



## Abstracts Asociación Mexicana de Hepatología (AMH) 2023

### Bouveret syndrome, a rare clinical presentation of abdominal pain in a patient with diabetic ketoacidosis: A case report.

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**Introduction and Objectives:** To present a 70-year-old female with type 2 diabetes and a history of multiple episodes of cholecystitis within Bouveret's Syndrome.

**Materials and Patients:** 70-year-old female with type 2 diabetes and a history of multiple episodes of cholecystitis refusing surgical treatment. She was admitted to the emergency department due to a clinical picture of 10 days of evolution characterized by severe abdominal pain localized in the right hypochondrium that was exacerbated after food intake. Symptoms included nausea, vomiting and malaise. Physical examination revealed a Glasgow score of 15 points, cardiopulmonary normal, abdomen tenderness on palpation, increased peristaltic sounds, and negative Murphy and Blumberg signs with no evidence of peritoneal irritation. Rest normal. Leukocytes 17.1, neutrophils 15.4, hemoglobin 12.3, platelets 45,000, glucose 614, BUN 54, urea 117, creatinine 3.3, AST 82, ALT 52, LDH 264, alkaline phosphatase 155, total bilirubin 0.56, albumin 1.9, gamma glutamyl transpeptidase 99, serum electrolytes normal. Urine tests with ketones and arterial blood gases with metabolic acidosis. Management for diabetic ketoacidosis was started with poor clinical progression and, worsening of abdominal pain and absence of bowel movements. Abdominal ultrasound showed a hepatic image in segment IVa with defined borders; it measured 47 × 38 millimeters, suggestive of a biloma. The gallbladder had heterogeneous content with multiple stones and acute lithiasic cholecystitis. The CT identified a stone in the first and second portions of the duodenum, biliary ileus and a cholecystoduodenal fistula.

**Results:** Bouveret syndrome was diagnosed by performing a duodenoscopy in which a fistulous orifice with bile outlet was observed, posteriorly removing the stone with no complications during the procedure. Image-guided drainage of the biloma was performed with a multipurpose catheter placement with total resolution. Diabetic ketoacidosis was treated under usual

measures, observing a general and important improvement in the patient.

**Conclusions:** Bouveret syndrome is a rare clinical entity and its simultaneous appearance with an acute episode of diabetic ketoacidosis is rarely described in the literature. Only 6% of patients with cholecystoenteric fistulas develop a clinical picture of intestinal obstruction, with duodenal obstruction being the less frequent (<5%).

#### Ethical statement

The patient's identity was protected. Consentment was obtained directly from the patient.

#### Declaration of interests

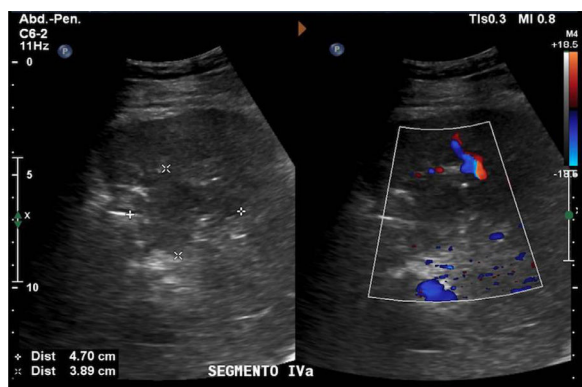
None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



**Figure 1.** CT scan identified a stone between the first and second portion of the duodenum, gallstone ileus and cholecystoduodenal fistula.



**Figure 2.** Abdominal ultrasound identified an image in hepatic segment IVa with defined borders which measured  $47 \times 38$  mm with the appearance of a biloma. Gallbladder with heterogeneous content due to multiple stones and data suggestive of acute lithiasic cholecystitis.

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### Hepatocellular carcinoma and upper gastrointestinal bleeding

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**Introduction and Objectives:** Hepatocellular carcinoma represents the most frequent malignant tumor of the liver, being the 5th most frequent cancer in men and the 7th in women worldwide; it is the 3rd cause of death from cancer in the world. To present a case of hepatocellular carcinoma presenting with gastrointestinal bleeding.

**Materials and Patients:** A 39-year-old female began her condition two days ago with the presence of hematemesis, accompanied by nausea, asthenia, and adynamia. On examination, icteric conjunctivae, globose abdomen, with the presence of abdominal distension, grade I ascites. Edema in the lower limbs +. Liver ultrasound with liver nodular lesions, chronic lithiasic cholecystitis, and free fluid in the abdominopelvic cavity. A simple and contrasted CT scan of the abdomen is requested with the presence of tumor activity at the level of the liver, portal thrombosis, free fluid in the abdominal cavity, and marginal T12-L1 osteocytes.

**Results:** We proceeded to perform sclerotherapy of esophageal varices and ligatures. Later, alpha-fetoprotein was requested, which reports 3680 ng/ml. The diagnosis of hepatocarcinoma was established and he was referred to the oncology service.

**Conclusions:** The best results are obtained with multidisciplinary teams for the diagnosis and treatment of this disease.

### Ethical statement

The patient's identity was protected. Consentment was obtained directly from the patient.

### Declaration of interests

None

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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### Frailty and diet quality index in patients with chronic HCV infection with and without cirrhosis. Preliminary report

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**Introduction and Objectives:** It is estimated that 71 million people live with chronic hepatitis C viral infection (HCV). Part of the comorbidities associated with cirrhosis is frailty. Remarkably, diet is highly important in the management of cirrhosis and liver diseases. Therefore, it is necessary to evaluate the quality of the diet in this population. In this context, we evaluated the frailty and quality of the diet in patients with chronic HCV infection with or without cirrhosis, as well as the association between demographic, clinical, and anthropometric variables.

**Materials and Patients:** A cross-sectional study was conducted in the hepatitis clinic of the Civil Hospital of Guadalajara Fray Antonio Alcalde. Each participant was required to complete the Liver Frailty index (LFI) which include hand grip strength, chair stand test and balance test. Additionally, the mini survey was applied to evaluate the quality of food consumption (Mini-ECCA v.2). This questionnaire includes 14 questions, each with 3 or 4 response options on a Likert scale. The outcome yields three classifications: "healthy food intake, habit to be improved, and unhealthy food intake." Finally, upper arm anthropometry was performed.  $P < 0.05$  was considered statistically significant.

**Results:** A preliminary sample of 20 patients was assessed. Of them, 60% ( $n=12$ ) had only chronic HCV infection, 85% ( $n=17$ ) of LFI were considered pre-frail, while the rest of the participants were classified as frail. The quality of the diet, 65% ( $n=13$ ), was considered "a habit to be improved." A relationship was found between the quality of the diet and LFI. Likewise, a negative correlation was also found between the mean arm muscle circumference (MAMC) and the LFI score ( $r=-0.577$ ;  $p=0.008$ ) as well as MAMC and time in chair supports ( $r=-0.504$ ;  $p=0.023$ ). In addition, we found a positive correlation between the MAMC and hand grip strength ( $r=-0.624$ ;  $p=0.003$ ).

**Conclusions:** Some degree of frailty was found in the participants, and the quality of the diet was found to be "a habit to be improved" in most of the population sample.

### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

### Declaration of interests

None

### Funding

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**Hepatic Steatosis Index (HSI): A Valuable Biomarker in Subjects with Metabolic Dysfunction-associated Fatty Liver Disease (MAFLD)**

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**Introduction and Objectives:** Metabolic Dysfunction-associated Fatty Liver Disease (MAFLD) has been recognized as the hepatic component of metabolic syndrome and has become a growing public health concern. Early and accurate detection of MAFLD is crucial for implementing appropriate intervention strategies and preventing progression to serious complications such as liver cirrhosis. We aimed to describe the diagnostic performance of the Hepatic Steatosis Index (HSI) in subjects with MAFLD and compare it with the Homeostatic Model Assessment of Insulin Resistance (HOMA), Waist-to-Hip Ratio (WHR), and Visceral Fat (SECA).

**Materials and Methods:** Retrospective design study. Bioanthropometric, clinical, and biochemical variables were collected. The HSI was calculated using the formula  $HSI = 8 \times ALT/AST + BMI + 2$  (if diabetic) + 2 (if female). ROC curves and their areas were generated. Statistical significance was determined at  $p < 0.05$ .

**Results:** A total of 585 subjects were evaluated, of whom 279 were classified with MAFLD (65.5% females) and 306 without MAFLD (76.8% females). Subjects with MAFLD exhibited higher values of age, BMI, WHR, HOMA, CAP, and HSI (Table 1). The HSI showed a diagnostic performance with an area under the curve (AUC) of 0.80. A cutoff point of 39.9 was established for the HSI, with a sensitivity of 63%, specificity of 74%, positive predictive value (PPV) of 73%, and negative predictive value (NPV) of 64%. The HSI demonstrated superior diagnostic performance compared to visceral fat (0.70), HOMA (0.70), and WHR (0.66) (Fig 1).

**Conclusions:** The results of this study demonstrate that HOMA, visceral fat, and ICC can be useful as screening strategies in MAFLD. However, the Hepatic Steatosis Index (HSI) showed superior diagnostic performance compared to the other evaluated biomarkers. Therefore, it is suggested that HSI be considered a useful diagnostic tool in MAFLD.

**Ethical statement**

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

**Declaration of interests**

None

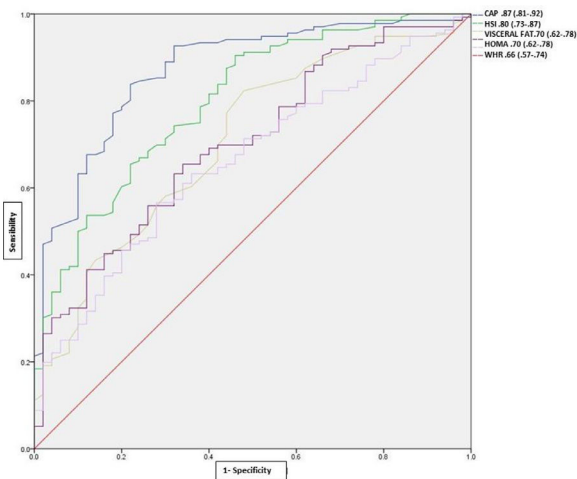
**Funding**

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**Table 1**

Comparison of variables in subjects with MAFLD and without MAFLD. Numerical variables are expressed as medians and interquartile ranges, and categorical variables with frequency and percentage. Student's t-test or Wilcoxon test was used for the difference of means as appropriate. Categorical variables were compared using Chi-square test. HOMA, Homeostasis Model Assessment of Insulin Resistance; WHR, Waist-Hip Ratio Index; MAFLD, Metabolic Associated Fatty Liver Disease.

| Variable                | MAFLD (n=279)    | Non MAFLD n=306  | P-value |
|-------------------------|------------------|------------------|---------|
| AGE                     | 51 (41.7-59)     | 47 (35-57)       | <.0001  |
| Gender                  |                  |                  | .002    |
| -Male                   | 96 (34.5%)       | 71 (23.2%)       |         |
| -Female                 | 183 (65.5%)      | 235 (76.8%)      |         |
| BMI                     | 31.8 (28.9-35.3) | 26.2 (23.9-30.6) | <.0001  |
| Visceral Fat (SECA)     | 3.4 (2.7-4.5)    | 2.5 (2-3.2)      | <.0001  |
| WHR                     | .93 (.86-.98)    | .86 (.81-.92)    | <.0001  |
| Glucose                 | 94 (86-105)      | 89 (83-95)       | <.0001  |
| Insuline                | 8 (5.9-11.6)     | 6.3 (4.5-8.9)    | <.0001  |
| HOMA                    | 1.8 (1.3-2.9)    | 1.3 (.94-1.9)    | <.0001  |
| Hepatic steatosis index | 42.9 (39.6-47.9) | 38 (33.8-42)     | <.0001  |



**Figure 1.** Diagnostic performance of non-invasive biomarkers in subjects with Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD). Receiver Operating Characteristic (ROC) curves were plotted, and the area under the curve was calculated. The Youden index was used to select the optimal cutoff point. CAP, Controlled Attenuation Parameter; HSI, Hepatic Steatosis Index; HOMA, Homeostatic Model Assessment of Insulin Resistance; ICC.- Waist-to-Hip Ratio.

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**Secondary Attack Rate of Hepatitis C Virus (HCV)**

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**Introduction and Objectives:** The transmission routes of Hepatitis C Virus (HCV) are categorized as horizontal and vertical. The former includes sexual contact, parenteral exposure, and intrafamilial transmission, while the latter pertains to mother-to-child transmission. Although extensive literature has documented the parenteral route and sexual contact, there is a paucity of studies examining intrafamilial transmission within the Mexican population. This study aims to determine the rate of horizontal viral transmission among first-degree relatives of patients diagnosed with HCV infection who received treatment at Hospital de Especialidades No. 14, Centro Médico Nacional "Adolfo Ruiz Cortines."

**Materials and Methods:** The study design is observational, descriptive, and retrospective. Patient records from outpatient clinics were scrutinized for the period spanning January 2018 to January 2022. Clinical and epidemiological characteristics, risk factors obtained from medical histories, and laboratory results (including positive HCV viral load and HCV serum PCR test) were evaluated to classify cohorts. Informed consent was obtained from all patients. The research work was registered and approved by the Local Research Committee (R-2022-3001-088).

**Results:** A total of 129 patients were analyzed, with an average age of 39.56 years. Female gender predominated among 68 patients (52.7%), and 29 patients (22.5%) acquired HCV infection. The primary risk factors identified were Systemic Arterial Hypertension (RR: 7.47, 95% CI: 2.951-18.914,  $p<0.05$ ), Type 2 Diabetes Mellitus (RR: 16.125, 95% CI: 5.985-43.441,  $p<0.05$ ), and Chronic Kidney Disease (RR: 10.795, 95% CI: 3.736-31.188,  $p<0.05$ ) (Table 1). Only two patients (6.89%) were classified as having chronic infection based on measured viral load. All patients received Direct-Acting Antiviral treatment, resulting in sustained viral response at three months post-treatment completion. The primary attack rate was 22.48%, the secondary attack rate was 412.5%, and the  $R_0$  was 1,492,953 (Table 2).

**Conclusions:** The study demonstrated that first-degree relatives with comorbidities are at a higher risk of contracting HCV infection. The study's findings also revealed that the prevalence of HCV infection is higher than the reported rate in the general population. These results highlight the importance of targeted screening programs, especially in high-risk populations with comorbidities, to identify and treat HCV infections promptly. Such efforts will contribute significantly to the international goals for eradicating this virus and preventing further transmission. Moreover, the study's findings underscore the need for increased awareness and preventive measures to reduce the impact of HCV within the Mexican population.

**Ethical statement**

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

**Declaration of interests**

None

**Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Table 1**  
Frequency Distribution of Risk Factors in first-degree relatives diagnosed with Hepatitis C Virus (HCV) infection.

| Risk Factors         |          | Hepatitis C Virus Infection |     | p    | RR    | Lower 95% CI | Upper 95% CI |
|----------------------|----------|-----------------------------|-----|------|-------|--------------|--------------|
|                      |          | No                          | Yes |      |       |              |              |
| Tobacco Use Disorder | Negative | 90                          | 24  | 0.28 | 1.875 | 0.585        | 6.006        |
|                      | Positive | 10                          | 5   |      |       |              |              |
| Alcoholism           | Negative | 87                          | 22  | 0.14 | 2.129 | 0.759        | 5.791        |

(continued)

|                                        |          |     |    |       |        |       |        |
|----------------------------------------|----------|-----|----|-------|--------|-------|--------|
| Hypertension                           | Positive | 13  | 7  | <0.05 | 7.471  | 2.951 | 18.914 |
|                                        | Negative | 74  | 8  |       |        |       |        |
| Diabetes Mellitus, Type 1              | Positive | 26  | 21 | 0.58  | 0.773  | 0.704 | 0.849  |
|                                        | Negative | 99  | 29 |       |        |       |        |
| Diabetes Mellitus, Type 2              | Positive | 1   | 0  | <0.05 | 16.125 | 5.985 | 43.441 |
|                                        | Negative | 86  | 8  |       |        |       |        |
| Pulmonary Disease, Chronic Obstructive | Positive | 14  | 21 | 0.09  | 3.731  | 0.711 | 19.578 |
|                                        | Negative | 97  | 26 |       |        |       |        |
| Renal Insufficiency, Chronic           | Positive | 3   | 3  | <0.05 | 10.795 | 3.736 | 31.188 |
|                                        | Negative | 93  | 16 |       |        |       |        |
| Immunocompromised                      | Positive | 7   | 13 | <0.05 | 0.187  | 0.129 | 0.27   |
|                                        | Negative | 100 | 23 |       |        |       |        |
|                                        | Positive | 0   | 6  |       |        |       |        |

**Table 2**  
Calculation of attack rate, secondary attack rate, and  $R_0$  in first-degree relatives diagnosed with Hepatitis C Virus (HCV) infection.

| Rate                  | %         |
|-----------------------|-----------|
| Attack Rate           | 22.48     |
| Secondary attack rate | 412.50    |
| $R_0$                 | 1,492,953 |

Number of new cases of the disease: 29  
Number of infectious contacts: 129  
Total number of individuals exposed to an infection, outbreak, or epidemic: 29  
Number of individuals who have developed the disease: 129  
Total number of susceptible individuals exposed: 169  
Transmissibility: 161

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**Association of IFNL3 gene rs4803217 with spontaneous clearance of Hepatitis C virus in patients from West Mexico**

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**Introduction and Objectives:** Cytokines are crucial in modulating immune responses and the outcome of hepatitis C virus (HCV) infection. Polymorphisms in the IL10 and IFNL3 genes have been associated with spontaneous clearance (SC) in populations worldwide. However, their effect on the Mexican population remains unknown. This study aimed to analyze the association of polymorphisms in the IL10 (rs1800871, rs1800872, and rs1800896) and IFNL3 (rs4803217) genes with SC in HCV patients from West Mexico.

**Materials and Patients:** A total of 203 treatment-naïve, anti-HCV-positive patients were included in the study. Among them, 60 had undetectable viral load, and 143 had a detectable viral load. Genotyping was performed using Real-Time PCR. Biochemical and serological analyses were conducted. Comparative statistical analysis was performed using SPSSv24 software. Written informed consent was obtained from all participants. The Institutional Review Board approved this study.

**Results:** The CC genotype of the IFNL3 rs4803217 gene was associated with SC (OR=2.046,  $p=0.026$ ). In SC patients, the CC genotype increased total cholesterol (TChol) compared to AA+AC genotypes (209.76 vs. 176.86 mg/dL,  $p=0.061$ ). The IL10 rs1800871, rs1800872, and rs1800896 polymorphisms were not associated with SC. In SC patients, the CC+CT genotypes of IL10 rs1800871 and CC+CA genotypes of IL10 rs1800872 were associated with higher TChol levels



compared to the TT genotype (198.68 vs. 177.85 mg/dL,  $p=0.010$ ) and the AA genotype (196.81 vs. 178.58 mg/dL,  $p=0.006$ ), respectively. In chronic patients, the GG+GA genotypes of *IL10* rs1800896 were associated with high insulin levels compared to the AA genotype (17.22 vs. 12.04 IU/mL,  $p=0.021$ ).

**Conclusions:** The CC genotype of the *IFNL3* rs4803217 gene was associated with SC in patients from West Mexico. *IL10* and *IFNL3* polymorphisms increased TChol in SC patients. These results suggest an interaction between metabolic and immune factors in the outcome of HCV infection.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

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### 25-hydroxyvitamin D deficiency as a factor associated with the development of Hepatic Encephalopathy in the Mexican population.

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**Introduction and Objectives:** Hepatic Encephalopathy (HE) is a common complication in patients with Chronic Liver Disease (CLD), and the development of this decompensation is multifactorial, including ammonia levels, inflammatory status, and sepsis, among others. A poorly studied factor in our population is the serum levels of 25-hydroxyvitamin D (25-OHD), which could act as a co-factor in HE. To assess if serum 25-hydroxyvitamin D (25-OHD) deficiency acts as a cofactor in the development of HE.

**Materials and Patients:** Observational, retrospective, analytical, case-control study; included subjects of both sexes, 18 years old and over, diagnosed with Chronic Liver Disease of different etiologies. Complete blood count, liver and kidney function, serum electrolytes, coagulation profile, and serum levels of 25-hydroxyvitamin D were recorded. They were evaluated using the West-Haven Criteria (WH).

**Results:** Independent samples T-test was used to compare differences between 25-hydroxyvitamin D levels in patients with and without HE. The association between 25-OHD deficiency and HE was assessed using a chi-square test, with a significance level set at  $\alpha=0.05$ . Out of a total of 96 patients, 36.5% had HE. The mean 25-OHD level in the HE group was  $18.78 \pm 8.56$ , compared to  $22.77 \pm 9.94$  in the group without HE. The T-test was significant:  $T(1)=2.072$ ,  $p=0.041$ . Among patients with deficiency, 20/35 (57.1%) had EH, while 22/61 (36.1%) did not have HE. The chi-square test for the association between deficiency and HE was positive, with a value of  $(1)=4.015$ ,  $p=0.045$ .

**Conclusions:** A causal relationship between 25-hydroxyvitamin D (25-OHD) deficiency and the development of HE cannot be attributed, as this is multifactorial. However, 25-OHD deficiency is common in patients with Chronic liver disease, and our study demonstrates that this deficiency acts as a cofactor, as there is a significant difference between the groups. It is necessary to validate these findings in the future through multivariate analysis to confirm our results.

#### Ethical statement

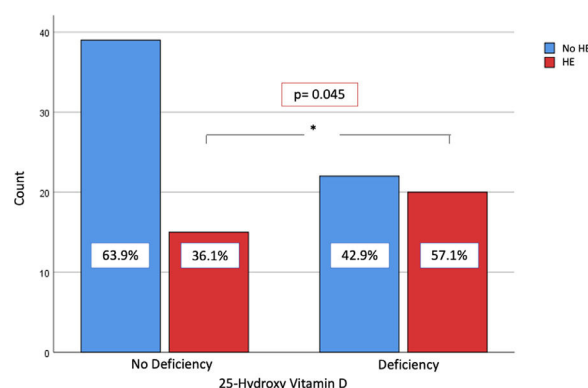
The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

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**Figure 1.** Percentage of patients with 25-OHD deficiency and HE

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### Incidence and Associated factors to development of hyponatremia in a cohort of ambulatory patients with compensated liver cirrhosis

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**Introduction and Objectives:** Hyponatremia is associated with ascites, hepatic encephalopathy, primary bacterial peritonitis, and increased mortality. However, the information about incidence and factors associated with hyponatremia in ambulatory patients with compensated cirrhosis is scarce. The aim of the study was to estimate the incidence and associated factors to the development of hypervolemic hyponatremia.

**Materials and Patients:** Ambulatory patients with compensated cirrhosis seen at Medical Center Siglo XXI were selected. All variables included in Child-Pugh Index and in the MELD Score and the types of treatment diet were analyzed. Hyponatremia was considered when

serum concentration of sodium was <135 mEq/L in hypotonic state and water retention.

**Results:** The incidence of hyponatremia was 9.6% (13/135). A prognostic risk index was identified based on fluid retention and the baseline MELD score (RH-MELD Index) (Table 1). A higher incidence of hyponatremia was observed in patients in category III [RR: 7.96 (95%CI: 1.17-54.06, p=0.034)], when adjusting for diet; patients with protein supplement consumption without a structured diet had a higher risk of hyponatremia [RR: 17.72 (95%CI: 3.50-89.52), p=0.001].

**Conclusions:** The results suggest that the incidence of dilutional hyponatremia in outpatients with cirrhosis is frequent; mild alterations in water retention and liver function in the compensated phase represent an early indicator of its development, which can be modified by the indicated diet.

**Ethical statement**

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

**Declaration of interests**

None

**Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Table 1**  
RH-MELD Index.

| Risk categories for Hyponatremia |             |           |
|----------------------------------|-------------|-----------|
| (RH-MELD) Categories             | N (%)       | P value   |
| I: No water retention, MELD ≤9   | 2/62 (3.2)  | Reference |
| II: Water retention or MELD ≥10  | 6/55 (10.9) | 0.201     |
| III: Water retention + MELD ≥10  | 5/18 (27.8) | 0.010*    |

\* Fisher exact test.

Unadjusted risk: RH-MELD I (reference), II (RR:3.67, CI 95%:0.71-19.01, p=0.121), III (RR:11.53, CI 95%: 2.01-66.13, p=0.006).

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**“Explosive” worsening of chronic hepatitis C-associated cryoglobulinemia vasculitis, as unmasking of lymphoma a case report.**

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**Introduction and Objectives:** Hepatitis C virus (HCV)- related lymphoproliferative disease from cryoglobulinemia to B-cell non-Hodgkin lymphoma (B-NHL) through cryoglobulinemic vasculitis (CryoVas). The CryoVas is difficult to diagnose; once diagnosed, we must rule out the HCV infection. We presented a patient with HCV and CryoVas, which presented a sudden “explosive” worsening, warning about the development of a B-NHL.

**Materials and Patients:** 55-year-old male with HCV and CryoVas; what was the trigger for the diagnosis of HCV twenty years before? He received pegylated interferon and ribavirin without response. The virological, biochemical, and immunological characteristics are shown in Table 1. The flare of CryoVas appeared twice a year at most,

limited to purpuric lesions on the legs, below the knees, arthralgia, and fatigue; was often triggered by infections, self-limiting throughout 2 to 3 weeks. The last flare started as usual but getting worse rapidly, spreading to the thighs, abdomen, chest, and upper extremities, plus fever, nocturnal diaphoresis, severe wasting, and inguinal, axillary lymph nodes. Lymph node biopsy shows diffuse large B-cell lymphoma (DLBCL)

**Results:** He received chemotherapy (CT), previously was re-treated with sofosbuvir/velpatasvir for 12 weeks. Five months after first-line treatment for DLBCL he presented an early relapse and received a second line of CT; at 3-year follow-up is in remission with no relapse of CryoVas, waiting for a bone marrow transplant.

**Conclusions:** Clinicians treating hepatitis C should be aware of the need to carry out immunological parameters at the basal evaluation, such as cryoglobulins, rheumatoid factor, C4 fraction, and even a flow cytometry in specific patients to the detection of leukemias and/or related lymphomas.

**Ethical statement**

The identity of the patients is protected. Consentment was obtained.

**Declaration of interests**

None

**Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Table 1**  
Viral, biochemical and immunological parameters during the HCV infection, CryoVas and B-LNH.

| Variable                     | 2006<br>year (y) | Basal<br>2019 y  | SVR12 | Last follow<br>up 2022y |
|------------------------------|------------------|------------------|-------|-------------------------|
| Viral load, UI/mL (log)      | 13466<br>(4.13)  | 867277<br>(5.94) | ND    | NR                      |
| Genotype                     | 1b               | 1b               | NR    | NR                      |
| Hemoglobin g/dL              | 9.9              | 10.6             | 12.8  | 13                      |
| Total leukocytes K/ $\mu$ L  | NR               | 8.6              | 7.6   | 9                       |
| Total lymphocytes K/ $\mu$ L | NR               | 2.3              | 1.5   | 1.9                     |
| Platelets                    | 152              | 88               | 80    | 122                     |
| AST                          | 40               | 79               | 20    | 21                      |
| ALT                          | 83               | 108              | 20    | 29                      |
| GGT                          | 38               | 66               | 33    | NR                      |
| LDH                          | 130              | 370              | 180   | 100                     |
| AFP                          | 1                | 2                | 3     | 2                       |
| FIB4                         | 1.16             | 4.76             | 3     | 0.49                    |
| APRI                         | 0.75             | 2.57             | 0.71  | 1.86                    |
| Crioglobulins                | NR               | Positive         | NR    | Negative                |

SVR12: Sustained viral response at 12 weeks after treatment, AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; GGT, gamma glutamyl transpeptidase; LDH, lactate dehydrogenase; AFP, alpha-fetoprotein; ND, No detected.

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**Intrahepatic Cholestasis Induced by Leflunomide: An Unusual Presentation of DILI**

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**Introduction and Objectives:** Leflunomide is a drug used to treat autoimmune diseases. However, despite its therapeutic benefits, adverse effects have been reported after six months of treatment, including liver damage.

**Materials and Patients:** A 19-year-old female from Acayucan, Veracruz, without significant hereditary or family history, drug addiction denied, with a pathological history of hypothyroidism for 2 years and rheumatoid arthritis since the age of 15, treated with leflunomide 20 mg, chloroquine 150 mg, levothyroxine 100 mcg. She presented in October 2022 with nausea, vomiting, postprandial abdominal pain, jaundice. Abdominal ultrasound revealed chronic calculous cholecystitis. Laparoscopic cholecystectomy was performed in December 2022 without complications. After surgical treatment, he persisted with jaundice, alteration of liver function tests of mixed pattern that evolves to cholestatic pattern (R factor 0.2, see Table 1). Non-reactive to viral hepatitis A, B and C, HIV, negative antibodies ANA, AML, AMA, anti-DNAs, anti-Smith, anti-Rho, complement C3 145 and C4 33. Cholangiography, with hepatomegaly, diffuse hepatic steatosis without evidence of biliary lesions. Liver biopsy showed features of portal and lobular hepatitis, intracytoplasmic and intracanalicular cholestasis, macrovesicular steatosis, and F2 fibrosis according to METAVIR (Fig. 1), which were not consistent with autoimmune or viral disease. RUCAM score with possible relation to hepatotoxicity (4 points), so it is considered drug-induced liver injury (leflunomide).

**Results:** Leflunomide was discontinued and treatment was adjusted to chloroquine 150 mg and prednisone 50 mg. Clinical and biochemical improvement was observed.

**Conclusions:** This case highlights the importance of suspecting DILI in patients treated with potentially hepatotoxic drugs and with alterations in liver biochemistry. It is a rare disease for which there are no specific markers. Therefore, liver biopsy is a useful tool for early diagnosis.

**Ethical statement**

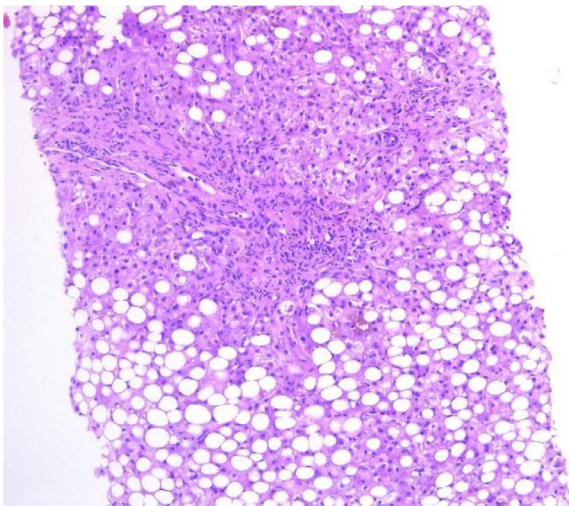
The identity of the patients is protected. Consentment was obtained.

**Declaration of interests**

None

**Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



**Figure 1.** Liver tissue with widened portal spaces, mild inflammatory portal infiltrate, thick droplet steatosis, intracytoplasmic and ductal cholestasis.

**Table 1**  
Control of laboratory studies

| Leflunomide is discontinued |        |        |        |        |        |       |
|-----------------------------|--------|--------|--------|--------|--------|-------|
| PARAMETER                   | 11-Feb | 23-Feb | 23-Mar | 21-Apr | 24-May | 5-Jul |
| Total bilirubin (mg/dL)     | 3.8    | 4.1    | 8.61   | 14.5   | 8.15   | 0.76  |
| Direct bilirubin (mg/dL)    | 2.47   | 3.3    | 6.64   | 7.81   | -      | 0.34  |
| Indirect bilirubin (mg/dL)  | 1.33   | 0.8    | 1.97   | 6.77   | -      | 0.42  |
| AST (U/L)                   | 65     | 95     | 277    | 236    | 168    | 48    |
| ALT (U/L)                   | 18     | 29     | 41     | 64     | 101    | 50    |
| Alkaline phosphatase (U/L)  | 253    | 142    | 569    | 217    | 146    | 132   |
| GGT (U/L)                   | 245    | 413    | 322    | 702    | 607    | 154   |
| TG (mg/dL)                  | -      | -      | 803    | 411    | 225    | 155   |
| Cholesterol (mg/dL)         | -      | -      | 324    | 289    | 296    | 194   |

| PARAMETER                  | 11-Feb | 23-Feb | 23-Mar | 21-Apr | 24-May | 5-Jul |
|----------------------------|--------|--------|--------|--------|--------|-------|
| Total bilirubin (mg/dL)    | 3.8    | 4.1    | 8.61   | 14.5   | 8.15   | 0.76  |
| Direct bilirubin (mg/dL)   | 2.47   | 3.3    | 6.64   | 7.81   | -      | 0.34  |
| Indirect bilirubin (mg/dL) | 1.33   | 0.8    | 1.97   | 6.77   | -      | 0.42  |
| AST (U/L)                  | 65     | 95     | 277    | 236    | 168    | 48    |
| ALT (U/L)                  | 18     | 29     | 41     | 64     | 101    | 50    |
| Alkaline phosphatase (U/L) | 253    | 142    | 569    | 217    | 146    | 132   |
| GGT (U/L)                  | 245    | 413    | 322    | 702    | 607    | 154   |
| TG (mg/dL)                 | -      | -      | 803    | 411    | 225    | 155   |
| Cholesterol (mg/dL)        | -      | -      | 324    | 289    | 296    | 194   |

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**Evaluation of the effect of Cinnamomum cassia oil on markers of oxidative stress and its modification in gene expression in a diabetic rat model induced with alloxane.**

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**Introduction and Objectives:** Diabetes Mellitus (DM) is a chronic hyperglycemia disorder presenting alteration of biochemical markers, proinflammatory activity, and oxidant stress (OS). There are treatments for DM but they can have adverse effects, so plants are an alternative to new therapeutic compounds. Cinnamomum cassia (cinnamon) has been shown to have antidiabetic and antioxidant activity. The objective of this study was to evaluate the effect of Cinnamomum cassia oil (CCO) on oxidative stress markers and their modification in gene expression in a diabetic rat model induced with alloxan.

**Materials and Methods:** Experimental, prospective and comparative study with female and male Wistar rats. Groups (n=6): Sham (SH), Diabetic (D), CCO, D with CCO (D+CCO) and D with metformin (D+MET). From serum and liver tissue, biochemical and antioxidant markers were measured respectively, as well as gene expression. Ethics Committee approval under HI17-00002 registry.

**Results:** No significant difference in ALT and AST was observed between the SH and CCO groups at the dose used (300 mg/kg) (Figure 1A y B). Group D presented an increase in glucose (GLU) compared to SH (Figure 1C). A significant decrease in GLU, urea nitrogen (BUN),



AST and ALT were observed in the D+CCO group compared to D group, but not in cholesterol (COL), triglycerides (TG), creatinine (CREA) (Figure 1D-J). No significant changes were observed in the levels of malondialdehyde (MDA), glutathione (GSH) and superoxide dismutase (SOD) when comparing the D+CCO group with respect to D (Figure 2A-C), but there was a significant decrease in the expression of *Rela* and *Gpx* in the D+CCO group with respect to D (Figure 2 E and D).

**Conclusions:** CCO at the dose used and during the study period was not hepatotoxic, had a hypoglycemic effect from the first dose and decreased ALT, AST and BUN levels. CCO has an anti-inflammatory effect by decreasing *Rela* gene expression.

### Ethical statement

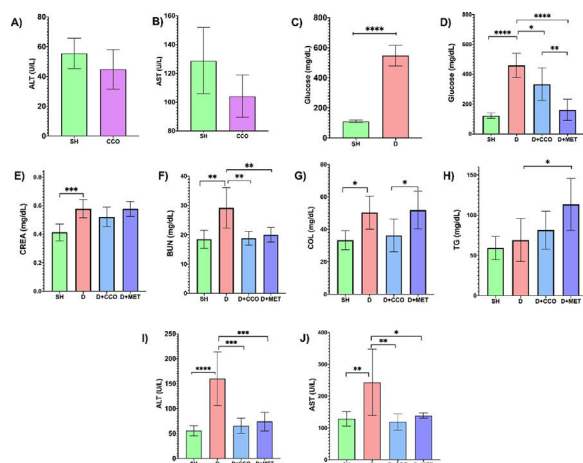
The protocol was registered and approved by the Ethics Committee.

### Declaration of interests

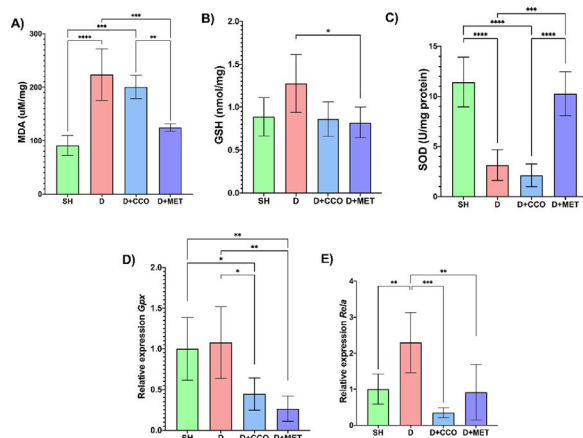
None

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



**Figure 1. Results of the biochemical markers in the different study groups.** (A and B) ALT and AST levels in SH groups and D. (C) Glucose levels after one week of administration with alloxane. (D-J) Glucose, CREA, BUN, COL, TG, ALT and AST levels in the various study groups after the administration period. Values are expressed as mean  $\pm$  SD. P values: \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$  and \*\*\*\*  $p < 0.001$ .



**Figure 2. Results of oxidative stress and gene expression markers in the different study groups.** (A, B and C) MDA, GSH and SOD oxidative stress markers. (E and D) Relative expression of *Gpx*

and *Rela* in the various study groups. Values are expressed as mean  $\pm$  SD. P values: \*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$  and \*\*\*\*  $p < 0.001$ .

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### Hepatoprotective effects of N-acetylcysteine prevents hepatocellular carcinoma development induced experimentally.

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**Introduction and Objectives:** Hepatocellular carcinoma (HCC) development involves imbalance of cellular processes such as oxidative stress, inflammation, fibrogenesis and cell proliferation. N-acetylcysteine (NAC) is an effective drug used clinically to treat drug-induced liver injury, but its ability to modulate molecular mechanisms activated during HCC establishment is unknown.

This study aimed to evaluate antioxidant, antifibrogenic, and antiproliferative NAC properties in the HCC induced experimentally.

**Materials and Patients:** Male Fisher 344 rats divided into 3 groups: 1. Control (CTL); 2. HCC: Diethylnitrosamine (DEN) + 2-acetylaminofluorene (2-AAF). 3. HCC/NAC: DEN+2-AAF and NAC. Liver damage, oxidative stress, fibrogenesis and proliferation markers were evaluated by colorimetric methods, Western blot, Dot blot, immunofluorescence, immunohistochemistry, respectively. H&E and Masson's Trichrome stains were also performed. This project was conducted in accordance with the guidelines of the University of Guadalajara under the approval number of the bioethics, research, and ethics research committees CI-01723.

**Results:** NAC exerts hepatoprotective effects, by preserving hepatic micro and macrostructure, slowing dysplastic nodules formation, and preventing an increase in ALT and GGT enzymatic activity. This drug also is able to exert anti fibrogenic effects by repressing extracellular matrix accumulation through to inhibition of  $\alpha$ -SMA and TFG- $\beta$  expression. Likewise, NAC demonstrated antiproliferative capacity by reducing Glypican-3 and Ki-67 expression.

Furthermore, NAC exerts its antioxidant effects by regulating Nrf2 signaling pathway, modulating CAT and SOD expression, and GSH levels. Finally, this drug prevents DNA oxidative damage through increasing enzyme 8-oxoguanine-DNA glycosylase (OGG1/2) expression, and therefore, reducing 8-oxoguanine (8oxoG) levels.

**Conclusions:** In this work, we demonstrate that NAC exerts antioxidant, antifibrogenic and antiproliferative effects useful in the prevention of the development of this disease. It is necessary to carry out additional analyzes that allow a more precise clarification of NAC hepatoprotective mechanisms, and that allow it to be repositioned as an adjuvant therapy in HCC treatment.

### Ethical statement

All experimental procedures were approved by the Research Committee, the Research Ethics Committee, and the Biosafety Committee of the University of Guadalajara, with the approval number CI-01723.



## Declaration of interests

None

## Funding

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## Pirfenidone slows the development of fibrosis and malignant neoplasms by modulating inflammation in an experimental model of hepatocarcinoma.

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**Introduction and objectives:** Hepatocellular carcinoma (HCC) is the most common liver neoplasm in the world. Inflammatory, oxidative and fibrogenic processes are key in tumor development and propagation. Pirfenidone (PFD) has been shown to have hepatoprotective, anti-fibrogenic and immunomodulatory properties during hepatocarcinogenesis. However, its effect on established HCC is unknown. Our aim is to evaluate the effect of PFD administration on the tumor and inflammatory microenvironment in an experimental hepatocellular carcinoma model.

**Materials and Patients:** Fischer-344 rats (n=18) protocolized into three groups: CTL: control, HCC: damage group, (induced by diethylnitrosamine (DEN) 50 mg/kg and 2-acetaminofluorene (2AAF) 25mg/kg/weekly for 16 weeks), HCC/PFD: damage group + administration of PFD 300 mg/kg/daily. Subsequently, immunoassays and histological analyzes were performed to assess inflammatory patterns, fibrosis, and malignancy.

All animals received human care, and all the experiments were performed according to the Guide for the Care and Use of Laboratory Animals, under the approval of the Research, Ethics, and Biosafety committees of the CUCS with approval number CI-03020.

**Results:** In the HCC/PFD group, the observed nodules were smaller in number, size, and protrusion compared to the HCC group. Additionally, there was a decrease in fibrosis development, extracellular matrix synthesis, as well as collagen and  $\alpha$ -SMA expression. The loss of hepatic architecture was restored, and there was a decrease in the percentage of transformed hepatocytes positive for Glypican-3 expression, in contrast to the HCC group. Furthermore, there was a restoration of p53 expression. Moreover, the local secretome showed a decrease in IL-10 and an increase in IL-6 and IL-1 $\beta$  compared to the HCC group. Finally, the expression and localization of CD45 and CD161 were observed to be increased within the tumor niches compared to the HCC group.

**Conclusions:** Treatment with PFD slows the development of both macroscopic and microscopic patterns of malignancy and fibrosis, decreases the activation of hepatic stellate cells, the local inflammatory secretome, and modulates the components of the tumor microenvironment, thus improving the conditions and progression of the

neoplasia. Therefore, pirfenidone could mean an improvement in the quality of life and an increase in the survival of patients with HCC in advanced stages.

## Ethical statement

The protocol was registered and approved by the Ethics Committee.

## Declaration of interests

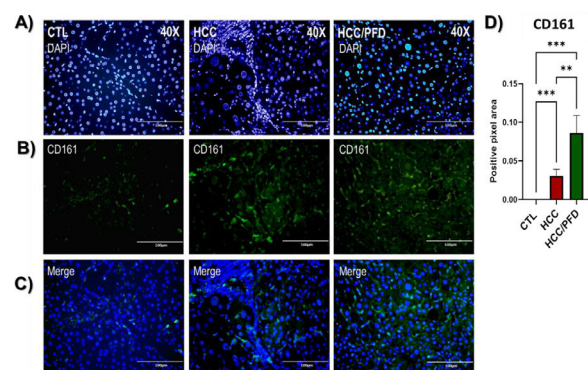
None

## Funding

Programa de Fortalecimiento de Institutos, Centros y Laboratorios de Investigación 2022, otorgado al Instituto de Biología Molecular en Medicina y Terapia Génica Programa para el

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Profesores de Tiempo Completo, 511-6/2020-8586 PTC-1534. Fondo para Proyectos de Impulso a la Investigación (PIN 2020- I).



**Figure 2. Immunofluorescence for CD161 detection.** In the blue channel (A), cell nuclei stained with DAPI. In the green channel (B), Alexa-green for CD161. (C) Merge. It is observed that the PFD treatment increased the infiltration of CD161-positive cells, with co-localization in tumor niche centers, suggesting enhanced cytotoxic activity by these cells. (D) Quantification of positive pixel areas, showing a higher positive area in the PFD-treated group. One-way ANOVA analysis considered statistically significant at  $p < 0.05$ ,  $*p < 0.05$ ,  $**p < 0.01$ ,  $***p < 0.001$ ,  $****p < 0.0001$ .

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## Pirfenidone induces translocation of sirt1 to nucleus and deacetylation of histone 3 slows down the development of fibrosis and tumorigenicity in a experimental model of hepatocarcinoma.

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**Introduction and objectives:** Hepatocellular carcinoma (HCC) is the most common liver neoplasm worldwide. Pro-inflammatory and

pro-fibrogenic processes are key in tumor development. On the other hand, Pirfenidone (PFD) has anti-inflammatory and antifibrogenic properties useful to counteract hepatocarcinogenesis; however, the effects of this drug on SIRT1, and histone H3 regulation in this disease are unknown.

The objective this work is evaluate PFD effects on SIRT1 translocation, and histone H3 lysines 9 and 14 (H3K9 and H3K14) deacetylation in an experimental model of HCC.

**Materials and Patients:** Fischer-344 rats were divided into three groups: CTL: control group, HCC: group damaged with diethylnitrosamine (DEN), 50 mg/kg and 2-aminofluorene (2AAF), 25 mg/kg/p.o. HCC/PFD group: damage group and with PFD (300 mg/kg/day) for 16 weeks. Histological and molecular analyzes were performed evaluating patterns of protein acetylation, fibrosis, and malignancy.

**Results:** Normal liver architecture is disturbed by dysplastic nodules formation surrounded by extracellular matrix and fibrosis, also an increase in cells with anaplasia and steatotic foci was observed in liver tissues of HCC group. PFD administration was effective to prevent these changes. Immunohistochemistry reveals an overexpression of GPC3 and  $\alpha$ -SMA in damage group, which is correlated with malignant degeneration, these responses was prevented by PFD too. Finally, western blots evidence a SIRT1 overexpression in nuclear fraction of PFD group, triggering H3K9 and H3K14 deacetylation, in addition, a decrease in p300 acetylase expression in nuclear fractions. Notably, c-Myc was reduced and p53 increased significantly.

**Conclusions:** PFD treatment reduces fibrotic and malignant patterns development. Likewise, PFD induces SIRT1 expression and nuclear translocation, and H3K9 and H3K14 deacetylation, decompacting chromatin and possibly increasing tumor suppressor genes expression for example c-MYC. These results demonstrate for the first time the capability of PFD to regulate epigenetic hallmarks on histones.

#### Ethical statement

All the experiments were carried out in accordance with the guidelines approved by the Ethics, Research and Biosafety committees of the CUCS with approval number CI-03020.

#### Declaration of interests

None

#### Funding

Programa de Fortalecimiento de Institutos, Centros y Laboratorios de Investigación 2022, otorgado al Instituto de Biología Molecular en Medicina y Terapia Génica Programa para el Desarrollo Profesional Docente, para el Tipo Superior (PRODEP), Apoyo a Nuevos Profesores de Tiempo Completo, 511-6/2020-8586 PTC-1534. Fondo para Proyectos de Impulso a la Investigación (PIN 2020- I).

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#### Bovine matrix scaffold implanted in rat liver improve regeneration in a partial hepatectomy model.

Moises Martinez-Castillo<sup>1</sup>, Benjamin León-Mancilla<sup>2</sup>, Gerardo Ramirez-Rico<sup>3</sup>, Marisela Hernandez-Santillan<sup>1</sup>, Abigail Hernández-Barragán<sup>1</sup>, Cristina Piña-Barba<sup>4</sup>, Gabriela Gutiérrez-Reyes<sup>1</sup>

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**Introduction and objectives:** Liver transplant is the recommended therapeutic option for advanced liver damage in chronic liver disease. However, the biocompatibility and low donation rates significantly reduce the chances of performing a successful transplant. The use of inert biomaterials such as collagen matrix scaffolds (CMS) has been suggested as a promising option to restore the function of organs, including liver. The objective was to evaluate the biocompatibility and liver restoration after partial hepatectomy and the implant of bovine matrix scaffold in a rat model.

**Materials and Patients:** Three groups of Wistar rats were evaluated: Sham, Partial hepatectomy (PH) (40%, left lobe) and PH + Collagen Matrix (CM). After surgical procedure the animals were monitored and the exploratory laparoscopy and histological analysis at 14 and 30 days was performed. The liver function was also compared in the three animal groups. The study was approved by the ethics committee of the School of Medicine at the Universidad Nacional Autónoma de México (UNAM). All procedures were performed according to official Mexican policy (SAGARPA, 1999). Our institution fulfills all technical specifications for the production, care, and use of laboratory animals and is certified by national law (NOM-062-ZOO-1999).

**Results:** The biomaterial showed evidence of reabsorption, the animals did not display signs of infection or systemic alterations. Moreover, the histopathological evaluation showed abundant hepatocyte proliferation and angiogenesis near to the site of CM implantation. An incipient inflammation or exacerbate macrophages, Langhans-type, and foreign-body giant cells were observed; these findings strongly suggest not rejection at 30 days. Furthermore, no statistical differences in albumin, bilirubin, cholesterol, triglycerides, alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase were observed at day 14 in sham, PH and PH + CM.

**Conclusions:** Bovine collagen matrix showed great compatibility with the liver and was bioabsorbable. The incorporation of this biomaterial does not interfere with liver function and promotes the proliferation of hepatocytes and vessels, showing typical arrangement of the hepatic parenchyma. The use of the biomaterial could be beneficial to reduce the current limitation of organ transplant.

#### Ethical statement

This study was approved by the ethics committee of the School of Medicine at the Universidad Nacional Autónoma de México (UNAM). All procedures were performed according to official Mexican policy SAGARPA, 1999). Our institution fulfills all technical specifications for the production, care, and use of laboratory animals and is certified by national law (NOM-062-ZOO-1999).

#### Declaration of interests

None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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### Collagen matrix scaffold as vehicle of WP1066, STAT-3 inhibitors, in an in vitro hepatocellular model.

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**Introduction and objectives:** Liver disease causes approximately 1.75 million deaths per year and chronic liver disease (CLD) and is usually detected in advanced stages (cirrhosis or hepatocellular carcinoma) that require partial ablation or transplant. STAT-3 has been identified as a therapeutic target in cancer. Moreover, collagen matrix scaffolds (CMS) can be used as carriers of antineoplastic drugs for hepatocellular carcinoma. The objective was to determine the capacity of CMS as vehicle of WP1066 (inhibitor of STAT3) in an in vitro HCC model.

**Materials and Patients:** WP1066 was incubated with HCC cell lines to determine the IC<sub>50</sub> by the Resazurin method. After this, the IC<sub>50</sub> concentration of WP1066 was added to CMS during 1, 3 and 7 days before the incubation with each HCC cell, then the WP1066 stability was evaluated by mass spectrometry. The pH of the RPMI medium was evaluated in all the experimental conditions using a potentiometer. Whereas the cell viability was compared with untreated cells and CMS without WP1066 by Resazurin method.

**Results:** The IC<sub>50</sub> of WP1066 for HEPA 1-6 and HEPG2 was similar 1.54  $\mu\text{M} \pm 0.07$  and 1.68  $\pm 0.16 \mu\text{M}$ , respectively. WP1066 showed stability after 7 days of preparation in DMSO. The pH evaluation of RPMI with WP1066, CMS and WP1066+CMS was similar (pH 7.2) at 72 h of incubation. Cell viability of both HCC cell lines was reduced 80% in the combination of CM plus WP1066 ( $p < 0.001$ ), however, CM alone also promotes the reduction of cell viability like WP1066 alone (50%) ( $p < 0.001$ ).

**Conclusions:** Previously, we reported that CM allows the survival and proliferation of mesenchymal stem cells. CM can be used as a vehicle of WP1066; moreover, CM alone or in combination with WP1066 promotes reduction of HCC cell lines. It is possible that hydroxyapatite from CM promotes reduction of cell viability of cancer cells but does not cause negative effects in mesenchymal stem cells.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee.

#### Declaration of interests

None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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### Segmental portal hypertension secondary to chronic pancreatitis

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**Introduction and objectives:** Case presentation of a male patient with portal hypertension secondary to chronic pancreatitis

**Materials and Patients:** This is a 38-year-old male patient, occasional drinker, risky consumption, history of diagnosis of diabetes mellitus, with adequate adherence to hypoglycemic treatment with metformin, presented a clinical picture of 3 years of evolution consisting of severe pain in the upper abdomen with irradiation to the back on the left side, which required emergency admissions with stabilization and discharge with subsequent recurrence, as well as significant weight loss of 10% over a period of 8 months. He was admitted to the emergency department with clinical symptoms compatible with upper gastrointestinal bleeding due to the presence of melanic bowel movements on multiple occasions, associated with anemic syndrome, biochemically highlighting a Hb of 2.4 mg/dl, with normal liver function tests and other laboratories, with no changes of chronic hepatopathy by ultrasound.

**Results:** Regarding the approach to the digestive tract bleeding, Panendoscopy was performed, showing mucosa without alterations, without observing bleeding during the study, ruling out the presence of varices at esophageal level, proceeding to the realization of contrasted Angio Tomography, where findings of segmental portal hypertension with spleno-portal collateral vessels, splenic thrombosis and pancreatic calcifications suggestive of changes due to chronic pancreatitis were observed, with an area of enhancement at the level of the gastric fundus at the site of gastric varices, splenomegaly was not reported. For treatment selection, interventional radiology was evaluated, offering as a therapeutic option the recanalization of the splenic vein with stent placement; however, since Splenectomy was still considered as the definitive treatment for segmental portal hypertension, the latter intervention was chosen for resolution, with adequate evolution after the procedure, remission of bleeding and corroborating adequate flow redistribution after surgery by means of new Angio-CT. The patient attends his consultations on a regular basis, with good evolution, good glycemic control and improvement in nutritional status.

**Conclusions:** Segmental portal hypertension (SPH) is due to the presence of isolated obstruction of the splenic vein by thrombosis or extrinsic compression.

Pancreatitis conditions the development of thrombosis because the inflammatory state induces stasis and damage of the intima related to the contact of the splenic vein and the pancreas.

The presence of isolated gastric varices makes it necessary to rule out splenic venous thrombosis.

The definitive treatment continues to be splenectomy, reducing the flow to the varices and collateral circulation.

#### Ethical statement

The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

<https://doi.org/10.1016/j.aohep.2024.101404>



## Primary Hepatic Leiomyosarcoma (PHL) with pulmonary metastatic activity. Case report and literature review

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**Introduction and Objectives:** Sarcomas from the liver are rare, constituting only 1%-2% of all primary hepatic malignant tumors. Leiomyosarcoma accounts for 8%-10% of all hepatic sarcomas. However, these are generally metastatic tumors, arising from the GI tract, uterus, retroperitoneum, or lungs. So far, less than 100 cases of primary hepatic leiomyosarcoma (PHL) have been reported in the literature. PHL is a rare mesenchymal hepatic tumor whose clinical manifestations are often nonspecific and remain asymptomatic until there is a significant increase in tumor size, causing a mass effect. Furthermore, alpha-fetoprotein and other serological markers are usually normal. Thus, histological examination is the only way to achieve the diagnosis. The pathological features of leiomyosarcoma include spindle-shaped cells, abundant cytoplasm, nuclear atypia, and the presence of mitotic figures. Immunohistochemical staining of tumors is positive for vimentin, desmin and actin, and negative for a-fetoprotein, CD34, CD117, cytokeratin, and hepatocytes.

No risk factors have yet been identified. Interestingly, many of these tumors occur in immunocompromised individuals, such as post-transplantation and AIDS patients. This is postulated to be secondary to the effect of the uninhibited Epstein-Barr virus (EBV) on smooth muscle proliferation and previously treated Hodgkin's lymphoma. However, patients without any predisposing condition have also been described in the literature.

Surgical resection is considered to be the only potentially curative treatment. Standard chemotherapies (doxorubicin, ifosfamide; gemcitabine and docetaxel) have modest activity with single-agent and combination response rates of 10%-20% and 17%-40%, respectively.

**Materials and Patients:** A 43-year-old male with a history of alcoholism consuming 135 g/week for three years, smoking index of 1.8 packs/year, and six years diagnosis with type 2 diabetes mellitus. The clinical presentation started with pain in the upper right quadrant, nocturnal diaphoresis, and weight loss, progressing to hiccups, nausea, and vomiting.

**Results:** Dynamic CT revealed an irregular heterogeneous liver tumor involving the entire right lobe, with attenuation ranging from 7-45 HU in the non-contrast phase, showing heterogeneous enhancement in arterial phase up to 138 HU, with hypodense areas suggestive of necrosis, isodense to the parenchyma in the portal and delayed phases, measuring 174 × 138 × 170 mm. There were adenopathies and pulmonary nodules, the largest measuring 7.3 × 6.2 mm. Liver biochemistry and tumor markers AFP, Ca 19-9, and CEA were within normal limits. Liver biopsy revealed a malignant mesenchymal neoplasm composed of spindle cells with nuclear pleomorphism and atypical mitotic figures within the hepatic parenchyma. Immunohistochemistry showed positive staining for smooth muscle actin, desmin, calponin, DOG1, and negative for CD34, cytokeratin, CD117, ACE, consistent with leiomyosarcoma.

**Conclusions:** Palliative chemotherapy with doxorubicin and ifosfamide was initiated in 2021. A year later, clinical evolution ECOG 1, but follow-up CT showed a lesion measuring 314 × 159 × 155mm, leading to the decision for supportive care.

## Ethical statement

The identity of the patients is protected. Consentment was obtained.

## Declaration of interests

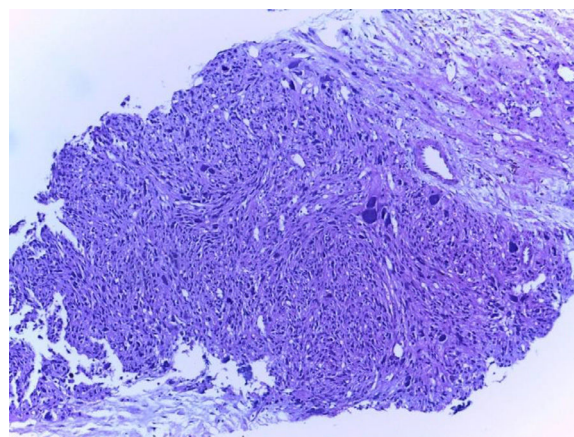
None

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



**Figure 1.** Triphasic CT in arterial phase, coronal section, showing an irregular and heterogeneous liver tumor, which fully involves the right hepatic lobe, dimensions 174 × 138 × 170 mm, with heterogeneous enhancement in the arterial phase of up to 138 HU, and hypodense areas in relation to necrosis.



**Figure 2.** Hematoxylin-eosin stained liver biopsy showing spindle cell neoplasm with eosinophilic cytoplasm, nuclear pleomorphism and atypical mitotic figures.

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## Hepatocellular carcinoma with metastasis to the inferior cava vein and right atrium, an unusual cause of Budd Chiari Syndrome

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**Introduction and Objectives:** Hepatocellular carcinoma (HCC) represents 80-85% of primary liver malignancies, ranks fifth in annual incidence of cancer, with an annual risk in patients with cirrhosis due to hepatitis B virus (HBV) of 3-8%. It has a tendency to involve vascular structures in the liver, such as the portal vein (VP) and hepatic veins (VH). Although HCC involvement of VH is seen less frequently compared to PV, tumor thrombi (TT) have been found to extend into the inferior vena cava (IVC) and right atrium (RA) through the HV. In patients with cardiac metastasis, secondary Budd-Chiari, pulmonary infarction and/or pulmonary metastasis have been documented mainly. A certain number of patients with TT-VH may develop Budd Chiari syndrome <3%, associated with chronic HBV infection.

**Materials and Patients:** A 58-year-old male patient with a history of human immunodeficiency virus and HBV coinfection, E antigen negative, with virological response. He presented with intense abdominal pain in the left hypochondrium that radiated in a generalized way to the inguinal region bilaterally. During the evaluation, ultrasonographic data of cirrhosis, ascites, Budd-Chiari syndrome, extensive portal thrombosis and hepatocellular carcinoma are found.

**Results:** Angiotomography showing areas of ischemia and necrosis in the left hepatic lobe, with the presence of a heterogeneous lesion measuring 5.2 cm that involves segments II, III, IVA, and IVB with enhancement in the arterial phase, portal vein thrombosis, and middle suprahepatic veins. Left, as well as a cardiac tumor dependent on the right atrium with extension to the ipsilateral ventricle and inferior vena cava. A transthoracic echocardiogram shows the involvement of the right heart cavities. Laboratory findings: Valued for oncology services without being a candidate for any therapy.

**Conclusions:** We present a case with symptoms compatible with acute Budd Chiari syndrome with extension to the right atrium and right ventricle secondary to hepatocellular carcinoma. Due to the extension of the tumor, it was not a candidate for surgical therapy, thrombolysis or systemic therapy, presenting with a torpid evolution. Metastasis to the inferior vena cava and right atrium secondary to HCC are uncommon. Imaging studies play an important role in determining the type of lesion and its extension. There are few investigations on treatment since high mortality rates are reported with the performance of lumpectomy combined with thrombectomy. Gaining relevance in the search for therapeutics mainly in tertiary level hospitals and in the scrutiny to rule out HCC and HBV infection in a timely manner.

### Ethical statement

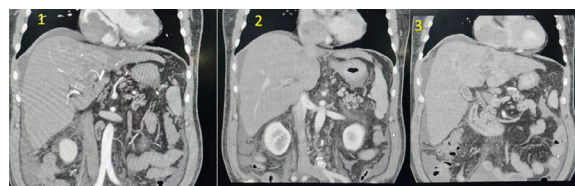
The identity of the patients is protected. Consentment was obtained.

### Declaration of interests

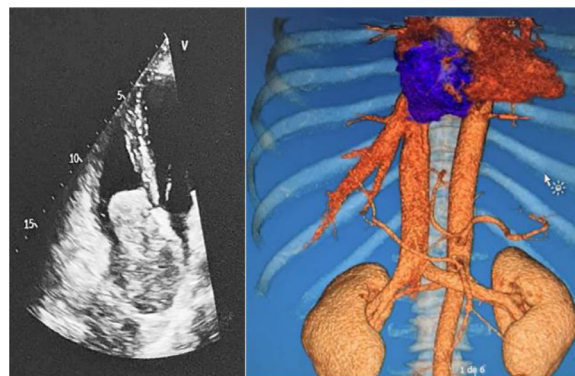
None

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



**Figure 1:** Triphasic computed tomography. 1) Arterial phase: arterial enhancement stronger than the surrounding liver (wash-in). 2) Venous phase: hypodensity or hyposignal intensity compared to the surrounding liver (wash-out) in the venous phase.



**Figure 2:** Comparison between echocardiography and tomographic reconstruction

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## Pirfenidone decreases insulin, glucagon, leptin, plasminogen activator inhibitor 1, preventing nonalcoholic steatohepatitis and myocarditis in an obesity model

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**Introduction and Objectives:** Obesity is an epidemic in the world, linked with insulin resistance, nonalcoholic steatohepatitis (NASH), and cardiovascular diseases (CVDs), being the latter main cause of global death. NASH progresses with inflammation with or without hepatic fibrosis, including a hormonal dysregulation. Pirfenidone (PFD) have anti-inflammatory and anti-fibrotic effects. However, its effects on hormonal regulation are completely unknown. The aim of this study was to investigate the effects of PFD on hormonal expression levels, related to the lipids and carbohydrates metabolism in high-fat/high-carbohydrate (HFHC)-diet-induced obese male C57BL/6J mice.

**Materials and Patients:** Twenty-week-old mice were fed with normal diet (ND, 3.1 kcal/g, n=7) and HFHC (65.1 kcal/g, water with 2.31% fructose and 1.89% sucrose, n=14) diet for 16 weeks; at 8 weeks, seven mice with HFHC were administered PFD (300 mg/kg/day) by gavage. ITT, ELISA, dry-chemistry, ELISA, histologies and SPSS were analyzed.

**Results:** HFHC mice development NASH and myocarditis with fibrosis in both tissues ( $P \leq 0.05$ ). HFHC showed elevated resistin and

aspartate aminotransferase ( $P \leq 0.05$ ). Parameters significantly increased in HFHC ( $P \leq 0.05$ ), were ameliorated by PFD, such as weight (body, liver, and heart), tibia length, epididymal fat, hepatic steatosis, hormones (insulin, glucagon, leptin, plasminogen activator inhibitor 1), lipid profile (total cholesterol, triglycerides, LDL, and VLDL), as well as inflammatory foci and fibrosis in hepatic and cardiac tissue ( $P \leq 0.05$ ). Moreover, PFD reduced alanine aminotransferase ( $P \leq 0.05$ ).

**Conclusions:** In the current work, we showed that PFD increases hormone expression levels, which are implicated in the lipids and carbohydrates metabolism, and also improves expression levels of lipid profile and lipoproteins related with NASH and CVDs. These findings contribute and support the potential therapeutic of PFD for the prevention of NASH and cardiovascular disease development induced by obesity.

### Ethical statement

All experiments in the mice were done and results were reported in accordance with the ARRIVE guidelines. The protocol was approved by the CUCS Research

Committee at the University of Guadalajara (protocol number: CI-01419).

### Declaration of interests

None

### Funding

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### Metabolic dysfunction-associated fatty liver disease in overweight and obese pediatric population: clinical and biochemical characterization

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**Introduction and Objectives:** Metabolic dysfunction-associated fatty liver disease (MAFLD) is currently the most common chronic liver disease in children and adolescents. In Mexico, there are no studies that demonstrate its incidence and prevalence, nor its clinical and biochemical characteristics; we don't have a clinical practice guideline, nor guidelines for screening, treatment, and follow-up. Our objective is to identify the clinical and biochemical features of MAFLD in overweight and obese pediatric patients.

**Materials and methods:** Observational, descriptive, ambispective and cross-sectional study. Patients were recruited from the Pediatric Gastroenterology outpatient clinic of the University Hospital of Puebla for a period from 2019 to 2022, selecting those with overweight and obesity, who were confirmed with a diagnosis of MAFLD through biochemical and imaging tests.

**Results:** 38 patients met criteria; 63.2% ( $n=24$ ,  $\pm 4.03$ ) correspond to the male sex, compared to 36.8% ( $n=14$ ,  $\pm 3.56$ ) of the female sex. It was more frequent in adolescents (78.9%) and with a higher proportion of patients with obesity (76.3%); no school patient was diagnosed as overweight; all patients in this age group presented obesity at the time of diagnosis.

The total number of patients who presented ALT elevation in diagnostic criteria was 52.6%. Regarding metabolic alterations, the following were found more frequently: Hypoalbuminemia (50%), Hypertriglyceridemia (42.1%) and elevation of HOMA-IR (91.9%). When evaluating Vitamin D levels, all were altered in insufficiency (42.9%) and deficiency (57.1%). NonHDLc/HDLc index levels have a statistically significant correlation ( $p=0.039$ ) with ALT levels.

**Conclusions:** MAFLD development is more frequent in male adolescents who are overweight and obese. Using ALT levels as criteria for hepatic steatosis by biochemical marker in the absence of an imaging study may facilitate diagnosis in the MAFLD algorithm. The indices associated with lipid levels (TG/HDLc and nonHDLc/HDLc) may indicate an increased risk for developing MAFLD.

### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

### Declaration of interests

None

### Funding

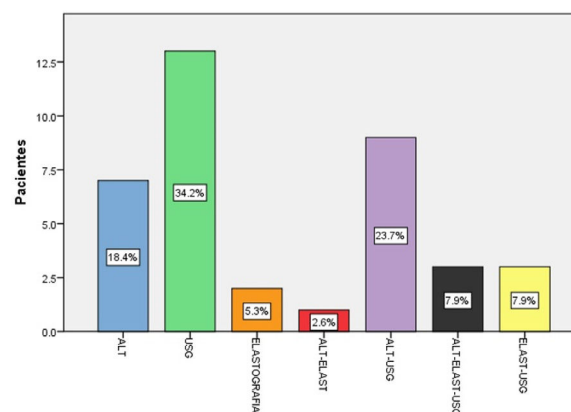
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Table 1**

Anthropometric and biochemical data for overweight and obesity

| Variable                 | Overweight (n=9)<br>Media y DS | Obesity (n=29)<br>Media y DS | p            |
|--------------------------|--------------------------------|------------------------------|--------------|
| Age                      | 14 (1.73)                      | 12.5 (3.68)                  | <b>0.013</b> |
| Stature (mts)            | 1.63 (0.08)                    | 1.55 (0.16)                  | 0.163        |
| Weight (kg)              | 67.93 (10.11)                  | 68.37 (20.4)                 | 0.931        |
| CC (cm)                  | 93.35 (9.57)                   | 90.99 (11.08)                | 0.609        |
| IMC (kg/m <sup>2</sup> ) | 25.16 (2.22)                   | 27.47 (4)                    | 0.110        |
| ALT (U/L)                | 50.66 (26.5)                   | 72 (82.4)                    | 0.452        |
| AST (U/L)                | 42.11 (21.8)                   | 43.84 (35.39)                | 0.891        |
| CT (mg/dl)               | 167.88 (46.5)                  | 147.5 (40.3)                 | 0.263        |
| LDL (mg/dl)              | 90.62 (37)                     | 73.97 (25.54)                | 0.144        |
| HDL (mg/dl)              | 42.28 (16.82)                  | 42.99 (18.67)                | 0.921        |
| TG (mg/dl)               | 175.88 (105.33)                | 140.15 (77.42)               | 0.285        |
| Insulin (uU/ml)          | 21.02 (6.44)                   | 25.73 (13.4)                 | 0.166        |
| Glucose (mg/dl)          | 90.22 (4.99)                   | 89.46 (6.63)                 | 0.703        |

Statistically significant p values were underlined. mts: meters, kg: kilograms, cm: centimeters, mg/dl: milligrams/deciliters, uU/ml: microunits per milliliter.



**Figure 1.** Type of diagnosis

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## Sword of Damocles: a hard blow from hepatitis A.

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**Introduction and Objectives:** The global incidence of liver failure associated with hepatitis A virus infection is reported in 0.5% of all cases, among which the associated risk factors are age over 40 years and pre-existing liver disease, and about 40% of the cases require liver transplantation.

**Materials and Patients:** A 29-year-old man, previously healthy and without any identified risk factors. One week prior to his admission, after eating shellfish, he presented intense colicky abdominal pain without radiation, nausea, vomiting, abundant non-steatorrhea, diarrheal stools, and unquantified fever.

He went to a private clinic where unspecified medication was administered and an abdominal ultrasound was performed, where hepatomegaly was reported. Laboratory studies showed alteration in liver biochemistry integrating hepatocellular damage 10 times above the normal upper limit as well as prolongation of coagulation times. Three days after the onset of the symptoms, generalized jaundice, aggressiveness and drowsiness were added, for which he was referred to our hospital unit. Upon admission, he presented a stupor and was taken to invasive mechanical ventilation.

**Results:** The approach was started, and results were reactive for IgM to hepatitis A virus and non-reactive for HIV, hepatitis B and C viruses. He remained intubated for five days and presented acute kidney injury that required hemodialysis and coagulopathy without presenting clinical data of bleeding; subsequently, he gradually presented clinical and laboratory improvement, and after 12 days of hospitalization, he was discharged home.

**Conclusions:** In the approach to acute liver failure, it is important to consider infection by the hepatitis A virus, because, despite the fact that the incidence of infection in Mexico is 5%, not all of the Mexican population has access to the vaccination and is the only effective measure to prevent this disease.

In the case of our patient, he did not present these risk factors and had a spontaneous recovery. Within the approach to fulminant hepatitis, it is important to consider infection by the hepatitis A virus, because even though the incidence in our country is 5%, not the entire Mexican population has access to vaccination.

### Ethical statement

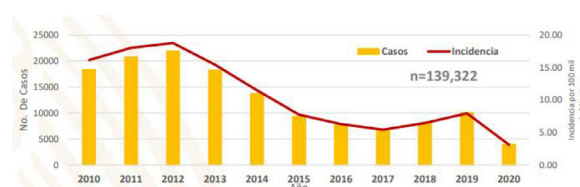
The identity of the patients is protected. Consentment was obtained.

### Declaration of interests

None

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



**Figure 1.** Cases and incidence per year of hepatitis A virus infection in Mexico



**Figure 2.** Cases and incidence by state of hepatitis A virus infection

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## Retreatment experience with Glecaprevir/ Pibrentasvir (G/P) for hepatitis C infection in patients failing first-line direct-acting antiviral agents.

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**Introduction and Objectives:** First-line direct-acting antiviral agents (DAAs) achieved a sustained viral response (SVR) in >95%, failure to follow the scheme is rare and the option of retreatment with sofosbuvir/velpatasvir/voxilaprevir does not exist in our setting, therefore although G/P is considered an alternative, it is the only available option. There are few reports evaluating it; due to this, we describe the frequency and characteristics of patients with failure to first-line DAA schemes and the result of retreatment with G/P during the period from January 2017 to January 2023 in 3 tertiary hospital centers.

**Materials and Patients:** The intentional search for cases with failure to achieve SVR with first-line DAAs was carried out in 2 Mexican reference centers and one Ecuadorian center during the period from January 2017 to January 2023. Characteristics and results of patients treated with the scheme were documented. of G/P. No conflict of interest was reported by the researchers.

**Results:** From a total of 2,397 HCV-infected patients treated with the first-line DAA scheme, without cirrhosis or with compensated cirrhosis, a total of 9 patients presented virological failure, the average



age was 52.4 years, five women and four men, of these, six patients had fibrosis grade F4, 3 of them F1, the predominant genotype was 1a, the initial regimens were SOF/VEL or SOF/LED in the majority, only one case used Paritaprevir/Ritonavir/Ombitasvir/Dasabuvir + Ribavirin, all the patients re-treated with G/P had SVR at 12 weeks, no resistance profile was routinely performed, adverse effects were mild, and were reported in 22.2% of the total, none of them abandoned treatment.

**Conclusions:** First-line DAAs are effective; virological failure in our sample is lower (0.37%) than reported in the literature. G/P is an effective and safe scheme for retreatment of patients with failure without cirrhosis or with compensated cirrhosis (100% response in our study), without serious adverse effects, which makes it possible to eliminate and meet the WHO 2030 goals.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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#### Hepatitis A at the Hospital de Especialidades Centro Medico Nacional La Raza. Preliminary report.

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María C. Bernardino-del Río,  
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**Introduction and Objectives:** The hepatitis A virus in our country is an endemic disease with a benign course that presents in early stages of life, generating lasting immunity so that the frequency of presentation decreases in adulthood. Serious cases often occur at the extremes of life. We have observed an increase in cases of Hepatitis A requiring hospitalization with severe liver dysfunction.

This study aimed to determine the clinical, biochemical, complications, and mortality characteristics of patients with acute hepatitis A virus admitted to a tertiary-level hospital.

**Materials and Patients:** A descriptive, cross-sectional, retrospective, observational study was carried out in patients with acute hepatitis A virus hospitalized in the Gastroenterology service of the Hospital de Especialidades CMN La Raza from February 2022 to April 2023. Age, gender, clinical presentation, complications, and comorbidities were assessed. The results were analyzed with relative and central frequency measures to obtain percentages, mean, and arithmetic mean.

**Results:** 31 patients were registered, 29 men (94%) and two women (6%). The average age was 35 years (18–56). 11 patients (35%) presented acute liver failure, and 1 case was a prolonged cholestatic atypical hepatitis. The most frequent complications presented during

the hospital stay were the following: coagulopathy (INR>1.5) 64%, acute kidney injury 38%, anemia 35%, encephalopathy 35% (Table 1). Mortality was 13% (4 patients) due to acute liver failure and without comorbidities. The average of relevant biochemical alterations: AST 1849 U/L, ALT 2602 U/L, total bilirubin 18.24 mg/dL, creatinine 2.05 mg/dL, INR 2.56. (Table 2). 64% of patients had no comorbidities. The comorbidities found were cirrhosis, polycystic liver disease, essential thrombocytosis, multiple sclerosis, Evans syndrome, arterial hypertension, diabetes, obesity, dyslipidemia and HIV.

**Conclusions:** The presence of acute liver failure and mortality in our population was high in comparison to what has been reported in the international literature. Coagulation disorders, acute kidney injury and anemia were the most frequent complications in our cases of hepatitis A. It was relevant that most of the patients were <40 years old and 94% were male.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Table 1**

Complications presented in patients with acute hepatitis A infection.

| COMPLICATIONS             | N  | %    |
|---------------------------|----|------|
| Coagulopathy              | 20 | 64.5 |
| Acute Kidney Injury       | 12 | 38.7 |
| Anemia                    | 11 | 35.4 |
| Encephalopathy            | 11 | 35.4 |
| Thrombocytopenia          | 6  | 19.5 |
| Acute Pancreatitis        | 1  | 3.2  |
| Cerebral Haemorrhage      | 1  | 3.2  |
| Rhabdomyolysis            | 1  | 3.2  |
| Intracranial Hypertension | 1  | 3.2  |

**Table 2**

Biochemical alterations in patients with acute hepatitis A infection.

| VALUES                  | MIN  | MAX  | MEAN    | ST      |
|-------------------------|------|------|---------|---------|
| Total Bilirubin (mg/dL) | 4    | 45.6 | 18.3    | ± 9.49  |
| Creatinine (mg/dL)      | 0.7  | 8.07 | 2.02    | ±2.09   |
| INR                     | 1.01 | 9.29 | 2.4     | ±2.01   |
| AST(U/L)                | 88.7 | 5527 | 1795.1  | ±1619.2 |
| ALT(U/L)                | 137  | 5810 | 2499.03 | ±1507.3 |

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#### Chronic liver damage in hemodialysis users. The importance of molecular tests for detection of hidden infection by hepatotropic viruses in high-risk groups

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**Introduction and Objectives:** Worldwide, cirrhosis secondary to the hepatitis C virus is the first indication for liver transplantation. In Mexico, alcohol abuse, viral hepatitis, and obesity are the highlighted causes. Hepatitis C virus (HCV) eradication leads to reduced morbidity, mortality and transmission. Hemodialysis users are a high-risk group with high prevalence of HCV. The aim of this study was to identify patients with liver damage in hemodialysis users and their relationship with viral hepatitis, diagnosis, and management.

**Materials and Patients:** We reviewed the electronic medical records of hemodialysis users from January 1, 2017, to December 31, 2019. All patients who underwent at least one hemodialysis procedure were included. We used descriptive statistics with the SPSS v21 program.

**Results:** We analyzed 362 patients, 57% of whom were men, with a mean age of 52. The most frequent etiology attributable to kidney damage was hypertension 96% and diabetes mellitus 59%. The mean time on hemodialysis was 19 months. The biochemical and serological characteristics of the group are shown in Table 1. We found forty-seven patients with transaminasemia, of which thirteen had liver cirrhosis, evaluated by FIB4/APRI. A viral load was requested for hepatitis C in only one patient, with a positive result, who received treatment with glecaprevir/pibrentasvir for 12 weeks without complications. Retrospective review limits us in identifying the cause for which the patients did not undergo molecular tests for hepatitis B and C. These patients have significant depression of immunity with negative serology on the presence of viral replication "hidden infection."

**Conclusions:** Hemodialysis users should be exhaustively studied, and molecular tests should be performed on suspicion of viral hepatitis.

## Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

## Declaration of interests

None

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Table 1**  
Biochemical and serological characteristics of hemodialysis users

| Variable                | Without transaminasemia<br>n=315 | With transaminasemia<br>n=47 |
|-------------------------|----------------------------------|------------------------------|
| Hemoglobin g/dL         | 9                                | 9                            |
| Platelet K/ $\mu$ L     | 228                              | 217                          |
| AST                     | 23                               | 74                           |
| ALT                     | 25                               | 70                           |
| Antibodies HBV, HCV (n) |                                  |                              |
| 2017 y (32)             | 27                               | 5                            |
| 2018 y (101)            | 89                               | 12                           |
| 2019 y (229)            | 200                              | 29                           |

Footer: y (year)

## Epidemiology and demographic aspects in patients with acute on chronic liver failure in a third-level care hospital in Mexico.

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**Introduction and Objectives:** Patients presenting with acute on chronic liver failure (ACLF) is a syndrome characterized by acute decompensation of cirrhosis associated with failures of different organs as well as leading to high mortality in the short term, being its demographic and epidemiological characteristics important points to evaluate predictors of poor prognosis in this group of patients. This study aimed to characterize the demographic aspects of patients with acute on chronic in the Mexican population.

**Materials and Patients:** A retrospective, observational, descriptive and unicentric study was carried out, which included patients with a confirmed diagnosis of ACLF who had been hospitalized during the period from 2017 to 2022 in the gastroenterology service of Centro Médico Nacional Siglo XXI "Bernardo Sepulveda," IMSS.

**Results:** 186 patients were included, 95 women (51%) and 91 men (49%) being more prevalent in the range between 56-65 years 59 patients (32%). The most frequent etiology of cirrhosis was NAFLD (esteatohepatitis not alcoholic) in 54 (29%) and ethylism in 42 (23%). A MELD of 31-35 predominated in 50 patients (27%) and a Child Pugh C in 163 patients (87%). The antecedent of at least one previous decompensation was found in 161 (85%), the most common being ascites in 141 (76%) followed by hepatic encephalopathy in 95 (51%). 25 patients (13%) had no previous decompensation. The infection was identified as precipitating in 111 (60%) and without precipitating factor identified in 21 (11%). The most frequently identified infectious focus was abdominal in 60 (36%) and urinary in 40 (24%). The most frequent isolated agent was *Escherichia coli* in 22 (12%). Hepatorenal syndrome was found in 12 patients (6%). At admission, grade I ACLF occurred in 37 (20%), grade II 72 (39%), grade III 77 (49%) with a predominant CLIF C between 51-60 points in 99 patients (53%) requiring an average of 8 days of hospitalization.

**Conclusions:** We found that the ACLF does not present gender predilection as being more frequent between 56-65 years. The main etiology of cirrhosis was NAFLD, the majority being found in Child-Pugh C. Most have a history of at least one decompensation, the most frequent being ascites. 13% debuted with ACLF as the first decompensation. The most common precipitant was infectious, with the abdominal focus manifested as PBE as the main one. The most common agent was *Escherichia coli*. At admission, ACLF grade III was the most common.

## Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

## Declaration of interests

None

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Table 1. Baseline characteristics of patients with ACLF**

| Characteristics                | No. patients | Percentage |
|--------------------------------|--------------|------------|
| Average age                    |              |            |
| 56 years                       |              |            |
| Gender                         |              |            |
| Female                         | 95           | 51%        |
| Male                           | 91           | 49%        |
| Etiology                       | No. patients | Percentage |
| Bile duct atresia              | 1            | 1%         |
| CBP                            | 13           | 7%         |
| CBP/HAI                        | 8            | 4%         |
| CEP                            | 5            | 3%         |
| Portal cholangiopathy          | 1            | 1%         |
| Alpha 1 antitrypsin deficiency | 1            | 1%         |
| NAFLD                          | 54           | 29%        |
| Wilson's disease               | 1            | 1%         |
| Ethylism                       | 42           | 23%        |
| HAI                            | 10           | 5%         |
| Not determined                 | 20           | 11%        |
| HBV                            | 4            | 2%         |
| HCV                            | 25           | 13%        |
| HCV/CBP                        | 1            | 1%         |
| CLIF C ACLF                    |              |            |
| 71-80                          | 4            | 2%         |
| 61-70                          | 41           | 22%        |
| 51-60                          | 99           | 53%        |
| 41-50                          | 38           | 20%        |
| 31-40                          | 4            | 2%         |
| MELD                           |              |            |
| 51-55                          | 2            | 1%         |
| 46-50                          | 10           | 5%         |
| 41-45                          | 20           | 11%        |
| 36-40                          | 39           | 21%        |
| 31-35                          | 50           | 27%        |
| 26-30                          | 32           | 17%        |
| 21-25                          | 26           | 14%        |
| 16-20                          | 7            | 4%         |

CBP: Primary biliary cholangitis, AIH. Autoimmune hepatitis. CEP: Primary sclerosing cholangitis. NAFLD: Steatonepatitis not alcoholic. HCV: hepatitis C virus. HBV: hepatitis B virus. CLIF C ACLF: scale for mortality of acute on chronic liver failure. MELD: Model for end-stage liver disease

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### CLIF-C-ACLF scale to predict mortality in pediatric patients with acute-on-chronic liver failure

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**Introduction and Objectives:** The acute decompensation of liver cirrhosis associated with organ failure is known as acute-on-chronic liver failure (ACLF); in pediatrics, it develops >22%, with mortality >33% per month; Based on prognosis, CLIF-C ACLF is a score with greater discriminative capacity to predict short-term mortality (25%) compared to already established scales, which require more complex variables. To describe the utility of the CLIF-C ACLF scale in pediatrics. Specific: In children with cirrhosis who developed ACLF: Describe the sociodemographic, clinical, and biochemical characteristics; Determine the MELD, PELD, Child Pugh, AARC and CLIF-C ACLF scales and compare their predictive value.

**Materials and Patients:** Retrospective cohort, age: 6 months to 18 years, temporality: March 2018 - February 2022. Frequency and percentage were reported for qualitative variables, and median variables and range for quantitative variables; Inferential with Pearson and Spearman correlation between the scales at admission, 28 and 90 days, an area under the receiver operating characteristics (AUROC) and Whitney U were calculated.

**Results:** Out of 95 cases with chronic liver disease, 63.1% presented ACLF, mostly stage II (35.3%). The female sex predominated (72.1%) and bile duct atresia was the most common entity (80%), with a mean age at diagnosis of 38 months and mortality of 55%. Ascites (97%) and hepatic encephalopathy (58.3%) were the main complications. The major precipitating factors described were infections (57.4%): bacterial cholangitis (16.2%) and pneumonia (8.8%). Through AUROC we compared CLIF cACLF with PELD, MELD, Child Pugh and AARC, observing greater statistical significance at 28 and 90 days (sensitivity: 0.63, specificity: 0.85) and through the U test, we observed that coagulopathy is the biochemical index with higher prediction for acute decompensation in ACLF.

**Conclusions:** CLIF-C ACLF compared to ACLF scores predicted increased risk of 28-day mortality (AUROC: 0.758) relative to PELD, MELD (AUROC: 0.721), Child Pugh (AUROC: 0.746), AARC (AUROC: 0.621), and at 90 days (AUROC: 0.663) with PELD, MELD (AUROC: 0.505), Child Pugh (AUROC: 0.598), AARC (AUROC: 0.357). We established a CLIF-C ACLF score  $\geq 77.5$  as a high predictor of mortality (95% CI). The scale is useful in pediatrics.

### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

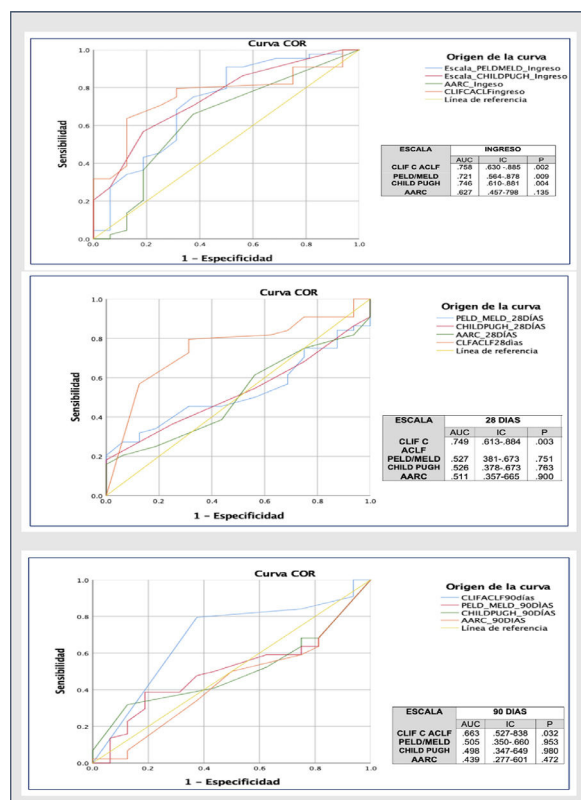
### Declaration of interests

None

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

# **AUROC of CLIF-C ACLF, MELD/PELD, Child Pugh, AARC in predicting at admission, 28- and 90 - days mortality.**



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## **Extrahepatic disease in a cohort of HCV infected patients successfully treated with direct acting antivirals. One year follow up.**

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**Introduction and Objectives:** The hepatitis C virus (HCV) infects hepatocytes and B lymphocytes. The ability to infect B lymphocytes has been linked to cryoglobulinemia, cryoglobulinemia syndrome, lymphomas, and organ-specific and systemic autoimmune diseases (AD). Among the AD, diabetes mellitus, thyroiditis, and Sjögren syndrome stand out as extrahepatic diseases (EH). The aim of a study was identify HCV-related EH, during infection and one year after successfully direct-acting antiviral (DAA) treatment

**Materials and Patients:** We conducted a prospective study in a Regional Hospital of reference for the treatment of Hepatitis C, from 14 hospital units in the Northeast of Mexico. From June 15, 2018, to January 1, 2023.

**Results:** Of 364 patients with positive serology, 153 had viremia, and 127 received DAA, with different schemes aligned to the guidelines of treatment of hepatitis C. 50% were women, with a mean age of 54. 80% received regimens based on sofosbuvir. 96.8% achieved a

sustained viral response 12. Before the treatment with DAA, we identified nine hypothyroidisms, eight cryoglobulinemic vasculitis, one with anemia and thrombocytopenia autoimmune, and 25 with diabetes. At basal visit for treatment, 17 hypothyroidisms, eight prediabetes, eight diabetes, one lymphoma, one monoclonal gammopathy of uncertain significance, three rheumatoid arthritis, and three hepatocellular carcinomas. At one year of follow-up, plus sixteen with diabetes mellitus, three with hepatocarcinoma, 6 with xerophthalmia, and one with breast cancer, increasing obesity, and fatty liver were identified.

**Conclusions:** EH is frequent and carries out morbidity, especially proliferative disorders of B lymphocytes and AD as some can persist even after the treatment of HCV infection. The intentional search for EH should be mandatory and, once identified, will be multidisciplinary follow-up, for the timely identification of worsening or malignant transformation, to offer timely diagnosis and treatment.

## **Ethical statement**

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

## **Declaration of interests**

None

## **Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

<https://doi.org/10.1016/j.aohep.2024.101415>

## **Evaluation of the hepatoprotective effect of an hydroalcoholic extract of *Jatropha dioica* against the damage induced by valproic acid in Wistar rats**

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**Introduction and Objectives:** Liver diseases have gained importance due to their prevalence, incidence and because most chronic liver diseases have no cure, except for hepatitis C. Liver damage induced by drugs such as valproic acid (VPA) has been used to study therapeutic alternatives. *Jatropha dioica* may be one of these alternatives as it has metabolites with potential antioxidant activity. The objective of this study was to evaluate the hepatoprotective effect of a hydroalcoholic extract of *J. dioica* against VPA-induced damage in Wistar rats.

**Materials and Patients:** 24 Wistar rats of both sexes were used. Groups: Sham (SH), Non-Toxicity(JdTox), VPA and *J. dioica*+VPA (JdVPA) (n=6). *J. dioica* (300 mg/kg, p.o) was administered for 7 days, followed by VPA (500 mg/kg, i.p, for four days) injected concomitantly. Biochemical markers, oxidative stress, and histological analysis were determined. Ethics Committee approval under HI22-00003 registry and PAICYT 143-CS-2022 financing. The research group declares no conflict of interest.

**Results:** VPA group showed a significant increase in ALT and AST against Sham, JdVPA group showed a significant decrease in these parameters vs. VPA (Figure 1), and the remaining biochemical markers showed no statistically significant differences between the groups. The VPA group presented statistically significant alterations in the concentrations of malondialdehyde (MDA), reduced glutathione (GSH), and superoxide dismutase (SOD) vs. SH. The JdVPA group significantly improved the damage caused by VPA, decreasing MDA and increasing GSH and SOD (Figure 2). Histologically, VPA presented an inflammatory infiltrate, which decreased in the JdVPA group. However, this difference was not statistically significant.

**Conclusions:** In murine models, VPA has been able to induce alterations in transaminase levels and oxidative stress markers, both of which may indicate the presence of liver damage. Plants of the *Jatropha* genus have been shown to possess phenolic and flavonoid compounds with antioxidant capacity, which may be responsible for the hepatoprotective effect observed in this study using *J. dioica* at the evaluated dose without showing toxicity.

#### Ethical statement

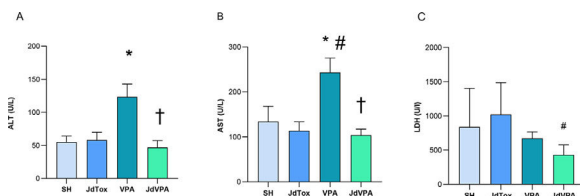
The protocol was registered and approved by the Ethics Committee.

#### Declaration of interests

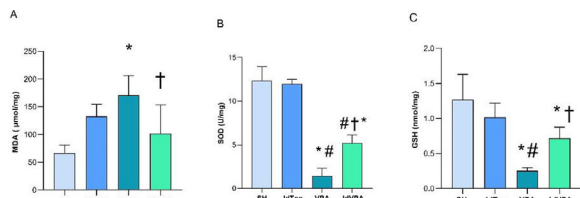
None

#### Funding

Funding for this project came from PAICYT under registration number 143-CS-2022.



**Figure 1. Serum biochemical markers.** (A) Serum ALT levels, \*P=0.036 vs. SH, †P=0.0015 vs. AVP-C. (B) Serum AST levels, \*P<0.0001 vs. SH, #P<0.0001 vs. JdTox, †P<0.0001 vs. AVP-C. (C) Serum LDH levels, #P<0.0498 vs. JdTox. Kruskal-Wallis with Dunn's post hoc (A) and One-way ANOVA with Tukey's post-hoc (B-C)



**Figure 2. Liver tissue concentrations of oxidative stress biomarkers.** (D) MDA, \*P=0.0012 vs. SH, †P=0.0283 vs. AVP-C. (E) SOD, \*P<0.0001 vs. SH, #P<0.0001 vs. JdTox, †P<0.0003 vs. AVP-C. (F) GSH, \*P<0.007 vs. SH, #P=0.0007 vs. JdTox, †P=0.0221 vs. AVP-C. One-way ANOVA with Tukey's post-hoc (A-C)

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#### Evaluation of the hepatoprotective effect of *Flourensia cernua* against the damage induced ischemia-reperfusion in Wistar rats.

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**Introduction and Objectives:** Liver transplantation is the optimal treatment in patients with irreversible liver damage. The principal complication of a transplant is ischemia-reperfusion injury (I/R), which induces primary graft rejection. Treatment with plant extracts prior to I/R has decreased the severity of this injury due to their potential anti-inflammatory and antioxidant activity. A plant that presents potential antioxidant activity is *Flourensia cernua* (Fc). The objective was to evaluate the hepatoprotective effect of *Flourensia cernua* against the damage induced by ischemia-reperfusion in Wistar rats.

**Materials and Patients:** 42 mixed Wistar rats were sorted into 7 groups (n=6). Fc was administered (200 mg/kg, p.o/5 days) followed by I/R clamping of the left portal triad producing 1hr of 70% ischemia and 2 or 24hrs of reperfusion. Biochemical and oxidative stress biomarkers, proinflammatory cytokine and gene expression were determined. Ethics Committee approval under HI17-00002 registry and PAICYT 152-CS-2022 financing. The research group declares no conflict of interest.

**Results:** The I/R groups with 2 (IR2hr) and 24 hour (IR24hr) reperfusion displayed significantly elevated ALT and AST concentrations vs. Sham (SH); only FcIR2hr significantly decreased these enzymes (Figure 1). The remaining biochemical parameters did not show any significant differences between the groups. IR2hr group induced a statistically significant alteration of oxidative stress biomarkers, Fc counteracted these effects, with a decrease of malondialdehyde (MDA) and an increase of reduced glutathione (GSH) and the superoxide dismutase(SOD) (Figure 2). The gene expression of NFκβ was increased in IR2hr group, the treatment with *F. cernua* counteracted this increase. TNF-α was significantly increased in the IR2hr group and decreased in the treatment group.

**Conclusions:** I/R is a widely studied injury model, capable of inducing pathological changes in several spheres, not unlike the observed results in the present study; the hydroalcoholic extract of Fc displayed anti-inflammatory and antioxidant activity at 200mg/kg, it was not toxic and proved to be hepatoprotective against I/R.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee.

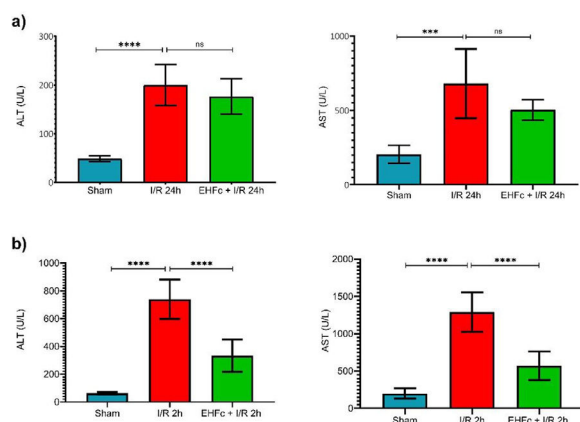
#### Declaration of interests

None

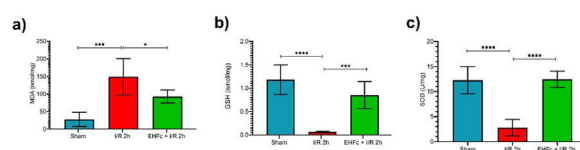
#### Funding

Financing from PAICYT 152-CS-2022





**Figure 1.** Evaluation of the hepatoprotective activity of the hydroalcoholic extract of *Flourensia cernua* (EHFc). Levels of serum ALT and AST in different study groups. a) I/R at 24h after reperfusion, b) I/R at 2h after reperfusion. (Mean  $\pm$  SD. \*\*\*\*  $P < 0.0001$ , \*\*\*  $P < 0.001$  vs. the I/R group;  $n = 6$  for each group). Sham (healthy control group), I/R (damage control group), EHFc + I/R (treatment group).



**Figure 2.** Evaluation of oxidative stress in hepatic tissue. a) Malonaldehyde (MDA), b) Reduced glutathione (GSH), c) Superoxide dismutase (SOD). (Mean  $\pm$  SD. \*\*\*\*  $P < 0.0001$ , \*\*\*  $P < 0.001$ , \*  $P < 0.05$  vs. the I/R at 2h after reperfusion group;  $n = 6$  for each group). Sham (healthy control group), I/R (damage control group), EHFc + I/R (treatment group).

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## Overlap syndrome: Report of a case and review of the literature.

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**Introduction and Objectives:** Autoimmune liver disorders, like autoimmune hepatitis, primary biliary cholangitis, and primary sclerosing cholangitis, are characterized by an atypical immune response that targets bile duct damage in primary biliary cholangitis and significant portal and lobular lymphoplasmacytic inflammation in autoimmune hepatitis. Most patients have no difficulty distinguishing between the two entities. However, certain individuals exhibit symptoms of a confluence of two autoimmune liver disorders, referred to as Overlap Syndrome.

We present the case of a woman who has been diagnosed with primary biliary cholangitis with some features of autoimmune hepatitis.

**Materials and Patients:** A 48-year-old woman presents with a 3-year history of jaundice, night-time pruritus, fatigue, and a 10-kilogram weight loss. Her medical record includes arterial hypertension for one year of evolution and weekly consumption of 50 g of alcohol for 20 years.

**Results:** Blood analysis showed BT 1.4, BD 0.63, TGO 236, TGP 220, FA 2505, DHL 441, AFP 1.89, CA19-9 6.43, and a negative viral panel.

Liver ultrasonography showed early-stage liver cirrhosis. Endoscopy revealed erosive gastritis. A percutaneous liver biopsy showed portal and periportal nonspecific chronic inflammation with localized necrosis. The patient was prescribed ursodeoxycholic acid TID and prednisone 50 mg QD based on the initial suspicion that he had primary biliary cholangitis. At a subsequent appointment, she presented AST 132, ALT 114, FA 583, GGT 474, positive ASMA, and ANA 1:160. The diagnosis of an overlap syndrome between primary biliary cholangitis and autoimmune hepatitis was made in accordance with the Paris criteria. The patient received prednisone 25 mg QD, azathioprine 50 mg QD, and ursodeoxycholic acid TID.

**Conclusions:** In the present case report, the patient's condition progressed, manifesting symptoms indicative of chronic liver injury. Immunosuppressants and ursodeoxycholic acid were administered according to guidelines, improving symptoms and biochemical indicators. Liver biopsies and noninvasive methods for liver fibrosis staging and disease progression deserve further investigation.

Autoimmune liver disorders are distinguished by an atypical immune reaction that targets the hepatocytes or bile ducts. Certain individuals exhibit symptoms of a co-occurrence of two medical conditions, referred to as Overlap Syndrome, which is associated with more severe outcomes. These outcomes include Crohn's disease, Sjögren's syndrome, cirrhosis, and hepatocellular carcinoma.

The variability of presentation and clinical characteristics in autoimmune liver disorders has made Overlap Syndrome classification, diagnosis, and treatment debated. The Paris criteria (Chazouillères 1998) are the most practical option for implementation due to their inherent simplicity and precision. Nevertheless, certain guidelines recommend against the utilization of the Paris criteria due to certain limitations. Future studies and validation of diagnostic and prognostic scores are needed for effective and timely therapy.

## Ethical statement

The identity of the patients is protected. Consentment was obtained.

## Declaration of interests

None

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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## One-year survival after liver transplantation in a group of geriatric patients

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**Introduction and Objectives:** Prevalence of patients with decompensated cirrhosis with requirement of liver transplantation (LT) has increased in our country. A significant percentage of patients with this condition belongs to a geriatric population, which could contraindicate LT, although trends in other countries indicate that the results of LT in geriatric patients are excellent.

To assess one-year survival of LT patients over 60 years

**Materials and Patients:** Retrospective, observational, and analytical study of patients over 60 years who underwent LT, evaluating survival, cold ischemia time (CIT), hot ischemia time (HIT), and donor age (DA), compared with a group of patients under 60 years who underwent LT.

We evaluated survival over time in months with a follow-up at one year of recipients under 60 years and older than 60 using the Kaplan-Meier curve and the log-rank test, with a significant alpha level <0.05.

**Results:** A total of 81 patients were included: 51 under (44.33 ±10.59) and 30 over 60 years (64.13 ±3.30), 31 females (38.27%) 50 males (61.72%). Etiologies of cirrhosis: alcohol intake 30.86%, autoimmune diseases 24.69%, MALFD 11%, hepatocellular carcinoma 9.88%. CIT and HIT in under and over 60 years were 313.64 ±97.69min and 29.91 ±6.14min, and 307.39 ±101.85min and 30.36 ±7.57min, respectively. DA was 35.55 ±14.33 years. Mortality rates were 11.76% (6/51) and 13.3% (4/30) in patients under and over 60 years, respectively, with a cumulative rate of 12.34% (10/81). The average survival in months was 12.27 (11.45-13.1, 95%CI) and 10.83 (9.6-12.0, 95%CI) in under and over 60 years, respectively. Comparison based on age was not statistically significant (log-rank test, Chi-square 1=0.742, p=0.389).

**Conclusions:** One year survival in geriatric patients after LT is equal to that of younger patients, indicating that age should not be a contraindication for LT.

#### Ethical statement

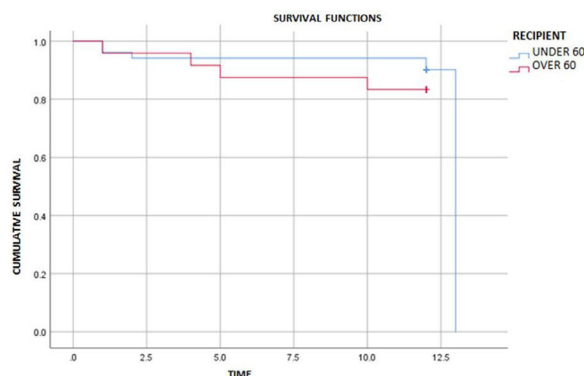
The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



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#### Development of hepatic steatosis in liver transplant recipient patients.

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**Introduction and Objectives:** It has been reported that up to 39.7% of liver transplant recipients develop hepatic steatosis at some point during follow-up, with recurrence being more likely than de novo appearance. Specifically in patients previously known to have MAFLD, this condition is favored by the components of the metabolic syndrome (particularly being overweight), to which is added the use of immunosuppressive drugs. The objective is to determine the prevalence of hepatic steatosis by ultrasound in patients receiving liver transplants at the Hospital de Especialidades del Centro Médico Nacional La Raza.

**Materials and Patients:** In this study were included liver transplant recipients treated in the period from 2017 to 2023 who had a liver ultrasound at least six months after transplantation. The diagnosis of hepatic steatosis was established by an increase in the echogenicity of the liver parenchyma, which is equal to or exceeds the echogenicity of the pancreas.

**Results:** A sample of 40 patients was analyzed, 19 men (47.5%) and 21 women (52.5%), with age of 52.05 ±10.49 years. The most common causes of liver disease were hepatitis C virus infection (32.5%), MAFLD (17.5%), and autoimmune hepatitis (15%). The most frequent comorbidity was diabetes (20%) (Chart 1). Hepatic steatosis was found in 25% of cases (50% men and 50% women) (Graph 1). The most frequent etiology of liver disease in patients who developed steatosis was MAFLD (20%), while in those who did not develop steatosis it was HCV infection (40%), without statistical significance. When compared with patients without steatosis, there were no statistically significant differences in post-transplant weight and BMI (69.2 vs. 67.0 kg, p= 0.601; BMI 26.0 vs. 25.0, p=0.529) or pre-transplant MELD (14.3 vs. 16.4, p= 0.251)

**Conclusions:** In our study, the prevalence of steatosis found was similar to that reported by other authors. They have not evidenced statistically significant differences in age, gender, comorbidities, anthropometry, or etiology of cirrhosis. Patients need close monitoring to identify the development of this complication in a timely manner.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Table 1**

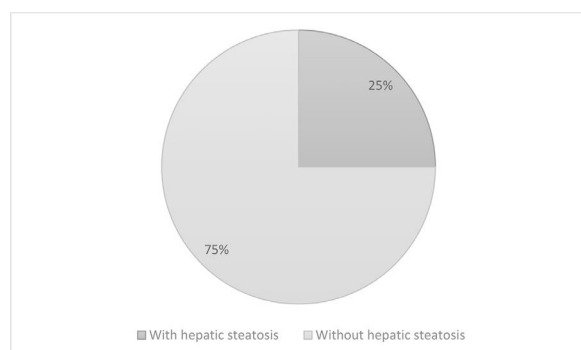
Characteristics of people who developed hepatic steatosis.

| Variable       | Patients who developed steatosis (%)<br>n= 10 (24.3) | Patients who didn't develop steatosis (%)<br>n= 31 (75.6) | p value      |
|----------------|------------------------------------------------------|-----------------------------------------------------------|--------------|
| Sex            |                                                      |                                                           | <b>0.023</b> |
| Male           | 8 (80)                                               | 12 (38.7)                                                 |              |
| Female         | 2 (20)                                               | 19 (61.2)                                                 |              |
| Age            | 52.4±12.3                                            | 51.3±10.3                                                 | 0.818        |
| Comorbidities  |                                                      |                                                           |              |
| Diabetes       | 4 (40)                                               | 4 (12.9)                                                  | 0.060        |
| Hypertension   | 1 (10)                                               | 2 (6.4)                                                   | 0.708        |
| Hypothyroidism | 0 (0)                                                | 4 (12.9)                                                  | 0.232        |
| Etiology       |                                                      |                                                           | 0.192        |
| MALFD          | 4 (40)                                               | 3 (9.6)                                                   |              |

(continued)

|                                     |          |           |              |
|-------------------------------------|----------|-----------|--------------|
| Autoimmune hepatitis                | 2 (20)   | 5 (13.8)  |              |
| Primary biliar cholangitis          | 1 (10)   | 2 (6.4)   |              |
| Primary sclerosing cholangitis      | 0 (0)    | 1 (3.2)   |              |
| Ethylism                            | 0 (0)    | 2 (6.4)   |              |
| Chronic hepatitis C virus infection | 2 (20)   | 11 (35.4) |              |
| AIH-PBC overlap                     | 0 (0)    | 4 (12.9)  |              |
| Polycystic disease                  | 0 (0)    | 3 (9.6)   |              |
| Cryptogenic                         | 1 (10)   | 0 (0)     |              |
| BMI pre-transplant                  | 27.5±3.7 | 24.0±3.1  | <b>0.032</b> |
| BMI pre-transplant interpretation   |          |           | <b>0.049</b> |
| Low                                 | 0 (0)    | 2 (6.4)   |              |
| Normal                              | 3 (30)   | 19 (61.2) |              |
| Overweight                          | 4 (40)   | 2 (6.4)   |              |
| Class 1 obesity                     | 3 (30)   | 1 (3.2)   |              |
| BMI post transplant                 | 27.6±3.7 | 24.8±2.9  | 0.054        |
| BMI post- trasplant interpretation  |          |           | 0.162        |
| Low                                 | 0 (0)    | 0 (0)     |              |
| Normal                              | 2 (20)   | 14 (45.1) |              |
| Overweight                          | 6 (60)   | 16 (51.6) |              |
| Obesity                             | 2 (20)   | 1 (3.2)   |              |

MASLD, metabolic dysfunction-associated steatotic liver disease; AIH, autoimmune hepatitis; PBC, primary biliary colangitis; BMI, body mass index.



**Figure 1.** Prevalence of steatosis in patients receiving liver transplantation.

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### Observational Study of Biliary Duct stenosis in patients with Post-Liver Transplant

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**Introduction and Objectives:** Liver transplant is a surgical procedure indicated in terminal hepatic diseases or patients who fail any other type of treatment. Complications of liver transplant are stenosis of biliary tract, with an incidence of 5–25%, which influences both morbidity and mortality.

Nowadays, treatment has evolved with Endoscopic Retrograde Cholangiopancreatography (ERCP). This treatment consists of dilation, prosthesis placement and stents.

The main objective of this study consists in describing the clinical characteristics, therapeutic strategies, results and impact in post-liver transplant patients with bile duct stenosis at the National Medical Center “20 de Noviembre”.

**Materials and Patients:** In this retrospective observational study, a total of 39 post-liver transplant patients who presented bile duct stenosis complications were included, receiving endoscopic treatment from 2018 to 2023 with ERCP at the National Medical Center “20 de Noviembre”.

**Results:** A total of 39 post-liver transplant patients with bile duct stenosis were included. The mean age was 49.8 years, with equal distribution between genders. The main causes of liver transplantation were autoimmune diseases (41%) and alcohol-induced liver cirrhosis (23%). The immunosuppressive treatment they received consisted of mycophenolate mofetil (MMF), tacrolimus, and prednisone in 92% of the cases. Regarding endoscopic procedures, a total of 163 ERCP were performed, an average of 4 per patient with prosthesis placement in 64%, mainly plastic (64%). Pneumatic dilation was the most used method (64%). The complication related to endoscopic procedure was cholangitis in 17.9%, without pancreatitis. Bile duct rehabilitation was successful in 64%. Three patients presented death, all related to graft rejection.

**Conclusions:** Bile duct stenosis is a significant complication in post-liver transplant patients, which must be treated individually. Bile duct rehabilitation was successful in more than half of the cases. That said, placement of prosthesis is the most effective strategy in these cases. However, additional research is required to identify success predictors and improve the management of post-transplant complications.

### Ethical statement

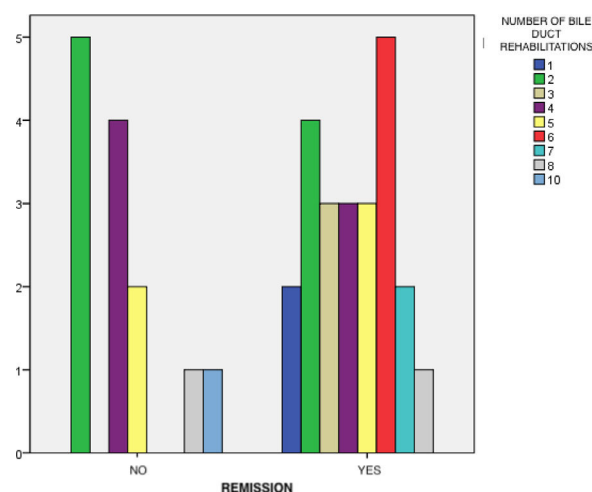
The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

### Declaration of interests

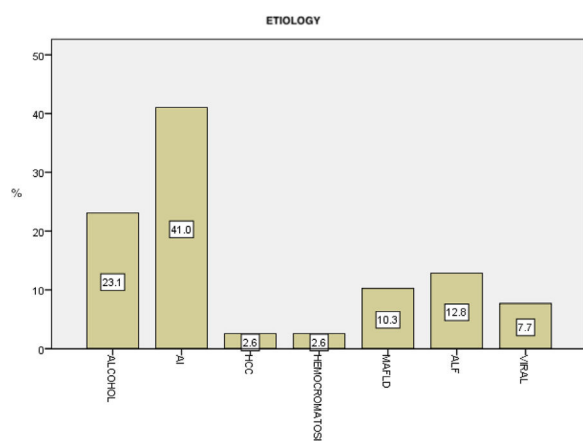
None

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



**Figure 1.** Number of bile duct rehabilitations and remission (N=39)



**Figure 2.** Etiology of liver transplantation (N=39)

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### N-acetyl cysteine prevents alterations generated during experimental liver steatosis induced by a chronic consumption of alcohol plus a hypercaloric diet.

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**Introduction and Objectives:** Metabolic alterations and alcohol consumption are the most common etiological agents related to hepatic steatosis (HS) development. There is little evidence that shows the effects generated by synergy of both etiologic agents. N-acetyl cysteine (NAC) is a drug whose efficacy in the early stages of SH, generated by a hypercaloric diet plus alcohol consumption, is unknown.

The aim of this work was to evaluate NAC effects on oxidative stress, and metabolic alterations induced in HS experimentally induced by chronic ethanol consumption plus a hypercaloric diet.

**Materials and Patients:** C57BL/6J mice (n=4) grouped into 1) Control; 2) HF/OH, administrated with hypercaloric diet and ethanol; 3) HF/OH+NAC, same treatments of group 2 plus NAC. Serum markers of liver damage and anorexigenic and orexigenic adipokines were evaluated; oxidative stress markers in liver samples were analyzed; finally, a H&E stain was performed. This project was conducted in accordance with the guidelines of the University of Guadalajara under the approval number of the bioethics, research, and ethics research committees CI-02920.

**Results:** NAC prevents weight gain and metabolic alterations generated by concomitant consumption of a hypercaloric diet and alcohol; this drug improves changes in anorexigenic and orexigenic adipokines such as leptin, ghrelin, resistin, GLP-1, and modulates total, HDL, and LDL cholesterol levels. On the other hand, NAC reduces CYP2E1 and alcohol dehydrogenase expression, as well as the oxidative environment induced by both etiologic agents, by avoiding an increase in malondialdehyde levels, promoting Nrf2 transcription factor expression and superoxide dismutase; also preventing an increase in the expression of Catalase. Finally, H&E staining showed that NAC prevents the development of tissue alterations in

the liver parenchyma generated by the consumption of a hypocaloric diet plus alcohol.

**Conclusions:** In this work, we demonstrate that NAC prevents metabolic alterations and oxidative damage related to early phases of HS induced by concomitant consumption of alcohol plus a hypercaloric diet. These effects would slow down the development of more severe stages of this disease.

### Ethical statement

The study was conducted according to the guidelines of the Institutional Animal Care and Use Committee of UPAE-Bioterio at CUCS, University of Guadalajara (CI-02920).

### Declaration of interests

None

### Funding

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### Hepatology at the Civil Hospital of Guadalajara, Fray Antonio Alcalde (HCGFAA) in the last 25 years and its international scientific productivity

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**Introduction and Objectives:** With the creation of the Doctorate Program in Molecular Biology in Medicine, the first clinical and molecular hepatology research studies began at the HCGFAA in 1998. SCOPUS uses the H-Index to assess researchers' quality and scientific productivity; however, this parameter does not evaluate co-authorship, first author, or corresponding author. This bibliometric study aimed to evaluate the scientific productivity of the Department of Genomic Medicine in Hepatology-HCGFAA (Jalisco) and its current ranking in Mexico.

**Materials and methods:** We searched the CONAHCYT database and selected the active hepatology researchers according to the platform's classification categories (July 2022). Subsequently, we recollected SCOPUS's H-Index and estimated the co-author's number (collaboration index) per article, first author and corresponding author.

**Results:** We identified 31 hepatology researchers in the National Researchers' System (SNI): 18 level I, 5 level II, and 7 level III categories. A 78% of them are located in: Mexico City (13), Jalisco (7), and Nuevo Leon (4). The average number of scientific publications/H-Index was 20/7.6 in the SNI researchers' level I, SNI II 24/9.4, and SNI III 142/31. A 29% of SNI I researchers' publications belonged to the first author and corresponding author articles, SNI II had 36%, and SNI III had 43%. The maximum number of authors per article ranged from 3 to 1055. The average of international citations in the SNI I category was 271, SNI II 619, and SNI III 3566.

**Conclusions:** The data shows a consolidation of hepatology at HCGFAA in Jalisco, as well as in Mexico City and Nuevo Leon. The bibliometric parameters allowed us to evaluate the researcher's contribution as the first or corresponding author. It also revealed that cases with many co-authorships and highly cited articles in first-quartile journals are related to the consensus, pharmaceutical industry, and epidemiological studies.



### Ethical statement

This study did not involve any patients or animal models and did not require approval.

### Declaration of interests

None

### Funding

U. de G. Programa de Fortalecimiento.

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### Prevalence of pregnancy liver diseases in patients at National Medical Center “La Raza” IMSS.

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UMAE Hospital of Specialties “Dr. Antonio Fraga Mouret” CMN “La Raza” IMSS

**Introduction and Objectives:** There are physiological changes in the hepatobiliary system during pregnancy. However, there are also pregnancy-related liver diseases, which occur in up to 3% of all pregnancies and can have potentially serious consequences for the mother and fetus. The most frequent are hyperemesis gravidarum, preeclampsia/eclampsia, elevated liver enzymes and low platelet count syndrome (HELLP), intrahepatic cholestasis of pregnancy (ICP) and acute fatty liver of pregnancy (AFLP). The prognosis depends on timely diagnosis and treatment. This study aimed to report the epidemiological characteristics of liver diseases in a Mexican population of pregnant women.

**Materials and Patients:** A retrospective descriptive observational study that included information collected from the electronic file of pregnant patients treated at UMAE HGO No. 3, of CMN La Raza, assessed by the Gastroenterology service of HE CMN “La Raza” in the period March 2021– May 2023.

**Results:** 142 patients were included, the mean age was 30 years, 54% were multiparous women, 8.4% of the patients were in the first trimester, 27% in the second trimester and 64% in the third trimester. In our total sample, alterations in liver biochemistry that met clinical and biochemical criteria for pregnancy-associated liver disease were analyzed, where 49% reported hypertransaminasaemia due to etiologies such as preeclampsia, HELLP syndrome, metabolic dysfunction associated fatty liver disease (MAFLD) and biliary pathology, 41% met criteria for ICP, 6% hyperemesis gravidarum, 1.4% were diagnosed with portal hypertension and liver cirrhosis, only 0.7% were diagnosed with autoimmune hepatitis and AFLP.

**Conclusions:** Based on solicited assessments over a 2-year period of women at any stage of pregnancy, hospitalized due to changes in liver biochemistry, most changes occurred in the third trimester of pregnancy, the most frequent disorder was intrahepatic cholestasis of the pregnancy, the rest of the pathologies were included in the hypertransaminasaemia group, where the most frequent causes were: MAFLD and cholelithiasis, less frequently: preeclampsia, HELLP syndrome or intrahepatic bile duct disorders.

### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

### Declaration of interests

None

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

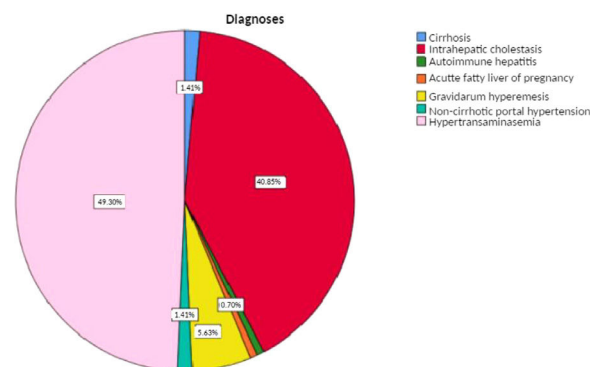


Figure 1. Prevalence of diagnoses.

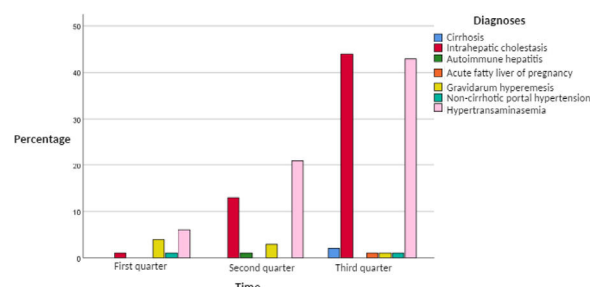


Figure 2. Frequency of diagnoses according to trimester.

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### Regulation of TGF-β1, 2, and 3 and IL-10 at systemic level in chronic liver disease

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**Introduction and Objectives:** Chronic liver disease (CLD) is considered an important health problem worldwide. The production of IL-10 regulated the hepatic inflammation. Whereas TGF-β plays a crucial role during the progression of CLD, promoting the dysregulated production of extracellular matrix in the liver. However, the role of TGF-β1, 2, and 3 and IL-10 in CLD is not completely understood. To evaluate the circulatory values of TGF-β1, 2, and 3 and IL-10 in hepatitis C virus (HCV), Non-alcoholic fatty liver disease (NAFLD) and alcoholic cirrhosis (OHCi) and control subjects (CT).

**Materials and Patients:** A prospective, cross sectional, observational and multicentric study. HCV (n=33), NAFLD (n=33) and OHCi patients (n=22) and CT (n=26) were enrolled. The anthropometric variables, detailed clinical history and biochemical parameters were

considered. TGF- $\beta$ 1, 2, and 3 and IL-10 (pg/mL) were evaluated using multiple suspension arrays. Kruskal-Wallis and Mann-Whitney U test were used for the statistical analysis. The study has the approval of the Research and Ethics Commissions with code FM/DI/135/2017 and the Research Ethics Committee of the Hospital General de México Dr. Eduardo Liceaga with code DI/16/107/03/031 as well the consent informed of the patients.

**Results:** The age of CT group was estimated at 33 yrs., while the average of the different hepatopathies was 47 yrs. Male predominance was marked in OHCi and CT, but in NAFLD the distribution of women was similar. Multiple comparison analysis revealed that serum levels of TGF- $\beta$ 1, 2, and 3 did not present statistical differences in each CLD group. Nevertheless, TGF- $\beta$ 2 isoform showed significant difference in NAFLD and OHCi vs. CT ( $p < 0.05$ ), showing a ratio of 1.8 and 1.6, respectively. The levels of the anti-inflammatory cytokine IL-10 were distributed as follows: OHCi>NAFLD>HCV showing correlation with the increment of the ratio of 4.4, 2.7, and 2.3 folds compared to CT, respectively.

**Conclusions:** Our data showed no differential changes of TGF- $\beta$ 1, 2, and 3 in accordance with CLD. The up regulation of TGF- $\beta$ 2 isoform could be related to different inflammatory responses in NAFLD and OHCi. On the other hand, IL-10 was upregulated in all the chronic conditions reflecting its role as pro-inflammatory mediator.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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#### Levels of IGFBP-1, 3 and 7 in human serum induced by alcohol consumption, NAFLD and dual insult

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**Introduction and Objectives:** Alcoholic liver and non-alcoholic liver disease causes liver disease. Dual damage has been gaining great relevance. Insulin growth factor binding proteins (IGFBPs) regulate the signaling pathways of IGF; IGFBP-3 have emerged as promising biomarkers in HGNA; however, in alcohol intake and dual damage has not been previously reported the levels of IGFBPs. To demonstrate the changes in the serum levels of IGFBP-1, 3 and 7 in alcohol consumption, NAFLD and dual insult

**Materials and Patients:** Prospective, cross-sectional and multi-center study; approved by the research and ethics commission of the UNAM and the General Hospital of Mexico. A clinical history was taken and an informed consent was requested. IGFBP-1, 3 and 7 were evaluated in alcoholism (OH), alcoholic liver disease (cirrhosis (CiOH)), alcoholic hepatitis (AH), NAFLD, dual patients and control group (CT) using multiple suspension arrays. Kruskal-Wallis, Mann-Whitney U test were used for the statistical analysis.

**Results:** The data showed that alcohol dependence increased the serum levels of IGFBP-1, 3 and 7 (ng/mL) vs. CT, and vs. the other hepatopathies as follows OH>AH>CiOH>HGNA>Dual. Whereas in CiOH the levels of IGFBP-1, 3 and 7 were reduced vs. CT, but a slight increment was observed in AH; however, it never reached similar values to CT. On the other hand, in NAFLD the serum concentrations of all the IGFBPs evaluated were downregulated vs. CT.

**Conclusions:** The serum levels of IGFBPs were regulated in a differential manner in accordance with the negative liver stimuli, these changes were more evident in alcoholism. The dual stimulus showed the clear synergistic effects of alcohol consumption and diet in IGFBP regulation. IGFBPs could be used as biomarkers or targets in the control of different hepatopathies.

#### Ethical statement

The study was previously approved by the institutional ethics committees of the Hospital General de México (HG/DI/16/107/03/082) and the Universidad Nacional Autónoma de México

(FMD/DI/15/2015), guaranteeing its performance in accordance with the ethical principles described in the 1975 Declaration of Helsinki. A clinical history was taken and an informed consent was requested.

#### Declaration of interests

None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

<https://doi.org/10.1016/j.aohep.2024.101426>

#### Clinical and epidemiological characterization of patients with hepatocarcinoma

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**Introduction and Objectives:** Hepatocellular carcinoma (HCC) represents more than 80% of liver cancers with a direct impact on morbidity and mortality. Viral hepatitis is responsible for most cases, in addition to the progression of liver cirrhosis from other causes. There are various risk factors of importance for identification and screening programs for adults at risk of HCC. The aim of this study was to characterize the clinical and epidemiological profile of patients diagnosed with HCC.

**Materials and Patients:** Prospective study of patients diagnosed with HCC. Data from clinical history, laboratory results, histopathology, and imaging studies were obtained. Univariate analyzes were carried out and Kolmogorov-Smirnov and Shapiro-Wilk normality tests were performed for continuous variables to determine the appropriate statistical test, performing bivariate analyzes with the Mann-Whitney or T-Student test. Non-parametric correlations were

determined by Rho Spearman calculated with a 95% confidence interval and statistical significance  $p<0.05$ .

**Results:** We identified 50 patients (n=50) with HCC with a mean age of diagnosis 66 years ( $SD \pm 12.91$ ), 70% predominating in men and 88% with liver cirrhosis, the majority being Child-Pugh C (34%). The main etiology of liver cirrhosis was hepatitis C (42%) and alcohol consumption (30%); others were MASLD 4% and hepatitis B 4%. The performance status by ECOG scale was (0-2) in 70% and (3-4) in 30%. Most patients were identified in Barcelona (BCLC) D (38%) and all were diagnosed by imaging criteria or histopathology combined AFP (alpha-fetoprotein) levels. Biopsies were performed in 34% of the patients, with a predominance of moderately differentiated type (14%), identifying metastases in 8%. Mortality was 28% presenting statistical significance with AFP levels ( $p=0.028$ ) and hepatic encephalopathy ( $p=0.004$ ). The ECOG scale showed a positive correlation with the presence of ascites ( $r=.567$ ,  $p= <0.001$ ), hepatic encephalopathy ( $r=.337$ ,  $p=0.017$ ) and Child-Pugh Scale ( $r=0.615$ ,  $p=<0.001$ ).

**Conclusions:** Most cases were identified at an advanced stage, highlighting the importance of early detection, with screening programs focused on eliminating risk factors, treatment of viral hepatitis, cessation of alcohol consumption, and periodic follow-up of patients with liver cirrhosis to prevent disease progression and impacts on quality of life.

Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

Declaration of interests

None

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

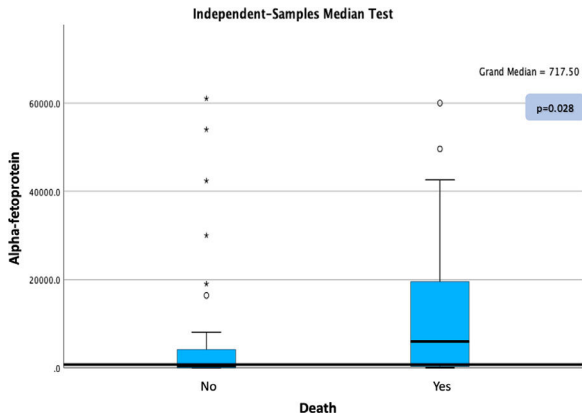


Figure 1. Relationship of AFP Levels with Mortality

| Table 1                                                                |                         |           |
|------------------------------------------------------------------------|-------------------------|-----------|
| Correlation of ECOG Performance Status Scale with Liver Decompensation |                         |           |
| ECOG Performance Status Scale                                          | Correlation Coefficient | p-value   |
| Ascites                                                                | $r=.567$                | $p<0.001$ |
| Hepatic Encephalopathy                                                 | $r=.337$                | $p=0.017$ |
| Child Pugh Scale                                                       | $r=.615$                | $p<0.001$ |

Survival of patients with hepatocellular carcinoma treated with immunotherapy experience of a third level center.

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**Introduction and Objectives:** Hepatocellular carcinoma (HCC) ranks sixth among tumors, the third cause of death worldwide and accounts for 85-90% of primary liver tumors. Recently, the use of immunotherapy as first-line treatment offers a survival of 18 months. The objective of this study is to assess the survival and adverse effects of the different immune checkpoint inhibitor therapies in our population

**Materials and Patients:** Patients who received immunotherapy at the Central Military Hospital from January 2021 to April 2023 were included. The following were recorded: leukocytes, hemoglobin, platelets, PT, INR, BT, AST, ALT, ALP, albumin, MELD, MELD-Na, ALBI, MELD 3.0 before and after treatment, calculation of survival, progression-free time and adverse effects

**Results:** 18 patients with stage A were included 2 patients, BCLC B 6 patients and BCLC C 10 patients, age  $67.72 \pm 14.40$  years, 11 (61%) men, the following immunotherapy schemes were given: atezolizumab + bevacizumab 13 patients and 5 patients with Nivolumab. The following variables were compared before and after immunotherapy: leukocytes, hemoglobin, platelets, PT, INR, BT, AST, ALT, ALP, albumin, MELD, MELD-Na, ALBI, MELD 3.0. Without finding statistical differences (Table 1). Adverse effects were 1 patient presented with clostridiode and 2 with immune-mediated hepatitis without improvement after treatment, which required suspension of immunotherapy and initiation of second line treatment. Overall survival was 19 months and progression-free time 15 months.

**Conclusions:** The overall survival of the patients was 19 months, the adverse effects that the patients appeared were similar to those reported in the literature.

Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

Declaration of interests

None

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



**Table 1**  
Blood chemistry, complete blood count and liver function tests in patients with Ca undergoing treatment before and after immunotherapy (n=18).

|                                 | Patients before immuno-therapy (n= 18) | Patient after immunother-apy (n=18) |                  |             |                            |                          |
|---------------------------------|----------------------------------------|-------------------------------------|------------------|-------------|----------------------------|--------------------------|
| Pattern (units)                 | Values (media ± DE)                    | Values (media ± DE)                 | t (gl)           | P<0.05      | IC 95%                     | Reference ranges (años)  |
| Age                             | 67.72 ± 14.40                          | 69.63 ± 14.05                       | -3.15 (17)       | 0.006       | -3.1 – -0.6                |                          |
| Gender                          |                                        |                                     |                  |             |                            |                          |
| • Man                           | 11                                     | 11                                  |                  |             |                            | n=11                     |
| • Woman                         | 7                                      | 7                                   |                  |             |                            | n=7                      |
| CHILD PUG                       | 6.56± 1.33                             | 6.72± 1.74                          | -0.54 (17)       | 0.59        | -0.81 – 0.47               |                          |
| MELD                            | 9.11± 2.11                             | 10.39± 5.34                         | -1.11(17)        | 0.28        | -3.69– 1.13                |                          |
| MELD NA                         | 9.17± 2.22                             | 10.89± 6.07                         | -1.36 (17)       | 0.18        | -4.38 – 0.93               |                          |
| MELD 3.0                        | 10.56± 2.79                            | 12.06± 5.62                         | -1.11 (17)       | 0.28        | -4.34– 1.34                |                          |
| ALBI                            | -1.95± 0.81                            | -1.91± 0.68                         | -0.14 (17)       | 0.88        | -0.56 – -0.49              |                          |
| Leukocytes x103/μL              | 6.15± 2.94                             | 5.57± 2.45                          | 0.87 (17)        | 0.39        | -0.80– 1.95                | 5 - 10                   |
| Hemoglobin g/dL                 | 13.02 ± 2.67                           | 13.02 ± 2.77                        | 0.00 (17)        | 1.00        | -1.36 – 1.36               | 13.5 – 18                |
| Platelet x10 <sup>9</sup> /μL   | <b>265.59± 80.79***</b>                | <b>169.00 ± 80.80***</b>            | <b>1.54 (16)</b> | <b>0.14</b> | <b>-36.24– 229.41</b>      | <b>150 – 450</b>         |
| PT (seconds)                    | 12.95 ± 4.11                           | 11.41 ± 3.63                        | 1.13 (17)        | 0.27        | -1.32– 4.40                | 11.0 – 13.5              |
| INR                             | <b>1.94± 3.34***</b>                   | <b>1.14 ± 0.22***</b>               | 1.01 (17)        | 0.32        | -0.87 – 2.48               | ≤1                       |
| Total Bilirubin (mg/dL)         | <b>1.27± 0.63***</b>                   | <b>1.58± 1.26***</b>                | -1.24 (17)       | 0.22        | -0.82 – 0.21               | 0.2 – 1.2                |
| Direct Bilirubin (mg/dL)        | <b>0.44 ± 0.43***</b>                  | <b>0.57 ± 0.69***</b>               | -0.83 (17)       | 0.41        | -0.45 – 0.19               | 0 - 0.2                  |
| No Direct Bilirubin (mg/dL)     | <b>0.83± 0.52***</b>                   | <b>1.01± 0.77***</b>                | -1.36 (17)       | 0.19        | -0.46 – 0.10               | 0 - 0.8                  |
| ALT (TGP) (UI/L)                | <b>82.11± 128.12***</b>                | <b>48.56± 42.60***</b>              | 1.07 (17)        | 0.30        | -32.63–99.74               | 10 - 35                  |
| AST (TGO) (UI/L)                | <b>88.55 ± 86.06***</b>                | <b>78.22± 55.96***</b>              | -0.42(17)        | 0.67        | -41.15 – 61.81             | 5 - 34                   |
| ALP (Alkaline phosphatase) UI/L | <b>250.72 ± 205.12***</b>              | <b>307.22 ± 179.99***</b>           | -1.56(17)        | 0.13        | -132.50 – 19.50            | <138                     |
| Albumin g/dL                    | 3.39± 0.66                             | 3.28± 0.77                          | 0.60 (17)        | 0.55        | -0.27 – 0.49               | 3.5 - 4.8                |
| Alpha-fetoprotein (nanograms)   | <b>6455.04± 21565.83***</b>            | <b>2570.74± 5706.40***</b>          | <b>0.63 (13)</b> | <b>0.53</b> | <b>-9346.56 – 17115.18</b> | <b>&lt;300 nanograms</b> |

\*\*\*Out of clinical reference value // t-test for related samples pre-post, \*P<0.05 // AST- Aspartate aminotransferase, ALT- Alanine aminotransferase, ALP- alkaline phosphatase, GGT- Gamma glutamyl transferase. // + OS actual overall survival

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**Clinical characteristics, therapeutic approach, and outcomes in patients with hepatocellular carcinoma at a third-level hospital.**

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**Introduction and Objectives:** Hepatocellular carcinoma (HCC) is the most common malignant tumor in patients with advanced cirrhosis, posing a significant challenge to the healthcare system. Treatment involves a multidisciplinary approach; however, advanced disease limits the available options. Effectiveness and outcomes can differ depending on the stage of the disease, the patient's functional reserve, and other factors. This study aims to describe the clinical characteristics, staging, treatment, and outcomes of patients with HCC at a third-level hospital

**Materials and Patients:** A retrospective, descriptive study of HCC patients. Demographic variables, treatment received according to the Barcelona Clinic Liver Cancer (BCLC) staging system, and treatment response according to the Response Evaluation Criteria in Solid Tumors (RECIST) were evaluated. Descriptive statistics with measures of central tendency and dispersion were performed.

**Results:** The study included 50 patients (20 females, 30 males; mean age 62 ±8). Etiology of cirrhosis: MAFLD (19), alcohol-related (14), Hepatitis C (11), and other causes (6). The average MELD score was 12.5 ±6.22, and the MELD-Na score was 14.7 ±5.44. BCLC staging: A (9), B (28), C (4), D (9). Eligible for treatment (30), categorized as Child-Pugh A(2), B(22), C(6). Radiological treatment (21) included Transarterial Chemoembolization (TACE) in 13 cases, ablation (4),

and a combination TACE/Ablation (4). Medical treatment with Lenvatinib (1). Combination of medical and radiological treatments (3). TACE followed by transplantation (4), and transplantation alone (1). Treatment response evaluation: Complete response (4), partial response (9), stable disease (7), and progression (8). The 3-month mortality rate was 8.3%.

**Conclusions:** In our group, most of the patients were males, with a relatively equal distribution between compensated and decompensated cirrhosis. MAFLD was the most prevalent etiology, and a significant portion of cases presented at an intermediate stage (BCLC B), qualifying them as candidates for treatment. The response rates to treatment were 13% for complete response and 30% for partial response. Furthermore, the calculated mortality rate at 3 months was relatively low.

**Ethical statement**

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

**Declaration of interests**

None

**Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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**Characteristics and outcome of patients with liver abscess, a retrospective cohort.**

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**Introduction and Objectives:** Liver abscess (HA) is currently a rare entity, the prevalence is low, the epidemiological transition from

amoebic to pyogenic in recent years may have modified its characteristics and outcome. Therefore, knowing its presentation, evolution, management and outcome is relevant. Describe the characteristics and outcome of patients with liver abscess

**Materials and Patients:** Retrospective and observational study of patients diagnosed with HA, epidemiological variables, presentation, treatment, drainage, and outcome were evaluated. Descriptive statistics were performed with measures of central tendency and dispersion

**Results:** Records of patients with HA were reviewed, in a period from 2018 to 2023. A total of 103 patients with HA were included, age  $48.3 \pm 15.7$ , 70% men and 30% women, 84.5% pyogenic and 14.5% amoebic with 0.9% of deaths. 25.2% of the patients were diabetic. 42.7% were single liver abscesses, the most frequent location was segment VII in 50.4%. Regarding antibiotic treatment, 80.4% were treated with metronidazole and ceftriaxone, followed by carbapenems in 14.5%. Of the total number of patients, 73.7% required percutaneous drainage, 60.1% underwent culture, of the identified agents *E. Coli* was the most frequent in 9.7%. Only one patient died due to septic shock.

**Conclusions:** The most frequent etiology of HA is now pyogenic, much higher than amoebic, mortality is low, the outcome is healing without sequelae with the use of antimicrobials and percutaneous drainage.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

None

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#### Detecting the risk for fatty liver, MASH, and insulin resistance using different indexes and markers of liver damage in young adults from West Mexico

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**Introduction and Objectives:** Previous studies conducted by our research group have demonstrated a high frequency of fatty liver and metabolic-associated steatohepatitis (MASH) in young Mexican population. Therefore, early detection of risk factors and metabolic abnormalities is important to prevent or reverse the progression to MASH. The objective of this study is to use non-invasive markers for the detection of insulin resistance (IR), the risk of fatty liver disease (FLD), liver damage, and metabolic-associated steatohepatitis (MASH) in young adult population from West Mexico

**Materials and Patients:** A cross-sectional study assessing the presence of IR using HOMA-IR and non-invasive assessment of the risk of fatty liver disease (FLD) (FLI  $\geq 60$ ), liver damage (HCG markers 19.6% to 58.8%), and metabolic associated steatohepatitis (MASH) (FIB-4: 1.45-3.25; APRI:  $\geq 0.7$ -1.0; NAFLD Fibrosis Score:  $> 0.675$ ) in young adults aged 18 to 45 years. Written informed consent was obtained from all participants. The Institutional Review Board approved this study.

**Results:** Fifty-three participants (37 women and 16 men) with an average age of  $29.53 \pm 8.33$  years were recruited. A 80.7% had overweight and obesity (class I, II, III), with an average waist-to-height ratio of  $0.55 \pm 0.09$ . Additionally, 80.8% of the participants had one or more metabolic abnormalities; hypercholesterolemia (25%), hypertriglyceridemia (39.2%), hypoalbuminemia (64%), and IR (54.3%). A risk of 39.6% for NAFLD (FLI), 42.95% for liver damage (HCG markers), and 2% - 4% for MASH with intermediate hepatic fibrosis (F2-F3) and significant according to the FIB-4, APRI, and NAFLD Fibrosis Score markers, respectively, were identified.

**Conclusions:** A high prevalence of metabolic disorders and IR was detected, which may be related to a high risk of developing fatty liver disease (39.6%) and liver damage (42.95%), as well as MASH (2-4%) in the young Mexican adult population, suggesting the need of early prevention strategies.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

University of Guadalajara-Programa de Fortalecimiento de Institutos, Centros y Laboratorios.

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#### Poor correlation between HOMA index and Triglycerides/HDL-C ratio as markers of insulin resistance in adult patients with MAFLD.

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**Introduction and Objectives:** In children, studies have demonstrated that Triglycerides/HDL-C ratio can be a good alternative to the HOMA index for measuring insulin resistance as a more accessible and widely available method in MAFLD. However, this has not been replicated in adults. Our goal is to show the correlation that exists between the HOMA index and the Triglycerides (TG) to High-Density Lipoprotein (HDL) ratio as markers of insulin resistance in adult patients with fatty liver disease.

**Materials and Patients:** Descriptive and retrospective study. It included 80 adult patients with MAFLD between July 2021 and May 2023. Insulin resistance (RI) was defined as a HOMA index  $\geq 2.71$  or a TG/HDL-C ratio  $\geq 1.36$  mmol/L. The results were analyzed using measures of central tendency, dispersion, and Pearson's test.

**Results:** 80 patients were evaluated, with 65% of the sample corresponding to women, with a mean age of 52.5 years. 64% of patients (n=51) with MAFLD showed insulin resistance measured by HOMA-IR, while 57.7% (n=46) had a Trig/HDL-C ratio  $\geq 1.36$ . 8 patients who showed extreme data, possibly due to laboratory measurement error, were excluded. When applying the Pearson's test, a score of 0.25 was obtained, indicating a weak correlation between both markers (Table 1 and Figure 1).

**Conclusions:** In our study, we found a low correlation between the HOMA index and the Triglycerides/HDL-C ratio, suggesting that the Triglycerides/HDL-C ratio may not be a suitable marker for insulin resistance in adult patients with MAFLD. Therefore, we do not currently recommend its use in this patient population.

Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

Declaration of interests

None

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

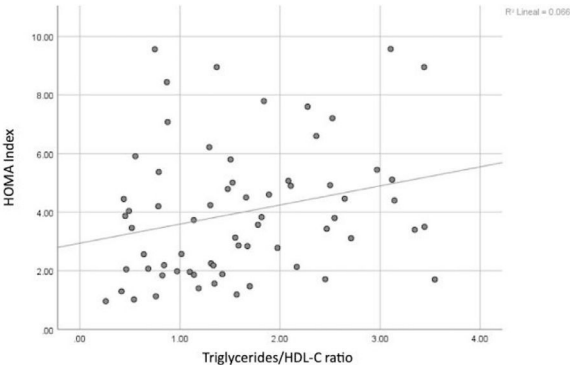


Figure 1. Simple scatter plot with HOMA index line fit by TG-HDL ratio.

|                           |                     | HOMA Index | Triglycerides/HDL-C ratio |
|---------------------------|---------------------|------------|---------------------------|
| HOMA Index                | Pearson correlation | 1          | .257                      |
|                           | Sig. (bilateral)    |            | .037                      |
|                           | N                   | 67         | 66                        |
| Triglycerides/HDL-C ratio | Pearson correlation | .257       | 1                         |
|                           | Sig. (bilateral)    | .037       |                           |
|                           | N                   | 66         | 71                        |

Table 1. Correlation between HOMA and Triglycerides/HDL-C ratio using Pearson's test.

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Rapidly progressive glomerulopathy in a patient with hepatitis C virus not diagnosed. Case Report.

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**Introduction and Objectives:** Hepatitis C virus (HCV) related-Kidney disease, mostly due to the formation of immune complexes and cryoglobulins with cryoglobulinemic vasculitis (CryoVas), and a direct cytopathic effect. We present a case of HCV-nephritic syndrome associated with focal segmental glomerulosclerosis without CryoVas that reported anecdotally in the literature.

**Materials and Patients:** 63-year-old female with 15 years of stable essential hypertension. She suddenly presented lower extremity

edema, headache, phosphenes, hypertensive uncontrol, hematuria, proteinuria and decreased glomerular filtration. She received steroids with partial response, for which phenolic acid was started after six months without complete response. A renal biopsy with immunofluorescence, serum antinuclear antibodies (SS-A, SS-B, Sm, RNP, Jo1, Scl70, dsDNA, ANCA-c, ANCA-p, anticardiolipin, cryoglobulins) rheumatoid factor, C4 electrophoresis of immunoglobulins and liver function tests carry out.

**Results:** All liver and immunological parameters was normal. The renal biopsy were atypical damage associated with HCV finding focal segmental glomerulosclerosis with areas of extra-capillary proliferative glomerulosclerosis pauci-immune, shown in Figure 1. Hepatitis C serology and viral load were positive, she received glecaprevir/pibrentasvir for 12 weeks with a sustained viral response at week 12. During the 3-year follow-up, the patient is on peritoneal dialysis, with no viral relapse.

**Conclusions:** We should emphasize that the control of focal segmental glomerulosclerosis-associated nephritic syndrome was achieved with direct-acting antivirals (AAD). This type of kidney injury is described as a direct lesion from virus replication to direct injury to podocytes, so the isolated use of other immunosuppressive therapies (steroids/immunosuppressors) can accelerate the renal damage, early identification of HCV involvement is necessary to start appropriate treatment with AAD as soon as possible.

Ethical statement

The identity of the patients is protected. Consentment was obtained.

Declaration of interests

None

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

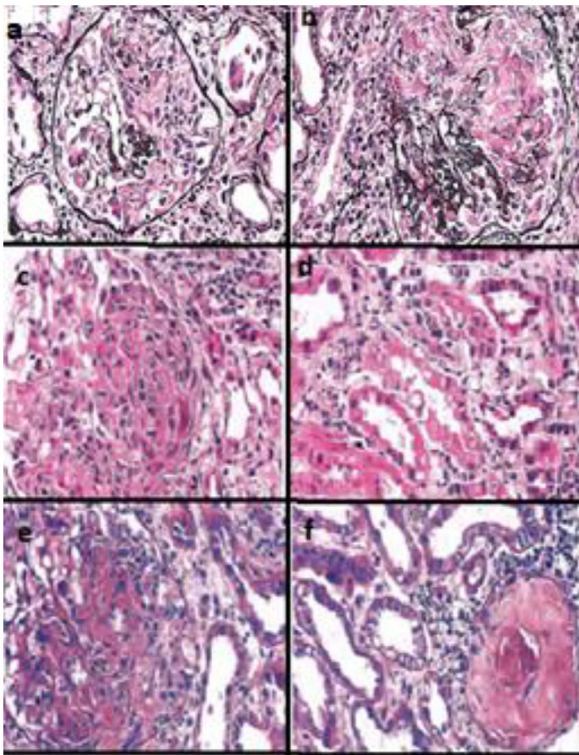


Figure 1. Light micrograph, renal biopsy. a, b: Jones' metamine stain, showing a thickened Bowman's capsule, folded, without spicules or filling defects with the stains used, fibrous crescents with an index of interstitial fibrosis 30-35%. c, d. HE stain, glomerulus with



extra capillary proliferative and segmenting extra capillary proliferative lesions partially the tangles, cariorexis and fibrinoid necrosis. e, f: Masson's trichome stain, interstitium tubular with fibrosis and atrophy, scant infiltrate inflammatory with lymphocytes and cells plasmatic, tubular epithelium with regenerative changes accentuated and intratubular proteinaceous material. Negative immunofluorescence (IgA, G4, kappa, C3), not showed.

<https://doi.org/10.1016/j.aohep.2024.101433>

### Demographic and clinical characteristics of patients with chronic HCV infection in a third-level IMSS Hospital in Mexico City

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**Introduction and Objectives:** Hepatitis C virus (HCV) infection is a major cause of chronic liver disease, there are approximately 71 million infected individuals worldwide, up to 40% of them will have spontaneous resolution and 60% will develop chronic infection with risk of developing cirrhosis and hepatocellular carcinoma. In Mexico it is the fourth cause of death and one of the main causes of disability. Current HCV treatment with direct-acting antivirals (DAAs) has a high rate of sustained viral response that ensures the cure of the infection, decreases the progression of liver fibrosis and decompensation rates in patients with cirrhosis. This study aimed to describe the demographic and clinical characteristics of patients with chronic HCV infection, treated at a third-level care hospital in Mexico City.

**Materials and Patients:** A retrospective cohort study in a part of the patients from the HCV clinic of an IMSS third-level hospital, which included cases with confirmed HCV infection, who received treatment with direct-acting antivirals +/- ribavirin, in the period of 2017-2022.

**Results:** Data from 222 treated patients was collected; a mean age of 53 years was reported, with a male-female ratio of 1:1. Among candidates for treatment with direct-acting antivirals 50.5% had advanced chronic liver disease at the time of diagnosis. Of these patients 76.1% were classified as a compensated chronic liver disease with a stage of Child Pugh A and 86.7% had a MELD-Na score of less than 14 points. The sustained virologic response rate in this population was 99%.

**Conclusions:** It was observed that the collected treated population was on average in the sixth decade of life, with no gender predilection. Half of this population had advanced chronic liver disease at the time of diagnosis and initiation of treatment with direct antivirals. The majority of patients were in a compensated stage by Child Pugh, and showed a low MELD-Na score which was favorable for follow-up and subsequent management.

### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

### Declaration of interests

None

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

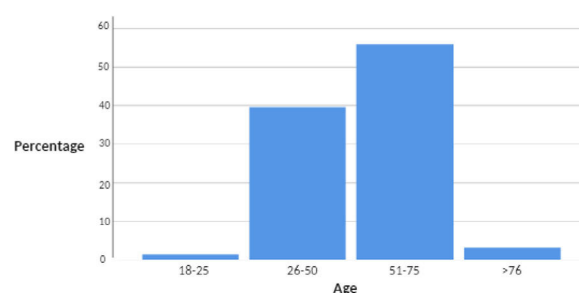


Table 1. Prevalence of ages.

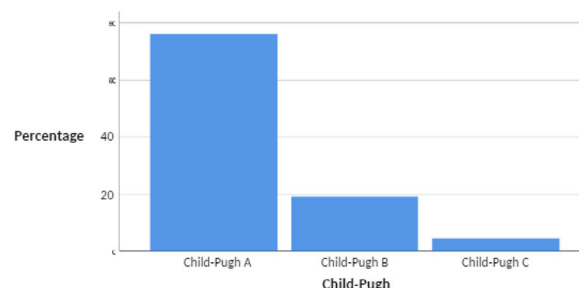


Table 2. Prevalence of Child-Pugh stage.

<https://doi.org/10.1016/j.aohep.2024.101434>

### Factors associated with mortality in patients with cirrhosis.

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**Introduction and Objectives:** Chronic liver disease is increasingly prevalent, the causes range from MAFLD, alcohol consumption, HCV, autoimmune disease, and others. They develop complications such as: portal hypertension with esophageal and gastric varices, hepatic encephalopathy, ascites, renal injury, among others, conditioning the final stage of the disease and death; therefore, knowing the factor that has the greatest impact on mortality is relevant. To evaluate which decompensations are associated with higher mortality in patients with cirrhosis of different etiologies.

**Materials and Patients:** Retrospective, analytical, observational study of patients with cirrhosis. To determine the factors associated with 28- and 90-day mortality, proportional hazard curves were performed for COX with encephalopathy, gastrointestinal bleeding, ascites, renal injury, ACLF and infection, with absence of the factor as reference. Considering significant  $\alpha \leq 0.05$ , SPSS-V 25.0 was used

**Results:** 200 patients, men 53%, women 47%. Etiology: alcohol 86, MAFLD 58, autoimmune 27, dual 16 and HCV 13; 37 died at 28 days and 49 at 90 days. Cumulative mortality rate 28 days 18.4%, 90 days 24.4%, with CHI square test for the model was significant, 109.34 (10),  $p < 0.001$ , being significant with WALD statistic for ACLF with OR of 4.78 (1.24-18.37; 95%IC),  $p = 0.023$  for 90 days, the model was significant CHI square 118.22 (10),  $p < 0.001$ , being significant encephalopathy grade 2 OR of 11.95 (1.49-57.16; 95%IC)  $p = 0.02$ , ascites OR 2.63 (1.24-5.58; 95%IC)  $p = 0.12$ , acute kidney injury OR 4.02 (1.16-

13.88;95%IC)  $p=0.28$ , ACLF grade 2 OR 2.73 (1.001-7.43;95%IC)  $p=0.05$ , ACLF grade-3 OR 5.94 (1.83-19.2;95%IC)  $p=0.03$ , and infection OR 1.96 (1.014-3.79;95%IC)  $p=0.45$

**Conclusions:** In our study group, the factors associated with mortality were the degree of ACLF, greater degree of encephalopathy and development of renal failure, with HD standing out with an OR of 11.95.

### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

### Declaration of interests

None

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

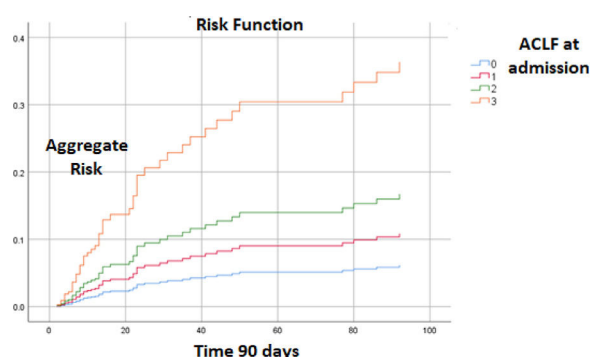


Figure 1. ACLF grade and its relationship with 90-day mortality

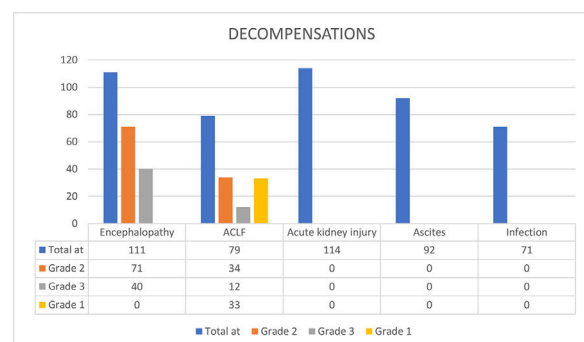


Figure 2. Main decompensations in patients with cirrhosis

<https://doi.org/10.1016/j.aohep.2024.101435>

### Impact of spontaneous bacterial peritonitis on the outcome of patients with cirrhosis

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**Introduction and Objectives:** Spontaneous bacterial peritonitis (SBP) is a severe complication that can occur in patients with

cirrhosis and is associated with high mortality rates. Evaluating SBP as a risk factor in the outcome of patients with cirrhosis is important because it helps understand the impact of this complication on the overall prognosis of these patients. Therefore, the objective of this study is to identify risk factors, treatment outcomes, and mortality rates associated with SBP in this population.

**Materials and Patients:** A retrospective and analytical study was conducted on patients with cirrhosis who developed SBP. The cause of cirrhosis and Child-Pugh score were evaluated. They were classified into early responders (ER) (more than 25% decrease in polymorphonuclear cells on the second day of effective antibiotic treatment), development of renal injury, acute-on-chronic liver failure (ACLF), and 28-day mortality. Statistical analysis included evaluating the mortality rate using the Kaplan-Meier curve, log-rank test, considering significance at  $p \leq 0.05$ . Renal injury, ACLF, and non-early responders were independently compared.

**Results:** A total of 79 patients were included in the study, 40 males (50.63%) and 39 females (49.36%). Alcohol-related in 49.36% of cases. Child-Pugh C was found in 67 cases (84.81%). Antibiotics were cephalosporins in 66 cases (84.81%) and carbapenems in 13 cases (16.45%). There were 6 deaths among early responders and 29 among non-early responders, with a mean survival of 25.76 days for early responders versus 9.78 days for non-early responders,  $p < 0.001$  (Figure 1). Regarding Acute-on-Chronic Liver Failure (ACLF), there were 2 deaths in patients without ACLF and 33 deaths in patients with ACLF. The mean survival for patients without ACLF was 26.93 days, compared to 14.6 days for those with ACLF,  $p < 0.001$ . Patients without renal injury had 3 deaths, while those with renal injury had 32 deaths. The mean survival for patients without renal injury was 25.65 days, compared to 16.17 days for those with renal injury,  $p < 0.001$  (Figure 2)

**Conclusions:** SBP in patients with cirrhosis is associated with a high mortality rate. However, several factors such as treatment response, the presence of ACLF, and renal injury have a significant impact on patient survival.

### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

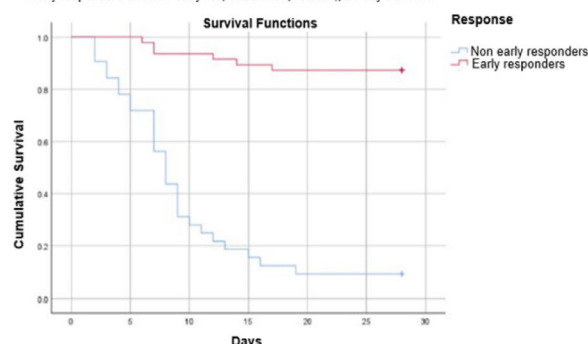
### Declaration of interests

None

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Figure 1. Area Under Receiver. Operating Characteristics Curve (AUROC) of early responders and non-early responders for predicting 28-day survival.



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## The role of cirrhosis etiology in the development of acute kidney injury and death

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**Introduction and Objectives:** Patients with hepatic cirrhosis (HC) are at risk of developing acute kidney injury (AKI) due to multiple factors. The main types of AKI are hypovolemia, acute tubular necrosis (ATN), and urinary obstruction. Common causes of HC include MAFLD, alcohol consumption, viral and autoimmune diseases, which may have a different role in the risk for AKI and mortality. This study aims to assess the etiology of cirrhosis in the development of acute kidney injury (AKI) and mortality.

**Materials and Patients:** Retrospective, analytical, observational study of patients with CH, analyzing etiology, type of AKI, and mortality. Statistical analysis: Using the Log-Rank test, the Kaplan-Meier curve was performed considering death at 28 and 90 days to assess the mortality rate associated with etiology. The Chi-square test with Bonferroni correction was conducted to evaluate the association between etiology and type of AKI; a significance level of  $\leq 0.05$  was considered.

**Results:** A total of 201 patients with CH were included, 106 of them being male (52.73%), with an average age of  $55 \pm 10.4$  years. Child-Pugh classification distribution was as follows: A: 25 (12.43%), B: 70 (34.82%), and C: 106 (52.73%). The average MELD-Na score was  $21.8 \pm 9.45$  points. The cumulative mortality rate at 28 days was 18.4% (37); the comparison by etiology showed statistical significance with a Chi-square test of 13.23 (4),  $p=0.01$ . The mean survival for MAFLD was 27.7, alcohol-related was 23.8, autoimmune was 24.1, viral was 25.92, and dual etiology was 22.56, with an overall survival of 24.88. The comparison at 90 days was significant, with a Chi-square test of 10.46 (4),  $p=0.033$ , and a cumulative mortality rate of 24.4% (49). The mean survival for MAFLD was 86.82, alcohol-related was 70.02, autoimmune was 67.03, viral was 80.07, dual etiology was 66.56, and the overall survival was 74.84. Association tests between etiology and type of renal injury showed statistical significance, with a Chi-square test of 29.65 (8),  $p<0.001$ . Differences were found between the alcohol-hypovolemic group and the non-renal injury and ATN groups.

**Conclusions:** Dual etiology and autoimmune factors confer higher mortality at 28 and 90 days, respectively, while alcohol consumption increases the risk of AKI due to hypovolemia.

### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

### Declaration of interests

None

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Figure 2. Area Under Receiver, Operating Characteristics Curve (AUROC) of renal injury and non-renal injury for predicting 28-day survival

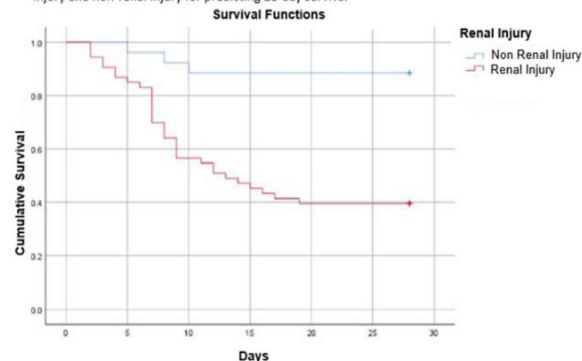


Figure 1. 28-day survival by etiology of Hepatic Cirrhosis.

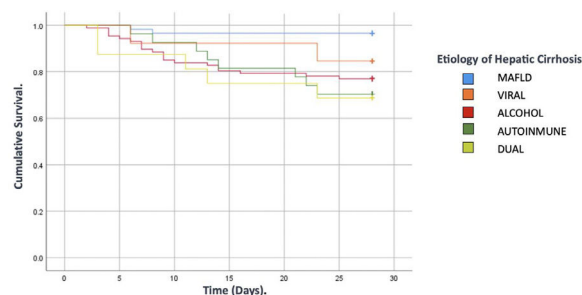


Figure 2. 90-day survival by etiology of Hepatic Cirrhosis.

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## Evaluation of severity and survival scales in acute-on-chronic liver failure(ACLF) in a Mexican population sample.

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**Introduction and Objectives:** ACLF is a syndrome characterized by multiorgan failure due to acute decompensation in chronic liver disease, with high short-term mortality. Therefore, scales have been designed to predict prognosis and early mortality. Evaluation of MELD, MELD NA, MELD LACTATE, and MELD 3.0 scales for survival prediction in ACLF patients

**Materials and Patients:** Observational, retrospective, and analytical study, scales were calculated, and sensitivity (S) and specificity (E) were determined using CLIF-C-ACLF as reference through ROC curves. Cut-off points were established at the maximum values of S and E. Cumulative mortality percentage by Kaplan-Meier, and comparison of ACLF grades with the Long-Rank test with  $p<0.005$ .

**Results:** 233 patients were included, 165 (71%) males, with a mean age of  $52 \text{ years} \pm 12.96$ . The etiology was alcohol-related in 158 (68%) cases. ACLF grade distribution, it was 1: 37%, 2: 41%, and 3: 22%. The MELD 3.0 showed the highest discriminatory power for ACLF grade 3, with AUC of 0.91 (95% CI:0.86-0.96), a cut-off point of 34.5, sensitivity of 86%, and specificity of 80% (Figures 1). The 2-year mortality rate was 123 (52%); 30 (35%), 51 (53%), and 42 (82%) for grades 1, 2, and 3, respectively, with a significant Log-Rank test, chi-square = 34.99,  $p$



<0.001. The mean survival by grades was 17 months for grade 1, 13 months for grade 2, and 5 months for grade 3 (Figure 2)

**Conclusions:** The MELD 3.0 scale showed better performance as a tool to evaluate severity and predict short-term mortality risk in ACLF patients.

#### Ethical statement

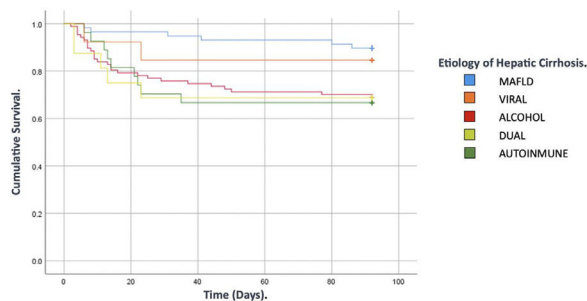
The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

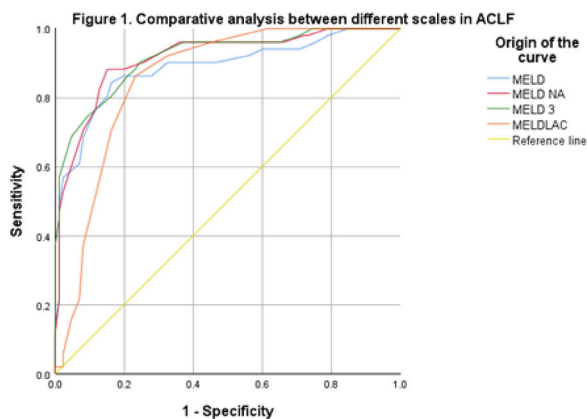
None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



**Figure 1.** Comparative analysis between different scales in acute on chronic liver failures (ACLF). Meldlac: Meld Lactato



**Figure 2.** Kaplan-Meier. Survival by grades of acute on chronic liver failure (ACLF).

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#### BUN/creatinine ratio associated with mortality in patients with cirrhosis and acute kidney injury.

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**Introduction and Objectives:** Cirrhosis is a prevalent disease worldwide, with complications such as acute kidney injury (AKI) that increase the risk of fatal outcomes. A high BUN/creatinine ratio (IBC) has been associated with mortality in other diseases. Therefore, evaluating this index in patients with cirrhosis could predict mortality. To determine whether a high BUN/creatinine ratio is associated with mortality in patients with cirrhosis and AKI.

**Materials and Patients:** Retrospective analysis was conducted on a cohort of cirrhotic patients with and without AKI, calculating the IBC and assessing its association with mortality.

**Results:** A total of 201 patients with cirrhosis were included, of whom 106 were male (52.73%), with a mean age of 55±10.4 years. The distribution of Child Pugh scores was as follows: A (25, 12.43%), B (70, 34.82%), and C (106, 52.73%); the mean MELD-Na score was 21.8±9.45. The cumulative mortality rate at 28 days was 37 (18.4%) and at 90 days was 39 (24.4%). The model was not significant at 28 days but was significant at 90 days with a X2 value of 48.18 (2) and p<0.001.

At 90 days, the model was significant with a x2 value of 49.7 (2) and p<0.001, with an OR (IBC) of 2.78 (1.08-7.11, 95% CI, p=0.33), and for AKI OR of 7.97 (2.2-28.8, 95% CI, p=0.02) (Figure 1). Considering either factor present, the model was significant at 28 days with a X2 of 27.75 (1) and p<0.001, with an OR of 7.2 (3-17.3, p<0.001), and at 90 days with a X2 of 35.59 (1) and p<0.001, with an OR of 6.67 (3.23-13.76, p<0.001).

**Conclusions:** The Cox proportional hazards model was used to compare factors associated with mortality separately for AKI (present vs. absent) and IBC (>20 mg/dl vs. <20 mg/dl) at 28 and 90 days, as well as if both factors were present. The model was considered significant if the p-value was less than 0.5. The study concluded that a higher IBC (>20 mg/dl) could predict mortality in patients with cirrhosis, as the odds ratios at 28 and 90 days were significant.

#### Ethical statement

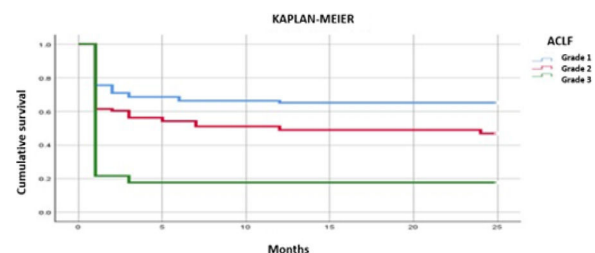
The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



**Figure 1.** IBC and AKI at 90 days associated with mortality.

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#### Evaluation of the ALBI, MELD, MELD-Na, MELD 3.0 score in patients with hepatocellular carcinoma treated with Yttrium-90 (90y)

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Salvador Amezcua-Pérez<sup>3</sup>,  
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**Introduction and Objectives:** Hepatocellular carcinoma (HCC) occupies the third cause of mortality worldwide. 10% of patients receive curative therapy. There are loco-regional therapies to improve patient survival such as (TACE) and radioembolization with Yttrium-90. There are prognostic scales, such as ALBI, MELD, MELD-Na, MELD 3.0, to identify those who will respond better to treatment.

To evaluate the potential of the ALBI, MELD, MELD-Na, MELD 3.0 index as a predictor of mortality in patients who received treatment with Yttrium-90

**Materials and Patients:** Patients with cirrhosis and HCC who were candidates for radiation embolization with Yttrium-90 were evaluated. The following scores ALBI, MELD, MELD-Na, MELD 3.0 were assessed before and after therapy.

**Results:** There were 7 patients, age  $70 \pm 11.3$  years, 60% women, all BCLC B and Child Pugh B, etiology of CH was 3 patients due to alcohol-associated liver disease, 2 patients due to MASLD and 2 cryptogenic, 4 patients had 2 sessions and 3 patients 1 session, complete response in 3 patients and 5 progressed. 3 patients died. The variables of leukocytes, hemoglobin, platelets, PT, INR, BT, AST, ALT, albumin, ALBI, MELD, MELD 3.0, MELD-Na, Child Pugh were compared without obtaining statistical significance (Table 1). The survival of the patients was 14.6 months. There were no complications or adverse effects with the Yttrium-90 treatment.

**Conclusions:** ALBI, MELD, MELD 3.0, MELD-Na score do not predict mortality in patients treated with Yttrium-90. A study with a larger number of patients is needed to correlate and obtain more significant results

#### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

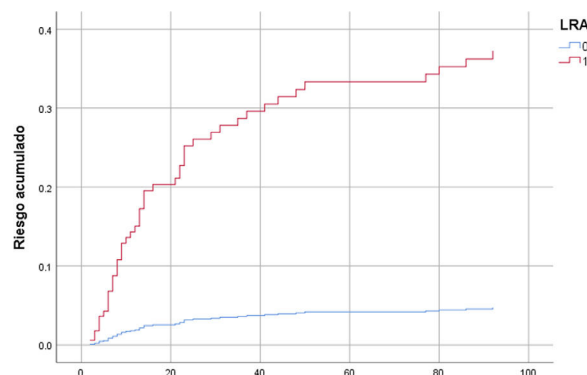
#### Declaration of interests

None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Table 1.** Blood cytometry, Liver Functional Tests & cancer scales systems in patients with cancer and treatment transarterial radioembolization (TARE) with Yttrium-90.



\*\*\* Outside clinical reference value // Paired Samples t Test (pre-post) \*P<0.05 // AST- Aspartate transaminase, ALT- Alanine transaminase, ALP- Alkaline phosphatase, GGT- Gamma-glutamyltransferase, INR- International Normalized Ratio, PT-Prothrombin time // \*BCL PRE A=1, B=6 y POST BCL A=1, B=4 y C=2//

<https://doi.org/10.1016/j.aohep.2024.101440>

#### Efficacy and safety of intravenous L-ornithine L-aspartate in patients with grade III and IV hepatic encephalopathy

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**Introduction and Objectives:** Hepatic encephalopathy (HE) is a common and serious complication of cirrhosis, associated with high morbidity and mortality. Ammonia and inflammation are the main triggers of HE. The use of L-ornithine-L-aspartate (LOLA) provides precursor substances for glutamine synthesis in perivenous cells, accelerating ammonia detoxification.

This study aims to evaluate the efficacy and safety of intravenous L-ornithine-L-aspartate (LOLA) in patients with grade III-IV hepatic encephalopathy (HE).

**Materials and Patients:** Retrospective and analytical study of patients with grade III-IV hepatic encephalopathy (HE).

All patients received intravenous LOLA 50 g for up to 48 hours, excluding those with renal failure. Descriptive statistics with measures of central tendency and dispersion were performed. Improvement was considered when HE regressed by at least one grade, and adverse events were evaluated.

**Results:** A total of 32 patients were included, with a mean age of 55 years  $\pm$  9.6. There were 13 females (40.6%) and 19 males (59.4%). Eight patients (25%) were classified as Child-Pugh B, while 24 patients (75%) were classified as Child-Pugh C. The mean MELD score was  $19.03 \pm 6.08$ , and the mean MELD NA score was  $7.19 \pm 7.19$ . The most common etiology was alcohol-related (43.8%), followed by MAFLD (29.1%) and viral (9.5%). All patients had grade III hepatic encephalopathy. The precipitating factors were sepsis (53%), hemorrhage (25%), constipation (12.5%), diuretics (6.3%), and electrolyte imbalance (3.1%). A total of 24 patients (75%) responded to the treatment, while 8 patients (25%) did not. Nineteen patients were found to have some degree of acute-on-chronic liver failure (ACLF). No adverse events were reported.

**Conclusions:** The use of intravenous LOLA for the treatment of grade III-IV hepatic encephalopathy is effective and safe. These results support the use of LOLA as a therapeutic option in the management of hepatic encephalopathy in this patient population.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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**Lactate-albumin ratio as a predictor of mortality in patients with acute on chronic liver failure in a third-level care hospital in Mexico**

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**Introduction and Objectives:** Acute-on-chronic liver failure (ACLF) is an abrupt worsening of clinical conditions in patients with chronic liver disease. It has a higher mortality rate with respect to patients who do not develop this entity (33.9% vs. 4.7%). The lactate/albumin ratio is a statistically significant predictor ( $p<0.001$ ) of mortality during hospitalization in these patients. This study aimed to determine whether the lactate-albumin ratio predicts mortality in patients with ACLF in Mexican population, identify the sociodemographic characteristics of this group of patients and to determine the related mortality at 7, 28, 90 and 180 days.

**Materials and Patients:** An observational, retrospective, single-center study was conducted where patients with diagnosis of ACLF according to the EASL-CLIF criteria who were hospitalized during the period from 2017 to 2022 in the Gastroenterology department at National Medical Centre "Siglo XXI" were included. Patients diagnosed with terminal chronic extrahepatic diseases, hepatocellular carcinoma and extrahepatic neoplasms were excluded.

**Results:** A total of 186 patients were enrolled, 51% were women, with an age range of 56-65 years, 29% were secondary to fatty liver disease associated with metabolic dysfunction, obtaining that the most frequent precipitant was the infectious origin in 111 patients (60%), with abdominal origin being the most prevalent (36%). Renal failure was present in 71%, followed by coagulopathy (50%) and neurological failure (49%). On admission, grade I ACLF was present in 37 patients (20%), grade II in 72 (39%), grade III in 77 (49%). At 7, 28, 90 and 180 days 73 patients (39.5%), 146 patients (78.9%), 159 (85.9%) and 172 patients (93%) died respectively, with a lactate albumin ratio for each of these, with a cut-off point 1.24 (AUC 70.70%), 0.87(AUC 71.20%), 0.84 (AUC 73.5%) and 1.04(AUC 64.90%) respectively with statistically significant values  $p < 0.05$ .

**Conclusions:** Lactate levels and its clearance have been shown to predict outcome of critically ill patients with liver cirrhosis, improving the prediction of mortality. The lactate albumin ratio is useful for predicting mortality in this group of patients at 7, 28, 90 and 180 days with adequate sensitivity and specificity. The values obtained were statistically significant as shown in the complementary tables.

**Ethical statement**

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

**Declaration of interests**

None

**Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Table 1.**  
Lactate/albumin ratio.

| Category             |       | Mean Lactate/<br>albumin ratio | Standard<br>deviation | p        |
|----------------------|-------|--------------------------------|-----------------------|----------|
| General population   |       | 1.74                           | 1,542                 | <0.001*  |
| ACLF grade at 1 day  | i     | 1.31                           | 1,055                 | 0.026‡   |
|                      | ii    | 1.54                           | 1,214                 |          |
|                      | ii    | 2.15                           | 1,891                 |          |
| ACLF grade at 3 days | i     | 1.40                           | 1,146                 | 0.048‡   |
|                      | ii    | 1.48                           | 1,108                 |          |
|                      | ii    | 2.20                           | 1,942                 |          |
| Outcome at 7 days    | Alive | 1.28                           | 0.961                 | < ¥0.001 |
|                      | Death | 2.46                           | 1,954                 |          |
| Outcome at 28 days   | Alive | 1.08                           | 0.901                 | < ¥0.001 |
|                      | Death | 1.93                           | 1,633                 |          |
| Outcome at 90 days   | Alive | 0.93                           | 0.696                 | < ¥0.001 |
|                      | Death | 1.88                           | 1,605                 |          |
| Outcome at 180 days  | Alive | 1.11                           | 0.86                  | ¥0.072   |
|                      | Death | 1.80                           | 1,576                 |          |

\*Kolmogorov-Smirnov test, ‡Kruskal-Wallis test, ¥Mann-Whitney U test.

| Assessment                                     | Area down<br>the curve | Cutt off<br>point | Sensitivity | Specificity | p      |
|------------------------------------------------|------------------------|-------------------|-------------|-------------|--------|
| Lactate/albumin ratio mortality<br>at 7 days   | 70.70%                 | 1.24              | 64.40%      | 60.40%      | <0.001 |
| Lactate/albumin ratio mortality<br>at 28 days  | 71.20%                 | 0.87              | 71.00%      | 61.50%      | <0.001 |
| Lactate/albumin ratio mortality<br>at 90 days  | 73.50%                 | 0.84              | 72.20%      | 61.50%      | <0.001 |
| Lactate/albumin ratio mortality<br>at 180 days | 64.90%                 | 1.04              | 60.20%      | 61.50%      | 0.034  |

Roc curves.

<https://doi.org/10.1016/j.aohep.2024.101442>

**Neutrophil/Lymphocyte ratio in patients with spontaneous bacterial peritonitis.**

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**Introduction and Objectives:** Spontaneous bacterial peritonitis (SBP) is a complication secondary to hemodynamic and structural changes and portal hypertension generating an increase in intestinal permeability and proinflammatory state. In cirrhosis it has been shown there is an immune dysfunction with changes in the cellular response associated with lack of regulation of neutrophils, a decrease in lymphocytes and synthesis of anti-inflammatory cytokines which make the response to an infectious agent deficient due to these changes the use of inflammatory biomarkers is limited. The neutrophil/lymphocyte ratio (NLR) has been shown to be a prognostic and diagnostic predictor in different pathologies but in liver their use has been inconclusive.

Our objective is to determine the role of the neutrophil/lymphocyte ratio in hospitalized patients with acute on chronic liver failure (ACLF) and without ACLF in hospitalized patients with spontaneous bacterial peritonitis at the Gastroenterology Department of the Hospital Juárez de México.

**Materials and Patients:** Observational, descriptive, retrospective, longitudinal study; patients with PBE were selected and divided into



two populations: with ACLF criteria and without ACLF accord EASL guidelines. Inclusion criteria: Patients with ascites secondary to cirrhosis, without the use of primary SBP prophylaxis, admitted to the hospitalization service without other identified sources of infection. NLR was performed at the time of hospitalization and after antibiotic use. Measures of central tendency for dispersion and Pearson correlation between Child Pugh and Meld Na scores with NLR were applied.

**Results:** A total of 128 patients were collected, 25 patients fulfilling the inclusion criteria: 15 without ACLF and 10 with ACLF. Mortality in both groups was 40%; in patients without ACLF it corresponded to 20%, whereas in patients with ACLF mortality was 70%, which corresponded to Grade 2 (50%) and Grade 3 (80%). Regarding the NLR index, patients with ACLF did not have higher values compared to those without ACLF. The correlation with the scores was not significant between ACLF - NLR (r=0.35) and Meld Na - NLR (r=0.035). Seventeen patients responded to antibiotic treatment, 13 in the group without ACLF and 4 in the group with ACLF, in all of which there was a decrease in the NLR after ascites fluid control. However, it was found that the index values were correlated before and after the use of antibiotics at 48 hours of treatment (r= 0.88) in comparison with the NLR before and after no response to treatment at 48 hours (r= 0.31).

**Conclusions:** We found that NLR was not associated with severity, stage and mortality in patients with SBP, however there is a strong relationship between NLR values before and after antibiotic use at 48 hours, which could allow its use as a biomarker for assessment of antibiotic response.

Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

Declaration of interests

None

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Table 1.  
Study population characteristics.

|                                      | Without ACLF (n=15)                    | ACLF (n=10)                             |
|--------------------------------------|----------------------------------------|-----------------------------------------|
| <b>Gender</b>                        |                                        |                                         |
| Male                                 | 4 (26.6%)                              | 8 (80%)                                 |
| Female                               | 6 (73.4%)                              | 2 (20%)                                 |
| <b>Age</b>                           | 49 años (30 -67)                       | 58.2 años (44 -78)                      |
| <b>Etiology.</b>                     |                                        |                                         |
| Alcohol.                             | 6 (73.4%)                              | 6 (60%)                                 |
| Autoimmune Hepatitis.                | 0                                      | 1 (10%)                                 |
| Primary biliary cholangitis.         | 1 (6.6%)                               | 1 (10%)                                 |
| Overlap Syndrome                     | 2 (13.2%)                              | 0                                       |
| Hepatitis C virus.                   | 3 (19.8%)                              | 0                                       |
| Cryptogenic.                         | 3(19.8%)                               | 2 (20%)                                 |
| <b>CHILD PUGH</b>                    |                                        |                                         |
| A                                    | 1 (6.6%)                               | 0                                       |
| B                                    | 6 (39.6%)                              | 2 (20%)                                 |
| C                                    | 8 (52.8%)                              | 8 (80%)                                 |
| <b>Meld- Na</b>                      | 19.53 points (8 -28)                   | 27 points (14 - 40)                     |
| <b>Mortality.</b>                    | 3 (20%)                                | 7 (70%)                                 |
| <b>ACLF</b>                          |                                        |                                         |
| Grade II                             |                                        | 4 (40%)                                 |
| Grade III                            |                                        | 6 (60%)                                 |
| Polymorphonuclear cells at diagnosis | 2150 cels/mm <sup>3</sup> (50 -16,200) | 1782.6 cels/mm <sup>3</sup> (188 -6180) |
| Response to treatment.               |                                        |                                         |
| Yes.                                 | 13 (87%)                               | 4 (40%)                                 |
| No.                                  | 2 (13%)                                | 6 (60%)                                 |
| Ascites Fluid Proteins.              | 1.76 g/dl (0.5 - 4.6)                  | 1.84 (0.6 - 4.6)                        |
| <b>NLR</b>                           |                                        |                                         |
| Before treatment.                    | 8.82 (1.86 - 21.16)                    | 23.65 (1.60 - 59.60)                    |
| After treatment.                     | 4.87 (1.4 - 14.61)                     | 18.62 (1.2 - 52.8)                      |

Impact of cholemic nephrosis on renal failure in cirrhotic patients

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**Introduction and Objectives:** : The development of acute kidney injury (AKI) in cirrhotic patients is of multifactorial origin, including urinary tract infection, diuretics, portal hypertension, shock, etc. Another important factor is cholemic nephrosis, it is considered when total bilirubin exceeds 20 mg/dl, this implies that bile pigments damage the distal tubule with deterioration of renal function, increasing morbidity and mortality. This study aimed to evaluate the levels of hyperbilirubinemia in the development of AKI and its association with biomarkers of renal failure.

**Materials and Patients:** : Retrospective and analytical study of a cohort of cirrhotic patients, to evaluate the development of AKI associated with bilirubin levels. Statistical analysis: A binary logistic regression model was performed considering bilirubin (greater than 20), NGAL (greater than 150) and cystatin (greater than 0.95) as associated factors. The significance of the model was considered with an alpha level less than 0.05.

**Results:** 109 patients were included, 45 women 64 men, age 54.67 ± 11.6, Child Pugh A: 2, B: 29, C: 78. The binary logistic model was significant W(1)=11.089, p=0.001. The OR for bilirubin was 4.37 (1.168-16.35, 95% CI P=.027), for NGAL OR 2.7 (1.08-6.71, 95% CI; p=.032), cystatin 0.64 (0.35-11.66, CI 95%; p=0.764) not significant.

**Conclusions:** Hyperbilirubinemia increases the risk of developing AKI by up to 4 times. The useful biomarker for AKI was NGAL.

Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

Declaration of interests

None

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

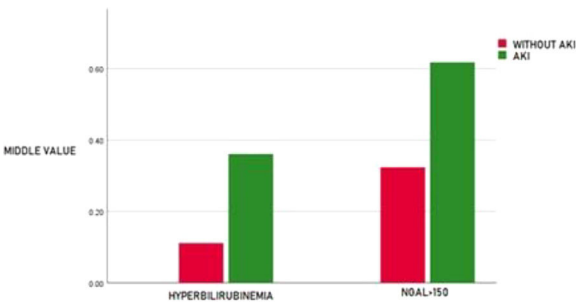


Figure 1. Grouped Bar Graph: mean value of bilirubin and NGAL in patients with AKI

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Evaluation of the MELNa AGIB Scale to Predict Mortality in Patients with Cirrhosis and Variceal Hemorrhage.

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**Introduction and Objectives:** Patients with decompensated cirrhosis are at risk of variceal hemorrhage, which increases the risk of mortality. Validated scales exist to assess this risk, but there is currently no scale that evaluates the risk of variceal hemorrhage and death simultaneously. The MELDNa AGIB (acute gastrointestinal bleeding) scale incorporates sodium (Na) levels, albumin levels, the corrected QT interval (QTc), and a history of hemorrhage to calculate mortality at 6 weeks. While it has been evaluated in other centers, further studies are needed to validate its utility. To evaluate the MELDNa-AGIB scale for predicting the risk of mortality in decompensated cirrhotic patients.

**Materials and Patients:** This was a retrospective, analytical, observational study conducted on a cohort of patients with decompensated cirrhosis and variceal hemorrhage. The MELDNaAGIB scale was calculated for each patient and compared with other scoring systems, including MELD, MELD NA, MELD LACTATE, and MELD 3.0, to assess its effectiveness. Statistical analysis involved the construction of ROC curves to determine the prognostic value of each scoring system in predicting mortality among patients with variceal bleeding. A significance level of  $p<0.05$  was considered, and sensitivity and specificity were determined based on the cutoff points obtained from the significant ROC curves.

**Results:** A total of 32 patients were included in the study, of whom 56.2% were male, with an average age of  $57\pm11$ . The etiologies of cirrhosis included alcohol-related, metabolic-associated fatty liver disease (MAFLD), dual injury, hepatitis C virus (HCV), autoimmune hepatitis (AIH), and unidentified causes (34.37%, 31.25%, 21.87%, 6.25%, 3.12%, 3.12%, respectively). Fifty percent of the patients had a prolonged QTc interval ( $>456$ ms) as calculated using the Fridericia formula, and 67.2% had a history of previous variceal hemorrhage. The MELDNa-AGIB scale demonstrated an area under the receiver operating characteristic (AUROC) curve of 0.849 (95% confidence interval: 0.681-0.950,  $p=0.004$ ), with a sensitivity of 87.5% and specificity of 83% when a cutoff point of 17 was applied for MELDNa-AGIB. The AUROC for predicting mortality was significantly lower for MELD/Lactate.

**Conclusions:** Although the study group was small, the MELDNa-AGIB scale showed significant performance in predicting 6-week mortality in patients who developed variceal hemorrhage.

Ethical statement

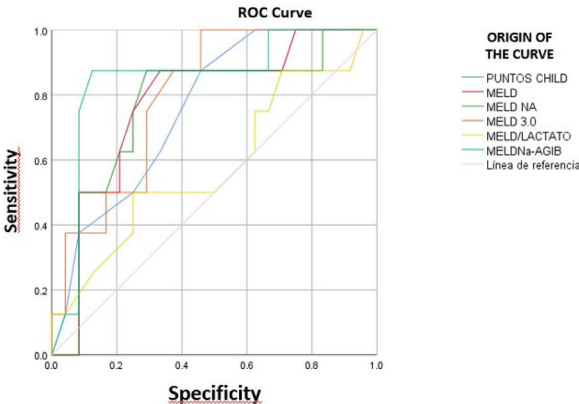
The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

Declaration of interests

None

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



| AREA UNDER THE CURVE |       |                          |                                      |                                    |             |
|----------------------|-------|--------------------------|--------------------------------------|------------------------------------|-------------|
| TEST VARIABLES       | Area  | Desv. Error <sup>a</sup> | Asymptotic significance <sup>b</sup> | 95% Asymptotic Confidence Interval |             |
|                      |       |                          |                                      | Lower limit                        | Upper limit |
| CHILD PUGH SCORE     | 0.758 | 0.089                    | 0.031                                | 0.584                              | 0.932       |
| MELD                 | 0.776 | 0.094                    | 0.021                                | 0.592                              | 0.960       |
| MELD NA              | 0.766 | 0.102                    | 0.026                                | 0.566                              | 0.965       |
| MELD 3.0             | 0.797 | 0.080                    | 0.013                                | 0.639                              | 0.955       |
| MELD/LACTATE         | 0.583 | 0.124                    | 0.486                                | 0.341                              | 0.826       |
| MELDNa-AGIB          | 0.849 | 0.086                    | 0.004                                | 0.681                              | 1.000       |

The test result variables: CHILD PUNTOS, MELD, MELDNa, MELD 3.0, MELD/LACTATE, MELDNa-AGIB have at least one tie between the positive true state group and the negative true state group.

a. Under the non-parametric assumption.

b. Null hypothesis: true area = 0.5

Figure 1. Comparative analysis among different scales in patients with variceal hemorrhage and hepatic cirrhosis.

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Validation of S-ANT for the diagnosis of minimal hepatic encephalopathy

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**Introduction and Objectives:** Hepatic encephalopathy (HE) is one of the most frequent complications of cirrhosis, minimal hepatic encephalopathy (MHE) is the initial stage and is characterized by the fact that it has no clinical data, its diagnosis is made with neuropsychological tests, the MHE produces a deterioration in the quality of life of patients and an increased risk of accidents. Hence, it is relevant to diagnose. Performing neuropsychological tests requires prolonged time, so validating an MHE count test that is easy, reproducible, and in less time is recommended. The simplified-animal naming test (S-ANT) test is performed by asking the patient to nominate 20 animals in one minute. In the reference cutoff for the non-Mexican population, a score lower than 15 suggests MHE.

We aimed to assess the validity of the S-ANT scale as a screening test in patients with cirrhosis without overt HE.

**Materials and Patients:** We present a prospective, descriptive, and analytical study of patients with cirrhosis of different etiology

without overt HE who underwent S-ANT, PHES, and Flicker tests. We determine the area under the receiver operator characteristic (AUROC) curve to validate the S-ANT test. MHE was detected if the PHES and Flicker tests were abnormal.

We compared the S-ANT scores of both groups with and without MHE with the student's t-test for independent groups. Sensitivity (S) and specificity (SE) were calculated with the AUROC cutoff point for MHE.

**Results:** Detection of MHE was in 12/83 patients (14.5%); 43 (51.83%) women, mean age  $52.7 \pm 7.5$  years, median schooling 8.3 years (range 0-17), the etiology of cirrhosis was: 39 (47.0%) alcohol, 9 (28.9%) primary biliary cirrhosis, 17 (20.5%) metabolic fatty liver, 18 (21.7%) hepatitis C virus According to Child-Pugh: 57 (68.7%) A, 25 (30.1%) B, and 1 (1.2%) C. The mean S-ANT for non-MHE was  $19.35 \pm 5.4$ , and for MHE,  $14.7 \pm 5.6$ ,  $p=0.024$  AUROC was significant .760 (.577-.942, 95%CI);  $p=0.037$  with  $S=83\%$  and  $SE=77\%$  cutoff= 17.5 words, which is higher than for other populations.

**Conclusions:** In the Mexican population, S-ANT reliably discriminates against patients with cirrhosis without overt HE with cognitive impairment, confirmed by PHES and Flicker test

### Ethical statement

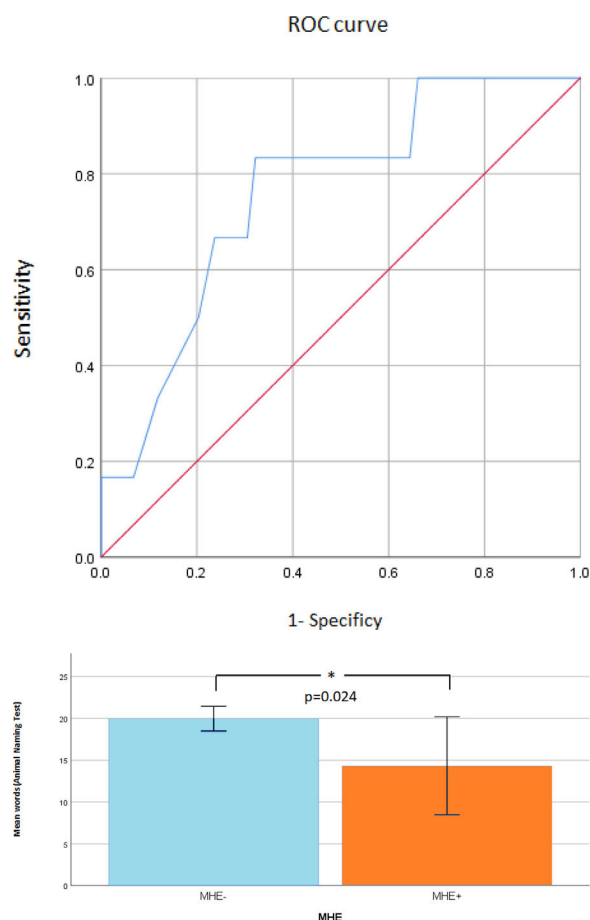
The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

### Declaration of interests

None

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



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## Hepatitis secondary to consumption of piñalim

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**Introduction and Objectives:** The use of natural products without proper assessment is common and favored by the popularity of phytotherapeutics. The regulations related to the prescription and use of these products are scarce, which leads to their being widely used in self-medication. We present the clinical case of a woman who consumed piñalim and presented hepatotoxicity

**Materials and Patients:** A 29-year-old woman without significant history. She was admitted to the general surgery service for cholecystectomy. After preoperative evaluation, abnormalities in liver function tests (LFT) stood out, for which reason they intentionally asked about the consumption of alcohol, drugs, supplements or herbal and/or homeopathic products, referring to the daily consumption during the last year of PIÑALIM (red, green and white tea) in order to lose weight. Ultrasound of the liver and bile ducts reported: liver of normal shape, size and situation, with no evidence of solid or cystic lesions. Bile duct without dilatation. Gallbladder with a 5.6mm thick wall, without images suggestive of stones. The surgical report showed a lack of findings in the gallbladder and liver. The jaundice and altered LFT persisted in the postoperative period (mixed pattern); additional tests were performed: HBV-HCV-HAV-HIV viral panel: TORCH negative. Negative Tomography of the abdomen without relevant findings. ANA: Negative Until now, the only hepatotoxic agent identified (PIÑALIM) had already been suspended, so this behavior was maintained, avoiding the consumption of any drug. In the following control, the LFT maintained a downward trend, until normalizing 6 months after the definitive suspension of the infusion. (Table 1)

**Results:** After the definitive suspension of the tea, the LFT were normalized, thus concluding the direct relationship of the product by having a score on the CIOM/RUCAM scale of 9 (definitive cause of hepatotoxicity).

**Conclusions:** The report of hepatitis associated with infusions is becoming more frequent, it is important to raise awareness about our patients in the "non-safety" of natural products and in the medical team to alert about these products and avoid procedures unnecessary surgeries.

### Ethical statement

The identity of the patients is protected. Consentment was obtained.

### Declaration of interests

None

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Table 1**  
Liver Function Tests

| Preoperative                                                                                              | Postoperative                                                                                             | 6 months of suspension of the hepatotoxic                                                              |
|-----------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|
| TB: 11.1mg/dl, DB: 8.1mg/dl, IB: 3.0mg/dl, TSA: 159U/L, TLA: 356U/L, AF: 281U/L, HDL: 545U/L, TGG: 459U/L | TB: 8.0mg/dl, DB: 6.3mg/dl, IB: 1.7mg/dl, TSA: 111U/L, TLA: 242U/L, AF: 180U/L, HDL: 400U/L y TGG: 298U/L | TB: 1.3mg/dl, DB: 0.7mg/dl, IB: 0.6mg/dl, TSA: 36U/L, TLA: 44U/L, AF: 120U/L, HDL: 250U/L y TGG: 66U/L |

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From Hepatitis E to Autoimmune Hepatitis:  
Aftermath of a trip to Qatar

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**Introduction and Objectives:** Autoimmune hepatitis (AIH) is a chronic immune-mediated disease with an estimated frequency of 11 to 25 subjects per 100 000 population. It has been reported that viral hepatitis can be a trigger for chronic active hepatitis with AIH criteria. Hepatitis E virus is infrequent in our environment, but it is recognized as the cause of about 20 million new infections per year, being described in case reports as a triggering factor of AIH.

**Materials and Patients:** We present the case of a 39-year-old woman who debuts with jaundice and general condition attack, this, 20 days after her return from Qatar, referring to have consumed raw meat during her stay, denying chronic degenerative history, alcohol and drug consumption. Liver function tests showed changes with R factor >5 compatible with hepatocellular pattern, liver ultrasound showed no liver or biliary changes. AgsVHB (-), HCV (-), VHA IgG (+), IgM (-), AC VHE IgG (-), IgM (+), immunoglobulins IgA 342, IgG 1777 U, IgM 97 U, negative ANA, AML, AMA, anti-LKM-1 antibodies were reported, which was considered probable acute hepatitis E. Cholangioresonance was performed due to the increase in bilirubin at the expense of direct bilirubin, confirming the absence of biliary tract changes.

**Results:** The patient was stable for 4 weeks with clinical improvement and a gradual decrease in bilirubin and transaminases, without evidence of liver damage or encephalopathy. After this period, the patient presented again with an abrupt rise in transaminases of more than 20 times the LSN. In view of these findings, an ultrasound-guided liver biopsy was performed. The histopathological report was consistent with autoimmune hepatitis, and treatment with prednisone and azathioprine was initiated, to which the patient responded favourably. The patient is currently asymptomatic and stable.

**Conclusions:** It is important to consider that acute hepatitis due to HEV is increasingly recognised, although sometimes misdiagnosed and confused with other liver diseases. It is also important to highlight that autoimmune diseases may be preceded by a viral infection due to an inadequate immune response, which forces us to highlight liver biopsy as a useful tool when serological markers are insufficient.

Ethical statement

The identity of the patients is protected. Consentment was obtained.

Declaration of interests

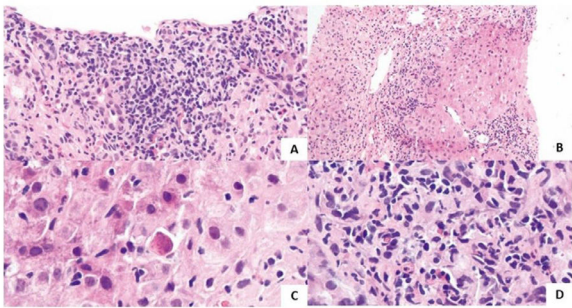
None

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Table 1.  
Biochemical evolution

| PARAMETRO | 21.12.22 | 26.12.22 | 28.12.22 | 07.01.23 | 09.01.23 | 14.01.23 | 28.01.23 | 18.02.23 | 28.03.23 |
|-----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| BT        | 8        | 16.3     | 7.56     | 3.2      | 14.31    | 2.21     | 1.9      | 0.89     | 0.91     |
| BD        | 6.81     | 14.36    | 6.16     | 1.8      | 12.3     | 1.21     | 1.3      | 0.6      | 0.8      |
| BI        | 1.19     | 1.94     | 1.4      | 1.4      | 2.01     | 1        | 0.6      | 0.29     | 0.11     |
| AST       | 2749     | 2012     | 242      | 93       | 1649     | 250      | 234      | 40       | 25       |
| ALT       | 3662     | 3017     | 1176     | 358      | 2687     | 562      | 211      | 88       | 28       |
| FA        | 621      | 237      | 134      | 190      | 255      | 188      | 219      | 135      | 72       |
| INR       | 1.27     | 1.47     | 1.2      | 1.23     | 1.54     | 1.05     |          |          |          |



**Image 1:** **A)** The inflammatory infiltrate consists predominantly of lymphocytes with damage to the ductal epithelium, with occasional neutrophils. **B)** Identical fibrous dilatation of the portal spaces forming occasional porto-portal bridges. **C)** Necrotic hepatocytes and occasional lymphocytes in the cytoplasm of the hepatocytes (emperipolesis). **D)** Detail of the inflammatory infiltrate in the portal spaces, consisting of lymphocytes, isolated plasma cells and neutrophils.

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Characteristics of patients with overlap syndrome  
of autoimmune liver diseases in a third level  
hospital.

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**Introduction and Objectives:** Autoimmune liver disease is classified into 3 well-defined entities: autoimmune hepatitis, primary biliary cholangitis and primary sclerosing cholangitis, there is a group of patients who show characteristics of more than one entity and is called overlap syndrome (OS), according to the Paris criteria they are classified, the prevalence of overlap in our country is low. We describe the clinical and biochemical characteristics of patients with OS treated at the liver clinic at the Hospital General de México.

**Materials and Patients:** It is a retrospective and descriptive study, records of the autoimmune liver disease consultation were reviewed, searching for patients with OS using the Paris criteria in the period 2014-2023, descriptive statistics were performed with measures of central tendency and dispersion using SPSS 25.0.

**Results:** 22 patients were included, all of them with liver biopsy, 95% women aged 47 ± 12.6 years, the most common phenotype was PBC/HAI (59%). The time to diagnosis from initial manifestations ranged from 1 to 6 years, the most frequent tests were ANA (81%), AMA (63%), ASMA (18%) and LKM1 (18%), Immunoglobulin G levels on average 2048 ±643.8. The most frequent comorbidities were systemic sclerosis, arterial hypertension and hypothyroidism, the predominant symptoms were fatigue and pruritus reported in 36%; 90% were cirrhotic, Child Pugh A 70%, B 25% and C 5%. The most frequent decompensation was variceal hemorrhage (22.7%), 4.7% reported portal thrombosis, and 2 patients were transplanted.

**Conclusions:** Overlap syndromes are rare, we found the majority of patients are women with advanced stage of liver disease, the most frequent overlapping is PBC/HAI with a high proportion of positive serology tests and concordant biopsy, two patients underwent



liver transplantation. It is important to always look for this rare syndrome.

Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

Declaration of interests

None

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

| Characteristics of patients with overlap syndrome of autoimmune liver diseases. |              |              |
|---------------------------------------------------------------------------------|--------------|--------------|
| Sex                                                                             | Male         | n = 21 (95%) |
|                                                                                 | Female       | n = 1 (5%)   |
| Phenotype                                                                       | PBC/HAI      | n = 13 (59%) |
| Antibodies                                                                      | ANA          | n = 18 (81%) |
|                                                                                 | AMA          | n = 14 (63%) |
|                                                                                 | ASMA         | n = 4 (18%)  |
|                                                                                 | LKM1         | n = 4 (18%)  |
| Child-Pugh classification                                                       | Child-Pugh A | n = 14 (70%) |
|                                                                                 | Child-Pugh B | n = 5 (25%)  |
|                                                                                 | Child-Pugh C | n = 1 (5%)   |

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Epidemiological changes in the incidence of acute liver failure at a hospital in Mexico City

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**Introduction and Objectives:** Acute liver failure is a condition that can rapidly progress to multiple organ failure. The main reported cause is paracetamol ingestion in 47%, followed by drug-induced liver injury in 11% and viral hepatitis in 10%. An increase in the incidence in our hospital and a change in the etiology were observed. This study aimed to determine the frequency and etiology of acute liver failure, presentation and outcome of patients in the last 3 years at Juarez Hospital of Mexico.

**Materials and Patients:** Retrospective, descriptive, observational, cross-sectional study. 20 files with a diagnosis of acute liver failure from May 2020 to May 2023 at Juarez Hospital of Mexico were reviewed. Epidemiological data, clinical manifestations, biochemical parameters, evolution and outcome of the studied population were obtained.

**Results:** 15 patients were included, 86.6% were male, 13.3% female, 73.3% of the patients were under 35 years of age. 66.6% were secondary to hepatitis A virus, 13.3% to drug-induced liver injury and 20% autoimmune. In the last 5 months, 53.3% of the cases were presented. 73.3% manifesting as hyperacute, 20% acute and 6.6% sub-acute. The pattern of presentation of liver injury was hepatocellular in 80% and mixed in 20%. 3 patients received liver transplant (20%), 5 received plasmapheresis (33.3%), and 7 patients received support measures (46.6%). Mortality was 20%.

**Conclusions:** An increase in cases of acute liver failure was determined in the last 5 months, all secondary to hepatitis A virus, with a hyperacute presentation pattern, all required intensive care management, with 100% survival in patients undergoing liver transplantation or plasmapheresis. Due to these findings, it is necessary to perform

multicenter studies to determine a change in the behavior of this virus.

Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

Declaration of interests

None

Funding

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Utility of the MELD and MELD-Lactate scale in patients with severe Alcoholic Hepatitis as a predictor of severity and early mortality.

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**Introduction and Objectives:** Alcoholic Hepatitis (AH) causes acute inflammation of the liver. The prognosis depends on the recovery of the liver from rapid improvement to multi-organ failure and death. There are scales that establish the prognosis and respond to steroid in AH, based on biochemical markers, none uses lactate levels. The lactate level in a patient with hepatitis may be increased. To determine if the MELD-Lactate scale is better than MELD for predicting with greater accuracy the severity and early mortality in patients with Alcoholic Hepatitis.

**Materials and Patients:** Retrospective, retrospective and analytical study, from 2019 to 2022. The variables were obtained with laboratories upon admission, including lactate levels. The area under the curve for sensitivity and specificity was calculated for predictive scales and MELD-lactate to determine mortality at 28 and 90 days.

**Results:** Include 70 patients, 59 men (84.2%) and 11 women (15.7%), age 43.2 ±9.8 years. The mortality at 28 days was 19 patients (27.1%) and at 90 days it was 18 patients (25.7%), a total of 37 (52%). The area under the curve for MELD-Lactate was in general mortality 0.823; 0.705-0.941 (sensitivity 81.8% specificity 72.4%), at 28 days 0.874; 0.780-0.968 (sensitivity 88.9%; specificity 71.3%) and 90 days there was no significance, compared with MELD which was general mortality 0.741; 0.603-0.878 (sensitivity 81.8% specificity 66.1%), at 28 days MELD 0.766; 0.615-.916 (sensitivity 88.9% specificity 63.3%) and at 90 days there was no significance, with the rest of the scales (MELD 3.0, ABIC, Maddrey, MELD- Na and Glasgow, it was less than that of MELD-Lactate. (Figure 1,2).

**Conclusions:** Patients with severe AH have higher mortality, either early or late. In our study we showed that the MELD-lactate scale may be a better prognostic scale for early mortality in patients with alcohol hepatitis, since it showed a better performance than all the other scales used, although these results must be confirmed in other hospital centers, we can recommend their use.

Ethical statement

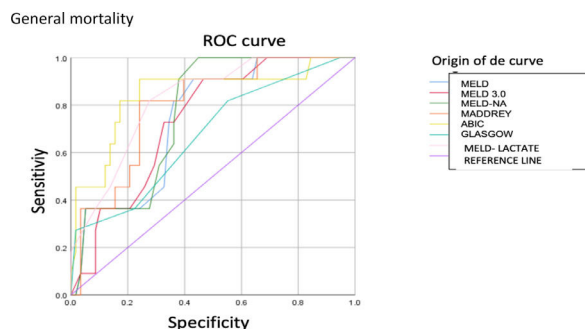
The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

**Declaration of interests**

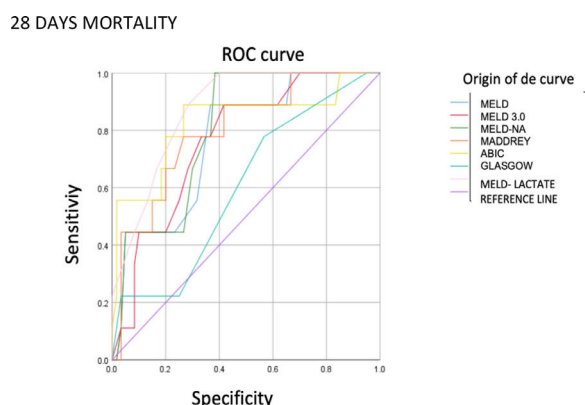
None

**Funding**

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**General mortality**

**Figure 1.** Sensitivity and specificity of scales used in alcoholic hepatitis to predict mortality.

**28 DAYS MORTALITY**

**Figure 2.** Sensitivity and specificity to predict 28 days mortality.

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### Comparison of non-invasive scores for the evaluation of liver fibrosis in subjects with metabolic dysfunction-associated fatty liver disease (MAFLD)

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**Introduction and Objectives:** Metabolic-associated fatty liver disease (MAFLD) poses a significant risk for progression to advanced liver diseases, underscoring the need for early detection. This study aims to assess and compare the diagnostic efficacy of non-invasive markers (APRI, FIB-4, Hepamet, and NAFLD Score (NFS)) in detecting hepatic fibrosis among MAFLD patients.

**Materials and Patients:** A retrospective examination was performed on adults with MAFLD who had undergone transient liver elastography. Hepatic fibrosis was identified at a cut-off point of  $\geq 8$  kPa. APRI, FIB-4, Hepamet, and NFS scores were evaluated with cut-off points determined via the Youden index. Receiver Operating Characteristic (ROC) curves and their areas were computed. All participants provided informed consent.

**Results:** Our cohort consisted of 150 MAFLD patients, the median age of 55 years (48-65), comprising 66.2% (129) females and 33.88% (66) males. The median BMI was 32.1 (28.8-35.6), kPa was 5.6 (4.6-7.8), and CAP was 310 (280-341). Hepatic fibrosis was evident in 24.7% (37) of the participants. Among the evaluated scores, APRI exhibited superior diagnostic performance, achieving an area under the curve of 0.72, followed by FIB-4 (0.66), Hepamet (0.64), and NFS (0.62). The cut-off points of 0.50 for APRI, 1.65 for FIB-4, 0.05 for Hepamet, and -0.75 for NFS yielded sensitivities of 86%, 82%, 86%, and 81%, respectively (Fig 1).

**Conclusions:** Non-invasive scoring systems, notably APRI, demonstrate valuable potential in evaluating hepatic fibrosis among Mexican MAFLD patients. Utilization of adjusted cut-off points enhances test efficiency, thereby facilitating early detection of individuals at greater risk of disease progression.

**Ethical statement**

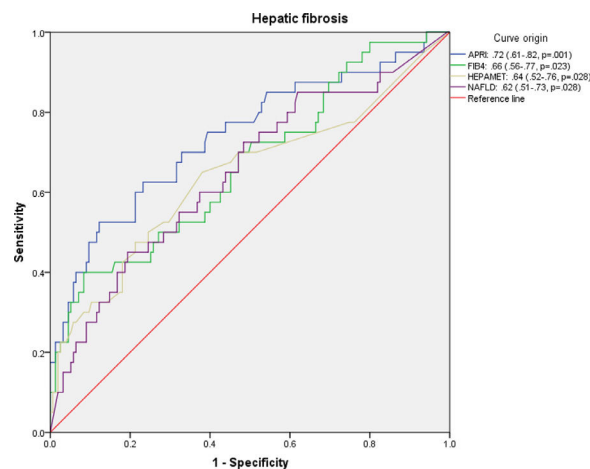
The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

**Declaration of interests**

None

**Funding**

This research was supported by CONAHCYT grant CVU 1138232 and Proyecto de Ciencia Básica #256235



**Figure 1.** Receiver operating characteristic (ROC) curves were constructed to evaluate the diagnostic performance of different non-invasive scores for hepatic fibrosis in subjects with metabolic-associated fatty liver disease (MAFLD). Hepatic fibrosis was assessed using liver transient elastography, with a threshold of  $\geq 8$  kPa indicating the presence of fibrosis.

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## IGFBP2: a possible molecular link between liver, heart, and bloodstream during metabolic dysfunction-associated steatotic liver disease

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**Introduction and Objectives:** Metabolic dysfunction-associated steatotic liver disease (MASLD) is highly prevalent worldwide, the concomitant presence of fibrosis is considered the most important risk factor of cardiovascular death. IGFBP2 is expressed mainly in the liver and at very low levels in heart. This peptide is associated with metabolic affection including obesity and type 2 diabetes. IGFBP2 role in MASLD is not clear. We aimed to assess the expression of IGFBP2 protein in the liver and associate it with its blood levels and cardiac expression in a rodent model of MASLD.

**Materials and Patients:** Male C57BL/6 mice weighing  $23 \pm 2$ g were included and fed a high-fat diet with water added with sugar (HF-SF) or control diet up to 30 weeks. Liver damage was assessed by biopsy. IGFBP2 was assayed by ELISA in serum, liver, and heart. Data is shown as Mean  $\pm$  SD, analyzed by ANOVA,  $p < 0.05$ .

**Results:** HF-SF mice exhibited increased bodyweight, visceral adiposity, and fasting glycemia compared to controls. HF-SF group developed steatosis with or without fibrosis. Mice showing fibrosis were assessed as F1C, portal fibrosis. IGFBP2 was significantly lower in steatosis regardless of the presence of fibrosis, both in serum and liver. Cardiac expression of IGFBP2 was diminished in steatosis with fibrosis compared with controls. Significant, moderate, positive correlations were observed between serum IGFBP2 and its hepatic expression, as well as IGFBP2 cardiac expression. IGFBP2 in serum negatively correlated with visceral adiposity and bodyweight.

**Conclusions:** IGFBP2 expression in liver and heart depends on the stage of MASLD and is associated with visceral adiposity. IGFBP2 in the bloodstream is produced mainly by the liver, and with lower contribution from heart. Serum IGFBP2 can be considered as a marker of its hepatic and cardiac expressions which are closely related with the stage of MASLD. IGFBP2 might be considered a molecular link between liver and heart during MASLD.

### Ethical statement

All procedures were approved by CICUAL-FM-UNAM (002-CIC-2022).

### Declaration of interests

None

### Funding

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## Endoscopic ultrasound guided portal pressure gradient: safety aspects, clinical relevance and technical issues to improve the procedure

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**Introduction and Objectives:** Endoscopic ultrasound guided portal pressure gradient measurement (EUS-PPGm) would provide useful clinical information in patients with liver diseases. However, there is yet scarcely data on the clinical relevance of this EUS-guided procedure.

We report our experience on EUS-PPGm focus on safety, clinical relevant findings, technical drawbacks and how to overcome them, aiming to make this procedure more safe, accurate and available.

**Materials and Patients:** EUS-PPGm was performed with a therapeutic echoendoscope and a dedicated 25G needle in 30 consecutive patients. Assessment of NAFLD 25; idiopathic portal hypertension 3; evaluation for curative therapy in hepatocellular carcinoma (HCC) 2. EUS-guided bilobar liver biopsies (EUS-BLB) were also immediately performed in 26 patients (87%) with a 19G needle

**Results:** EUS-PPGm was obtained in 25/30 patients (83%) being  $>5$  mmHg in 10/22 NALFD patients (45%) without endoscopic and/or ultrasonographic signs of portal hypertension neither liver fibrosis on EUS-BLB. Mean time to obtain EUS-PPGm was  $21 \pm 2$  minutes.

EUS-PPGm was not obtained in 5 cases. In 4 cases for excessive use of the elevator and up&down wheel and bending of the needle. In another case for exacerbating breathing movements. The hepatic and portal vein were difficult to puncture in one and two cases, respectively having to transverse the vessels and reposition the needle.

A self-limited bleeding from the cardias and a mild epigastric pain 2 day after a combined procedure were observed without other adverse events one month later.

**Conclusions:** EUS-guided PPGm, even when combined with EUS-BLB, seems safe providing useful clinical information. Almost half of patients affected with NAFLD have portal hypertension diagnosed precociously in reversible stages providing a useful tool in precision Medicine, especially in the setting of obesity pandemic. There are technical aspects related to the needle and the position of the echoendoscope that should be known to improve the safety, accuracy and availability of this procedure.

### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

### Declaration of interests

None

### Funding

None

<https://doi.org/10.1016/j.aohep.2024.101454>

# **The use of molecular adsorbent recirculating system and single-pass albumin dialysis as liver support: The experience of the Centro Médico Nacional 20 de Noviembre**

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**Introduction and Objectives:** Acute on chronic liver failure (ACLF) describe a state of severe liver dysfunction. Extracorporeal liver support (ECLS) is a system that performs filtration and detoxification functions within an external device with the goal of reducing mortality or bypassing liver transplantation. The objective was to evaluate the effects of the molecular adsorbent recirculating system (MARS) and single-pass albumin dialysis (SPAD) in patients with acute-on-chronic in a tertiary Mexican hospital.

**Materials and Patients:** : Retrospectively, a search was performed in the internal electronic system with patients who required MARS or SPAD from 2016 to 2022.

**Results:** The results show a total of 18 patients with the diagnosis of acute on chronic liver failure who received treatment with MARS or SPAD. It was observed that 50% of the patients were women, with a mean age of 37.8 years.

The cause of the chronic liver disease was autoimmune hepatitis in 5 cases, 5 primary biliary cholangitis, 3 as cryptogenic cirrhosis, 2 viral, 1 hepatocarcinoma, 1 metabolism errors and 1 graft rejection. Within the support therapies used, it was found that 28% of the patients received MARS and 72% received SPAD, with a total of 49 sessions.

Clinically 77% of patients experienced improvement in hepatic encephalopathy and 66% improvement in renal function. At the end of the 90-day follow-up period, an overall survival rate of 52.94% was recorded.

**Conclusions:** These findings support the effectiveness of MARS and SPAD as viable ECLS options in patients with ACLF. The positive results in the improvement of encephalopathy and renal function, together with the survival rate, indicate the potential of these therapeutic approaches in the management of patients in this clinical setting. The sample size was small, which may affect the generalizability of the results.

## **Ethical statement**

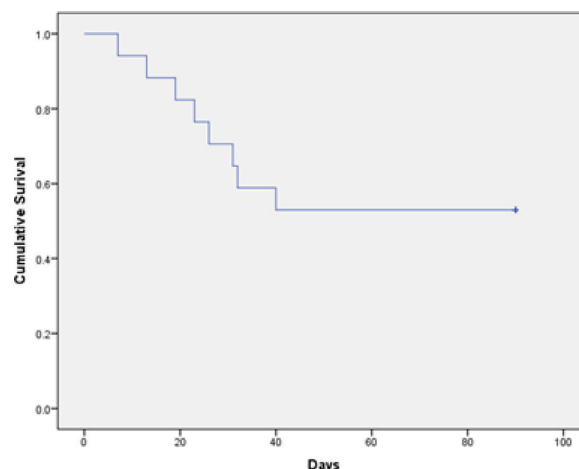
The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

## **Declaration of interests**

None

## **Funding**

None



**Figure 1.** Cumulative survival of patients treated with extracorporeal liver support.

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## **Hepatitis C Virus NS5A and Core protein induce hepatic stellate cells activation promoting fibrosis-related gene regulation on hepatocytes.**

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**Introduction and Objectives:** Chronic HCV infection leads to the development of liver fibrosis mediated by intercellular communication between hepatocytes and hepatic stellate cells (HSCs). The diverse molecular pathways involved in the development of fibrosis in hepatocytes derived from HSC activation induced by viral proteins remain to be fully determined. Our aim is to determine differentially expressed genes associated with fibrotic processes in hepatocytes (Huh7) that express the HCV NS5A or Core protein during co-culture with HSC (LX2).

**Materials and methods:** Huh7 cells were transfected to express NS5A or Core proteins and co-cultured with HSC-LX2 cells. Viral protein expression and expression of TGFβ1, Col1, and αSMA was



determined to assess LX2 activation. A profile of 84 genes associated with fibrosis during co-cultivation was determined and analyzed.

**Results:** HSC-LX2 co-cultured with transfected Huh7 showed an 8.3, 6.7 and 4-fold increase in collagen1, TGF $\beta$ 1 and timp1 expression respectively induced by NS5A and a 6.5, 1.8 and 6.2-fold increase respectively induced by Core, all these compared to HSC-LX2 co-cultured with untransfected Huh7. We detected 28 overexpressed genes in Huh7 (NS5A+) and 46 differentially expressed genes in Huh7 (Core +) in co-culture with HSC-LX2, compared to untransfected Huh7 in co-culture with HSC-LX2. Analysis of the expression profile showed that the TGF $\beta$ 1, the ECM regulation, and growth factors pathways are the molecular mechanisms involved during the co-culture of Huh7 transfected with NS5A or Core with HSC-LX2.

**Conclusions:** HCV NS5A and Core proteins expression in Huh7 cells induces the HSC-LX2 activation, regulating the expression of diverse genes in hepatocytes that trigger different molecular mechanisms involved in the fibrosis development, this information provide the identification of possible anti-fibrotic targets drugs associated with HCV infection for further study.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee.

#### Declaration of interests

None

#### Funding

The study was funded by the Department of Biochemistry and Molecular Medicine and CIIViM, School of Medicine, and by PAICYT 171-CS-2022 from Universidad Autónoma de Nuevo León (UANL), Monterrey, Nuevo León 64460, Mexico.

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#### Hepatitis C virus-infected patients carriers of the TT (C\*52T, rs14158) genotype of the LDL receptor and Apo3 present severe liver damage in West Mexico

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**Introduction and Objectives:** The clinical course of hepatitis C virus infection (HCV) is modulated by environmental factors and genetic polymorphisms that interact with the virus, such as the low-density lipoprotein receptor (LDLR) and ligand Apolipoprotein E (ApoE); both are associated with lipid metabolism. However, the relationship of these genes with liver damage has not been jointly evaluated in Mexicans. The study aimed to identify a relationship between the LDLR polymorphism (C\*52T, rs14158) and ApoE haplotype in anti-HCV positive patients with liver damage in a subpopulation of West Mexico.

**Materials and Patients:** This cross-sectional study included 152 naïve anti-HCV positive patients; 110 were viral load (VL) positive (+ve), and 42 were VL negative (-ve). A medical-nutritional evaluation was registered. LDLR and ApoE genotypes were assessed by allelic discrimination. Comparative statistical analysis was performed between VL+ve and VL-ve adjusted by genotype distribution and liver damage.

Written informed consent was obtained from the participants. The Institutional Review Board approved this study.

**Results:** The patients (85F/67M) were 49.8 $\pm$ 12 years of age with a BMI of 27.7 $\pm$ 5.4. VL +ve patients showed glucose homeostasis abnormalities (glucose >100 mg/dL, HOMA-IR >2.5); low levels of cholesterol, triglycerides, VLDL, and LDL, compared to VL-ve patients (p<0.001), as well as high-above-normal ALT, AST, GGT (p<0.001) and low platelets (p<0.001). A 61.1% (58/95) of the VL+ve patients had a high risk for fibrosis (FIB-4), and 35.7% (35/98) had severe fibrosis (APRI). A 10% (11/110) of the VL+ve patients were carriers of the TT LDLR/ApoE3 genotype in which 90% (10/11) had moderate/severe liver damage compared to the C allele carriers (CC, CT), whereas the VL-ve patients had 0% of the TT LDLR genotype (p=0.035) with a lower proportion of liver damage.

**Conclusions:** The presence of the TT LDLR/ApoE3 genotypes in VL +ve patients with hepatic function abnormalities suggests that it may be a valuable marker for risk of liver damage to avoid disease progression and to implement preventive strategies among the Mexican population.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

None

<https://doi.org/10.1016/j.aohep.2024.101457>

#### LILLE-4 vs. LILLE-7 to predict short-term mortality in patients with severe alcoholic hepatitis

Claudia L. Dorantes-Nava<sup>1</sup>, María F. Higuera-de la Tijera<sup>1</sup>, Alfredo Servín-Caamaño<sup>2</sup>, Gabriela Gutiérrez-Reyes<sup>3</sup>, Miguel Y. Carmona-Castillo<sup>1</sup>, Sandra Teutli-Carrion<sup>1</sup>, Ernesto J. Medina-Avalos<sup>1</sup>, José L. Pérez-Hernández<sup>1</sup>

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**Introduction and Objectives:** Alcoholic hepatitis (AH) is an acute liver inflammation associated with excessive alcohol consumption. The pharmacological treatment for AH is corticosteroids. There is a study that has proposed calculating the Lille model on day 4 (Lille-4), which apparently has comparable accuracy to the Lille model calculated on day 7 (Lille-7). However, this finding has not been validated. Therefore our objective is to determine if Lille-4 is equivalent to Lille-7 in predicting 28-day mortality in patients with probable severe alcoholic hepatitis (AH) as defined by the 2016 consortium criteria sponsored by NIAAA.

**Materials and Patients:** Observational, prospective, ambidirectional, analytical cohort study conducted from January 2010 to April 2023. We collected clinical and biochemical variables upon admission, calculated Lille models, assessed response and 28-day mortality. Comparative analyses were performed based on survival versus

mortality. Sensitivity, specificity, PPV, NPV, and accuracy of the models were calculated.

**Results:** A total of 327 patients were included, 297 (90.8%) being male. Mean age was 43.4±9.3 years. The 50th percentile for alcohol consumption was 320 g/day (5th-95th percentile: 100.8-662). At day 28, 207 patients (63.3%) died. Upon admission, the patients who died showed a significant difference compared to survivors in: Maddrey (90 [95%CI: 81-99] vs. 70 [95%CI:65-75]; p<0.0001); ABIC (8.8±1.8 vs. 8.1±1.3; p<0.0001); MELD (32±8 vs. 27±4; p<0.0001); MELD-Na (33±6 vs. 30±4; p<0.0001). Lille-7 model had an AUROC of 0.71 [0.65-0.77], where a value >0.45 had a sensitivity (S) of 78% and specificity (E) of 45% in predicting early mortality. Lille-4 model had an AUROC of 0.68 [0.63-0.74], where a value >0.45 had an S of 81% and E of 54% (Figure 1).

**Conclusions:** Lille-7 is the model with the highest accuracy, according to the obtained AUROC, for predicting early mortality in severe alcoholic hepatitis (AH). Therefore, the determination of total bilirubin should not be done prematurely (before day 7), and steroid therapy should be provided to patients for up to 7 days to classify treatment response.

Ethical statement

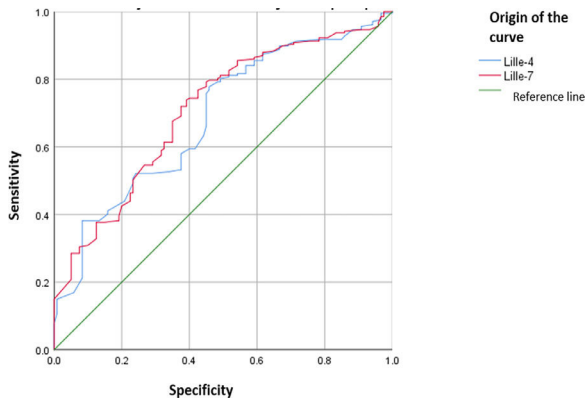
The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

Declaration of interests

None

Funding

None



**Figure 1.** Area Under the Receiver Operating Characteristic Curve (AUROC) of Lille-4 and Lille-7 for predicting 28-day mortality.

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Hepatic injury biomarkers in COVID-19

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**Introduction and Objectives:** C-reactive protein (CRP) and D-dimer have been shown to be predictors of severity in patients with COVID-19. The FIB-4 and APRI scoring systems are tools calculated using routine laboratory parameters that allow non-invasive evaluation of liver fibrosis. Some studies have demonstrated that the parameters comprising these scores predict mortality in COVID-19. The objective of this study was to determine the role of various liver injury biomarkers in stratifying the severity of hospitalized patients with COVID-19.

**Materials and Patients:** Analytical and retrospective study. Patients with COVID-19 were included, while those with liver disease were excluded. A receiver operating characteristic (ROC) analysis with 95% confidence intervals (CI) was performed to determine the predictive performance of FIB-4, APRI, D-dimer, and CRP in terms of the need for invasive mechanical ventilation (IMV) and mortality.

**Results:** A total of 448 hospitalized patients with COVID-19 were included in the study. 68.2% were male, with a mean age of 56.27 ± 14.7 years. 35.1% had systemic arterial hypertension, 29.2% had diabetes mellitus, 6% had cancer, 5% had chronic obstructive pulmonary disease, and 3.3% had chronic kidney disease. 21.4% required nasal cannula support, 29.4% required mask with reservoir, 35.5% required high-flow oxygen therapy, and 13.1% required IMV. 48% had severe disease, and 28.1% died. ROC analysis with 95% CI revealed that the best predictor of the need for IMV was the FIB-4 index, with an AUC of 0.637 (95% CI 0.545 - 0.732, p= 0.003), followed by APRI with an AUC of 0.596 (95% CI 0.504-0.687, p=0.04). The best predictor of mortality was FIB-4 with an AUC of 0.689 (95% CI 0.620 - 0.785, p= <0.001), followed by D-dimer with an AUC of 0.608 (95% CI 0.528 - 0.688, p= 0.041).

**Conclusions:** The application of the FIB-4 index with a cutoff point of ≥1.9 predicts IMV and mortality in SARS-CoV-2 infection and is superior to the standard severity biomarkers (CRP and D-dimer).

Ethical statement

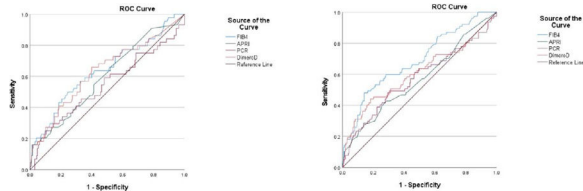
The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

Declaration of interests

None

Funding

None



**Figure 1:** ROC curves.

**Table 1**

Mortality and invasive mechanical ventilation markers in SARS-CoV-2: Analysis of ROC curves

| Mortality                       |       |             |               |             |             |         |
|---------------------------------|-------|-------------|---------------|-------------|-------------|---------|
| Marker                          | AUC   | CI 95%      | Cut-off point | Sensitivity | Specificity | P value |
| FIB-4                           | 0.689 | 0.620-0.785 | 1.905         | 0.610       | 0.384       | <0.001  |
| APRI                            | 0.569 | 0.493-0.645 | 0.605         | 0.429       | 0.308       | 0.066   |
| CPR                             | 0.572 | 0.493-0.651 | 184.50        | 0.494       | 0.312       | 0.055   |
| D Dimer                         | 0.608 | 0.528-0.688 | 747.50        | 0.455       | 0.236       | 0.041   |
| Invasive mechanical ventilation |       |             |               |             |             |         |
| FIB-4                           | 0.637 | 0.545-0.732 | 2.225         | 0.545       | 0.324       | 0.003   |
| APRI                            | 0.596 | 0.504-0.687 | 0.505         | 0.545       | 0.412       | 0.41    |
| CPR                             | 0.541 | 0.439-0.644 | 168.70        | 0.455       | 0.399       | 0.52    |
| D Dimer                         | 0.631 | 0.536-0.726 | 488.50        | 0.568       | 0.378       | 0.005   |

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### **In vitro analysis of apoptosis in hepatic stellate cells cultured under steatogenic conditions**

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**Introduction and Objectives:** Hepatic stellate cells (HSC) are responsible for the development of fibrosis during chronic liver disease. Cell death is among the most common cellular causes of increased tissue damage. From the different types of cell death, apoptosis and necrosis of hepatocytes are associated with the development of inflammation and the progress of liver disease. We aimed to assess cell death by apoptosis and necrosis in LX-2 hepatic stellate cells in an *in vitro* model of steatosis.

**Materials and methods:** LX-2 HSC were cultured under different conditions: control (C), mild steatosis (MS), severe steatosis (SS) and activation (TGF $\beta$ ). Cell death was identified by trypan blue staining. Apoptosis and necrosis were analyzed by flow cytometry at 24, 48 y 72h. Data: Mean $\pm$ SD, analyzed by one-way ANOVA,  $p < 0.05$  was considered significant.

**Results:** Cell death was similar between HSC cultured under control or activation conditions at the different times studied. Increased cell death was observed in MS at 72h and in SS from 24h. Accordingly, percentage of apoptotic cells was significantly increased in MS at 72h compared with other conditions at that time (C72h=14.1 $\pm$ 6.1, TGF $\beta$ 72h=11.8 $\pm$ 5.2, MS72h=57.7 $\pm$ 8.4, SS72h=3.8 $\pm$ 2.7 %,  $p < 0.05$ ). In contrast, SS group showed its peak in apoptosis at 24h (C24h=27.4 $\pm$ 2.8, TGF $\beta$ 24h=21.7 $\pm$ 7.5, MS24h=25.7 $\pm$ 3.2, SS72h=50.8 $\pm$ 9.5 %,  $p < 0.05$ ), showing that apoptosis begins early at 24h but is evidenced by trypan blue up to 48h. Activation of HSC was not associated with changes in apoptosis. No differences were observed in necrosis.

**Conclusions:** Apoptosis in LX-2 HSC was associated with the severity of the steatogenic condition, the higher the amount of free fatty acids in the medium, the higher the mortality at short term. Apoptosis explained most of the mortality observed by trypan blue in HSC; however, other death processes, including pyroptosis or necroptosis, should not be discarded yet, since they might also contribute to HSC cell death during steatosis.

#### **Ethical statement**

The protocol was registered and approved by the Ethics Committee.

#### **Declaration of interests**

None

#### **Funding**

None

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### **Prevalence of Immunoglobulin G against Hepatitis A Virus and Hepatitis E Virus in healthcare personnel**

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**Introduction and Objectives:** The hepatitis A and hepatitis E viruses are organisms that stand out for their high resistance to acid

and alkaline media, as well as to freezing temperatures. Despite presenting an approximate mortality of 1% for both viruses, a seroprevalence of up to 81.3% has been reported in previous decades, so it is important to know the current epidemiological status of both diseases.

**Materials and Patients:** Cross-sectional, descriptive, prospective and observational study. Individuals over 18 years of age were recruited, who were studying or had the degree of gastroenterologists at the Hospital de Especialidades Centro Médico Nacional Siglo XXI, in a period of time between June 01 and June 30, 2023. Blood samples were collected for detection of immunoglobulin G against hepatitis A and hepatitis E viruses and a demographic questionnaire was conducted to each of the participants.

**Results:** 23 individuals were recruited, 60.9% men ( $n=14$ ) and 39.1% women ( $n=9$ ), with a median age of 29 years, 13.0% corresponding to individuals from Mexico City ( $n=3$ ) and 86.9% from other states of the Mexican Republic ( $n=20$ ). A seroprevalence of 17.3% ( $n=4$ ) and 4.3% ( $n=1$ ) was reported for hepatitis A virus and hepatitis E virus, respectively.

**Conclusions:** There is a lower seroprevalence for hepatitis A and hepatitis E viruses than reported, so it is vitally important to take preventive measures in populations at risk of infection, such as health personnel.

#### **Ethical statement**

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### **Declaration of interests**

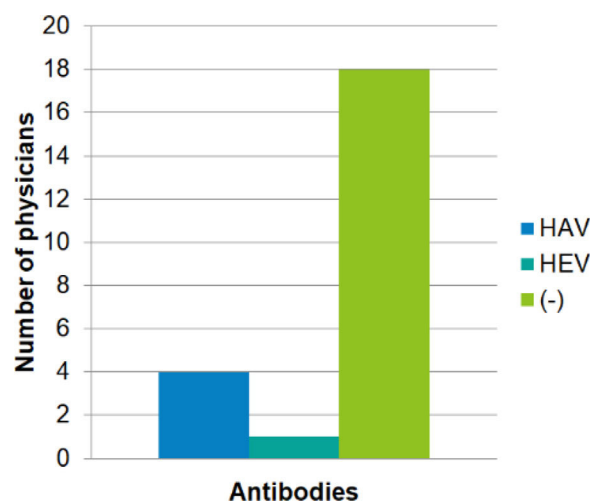
None

#### **Funding**

None

**Table 1.**

Number of physicians with antibodies against hepatitis A virus (HAV), hepatitis E virus (E) or a negative test (-).



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### **Noninvasive markers of hepatic fibrosis and their clinical application in coronary artery disease.**

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**Introduction and Objectives:** Coronary artery disease (CAD) is a leading cause of morbidity and mortality worldwide. Reliable knowledge of the prevalence of occult CAD, particularly anatomically confirmed CAD is limited and cardiovascular risk (CVR) models only predict the risk of an acute coronary event within a set period. It has been described that a FIB-4 score is associated with a higher CVR. Determine what is the utility of noninvasive markers of liver fibrosis in CAD.

**Materials and Patients:** A cross-sectional study was conducted in two tertiary centers in central and western Mexico from March 2019 to April 2023. Patients who required percutaneous coronary angiography were studied and demographic data and coronary angiographic were recorded. Noninvasive fibrosis indexes were calculated. Continuous variables were subjected to a distribution analysis and equality of variances to subsequently perform a mean comparison analysis with U-Mann-Whitney test between patients with monovascular, bivascular and trivascular involvement. A correlation analysis was also performed between the invasive markers and the Syntax index.

**Results:** A total of 168 patients were included with a mean age of  $66 \pm 12$  years with a predominance of male sex with 75.6% (n= 127). Angiographic findings included 37.5%, monovascular, 32.7%, bivascular and 29.8% trivascular involvement. Comparison of means of non-invasive markers of fibrosis demonstrated a significant difference in HFS between patients with monovascular ( $0.17 \pm 0.18$ ), bivascular ( $0.27 \pm 0.18$ ) and trivascular ( $0.30 \pm 0.25$ ) coronary artery disease,  $p < 0.001$ . A correlation was also demonstrated between non-invasive markers and Syntax score: FIB-4 ( $r = 0.820$ ,  $p < 0.001$ ), APRI ( $r = 0.766$ ,  $p < 0.001$ ), HFS ( $r = 0.869$ ,  $p < 0.001$ ), ( $r = 0.820$ ,  $p < 0.001$ ), NFS ( $r = 0.807$ ,  $p < 0.001$ )

**Conclusions:** The score of noninvasive tools to assess liver fibrosis correlates positively with the complexity of CAD and could be considered as noninvasive tools to be used in the assessment CVR.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

None

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#### Correlation between steatosis and fibrosis in patients with metabolic syndrome

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**Introduction and Objectives:** MAFLD is a highly prevalent cause of chronic liver disease, present in 70% of overweight people, 70% of diabetics, and 90% of morbidly obese people. It is the hepatic manifestation of the metabolic syndrome, defined by the presence of central obesity, insulin resistance, hyperlipidemia, hyperglycemia, and hypertension. The development of liver fibrosis is secondary to several factors, steatosis being one of them. To evaluate the correlation of steatosis with hepatic fibrosis in patients with metabolic syndrome using transition elastography.

**Materials and Patients:** Patients older than 18 years who met MALFD criteria were included, transition elastography was performed to calculate CAP and kilopascals, steatosis degree and fibrosis degree were calculated according to the myfibrosan application, for statistical analysis Pearson's bivariate correlations were used between CAP and kilopascal values. The association between the degree of steatosis and fibrosis was performed using the chi-square test. Was considered significant at  $p < 0.05$ .

**Results:** 94 patients were included, 20 men (21.3%), 74 women (78.7%), mean age  $40.5 \pm 10.02$ , CAP  $300.6 \pm 63.4$ , kilopascals  $6.4 \pm 2.7$ , steatosis grade S0: 8, S1: 8, S2: 20, S3: 58, degree of fibrosis F0: 58, F1: 14, F2:14, F3: 6, F4:2. The correlation between CAP and kilopascals was moderate and significant  $RHO=0.343$   $P=0.001$ . A significant association was found between the degree of steatosis and that of fibrosis chi-square (12) =25.1,  $p=0.015$ . The proportions were 50% (S0:F0), 16% (S1:F3), 50% (S2:F3), 100% (S3:F4).

**Conclusions:** The correlation between steatosis and fibrosis is moderate, implying that there are other factors that influence the development of fibrosis and its progression, so metabolic control and other factors in patients with MALFD are highly relevant to prevent fibrosis progression.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

None

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#### Acute liver failure secondary to co-infection of Hepatitis B and HIV

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**Introduction and Objectives:** We present the case of a man with hepatitis B and HIV coinfection diagnosed by serological studies which presented acute liver failure; the diagnostic approach, its treatment and outcome are described.

**Materials and Patients:** Provide information on the association of hepatitis B virus and HIV. When hepatotropic viruses are identified, intentionally find the association with other factors that cause acute



liver failure, including infectious agents, drugs, and coexisting diseases.

Brief description of the management to be carried out in cases of acute liver failure secondary to viral infections.

**Results:** This is a 31-year-old man who was hospitalized when presenting in his house with jaundice syndrome, abdominal pain and a drowsy state:

In his important history, he presented consumption of crystal and marijuana in a time of 8 months, high-risk sexual relations without the use of condoms, multiple sexual partners (Man who has Sex with Men), had been evaluated 7 days before as probable autoimmune hepatitis due to present positive anti-smooth muscle antibodies 1:80.

On admission to our unit, he presented 7 days of evolution with hyposthenia, hypodynamia, diffuse abdominal pain, being treated at the time as autoimmune hepatitis, treatment with steroids was given, later he presented an increase in the abdominal girth and was sent to our medical institution, we received the patient in stupor state with Glasgow Coma Scale 10pts, jaundiced tint in sclerae and skin, due to the aforementioned history, a panel was performed for hepatotrophic viruses and sexually transmitted diseases such as HIV and syphilis. Finding positive HBsAg, positive rapid test for HIV and positive VDRL, later in his first 24 hours of admission to our unit, he developed prolongation of coagulation times (PT 55.5, aPTT 82.8), quantification of Total Bilirubin at 21.2mg/dl, with liver enzymes. > 6 times its normal value (AST 353, ALT 195), INR 5.15, and hepatic encephalopathy, for which an acute liver failure approach was initiated, fulfilling the defining criteria to be met: BT elevation >4mg/dl, prolonged treatment times coagulation and hepatic encephalopathy (Table 1).

We report the case of a patient who presented an important history to guide viral infections as the cause of the acute hepatic process; a complete viral panel was requested that included HIV, Hepatitis A, B, C and VDRL Viruses, where the Hepatitis Antigen was positive. Hepatitis B virus surface, the rapid test for HIV, as well as the VDRL. However, in the first hours of admission, defining clinical data of acute liver failure were established by presenting Prolonged coagulation times with INR >1.5, hyperbilirubinemia >5 and type A acute hepatic encephalopathy according to the Vienna classification, for which reason management began with disaccharide laxatives (lactulose), luminal-acting antibiotics (rifaximin), fluid replacement (30ml/kg) and administration of albumin (1g/kg/day), however, according to mortality and survival scores, the patient presented a high mortality (MELD Na 49pts, 90-day mortality of 66%, NACSELD 30-day mortality of 96%), according to Factor R a mixed pattern was obtained, which is associated with hepatotropic virus infection among the main causes, and The coexistence of HBV and HIV was established as the cause of acute liver failure, since it has been established that when there is a coinfection between HBV and HIV, the possibilities of acute liver failure increase to >10%, emphasizing that in cases of liver failure acute due to viral causes, other associated factors should be sought, such as coinfection with other viruses, since the incidence of cases of acute liver failure due to a single viral agent is less than 5%. It is worth mentioning that cases have been reported that establish syphilis infection as the cause of liver failure, so it could even be considered a triple coinfection. After 48 hours of admission, the patient did not present improvement; he progressed with deterioration of renal function and hepatic encephalopathy, requiring advanced management of the airway. This procedure is the one that his relatives did not accept and for this reason, no therapy could be provided. Renal replacement or management in the intensive care unit.

**Conclusions:** This case is highly relevant since when addressing acute liver failure, causes of viral origin must be intentionally sought. Among the viral causes, the hepatitis B virus is the one that has been most associated with developing acute liver failure. It is established that up to 4% of patients with HBV will develop this entity. In this case, the patient was infected with HIV, estimating an association between both infections of 10% as causes of acute liver failure. These

patients who present coinfection should urgently start management with HAART, which presents activity for HBV. However, it is estimated that Coinfected patients who progress to acute liver failure have a poor prognosis and high mortality, leading in most cases to death. Likewise, during the course of the disease, the use of steroids is not recommended for the management of patients with virus infection. hepatotropes, so they should be avoided. In this case, despite having started treatment in the first 24 hours, the patient did not improve and once they present renal failure, renal replacement therapy and management in intensive care should be provided in order to reduce mortality and allow recovery. Liver transplantation can be used as definitive treatment provided that this resource is available and when the criteria for acute liver transplantation are met, the Kings College criteria and the Clichy criteria have been established for this purpose, an 80% success rate is estimated in cases of acute liver failure undergoing transplantation.

**Ethical statement**

The identity of the patients is protected. Consentment was obtained.

**Declaration of interests**

None

**Funding**

None

**Table 1**

| ESTUDIOS DE LABORATORIO |                         |
|-------------------------|-------------------------|
| Prothrombin Time        | 55.5 seconds            |
| INR                     | 5.15                    |
| aTTP                    | 82.8 seconds            |
| Alcaline Phophatase     | 84 U/L                  |
| ALT                     | 195 U/L                 |
| AST                     | 353U/L                  |
| Glucose                 | 171 mg/dl               |
| Urea                    | 113.4 mg/dl             |
| BUN                     | 53 mg/dl                |
| Creatinine              | 3.87 mg/dl              |
| Cholesterol             | 50 mg/dl                |
| Uric Acid               | 5.1 mg/dl               |
| Triglycerides           | 58 mg/dl                |
| Albumine                | 2.0 g/dl                |
| Total Bilirrubin        | 21.2 mg/dl              |
| Direct Bilirrubin       | 13.9 mg/dl              |
| Indirect Bilirrubin     | 7.3 mg/dl               |
| Total Proteíns          | 4.6 g/dl                |
| Globulins               | 2.6 g/dl                |
| A/G Relation            | 0.77                    |
| Hepatitis B sAg         | Reactive 5629.17 copies |
| Syphilis                | Positive                |

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**MexMix supplementation prevented MAFLD development by restoring microbiota-gut-liver axis in a mice model.**

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**Introduction and Objectives:** The microbial communities' control is crucial to maintaining homeostasis of gut-liver axis; clinical evidence demonstrates disruptions of microbiota-gut-liver in individuals with Metabolic-associated fatty liver disease (MAFLD). Foods rich in fiber and polyphenols have been associated with an improvement in microbiota diversity, index and miRNAs expression. The aim of this study was to evaluate the effect of a supplementation with a mixture of Mexican foods (MexMix): *Opuntia ficus indica* (nopal), *Theobroma cacao* (cocoa) and *Acheta domesticus* (crickets) on gut-liver axis in a MAFLD mice model.

**Materials and Patients:** Thirty C57BL/6J mice were divided into three groups: 1) control: normal diet. 2) HF: high fat diet (60%) and fructose/sucrose water 3) MexMix: HF diet up to week 10, followed by HF diet supplemented with 6.7% nopal, 8.7% cocoa, and 8.7% cricket for 8 weeks.

**Results:** The MexMix animals showed a significantly decreased in body weight, visceral and epididymal fat, adipocyte size, triglycerides, insulin, leptin, and PAI-1; while adiponectin levels increased. Using 16S rRNA gene sequencing, MexMix increased phylogenetic diversity, Firmicutes abundance, and enrichment of 10 beneficial genera, including *Lachnospiraceae*, *Ruminococcaceae*, *Akkermansia*, and *Eubacterium\_coprostanoligenes\_group*. In the gut, MexMix supplementation significantly increased SCFAs concentration, intestinal crypts depth, *Ocln* and *Cldn1* expression, and decreased *Il6* and *Tnf-α* expression. In liver, MexMix significantly reduced steatosis and *Tnf-α* expression. Besides, MexMix increased nuclear translocation of NFR2 and, in consequence, a higher hepatic expression of *Cat* and *Sod*. MexMix also decreased hepatic expression of miRNA-34a, miRNA-103, and miRNA-33a.

**Conclusions:** Synchronous supplementation with three nutraceuticals, nopal, cacao, and cricket, produced better results compared to previous studies where foods were administered individually. MexMix demonstrated its efficacy as a prebiotic, promoting the growth of beneficial genera and improving intestinal health. These findings indicate that MexMix has the potential to serve as a therapeutic approach for treating MAFLD in patients, as well as other conditions associated with excessive consumption of fats and sugars.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee.

#### Declaration of interests

None

#### Funding

None

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#### Effect of methyl donor supplementation on gut microbiota and hepatic expression of key miRNAs in a murine model of MAFLD

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**Introduction and Objectives:** Metabolism-associated fatty liver disease (MAFLD) is the most common liver disease worldwide, and intestinal dysbiosis is associated with its development. Methyl donor

supplementation has shown beneficial effects for MAFLD treatment; however, its role on the intestinal microbiota and miRNAs hepatic expression has been poorly studied. The aim of this study was to evaluate the effect of methyl group donor supplementation on gut microbiota and hepatic expression of key miRNAs in a murine model of MAFLD.

**Materials and Patients:** Twenty-four male C57BL/6J mice were divided into three groups: 1) Control: Conventional diet. 2) HF/FS: Diet rich in fats and sugars for 18 weeks. 3) HFMS: HF/FS diet for the first 10 weeks, followed by a HF/FS diet plus orogastric supplementation with methyl group donors for the last 8 weeks.

**Results:** The intestinal microbiota was characterized by 16S rRNA gene sequencing; supplementation with methyl donors modified microbial composition analyzed by beta diversity. In addition, HFMS group strongly tended to increase alpha diversity and induced enrichment of six genus: *Acinetobacter*, *Anaeroplasm*, *Pseudomonas*, *Stenotrophomonas*, *Tuzzerella*, and *Moraxellaceae* family. HFMS group significantly increased SCFAs fecal concentration and restored intestinal permeability dysfunction by increasing *Ocln* and *Cldn1* expression; consequently, a decrease in liver inflammation was observed due to a decrease in *Tnf-α* expression. On the other hand, HFMS group significantly increased hepatic expression of miR-122 and decreased miR-33a expression.

**Conclusions:** This study offers valuable insights into the role of methyl donors as microbiota modifiers, highlighting their ability to promote restoration of intestinal health and liver metabolism. These findings contribute to the proposition that methyl donors could be a promising strategy for treating MAFLD and hepatic related conditions.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee.

#### Declaration of interests

None

#### Funding

None

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#### Exploring the metabolic and molecular benefits of methyl donor supplementation in a model of metabolic and fatty liver disease

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**Introduction and Objectives:** Metabolic fatty liver disease (MAFLD) is currently the most common cause of chronic liver damage worldwide. Differential methylation in genes and histones has been correlated with metabolic alterations present in the disease. Supplementation with methyl group donor molecules could work as a therapeutic strategy to reverse the progression of the disease.

**Materials and patients:** Male C57BL/6J mice of 20-25g of initial weight were fed with a conventional diet (ND n=8); or a diet high in

fat and sugar (HF n=8) for 18 weeks, or a diet high in fat and sugar for 10 weeks, plus 8 weeks of HF diet + methyl group donor supplementation (HFMS n=8). Insulin Tolerance test was performed before sacrifice. Liver, epididymal and visceral fat, and serum samples were collected. Biochemical and histological analyzes were performed. In the liver, global DNA methylation was quantified and the transcriptome was analyzed using dual-channel microarrays. Proteomic analysis was carried out by immunoblotting.

**Results:** The supplemented animals (HFMS) showed a decrease in body weight epididymal and visceral fat ( $p<0.001$ ). The HFMS group showed reduced serum levels of triglycerides and glucose and increased insulin sensitivity. Histological analysis of livers from ND and HFMS animals did not show characteristic MAFLD damage. Global DNA methylation was increased in the HFMS animals. Transcriptome analysis in the HFMS group showed a decrease in metabolic pathways associated with the development of MAFLD and an increase in lipid and cholesterol metabolic pathways. The proteomic analysis revealed an increase of the expression of H3K9 and DNMT1 and a decrease of H3K4, MJD2B and EZH1 proteins involved in the development of the disease.

**Conclusions:** Supplementation with methyl group donors has beneficial effects on weight and body composition, improves hepatic metabolism of lipids, and increases the expression of molecules that regulate DNA methylation and histones, even when consumption of a high-fat diet is continued.

Ethical statement

The protocol was registered and approved by the Ethics Committee.

Declaration of interests

None

Funding

None

**Table 1**  
Differences between diet groups

|                            | ND              | HF                | HFMS            |
|----------------------------|-----------------|-------------------|-----------------|
| Final weight (gr)          | 30.25 ± 2.25**  | 46 ± 4.39***#     | 33.83 ± 2.92#   |
| Feed consumption (gr)      | 3.417 ± 0.37    | 3.37 ± 0.53       | 3.164 ± 0.36    |
| Liver weight (gr)          | 1.918 ± 2.27*   | 2.3 ± 0.36*       | 2.12 ± 0.15     |
| Visceral fat weight (gr)   | 1.027 ± 0.12*   | 1.433 ± 0.39*#    | 0.98 ± 0.19#    |
| Epididymal fat weight (gr) | 1.58 ± 0.31***  | 3.4 ± 0.85***#    | 2.24 ± 0.41#    |
| Glucose (mg/dL)            | 116.6 ± 10.93*  | 137.13 ± 19.19*#  | 132.9 ± 13.3#   |
| Global Methylation (%)     | 0.6033 ± 0.061* | 0.5200 ± 0.062*## | 0.8967 ± 0.17## |
| Triglycerides (mg/dL)      | 82.67 ± 5.508*  | 104.4 ± 6.841*##  | 81.2 ± 6.017##  |

All the results are expressed as the mean ± SD. Statical analysis were performed using One-Way Anova and Tukey Post hoc test. The “#” symbol represents (# $p<0.05$ ) (## $p<0.01$ ) differences between HF vs. HFMS and “\*\*\*” is used for HF vs. ND differences (\* $p<0.05$ ) (\*\* $p<0.01$ ) (\*\* $p<0.001$ ).

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**Methyl-group donor supplementation beneficial effects on metabolic, histological, and inflammatory parameters in a murine model of alcoholic steatohepatitis**

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**Introduction and Objectives:** Chronic alcohol consumption is the main cause of alcohol-related liver disease (ARLD) ranging a spectrum characterized by inflammation and progressive fibrosis. Currently, abstinence is the main treatment for ARLD; for this reason, it becomes indispensable to evaluate therapeutic alternatives as methyl group donors which have the potential to influence the development and progression of the disease. To evaluate the effect of chronic alcohol consumption coupled with methyl-group donor supplementation on metabolic and histologic features and gene expression of proinflammatory cytokines in a murine model of ARLD.

**Materials and Patients:** : 24 male C57BL/6J mice divided into groups with conventional diet (ND n=8); alcohol-induced liver-injury induced with *ad libitum* consumption of a 20% ethanol-aqueous drink and a 45%-fat diet (OH n=8) for 18 weeks; or latter diet for 10 weeks, plus 8 weeks of this diet and methyl group (OH +METMIX n=8). This protocol is in the process of being approved by the CUCS Ethics, Research and Biosafety Committees.

**Results:** Serum biochemical studies and histological analysis performed in the methyl-donor supplemented group (OH+ METMIX) -zinc sulfate, methionine, vitamin B12, folic acid, betaine and choline- showed a significant decrease in body weight, epididymal and visceral fat ( $p<0.05$ ), and serum levels of cholesterol, HDL and LDL. Whilst, serum levels of AST, ALT, TG and VLDL, as well as IL-6 and TNF- $\alpha$  mRNA from hepatic tissue, and the hormones insulin, leptin, glucagon, and resistance, demonstrated a tendency to decrease their concentrations compared to the OH group.

**Conclusions:** Treatment with methyl-group donors improves body weight, body composition, cholesterol, LDL and HDL concentrations, exerting beneficial and protective effects even when consuming an ethanol-aqueous drink.

Ethical statement

The protocol was registered and approved by the Ethics Committee.

Declaration of interests

None

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**Passenger lymphocyte syndrome, an unusual cause of anemia after liver transplantation**

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**Introduction and Objectives:** The prevalence of anemia after liver transplantation ranges from 4.3% to 28.2%. Causes that occur in the first two weeks include bleeding, sepsis, medications, and hemolysis. Immune hemolysis represents less than 1% of the cases and includes graft-versus-host disease and hemolysis associated with ABO incompatibility. We present a case of passenger lymphocyte syndrome as a cause of immune hemolytic anemia two weeks after a liver transplant.

**Materials and Patients:** A 43-year-old woman, blood group A+, with a history of HCV-related liver cirrhosis and BCLC-A hepatocellular carcinoma, was chosen for a liver transplant. Surgery was uneventful, requiring the transfusion of an O+ blood unit. The postoperative evolution was carried out without complications. On day 10, after the transplant, she presented a drop of 3 g/dL in hemoglobin, leukocytosis, elevated acute phase reactants, and mixed hyperbilirubinemia. An esophagogastroduodenoscopy and colonoscopy showed no active bleeding. The hemolysis profile showed a decrease in the haptoglobin value and an increase in DHL, negative Coombs, without schistocytes. An MRCP was requested, with no evidence of bile leakage or active bleeding. Because of the suspicion of hemolysis due to drugs, tacrolimus was changed to mycophenolate mofetil, and because of possible hemolysis due to sepsis, broad-spectrum antibiotic coverage was added without improvement. On day 14, there was a suspicion of transient lymphocyte syndrome. Isohemagglutinin levels were requested and became positive, and two O+ blood units were transfused. The following day, she presented a significant improvement in all laboratory parameters, and on day 20 she was discharged from the hospital without any abnormality in her laboratory parameters.

**Results:** In our management of hemolytic anemia after liver transplantation, two theories initially emerged: 1) Hemolysis due to tacrolimus, for which it was suspended and changed to mycophenolate mofetil, and 2) Hemolysis due to sepsis, due to leukocytosis and inflammation, initiating coverage with meropenem and vancomycin. But without improvement after both interventions. Finally, due to suspicion of transient lymphocyte syndrome, isohemagglutinins were requested and were positive, and after the transfusion of 2 O+ blood units, containing anti-A+ antibodies, she showed improvement, confirming the diagnosis.

**Conclusions:** In the passenger lymphocyte syndrome, there is a donor B lymphocyte production of antibodies causing a primary or secondary response to recipient erythrocytes. The incidence is higher in the heart-lung transplant, followed by liver transplantation. The risk also increases according to the donor-recipient ABO mismatch, being more common with group O donors and group A recipient (61%), followed by group O donors and group B recipients (22%). The clinical picture is characterized by fever, diarrhea, rash and hemolysis. The hemolysis usually occurs on days 3 to 24 after the liver transplantation and tends to be mild and self-limited. The diagnosis is made when the recipient had a positive direct antiglobulin test and there were donor antibodies in the serum against the recipient's red blood cell antigens. Treatment options include the transfusion of O red blood cell units and, in cases of severe hemolysis, immunosuppressors or plasmapheresis.

#### Ethical statement

The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

None

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#### Effect of the combination of orlistat and l-carnitine on the quality of life (sf-36) in 16 overweight patients. a preliminary result

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**Introduction and Objectives:** Orlistat is a drug widely used in overweight/obese patients, while the combination with l-carnitine could offer an improvement in its effectiveness. To our knowledge, the effect of this combination on the quality of life of overweight patients has not been determined.

To evaluate the effects on the quality of life of patients who took the combination of orlistat and l-carnitine at 4 and 8 weeks of treatment.

**Materials and Patients:** : We evaluated the quality of life (Short Form-36) in 16 patients [41.81±8.26 (37.77-45.86) years, 81% women] undergoing pharmacotherapy of the combination of orlistat and l-carnitine (once a day) at 4 and 8 weeks of treatment. Data express mean±SD and 95%IC or percentages as correspond. We use paired Student t Test, two tails with an alpha=0.05.

**Results:** Patients lowered their weight by about 3%. Patients show improvement in body pain, general health, vitality and in both Mental [45.68±6.51 (42.49-48.86) vs. 49.88±3.21 (48.31-51.46), p=0.02] and Physical [59.4±8.92 (55.03-63.77) vs. 63.36±9.64 (58.63-68.08), p=0.01] summaries.

**Conclusions:** These results suggest a beneficial effect of the combination of Orlistat and l-carnitine on the treatment of overweight. Further studies compared with placebo and standard care are required.

#### Ethical statement

The protocol was approved by the local research and ethical committees.

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#### Declaration of interests

None

#### Funding

Laboratorios Liomont provided the medicament "orlistat and l-carnitine" for this study.

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#### METS-IR and its correlation with the diagnosis of nonalcoholic fatty liver disease corroborated by elastography.

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**Introduction and Objectives:** Nonalcoholic fatty liver disease (NAFLD) has become the leading cause of chronic liver disease worldwide, with a prevalence ranging from 25% to 40% (1,2). Its increase



has been related in parallel to the increase in the prevalence of obesity, insulin resistance (IR), type 2 diabetes (T2D) and other components of the metabolic syndrome (3).

Insulin resistance (IR) has been characterized as the main factor in the pathogenesis of NAFLD, and in turn, the presence of T2D is a predictor of advanced fibrosis and mortality (4). Insulin resistance assessments often require invasive and expensive methods, which has generated the search for indirect measures and precise RI. Currently, non-insulin based fasting IR indices have been developed, substituting insulin measurements for triglyceride measurements, fasting glucose and lipoproteins (5).

Recently, a novel surrogate index was developed to estimate the action of insulin without the determination of insulin. The metabolic score for insulin resistance (METS-IR) is calculated using fasting glucose, triglyceride, and HDLc measurements along with body mass index (BMI). METS-IR is an indirect method that correlates with fat intravisceral, intrahepatic and intrapancreatic and is useful for the prediction of T2D (5).

The identification of risk factors for NAFLD development and the availability of non-invasive tests for its diagnosis, offers a window of timely interventions that can modify the outcome of patients, improve the quality of life and reduce its impact on public health.

The primary objective in this work is to determine if there is a correlation between metabolic score for insulin resistance and the grade of hepatic steatosis in nonalcoholic fatty liver disease corroborated by elastography, in patients from Juarez Hospital of Mexico.

**Materials and Patients:** A retrospective, cross-sectional and analytical study was carried out. Patients aged 15 to 85 years were included, who had a diagnostic elastography and who had a diagnosis of NAFLD. Within the exclusion criteria, patients diagnosed with T2D who were under medical treatment, hepatitis B and C virus infection, history of autoimmune liver disease and history of chronic alcohol consumption, with a consumption greater than 30 g in men and 20 g in women, patients diagnosed with liver cirrhosis under medical treatment, patients with cholestatic syndrome and pregnant patients.

Descriptive statistics were performed with measures of central tendency and dispersion, inferential statistics using T student, and the correlations were determined with Pearson's correlation coefficient, being statistically significant  $P < 0.05$ .

**Results:** Elastographies with reports of fatty infiltrations and fibrosis and were gathered carried out between January 2017 and December 2018 in the Liver Clinic of the Gastroenterology service of the Juárez Hospital of Mexico. 283 elastography reports were obtained, of which, due to non-inclusion criteria, 207 were discarded, leaving a total of 76 patients for statistical analysis.

Within this population, 23.7% ( $n = 18$ ) were men and 76.3% ( $n = 58$ ) are women. According to the definitions of body mass index, the population was classified as normal weight, overweight and obesity. The population with normal BMI was 15.8% ( $n = 12$ ) of the population, overweight patients in 48.7% ( $n = 37$ ) and patients with obesity in 35.5% ( $n = 27$ ). The main number of patients was found in the overweight group, being higher in the group of women, with 48.3% ( $n = 28$ ).

A correlation was made between the METS-IR with the degree of fat infiltration and liver fibrosis, and a correlation of fat infiltration with body mass index. Correlation was obtained between the METS-IR index with the degree of fatty infiltration with statistical significance ( $p = 0.029$ ) in general and a correlation with any METS-IR index value and the different degrees of hepatic steatosis in particular.

**Conclusions:** The METS-IR index is a novel method for determining insulin resistance in patients with metabolic risk factors. This is

the first study to evaluate the relationship of the METS-IR index with NAFLD, and the correlation between IR and hepatic fat infiltration was verified. The higher the value of METS-IR, the greater the presence of fat infiltration. We consider the METS-IR as a valuable screening tool for liver disease in a population whose access to invasive diagnostic studies is limited.

#### Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

#### Declaration of interests

None

#### Funding

None

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#### Prolonged-release pirfenidone in patients with compensated cirrhosis. Final results of the multicenter study ODISEA, controlled against placebo, plus standardized care\_2023

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**Introduction and Objectives:** Advanced liver fibrosis (ALF) is a predictor of adverse prognosis in chronic liver disease. In addition to etiological treatment, a new approach to stop or reverse residual fibrosis would be desirable. Our aim was to assess the efficacy and safety of a prolonged-release pirfenidone formulation (PR-PFD) compared to placebo, plus standardized care, in patients with compensated liver cirrhosis.

**Materials and Patients:** 180 patients with ALF (F4 by elastography) of various causes were randomly assigned to 3 groups: placebo (G1), PR-PFD: 1200 mg/d (G2) or 1800 mg/d (G3), plus standardized care, during 24 months. All participants underwent standard lab tests, quality of life assessment, elastography, fibrotest, liver US, and endoscopy at baseline and at 12 and 24 months. Ethics Committee Registry H14-004. Patients signed an informed consent, which will be in custody for 15 years. This study was funded by CellPharma Laboratory.

**Results:** 165 patients were eligible for the efficacy and 180 for the safety analysis. At baseline, demographics, etiology, stage of cirrhosis, Child-Pugh or MELD scores, quality of life or fatigue scales, and liver stiffness (kPa) and Fibrotest (units) scores (mean ± 1SE) were similar between groups (multivariate mixed model). The estimated fibrosis scores presented a significant reduction, mainly in G2 (Table). Decompensations were detected in 19 patients: variceal bleeding (5), encephalopathy (4), hepatocarcinoma (4) with similar distribution between groups. Ascites (12) was more frequent in the placebo group (p=0.003). G2 patients presented significant improvements between baseline and 24 months in: ALT ( $43.5 \pm 3.8$  vs.  $31.3 \pm 4.8$  UI/L, p=0.003), albumin ( $4.2 \pm 0.06$  vs.  $4.5 \pm 0.07$  g/dL, p<0.001); total bilirubin ( $0.90 \pm 0.08$  vs.  $0.65 \pm 0.10$  mg/dL, p<0.001); platelets ( $121.7 \pm 7.8$  vs.  $144.3 \pm 9.7 \times 10^3/\mu\text{L}$ , p<0.001), MELD ( $9.73 \pm 0.32$  vs.  $9.03 \pm 0.40$ , p=0.022) and quality of life ( $83.7 \pm 1.5$  vs.  $90.9 \pm 1.9$  %, p=0.002). Adverse events were mainly mild from the GI tract (n=48, 46, and 35) and skin (n=15, 22, and 12) in G1, G2, and G3, respectively.

**Conclusions:** Prolonged-release pirfenidone at a dose of 1200 mg significantly decreased indirect fibrosis markers at 24 months and

induced improvement in LFTs, MELD, and quality of life in compensated cirrhosis and without safety concerns.

**Ethical statement**

HI14-004

**Declaration of interests**

None

**Funding**

CellPharma Laboratory

**Table.**

The estimated fibrosis scores presented a significant reduction, mainly in G2

| Elastography<br>kPa | Group 1<br>(Placebo) | Group 2<br>(1200 mg) | Group 3<br>(1800 mg) | Fibrotest<br>(units) | Group 1<br>(Placebo) | Group 2<br>(1200 mg) | Group 3<br>(1800 mg) |
|---------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| Basal               | 27.5 ±2.3            | 24.2 ±2.3            | 24.4 ±2.3            | Basal                | 0.86 ±0.02           | 0.86 ±0.02           | 0.87 ±0.02           |
| 24 mo               | 24.6 ±2.4            | 15.4 ±12.3           | 23.3 ±2.3            | 24 mo                | 0.84 ±0.02           | 0.82 ±0.02           | 0.84 ±0.02           |
| P-value             | 0.402                | 0.001                | 0.654                | P-value              | 0.101                | 0.001                | 0.045                |

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