hepatic repair in chronic hepatitis and fibrosis progresion

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Background and aim: During chronic Hepatitis C (CHC) is generates persistent inflammation that can progress to fibrosis. IL-1β is responsible for the initiation of inflammation, the action of IL-1β, its activity is regulated by IL-1RA which has also been implicated in the liver in cell proliferation. IFN-γ is the main initiating agents of the antiviral response, additionally promotes the production of CXCL-10 / IP-10 activating the chemotaxis of lymphocytes and NK cells. Objective. To evaluate the serum levels IL-1β, IL-1RA, IFN-γ and CXCL-10 in patients with CHC and its association with liver fibrosis.

Material and methods: A cross-sectional study, patients with CHC without comorbidities with grade of fibrosis for Fibroscan/Fibrotest and control group (CT) were included. Subjects CT with negative viral panel and without signs of liver disease. The quantification of IL-1β, IL-1RA, IFN-γ and CXCL-10 molecules in serum the multiple suspension method. Statistical analysis was performed using Mann-Whitney U test, $p < 0.05$ was considered significant. All patients signed informed consent. Protocol approved by the General Hospital of Mexico (HG/ DI/16/107/03/082) and UNAM (FMD/DI/15/2019).

Results: CHC (107) and CT (192) subjects were include. The concentration (pg/mL) of IL-1β was 7 ± 2 for CHC and 3 ± 0.1 for CT ($p = 0.048$), of IL-1RA was 44 ± 11 for CHC and 50 ± 13 for CT ($p = 0.734$). The serum levels of IFN-γ 9 ± 4 for CHC, and for CT 11 ± 3 ($p = 0.002$). In the case of CXCL-10, 938 ± 92 for of CHC and 361 ± 21 for the CT ($p < 0.001$). Comparing by grade of fibrosis for IL-1β, no significant difference was found. IL-1RA showed differences in F1vsF4 and F3vsF4. The IFN-γ in F1vsF4 and F2vsF4. Finally, CXCL-10, presented significance only in F1vsF4.

Conclusions: Higher levels of IL-1β and CXCL10 were found in HCc, as part of the active inflammatory response. Whereas in the comparison of fibrosis stages: IFN-γ and CXCL-10 showed participation in early stages. On the other hand, IL-1β does not display changes, however, their antagonist IL-1RA increases in F4 suggesting their participation in liver regeneration.

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Effect of pangenotype treatment on chronic hepatitis C. Real life studio

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Background and aim: Hepatitis C is the main cause of transplantation in the United States (USA) and worldwide, in Mexico it has a prevalence of 0.3-0.5% and represents one of the main causes of liver cirrhosis and alcohol consumption. Treatment has change with the arrival of direct-acting antivirals (DAAs), in particular with pangenotype schemes, reporting sustained viral response (SVR)> 95%. SVR reduces mortality from all causes, the need for liver transplantation, death related to cirrhosis and its complications. Aim: To determine the effect of pangenotype treatment with Glecaprevir / Pibrentasvir in patients with chronic hepatitis C.

Material and methods: Cross-sectional, retrolective, analytical and comparative study. All older subjects diagnosed with chronic hepatitis C, who received glecaprevir-pibrentasvir treatment and who had a viral load result at the end of treatment and APRI and baseline FIB-4 and post-treatment were included. Descriptive statistics and group comparisons were performed with t-Student, to show differences the Wilcoxon test. The project was submitted for approval by the institutional ethics committee.

Results: We analyzed 50 patients, 33 (66%) women, genotype 1b was the most frequent (36%), 41 patients received treatment for 8 weeks (82%), the mean age was 56 ± 13.78 and the median mass index body 26 (23-30). 18% (9) had diabetes mellitus, 2 (4%) patients with chronic kidney disease on hemodialysis. 16% (8) had cirrhosis. SVR 12 was 98%. A significant difference of $p < 0.05$ was shown in the fibrosis markers APRI and FIB-4 when comparing baseline and post-treatment. There were no adverse effects that caused the suspension of the treatment.

Conclusions: Pangenotype treatment with glecaprevir-pibrentasvir is effective in achieving SVR 12 in 98% and improves fibrosis parameters measured with biomarkers as has been shown in previous studies.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Experience in treatment with direct action antivirals in patients with HCV-HIV coinfection

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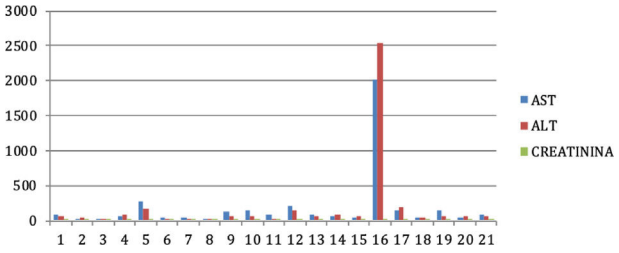
Background and aim: Near 25% of people infected with Human Immunodeficiency Virus (HIV) are also carriers of the Hepatitis C Virus (HCV). Hepatitis C virus infections are generally asymptomatic, and because HIV-infected individuals have a decreased immune response, these infections can escape immune control and lead to chronic asymptomatic disease. The use of direct-acting antivirals (DAAs) decreases the inflammation and liver fibrosis in this group of patients. Aim: To describe the characteristics of patients coinfected with HIV with HCV and analyze the changes in liver inflammation assessed by aminotransferases and liver fibrosis measured by transitional elastography.

Material and methods: Cross-sectional, retrolective, analytical and comparative study. We included elderly subjects with a diagnosis of chronic HCV infection coinfected with HIV, treated with DAAs and who had a viral load result 12 weeks after treatment, aminotransferases and basal transition and post-treatment elastography. Descriptive statistics and group comparison were performed with the Student's t test, and the Wilcoxon test was shown to show differences.

Results: 21 male subjects were analyzed, the mean age was 44 ± 12.3 and 66% (14) were genotype 1 and 34% (7) genotype 4. The median AST 77 (42-1459) and ALT was 64 (35-87). The median fibrosis by transitional elastography was 6.5 (4.1-12.3). 100% percent of the participants received sofosbuvir and ledipasvir. The SVR was 95% in the analyzed group. The decrease in fibrosis measured by elastography before and after treatment was not statistically significant. There is a decrease in aminotransferases after treatment with AAD (Table 1).

Table 1
Baseline Values of Aminotransferases and Creatinine in HCV-HIV Co-infected Patients.



Conclusions: Treatment with ADD in patients coinfected with HIV and HCV has SVR rates similar to those described in monoinfected patients (95% in our group) and decreases inflammation and fibrosis as measured by transitional elastography.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Hepatic and gastrointestinal manifestations of SARS-COV-2 infection (COVID-19)

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Background and aim: Abnormal liver function tests (LFTs) and gastrointestinal (GI) symptoms have been reported up to 50% in patients with COVID-19, and in 5% they can precede respiratory symptoms. The objective of this work is to describe the LFTs and GI symptoms of patients with COVID-19 and their association with admission to the intensive care unit (ICU) and mortality.

Material and Methods: We conducted a retrospective, cross sectional, descriptive study, using files from patients with a positive Gen Finder COVID-19 test, admitted to Medica Sur Clinic and Foundation between March 13th through May 14th, 2020. We performed descriptive analysis of data and its association with clinical outcomes.

Results: A total of 108 patients with COVID-19 were identified; 68.5% ($n=74$) were men, the mean age was 53 ± 14 years and the body mass index was 28.6 ± 5.8 kg/m^2. The most frequent comorbidity was hypertension with 24% ($n=26$). The presence of comorbidities was associated with risk of ICU admission (OR 3.9 [95% CI 1.6-9.9], $p=0.002$). The most frequent symptoms were cough (72.2%, $n=78$), fever (69.4%, $n=75$) and dyspnea (48.1%, $n=52$). At least one abnormal LFT was present in 94% ($n=103$) of patients at admission, the most frequent was LDH (88.9%, $n=96$), AST and GGT (63%, $n=65$), which are summarized in Table 1. Patients presented abnormal LFTs and respiratory symptoms in 48.1% ($n=52$), while 16.6% ($n=18$) presented abnormal LFTs without respiratory symptoms. Among GI symptoms, 37% ($n=4$) reported at least one, including diarrhea (28.7%, $n=31$), hyporexia (9.3%, $n=10$), nausea (8.3%, $n=9$) or vomiting (4.6%, $n=5$). Of patients admitted to the ICU ($n=39$), 27.5% ($n=10$) presented at least one GI symptom. Mortality was 7.4% ($n=8$). No associations were found between abnormal LFTs, GI symptoms, and outcomes of mortality and ICU admission.

Table 1
Initial liver function tests of patients with COVID-19 ($n=108$).

Parámetro	M [IQR]
Hemoglobin (g/dL)	14.6 [13.7-15.7]
Platelets (cells $\times 10^3$/L)	110.5 [100-136.6]
Albumin (g/dL)	3.2 [2.8 -3.5]
Total bilirrubin (mg/dL)	0.94 [0.67-1.01]
Direct bilirrubin (mg/dL)	0.23 [0.16-0.24]
Alanine aminotransferase (IU/L)	42 [28-52.7]
Aspartate aminotransferase (IU/L)	52.1 [33-55]
Alkaline phosphatase (IU/L)	72.5 [55-75.7]
Gamma-glutamyl transpeptidase (IU/L)	73 [34-77]
Lactate dehydrogenase (IU/L)	303 [222-360]

Conclusions: In patients with COVID 19, the presence of metabolic comorbidities confers a higher risk of ICU admission, in contrast to abnormal LFTs and GI symptoms that were not associated with clinical outcomes.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Effect of chronic alcohol intake in a pre-clinical model with cholesterol overload

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Background and aim: Obesity and alcohol consumption are two of the main risk factors in liver diseases, which coexist frequently and are considered to accelerate the progression of liver damage, from simple steatosis to steatohepatitis, cirrhosis and cancer. The Mexican diet is high in cholesterol, in addition to being frequently found elevated in patients and animal models with obesity. Therefore, our goal is to determine the effect of alcohol intake in an environment with cholesterol overload.

Material and methods: Male and female mice of the C57BL / 6J strain 8-10 weeks old were used. The NIAAA model was used, which consists of consuming a Lieber-DeCarli diet added with ethanol (5% v / v final concentration) for 10 days, followed by acute dose intragastric (5 g / kg) of ethanol. Cholesterol overload was induced by adding cholesterol (1.25 w / v) to the liquid diet. Liver damage was assessed using liver function tests. Biochemical tests were carried out to determine the degree of apoptosis and the amount of cholesterol in the different experimental groups.

Results: The alcoholic diet added with cholesterol exacerbates liver damage and causes premature death of males. Also, the enzymatic activity of ALT and AST were increased, both in males and in females groups. Liver caspase 3 activity, indicative of apoptosis, was also found increased with respect to the other groups. At the macroscopic level, a liver with higher steatosis was observed in the group treated with alcohol and cholesterol, data that was corroborated by H&E in histological sections with a 5.15-fold increase in the total cholesterol content in the liver compared to the control group. Females had higher liver cholesterol content than males (18.66 μg cholesterol / mg protein vs. 15.6 μg cholesterol / mg protein), however, the activity of transaminases were similar in both genders.

Conclusions: The data obtained suggests that liver cholesterol overload increases susceptibility to alcohol damage. An increase in cell death was observed in this group, as well as in liver damage tests. Further studies are required to determine the mechanism by which greater damage is caused in the presence of both agents.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Acute liver injury and survival in patients with SARS-Cov-2 from the Hospital Central Militar

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Background and aim: Recent studies on SARS-CoV-2 have shown that the incidence of liver injury varies between 14.8% and 53%, mainly demonstrable by abnormal ALT / AST levels accompanied by slightly elevated bilirubin levels. Reports of autopsies around the word of patients that death from COVID-19 shows severe liver damage ranging from 58.06% to 78% of the cases.

There is evidence that the elevation of transaminases (ALT / AST) translates into a more serious clinical profile. Besides, the elevation of AST is related with a high risk of mortality, so it must be monitored during hospitalization. Thus, it is important to know the behavior of liver injury and mortality in our population. Aim: To determine transaminase levels in patients with SARS-Cov-2 and its relationship with mortality.

Methods: All the patients admitted with a positive SARS-Cov-2 PCR test were analyzed, the mean and standard deviation of AST, ALT, and other variables of the liver biochemistry, hemoglobin, leukocyte, fibrinogen, and TP were obtained. A Kapplan Meier curve was made for survival to compare patients with and without transaminases elevation.

Results: We studied a total of 92 patients: 79 (86%) were male, age 56.62 ± 13.70 years, weight 72.5 ± 14.30 kg, height 1.63 ± 0.10

m, BMI 27.09 ± 5.04 kg / m2. Of the 92 patients, 68 (73%) had an elevation of transaminases at admission.

Patient's whit elevation of transaminases (68): 63 (93%) were males, the mean values at admission of AST and ALT were 74.91 ± 5.83 and 72.75 ± 5.74, respectively. The average hospital stay was 6.1 ± 4.1 days in de group with no elevation of transaminases and 7.25 ± 5.3 days for the group with elevation. Other variables of liver biochemistry, hemoglobin, leukocyte, fibrinogen, and TP are presented in Table 1. The data referring to the probability

Table 1
Variables determined in the total of SARS-Cov-2 positive patients.

Variable	Media	DE	Variable	Media	DE	Variable	Media	DE
AST (U/L)	74.91	5.83	PCR	141.18	113.66	Bilirrubina directa	0.25	0.09
ALT (U/L)	72.75	5.74	Deshidrogenasa láctica	447.59	175.81	Bilirrubina indirecta	0.43	0.24
Leucocitos	9324	4.91	Albúmina (g/dl)	3.42	0.631	Fibrinógeno	699.26	153.36
Hemoglobina (g/dl)	14.12	2.14	ALP (U/L)	90.72	35.09	TP (seg)	14.95	2.16
Plaquetas	207250	797006	Bilirrubina total	0.96	1.29			

of requiring ICU income. And probability of requiring mechanical ventilation are presented in Table 2.

Table 2
Risk of admission to the ICU. And the risk of requiring mechanical ventilation in patients with elevated transaminases.

Patients with transaminases elevation	Marginal odds	Conditional odds	Bayes Factor
ICU admission	0.04	0.15	3.81
Mechanic ventilation	0.14	0.28	2.02

The group without and with elevated transaminases were compared to observe if elevation of transaminases could influence mortality, obtaining a non-statistically significant p. ($x2 = 0.087$, $p = 0.782$).

Conclusions: In the studied population, the predominant gender was male, the population with elevated transaminases had a 3.82 risk of entering the ICU and 2.02 times more of requiring mechanical ventilation. The elevation of transaminases does not influence survival. The analysis of the entire database will have to be done, since this is a preliminary study (Fig. 1).

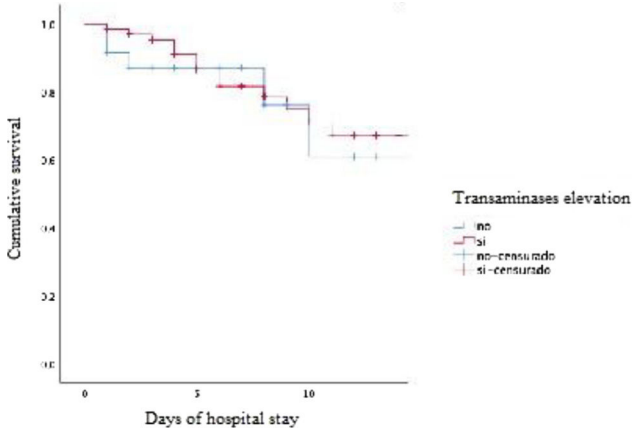

Figure 1. Kaplan Meier curve. The group of patients with and without transaminase elevation is displayed. Elevation of transaminases does not influence in survival.

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Evaluation of cyclooxigenase inhibitors in hepatic isquemia-reperfusion injury in Wistar rats

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Background and aim: Ischemia-reperfusion (IR) is one of the main causes of liver graft rejection, therefore the search for new alternatives that reduce this damage continues. Inhibition of the enzyme cyclooxygenase (COX) has been reported to contribute to modulation of IR injury in various organs such as the stomach, brain, lung, heart, and liver. The aim for this work was to determine if the administration of COX inhibitors, acemetacin (ACE) and mefenamic acid (AMF) have a hepatoprotective effect in Wistar rats.

Material and methods: Female Wistar rats were used (200-300 g) and divided into 4 groups ($n = 6$): Sham (laparotomy), IR (20 min of ischemia, 60 min of reperfusion), AMF+IR y ACE+IR (both at a dose of 10 mg / kg for 5 days with subsequent IR). Serum levels of ALT, AST, LDH were determined. Expression of IL-1β, GPx, MPO, SOD-1 and NF-κβ genes was evaluated in total liver tissue RNA using qPCR ($\Delta\Delta Ct$). Cytokines IL-6, IL-1β and TNF-α were evaluated in tissue homogenate using ELISA and oxidative stress markers SOD, GPx and MDA by spectrophotometry. The procedures were performed in accordance with NOM-062-ZOO-1999 and approval of the ethics committee (HI19-00002).

Results: A decrease in ALT and LDH biochemical markers was observed in the AMF + IR group, while in ACE + IR the levels of ALT, AST, LDH were significantly reduced in addition to the relative expression of NF-κβ and GPx, however, the relative expression of IL-1β and the lipid peroxidation marker MDA were significantly increased. No significant difference was observed in the rest of the evaluated markers (Figure).

Conclusions: A hepatoprotective effect of ACE and AMF on IR damage was demonstrated when a decrease in markers of liver damage was observed.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Evaluation of atherosclerotic risk in patients with chronic hepatitis C infection

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Background and aim: Chronic hepatitis C virus infection (HCV) is an independent risk factor for atherosclerosis and is associated with the development of cardiac and cerebrovascular events. Among the mechanisms are the production of proinflammatory

cytokines, endothelial dysfunction and increased oxidative stress. The effect of sustained virologic response with direct-acting antiviral agents (DAA) on the progression of atherosclerotic disease has had little study.

Objective: Analyze atherosclerotic risk in patients with chronic hepatitis C infection treated with DAA.

Material and methods: Observational, prospective, analytical, comparative study. Adult subjects with a diagnosis of chronic hepatitis C, without coinfections, cardiovascular diseases, type 2 diabetes, or kidney failure and who signed an informed consent letter. We measured body mass index (BMI), blood cell count, lipid profile, liver function tests, glucose, glycated hemoglobin, uric acid, fibrinogen, C-reactive protein (CRP). Carotid doppler ultrasound to measure carotid media-intima thickness (CIMT).

The two proportions formula was used, descriptive statistics and group comparison with t-Student, dichotomous variables with X^2 and to show differences the Wilcoxon tests. Project with the approval of the institutional ethics committee.

Results: We analyzed 24 participants 19 (79%) women, the mean age 60 ± 11.4, genotype 1b was the most frequent (41.7%), 9 (37.5%) participants had cirrhosis and 4 of them were Child-Pugh B; mean BMI 28 ± 5.07, 6 participants (25%) were obese and 10 (41.7%) had a smoking history.

The analysis of inflammation markers showed a significant decrease in CRP $p < 0.05$. Pretreatment 19 participants (79.2%) had CIMT < 9 mm and 5 (20.8%) had CIMT $\geq$9 mm and posttreatment 22 (91.2%) CIMT <9 mm and 2 (8.3%) CIMT $\geq$9 mm, that is, there were fewer participants with risk CIMT after treatment (Figures 1 and 2).

Conclusions: Treatment with DAA decreases CIMT and improves inflammation markers such as CRP. However, it is necessary to increase the sample size to define whether there is a decrease in cardiovascular risk.

Conflicts of interest: The authors have no conflicts of interest to declare.

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