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# Oral Presentations at The XVI National Congress of The Mexican Association of Hepatology

## VARICEAL VERSUS NON-VARICEAL ETIOLOGY OF GASTROINTESTINAL BLEEDING IN PATIENTS WITH CIRRHOSIS AND RELATED SECONDARY COMPLICATIONS

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**Introduction and Objectives:** Liver cirrhosis is a highly prevalent worldwide disease and in the last decade, there has been an increase of 13%. Patients with advanced liver disease are at higher risk of developing life-threatening decompensations; one of these main complications is the presence of upper gastrointestinal bleeding, representing a frequent cause of hospital admission and mortality. Broad knowledge of these complications is essential to improve the diagnostic and therapeutic approach in these patients.

**Objectives:** To compare the different complications related to upper gastrointestinal bleeding of variceal vs. non-variceal origin and the characteristics of these patients.

**Methods:** Case-control study conducted in a cohort. The cohort was made up of cirrhotic patients due to any etiology who were admitted for hospitalization at our unit in a period from January 2017 to May 2021; two groups were extracted, those with variceal bleeding formed the cases group and, those with non-variceal hemorrhage the control group and a comparison between groups was made using X2 or Fisher's exact test or Student's test accordingly to the type and distribution of each variable, considering significant a value of $p < 0.01$

**Results:** A total of 294 cirrhotic patients with gastrointestinal bleeding were included, 169 men (57.5%); mean age 54.6 ± 11.9 years; mean days of hospital stay 2.19 ± 2.74. Regarding the etiology of liver cirrhosis, the main etiology was alcohol in 39.7% (117), followed by viral etiology in 6.4% (18), NASH in 5.8% (17) and, less frequently due to autoimmune causes in 3.4% (10), however, up to 44.7% remained with indeterminate etiology. Regarding the origin of gastrointestinal bleeding, 209 (71.1%) were of variceal origin and 85 (28-9%) were of non-variceal origin. A total of 94 (32%) developed acute kidney injury (AKI), and only the variceal origin was related to a higher risk of developing AKI 57/209 vs. 37/85, $p < 0.01$ (OR = 1.6; 95% CI: 1.2-2.2) but there was no difference regarding the etiology of gastrointestinal bleeding and development of other complications such as encephalopathy, ascites, jaundice, infections, need a transfusion, severe hypovolemic shock, death. See table.

**Conclusions:** The etiology (variceal vs. non-variceal) of the gastrointestinal bleeding has no impact on the development of other complications in cirrhosis; therefore, therapeutic prophylaxis and surveillance strategies should be prioritized in the patient with cirrhosis, regardless of the origin of bleeding. The risk of AKI should always be considered and monitored when the origin of the bleeding is variceal since this study shows the closest relationship between these two complications.

The authors declare that there is no conflict of interest

The comparison regarding the development of additional complications in relation to variceal or non-variceal etiology in cirrhotic patients

| Complication | Total n=294 | Variceal bleeding n=209 | No-variceal bleeding n=85 | P |
|---|---|---|---|---|
| **Acute kidney injury** | 94 (32.0) | 57 (27.3) | 37 (43.5) | <0.01 |
| **Hepatic encephalopathy, n(%)** | 128 (43.5) | 86 (41.1) | 42 (49.4) | 0.19 |
| **Ascites, n (%)** | 55 (18.7) | 36 (17.2) | 19 (22.3) | 0.31 |
| **Jaundice n (%)** | 51 (17.3) | 32 (15.3) | 19 (22.3) | 0.14 |
| **Infections, n (%)** | 65 (22.1) | 48 (23.0) | 17 (20.0) | 0.58 |
| **Need of transfusion, n(%)** | 138 (46.9) | 99 (47.4) | 39 (45.9) | 0.82 |
| Hypovolemic shock **n(%)** | 17 (5.8) | 13 (6.2) | 4 (4.7) | 0.78 |
| **Death, n(%)** | 4 (1.4) | 3 (1.4) | 1 (1.2) | 1.0 |

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## CORRELATION BETWEEN SARCOPENIA AND HEPATIC ENCEPHALOPATHY IN PATIENTS WITH CIRRHOSIS

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**Introduction and Objectives:** Malnutrition is a frequent complication in patients with cirrhosis, associated with greater disease progression, complication rate, and mortality. Sarcopenia is one of the main indicators of malnutrition, characterized by a general decrease

in muscle mass and functional deterioration. CT determination of muscle mass is not easily accessible in routine clinical practice, so practical measurement tools are essential. It has been proposed to classify sarcopenia as severe when decreased muscle strength, muscle mass, and low physical performance coexist. The impact of severe sarcopenia on the risk of developing hepatic encephalopathy is currently unknown. Primary outcome: Determine if there is a significant correlation between the degree of sarcopenia and hepatic encephalopathy. Secondary outcomes: to determine the prevalence of sarcopenia in patients with cirrhosis, the association between sarcopenia and liver decompensation events, to determine the correlation between individual tests (battery of functional physical performance tests [SPPB], grip strength, and skeletal muscle mass) with hepatic encephalopathy.

**Materials and methods:** Prospective, cross-sectional, observational, descriptive, and analytical study in patients with liver cirrhosis evaluated by outpatient consultation, with diagnosis confirmed by transitional elastography (Fibroscan® 502 ECHOSENS® equipment). The presence of sarcopenia was determined by measurement of grip strength with a hand-held hydraulic dynamometer (JAMAR® B001D7QDJG) and determination of muscle mass by tetrapolar electrical bioimpedance (OMRON® HBF 500). A positive case was considered when coexisting force ≤27 kg / ≤16 kg and skeletal muscle mass ≤20 kg / ≤15kg in men and women respectively, classifying it as severe sarcopenia with a score of ≤8 pts in SPPB. The presence of hepatic encephalopathy was determined by clinical evaluation and critical flicker rate (cut-off <39 Hz). Logistic regression analysis and Chi-square test were performed.

**Results:** 96 patients were included, of which 35 (36.4%) had sarcopenia and 21 (60%) were classified as severe sarcopenia. The demographic characteristics and severity of cirrhosis were comparable in patients with and without sarcopenia. In multivariate logistic regression analysis, a significant correlation was demonstrated between the presence of sarcopenia and manifest hepatic encephalopathy p = 0.014, HR 9.05, 95% CI (1.54-52). No significant correlation was shown with ascites (p = 0.08) or recent variceal bleeding (p = 0.53). A significant correlation was demonstrated between previous events of encephalopathy (p = 0.021) and ascites (p = 0.032) with the presence of sarcopenia. Regarding individual tests, a SPPB score ≤8 was independently associated with overt encephalopathy (0.009, HR 19.7, 95% CI (2.1-182). Handgrip strength, chair stand, and muscle mass were not statistically significant.

**Discussion and Conclusions:** This pilot study suggests that the presence of sarcopenia is significantly correlated with the risk of developing overt hepatic encephalopathy, and the presence of previous ascites could increase the risk of developing sarcopenia. Evaluation of physical performance by SPPB could be independently correlated with the development of hepatic encephalopathy.

The authors declare that there is no conflict of interest

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## PREVALENCE AND CHARACTERISTICS OF PORTAL VEIN RECANALIZATION IN CIRRHOTIC PATIENTS ADMITTED WITH PORTAL THROMBOSIS IN A THIRD LEVEL CARE CENTER

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**Introduction and Objectives:** Portal vein thrombosis (PVT) refers to the formation of blood clots within the trunk of the portal vein (PV) or its main branches, which can spread to the superior mesenteric (SMV) and splenic (VE) veins. The natural history of liver cirrhosis is a complication with a "rebalanced" coagulation system that can promote bleeding or a thrombotic tendency. The prevalence in compensated cirrhotic is 1% in and 8-25% in decompensated patients.

**Aim:** To determine the prevalence and characteristics of PV recanalization in cirrhotic patients with PVT.

**Material and methods:** Descriptive, cross-sectional/prevalence.

**Procedure:** We reviewed medical records of all cirrhotic patients admitted with PVT diagnosis from January 2019 to April 2021. We included patients with a diagnosis of PVT. Qualitative variables were expressed as frequencies and percentages. The numerical variables were expressed as means and standard deviations. We use X2, Fisher's exact, Student's t, and Mann-Whitney U to compare groups as appropriate.

**Results:** Of 553 cirrhotic patients admitted from January 2019 to April 2021, 48(8.67%) patients with PVT diagnoses were included. Of these, 27(56.3%) were women, with a mean age of 59.37±12.67 years, 9(18%) with a diagnosis of cancer, of which 8(16.7%) were hepatocellular carcinoma, 2(33.3%) extended to the two arms, 6(12.5%) received treatment, 100% of the treatment was based on low molecular weight heparin. According to the degree of recanalization: 37 (77.08%) recanalized, 27(56.3%) did so partially, of them, 24(88.9%) were spontaneous; 10(20.8%) recanalized utterly, of which 90% were without treatment, with no significant difference between recanalization to free progression vs. treatment ($p$=0.179) and 11(22.9%) did not recanalize. Regarding the characteristics of the thrombosis by imaging studies, 26(54.2%) were chronic, 28(58%) partial, only 9 (18.8%) with cavernomatous transformation, 30(62.5%) were located in the main trunk, 6(12.5%) extended to the SLM and 11(22.9%) presented flow <15cm/s.

**Discussion:** In cirrhotics with recent or partial occlusion (> 50% of the lumen) or thrombosis of the main PV or SMV, therapy should be considered. Anticoagulant or interventional therapy has no benefit complete chronic occlusion of the main PV or cavernomatous transformation. Spontaneous recanalization occurs in 40% in 3 months, and with therapy, it is 80%. Several cohort studies reported that near 50% recanalize partially or totally in the next three months, and up to 80% recanalize at 12 months. Clinical trial data are weak regarding the indications for treatment for PVT without ischemic symptoms. Our study showed that 77.08% of cirrhotic patients with PVT recanalized, most partially during follow-up and more than 80% spontaneously, and only a low percentage presented with cavernomatous transformation. In addition, more than 70% of the patients who recanalized have a low risk of re-thrombosis related to flow.

**Conclusions:** The prevalence of PVT in cirrhotic patients was relatively low (10%), complete or partial recanalization was very high, even spontaneously, there was no difference in the degree of recanalization with or without anticoagulation.

The authors declares that there is no conflict of interest

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## INITIAL EVALUATION OF KIDNEY FUNCTION IN PATIENTS WITH LIVER CIRRHOSIS OF CEIHET, HIDALGO

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**Introduction and Objectives:** Kidney injury has become one of the main causes of decompensation in cirrhotic patients. There are few studies in our country that compare various methods to assess kidney function in these patients. Objective: To evaluate the initial renal function in patients with liver cirrhosis from CEIHET, Hidalgo.

**Material and methods:** Observational, cross-sectional, retrospective and analytical study, selecting 186 files with a diagnosis of liver cirrhosis, from January 2020 to June 2021, evaluating renal function (MDRD-6, 24-hour urine creatinine clearance, KDIGO / CKD and Serum cystatin C) at the initial check-up appointment. Statistical analysis was performed through measures of central tendency, dispersion and correlation.

**Results:** 186 files were analyzed, 53.2% (n = 99) women; mean age of 63 years and a mean time since the diagnosis of cirrhosis of 2.2 years. 117 patients (63%) Child Pugh A. The main etiology of cirrhosis was metabolic fatty liver in 110 patients (53.8%). At the time of the first visit, 140 patients (75.3%) had serum creatinine levels between 1 and 2 mg/dl, with a mean of 1.3. Regarding 24-hour urine creatinine clearance, 93 patients (50%) showed levels greater than 90ml / min, and 47 (25.2%) had levels less than 45ml / min. When measuring filtration rate by MDRD-6, 86 (46.4%) showed levels higher than 90ml / min, and 40 (21.5%) had levels lower than 45ml / min. Regarding KDIGO / CKD, 100 individuals (53.8%) showed rates greater than 90ml / min, and only 27 (14.5%) rates less than 45ml / min. In serum Cystatin C, 103 (55.5%) had levels between 1 and 1.5mg / L, and 50 (27%) showed levels greater than 1.5mg / L. When comparing the various measurements, there was only a statistical difference between KDIGO / CKD and the other scales, showing a lower rate of detection of initial kidney injury (p 0.008, 0.07 and 0.04). In total, 89 (48%) of the patients had creatinine clearance less than 60ml / min at the initial consultation. Discussion. In our study, almost half of the patients with cirrhosis present a degree of kidney damage from the first visit to Hepatology. It was impossible to determine whether it is acute, exacerbated chronic, or definitive chronic disease. The use of 24-hour urine creatinine clearance, serum cystatin C, and MDRD-6 is helpful since serum creatinine levels alone erroneously estimate the degree of kidney injury in these patients. We essentially consider the initial kidney function evaluation in all cirrhotic patients to identify probable causes and treat them.

**Conclusions:** We found that up to 48% of patients with liver cirrhosis present some degree of kidney injury at the time of their first consultation with Hepatology. 24-hour urine creatinine clearance, serum cystatin C, and MDRD-6 appear useful in evaluating renal function in these patients.

The authors declare that there is no conflict of interest

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## IMPACT OF REFRACTORY ASCITES ON THE SURVIVAL OF PATIENTS WITH CIRRHOSIS

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**Introduction and Objectives:** Refractory ascites is an infrequent complication in patients with cirrhosis; it is considered in those who do not respond to diuretics or who have adverse effects with diuretics. Treatment is large-volume paracentesis, followed by plasma volume expansion to prevent paracentesis-induced circulatory dysfunction (PICD) to avoid deterioration in renal function and hyponatremia. Intermittent paracentesis could increase morbidity and mortality in these patients. Perhaps the classic prognostic scales, such as MELD, undervalue this factor that is not usually considered for prioritizing transplantation. The objective of this study is to assess the survival of patients with cirrhosis with refractory ascites.

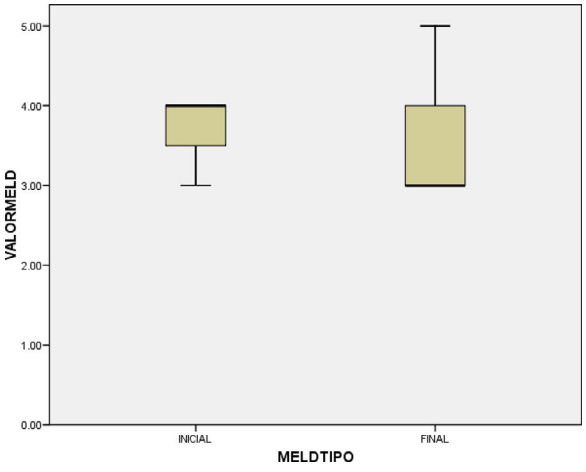
**Material and methods:** Observational, retrospective, descriptive and analytical study. Patients with cirrhosis and refractory ascites were included, who were subjected to intermittent paracentesis on several occasions from February 2019 to June 2021. Descriptive statistics were performed with central tendency and dispersion measures, baseline and final MELD were calculated, and mortality was evaluated.

**Results:** Eleven patients were included, six men (54.5%) and five women (45.5%), aged 54 ± eight years. The patients had a range of paracentesis performed from 3 to 30 occasions (median five interventions), with a follow-up of 1 to 40 months (median of 8 months). The etiology of cirrhosis was alcoholic 63.6%, MALFD 9.1%, and 27.3% other causes. The total amount of fluid drained per patient was 37 to 439 L, 90% of the patients classified as Child-Pugh grade C, and 10% B. The median of the initial MELD was 15 (range = 13), and the median of the final MELD was 22 (range=17). There was no significant difference according to the Wilcoxon test p = 0.317. The renal function between the first and the last paracentesis decreased mildly by 24% and from 36% to 45% severely. Overall mortality was six patients (54.5%). The causes of death were spontaneous bacterial peritonitis (SBP) 9%, ACLF (Acute on Cronic Liver Failure) 27%, infarction 9%, and sepsis 9%. Median survival was 18 months (range 13-23)

**Discussion:** Patients with refractory ascites have very high mortality (59%); Despite the amount of fluid drained, up to 439L in one patient (for example), it did not seriously affect kidney function overall. We found no statistically significant difference between the initial and final MELD values (Figure 1). However, the MELD score does not make them candidates for liver transplantation; therefore, refractory ascites should be considered with an additional score to enter them on the transplant list.

**Conclusions:** Refractory ascites is uncommon, but it has high mortality; the MELD scale may not accurately predict the possibility of death, so they should be entered with an additional score to consider them candidates for liver transplantation.

The authors declare that there is no conflict of interest

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## EXPERIENCE IN THE USE OF HUMAN ALBUMIN IN COMPLICATIONS OF LIVER CIRRHOSIS AT HOSPITAL JUÁREZ DE MÉXICO

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**Introduction and Objectives:** Controlled clinical studies have demonstrated the benefits of albumin in decompensated cirrhotic patients with ascites, elevated creatinine, spontaneous bacterial peritonitis, refractory ascites, hepatorenal syndrome and encephalopathy, in whom the use of albumin improves not only patient survival but also expands intravascular volume, improves microcirculation, binding to numerous substances such as bile acids, nitric oxide and cytokines. However, the time of administration and the dose remains controversial.

**Objective:** To present the experience of the administration of human albumin, the clinical and epidemiological factors associated with the success of the treatment in the different complications of hospitalized patients for decompensated cirrhosis in the Gastroenterology Department at Hospital Juárez de México from January 2019 to January 2021.

**Material and methods:** A descriptive, retrospective, observational and cross-sectional study of a cohort of patients hospitalized for decompensated liver cirrhosis in the Gastroenterology Department at Hospital Juárez de México. The records of 63 patients who were administered albumin at a dose of 0.7 gr/kg of body weight were reviewed according to the type of complication, reason for admission, in such a way that epidemiological data, values from laboratory studies, cause of prescription and administration results which were analyzed with measures of central tendency and percentages, obtaining Child Pugh and MELD scores.

**Results:** Of the population studied (N = 63); 42.8% were men (n = 27) with an average age of 57.7 years, 57.1% were women (n = 36) with an average age of 59.42 years. Regarding the etiology of liver disease, the following order was observed: alcohol-related liver disease in 42.8%, MAFLD (metabolic associated fatty liver disease) 42.8%, AIH (autoimmune hepatitis) 4.75%, PBC (primary biliary cirrhosis) 4.75% and HBV (hepatitis B virus) 4.75%. Indications for the use of albumin were spontaneous bacterial peritonitis 53.3%; an acute renal failure that does not respond to fluids, precipitated by: upper gastrointestinal bleeding in 14.2%, urinary tract infection 9.5%, alcoholic hepatitis 9.5%, liver failure due to hepatitis B virus 4%, hepatorenal syndrome 9.5%. 42.8% of the patients in the study cohort had at least one comorbidity. 77.7% of them had type 2 diabetes, 11.1% had type 2 diabetes and arterial hypertension, UC was observed in 11.1% of the population. 4.76% had Child-Pugh score A, 28.57% had Child-Pugh score B and Child Pugh score C 66.66% with an average MELD Na of 25 points. In 94.7% of the cases, effectiveness was observed in the resolution of the complication, 5.3% of the patients, despite the administration of albumin, died of septic shock (secondary to urinary tract infection n = 3, SBP n = 4 and pneumonia n = 1), these patients had Child Pugh C, mean MELD Na 32, and mean serum albumin of 1.8 mg / dl, in contrast to the respondents who had mean serum albumin of 2.62 mg / dl.

**Discussion:** Unlike what is reported in the literature, we observed that despite the lower doses administered than those recommended in the treatment guidelines, we obtained a 94.7% success rate in treated patients, observing that factors such as serum albumin value, comorbidities, Child Pugh score, MELD-NA and added infectious processes can be determining factors in the results of treatment, which raises the question of: whether the administration of albumin should be individualized according to the clinical characteristics of the patient and not a standardized dose according to their complication.

**Conclusions:** Serum albumin values, the presence of comorbidities, acute infections, and high Child Pugh and MELD Na scores are independent factors that affect the results of human albumin treatment in decompensated cirrhotic patients.

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## CHANGES IN CARDIAC FUNCTION IN PATIENTS WITH DECOMPENSATED CHRONIC LIVER FAILURE

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**Introduction and Objectives:** Cirrhotic cardiomyopathy is cardiac dysfunction, recently recognized as a clinical entity, present in up to 50% of liver cirrhosis in the absence of other heart diseases. Cirrhotic cardiomyopathy is characterized by a decrease in the contractile response of the heart in patients with CH, associated with the presence of an alteration in diastolic relaxation and electrophysiological alterations at rest, all in the absence of known heart disease and regardless of the etiology of liver disease. Hemodynamic and electrophysiological studies have made it possible to document alterations in cardiac behavior in 25 and 40-60% of patients with liver cirrhosis, respectively. Objective: Determine the alterations in cardiac function in patients diagnosed with decompensated chronic liver failure.

**Material and methods:** Descriptive, observational, cross-sectional and prospective study, carried out all the patients with decompensated liver cirrhosis who attended the Central Military Hospital from January 2021 to September 2021 and who underwent a laboratory study, echocardiogram, electrocardiogram, chest X-ray and laboratory studies. The mean, standard deviation and absolute and relative frequencies will be used for the quantitative variables for the statistical calculation. The statistical package SPSS version 20 will be used.

**Results:** Eleven older patients with a diagnosis of decompensated chronic liver failure were included. A new study carried out on the same basis as CANONIC, allowed to clarify the dynamic and evolutionary character of patients with ACLF, determining the average mortality at 28 and 90 days, according to the number of compromised organs. Thus, the presence of ACLF-1 determines a risk of death at 28 and 90 days of 18 and 39%, respectively, a figure that increases in ACLF-2. 54.5% were men, the average age 54.2 years ± 10.3, 27.3% had arterial hypertension and 9.1% DM2, the etiologies were by enol in 54.5%, HAI 18.2%, PBC 18.2% and 9.1% by MAFLD. Mean arterial pressure was 77.0 ± 8.1, QTc 449.9 ± 57.6, and HR 78.54. The Child-Pugh scale had mainly C score values in 36.4% of the cases, followed by 27.3% in 12-point scores, scores of 10, 11 and B had only one case, respectively (9.1%). The MELD score was 10 at 40 points, 27.3% of the patients reported 18 points, a case similar to the MELD-NA from 13 to 40, with 18.2% of the patients at 21 points and a similar percentage at 29 points. CLIF score was distributed in 54.5% in 1, 27.3% in 2 and 18.2% in 0. PSAP had a mean of 31.2 ± 8.3 and diastolic dysfunction, it appeared in two cases as isovolumic relaxation and in two as a slow relaxation pattern, the other patients had various types of diastolic dysfunction, the natriuretic peptide was 314.1 pg / ml with a range of 13.1 to 1270.0 pg / ml. Troponin in 45.5% of the cases was less than 0.1ng / L, in 27.3% <0.05 ng / L, in 18.2% <0.01 ng / L and 9.1% was 0.026 ng / L. CK-MB in 90.9% was less than 1.0 U / L and in 9.1% it was 1.8 U / L. TAPSE had an average of 23.2MM ± 4.3.

**Discussion:** 30% of these patients died in this hospitalization With an average of 30 ± 10 days hospitalized. The decompensating cause was 72% ascites, 20.5% hepatorenal syndrome and 7.5 other causes,

including gastrointestinal bleeding. Observing that with this number of patients, there is a great implication in mortality and in the number of days of hospital stay.

**Conclusions:** It was possible to characterize cardiac function alterations in patients with a diagnosis of decompensated chronic liver failure, being more affected patients with arterial hypertension, etiology attributable to alcoholism, Child-Pugh C, MELD of> 27 points and MELD-NA of> 18 points and mainly CLIF 1 and PSAP of 31. It is expected to increase the number of patients to obtain greater clinical relevance.

The authors declare that there is no conflict of interest.

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## EFFICACY AND SAFETY OF TERLIPRESSIN INFUSION VS BOLUS TREATMENT IN DIGESTIVE BLEEDING OF VARICEAL ORIGIN AT THE PUEBLA SPECIALTY HOSPITAL, PRELIMINARY RESULTS

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**Introduction and Objectives:** Digestive bleeding of variceal origin represents an emergency medical event, with a mortality rate close to 20% and drug treatment is one of the pillars of management. In our environment and according to international recommendations, terlipressin administered in boluses is the treatment of choice for this entity, with a high percentage of adverse effects related to its use, so it is relevant to find other strategies in its use, but without reducing its use effectiveness. Some studies suggest that the use of terlipressin by continuous infusion could represent a more effective or comparable strategy for the control of bleeding, a lower rate of adverse effects and a lower risk of rebleeding, so the objective of this study is to compare the efficacy and safety of terlipressin in intermittent dose vs. infusion for acute bleeding of variceal origin in patients with portal hypertension.

**Material and methods:** this is a randomized, open, comparative and prospective study that included adult patients with a diagnosis of portal hypertension of any origin, with manifest gastrointestinal bleeding, treated at the Puebla Specialty Hospital since March 1, 2021, who were randomly administered terlipressin by infusion and boluses. Study variables: treatment failure, adverse effects, days of hospital stay and transfusion requirement. The protocol was approved by the local committee and conbioethics 21-CEI-002-20180731, all patients participated with informed consent. Results were analyzed with frequency measures, Fisher's exact test was used to demonstrate hypotheses, and Student's t-test was used for unrelated normal distribution variables.

**Results:** Up to now, 10 patients have been admitted to the study, in which no significant differences have been obtained in the study variables; however, in the bolus terlipressin group, three of the five patients have presented adverse effects, unlike the infusion terlipressin group in which they have not been presented.

**Discussion:** At the moment, a total of 10 patients has demonstrated comparable effectiveness in both groups; however, in the bolus group, 60% of the patients have presented adverse effects that have led to the change of vasoactive drug, unlike the infusion group where there have been no adverse effects, however, no significant differences have been found between both groups, which is explained by the small number of patients at the moment.

**Conclusions:** We consider that a larger number of patients is required to demonstrate our hypothesis.

The authors declare that there is no conflict of interest.

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## DIABETES AS A CAUSE OF DECOMPENSATION IN HEPATIC CIRRHOSIS

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**Introduction and objectives:** Cirrhosis and diabetes mellitus are two chronic diseases with a significant impact on quality of life glucose intolerance has been observed in about 80% of patients with cirrhosis, 30-60% of patients with advanced cirrhosis develop diabetes. The development of diabetes as a complication of cirrhosis is referred to as hepatogenic diabetes and type 2 diabetes which the patient develops prior to the presence of cirrhosis. Hepatogenic diabetes, unlike diabetes mellitus, lacks a family history, less obesity, and a lower incidence of micro and macrovascular complications. Diabetes increases morbidity and mortality in patients with liver cirrhosis. The effect of type 2 diabetes and hepathogenic diabetes on the clinical outcome of cirrhosis has been evaluated in a few studies. Diabetes mellitus has been shown to be associated with an increased risk of complications and mortality. We consider it important to assess the association between the type of diabetes (hepatogenic and non-hepatogenic) with the presence of decompensation of cirrhosis (hemorrhage, hepatic encephalopathy, ascites, spontaneous bacterial peritonitis).

**Material and methods:** Ambispective, observational, descriptive study. Patients with a diagnosis of liver cirrhosis and diabetes from an outpatient clinic at the General Hospital of Ticomán and a review of the clinical record are included, collecting information on decompensation events (hemorrhage, hepatic encephalopathy, spontaneous bacterial peritonitis, ascites). Descriptive analysis is performed of the variables.

**Results:** Twenty-eight patients were included, of whom 15 suffer from type 2 diabetes mellitus and 13 of them were diagnosed with hepatogenic diabetes. Hepatogenic diabetes was diagnosed in 9 patients with impaired fasting glucose levels and in 4 patients with a glucose tolerance curve. In both groups, the male gender predominated (53.3 and 61% respectively), the main etiology of alcohol cirrhosis. In the group with hepatogenic diabetes, 76.92% presented some decompensation event, the most frequent being upper gastrointestinal bleeding in 80%. In this group of patients, they correspond to Child A 53.84%, Child B 38.46 and Child C 7.69%. 76.92% of the patients had a portal diameter greater than 10mm, 61.53% of the patients had large esophageal varices. In 53.84% of the patients, they were difficult to control, receiving treatment with a combination of insulin and metformin. On the other hand, in the group of patients with diabetes mellitus 69.23% presented decompensation, the most common hemorrhage in 46.66%, of these patients 33.3% Child A, 53.33% Child B and 13.33% Child C. 53.33% had a diameter of the portal greater than 10mm and 61.53 large esophageal varices. 33.33% of the patients were difficult to manage, being treated with combinations of insulin, metformin and linagliptin.

**Discussion:** The association of diabetes with decompensation events has been observed in some studies, Del Vecchio et al. found that diabetes was more frequent in subjects with decompensation than in those with compensated cirrhosis, with a prevalence of 63%. Targest et al. Diabetes is commonly associated with a significant increase in the development of spontaneous bacterial peritonitis. Goh et al. Diabetes is associated with an increased risk of mortality in patients with cirrhosis.

**Conclusions:** In our study, we observed that decompensation events were more common in the group of patients with hepatogenic

cirrhosis, being the main gastrointestinal bleeding, in addition to presenting a larger diameter of the portal vein on ultrasound and a higher percentage of large esophageal varices. And we observed this group of patients presented difficult management of glucose levels being treated with combinations of insulin and metformin.

The authors declare that there is no conflict of interest.

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## COMPLICATION ASSOCIATED WITH UPPER GASTROINTESTINAL BLEEDING AMONG MEXICAN PATIENTS WITH CIRRHOSIS

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**Introduction and Objectives:** Upper gastrointestinal bleeding is a common complication among cirrhotic patients and holds high mortality and morbidity; the most common cause is variceal hemorrhage. Nonetheless, non-variceal hemorrhage is also frequent; this study aims to determine the prevalence of upper gastrointestinal bleeding complications among Mexican patients with cirrhosis.

**Methods:** Retrospective, cross-sectional, an analytic study among patients with cirrhosis of all etiologies admitted to the Gastroenterology department of the Hospital General de Mexico "Dr. Eduardo Liceaga" with acute upper gastrointestinal bleeding of both etiologies (variceal and non-variceal hemorrhage) in the period comprised from January 2017 to May 2021. Complications associated with the bleeding events were evaluated. For statistical analysis, quantitative variables were described as mean and standard deviation for qualitative variables in frequencies and percentages.

**Results:** A total of 295 patients were included, 55.3% male, mean age was 54.6 ± 11.8 years, 16.27% patients were staged as Child A, 49.15% Child B y 34.57% Child C, with and an average MELD score of 16. Main cirrhosis etiology was alcohol-related liver disease in 39.7%, viral hepatitis 6.4%, NASH 5.8% and others 3.4%; however, in 44.7% of patients, we were not able to determine the etiology of liver disease. The main cause of gastrointestinal bleeding was variceal hemorrhage in 71.1% and 28.9% non-variceal. The shock was identified in 5.76% (17) of patients, 9 of them required vasopressors, hepatic encephalopathy was present in 42.71% (126), Ascites in 18.64% (55), jaundice in 16.94% (50), acute kidney injury in 31.52% (93), bacterial infections in 24.06% (71), four patients (1.35%) died. Complications related to gastrointestinal bleed according to disease severity are depicted in table 1.

**Discussion and Conclusions:** Complications associated with upper gastrointestinal bleeding among Mexican patients with cirrhosis are frequent. Encephalopathy is the most common (42.71%) followed by acute kidney injury (31.52%) preponderantly of high grade, patients with more advanced disease are more prone to present infections, mainly UTI and ascites. Therefore they must be monitored closely.

The authors declare that there is no conflict of interest.

| COMPLICATION | CHILD A (N=48) | CHILD B (N=145) | CHILD C (N=102) |
|---|---|---|---|
| **SHOCK %(N)** | 2.08% (1) | 6.89% (10) | 5.88% (6) |
| **ENCEPHALOPATHY %(N)** | 20.8% (10) | 34.44% (50) | 64.7% (66) |
| **ASCITES %(N)** | 8.3% (4) | 16.55% (24) | 26.47% (27) |
| **JAUNDICE %(N)** | 0% (0) | 7.58% (11) | 38.23% (39) |
| **ACUTE KIDNEY INJURY %(N)** | 2.08% (1) | 28.90% (42) | 49.01% (50) |
| Grade 1a | 0 | 0 | 0 |
| Grade 1b | 0 | 54.76% (23) | 44% (22) |
| Grade 2 | 100% (1) | 21.42% (9) | 26% (13) |
| Grade 3 | 0 | 23.8% (10) | 30% (15) |
| **INFECTIONS %(N)** | 6.25% (3) | 20% (29) | 38.23% (39) |
| SBP | 0 | 0 | 12.82% (5) |
| UTI | 100% (3) | 55.17% (16) | 56.41% (22) |
| Pneumonia | 0 | 17.24% (5) | 23.07% (9) |
| Others | 0 | 6.8% (2) | 17.94% (7) |
| **MORTALITY %(N)** | 0 | 2.06% (3) | 0.98% (1) |

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## TRENDS OF CHRONIC LIVER DISEASES IN THE UNIVERSITY HOSPITAL, UANL FOR 25 YEARS. A SINGLE-CENTER EXPERIENCE

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**Introduction and objectives:** Liver cirrhosis is one of the main leading causes of death in Mexico. Some chronic liver diseases (CLD) are Alcoholic Liver Disease (ALD), Autoimmune Liver Disease (AILD), Hepatitis B (HBV), Hepatitis C (HCV), and Non-Alcoholic Steatohepatitis (NASH). In Mexico, ALD and HCV are the leading causes of CLD. Objective: To analyze the incidence of CLD in a liver unit (LU) over 25 years.

**Methods and materials:** Clinical records of patients who attended for the first time to LU, from January 1995 to December 2019 were reviewed. There were 2780 patients with CLD, and 2668 filled the inclusion criteria with available clinical records. The diagnosis of CLD was made according to international guidelines. Inclusion criteria: patients with CLD in their first visit, with or without cirrhosis. Exclusion criteria: acute liver disease, <18 years old. Patients were divided by etiology. This study was observational, descriptive and the sampling was carried out in a non-probabilistic and convenient way. Intervals of time were group A ($G^A$) 1995-2003, group B ($G^B$) 2004-2011 and group C ($G^C$) 2012-2019. A one-way ANOVA was used to determine the differences between these groups.

**Results:** A statistically significant difference was found in the AILD, ALD and NASH groups, as determined by a one-way ANOVA (p=0.036, p=0.011 and p=<0.00). A Tukey post hoc test showed that AILD cases in GB were higher than GA (p=0.029). The same trend was observed in ALD cases, which also showed an increase between the GA and GC (p=0.012). For NASH cases, each period showed an increase (p=0.005AB, p=<0.001AC, p=0.013BC). HCV and HBV showed no statistically significant changes (Figure).

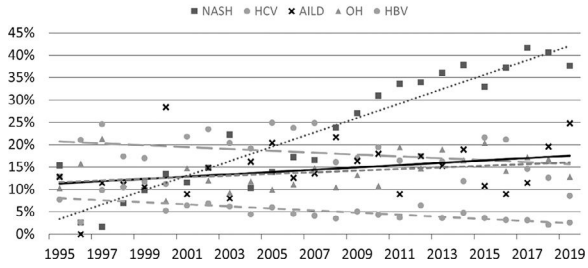
**Discussion:** In Mexico, there is scarce information on the incidence of CLD. This study showed a higher NASH incidence (43%) than the previously reported (29%)[1] as well as prevalence (23%)[2] in cirrhotic patients. The incidence of HAI in this study was 17%, similar to a previous study of 16%[1] in cirrhotic. Previously reported prevalence was 7.3%[2] in cirrhotic patients. ALD incidence was 15%, previously reported in 23%[1], and a prevalence of 31%[2] in cirrhotic patients. HCV

incidence had no significant changes (16%), but it was lower than previously reported (22%)[1].

**Conclusions:** This is the first study that reports an incidence of CLD in patients with or without cirrhosis. In the northeast of the country, the incidence of NASH has increased significantly during the last 25 years, becoming the most common CLD. This study found an AILD incidence similar to a previous report.[1] ALD showed moderate elevation compared to NASH, and HCV began to decrease.

The authors declare that there is no conflict of interest.

**Figure. Incidence of chronic liver diseases**

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## CAUSES OF DECOMPENSATION IN HOSPITALIZED CIRRHOTIC PATIENTS

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**Introduction and Objectives:** Decompensation of liver cirrhosis represents a turning point in the prognosis of cirrhotic patients presenting more complex medical needs that can lead to a prolonged hospital stay and a significant risk of in-hospital death. Likewise, mean survival decreases from 12 years for compensated cirrhosis to almost two years for decompensated cirrhosis. Apica BS et al. (2013) reported ascites as the most frequent cause of decompensation in 95.3% cases in the African population. On the other hand, the Colombian study of Sanchez (2016) conducted with the Latin population indicates as the leading cause of decompensation ascites (36.1%), variceal bleeding (28.4%). Unfortunately, in Mexico, we do not have data indicating the most frequent cause of decompensation in hospitalized patients. Therefore, knowing the frequency and most common causes of decompensation will direct prevention and timely treatment strategies. Objective: To determine the cause and prevalence of liver cirrhosis decompensation in patients admitted to the Hospital General de México.

**Material and Methods:** Observational, descriptive, retrospective study, Inpatients, hospitalized in the Gastroenterology Service of the General Hospital of Mexico "Dr. Eduardo Liceaga" with a diagnosis of liver cirrhosis, during the period from March 2019 to March 2021. The results were analyzed by descriptive statistics, frequency measures, and measures of central tendency (to obtain percentages, mean and average).

**Results:** We reviewed 454 records of patients diagnosed with liver cirrhosis with an average age of 59 years with a range of 18-75 years, predominantly male 59.25%. The most frequent etiology was alcohol in 44.71%, followed by non-alcoholic steatohepatitis 9.91%, autoimmune causes 7%, and viral (hepatitis B and C) 3.30%; however, up to 31.7% the etiology cannot be determined. According to the Child-Pugh classification, the predominant one was C up to 53.96%. The most frequent decompensation was gastrointestinal bleeding with 52.64%, of which 47.57% were of variceal origin, acute kidney injury with 50%, hepatic encephalopathy 46.03%, and ascites 40.96%. It should be noted that 15.19% presented acute on chronic hepatic failure, and 11.23% toxic-alcoholic hepatitis: less frequently hyponatremia 8.37%, spontaneous bacterial peritonitis (SBP) 7.92%, hepatorenal syndrome 1.98%, and hepatopulmonary syndrome 1.10%. See table 1.

**Conclusions:** In this study, the most frequent cause of decompensation was variceal bleeding, which differs from that reported in the literature in previous studies; however, this may be because the study population attends assessment in advanced stages of the disease and sometimes in the terminal phase to receive specialized care.

The authors declare that there is no conflict of interest.

**Table 1**
Anthropometric characteristics, Child-Pugh, etiology, and decompensations of Chronic Liver Disease.

| PARAMETER | n= 454 | interval or % |
|---|---|---|
| Average age (years) | 59 | 18-75 |
| **GENDER** | | |
| Male | 269 | 59.25% |
| female | 184 | 49.75% |
| **CHILD PUGH** | | |
| A | 42 | 9.25% |
| B | 167 | 36.78% |
| C | 245 | 53.96% |
| **ETIOLOGY** | | |
| ALCOHOL | 203 | 44.71% |
| UNAFFILIATED | 143 | 31.50% |
| NASH | 45 | 9.91% |
| PRIMARY BILIARY CHOLANGITIS | 23 | 5.07% |
| C VIRUS | 14 | 3.08% |
| AUTOINMUNE HEPATITIS | 8 | 1.76% |
| CARDIAC | 7 | 1.54% |
| HEPATOCARCINOMA | 5 | 1.10% |
| BILIARY TRACT LESION | 3 | 0.66% |
| BILIARY TRACT ATRESIA | 1 | 0.22% |
| PRIMARY SCLEROSING CHOLANGITIS | 1 | 0.22% |
| B VIRUS | 1 | 0.22% |
| DECOMPENSATIONS | | |
| GASTROINTESTINAL HEMORRHAGE | 239 | 52.64% |
| VARICEAL | 216 | 47.57% |
| NON - VARICEAL | 16 | 3,52% |
| VARICEAL/NON VARICEAL | 7 | 1.54% |
| HEPATIC ENCEPHALOPATHY | 209 | 46.03% |
| I | 0 | 0% |
| II | 158 | 34.80% |
| III | 51 | 11.23% |
| IV | 0 | 0% |
| ACUTE KIDNEY INJURY | 225 | 50% |
| IA | 80 | 17.62% |
| IB | 14 | 3% |
| II | 60 | 13.21% |
| III | 55 | 12.11% |
| CKD | 16 | 3.52% |
| ASCITES | 186 | 40.96% |
| GI | 4 | 0.88% |
| GII | 115 | 25.33% |
| GIII | 67 | 14.75% |
| SBP | 36 | 7.92% |
| HYPONATREMIA | | |
| <125 | 38 | 8.37% |
| ACLF | 69 | 15.19% |
| 1 | 21 | 4.62% |
| 2 | 34 | 7.48% |
| 3 | 14 | 3% |
| HEPATORENAL SYNDROME | 9 | 1.98% |
| HEPATOPULMONARY SYNDROME | 5 | 1.10% |
| TOXIC ALCOHOLIC HEPATITIS | 51 | 11.23% |

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## PREVALENCE AND CLINICAL CHARACTERISTICS OF FATTY HEPATIC DISEASE ASSOCIATED WITH METABOLIC DYSFUNCTION IN A POPULATION WITH NORMAL BODY MASS INDEX. (LEAN MAFLD)

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**Introduction and Objectives:** The prevalence of fatty liver disease associated with metabolic dysfunction (MAFLD) is estimated at 39.1%. 4.1% of patients with lean MAFLD are characterized by steatosis, normal BMI, and metabolic alterations. This work aims to describe the prevalence of lean MAFLD and metabolic characteristics in the Mexican population.

**Materials and Methods:** Retrospective study of patients with preventive medical check-up from 2019-2020 includes elastography for evaluation of fibrosis and steatosis (controlled attenuation parameter, CAP). Criteria to define lean MAFLD: BMI <24.9 and $^{3}2$ metabolic alterations: blood pressure> 130/85, previous diagnosis of hypertension, glucose alterations (100 - 125 mg / dl; 140 -199 mg / dl postprandial; HbA1c 5.7 - 6.4%, triglycerides> 150 mg / dl, HDL <40 mg / dl in men and <50 mg / dl in women, treatment for dyslipidemia, abdominal circumference ≥102 cm in men and ≥ 88 cm in women and C-reactive protein> 2mg / L). Exclusion: history of liver disease, significant hepatotoxic and/or alcohol consumption (> 2 drinks/day in women,> 3 drinks/day in men). Measures of central tendency and dispersion present data according to the distribution of the sample. A test was performed to analyze differences in clinical variables.

**Results:** 3863 patients were evaluated, 1754 (45.4%) presented steatosis (CAP> 263 dB / m) and 5.7% (n = 100) met criteria for lean MAFLD. 54% men with median age: 46 [40-56] years, BMI: 23.7 [22.8-24.4] kg / m2, CAP: 293 [271-314] dB / m and liver stiffness: 4.0 [3.5-4.7] kPa. 40% had grade 1 steatosis (> 263dB), 17% grade 2 (> 283 dB) and 43% grade 3 (> 296 dB). The clinical characteristics are shown in Table 1. The BMI showed a significant difference according to the degree of steatosis, being greater in patients with grade 3 (G1: 23.6 [IQR 22.8-24.3], G2: 23.3 [IQR 22.8 - 23.9] and G3: 24.1 [IQR 22.6 [24.1-24.7], p = 0.01)

**Discussion:** This study confirms the high prevalence of MAFLD / lean MAFLD in the Mexican population. The cut-off points to define the presence of steatosis (> 263 dB / m) has reported greater diagnostic precision (AUROC 0.97) than that used in the clinic (> 232 dB / m); When using the latter, the prevalence of steatosis rises to 65.9%; however, the prevalence of lean MAFLD does not change. This is the first report on the prevalence of Lean MAFLD in Mexico according to different cut-off points of CAP. With more inclusive MAFLD criteria, the prevalence of lean MAFLD does not change. Therefore, it is possible to start non-pharmacological therapy early in patients with overweight, obesity, or normal BMI.

**Conclusion:** The prevalence of lean MAFLD in the Mexican population is high, with a higher proportion of patients with grade 3 steatosis presenting a higher BMI. The prevalence does not change when using different cut-off points for CAP.

The authors declare that there is no conflict of interest.

**Table 1**
Clinical characteristics of patients with lean MAFLD

| Characteristics | Median [IQR]/ % (n) |
|---|---|
| **Age** | 46 [40-56] |
| **Weight** | 66.1 [59-74] |
| **BMI** | 23.7 [22.8 – 24.4] |
| **kPa** | 4.0 [3.5-4.7 |
| **CAP** | 293 [271-314] |
| **IQR CAP** | 24 [17-29] |
| **Systolic blood pressure** | 110 [104-122] |
| **Diastolic blood pressure** | 73 [69-80] |
| **Fasting glucose** | 94 [89-99] |
| **Triglycerides** | 171 [110-236] |
| **HDL** | 40 [34-47] |
| **PCR** | 1.6 [0.82-3.0] |
| **HbA1c** | 5.3 [5.1-5.5] |
| **Waist circumference** | 89 [83-93] |

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## INCIDENTAL FINDING OF FATTY LIVER IN AUTOPSIES

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**Introduction and Objectives:** Non alcoholic fatty liver disease (NAFLD) and alcoholic fatty liver disease (ALD) are the most common emergent causes of chronic liver disease; they evolve from simple steatosis, steatohepatitis, fibrosis/cirrhosis and hepatocellular carcinoma. Knowing the factors that influence their development and screening can improve the prognosis of these patients.

**Objective:** To determine the prevalence of incidental findings of fatty liver in necropsies performed for all causes of mortality and to analyze the main characteristics of these patients.

**Materials and Methods:** Type and design of the study: Observational, descriptive, transversal study.

**Procedure:** All necropsy records for all causes of mortality registered at the Pathology Department in our center in the last 10 years were reviewed (January 2010 – December 2019). We search the following findings: “liver steatosis,” “steatohepatitis,” degree of fibrosis/cirrhosis, “atherosclerosis,” “heavy alcohol intake,” “diabetes, obesity, dyslipidemia, metabolic syndrome.” We used descriptive and analytical statistics: $X^2$, exact Fisher’s test, univariate and multivariate logistic regression models.

**Results:** 4557 necropsies were registered. Fatty liver was found in 6.4% of the cases. 53.3% were women; 51±15 years old; There was simple steatosis in 156 cases (53.6%) and steatohepatitis with necroinflammatory activity in 135 (46.4%). A 49.8% presented liver fibrosis (F1=38 [13.1%]; F2=48 [16.5%]; F3=15 [5.2%]; F4=44 [15.1%]). The etiology through clinical history and histological findings compatible with alcoholic liver injury occurred in 67 cases (23%), NAFLD in 98 (33.7%), mixed type (NAFLD+ALD) in 19 (6.5%), the etiology could not be identified in 107 (36.8%). The multivariate analysis showed alcohol intake as the main risk factor for necroinflammation (OR=2.58; ICal95%= 1.52-4.38; p<0.0001). History of alcohol intake (OR=2.52; ICal95%= 1.40-4.54; p=0.002) and presence of necroinflammatory activity (OR=6.53; ICal95%= 3.72-11.47; p<0.0001) were predictive factors of fibrosis F2-F4. (Table 1)

**Conclusions:** In this study, which included all causes of death, incidental findings of steatosis, steatohepatitis, and fibrosis/cirrhosis

were found in a high proportion. Alcohol consumption continues to contribute significantly to liver injury in Mexico.

The authors declare that there is no conflict of interest.

**Table 1**
Multivariate predictive models

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

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

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

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

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## FREQUENCY OF RISK FACTORS FOR DEVELOPMENT OF METABOLIC FATTY LIVER DISEASE (MAFLD) IN A CENTER OF CONCENTRATION OF LIVER DISEASES

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**Introduction and Objectives:** Metabolic fatty liver disease (MAFLD) includes a wide spectrum of presentations, ranging from simple steatosis and non-alcoholic steatohepatitis to liver cirrhosis, leading to hepatocellular carcinoma; the etiology of this is multifactorial, with few studies on risk factors in the Mexican population.

**Objective:** Determine the frequency of risk factors in patients with MAFLD in a liver disease center: CEIHET, Mexico. Material and methods: An observational, cross-sectional and retrospective study selected 587 records from the CEIHET, Hidalgo, of patients with a diagnosis of MAFLD, from January 2017 to May 2020. Determine the frequency of risk factors. Statistical analysis was performed through measures of central tendency, dispersion and correlation.

**Results:** 587 files were analyzed, 56% (n = 329) women; mean age of 51.4 years. The group with simple steatosis had a mean age of 38 years, while in advanced liver cirrhosis, it was 63 years (p 0.005). In schooling, basic education was found for liver cirrhosis in 73.12% (n = 215), and, in previous stages, it was 21.84% (n = 64). In the AHF and APP, type 2 diabetes is shown as the main risk factor with 65.92% (n = 387) and 58.77% (n = 345), respectively; 6 out of 10 patients had two or more risk factors. 77.3% (n = 454) of patients did not meet the standards of adequate physical activity. Regarding BMI, 73% of patients with simple steatosis were overweight or obese, while, with liver cirrhosis, it was present in 98% without ascites or edema.

**Discussion:** A prevalence of fatty liver disease of 55.75% was found, being the main reason for liver Disease consultation, constituting the major cause of liver damage in females. The age of patients increases in direct proportion to the severity of liver damage. Of relevance is education, showing RR of 9.2 (p = 0.001), which indicates that the lower the level of education, a later detection is carried out. 77.3% of these patients did not comply with the physical activity standards established by the WHO. When studying the BMI, we noticed the presence of overweight/obesity in at least 88% of the population, correlating with that established in studies in the USA, where the Latino population has the highest BMI and in the highest frequency.

**Conclusions:** The present study shows that sedentary lifestyle, overweight, obesity and type 2 diabetes are the main determining factors for the presence of MAFLD in the Mexican population, and therefore the importance of its detection and management, to prevent its progression and improve the quality of life of patients.

The authors declare that there is no conflict of interest.

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## PREVALENCE OF COMBINED LIVER DAMAGE IN MEXICAN POPULATION

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**Introduction and Objectives:** Metabolic syndrome and alcohol consumption are the two main causes of liver steatosis. Often, one of them predominates for its development and the other acts as a cofactor. The impact of these entities separately and their damage in synergy in the Mexican population is currently unknown. Our objective is to determine the prevalence of non-alcoholic liver steatosis, alcoholic liver steatosis, and dual damage in donors from the blood bank of the Hospital General de México "Dr. Eduardo Liceaga" (HGMEL) using transient elastography (TE).

**Materials and Methods:** Pilot study. prospective, transversal, descriptive, and analytical. Healthy donors from the HGMEL blood bank who attended from June 8 to 29 2021 ≥18 years old, of any gender, will be included with a body mass index (BMI) ≥18.5. Donors with liver disease of any etiology and liver malignancy will be excluded. Donors who did not attend TE will be eliminated. The equipment used for TE was FibroScan® 502 Touch. Descriptive statistics will be used with measures of central tendency and dispersion.

**Results:** 30 donors were recruited, four were eliminated for not having performed TE. The age of the subjects was 36.53 ± 12.13 years. There were 13 female subjects and 13 males. Seven (26.92%) donors were classified with non-alcoholic fatty liver disease (NAFLD), 2 (7.69%) with alcoholic fatty liver disease (ALD), and 1 (3.84%) subject with liver steatosis due to combined damage; the 16 (61.55%) remaining subjects corresponded to a healthy population. From the NAFLD group, S1 steatosis was documented in 1 subject (14.28%), S2 in 2 (28.56%), and S3 in 4 (57.16%); F0-F1 liver stiffness was found in 6 (85.72%) subjects, and F4 in 1 (14.28%); Of this group, 3 (42.86%) subjects were classified as overweight, 3 (42.86%) with grade 2

obesity, and 1 (14.28%) with grade 3 obesity. On the other hand, from the ALD group, one donor was found with steatosis S1, and 1 with S2; one of them had liver stiffness F0-F1 with an AUDIT score of 17 and a risk pattern for excessive alcohol consumption (117 g 2 to 4 times a month), while the other subject had F4 fibrosis with an AUDIT score of 7 and a pattern risk of excessive consumption (208 g 2 to 4 times per month), both consume beer. Finally, one donor had liver steatosis due to combined damage, with S3 for steatosis and F4 liver stiffness (27.4 kPa, the highest record in the study); He has grade 3 obesity (BMI 44.41), an AUDIT score of 4, and a pattern of excessive consumption (78 g 2 to 4 times a month) of distillates.

**Discussion:** What is relevant about this work is that it studies an apparently healthy population and, according to our results, 38.45% (10) of the subjects already have a degree of liver steatosis and even 11.53% (3) showed advanced fibrosis. Our findings are similar to others about the prevalence of nonalcoholic liver steatosis, such as the work of the López-Velázquez group (26%) in 2014. Our study is novel in the investigation of alcoholic liver steatosis and the combined damage. Those issues are scarce addressed in our country. We also collect additional information, such as the identification of the consumption pattern of people with risky alcohol intake and the type of drink they consume.

**Conclusions:** Our study shows that liver steatosis in this sample of the Mexican population is predominantly non-alcoholic; all subjects within this group have high BMI. Excessive risk consumption is prevalent in subjects with alcohol-related steatosis, and beer is the most frequent drink. In combined damage, obesity and excessive consumption of distillates seem to be the cause of severe steatosis. The only patient in this group already shows advanced fibrosis, which makes us suspect that dual damage accelerates the rate of fibrosis progression.

The authors declare that there is no conflict of interest.

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## HEPATOCELLULAR CARCINOMA AFTER DIRECT ANTIVIRAL AGENTS FOR HEPATITIS C IN PATIENTS WITH DECOMPENSATED CIRRHOSIS

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**Introduction and Objectives:** If direct antiviral agents (DAA) are related to the development of HCC is controversial; therefore, exploring risk factors are crucial. We aimed to determine factors related to the development of hepatocellular carcinoma (HCC) in patients with hepatitis c (HCV) and decompensated cirrhosis (DC) treated with DAA.

**Materials and Methods:** A multicenter real-world cohort study including patients with HCV + DC treated with sofosbuvir (SOF) based on regimens free of inhibitors of protease (IPs).

**Results:** 222 patients, 118 (53.2%) were women, mean age 57.2 ±11.5-year-old, 209 (94.1%) achieved sustained virological response (SVR). According to Child-Pugh 44(19.8%) were A with history of any clinical decompensation event, 147(66.2%) B, and 31 (14%) C. After DAA, 134 (60.4%) improve in MELD, 45 (20.3%) had no change, and 43 (19.4%) worse, this worse in MELD was related to non-SVR [SVR 37/209 (17.7%) vs. non-SVR 6/13 (46.2%); OR=2.6, 95%CI:1.4-5.0, $p$=0.02]. Nineteen (8.6%) developed HCC during the follow-up after therapy with DAA; however, when we compared basal laboratory values between those who developed HCC and those who did not only alfa-fetoprotein (AFP) levels were different (without HCC 14.3 [mean 95%CI: 10.6-18.1] ng/mL vs. HCC 55.7 [mean 95%CI: 28.4-83.0] ng/mL; $p$<0.006). Univariate and multivariate analyses are shown in Table 1.

**Discussion:** Our study confirms that rather than DAA therapy, the most critical factors related to the development of HCC in DC patients with HCV treated with DAA, are non-achieve SVR and, most important basal AFP levels > 20ng/mL, it is essential to note that patients in this cohort had no any suspicious lesion in ultrasonography (USG) previous to start DAA therapy in their semestral screening as most of the guidelines recommend. AASLD, for example, recommends semestral HCC screening with USG with or without AFP, giving more weight to the imagen study. However, based on our results, we recommend always determining AFP levels as a compliment to USG.

**Conclusions:** In HCV patients with DC treated with DAA and with a negative basal screening USG for suspicious malignant lesions, basal AFP > 20ng/mL are the most critical factor related to the development of HCC and should be determined complementary to the USG study.

The authors declare that there is no conflict of interest.

**Table 1**
Risk factors related to the development of HCC after DAA in decompensated cirrhosis with hepatitis C infection

| Univariate analysis | | | | |
|---|---|---|---|---|
| Variable | HCC n=19 | Without-HCC n=203 | $p$ | OR (95%CI) |
| Age, year-old | 58±10.6 | 57±11.5 | 0.75 | - |
| Male gender, n(%) | 6 (30.6) | 98 (48.3) | 0.17 | 0.5 (0.2-1.3) |
| Use of ribavirin, n(%) | 13 (68.4) | 162 (79.8) | 0.25 | 0.5 (0.2-1.5) |
| Non-achieve SVR, n(%) | 4 (21.1) | 9 (4.4) | 0.008 | 5.7 (1.6-20.9) |
| Basal AFP level > 20ng/mL | 10 (52.6) | 30 (14.8) | <0.0001 | 7.3 (2.6-20.7) |
| Diabetes, n(%) | 5 (26.3) | 31 (15.3) | 0.21 | 2.0 (0.7-5.9) |
| Obesity, n(%) | 5 (26.3) | 36 (17.7) | 0.36 | 1.6 (0.6-4.9) |
| Progression of decompensation according to MELD | 6 (31.6) | 37 (18.2) | 0.17 | 2.1 (0.7-5.8) |

| Multivariate adjusted analysis | | |
|---|---|---|
| Variable | $p$ | OR (95%CI) |
| Non-achieve SVR, n(%) | 0.16 | 3.0 (0.6-14.5) |
| Basal AFP level > 20ng/mL | <0.0001 | 6.6 (2.3-19.0) |

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## HEPATOCELLULAR CARCINOMA IN VERACRUZ: A SURVEILLANCE COMPARISON BETWEEN TREATMENTS

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**Introduction and Objectives:** In Mexico, hepatocellular carcinoma (HC) represents >90% of primary hepatic tumors. The diagnosis is determined by imaging findings (CT or MR). A biopsy is necessary for specific situations. The staging method is the Barcelona classification (BCLC) which considers hepatic biomarkers, the tumor burden and the performance status. Treatment options include transplantation, liver resection (LR), radiofrequency ablation (RFA), transarterial embolization (TACE/TAE) and systemic treatment (ST). Nonetheless, there are few surveillance studies in Mexico. The study aims to describe the surveillance of HC subjects after different therapeutic approaches.

**Materials and Methods:** Descriptive and retrospective study with a database including 130 patients diagnosed with HC by imaging findings (or biopsy if needed) between 2005 and 2021 in Veracruz. For statistical analysis, surveillance data was first summarized by descriptive statistics and 5-year-overall survival rates (5OS). Subsequently, a comparison of surveillance between therapeutic options was made by Log-Rank, Cox regression and $\chi 2$. We considered statistical significance at $p<0.05$.

**Results:** A total of 130 patients were diagnosed with HC,128 patients were analyzed after 2 exclusions due to missing data, 45 (35%) of them died during the follow-up. The distribution of descriptive data is detailed in Table 1. We observed longer accumulated overall surveillance in patients who underwent LR (5OS: 73%), followed by RFA (5OS: 28%), $\chi 2$: 10.7, p=0.02. When analyzing data by BCLC we found a poor difference in surveillance between treatments ($p>0.05$). Recurrence of the tumor was only observed in stage B: 5 cases after LR (29.4%), and 2 cases after RFA (22.2%), $\chi 2$=12.084 p=0.017. The mean time for recurrence detection was 19 months and five months for LR and RFA, respectively. Discussion: This analysis showed higher accumulated surveillance for patients with LR, followed by RFA. Furthermore, Log-Rank curve of RFA showed a pronounced inclination of surveillance around the 25th month, after which it reached a plateau and deceleration until the 75th month. However, five year-OSr seemed to be lower than in other studies.

**Conclusion:** Our results suggest that LR is a feasible treatment alternative. In the meantime, RFA seems a worthy option when patients are not candidates for LR, showing promising results.

The authors declare that there is no conflict of interest.

**Table 1**
Surveillance time according staging

| | | $\chi^2$ | p | Tx | n 128 (%) | Surveillance (Months) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | M | SD | Me | SD |
| **Barcelona Classification** | **A** | **3.0** | **0.3** | **NT** | 4 (10.8) | 10 | 3 | 10 | 6 |
| | | | | **LR** | 12 (32.4) | 49 | 14 | 24 | 50 |
| | | | | **RFA** | 8 (21.6) | 14 | 4 | 12 | 11 |
| | | | | **ST** | 13 (35.1) | 11 | 3 | 9 | 10 |
| | | | | **Global** | 37 (100) | 24 | 6 | 10 | 34 |
| | **B** | **3.2** | **0.5** | **NT** | 16 (21.9) | 7 | 1 | 7 | 6 |
| | | | | **LR** | 18 (24.7) | 34 | 8 | 25 | 35 |
| | | | | **RFA** | 11 (15.1) | 26 | 7 | 15 | 24 |
| | | | | **ST** | 25 (34.2) | 12 | 2 | 11 | 9 |
| | | | | **TACE** | 3 (4.1) | 7 | 3 | 6 | 5 |
| | | | | **Global** | 73 (100) | 18 | 3 | 11 | 23 |
| | **C** | **5.9** | **0.1** | **NT** | 7 (53.8) | 5 | 2 | 4 | 4 |
| | | | | **LR** | 1 (7.7) | 3 | N/A | 3 | N/A |
| | | | | **RFA** | 1 (7.7) | 10 | N/A | 10 | N/A |
| | | | | **ST** | 4 (30.8) | 23 | 6 | 25 | 12 |
| | | | | **Global** | 13 (100) | 11 | 3 | 7 | 11 |
| | **D** | N/A | N/A | **NT** | 5 (100) | 5 | N/A | 5 | 2 |
| | | | | **Global** | 5 (100) | 5 | N/A | 5 | 2 |

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## HEPATOCELLULAR CARCINOMA: CLINICAL AND EPIDEMIOLOGICAL FEATURES IN VERACRUZ

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**Introduction and Objectives:** Hepatocellular carcinoma (HCC) is the most frequent liver tumor and it occupies sixth place of the malignant neoplasms worldwide. In the last decades, In Mexico has been reported an increase of 95% in incidence and 14% in mortality, becoming the second most lethal neoplasm after pancreatic cancer. Few studies describe the HCC epidemiological behavior in our population.

**Objective:** To describe the clinical and epidemiological features of HCC in patients from Veracruz city.

**Material and methods:** A descriptive and retrospective study was done from a patient database with diagnosed HCC by imaging and, if required, with a biopsy confirmation between 2005 and 2021 in Veracruz. Central tendency and dispersion measures were done for the analysis.

**Results:** 130 patients with HCC were studied, the mean diagnosis age was 66.9±11 (29-62 rate), with a female genre lead 1.2:1. Eighty-six patients (66.2%) had cirrhosis at the diagnosis, 32 (24.6%) were secondary to chronic alcohol consumption, 8 (6.2%) with hepatitis C infection, 20 (15.4%) MAFLD/ Cryptogenic and 3 (2.3%) with hepatitis B infection. The comorbidities reported were overweight in 58 patients (43.9%), obesity 19 (14.4%), high blood pressure 54 (40.2%) and diabetes mellitus 51 (38.6%). The most frequent biochemical disturbance was hyperbilirubinemia (1.27± 1.26). The rest f biochemical features are described in table 1. Sixty-six patients (50%) were found with Child-Pugh A with a MELD score of 9.86±3.0. In this stage, we found 74 patients (56.9%) with Barcelona B, 80% had a lone tumor, the mean tumoral size was 7.13±3.7 cm. 69.2% of patients had a tumoral size greater than 5 cm at the diagnosis.

**Discussion:** Our results show that the HCC behavior is similar to the reported in previous Mexican studies, predominating in patients with advanced liver injury and tumor outside criteria of local treatment at the diagnosis. The high frequency of comorbidities associated with metabolic syndrome is remarkable as one of the main risk factors with chronic C virus infection.

**Conclusion:** HCC in Mexico has been increasing. It shows similar epidemiological features with the reported in other populations due to its relationship with metabolic risk. Early screening in high-risk patients results in greater resectability and survival.

The authors declare that there is no conflict of interest.

**Table 1**
Clinical and biochemical features in patients with Hepatocellular carcinoma

| | |
|---|---|
| **Age** | 66.9±11 |
| **Sex** % (Female / Male) | 53.8 (70) / 46.2 (60) |
| **HC etiology** % (Alcohol/ Cryptogenic MAFLD/ HCV / HBV) | 32(24.6) / 20(15.4) / 8(6.2) / 3(2.3) |
| **Comorbidities** (Overweight/ Obesity/ HBP/DMT2) | 58 (43.9) / 19(14.4) / 53(40.2) / 51 (38.6) |
| **Child-Pugh** % (A, B, C) | 50% (65)/ 14.6% (19)/ 1.5% (2) |
| **BCLC** % (A, B, C, D) | 28.5% (37)/ 56.1% (74)/ 10.8% (14)/ 3.8% (5) |
| **ECOG** % (0,1,2,3) | 21.2% (11)/ 50% (26)/ 26.9% (14)/ 1.9% (1) |
| **Ascites** % | 10.8% (14) |
| **ALT** (UI/L) | 46±29 |
| **AST** (UI/L) | 67.6±54 |
| **BT** (mg/dl) | 1.27±1.6 |
| **Albumin** (mg/dl) | 3.55±0.6 |
| **Platelets** (x 1,000) | 174±103 |
| **Prothrombin time** (s) | 15±3.4 |
| **INR** | 1.17±0.1 |
| **Serum alphafetoprotein** (ng/nL) | 5135.1±26422 |
| **MELD** | 9.86±3.0 |
| **Tumor diameter** (cm) | 7.13±3.7 |
| Number of tumors | 1.37±1 |

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## A MULTICENTER REAL-WORLD COHORT TO VALIDATE THE EFFICACY AND SAFETY OF DIRECT ANTIVIRAL AGENTS FOR HEPATITIS C, AND RELATED RISK FACTORS FOR NON-SVR IN DECOMPENSATED CIRRHOSIS

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**Introduction and Objectives:** Clinical trials demonstrated the efficacy and safety of direct antiviral agents (DAA) to treat hepatitis C virus infection (HCV) in patients with decompensated cirrhosis (DC); however, very few real-world studies have been reported in this group. Moreover, predictive factors for non-achieving sustained virological response (SVR) in DC are not entirely understood. Therefore, the aim was to verify the efficacy and safety of DAA and to identify risk factors for failure to achieve SVR in DC.

**Materials and Methods:** A real-world cohort study included HCV patients with DC [Child-Pugh B/C or A but with a history of previous clinical decompensation events like variceal bleeding (VB), hepatic encephalopathy (HE), or ascites]. All patients treated before transplant had MELD ≤ 20 and Child-Pugh ≤ 12 according to AASLD guidelines.

**Results:** 222 patients, 118 (53.2%) were women, mean age 57.2±11.5 year-old, 61 (27.5%) were treated with Sofosbuvir (SOF)/Ledipasvir, 152 (68.5%) with SOF/Velpatasvir, and 9 (4.1%) with SOF/Daclatasvir, 175 (78.8%) used also ribavirin, 209 (94.1%) achieved SVR, despite non-significant difference, Child-Pugh C patients had a suboptimal response (SVR < 95%): A 42/44 (95.5%), B 140/147 (95.2%), C 27/31 (87.0%), $p$=0.2. Related adverse events were fatigue 60 (27%), nausea 44 (19.8%), headache 43 (19.4%), non-severe peripheral edema 10 (4.5%), anasarca 4 (1.8%), jaundice 6 (2.7%), 3 hemolytic anemia (1.4%), 1 dermatosis (0.4%), congestive cardiac failure 2 (0.9%), need to suspend therapy due to liver-related adverse events 2 (0.9%) they also died. In those who achieved SVR, MELD improved (basal 12.4±3.3 vs. post-SVR 10.9±3.5; $p$<0.0001); but was worse in those without SVR (basal 16.2±3.9 vs. without-SVR 17.3±6.2; $p$=0.24). Times/year needing hospitalization for liver-related decompensation events were less frequent in those who achieved SVR (basal 1.7±1.3 vs. after SVR 0.4±0.7; $p$<0.0001) but remained without change in that without-SVR (basal 1.5±1.5 vs. after non-achieve SVR 2.2±1.9; $p$=0.04).

**Discussion:** A few real-world studies have been conducted in DC with hepatitis C. However, in the Mexican population, our study is the first that demonstrated in a real-world setting, similar to clinical trials, that DAA based on SOF and free of protease inhibitors (PIs) are effective and safe to cure HCV in DC. When to treat HCV before or after liver transplantation can be challenging. Classically, MELD >20 and Child-Pugh C >12 are related to non-SVR; however, our study also shows that additional clinical factors have a negative impact on SVR: history of recurrent VB and episodic and persistent HE; therefore, these criteria should also be considered to decide to treat previous or after liver transplantation. In addition, acute decompensation and mortality events are very high in those who do not achieve SVR.

**Conclusions:** SOF based on regimens without PIs are effective and safe in VHC with DC. Additional to classic criteria (MELD >20, Child-Pugh > 12), recurrent VB and HE are predictors of failure to achieve SVR in VHC with DC.

The authors declare that there is no conflict of interest.

**Table 1**
Comparison of characteristics of the cohort according to the response to DAA therapy

| Variable | SVR n=209 | Without-SVR n= 13 | $p$ | OR (95%CI) |
|---|---|---|---|---|
| Basal characteristics | | | | |
| Age, year-old | 57.3±11.3 | 55.7±14.9 | 0.63 | - |
| Transition elastography, KPa | 28.8±12.9 (n=181) | 41.7±21.6 (n=10) | 0.09 | - |
| Child-Pugh, points | 8±1 | 9±2 | 0.05 | - |
| MELD, points | 12.4±3.3 | 16.2±3.9 | <0.0001* | - |
| Viral load, IU/mL | 2,219,130 | 2,368,392 | 0.96 | - |
| Episode of variceal bleeding, n(%) | 137 (65.6) | 10 (76.9) | 0.55 | 1.2 (0.9-1.6) |
| Recurrent variceal bleeding, n(%) | 46 (22.0) | 10 (76.9) | <0.0001* | 3.5 (2.4-5.2) |
| Ascites, n(%) | 123 (58.8) | 10 (76.9) | 0.25 | 1.3 (0.9-1.8) |
| | 76 (36.4) | 9 (69.2) | 0.03* | 1.9 (1.3-2.9) |

(*continued*)

**Table 1** (*Continued*)

| Variable | SVR n=209 | Without-SVR n= 13 | *p* | OR (95%CI) |
|---|---|---|---|---|
| Basal characteristics | | | | |
| Episodic hepatic encephalopathy, n (%) | | | | |
| Persistent hepatic encephalopathy, n (%) | 28 (13.4) | 5 (38.5) | 0.03* | 2.9 (1.3-6.2) |
| History of spontaneous bacterial peritonitis, n(%) | 4 (1.9%) | 1 (7.7) | 0.26 | 4.0 (0.5-33.4) |
| Follow-up at 1-year after DAA therapy | | | | |
| Child-Pugh, points | 6±2 | 9±3 | 0.007* | - |
| MELD, points | 10.9±3.5 | 17.3±6.2 | 0.003* | - |
| Transition elastography, KPa | 23.2±11.6 (n=62) | 45.7±20.8 (n=9) | 0.01* | - |
| Variceal bleeding, n (%) | 26 (12.4) | 7 (53.8) | 0.001* | 4.3 (2.3-8.0) |
| Ascites, n(%) | 32 (15.3) | 9 (69.2) | <0.0001* | 4.5 (2.8-7.3) |
| Episodic hepatic encephalopathy, n (%) | 22 (10.5) | 7 (53.8) | <0.0001* | 5.1 (2.7-9.7) |
| Persistent hepatic encephalopathy, n (%) | 6 (2.9) | 3 (23.1) | 0.01* | 8.0 (2.3-28.6) |
| Spontaneous bacterial peritonitis, n (%) | 0 (0) | 1 (7.7) | 0.06* | 0.9 (0.8-1.1) |
| Mortality rate, n(%) | 1 (0.5) | 4 (30.8) | <0.0001* | 64.3 (7.7-534.9) |

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## STUDY OF CONCORDANCE BETWEEN THE DEGREE OF LIVER FIBROSIS ESTIMATED THROUGH APRI AND FIB-4 BIOCHEMICAL SCORES, AND ELASTORESONANCE IN PATIENTS WITH AUTOIMMUNE HEPATITIS

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**Introduction and Objectives:** Autoimmune hepatitis is a chronic and progressive necroinflammatory disease with a fluctuating course of activity and affects more frequently the female sex. The etiopathogenesis is still unknown and may be the result of an interaction between factors: genetic, immunological, autoantigens; Therefore, the interaction of genetic predisposition with an environmental trigger and the disorder in immunoregulation would result in chronic inflammation of the hepatocytes and with it the development of hepatic fibrosis. Diagnostic tests for the evaluation of liver fibrosis include liver biopsy and non-invasive elastographic methods, such as transition elastography and elastoresonance, as well as serum biomarkers, composed of different variables that help predict the degree of liver fibrosis.

**Objective:** Compare the concordance between the results obtained for the diagnosis of liver fibrosis by the APRI and FIB-4 score, with the elastoresonance, in patients with HAI.

**Material and methods:** Elastoresonance, APRI and FIB-4 were performed in 6 patients to assess the concordance between different degrees of fibrosis.

**Results:** A total of 6 patients with a recent diagnosis of HAI were included in the study. The mean age was 50.33 years and 100% were women. 66.66% of the patients presented an advanced degree of fibrosis (F2-F3-F4) due to elastoresonance. The values for the APRI index were: 3 patients (50%) had an advanced degree of fibrosis, 1 patient had a low degree of fibrosis (6%) and 2 patients (33.33%) had intermediate. The findings for the FIB-4 values were exactly the same. The agreement of elastoresonance in the different degrees of fibrosis against the APRI and FIB-4 score was 100%.

**Discussion:** Non-invasive methods to measure the degree of liver fibrosis in patients with chronic liver disease have shown to be useful, and in this study, it transcends that the correlation with the degree of fibrosis obtained by elastoresonance with the APRI and FIB-4 scores is 100%, this could avoid reaching the liver biopsy, which although it is the gold standard in measuring the degree of liver fibrosis, is an invasive and expensive method, which involves risks for the patient (puncture of other internal organs, infection and adverse reaction to contrast material).

**Conclusions:** In patients classified with advanced fibrosis, the concordance between the estimates obtained using the elastoMR and those derived from the APRI and FIB-4 scores are high. However, a limitation of this study is the size of the sample.

The authors declare that there is no conflict of interest.

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## GLUCOGENOSIS AS A CAUSE OF INTRAHEPATIC CHOLESTASIS

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**Introduction and Objectives:** Hepatic glycogen storage pathologies are very rare diseases among inborn errors of metabolism caused by the alteration of the enzymes involved in the metabolism of glycogen. GSDs are classified according to enzyme deficiency and affected tissue, including types 0, Ia, Ib, III, IV, VI, and XI. The clinical presentation can be very varied, including intolerance to fasting, growth retardation and hepatomegaly. It can present with hypoglycemia, hyperlactatemia, increased liver enzymes, and hyperlipidemia. The most common type of glycogen storage disease is GDS IX, its incidence is 1: 100,000 births and it is responsible for 25% of all cases. The most common GSD IX subtype is subtype IX a caused by mutations in PHKA2, which accounts for 75% of cases. Long-term complications include liver adenomas, kidney disease, cardiomyopathy, and muscle symptoms.

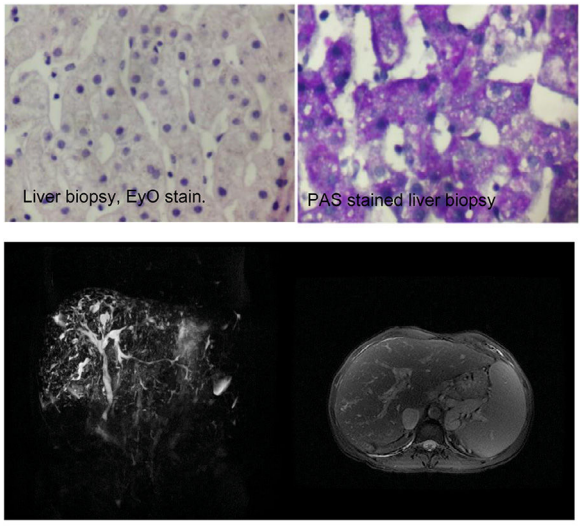
**Clinical case:** 27-year-old male patient. Important history, positive smoking with IT 1, positive alcoholism with consumption of 8 grams of alcohol per day for 10 years. During childhood, he presented hepatomegaly and an isolated event of jaundice. He began his condition one month before with asthenia, adynamia and weight loss (9 kg / 30 days), accompanied by generalized jaundice, later he presented abdominal pain in the right upper quadrant, with early satiety, acholia and choluria. On physical examination: hepatosplenomegaly, jaundice of the skin and integuments. Paraclinical: BT: 5.3 mg / dl, BD: 1.2 mg / dl 8, DHL: 444IU / L, TGP: 89 U / L, TGO: 168 U / L FA: 1050 U / L. HIV: non-reactive, HBV HCV non-reactive. Ultrasound with multiple nodular echogenic lesions without bile duct dilation, a 1.8 mm common bile duct, a 7 mm portal vein, and an enlarged spleen. Endoscopy: portal hypertensive gastropathy, extrinsic compression of the body and gastric fundus without evidence of varicose veins. Cholangioresonance without intra- and extra-hepatic bile duct dilation. Normal alpha 1 antitrypsin (2.08 g / dl). Given the evidence of intrahepatic cholestasis, it was decided to perform an ultrasound-guided liver biopsy where it was observed positive for intracytoplasmic glycogen in the hepatocytes, thus establishing a definitive diagnosis of Glycogenosis.

**Discussion:** Due to its low incidence, the diagnostic approach of Glycogenosis presents a challenge. The diagnosis is made at an early

age; the clinical data will depend on the affected tissue and type of Glycogenosis. The histopathological report is the mainstay of diagnosis in this type of case and making a differential diagnosis with other entities and a genetic study.

**Conclusions:** Glycogen storage disorders are part of a group of rare and few suspected pathologies. It is not frequent to find them in adult patients due to their complications. The prognosis must be individualized based on the affected tissue and the subtype presented.

The authors declare that there is no conflict of interest.




Collagioresonance

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## ADDRESSING THE INFILTRATIVE PATTERN: COMPLEX DIAGNOSIS

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**Introduction and objective:** Alterations in liver function tests are frequent, so the approach based on the predominant alteration and the patient's medical history is relevant. Carrying out a liver biopsy in cases of diagnostic doubt is imperative. The objective of this work is to describe a clinical case of an infiltrative pattern approach that culminated in the diagnosis of Hepatosplenic T-cell Lymphoma (HSCTL).

**Patients and Methods:** Clinical case report. Presentation. Woman, 72 years old. History of a sister with cirrhosis. Consumption of alcohol and herbalists; arterial hypertension and Sjögren. He was admitted for persistent fatigue and jaundice. Laboratories with anemia, thrombocytopenia and kidney injury; Hepatic biochemistry with a predominantly cholestatic pattern at the expense of alkaline phosphatase and direct hyperbilirubinemia. Without acute liver failure. By imaging the liver, vessels and normal bile duct; splenomegaly; Negative hepatitis viral panel, positive ANAs and Anti-actin, negative antimitochondrials, normal immunoglobulins. HAI vs. DILI / HILI is suspected. Liver biopsy reports HSTCL-type lymphoproliferative process (Figure 1). It was supplemented with bone marrow aspirate and PET-CT. He started prednisone and cyclophosphamide.

**Discussion:** The systematic approach to altered liver biochemistry requires integrating personal and family risk factors for liver disease. The infiltrative pattern that resembles the cholestatic one represents a diagnostic challenge as it is little recognized. In this case, we report a rare neoplasm corresponding to 5% of peripheral T lymphomas; they usually develop in young adults and in the absence of lymphadenopathy. It also has an adverse prognosis due to refractoriness to chemotherapy.

**Conclusion:** The HSTCL presented in this clinical case represents a complex and infrequent diagnosis. The symptoms and age group were atypical and the identification was possible through a systematic evaluation of the infiltrative pattern and differential diagnoses.

The authors declare that there is no conflict of interest.

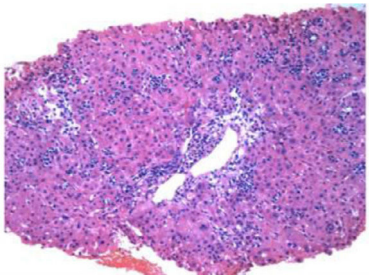

Figure 1. Atypical lymphocyte infiltrate in liver parenchyma.

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## PRIMARY BILIARY CHOLANGITIS COMPLICATED WITH ULCERATIVE COLITIS: A CASE REPORT

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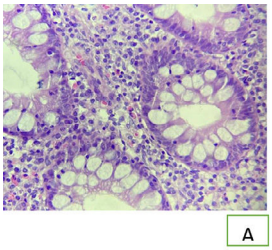
**Introduction and Objectives:** Liver involvement is not unusual in patients with inflammatory bowel disease (IBD), where one third of patients have abnormal liver biochemical tests, becoming a diagnostic challenge. Primary biliary cholangitis (CPB) is an autoimmune liver disease that presents with chronic cholestasis, the presence of specific antibodies and histological findings of destructive non-suppurative cholangitis. Genetic, immunological, and environmental factors that contribute to the pathogenesis of IBD may also contribute to associated hepatobiliary disorders. Objective: Present the case of a 67-year-old woman who consulted for cholestatic symptoms. Medical record of smoking for 25 years was suspended 15 years ago with a smoking index of 5. She reported a history of weakness, asthenia, self-limited palmar and plantar pruritus of 2 years of evolution, associated with abnormal liver function tests (total bilirubin 1.8 mg / dl, INR 1.40, albumin 3.2 g / dL). The initial physical examination revealed jaundice in the sclera, palmar erythema, evidence of telangiectasia in the abdomen, collateral circulation with medusa caput, positive ascitic wave, and splenomegaly. R factor is cholestatic, with alkaline phosphatase of 416 U / L, gamma glutamyl transpeptidase 660 U / L, alanine transferase 59 U / L, for which possible viral and autoimmune causes are addressed as the first possibility, reflecting antimitochondrial antibodies with high titers (278 U / L), associated with immunoglobulin G of 2490 mg / dl and immunoglobulin M of 734 mg / dl. During her one-year follow-up, she reported the onset of diarrheal stools Bristol 6, 2 to 3 episodes per day, with occasional urgency and with inflammatory characteristics, due to the presence of mucus and blood. Infectious causes are ruled out, elevated acute phase reactants are reported, followed up with a colonoscopy and

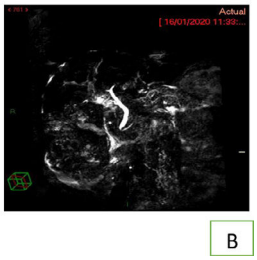
biopsy samples, reporting the presence of nonspecific proctitis, chronic colitis with focal ulceration, lymphoid aggregates, focal atrophy, and glandular distortion compatible with ulcerative colitis (UC). (Panel A) Due to the unusual association between UC and PBC, magnetic resonance cholangiography was requested, ruling out the overlap syndrome between primary biliary cholangitis and primary sclerosing cholangitis. (Panel B)

**Discussion:** A diverse heterogeneous group of hepatobiliary manifestations is reported in both UC and CD, and approximately 5% of adults with IBD have developed chronic liver disease. PBC is not usually associated with IBD, and concomitant reported cases are anecdotal. The presentations are different than the typical CBP without UC. PBC usually affects middle-aged women. The sex ratio is 10: 1 (female to male) and the mean age at diagnosis is 57.5 years. While the disease tends to affect men more often, with a female / male sex ratio of 2: 1 when associated with IBD. The distribution of ulcerative colitis in PBC patients is usually mild with limited bowel involvement. In a review by Tasa et al., eleven of 15 patients described left side colitis and proctitis.

**Conclusion:** The association between PBC and UC remains rare, as there are still few reported cases regarding the combined presentation of these diseases. Although PSC is the most specific hepatobiliary manifestation among UC patients with cholestasis, PBC should be considered in those with unexplained intrahepatic cholestasis. The use of a reliable test such as AMAs is of utmost importance to avoid misdiagnosis and/or under diagnosis.

The authors declare that there is no conflict of interest.




Panel A. Chronic and diffuse infiltrate of the basal lamina, with the presence of glandular distortion in rectal biopsies.

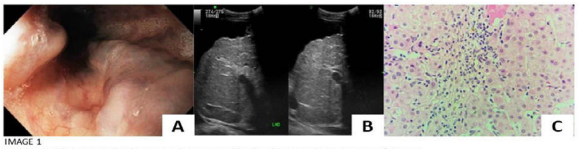



IMAGE 1
Panel A. Esophagogastroduodenoscopyshowing non-bleeding largeesophageal varices of Baveno
Panel B. Liver ultrasoundshowing the right lobe of the liver with irregularborders and a nodular pattern.
Panel C. HyE 40x staining.Hepatic parenchyma with pseudoacinartransformationis observed.

Panel B. The intra- and extra-hepatic bile duct preserved morphology without observing stenosis or dilations with normal signal intensity.

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## AUTO IMMUNE HEPATITIS AS A LIVER MANIFESTATION OF COMMON VARIABLE IMMUNODEFICIENCY: A CASE REPORT

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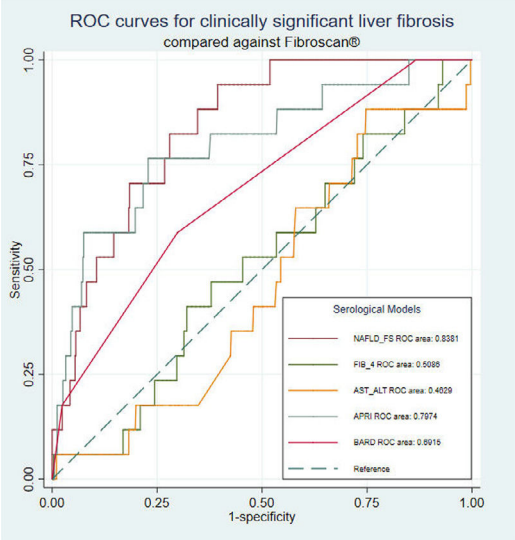
**Introduction and Objectives:** Common variable immunodeficiency (CVID) is a primary immunodeficiency disorder characterized by impaired differentiation of B cells with defective immunoglobulin production and paradoxically the development of autoimmune disorders. It is estimated that the prevalence of the liver disease is less than 10%. The most reported is focal nodular hyperplasia and, to a lesser extent, primary biliary cholangitis, primary sclerosing cholangitis and autoimmune hepatitis (AIH).

**Objectives:** present the case of a 22-year-old male who was admitted for hematemesis. He was diagnosed with immune thrombocytopenia 12 years ago without treatment and common variable immunodeficiency six years ago, currently three years without treatment. No family history of autoimmune or liver diseases. After extraction of the 4th molars, he presented swelling, redness, heat in the left submandibular region, unquantified fever, for which he received antibiotic treatment and non-steroidal anti-inflammatory drugs; 12 hours before admission, he began with hematemesis and hematochezia with data of hemodynamic instability, for which crystalloids are administered, the physical examination presents scleras with jaundice, an edematous, erythematous area with local heat in the left submandibular region, flat, symmetrical abdomen, absence of collateral circulation, Non-painful hepatomegaly, without shifting dullness. Laboratory admission with anemia, thrombocytopenia, cholestatic pattern in liver biochemistry tests, chronic viral infectious processes are ruled out and antibodies are made for autoimmune diseases, ANA 1:1200 is documented, other antibodies negative. Esophagogastroduodenoscopy where large esophageal varices of Baveno and severe portal hypertensive gastropathy (image 1 panel A). Doppler ultrasound reports diffuse liver disease, 14mm portal vein, with the presence of free fluid perihepatic and perisplenic, without biliary obstruction data (image 1 panel B). Percutaneous liver biopsy: fibrosis F2-3 on the scale of Metavir, interface hepatitis, associated with infiltrate lymphoplasmacytic integrating diagnosis of AIH (image 1 panel C).

**Discussion:** The prevalence of this condition is estimated at 1 in every 50,000 people worldwide. Up to 25% of patients with CVID will have an association with autoimmune diseases, representing the heterogeneous nature of the disease. The presentation of liver disease commonly reported in case series is anicteric cholestasis, and biopsies show evidence of non-cirrhotic portal hypertension. However, the association of CVID and AIH is rare; its diagnosis requires biopsies due to the lack of expression of antibodies in most cases.

**Conclusions:** In CVID patients with altered liver function tests, the association with autoimmune liver diseases should be ruled out to initiate timely treatment and avoid late complications.

The authors declare that there is no conflict of interest.




https://doi.org/10.1016/j.aohep.2021.100615

## PORTA VEIN THROMBOSIS (PVT) IN CIRRHOTIC PATIENTS PRE AND DURING THE PANDEMIC BY SARS-COV2

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**Introduction:** Determining the incidence and prevalence of PVT is difficult due to the heterogeneity of risk factors. The prevalence in cirrhotics is 1% in compensated patients and 8-25% in decompensated patients. SARS-COV2 infection presents extrapulmonary manifestations such as coagulation disorders with thrombotic angiopathy in 20-43%. In histopathological reports of necropsies or liver biopsies of patients who died from SARS-COV2, 30% had hepatic vascular thrombosis without chronic liver disease. IAM: To determine the prevalence of PVT in patients admitted to Gastroenterology before and during the SARS-COV2 pandemic.

**Material and Methods:** Research design: Descriptive, cross-sectional/prevalence. Procedure: We review medical records of all cirrhotic patients from March 2019 to February 2020 and from March 2020 to February 2021. We include cirrhotic patients diagnosed with PVT. Qualitative variables were expressed as frequencies and percentages. The numerical variables were expressed as means and standard deviations.

**Results:** In the pre-pandemic period: 491 cirrhotics admitted from March 2019 to February 2020 were identified, finding 24 cirrhotics with PVT (4.89%) 15(62.5%) were women with a mean age of 58.13 13.51 years. 6(25.0%) with neoplasms, of the latter 6(100.0%) with hepatocellular carcinoma. Regarding Child-Pugh: 11(45.8%) were B and 13(54.2%) were C and a mean MELD of 21.58. Regarding the location of the thrombus: 14(58.3%) occurred in the portal trunk, 6 (25.0%) in the trunk and branches, and 4(16.7%) only in one branch. During the pandemic period, we identified 189 cirrhotic patients; 24(12.60%) were cirrhotic with PVT. Of the latter, 12(50%) were men, with a mean age of 60.6311.93, 3(12.5%) had neoplasia and of these, 2(8.3%) were hepatocellular carcinoma. According to the Child-Pugh: 1(4.2%) was A, 12(50%) was B and 11(45.8%) was C with a mean MELD of 23.08, 15 (62.5%) had acute kidney injury, 4(16%) had atypical pneumonia upon admission, 16(66.7%) had ascites, of these 10(41.7%) were grade II. According to laboratory tests: creatinine 6.48±19.53, uric acid 9.22± 3.58, albumin 2.53±0.55, INR 1.81±1.07, and DHL 217.37±83.77. 95.8% underwent USG and 41.7% angiotomography. Regarding the thrombosis characteristics, 50% were acute, 29.2% had cavernomatosis, 66.7% were located in the portal trunk, and 54.2% had total occlusion. Regarding treatment, only 5(20.8%) received enoxaparin.

**Discussion:** Patients with COVID-19 experience a state of hypercoagulability, either in the arterial and/or venous system. Currently, only one case report has described a patient with suspected COVID-19, but without RT-PCR confirmation for SARS-COV2 and who developed PVT during hospitalization. On the other hand, patients with advanced liver disease are at higher risk of developing PVT. In the present study, there is no confirmatory evidence of infection by SARS-COV2. Still, there is evidence of an increase in the number of PVT cases three times more during the pandemic, so it is inferred that PVT could be associated with the presence of this infection.

**Conclusions:** We found that during the pandemic an increase in PVT was evidenced in patients with less advanced liver disease and fewer comorbidities, but with a more severe clinical picture, so it is suggested to investigate the presence SARS-COV2 in patients with liver decompensation and suspected of the PVT.

The authors declare that there is no conflict of interest.

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## HEPATIC FUNCTION ALTERATIONS IN SARS-COV 2 HOSPITALIZED PATIENTS AT HOSPITAL 450, DURANGO

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**Introduction and Aim:** Even if Sars-Cov 2 is an emergent, primarily respiratory illness, hepatic function alterations has been described by different countries. This work aims to describe the hepatic function alterations of patients with COVID-19 and their association with comorbilities and mortality.

**Material and Methods:** We conducted an observational, retrospective, cross-sectional, descriptive study, using files from patients Sars-COv 2 positive PCR test admitted at Hospital 450 between March 13th through October 31st 2020, including that patients with liver function test. Sociodemographic data, symptoms, hospitalization area, outcome and laboratory results were registered. In addition, a descriptive analysis, X2 test and OR risk association were performed.

**Results:** 466 patients were admitted at the hospital in this period of time, 69 patients without liver function test were excluded. A total of 397 patients were included: 60.2% were men, and 39.8% female. The mean age was 57 years old (16-95). 95.5% were communitary cases. Mean evolution days were 7.4 (1-37), and mean hospitalization days 8.6 (1-65). The symptoms related were: dyspnea (93.5%), cough (73%), fever (71%), myalgia (69.5%), headache (56.4%), odynophagia (27.7%), diarrhea(9.3%) and vomit (6%). Intubation were necessary in 27.2%, 28.8% had sepsis, and 15.1% were in shock status. The more frequent comorbidities were: hypertension (53%), DM (40.8%), obesity (43.1%), renal illness (14.1%) and other liver disease (3%). 33% of the patients were admitted to the intensive care unit. 63.7% demonstrated aminotransferase alterations (38% both AMT), most frequently AST (253 patients with twice normal values), hypoalbuminemia (64.7%), Alkaline Phosphatase (29.2%), and Total Bilirubin increased values (21.4%). In 61.2% of the patients anemia were detected, lymphopenia (55.4%), thrombocytopenia (17.9%), increased D dimer (79.8%), increased PCR (72.3 %). 41.1% of the patients died. Mortality association was found with: hypoalbuminemia (0.049) OR=1.548 IC95% (1.0-2.395); shock state (0.000) OR=13.995 IC95% (6.4-30.43); sepsis (0.000) OR=10.56 IC95% (6.2-17.72), intubation (0.000) OR=13.995 IC95% (12.5-45.0), renal illness (0.000) OR=5.45 IC95% (2.86-10.38), hypertension (0.000) OR=1.7 IC95% (1.13-2.55), and cardiovascular disease (0.01) OR=2.45 IC95% (1.21-4.95). No association between AMT and mortality was found.

**Discussion:** An elevated percentage of AMT anomalies was found, as in other works, almost one third of the patients presented with elevated AP, instead of 1.8% reported in other studies. A bad prognosis was associated with hypoalbuminemia.

**Conclusions:** Two thirds of the patients presented hypoalbuminemia and AMT increased, and in a few percentages with BT and AP anomalies. Hypoalbuminemia increases mortality risk.

The authors declare that there is no conflict of interest.

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## FREQUENCY OF HEPATIC FUNCTION ALTERATION IN MEXICAN PATIENTS WITH COVID-19 AND ITS ASSOCIATION WITH THE SEVERITY OF ACUTE RESPIRATORY DISTRESS SYNDROME: PRELIMINARY RESULTS

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**Introduction:** COVID-19 is a disease caused by the SARS-CoV-2 virus; atypical pneumonia and sepsis are the most severe manifestations of the disease. There is evidence that the virus affects the liver in different ways. The mechanism of liver damage has not yet been clearly established.

**Objectives:** To determine the frequency of alterations in the LFT (liver function tests) and its association with the severity of the ARDS (accute respiratory distress syndrome) in patients with COVID-19 and to determine if obesity, DM2 (diabetes mellitus) and HBP (high blood pressure) are associated with the severity of the ARDS.

**Material and methods:** Descriptive, cross-sectional and observational study of 56 patients with dx of ARDS due to COVID-19; Main variables: glucose, LFT and procalcitonin. Secondary variables: age, BMI, DM2, HBP, the severity of ARDS and days of stay. The frequency of qualitative variables was calculated in percentages, measures of central tendency and dispersion were determined for quantitative variables and the association between the increase in the parameters of the LFT and the severity of ARDS by calculating the Spearman correlation coefficient and the Mann-Whitney U test, stratifying according to those who survived or died. The medians of the quantitative values of the LFT between living and deceased were compared with the Mann W. U test for independent samples; due to the small sample size and the fact that the normality requirement was not met, statistically significant values were considered with $p < 0.05$.

**Results:** Of the 56 patients, 57% are women, all had tomographic data compatible with COVID-19. 41% presented moderate ARDS and 34% severe; 45% died. In the living, the frequency of DM2 and HBP was 22% in severe ARDS; An increase in AST (Aspartate aminotransferase) was found in 67% of admissions and in 100% there was an increase in its maximum peak. In mild ARDS, 33% of the living had increased GGT (gamma glutamyl transferase) at admission and 78% in severe ARDS. There was a statistically significant association between the increase in LDH (lactic dehydrogenase) at the maximum peak and the severity of ARDS ($p = 0.047$), the GGT at admission almost reached the statistically significant p value ($p = 0.053$), with a Spearman coefficient of 0.354 ($p = 0.051$). In the deceased, the frequency of DM2 in severe ARDS was 40%. 100% of those who died with severe ARDS had GGT and LDH increased values at their maximum peak. 100% with moderate ARDS and 90% of the severe ones had hypoalbuminemia upon admission, with a significant association with ARDS severity ($p = 0.033$). The LDH values at the maximum peak also showed a significant association with ARDS severity ($p = 0.043$) with a Spearman coefficient of 0.413 ($p = 0.040$).

**Discussion:** To date, this study is one of the few that has investigated the effects of the SARS-CoV-2 virus on liver function and its association with the severity of ARDS in Mexican population. Although our study has the weakness of having a small sample size, it has the strength of being carried out in a hospital that was converted into a COVID hospital, with which we will have access to data from a high number of patients, which will allow comparison alterations in liver function in living and deceased patients and relate it to the severity of ARDS.

**Conclusions:** Most of the patients had no history of DM2 or HBP; a large percentage had overweight / obesity and hyperglycemia on admission. There is a high frequency of patients who have alterations in LFT; however, with this sample, it was only possible to determine that the increase in LDH at the maximum peak during hospitalization and hypoalbuminemia on admission are associated with the severity of ARDS.

The authors declare that there is no conflict of interest.

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## RELIABILITY FACTORS FOR THE MEASUREMENT OF HEPATIC STEATOSIS BY MEANS OF A CONTROLLED ATTENUATION PARAMETER BY TRANSIENT ELASTOGRAPHY

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**Introduction and aim:** The controlled attenuation parameter (CAP) allows the indirect measurement of liver fat and the indirect the indirect measurement of liver fat and stiffness by transient elastography. Its diagnostic utility has been validated, but the factors for its reliability are unknown. Therefore, the objective is to evaluate the predictors of CAP quality by transient elastography.

**Material and methods:** Retrospective, observational design of transient elastography studies from January 2015 to December 2019 for fatty liver screening, fibrosis evaluation and esophageal varices screening, using Fibroscan 502 Touch with M and XL probes according to the manufacturer's recommendations. Sociodemographic and clinical data and reliability measures were evaluated: degree of liver stiffness (kpa), decibels / meter (db/m), interquartile ranges (IQR <40 and IQR <30), number of total and valid measurements. The data are shown in measures of central tendency and dispersion; for the reliability factors, a univariate and multivariate logistic regression analysis was performed.

**Results:** 1153 studies were analyzed, 52.6% (n = 606) were men, with a median age of 54 years [IQR 44-63] and BMI 27.4 kg / m2 [IQR 24.1-29.7]. The main indication was fatty liver screening 48.8% (n = 558), the median CAP was 262 (215-313) db / m with an interquartile range of 34 (24-47). In 26.2% (n = 302) an incorrect probe was used. The factors associated with reliability with IQR <40 were the XL probe (OR 0.34 CI95% 0.26-0.45), age <54 years (OR 0.71 CI95% 0.55-0.92) and IQR kPa <30 (OR 0.48 CI95% 0.28-0.82) and for the reliability of IQR <30 the use of the XL probe (OR 0.31 CI95% 0.23-0.42) and IQR kPa <30 (OR 0.35 CI95% 0.17-0.71). Evaluating only screening studies (n = 558), the use of the XL probe and age <54 years maintained an independent association for IQR <40 and with respect to IQR <30, only the XL probe maintained this association. Table 1.

**Discussion:** Current recommendations for quality CAP studies are to obtain valid measurements with IQR <30 and <40, although there is little evidence to support this. It was demonstrated that regardless of the indication, degree of fibrosis and BMI, the use of the XL probe favors the quality of the study and an adequate evaluation of liver stiffness (IQR kPa <30).

**Conclusions:** The main factor that favors the reliability of the CAP IQR <40 and 30 is the use of the XL probe regardless of the indication for use and the body mass index.

The authors declare that there is no conflict of interest.

**Table 1**
Factors associated with quality studies in patients undergoing liver steatosis screening. (n=558)

| Variable | IQR <40 | | | | IQR <30 | | | |
|---|---|---|---|---|---|---|---|---|
| | Univariate OR (IC95%) | p | Multivariate OR (CI95%) | p | Univariate OR (CI95%) | p | Multivariate OR (CI95%) | p |
| **XL probe** | 0.26 (0.18 – 0.38) | **≤0.001** | 0.24 (0.14 – 0.39) | **≤0.001** | 0.25 (0.17 – 0.36) | **≤0.001** | 0.18 (0.10 – 0.33) | **≤0.001** |
| **Obesity** | 0.51 (0.35 – 0.75) | **0.001** | | | 0.57 (0.39 – 0.83) | **0.003** | | |
| **<54 years** | 0.62 (0.43 – 0.89) | **0.01** | 0.67 (0.46 – 0.99) | **0.04** | 0.81 (0.58 – 1.1) | 0.26 | | |
| **IQR kPa <30** | 0.42 (0.20 – 0.88) | **0.02** | | | 0.35 (0.15 – 0.84) | **0.02** | | |
| **IQR kPa <10** | 0.74 (0.48 – 1.12) | 0.178 | | | 0.63 (0.43 – 0.93) | **0.02** | | |
| **BMI <27kg/m2** | 0.57 (0.39 – 0.55) | **0.005** | | | 0.61 (0.43 – 0.87) | **0.008** | | |

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## COMPARISON OF SEROLOGICAL MODELS OF LIVER FIBROSIS AGAINST TRANSIENT ELASTOGRAPHY BY FIBROSCAN® IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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**Introduction and Objectives:** Liver fibrosis is the most important prognostic factor in nonalcoholic fatty liver disease (NAFLD). The study's objective is to compare the serological models of liver fibrosis (NAFLD-FS, FIB-4, BARD, APRI and AST/ALT) against transient elastography by FibroScan® in patients with NAFLD.

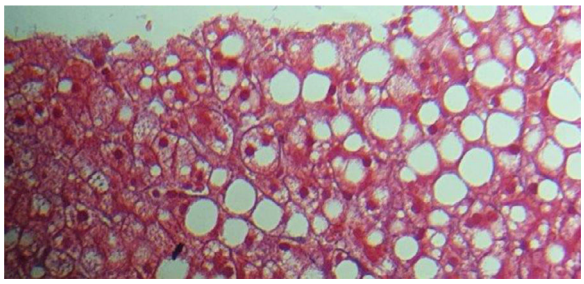
**Materials and Methods:** Observational, retrolective and cross-sectional study of records of patients diagnosed with liver steatosis by FibroScan® without significant alcohol consumption. A Pearson's correlation and heat maps were used for the correlation between results of FibroScan® and the serological models of liver fibrosis. ROC curves were analyzed to compare the serological models against FibroScan® as the gold standard for clinically significant liver fibrosis.

**Results:** Data from 976 files were collected, with a prevalence of 63% of liver steatosis by FibroScan® (CAP >232 dB/min) and 1.74% of significant liver fibrosis (LSM >7.0 kPa). In patients with NAFLD, a low positive correlation of NAFLD-FS (r=0.291; p<0.001) and BARD (r=0.021; p<0.001) and a very low positive correlation of APRI (r=0.184; p<0.001) with clinically significant liver fibrosis was reported. No correlation was observed with FIB-4 (r=-0.003; p=0.943) or with the AST/ALT ratio (r=-0.039; p=0.336). The NAFLD-FS reported an area under the curve (AUC) of 0.838 (95%CI 0.76-0.91) and the APRI of 0.797 (95%CI 0.68-0.92) compared to FibroScan® for clinically significant liver fibrosis (Figure 1).

**Discussion:** Liver biopsy is an invasive method and the gold standard for evaluating liver fibrosis; however, it is not exempt of complications. Transient elastography by FibroScan® is a non-invasive and validated method but with limited availability and accessibility. Serological models are widely available and can be easily used in daily practice. In a previous study, the NAFLD-FS reported an AUC of 0.72 (95% CI 0.60-0.83) compared against liver biopsy, which is comparable to the AUC reported in this study against FibroScan®.

**Conclusions:** The NAFLD-FS is the serological model for liver fibrosis with the best AUC and correlation with transient elastography in patients with NAFLD and is proposed as an evaluation method in places where FibroScan® or liver biopsy is not available.

The authors declare that there is no conflict of interest.



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## NEOBUXBAMIA TETETZO AS A CAUSE OF DRUG-INDUCED LIVER INJURY

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**Introduction and Objectives:** Drug-induced liver injury (DILI) is a rare clinical condition, the incidence is estimated from 14 to 19 cases per 100,000 population per year, it is responsible of 3 to 5% of jaundice hospitalizations, and it is the most frequent cause of acute liver failure in many of the western countries. Neobuxbaumia tetetzo is a species of flowering plant of the Cactaceae family, endemic to Mexico, distributed in Puebla and Oaxaca, and has been used within Mexican cuisine, without studies that establish the safety of its consumption, which predisposes to undocumented adverse effects, including probable liver injury.

**Materials and Methods:** The patient is a 19-year-old male, high school student and employee of a private company, single, originally from Tehuacán, Puebla, resident of Mexico City. Non-relevant family hereditary background. He denied experiencing any chronic degenerative diseases, allergies or traumas, but reported complications during an appendectomy in May of 2019. Has positive alcoholism, consuming it occasionally in social events; last consumption was seven months prior to the onset of symptoms. He denied the use of drugs, food supplements and herbalism. He began in June 30th of 2020 with asthenia, hyporexia, adinamia, nausea and unquantified fever, pain in epigastrium of moderate intensity, generalized pruritus, conjunctival jaundice and coluria were added, progressed to generalized jaundice, required hospitalization in August 2020. The laboratory results are Total Bilirubin 38.5 mg/dL, Direct bilirubin 26 mg/dL, ALT 60, AST 63, AP 329, GGT 33, General urine test that evidenced bilirubins 6 and urobilinogen 8. An ultrasonography and an abdominal tomography were performed, both reporting vesicular lithiasis, without obstruction or dilation of the bile duct. Subsequently, cholangioresonance was carried out on September 9, 2020, reporting liver gland with homogeneous parenchyma, bile duct without intra and extrahepatic dilation, gallbladder with the presence of lithic of 6.5 mm. Cholecystectomy and liver biopsy were performed, with histopathological result of gallbladder with chronic cholecystitis. Liver biopsy reporting: Hepatic parenchyma with preserved architecture, with few plasmatic and eosinophilic cells, and presence of severe intracanalicular and intracytoplasmic cholestasis corresponding to regenerative changes of grade 0 fibrosis on the Metavir scale and focal microvesicular steatosis, without regeneration nodules. Within its approach, serology Anti-Sm, IgM vs. CMV, IgM vs. Rubella, IgM vs. Toxoplasma, ANAs, anti Ro, SCL70 antibodies, HBV, HCV were negative.

**Discussion and Conclusion:** The only finding observed in the clinical case of our patient that we can appreciate is the elevation of bilirubin. After ruling out the main and possible causes that affected the health of our patient, it was decided to re-interrogate him and it was found that the patient had an antecedent of consumption of N. tetetzo, this highlights the importance of the clinical history in the approach of DILI and the need for of a clinician to contemplate this possibility. Although in this case, a RUCAM score of 6 points was calculated which makes the diagnosis possible, the score was created in order to avoid biopsy given that it is invasive; and before an anatomopathological finding compatible with DILI it is doubtful whether it is worth rechallenging the patient to the consumption of N. tetetzo to objectify the condition of bilirubins before exposure, there is a risk of acute liver failure, which creates an ethical dilemma and violates the principle of non-maleficence.

The authors declare that there is no conflict of interest.

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## HEPATIC MANIFESTATIONS OF INFECTIOUS DISEASES. PRESENTATION OF CLINICAL CASE

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**Introduction and Objectives:** There are infectious diseases that produce alterations in liver function tests and histology, through the activation, by endotoxins and other agents of the innate immunity pathway. This work aims to review the hepatic manifestations of diseases such as dengue and brucellosis in the pediatric age by means of clinical cases.

**Results:** Case 1: 17-year-old male with a history of travel to an endemic area and family members positive for dengue. Fever, myalgias, arthralgias, arthralgias and headache. On admission with leukocytes 6.93 thousand, platelets 189 thousand and positive IgG and IgM antibodies for dengue fever. Physical examination with hepatodynia and petechiae in the pelvic limbs. In control biochemistry with leukopenia and moderate thrombocytopenia, as well as alterations in liver function (Table 1). Ultrasound of the liver with data of acute inflammatory process. Seven days after admission, with clinical and biochemical improvement, it was decided the discharge of the patient. Caso 2: male, four years nine months old, with symptoms of 1 month of evolution characterized by fever, hyporexia and general malaise. Physical examination with icteric-pale color, hepatomegaly of $3 \times 5 \times 7$ cm and splenomegaly of 4 cm. Paraclinical tests showed anemia, leukopenia and mild-moderate thrombocytopenia, hypertransaminasemia, cholestasis and TTP prolongation (Table 2) with positive rose bengal, hepatic USG with hepatomegaly and echogenicity changes, for which he was sent to the third level of care.

**Discussion:** The mechanisms of liver injury can be divided into four pathways: vascular, toxic, immune and hormonal. In infections, the immune pathway is the cause of liver damage, being activated by endotoxins, leading to inflammatory infiltration, the release of cytokines, reactive oxygen species and necrosis. In dengue infection, liver injury manifests with hypertransaminasemia, with a peak between the seventh and ninth day, progressive decrease and normalization between 2 to 8 weeks. Hepatic involvement in brucellosis can occur in the acute or chronic phase of the disease. In the acute phase, establishing a non-specific granulomatous hepatitis, increasing in 63% of the cases the liver function tests.

**Conclusions:** The functions of the liver and the relationships it establishes with other organs may favor its injury during some infectious pathologies, being at this level one of the first manifestations in the context of an infectious disease, ruling out, in both cases, liver pathology by hepatotropic virus, metabolic, autoimmune and anatomical cause.

The authors declare that there is no conflict of interest.

**Table 1**
Case 1: Liver function test during the hospital stay

| Días de estancia | 2 | 4 | 7 | 8 | Semana 6 |
|---|---|---|---|---|---|
| ALT | 190 | 669 | 1106 | 857 | 227 |
| AST | 244 | 845 | 920 | 382 | 36 |
| GGT | | | 187 | 182 | 106 |
| ALP | 70 | 77 | | 91 | 123 |
| LDH | | 967 | 890 | 487 | 293 |
| TBili | 0.5 | 0.6 | 0.6 | 0.6 | 0.4 |
| IBili | 0.3 | 0.3 | 0.4 | 0.4 | 0.3 |
| DBili | 0.2 | 0.3 | 0.2 | 0.2 | 0.1 |
| PT | 12.2 | | 10.9 | | |
| PTT | 30.4 | | 24.1 | | |

**Table 2**
Case 1: Liver function test during follow up

| | 1 | 2 |
|---|---|---|
| ALT | 64 | 68 |
| AST | 109 | 137 |
| GGT | | 441 |
| ALP | 457 | 670 |
| DHL | | 967 |
| TBili | 1.30 | 0.88 |
| IBili | 1.22 | 0.25 |
| DBili | 0.08 | 0.63 |
| PT | 13.7 | 13.9 |
| PTT | 56.2 | 40.4 |

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## HEPATIC STEATOSIS IN CYSTIC FIBROSIS. APROPOS OF A CASE

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**Introduction and Objectives:** Cystic Fibrosis (CF) is a genetic disease characterized by dysfunction of the exocrine glands. Hepatic involvement is the leading non-pulmonary cause of death in CF patients. This paper aims to present the case of a schoolchild with hepatic alterations as the initial clinical manifestation of CF.

**Results:** 10-year-old male with a history of sibling death due to liver failure at three years of age, multiple respiratory symptoms in the first two years of life and hospitalization at 3 years of age due to bronchitis. The condition began one year before the assessment with growth arrest and in the last six months with two diarrheal episodes without mucus or blood. On physical examination, weight and height below p5 for age, icteric color, without hepatosplenomegaly, limbs with acropaquia (Image 1). Average bone age of 5-6 years, paraclinical tests with hypertransaminasemia, hypetriglyceridemia and decreased HDL (table 1), normal blood biometry, liver elastography with ARFI 2.1 m/s and liver biopsy with macro and microvesicular steatosis with moderate portoportal fibrosis (image 1-2). Negative approach for infectious hepatitis, Wilson's disease. 1 alpha-antitrypsin deficiency and lysosomal acid lipase deficiency. Diagnosis of CF with sweat electrolytes of 105 mmol/L was made. Currently under follow-up by gastroenterology and pediatric pulmonology.

**Discussion:** CF is the most common autosomal recessive disease in the Caucasian population, with multi-organ involvement. Liver disease has a high incidence in the first 10 years of life with 2.5/100 patient-years. However, no CFTR gene mutation has been directly associated

with the presence or severity of the liver disease. Clinical presentation varies from mild asymptomatic form to cirrhosis with the need for liver transplantation in these patients. The most common initial suspicion is hepatomegaly and transaminases alteration and laboratory studies and histology alteration. Hepatic fibroelastography represents an emerging method of study for diagnosis, as it represents one of the forms of confirmation of the criteria for liver disease associated with cystic fibrosis. Liver biopsy provides information on the predominant type of lesion (steatosis or focal cirrhosis) and the extent of portal fibrosis. However, it should be taken with caution because of the risk of underestimating the severity of the lesions.

**Conclusions:** Although the liver disease in cystic fibrosis does not represent the initial manifestation, the evaluation and monitoring in these patients are important for prognosis and survival since it can progress to cirrhosis and liver failure.

The authors declare that there is no conflict of interest.

**Table 1**
Liver function tests during evolution

| | 11.10.2018 | 19/01/21 | 05/06/21 |
|---|---|---|---|
| **TBil** | 0.33 | 0.38 | |
| **DBili / IBili** | 0.08 / 0.25 | 0.14 / 0.24 | |
| **AST /ALT** | 81 / 69 | 99 / 95 | |
| **GGT** | 99 | 70 | |
| **ALP** | 381 | 388 | |
| **LDH** | 586 | 309 | |
| **Protein/Alb** | 7,4 / 4.4 | 6.9 / 4.30 | |
| **PT/ INR/PTT** | 15 / 1.16 / 31 | 15 / 1.16 / 31 | |
| **TC** | | 127 | 119 |
| **TG** | | 81 | 174 |
| **HDL-C** | | 43.1 | 32.2 |
| **LDL-C** | | 78 | 72 |

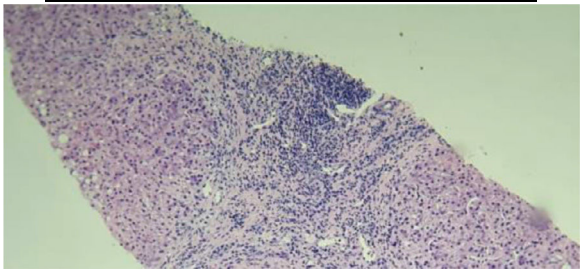

Image 1. Hepatic biopsy with steatosis

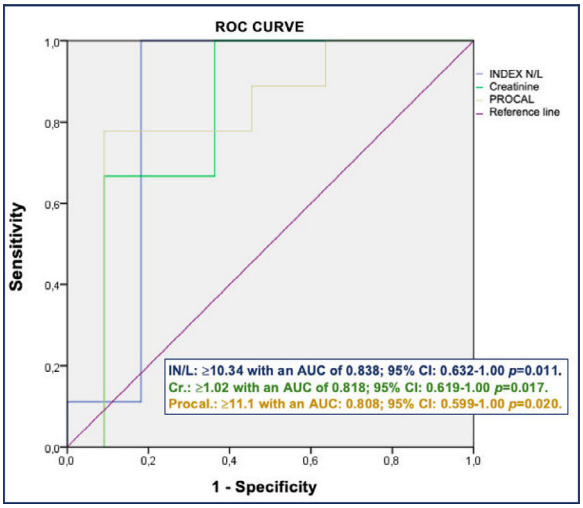


Image 2. Hepatic biopsy with moderate lymphoplasmacytic infiltrate

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## NEUTROPHILE/LYMPHOCYTE INDEX (IN/L), CREATININE (Cr), AND PROCALCITONIN (PROCAL) AS PREDICTORS OF AMEBIAN LIVER ABSCESS.

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**Introduction and Objectives:** A liver abscess (HA) is the accumulation of purulent material in the liver parenchyma that can be bacterial, parasitic, fungal, or mixed. The incidence ranges from 2.3 to 22 per 100,000 people. In Mexico, the annual incidence of amoebic HA is 6.7 per 100,000 inhabitants.

**AIM:** Determine the cut-off points for the neutrophil/lymphocyte index (IN/L), creatinine (Cr), and procalcitonin (Procal) to predict the etiology of liver abscess.

**Materials and Methods:** Research design: cross-sectional.

**Procedure:** We analyzed medical records of patients admitted during 2019 with HA diagnosis and amoeba PCR. The qualitative variables were expressed in frequencies and percentages. The numerical variables in means and standard deviation. We use X2, Fisher's exact, Student's t, and Mann-Whitney U to compare groups as appropriate. ROC curve was used to determine sensitivity (S), specificity (E), positive predictive value (PPV), negative predictive value (NPV), and likelihood value (+ LR). The p-value <0.05 was considered statistically significant.

**Results:** Out of a total of 32 patients diagnosed with HA during 2019, 20 patients treated with drainage and a PCR test for amoeba from the abscess fluid were included. Of these, 85%(17) were men, with a mean age of 45.33±10.93 years. 45%(9) were of amoebic etiology. In the latter group, the etiology can be predicted with the neutrophil/lymphocyte index with a cohort point of ≥10.34 with an AUC of 0.838, S: 100%, E: 81%, PPV: 81%, NPV: 100%. (9/11 vs 0/0 [81.8% vs 0.0%] + LR: 5.49; 95%CI:1.50-14 $p$=0.000). The creatinine value of ≥1.02 with an AUC of 0.818, S: 66.7%, E: 90.9%, PPV: 85.7%, NPV: 76.9%, (6/7 vs 3/13 [85.7% vs 23.1%] + LR: 7.33;95% CI:1.07-50 $p$=0.017) and with a procalcitonin cohort point of ≥11.1 with an AUC: 0.808, S: 77.8%, E: 90.9%, PPV: 85.7%, NPV: 87.5%, (7/8 vs 2/12 [87.5% vs 16.7%] + LR: 8.56;95% CI:1.28-57 $p$=0.005), with these cut-off points a significant difference was evidenced between the amoebic vs bacterial etiology, for IN/L: $p$=0.000, for Cr: $p$=0.017 and for procalcitonin: $p$=0.005, which are shown in figure 1.

**Discussion:** Amebic HA is etiologically more frequent in the West and generally in countries with poor infrastructure and development. It reports high mortality with conservative treatment and multiple abscesses, so it is crucial to identify their etiology. In the present study, we propose the cut-off points of biochemical markers for the diagnosis of amoebic HA through IN/L, Cr, and procal that are accessible in units where there is no amoeba CRP.

**Conclusions:** We were able to determine an adequate AUC and good sensitivity, specificity, positive and negative predictive value; therefore, we could use these biochemical markers to predict the etiology of liver abscesses.

The authors declare that there is no conflict of interest.

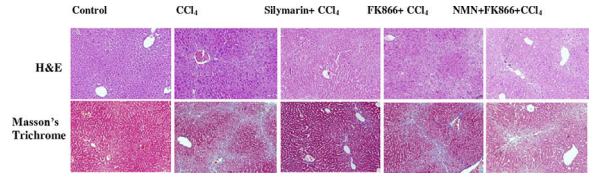


**Figure 1. ROC curve graph:** indicates the sensitivity and specificity of the cut-off point of the neutrophil/lymphocyte index, creatinine, and procalcitonin to predict abscess diagnosis amebic liver.

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## CLINICAL, BIOCHEMICAL, AND IMAGE CHARACTERISTICS IN PATIENTS WITH A DIAGNOSIS OF AMEBIC AND BACTERIAL LIVER ABSCESS.

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**Introduction and Objectives:** A hepatic abscess (HA) accumulates purulent material in the liver parenchyma and can be of bacterial, parasitic, fungal, or mixed origin. The incidence ranges from 2.3 to 22 per 100,000 people. In Mexico, the annual incidence of amoebic liver abscess is 6.7 per 100,000 population.

**IAM:** To determine the clinical, biochemical, and imaging characteristics in patients diagnosed with amoebic and bacterial liver abscess.

**Materials and Methods:** Research design: Descriptive, cross-sectional/prevalence.

**Procedure:** We analyzed medical records of patients admitted during 2019 with a diagnosis of liver abscess and who had an amoeba PCR test. The qualitative variables were expressed in frequencies and percentages; the numerical variables were mean and standard deviation. We use X2, Fisher's exact, Student's t, and Mann-Whitney U to compare groups as appropriate.

**Results:** Of a total of 32 patients admitted with a liver abscess in Gastroenterology during 2019, 20 patients treated with drainage and PCR test for amoeba of the abscess fluid were included. Of these, 85%(17) were men with a mean age of 45.35± 10.93 years, and 55%(11) were of bacterial etiology. Regarding the characteristics due to their etiology (amoebic vs. bacterial): 30%(6) were presented in segments VII and VIII; [33.3%(2/6) amoebic vs. 66.7%(4/6) bacterial]. According to the number, they were multiple; 28.6%(2/7) amoebic vs 71.4%(5/7) bacterial, unique; 53.8%(7/13) amoebic vs 46.2%(6/13) bacterial, without significant difference (p = 0.37). 60%(12) presented with pleural effusion, and of these, 58.3%(7) were amoebic. 100% were drained, of which 50% were by catheter with a diameter of 14Fr. Regarding the laboratory studies: 80%(16) of those with amoebic etiology had cultures of the abscess fluid without development, the leukocytes were 18.65 ± 6.55mm3 with a range of 16.5 in the amoebians vs. 14.58±6.51mm3 with a range of 17.6 in bacteria, Hb of 12.10±1.93 gr/dl in amoebians vs. 12.18 ± 1.72 gr/dl in bacteria and with procalcitonin of 18.06±12.77 gr/dl in amoebic vs. 19.98±59.76 gr/dl in bacterial. According to the imaging studies: the USG diameter was 10.67±2.78cm in amoebians vs. 10.53±4.91cm in bacteria and with a volume of 375.08±263.95 with a range of 782.0cm3 in amebic vs. 441.80±393.90 with a range of 1362.1cm3 in bacterial.

**Discussion:** Common etiologic agents for HA are E. histolytica (amoebic), bacterial (pyogenic), Mycobacterium tuberculosis, and various fungi. They tend to affect the younger population, especially men with immunosuppression, diabetes, and alcohol consumption. In developing countries, two-thirds are of amoebic origin and in need of puncture drainage. Our study observed that half had amoebic etiology corroborated by amoeba PCR, the majority unique, and almost all required drainage with diameters greater than 5cm by USG.

**Conclusions:** In the present work, we can show that half of the patients diagnosed with a liver abscess in the Gastroenterology Service are of amoebic origin and have similar characteristics to those described in the international bibliography.

The authors declare that there is no conflict of interest.

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## IMPACT OF RISK FACTORS IN THE SCRUTINY AND DIAGNOSIS OF HEPATITIS C

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**Introduction:** Chronic hepatitis C is considered a public health problem. Risk factors for infection traditionally identified as blood transfusion, major surgeries, organ donation, hemodialysis, vertical transmission have undergone an epidemiological transition. Other risk factors have become the main causes of new infections, such as intravenous drug use, sexual intercourse, prison, and tattoos.

**Objective:** To describe the risk factors associated with the positivity of Hepatitis C by analyzing the epidemiological profile of populations at high risk for Hepatitis C.

**Methods:** A cross-sectional study was carried out in the Mexican population as part of an HCV 2-years screening program implemented from December 2017 to December 2019. People were invited to participate in the program mainly in public health institutions, or through special campaigns in state and federal social rehabilitation centers and prisons. Adults (> 18 years) with informed consent were included for the study. Participants received a multiple-choice questionnaire to identify sociodemographic variables and the existence of any risk factor for HCV. A rapid test for HCV was performed and those participants whose results were reactive were applied a PCR test to determine quantification of HCV RNA. For the statistical analysis, the population was classified according to risk, as a general population with at least one risk factor and a high-risk population. A logistic regression model adjusted for sociodemographic variables and risk factors for the general population was developed to analyze the factors that may be associated with HCV positivity.

**Results:** This national cross-sectional cohort included 297,397 eligible subjects with a rapid test performed. Of the total number of rapid tests carried out, 13,085 subjects were reactive (4.4%) and 9,426 subjects (3.2% of the total population) were confirmed as positive by PCR test. The prevalence of viremia in the general population was 2.5%, while in the population with HIV was 3.1% and in persons deprived of their liberty (CERESO) was 18.5%. (Table) The median age in the total population was 43 years. Jalisco (10.1%) and Colima (7.7%) were the states with the highest percentage of positive results, followed by Baja California (7.4%). The percentage of people with viremia increases with age, going from 1.1% in the group of 18-29 years to more than 4.7% in those older than 60 years. In this cohort, the most common risk factors were history of acupuncture/ tattooing/ piercings (21%), intravenous drug use (15%), and high-risk sexual practices (12%). From the logistic regression by risk population, we found that having at least one risk factor increased the odds of being HCV positive by 62% (OR = 1.62, IC 95% 1.54-1.69), compared with the population without risk factors. When conducted the analysis by type of specific population, the results showed that incarcerated people were 55 times more likely to be positive for Hepatitis C and 14 times more likely to be positive to HCV, compared to the HIV positive population.

**Conclusions:** In this cross-sectional study with different high-risk populations for detecting hepatitis C, we identified 3.2% of viremic patients who were linearly related to older age and the existence of risk factors. Based on the results for this analysis, screening and

diagnosis in high-risk populations, even those that are routinely marginalized, could be more effective.

The authors declare that there is no conflict of interest.

| Population | RT performed (%) | RT reactive (%) | PCR positive (%) |
|---|---|---|---|
| Total | 297,397 | 13,085 (4.4) | 9,426 (3.2) |
| General population* | 245,156 (82.4) | 9,023 (3.7) | 6,225 (2.5) |
| Population in risk | | | |
| HIV | 33,292 (11.2) | 1,478 (4.4) | 1,028 (3.1) |
| PWID | 15,652 (5.3) | 1,268 (8.1) | 1,001 (6.4) |
| PRISON (CERESO) | 2,392 (0.3) | 1,098 (24.1) | 1,005 (18.5) |

RT: Rapid test. *General population with at least one risk factor. HIV: Subjects screened in HIV clinics. PWID: people who inject drugs.
CERESO: State Center for Social Re-adaptation

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## CLEAR CELL HEPATOCELLULAR CARCINOMA, A CASE REPORT

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**Introduction and Objectives:** Clear Cell Hepatocellular Carcinoma (CCHCC) represents 2.2 to 6.7% of all Hepatocellular Carcinomas (HCC), affects mostly women and is frequently associated with liver cirrhosis, viral infections (HBV, HCV), aflatoxins, hemochromatosis, oral contraceptives, obesity and type 2 diabetes mellitus. The most frequent manifestation is a solitary tumor with a pseudocapsule, which is more frequent than in other subtypes of HCC. Histologically, CCHCC can be observed as cells with an empty appearance with abundant cytoplasm, vacuolated and foamy due to the accumulation of glycogen and fat, constituting more than 50% of the total cells. Differential diagnosis with liver metastases can be difficult, so immunohistochemistry is an important diagnostic tool.

**Clinical Case:** 69-year-old female with a history of hepatitis C virus infection in 2018 receiving direct-acting antiviral treatment for 12 weeks with sustained viral response-12, Child Pugh B liver cirrhosis is documented. 2 years later, the follow-up ultrasound reports liver injury cystic and alpha-fetoprotein at 84.27 ng / ml, so a triphasic tomography was performed, observing liver lesion in segment VII of $35 \times 27 \times 31$ mm suggestive of hepatocellular carcinoma with atypical characteristics, no tumors were reported in another abdominal site, as there was no conclusive radiological criterion for hepatocellular carcinoma, a liver lesion biopsy was performed with a histological report of moderately differentiated clear cell carcinoma and immunohistochemistry with Hepatocyte antigen positive, Carcino-embryonic antigen negative, internal Arginase 1 positive, Glypican 3 positive and Internal renal carcinoma antigen negative, concluding diagnosis of clear cells hepatocellular carcinoma T1B, N0, M0, therefore the patient was referred for transarterial chemoembolization of the lesion.

**Discussion:** The importance of the current report is to identify histopathological characteristics and establish the usefulness of Immunohistochemistry to make a differential diagnosis with other tumors that can metastasize to and be confused with a primary CCHCC of the liver.

**Conclusions:** CHCC is a rare subtype of HCC with a more favorable prognosis than other forms of hepatocellular carcinoma, the histological differential diagnosis through immunohistochemistry should be performed with renal cell carcinoma, adrenal cortical carcinoma, clear cell sarcoma, angiolipomas, pulmonary and neuroendocrine clear cell variant, which can metastasize to the liver and be confused. The immunohistochemical study was decisive for the treatment and favorable prognosis of the patient.

The authors declare that there is no conflict of interest.

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## FRUCTOSE DIET INDUCES A METABOLIC REPROGRAMMING TO ENHANCE TUMOR AGGRESSIVENESS

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**Introduction and Objectives:** HCC is one of the main causes of cancer-related death worldwide and has third place in mortality. One of the main risk factors is metabolic-associated fatty liver disease (MAFLD), having hepatic steatosis, and related metabolic disorders. Mexican population has the highest obesity rate in both children and adults, and the consumption of hypercaloric diets has been related to that. Also, Mexico is in the top five countries with a higher fructose-enriched diet consumption and has been proved already the relation between fructose consumption and MAFLD. Likewise, fructose has been related to metabolic rewiring in transformed cells, enhancing aggressiveness and survival.

**Aim:** To analyze fructose role on aggressiveness promotion of HCC cells.

**Materials and Methods:** We used C57Bl/6J mice strain (both sex) with a high Fructose diet (Fru) (33% of fructose in the drinking water, *ad libitum*). Fru supplementation started with 15 days-old mice, two days after DEN was injected (10 $\mu$g/Kg, i.p), and the treatment was ended 8 months later. The UAM ethics committee approved the protocol. *In vitro* studies were carried out with the Huh-7 HCC cell line and we evaluated metabolic and biochemical parameters.

**Results:** Tissue samples were analyzed by H&E. We observed that the fructose-enriched diet group mice presented fat accumulation in the hepatocytes and also areas with a greater inflammatory infiltrate (Fru). Mice in the fructose-enriched diet + DEN (Fru/HCC) group showed a marked difference between the tumor area and the surrounding tissue and an increase in the number of bile ducts, indicating liver tissue damage. Also, we analyzed the protein content of some lipogenic enzymes and noticed an increment in fatty acid synthase (Fasn) in Fru and Fru/HCC. Due to that, we analyzed if Fru treatment was inducing metabolic rewiring in transformed cells. We obtained metabolic changes in fructose-treated cells, reducing the

glycolytic pathway and the traditional Warburg effect. Then we evaluated if the Huh-7 under a Fru treatment was more dependent on mitochondria or glycolysis ATP generation. We observed a reduction in proliferation under oligomycin treatment *vs*. 2-DG treatment. At least, we evaluated the pentose phosphate pathway (PPP) under a Fru treatment and obtained a higher glucose-6-phosphate dehydrogenase (G-6-P DH) activity with Fru *vs*. only glucose (Glc). Also, G-6-P DH had a more efficient activity in the presence of Fru because the time to reach the Vmax is lower *vs*. Glc.

**Conclusion:** Fructose induces a metabolic rewiring in cancer cells to enhance ATP production, NADPH, and nucleotides to sustain the active lipid synthesis and proliferation. The fructose-enriched diets promote an aberrant lipogenic phenotype enhancing tumor aggressiveness. Conacyt, Froteras de la Ciencia 1320.

The authors declare that there is no conflict of interest.

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## ANTIOXIDANT EFFECT OF SPINACH EXTRACT IN LIVER FIBROGENESIS ASSOCIATED TO ACTIVATION OF NRF2/HO-1 IN HYPERGLYCEMIC RATS

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**Introduction and Objectives:** In chronic hyperglycemia, increased oxidative stress plays an essential role in liver fibrogenesis. The spinach phytochemicals are shown to possess chemopreventive properties in this condition. Erythroid nuclear transcription factor 2 (Nrf2) is a transcriptional regulator expressing cytoprotective genes such as heme oxygenase-1 (ho-1). HO-1 is an enzyme present in the liver with antioxidant, anti-inflammatory, and anti-apoptotic capacities. However, the beneficial effect of spinach associated with endogenous activation of the Nrf2/HO-1 pathway is unknown. Objective: To evaluate the antioxidant effect of the spinach extract on injury hepatic associated with the Nrf2/HO-1 pathway in hyperglycemic rats.

**Materials and methods:** The study was approved by the ethics committee from the ENCB-IPN (CONBIOETICA/09/CEI/002/20190327). We used hyperglycemic Wistar rats induced with 60 mg / kg of streptozotocin (HG; n = 7); intragastrical-treated HG with 400mg / kg of spinach methanolic extract (HG-EME; n = 7) and normoglycemic rats (NG; n = 7). Histological sections were obtained at 12 weeks and evaluated by Sirius red staining and immunohistochemistry (Nrf2, HO-1). The oxidative damage by lipid peroxidation was determined by the tissues' malonaldehyde formation (MDA) levels. The H-score system quantified the percentage of nuclear staining of Nrf2 and the intensities of Sirius red and HO-1. Statistical analysis: The data were analyzed by one-way ANOVA with the Tukey test using the GraphPad Prism program (Version 5.0). Kruskal-Wallis and Dunn's test established the MDA training levels. Statistical significance was considered with $p < 0.05$.

**Results:** Collagen fibers were formed mainly in the centrilobular zone. The percentage of collagen fibers staining in the HG group was $50 \pm 10$, compared to HG-EME ($30 \pm 10$ $p < 0.05$). In NG, the percentage of fibers was $20 \pm 10$. The nuclear Nrf2 (nNrf2) and cytoplasmic HO-1 staining were localized in the hepatocytes of region 3 Rappaport. The percentage of nNrf2 in HG was $30 \pm 10$, compared to HG-EME ($70 \pm 10$ $p < 0.01$). In NG, the staining percentage for nNrf2 was $15 \pm 5$. For HO-1 staining, the values in the HG-EME group were higher than in the HG group ($p < 0.01$). Contrary, MDA levels in HG-EME decreased significantly compared to HG ($p < 0.05$).

**Conclusions:** Treatment with EME in hyperglycemic rats showed decreased liver damage generated by oxidative stress, associated with endogenous activation of the Nrf2/HO-1 pathway. The evaluation of liver biochemical tests can demonstrate a beneficial effect of EME. This work was supported by federal resources (HJM0713/19-I) and partially by INCICH.

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## NAMPT INHIBITION AND INCREASED NAD-BIOAVAILABILITY ATENUATE LIVER DAMAGE IN $CCl_4$-INDUCED MICE CHRONIC LIVER DISEASE

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**Introduction and Objectives:** Nicotinamide phosphoribosyltransferase (NAMPT) is the rate-limiting enzyme on the $NAD^+$ salvage biosynthetic pathway and a cytokine regulator with an important role in inflammation and fibrogenesis modulation. Use of FK866 (NAMPT inhibitor) has been proposed as a treatment on inflammatory diseases and cancer. However, FK866-induced depletion of NAD may also cause major impairment of the redox and bioenergetics homeostasis of the cell within the liver, thus limiting a favorable outcome for Chronic Liver Disease (CLD), as low NAD levels have been associated with higher Oxidative Stress and increased metabolic risk. The aim of this study was to evaluate the effects of NAMPT inhibition and concomitant NAD restoration on experimental CLD in vivo.

**Methods and Results:** NAMPT inhibition was evaluated within a $CCl_4$-induced CLD model on male BALB/c mice and a mild improved outcome was observed on the histological and biochemical features. NAD restoration strategy was accomplished by the concomitant administration of its precursor, NMN, resulting in significant improve on the histological analysis; lower inflammatory infiltrate and fibrosis were measured by image analysis on digitalized micrographies. Lower levels of Direct Bilirubin were also observed. NAMPT inhibition and adequate NAD restoration were confirmed by a colorimetric assay of NADH and $NAD^+$ and biochemical features were measured by routinary Liver Function Tests. Silymarin was used as a hepatoprotective control.

**Conclusion:** This study shows that NAMPT inhibition concomitant to NAD restoration significantly attenuate experimental liver damage.

The authors declare that there is no conflict of interest.

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## "THE EFFECT OF GROWTH DIFFERENTIATION FACTOR 11 (GDF11) ON THE RESPONSE OF TUMOR-ASSOCIATED MACROPHAGES IN HEPATOCELLULAR CARCINOMA DERIVED CELLS"

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**Introduction and Objectives:** Hepatocellular carcinoma (HCC) is the most common and aggressive form of liver cancer. Until 2020, worldwide, it has been ranked 5$^{th}$ and 3$^{rd}$ in terms of incidence and mortality, respectively. HCC has various etiologies, but tumors formed by high cholesterol intake induce an aggressive phenotype and high tumor-associated macrophages (TAM) infiltration. TAM acquires an alternative polarity (M2) with immunosuppressive and pro-tumoral activities. HCC patients with high TAM recruitment have a poor prognosis with a low free-survival rate. The design of therapies represents a challenge. The growth differentiation factor 11 (GDF11) has been proposed as a promising molecule for treating HCC, favors a reduction in proliferation, invasion, and lipid metabolism, and therefore reduces the aggressive phenotype. In our research group, we have found that GDF11 also has various effects on cells belonging to the tumor microenvironment, particularly in TAM.

**Aim:** To evaluate TAM polarity and their intercommunication with HCC-derived cells during treatment with GDF11.

**Materials and Methods:** THP-1-macrophages cell line was used; lipopolysaccharides were used for the M1 polarity acquisition and IL-4/13 or conditioned medium (CM) derived from Huh-7 cells for M2 polarity acquisition, flow cytometry (FCM) was used. GDF11 (50 ng/mL) was applied every 24 h up to 3 days. We used anti-Smad2 and 3 antibodies in Western blot (WB). Cell viability and proliferation studies were performed using crystal violet. The quantification of cholesterol was performed using o-Phthaldialdehyde and free radicals' detection was performed using dihydroethidium. Data were presented as mean ± standard error of the mean (SEM). The analysis of variance (ANOVA) test was used to compare the mean values between groups. Each result has at least 3 independent experiments. Statistical significance was indicated with an asterisk (*P<0.05).

**Results and Discussion:** GDF11 treatments induced Smad proteins activation by specific phosphorylation, indicating that THP-1 macrophages respond to treatment in times from 5 to 60 min, but maintaining their response up to 72 h. This could suggest that the difference in the subsequent response may be involved in the binding or activation of additional adapter proteins of this signaling pathway. Furthermore, it was observed that GDF11 does not affect the cell viability, proliferation, and morphology studied in their different polarities. Macrophage re-education or re-polarization assays were carried out by adding GDF11 for an additional 72h. The data obtained show that TAM populations lost CD206 marker, going from 90% to 40% of the population, suggesting a loss of this pro-tumor polarity and a re-education towards anti-tumor macrophages responses. However, experiments show a dual role of GDF11 in macrophages due to the increase of specific markers in non-activated cells, indicating that it has a different effect depending on the activation state. Since GDF11 compromises cholesterol metabolism, which is observed in a decrease in total cholesterol levels in non-activated macrophages, which is observed in other studies using HCC cell lines. Also, it was possible to corroborate that GDF11 is behaving like a statin used as a positive control in macrophages and Huh-7 cells. Finally, GDF11 increases ROS levels, specifically superoxide anion, characteristic of phagocytic M1 macrophages. To evaluate response on HCC cells, wound-healing assays indicated that macrophage secretion is a key factor for cell displacement rather than viability and proliferation.

**Conclusion:** In the present study, we found that GDF11 has immunomodulatory effects in TAM, decreasing pro-tumoral markers and lipid content that could be important to design HCC therapies.

The authors declare that there is no conflict of interest.

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## EFFECT OF SUPPLEMENTATION WITH TYPICAL MEXICAN FOODS (OPTUNA FICUS INDICA, THEOBROMA CACAO AND EDIBLE CRICKETS) IN HIGH-FAT/HIGH-SUGAR DIET-FED MICE

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**Introduction and objectives:** The obesogenic environment, including high fat/ high sugar diet, are risk factors for developing multiple diseases associated with obesity, such as metabolic-associated fatty liver disease (MAFLD) and metabolic syndrome, among others. An increase in physical activity and change of diet is the first therapeutic line to prevent or treat obesity; however, adherence to this treatment is negligible. Therefore, this communication's objective was to evaluate the effect of supplementation with a mixture of foods of Mexican origin: *Optuna ficus indica*, *Theobroma cacao* and edible crickets (MexTHER) on a diet high in saturated-fats and fructose-sucrose in obesogenic mice.

**Material and methods:** Twenty male C57BL/6J mice were divided into three groups between 7 and 8 weeks of age. Control group: Normal diet (ND) for 16 weeks; HF Group: Diet with 45% of Kcal from fat and water added with 55% fructose and 45% sucrose *ad libitum* for 16 weeks; and Therapeutic group: HF diet up to week eight and the last 8 weeks switched to a high fat/sugar diet supplemented with 10% nopal, 10% cocoa and 10% cricket (MexTHER). The animals were sacrificed at 16 weeks and histological, biochemistry and cognitive analysis were performed.

**Results:** Mice fed with MexTHER diet showed a significant reduction in weight at sacrifice. After two weeks MexTHER group equaled their weight to the ND group (ND = 35.92 ± 4.76, HF = 47 ± 7.11, MexTHER = 34.20 ± 6.71 p <0.001). Liver weight, visceral fat, and epididymal fat were also significantly reduced. The MexTHER group significantly decreased levels of triglycerides, cholesterol, LDL, insulin, glucose, GIP, leptin, PAI-1 and resistin. The livers of MexTHER and ND mice did not show histological alterations. The size of adipocytes showed significantly smaller diameters in the MexTHER group against HF group. Mice supplemented with MexTHER improved

cognitive parameters, obtaining higher Discrimination Index than the ND group in test novel object recognition (NOR).

**Discussion:** Supplementation with nopal or cocoa has been shown to reduce alterations caused by a diet high in fat and sugar; however, the simultaneous supplementation proposed in this project induced more noticeable benefits, being similar to those achieved with a switch from HF diet to ND diet.

**Conclusions:** MexTHER supplementation is a potential strategy for the treatment of diseases associated with excessive consumption of fat and sugars, such as MAFLD.

The authors declare that there is no conflict of interest.

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## EVALUATION OF THE HEPATOPROTECTOR EFFECT OF A SUPPLEMENT WITH CURCUMA LONGA AGAINST REPERFUSION ISCHEMIA DAMAGE IN AN EXPERIMENTAL MODEL IN WISTAR RATS

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**Introduction and Objectives:** Liver transplantation (LT) is the treatment for end-stage liver disease that may present graft rejection. Conditioning with natural products has shown great therapeutic utility, specifically against ischemia-reperfusion (IR). Curcumin has shown protective activity, which is why it is proposed to evaluate whether curcumin (AGROVITAE-UANL) reduces IR liver damage.

**Material and methods:** For thin layer chromatography, curcumin was started in 0.1% methanol using Si-60GF254 silica gel and chloroform: methanol (95: 5). To verify the presence of 3 curcuminoids, delay factors (Rf) equal to the curcumin standard (Sigma-Aldrich) were detected. For the 70% partial IR liver damage model, a midline laparotomy (L) was performed, the liver was dissected, the hepatic hilum clamped for 1 hour of IR and subsequent sacrificed by exsanguination. 4 groups were established: Sham (3% Tween 20; 500 $\mu$L x 3 days; L); IR (3% Tween 20; 500 $\mu$L x 3 days; L + IR); SIGMA + IR (3% Tween 20; curcumin 200 mg / kg x 3 days; L + IR); AGROVITAE+IR (3% Tween 20; curcumin 200 mg / kg x 3 days; L+IR). ALT, AST, LDH, FA, BIL, PT, ALB, MDA and Total Antioxidants (AOT) were quantified by UV-Vis. NF-k$\beta$ and MPO were evaluated by RT-qPCR. The protocol approved by the ethics committee with registration PI20-00002.

**Results:** The Rf of 3 curcuminoids was calculated: Curcumin (0.80), Demethoxycurcumin (0.69) and Bisdemethoxycurcumin (0.62). In the damage model, a significant increase in ALT, AST and LDH was achieved and a hepatoprotective effect against IR damage due to decreases in liver enzymes (Figure), there was no change in the rest of the markers.

No significant difference was found in the oxidative stress markers MDA and AOT and in the gene expression of NF-k$\beta$ and MPO associated with IR.

**Discussion:** Reyes et. al (2014) reported the presence of the 3 curcuminoids and their Rf, which agrees with our results. Wang et al. (2017) reported a decrease in ALT and AST values in the groups treated with curcumin in a partial IR model, which is consistent with this study. Lintz et al. (2017) reported in a partial IR model that LDH may not be affected, this contrasts with our results; however, in the curcumin groups, no significant difference was observed against IR. Zabala et al. (2019) reported elevation of ALT and AST that agrees with what was obtained in this study. Tinsay et al. (2014) reported that in IR, there was no effect on synthesis and cholestasis markers, as in this study, this can be explained because the damage produced is cell lysis. Regarding the non-difference in the gene expression of NF-k$\beta$ and MPO, other authors reported that the regulation of inflammatory response genes would have an effect at longer reperfusion times (3, 6, 12 and 24h), in hepatic partial IR models.

**Conclusions:** The presence of the 3 curcuminoids was confirmed in AGROVITAE-UANL. The IR damage model was effective in increasing ALT, AST, and LDH. A hepatoprotective effect of AGROVITAE-UANL, against IR by decreasing ALT and AST. No effect was observed on liver synthesis markers or cholestasis, so the damage was only associated with cell lysis. There was also no effect on MDA, AOT markers and inflammatory response genes at the established IR times, ruling out these pathways as possible mechanisms of action.

The authors declare that there is no conflict of interest.

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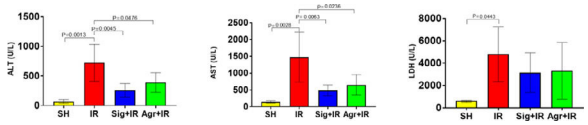


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## CHEMOSENSITIZING EFFECTS OF GDF11 IN HUMAN HEPATOCELLULAR CARCINOMA CELLS

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**Introduction and Objectives:** Hepatocellular carcinoma (HCC) ranks as the second leading cause of cancer death globally; this neoplasm accounts for approximately 90% of liver cancers, and about 850,000 new cases are reported annually. Several factors increase the likelihood of developing HCC, such as excessive alcohol consumption, hepatitis B and C virus infection, metabolic syndrome, and a diet high in lipids and cholesterol. The chronic lesions that the liver can suffer due to the aggression of these factors usually generate lower grade pathologies such as fatty liver, hepatitis, and cirrhosis, which can evolve into HCC. In 2019 Gerardo-Ramirez and collaborators from our group reported the ability of GDF11 to subtract aggressiveness to several HCC-derived cell lines HCC (Huh7, Hep3B, SNU-182, Hepa 1-6 and HepG2); they found that GDF11 reduced proliferation, metastatic capacity, colony, and spheroid formation and invasiveness in those cell lines. Findings by Gerardo-Ramirez *et al.* (2019) identified transcriptional repression of cyclins D1 and A and overexpression of p27. Additionally, an increase in the expression of epithelial markers E-

cadherin and Occludin was observed; conversely, mesenchymal-type features such as N-cadherin and Snail decreased with GDF11 treatment, confirming that this growth factor-induced a mesenchymal to epithelial transition. Furthermore, our group reported the effect of GDF11 in reducing lipid content, especially cholesterol and triglycerides. It was also confirmed that GDF11 reduced mevalonate pathway proteins in Huh7 and Hep3B liver cancer cell lines. Additionally, they reported that GDF11 was able to impair mitochondrial functionality and its structure. Moreover, GDF11 treatment induced an alteration of glycolytic capacity and oxygen consumption rate in these models.

**Objectives General:** To determine the sensitizing effect of GDF11 in the Hep3B cell line. Specific: To determine the capacity of GDF11 in the reduction of the EC50 of cisplatin.

**Methods:** We used the HCC cell line Hep3B (ATCC). A 72-h pretreatment with GDF11 or without was performed; then we treated the cells with cisplatin at various concentrations (0, 2.5, 5, 10, 15, 15, 25, 50, and 100 $\mu$M), incubated for 48 h, and cell viability assay was performed by crystal violet.

**Results:** In our experiments, GDF11 has shown an increased sensitivity of Hep3B cells to cisplatin treatment by significantly reducing the mean effective dose (EC50) from 22.26 $\mu$M to 8.11 $\mu$M this result was observed by crystal violet assay and by light microscopy.

**Discussion:** Results demonstrate that GDF11 has sensitizing effects against cisplatin treatment on the liver tumor cell line Hep3B. This agrees with previous results of our group where a detrimental impact in liver tumor cells is observed by the GDF11 treatment and contrast with other works where TGF-$\beta$ family members have chemoresistance effects.

**Conclusions:** GDF11 pretreatment sensitizes the HCC cell line Hep3B by reducing the cisplatin EC50.

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## HGF AND PROTECTIVE ROLL IN THE INTESTINAL COLLATERAL DAMAGE BY A-NAFTILISOTIOCIANATO- INDUCE CHOLESTASIS.

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**Introduction and Objectives:** he prevalence of cholestasis has been increasing in recent years; The excretion of bile acids via basolateral has been demonstrated to prevent the excessive accumulation in the hepatocyte, and the liver-intestine axis has been seen affected by enterohepatic circulation deregulation. The epithelial permeability loss caused by the tight junction ruptures leads to inflammation and reactive oxygen species (ROS) production. The hepatocyte growth factor is an essential cellular redox regulator and repair growth factor; it has been reported in its relevance in the intestinal mucosa regeneration and proliferative proprieties. This study aims to evaluate the protective effect of HGF in the intestine of animals subjected to cholestatic damage induced by ANIT. Material and methods: Twenty 10-12 weeks-old male CD-1 mice were used. ANIT (60mg/kg) was administrated at the beginning, 24 h later HGF (10 $\mu$g/kg) was injected, and 48 h later, the animals were subjected to euthanasia under anesthesia, and serum and intestines were collected. According to the National Institutes of Health of United Stated (NIH) guide, All mice have been cared for and the Norma Oficial Mexicana (NOM), NOM-062-ZOO-1999. The intestinal tissue was fixed and embedded in paraffin for the histological assessment, followed by routine H&E staining. The expression analysis of TNF- alpha, IL-1b and IL.6 were performed by RT-qPCR using a CFX96 Touch thermocycler with 5$\mu$g 2x SYBER Green, which included 1000ng of cDNA and 2$\mu$l of forward and reverse primers. The protein quantification was evaluated by Western Blot analysis; using 12% polyacrylamide gels, and the primary antibodies for anti-SOD-1, anti-GPx4, anti-Catalase were incubated. Data are presented as the average $\pm$ standard error media (SEM) using GrandPad (Prism 8) software. Variance analysis (ANOVA) was used for the statistical analysis and was considered $p<0.005$ to indicate a statistical significance.

**Results and Discussion:** Macroscopic changes reveal no apparent effect. Microscopic studies carried out by H&E staining showed a reduction of the intestinal lumen diameter in mice under ANIT treatment compared with Not treated control (NT). Interestingly, ANIT + HGF-treated group showed protective effects preserving lumen and tissue architecture. To corroborate the potential repair effect of HGF treatment to maintain the tissue and thus digestive process, the excreted stool for every group was addressed. The stools excretion level of ANIT- treated mice was significantly reduced compared with the control and co-treated mice. These results indicate that ANIT-cholestasis induce damage in the small intestine. However, results also found a vulnerability in the colon and ileum to cholestasis damage. To determine whether these sections received damage in ANIT- acute cholestasis model, by RT q-PCR, we examined the mRNA expression of inflammatory cytokines, which were increased in ANIT- treatment. By comparison, HGF co-treatment decreases inflammation like the control group. To check if this regulation of inflammation was for the HGF-induced redox regulation we evaluated, the protein expression of SOD-1, GPx4, and catalase. The treatment with HGF increased the expression of antioxidant enzymes of the intestine tissue. These results suggest that the damage in the intestine is supported by the regulation of ROS induced by cholestasis disease.

**Conclusion:** The current study demonstrated how HGF exerts a protective effect in the intestine triggered by ANIT. This effect seems to be the cellular redox regulation seen in the liver and renal tissue.

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The authors declare that there is no conflict of interest.

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## IGFBP-1 TO 7 AS BIOMARKERS IN STAGES OF LIVER FIBROSIS DURING VIRAL HEPATITIS C

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**Introduction and Objectives:** Diagnosis of liver disease (LD) is essential for the treatment and management of patients. The use of non-invasive methodologies is necessary despite the availability of direct-acting antivirals, some reports has been showed that treated patients can progress to cellular hepatocarcinoma (HCC). Continuous sampling that will evaluate liver tissue before and after treatment are essential for the prognosis of LD. Objective: To determine the sensitivity and specificity of insulin-like growth factor binding proteins (IGFBP) in the different stages of fibrosis in hepatitis C

**Material and methods:** A prospective, cross-sectional, observational study. The study included patients with CHC that were treatment naïve. The stages of fibrosis were classified as F0, 16 F1, F2, F3, or F4, according to international guidelines, through the FibroTest® and/or FibroScan® Patients with at-risk alcohol consumption (AUDIT>8), and without concordance between fibrosis diagnostic methods employed, and comorbidities were not included. Serum was obtained and multiple suspension array technology (Millipore®) was used to evaluated IGFBP-1,2, 3, 4, 5, 6, 7. Chi-square test, Mann-Whitney U test. Logistic regression models, odds ratios (ORs) and 5% confidence intervals were determined.

**Results:** A total of 128 patients diagnosed with CHC and 123 CT were included. Fibrosis stages were classified as follows: F0 (n=18), F1 (n=16), F2 (n=20), F3 (n=25), and F4 (n=48). IGFBP-1 to -7 showed an evident increment in patients mainly at F3 and F4. IGFBP-7 allows discriminate F3 vs F4 (72% sensibility, 62.5% specificity and cut of value of 2.74), whereas IGFBP-4 discriminates F3 vs F4 (83% sensibility, 68% specificity and cut of value of 14.68). P<0.001 was consider in statistical analysis.

**Discussion:** Although HCV treatment is available the progression from cirrhosis to HCC has been reported after clearance of HCV. Post-treatment studies evaluating the different stages of fibrosis should be performed. Therefore, the use of IGFBPs could be a tool in the continuous sampling previous and after treatment.

**Conclusion:** IGFBPs can be used as additional strategy for the diagnosis and discrimination of fibrosis stages in HCV.

Conflict of interest: The authors declare that there is no conflict of interest.

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## LYMPHOCYTE PROFILE ON PATIENTS WITH CHRONIC AND ACUTE ALCOHOL CONSUMPTION

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**Introduction and Objectives:** Several mechanisms participate in the physiopathology of chronic alcohol consumption and Alcoholic Liver Disease (ALD), such as deregulation in the immune system.

**Aim:** To analyze the lymphocyte subpopulations from patients with chronic and acute alcohol consumption.

**Material and methods:** A Cross-sectional study that included: G1: Controls with alcohol consumption <10g/day (CT); G2: Alcoholism, without clinical or biochemical stigma of liver damage (OH); G3: Patients with cirrhosis by alcohol (CiOH) and G4: Patients with Alcoholic Hepatitis (AH). Determination of T-CD3, T-CD4, T-CD8, NK and NKT lymphocytes from peripheral blood was performed by flow cytometry. Statistical analysis was performed by U-Mann Whitney test, p<0.05 was considered significant.

**Results:** 570 participants were included, the mean of age was: 29.5±10.8, 31±12.6, 47.6± 7.7 y 41.2±9.2 years for CT, OH, CiOH and AH respectively (p<0.001). Alcohol consumption was higher in CiOH 240(320,120) and AH 320(480,160) (p<0.001, p<0.05). Liver function test showed alterations in patients with CiOH and AH, AST 49.5 (75.3,38) for CiOH and 155 (177,121) for AH (p<0.001, p<0.001); ALT 32.5 (47.3,24) in CiOH and 49 (75,35.3) in AH (p<0.001, p<0.001), whereas GGT was 91.5 (191.8, 48) for CiOH, and 224 (525.5, 104) for AH (p<0.001, p<0.001). Cell percentages are described in Table 1.

Data expressed as the median and quartiles (Q3-Q1). a) Alcoholism vs. Control; b) Cirrhosis vs. Control; c) Alcoholic Hepatitis vs. Control; d) Alcoholism vs. Cirrhosis; e) Alcoholism vs. Alcoholic Hepatitis; f) Cirrhosis vs. Alcoholic Hepatitis.

**Discussion:** Changes in the proportion of innate cells affect their ability to repair tissues, which can be exacerbated when damage is perpetuated and chronic inflammation is established. To compare CiOH vs. CT groups we found the suppression of adaptive response and increase in innate population. Furthermore, when CiOH was compared vs. OH increased CD4+ cells and decreased the cytotoxic population, which could be explained due to factors such as active alcohol consumption or advanced cirrhosis. In AH, the innate responses are suppressed compared to other groups. When we compare acute damage (AH) vs. alcoholism (OH) cytotoxic populations decrease, while CD4+ cells increase. However, during acute damage (AH) vs chronic damage (CiOH) increase T and CD8+ cells.

**Conclusions:** The immunological abnormalities that occur during alcoholism, cirrhosis and alcoholic hepatitis are different, the most significant changes were observed in CD4+, CD8+, NK and NKT cells promoting an imbalance that could be related to progression of liver damage.

The authors declare that there is no conflict of interest.

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**Table 1**
Lymphocytic profile in patients with different types of liver damage

| | Control (n=300) | Alcoholism (n=102) | Cirrhosis (n=121) | Alcoholic Hepatitis (n=47) |
|---|---|---|---|---|
| T-Cells (CD3+) % | 66.5 (71.7, 61.1) | 62.3 (67.6, 56.2) a+ | 57.1 (66.5, 51.6) b*,d€ | 66.4 (78.3, 60) f€ |
| Helper Cells CD4+ (%) | 39.6 (45.4, 34.7) | 35.1 (42.1, 30) a+ | 42 (47.7, 32.6) d+ | 47.4 (51.5, 34.7) e€ |
| Cytotoxic Cells CD8+ (%) | 21.2 (27, 17) | 24.7 (30.8, 16.6) | 14.1 (18.9, 8.8) b*,d* | 18.9 (23.6,12.3) e€,f€ |
| CD4+/CD8+ Cells (%) | 1.87 (2.56, 1.37) | 1.5 (2.2, 1) a+ | 2.7 (4.1, 2) b*, d* | 2.7 (3.4, 1.7) e+ |
| NK Cells (%) | 11.1 (15.9, 8.4) | 15.5 (20.9, 10.7) a* | 13.2 (22.1, 8.1) b€ | 1.7 (12, 0.9) c+,e*,f* |
| NKT Cells (%) | 1.7 (2.8, 1.1) | 2.6 (4.5, 1.2) a+ | 1.4 (2, 0.7) d* | 0.5 (1.1, 0.3) c+,e*,f* |

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## IL-10 Y TNF-α IN SERUM OF PATIENTS WITH CHRONIC HEPATITIS C AND HEPATIC DAMAGE CHRONIC AND ACUTE FOR ALCOHOL CONSUMPTION

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**Introduction and Objectives:** The virus of hepatitis C (HCV) and alcoholic liver disease (ALD), are of the main causes of liver disease mortality. There is a need to determine biomarkers, serum cytokines are candidates since they participate in the immunopathogenesis of these diseases by activating the inflammatory process. Increased serum levels of IL-10 and TNF-$\alpha$ have been reported in cirrhosis and have been associated with progression to hepatocellular carcinoma. While TNF-$\alpha$ has become a key factor in the inflammatory process with high circulating levels in alcoholic hepatitis (HA). The objective of this work is to evaluate the serum levels of IL-10 and TNF-$\alpha$ in patients with chronic hepatitis C and ALD.

**Materials and methods:** A cross-sectional and multicenter study. Patients with chronic Hepatitis C (CHC) and CiOH (cirrhotic by alcohol) and alcoholic hepatitis (HA) with criteria for alcoholism (WHO) were included, personalized survey, clinical and biochemical evidence of ALD was recorder. The groups were compared with subjects with a negative viral panel obtained from the CT blood bank (controls). IL-10 and TNF-$\alpha$ from serum was quantified using the multiple suspension arrangement method (Milliplex®-MERCK ©). Statistical analysis was performed using SPSS software version 22 using Mann Whitney U test. It was considered statistically significant $p < 0.05$; values expressed as median (Q3, Q1).

**Results:** A total of 110 subjects were included, 25 for CHC, 25 CiOH, 10 HA and 50 CT. We observed a significant increase on bilirubin, mainly in HA vs CT ($p \leq 0.001$), also AST and GGT was overproduced in CHC, CiOH and HA vs CT ($p \leq 0.001$). IL-10 was found elevated in CHC vs CT ($p \leq 0.0001$) and in CiOH vs CT ($p \leq 0.05$), which confirms that this anti-inflammatory cytokine increases in accordance with liver disease progresses. TNF-$\alpha$ was found to be increased in CiOH vs CHC ($p \leq 0.05$), increased levels in HA vs three study groups CHC, CiOH and CT ($p \leq 0.001$).

**Discussion:** Overproduction of IL-10 in CHC and CiOH support that this anti-inflammatory cytokine increases as liver disease progresses, possibly due to its role as a regulator in inflammation. Has been reported the increment of IL-10 and TNF-$\alpha$ in patients with HA, it is related to the severity of HA and mortality[1]. Also, there are reports about high levels of TNF-$\alpha$ in patients with CHC[2], that contrast with our data, this may be because TNF-$\alpha$ acts differently in a chronic stage. The low concentration of TNF-$\alpha$ in HCc may reflect the regulatory mechanisms of the virus.

**Conclusions:** This study confirms the participation of IL-10 as a cytokine present in stages of chronic liver damage, elevated serum levels of TNF-$\alpha$ in HA compared to CiOH indicates that the inflammatory process actively participates in the acute damage induced by excessive alcohol consumption.

The authors declare that there is no conflict of interest.

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## DETERMINATION OF LEUKOCYTE PROFILE IN CHRONIC ALCOHOL CONSUMPTION

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**Introduction and objective:** Chronic alcohol consumption can induce Alcoholic Liver Disease (ALD) promoting biological alterations and liver damage; however, the immunological changes usually are underestimated. It has been reported, the increase of leucocytes in alcoholic hepatitis patients[1], but the regulation of other cell lineages has not fully evaluated.

**Objective:** To evaluate the leukocyte profile in patients with liver damage induces by chronic and acute alcohol consumption.

**Material and methods:** A Cross-sectional study. Patients were classified as follow: (1) Controls with alcohol consumption <10g/day, AUDIT <8 (CT); (2) Chronic alcohol consumption AUDIT> 8, without clinical or biochemical data of liver damage (OH, alcoholism); (3) Cirrhotic patients due to alcohol (CiOH) and (4) Patients with alcoholic hepatitis (AH). Leukocytes, lymphocytes, monocytes, neutrophils, eosinophils, and basophils were determined by hematic biometry. U-Mann Whitney was used for statistical analysis, $p < 0.05$ was considered significant.

**Results:** 570 patients were included. The mean in age was: 29.5± 10.8 for CT; 31±12.6 for OH; 47.6±7.7 for CiOH and 41.2±9.2 years old ($p<0.001$). Alcohol consumption was higher in CiOH 240 (320, 120; $p<0.001$) and AH 320 (480, 160; $p<0.05$). Albumin decreases in CiOH 2.9 (3.5, 2.2; $p<0.001$) and AH 1.9 (2.3, 1.6; $p<0.001$). On the other hand, AST, ALT and GGT increase in CiOH and AH, 49.5 (75.3, 38; $p<0.001$), 155 (177, 121; $p<0.001$) for AST, 32.5 (47.3, 24; $p<0.001$), 49 (75, 35.3; $p<0.001$) for ALT and 91.5 (191.8, 48; $p<0.001$), 224 (525.5, 104; $p<0.001$) for GGT. There was no a significant difference in eosinophils and basophils. The statistical number of leukocyte profile is described in Table 1.

Data is expressed as the median with interquartile values (Q3-Q1). a) Differences between Alcoholism and Controls; b) Cirrhosis and Controls; c) Alcoholic Hepatitis and Controls; d) Alcoholism and Cirrhosis; e) Alcoholism and Alcoholic Hepatitis; f) Cirrhosis and Alcoholic Hepatitis. €$p<0.05$; +$p<0.01$; *$p<0.001$.

**Discussion:** During alcoholism, lymphocytes decrease, whereas neutrophils increase; this could be related to a susceptibility to recurrent respiratory and gastrointestinal infections. Lymphocytes and neutrophils decrease in CiOH; the reduction in neutrophils could be explained because the stimuli in CiOH decrease. In patients with AH, monocytes and neutrophils increase, that in a consequence increases the inflammatory state, promoting liver fibrosis and mortality.

**Conclusion:** Chronic alcohol consumption, liver cirrhosis and alcoholic hepatitis promote cellular alterations, this phenomenon is more evident in AH. Our findings can be used to design novel detection strategies for the treatments of chronic and acute alcohol consumption.

Conflict of interest: The authors declare that there is no conflict of interest.

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**Table 1**
Leukocyte profile of patients with different types of alcohol-related liver damage

| | Control (n=300) | Alcoholism (n=102) | Cirrhosis (n=121) | Alcoholic Hepatitis (n=47) |
|---|---|---|---|---|
| Leukocytes (miles/mm$^3$) | 6.7 (7.7, 5.8) | 6.7 (7.8, 5.8) | 6.1 (9, 4.4) | 15 (20, 11) c*,e*,f* |
| Lymphocytes (miles/mm$^3$) | 2.2 (2.7, 1.8) | 1.9 (2.3, 1.7) a€ | 1.4 (2, 1)d* | 1.7 (4.9, 1) |
| Monocytes (miles/mm$^3$) | 0.4 (0.5, 0.27) | 0.4 (0.5, 0.3) a€ | 0.5 (0.7, 0.4) | 0.8 (1.2, 0.5) c+,e+,f€ |
| Neutrophils (miles/mm$^3$) | 3.6 (4.7, 2.9) | 4.1 (5, 3.3)a+ | 3.3 (5.7, 2.2) d€ | 12 (19, 7)c*, e*,f* |

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## SERUM DETERMINATION OF MMP-2 AND MMP-9 ACCORDING TO THE PATTERN OF ALCOHOL CONSUMPTION AND IN ALCOHOLIC HEPATIC DISEASE

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**Introduction and Objectives:** The damage caused by alcohol consumption generates liver fibrosis, which is characterized by the accumulation of extracellular matrix (ECM); To limit the liver damage, MMP-2 and MMP-9 gelatinases are produced as mediators to degrade ECM products. Their importance in liver damage proposes them as possible markers and target molecules in the diagnosis of alcohol consumption, as well as in alcoholic liver disease [1]. The objective of this work is to evaluate the serum concentrations of MMP-2 and MMP-9 gelatinases in subjects with different patterns of alcohol consumption and in alcoholic liver disease patients.

**Materials and methods:** A cross-sectional study was carried out in which subjects with different patterns of alcohol consumption were included. The inclusion was according to the AUDIT, DSM-IV, and clinical and biochemical data of liver disease: risk (Ri), abuse (Ab), dependence (OH), cirrhosis due to alcohol (CiOH) and alcoholic hepatitis (HA). A group without alcohol consumption (TC) was also included for comparison. For the quantification of MMP-2 and MMP-9, a multiple suspension assay (Milliplex®-MERCK ©) was used. Statistical analysis was performed using SPSS V.22 software using Mann Whitney U. P <0.05 was considered statistically significant; values were expressed as mean ± standard error.

**Discussion:** In 2015 Prystupa, A. et al. used MMP-2 and MMP-9 as markers of progression of damage in alcohol cirrhosis; however, there are no more related studies so far. Our data shows that the synthesis of MMP-2 and MMP-9 in consumption patterns and in liver disease are decreased from risky consumption, promoting the accumulation of ECM in liver tissue.

**Conclusion:** Serum levels of MMP-2 and MMP-9 gelatinases are affected by alcohol consumption, even in a risk pattern. MMP-2 and MMP-9 can be used as markers of alcohol-induced damage in early stages.

Conflict of interests: The authors declare that there is no conflict of interest.

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## COMPARISON OF CXCL-8 and IFN-γ PRODUCTION IN ACUTE AND CHRONIC STAGES OF LIVER DISEASE

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**Introduction and objective:** Hepatitis C virus and alcoholism are the main causes of Chronic Liver Disease. (1) The increase of CXCL-8 has been correlated with mortality in alcoholic hepatitis (AH), while in Chronic Hepatitis C (CHC) with the disease severity. (2) The IFN-$\gamma$ has an anti-viral and anti-fibrotic function. There are few comparative studies in patients regarding the production of these mediators and their possible implication in liver damage. The objective is to evaluate the concentrations of CXCL-8 and IFN-$\gamma$ in the serum of AH, alcoholic cirrhosis (CiOH) and CHC patients.

**Materials and methods:** A multicenter cross-sectional study was carried out. Four participant groups were included: AH, CiOH, CHC and control group (CT). For the quantification of CXCL-8 and IFN-$\gamma$ a multiple suspension array assay (Milliplex®-MERCK©) was used. Statistical analysis was performed by the SPSS V.22 software using Mann-Whitney-U-test. A p-value<0.05 was considered statistically significant. Values were expressed as median (Q3, Q1).

**Results:** 110 individuals were included: AH (10), CiOH (25), CHC (25) and CT (50). In CXCL-8 quantification, significant differences were detected in AH vs. CT, CiOH vs. CT, CHC vs. CT, CiOH vs. AH and CHC vs. AH ($p \leq 0.001$). While in IFN-$\gamma$, the differences were detected in AH vs. CT, CiOH vs. CT, CHC vs. CT, CiOH vs. AH and CHC vs. AH ($p \leq 0.001$).

**Discussion:** Differences were detected in both molecules when comparing the chronic stages (CiOH and CHC) with the acute stage (HA), while no differences were found when comparing both chronic stages. The highest CXCL-8 concentration corresponds to AH, reflecting its importance in prognosis and mortality. (2) The increase of IFN-$\gamma$ in CiOH and CHC may have a role in the regulation of fibrogenesis because of its anti-fibrotic function.

**Conclusion:** The deregulation of mediators such as IL-8 and IFN-$\gamma$ promotes systemic inflammation in both acute and chronic stages, being greater in AH. This may indicate an association with the susceptibility to persistent respiratory and gastrointestinal diseases.

The authors declare that there is no conflict of interest.

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## OXIDATIVE DAMAGE MARKERS IN ALCOHOLIC HEPATITIS

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**Introduction and objective:** Alcohol hepatitis (AH) is a clinical syndrome in patients with excessive and chronic alcohol consumption. Ethanol metabolism produces free radicals: reactive oxygen species (ROS) and reactive nitrogen species (RNS). This contributes to cellular damage in AH. The malondialdehyde (MDA) and carbonylated proteins are markers of oxidative damage in lipids and proteins. Our objective is to evaluate the levels of serum MDA and carbonylated proteins in AH patients with.

**Materials and methods:** This transversal study included 147 individuals divided into two groups: the control group (n=100), which consists of individuals with alcohol consumption ≤ 10 g/day and AUDIT score ≤ 7, and the group with AH patients (n=47). We measured the serum levels of MDA (thiobarbituric acid method) and carbonylated proteins (DNPH reaction). The statistical analysis was performed by the Windows SPSS v22 software. Data were expressed as mean values ± SEM. Comparisons were carried out by analysis of variance (ANOVA). A p-value <0.05 was considered statistically significant.

**Results:** The control group (CT), with a mean of 30.47±0.52 years old, had a consumption of 2.32±0.21g of alcohol daily (gOH/day) and an AUDIT score of 2.24±0.10. The AH patients, with a mean of 41.68± 1.3 years old, had a consumption of 354.25±39.54 gOH/day and an AUDIT score of 30±1.45. The AST, ALT, GGT, total and indirect bilirubin serum levels were higher in AH compared to CT (p<0.0001), with a ratio of AST/ALT ≥2. The albumin serum levels were lower (p<0.0001) in AH vs. CT. The carbonylated proteins serum levels were higher in patients with AH compared to CT (p<0.0001). No differences in MDA serum levels were found between both groups.

**Discussion:** We reported greater MDA serum levels (p=0.001) in alcoholic liver cirrhosis patients when compared to the control group; and an insignificant difference in carbonylated proteins serum level between both participant groups. The alcoholic hepatitis patients have an increase in carbonylated proteins oxidative damage while there is no lipidic damage.

**Conclusions:** Our results suggest that carbonylated proteins may a damage oxidative marker in the AH Mexican population. This damage may increase the risk of malnutrition, susceptibility to infections and sepsis, deficient coagulation factors production, gastrointestinal bleeding, among other complications that increase mortality. It is necessary to counteract oxidative damage to improve and complement the actual treatment in alcoholic hepatitis.

Competing interests. The authors declare they have no competing interests.

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## TOTAL CHOLESTEROL / HIGH DENSITY LIPOPROTEIN CHOLESTEROL RATIO, TRIGLYCERIDES / HIGH DENSITY LIPOPROTEIN CHOLESTEROL WITH THE CONTROLLED ATTENUATION PARAMETER (CAP) IN NON-ALCOHOLIC FATTY LIVER

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**Introduction and Objectives:** Non-Alcoholic Fatty Liver Disease (NAFLD) is a global public health problem. The ratio of Total Cholesterol (TC) to High Density Lipoprotein Cholesterol (HDL) and Ultrasensitive C-Reactive Protein have been a biomarker of cardiovascular risk. In a study of the Chinese population, the CT/HDL ratio was established as a predictor of metabolic syndrome and NAFLD >3.8 The optimal cut-off level to predict NAFLD according to the ratio triglycerides (TG)/HDL was established in women >0.9 and in men > 1.4, with sensitivity and specificity of 78 and 77.3% respectively. There are optimal cut-off values of CT/HDL and TG/HDL to predict NAFLD[4]. However, they have not been associated with the degree of hepatic fat infiltration using Transient Elastography (FibroScan®) study by CAP, with a sensitivity of 82% and specificity of 91%. Objective: To describe the relationship CT/HDL, TG/HDL with the controlled attenuation parameter in patients diagnosed with non-alcoholic fatty liver.

**Material and Methods:** Retrospective study in patients registered in the database of the Gastroenterology outpatient clinic of the Juárez Hospital in Mexico, with a diagnosis of NAFLD, from January 1, 2017 to April 30, 2019, who underwent Fibroscan. The data were obtained from the records of the outpatient clinic and clinical record, it was analyzed in the statistical program Jamovi 1.1.9, to obtain means, medians and percentages. Chi-square test was used for analysis of categorical variables and unidirectional analysis of variance (ANOVA) for continuous variables, establishing a $p<0.05$ as significant.

**Results:** In total 48 patients, middle age 49 years (20-76), female 38 (79.2%), with no previous history 29 (60.4%) metabolic syndrome 33 (68.8%) diabetic 19 (39.6%) obesity 27 (56.3%) The CAP for steatosis evaluation: S1, 4 (8.3%) S2, 20 (41.7%) and S3, 24 (50%), for degree of liver fibrosis in Fibroscan: F0, 33 (68.8%) and F1, 14 (29.2%) and by FIB4 scale (<1.30) with NAFLD scale indeterminate fibrosis. The median CT/HDL ratio is not higher with the degree of CAP per FibroScan, being S1, 3.9 (3.1- 4.1) S2, 3.8 (2.3- 6.8) S3, 4.5 (3.1-7.2), ($p$ 0.076). The higher the median TG/HDL ratio, the higher the degree of CAP per FibroScan, being S1, 2.3 (1.6- 2.7) S2, 3.8 (0.9- 7.9) S3, 4.6 (2-16.9) $p$ value 0.008. It was associated that the higher the degree of CAP per Fibroscan, the higher the triglyceride levels above the normal upper value and the greater the association of presenting metabolic syndrome with a p value of 0.009 and 0.003 respectively. (see table)

**Discussion:** Higher levels of the TG/HDL ratio, elevated triglyceride levels, and the presence of metabolic syndrome increase the degree of CAP in this group of NAFLD patients. This study the largest population was female (79.2%) so it cannot be inferred that the TG/HDL ratio and degree of CAP is relevant for male sex, so more studies should be carried out and these variables determined. This study has as a limitation that it was carried out in a single hospital center so the cohort sample should be increased and carried out prospectively to really determine whether or not it has utility CT/ HDL relationship in NAFLD, since in this study a result was obtained without statistical significance.

**Conclusions:** The CT/HDL ratio was not associated with the degree of CAP by Fibroscan. It was determined that the higher the median TG/HDL ratio, the higher the degree of CAP in Fibroscan. However, it is necessary to consider this study in patients with high

body mass index lowers its sensitivity and specificity, so it should be performed with other advanced imaging modalities.

The authors declare that there is no conflict of interest.

**Table**
Relationship of CT/HDL, TG/HDL, lipid profile and metabolic syndrome with the degree of CAP by FibroScan

| Parameters | Degree of CAP by FibroScan | | | P-value |
|---|---|---|---|---|
| | S1 | S2 | S3 | |
| **Triglycerides[a]** | 111.5 (14.82) | 178.75 (64.5) | 236.41 (113.10) | 0.009 |
| **HDL cholesterol[a]** | 51.02(9.09) | 46.49(10.17) | 41(9.24) | 0.068 |
| **LDL cholesterol[a]** | 126.75 (29.47) | 113.72 (31.55) | 115.94 (27.08) | 0.331 |
| **Total cholesterol[a]** | 193 (48.10) | 180.95(40.5) | 188(38.68) | 0.781 |
| **CT/HDL Ratio[b]** | 3.9 (3.1-4.1) | 3.8(2.3-6.8) | 4.5(3.1-7.2) | 0.076 |
| **TG/HDL Ratio[b]** | 2.3 (1.6-2.7) | 3.8 (0.9-7.9 | 4.6 (2-16.9) | 0.008 |
| **Metabolic syndrome[c]** | | | | |
| **Yes** | 1 (2.9) | 13 (38.2) | 20 (58.82) | 0.003 |
| **No** | 3 (21.42) | 7 (50) | 4 (28.5) | |

a: mean (standard deviation) b: median (ranges) c: number (percentage)
LDL: Low Density Lipoprotein HDL: High Density Lipoprotein

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## DIFFERENTIAL PROFILE OF PRO-INFLAMMATSORY / ANTI-INFLAMMATORY CYTOKINES AND MALONDIALDEHYDE IN PATIENTS WITH ALCOtHOL-INDUCED OR OBESITY OR MIXED INJURY

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**Introduction and Objectives:** Dysregulation of pro-inflammatory/anti-inflammatory cytokines and oxidative stress markers has been reported in Non-Alcoholic Steatohepatitis (NASH) and alcoholic steatohepatitis (ASH); however, in the disease recently known, as Both Alcoholic and Non-Alcoholic SteatoHepatitis (BASH) that meets the criteria of ASH and NASH have not been described. The objective was to evaluate the influence of alcohol and obesity on a differential profile of cytokines and malondialdehyde (MDA) in patients with these etiologies.

**Material and methods:** Cross-sectional, prospective, observational study. Patients from the "Dr. José E. González" from March 2019-March 2020, with a diagnosis of ASH (alcohol consumption ≥ 5 years, 30 g/day for men and 20 g/day for women), NASH (demonstrated by ultrasound, FibroScan or FibroMax) and BASH (ASH and NASH criteria). The serum cytokines interleukin-8 (IL-8), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-$\alpha$), interleukin-1$\beta$ (IL-1$\beta$), interleukin-10 (IL-10) and malondialdehyde (MDA) were determined. The protocol was approved by the ethics committee with registration MI19-000016.One-way analysis of variance was performed with Kruskal-Wallis and Dunn's post hoc. The results were expressed as median (interquartile range). The analysis was performed using Graph Pad Prism (v. 7.04, San Diego, CA, USA). A value of $p<0.05$ was considered significant.

**Results:** The patients were: 34 BASH, 43 NASH and 35 ASH. The severity of the patients with respect to clinical and biochemical parameters in increasing order was NASH <BASH <ASH. It was observed in increasing order that the levels of the cytokines IL-8, IL-6, IL-10 were: NASH <BASH <ASH; TNF-$\alpha$ levels were: BASH <NASH <ASH; IL-1$\beta$ levels show no significant difference between groups (Figure). The BASH group showed higher concentration levels of MDA [20.00 (9.00-30.50) pg/mL] with significant difference (p = 0.0434) compared to NASH [14.00 (3.00-19.00) pg/mL], but not with ASH (Figure). Serum levels of IL-6 (A; $p$ <0.0001), TNF-$\alpha$ (B; $p$=0.0014), IL-8 (C; $p$<0.0001), IL-10 (D; $p$<0.0001) and IL-1$\beta$ (E; Not significant) in the different study groups.

**Discussion:** In ASH and NASH, common pathogenetic mechanisms mediated by pro-inflammatory.

The authors declare that there is no conflict of interest.

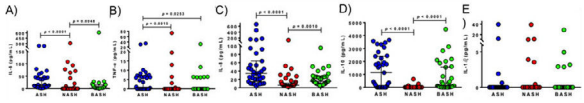


Figure. Serum levels of IL-6 (A; $p$ <0.0001), TNF (B; $p$= 0.0014), IL-8 (C; $p$<0.0001), IL-10 (D; $p$<0.0001) and IL-1$\beta$ (E; NS) in the different study groups. The values were expressed as median (interquartile range). NS: not significant.

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## PROFILE OF PRO AND ANTI-INFLAMMATORY CYTOKINES IN PATIENTS WITH CHRONIC LIVER DISEASE IN THE COMPENSATION, INFLAMMATION AND IMMUNOSUPPRESSION PHASES

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**Introduction and objectives:** Decompensated cirrhosis is defined by the onset of complications and is associated with immune dysfunction. This is the result of two processes: systemic inflammation and damage made by the immune system. Our objective was to determine the profile of pro and anti inflammatory cytokines in patients with chronic liver disease: alcoholic (OH), non-alcoholic steatohepatitis (NASH), autoimmune liver disease (AILD) and hepatitis C (HCV), in the phases of compensation, inflammation and immunosuppression, based on functional classifications and prognosis with the CHILD- PUGH, MELD and D'Amico scales.

**Methods and materials:** Prospective, observational, and cross-sectional study, made in the University Hospital, Dr. Jose E. Gonzalez during 2019-2020. A total of 108 patients were included: 28 OH, 27 NASH, 25 HCV and 27 AILD. The diagnosis and functional classification was made according to international guidelines. Inclusion criteria: over 18 years of age, signed informed consent. Exclusion criteria: hepatocellular carcinoma, other autoimmune pathologies. Blood samples (10 ml) were collected to quantify TNF-a, IL-8, IL-10, IL-1, IL-6. The protocol was approved by the ethics committee with registration MI20-0002. A one-way ANOVA was used to determine the differences between groups and stages

**Results:** In OH, there is an increase in IL-6 and IL-8 in the decompensation phase, Child-Pugh stage C, D'amico stage 5 and MELD from 25 to 34 points. NASH patients had an increase in IL-8 in the inflammation phase as assessed by Child-Pugh B and D'amico 3 and 4. There was an increase in IL-6 in the immunosuppression phase. In patients

with HCV and AILD, increased serum levels of IL-8 and IL-6 were shown in decompensation stages (Figure 1).

**Discussion:** In this study, we demonstrated a significant increase in the pro-inflammatory cytokine profile in patients in the inflammation and immunosuppression phases. Fischer J et al. reported that a greater understanding of the mechanisms associated with immune dysfunction has led to the identification of possible therapeutic targets, with the intention of reducing the risk of infection and preventing decompensation events and disease progression.

**Conclusion:** This study demonstrated a significant increase in the pro-inflammatory cytokine profile (IL-8 and IL-6) as cirrhosis progresses. This is consistent with in the inflammation and immunosuppression phases, assessed by the Child-Pugh severity scales in stages B and C, D'amico from stages 3 to 5 and MELD> from 16 to 24 points and from 25 to 34 points. in the four etiologies included, being statistically significant.

The authors declare no conflict of interest.

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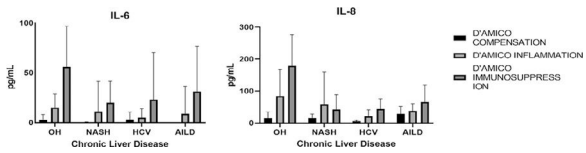


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## CONNECTIVE TISSUE GROWTH FACTOR (CTGF) AS A PROMOTER IN THE DEVELOPMENT OF FIBROSIS IN PATIENTS WITH PRIMARY BILIARY CHOLANGITIS

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**Introduction and Objectives:** Primary biliary cholangitis (PBC), an immune-mediated disease, is characterized by destroying the intrahepatic bile ducts, leading to progressive damage to the biliary tree, cholestasis, and development of progressive fibrosis leading to cirrhosis with all its complications. The development of fibrosis is multifactorial and includes connective tissue growth factor (CTGF). in a mouse model of cholestasis by bile duct ligation, the hepatic and serum increase in CTGF associated with the progression of fibrosis was demonstrated. Our goal was to determine the relationship between CTGF levels and their association with the development of fibrosis in patients with PBC.

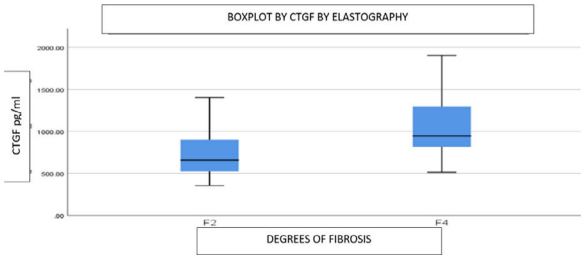
**Material and methods:** Prospective, cross-sectional, and analytical study, including patients with PBC. The degree of fibrosis was determined by transient elastography (Fibroscan). Serum concentrations of FCTC-8pg/ml were quantified, for statistical analysis, the SPSS version 25.0 software was used; the medians (Q3, Q1) of CTGF, alkaline phosphatase, gamma-glutamyl-transpeptidase, and degree of fibrosis were compared with the Mann-Whitney U test with significantly less than 0.05.

**Results:** We included 30 patients, 29 women (96.6%) and 1 man (3.4%), with a mean age of 55.5±12.4 years. Overexpression of CTGF protein was shown in 28 subjects (93.3%). Regarding the degree of fibrosis, all patients were categorized into one of two stages: Significant fibrosis (F2) and cirrhosis (F4). The F2 group had 11 patients with a median and standard deviation for CTGF of 915.9 and 522.9, respectively; The F4 group had 19 patients who showed a median: 945.7 (1313.85-738.32); p:**0.025**. In relation to the differences between fibrosis levels and markers of alkaline phosphatase cholestasis, the median and interquartile ranges F2: 79 (180.60) F4: 169 (266-5.84) p**: 0.066**; GGT: F2: 1.51(7.7-1,04); F4: 1.2(2-1.92) p:0.746 In (Figure 1) The difference in medians of patients with different degrees of fibrosis and different concentration of CTGF is shown, confirming the association between peptide and the development and progression of fibrosis.

**Discussion:** According to the results obtained in patients with CBP and chronic cholestasis, the increase in CTGF showed significant differences between the degree of fibrosis and its levels; this could perhaps be interpreted as if it were an important factor for the development and progression of liver fibrosis, taking into account the antecedent of the initial study in mice with bile duct ligation and secondary cholestasis, where this factor was overexpressed at the hepatic and serum level in subjects with advanced fibrosis. It will be important to add more samples to this work and compare it with healthy controls to have better evidence.

**Conclusions:** Connective tissue growth factor (CTGF) probably participates directly in the processes of synthesis of extracellular matrix and therefore in the progression of fibrosis in subjects with primary biliary cholangitis, which makes it a possibility of a therapeutic target to develop in future studies.

The authors declare that there is no conflict of interest.




(Figure 1) The difference in medians of patients with different degrees of fibrosis and different concentration of CTGF is shown, confirming the association between peptide and the development and progression of fibrosis.

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## Global real-world evidence of sofosbuvir/velpatasvir (SOF/VEL) as a highly effective treatment in underserved patient populations because of mental health disorders, incarceration or homelessness

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**Introduction and Objectives:** The treatment of vulnerable populations must be prioritized to accomplish the WHO HCV elimination goals by 2030, including patients with mental health disorders, incarcerated patients or homeless patients. Simplifying the treatment cascade and rapid treatment start is key to achieving this goal, even more so in the COVID-19 era. Sofosbuvir/velpatasvir (SOF/VEL) is a protease inhibitor-free, pangenotypic, panfibrotic, single duration, single tablet regimen, to be taken without regards to food and with limited drug-drug interactions, allowing treatment simplification. Purpose: This real world data (RWD) analysis evaluates the effectiveness and safety of SOF/VEL for 12 weeks in a heterogeneous HCV population who suffer a mental health disorder, are incarcerated, or homeless.

**Materials and Methods:** 33 clinical cohorts across Australia, Canada, Europe & USA included 1,888 patients, 280 of them (from 6 clinical cohorts) were treated in Canada and overall managed following local standards of care. Adults were included if SOF/VEL for 12 weeks was started before November 2019 and completed while suffering a mental health disorder, being incarcerated or homeless, irrespective of genotype (GT), presence of compensated cirrhosis (CC) or treatment experience. Exclusion criteria were history of decompensation, prior NS5A-inhibitor exposure, treatment duration >12 weeks or addition of ribavirin. Sustained virological response (SVR; ≥12 weeks after end-of-treatment) and time to treatment initiation were assessed.

**Results:** Overall analysis includes 1,888 (71.3% male) patients (1,422 with a mental health disorder, 526 incarcerated, 153 homeless) aged 50 years, 24.4% were taking antipsychotic drugs and 52.2% of patients had former or current intravenous drug use. 43.2% patients had HCV GT1, 11.6% GT2, 36.3% GT3, 5.9% GT4-6, and 3.0% mixed/unknown GT. 19.0% patients had CC and 12.4% were treatment-experienced. In 257 patients (13.6%), SVR was not evaluated due to non-virological or unknown reasons; 79.9% of those were lost to follow-up (LTFU). When SVR was measured, 98.0% (n=1598/1631) achieved SVR, with 97.6%, 98.9% and 100% in patients with a mental health disorder, incarcerated or homeless patients, respectively. SVR was 98.5% in non-cirrhotic and 95.4% in CC patients. SVR remained >95% under antipsychotic use or coexistence of two negative factors of non-response such as GT3 plus active drug use or psychiatric disorder. SVR was similar, irrespective of time from diagnosis to treatment. Detailed analysis of the Canadian cohort data will be presented at the conference.

**Conclusion:** A test-and-treat strategy, easily implemented with SOF/VEL, and supported by the AASLD/ALEH/APASL/EASL joint call to action, could further enhance the population-level efficacy of HCV therapy by reducing the rate of non-virologic failure due to LTFU and related factors.

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