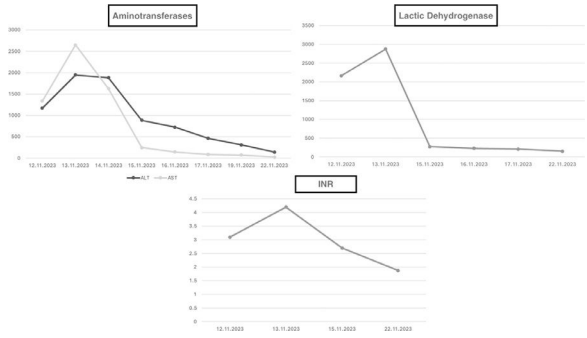
Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



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Novel bacterial cluster "Prevotella, Bacteroides and Suterella" associated with mortality in Mexican patients with acute-on-chronic liver failure (ACLF) and clinical utility of systemic hs-CRP and IL-6: A frontier approach involving next-generation sequencing at the intestinal level in a cohort by alcoholic etiology.

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Introduction and Objectives: ACLF is characterized by acute decompensation of cirrhosis, organ failure, and high short-term mortality. Several studies have demonstrated the relevance of intestinal microbiota (IM) in the pathophysiology of cirrhosis. To date, there are no studies in the Mexican population focused on IM in alcohol-associated ACLF and its relationship with mortality and inflammatory markers.

Aim: To analyze the composition and diversity of IM in patients with alcohol-associated cirrhosis and ACLF, healthy controls, and its correlation with inflammatory markers.

Materials and Patients: Cross-sectional study, which included 22 decompensated patients with ACLF, 16 decompensated patients without ACLF (CD) and 18 healthy individuals (HI), recruited at the Hospitales Civiles de Guadalajara. Fecal IM was characterized by NGS of the 16S-rRNA gene. Systemic levels of high-sensitivity C-reactive protein (hs-CRP) and interleukin 6 (IL-6) were quantified by ELISA, and bioinformatics analysis of IM was performed using the QIIME2 package. Quality filtering, which includes removal of chimeras and non-biological sequences, was performed using the DADA2 algorithm. Resulting ASVs were taxonomically assigned through a self-trained naïve Bayesian classifier, against the SILVA database. Furthermore, α and β diversity analyses, relative abundances, and ANCOM-BC compositional analysis were performed in the QIIME2 package. Predictive values and associations were performed using ROC curves and Spearman correlations, respectively.

Results: ACLF and CD patients showed significantly lower α-diversity compared to CS. The comprehensive bacterial taxonomy profile in ACLF was significantly dominated by pathogenic/inflammatory genera such as Escherichia/Shigella, Enterobacter and Prevotella. In contrast, we observed a depletion of Bacteroides compared to CD. Interestingly, the subanalysis of MI in ACLF patients categorized at 7 and 90 days of mortality showed consistency with the enrichment of the Prevotella, Bacteroides and Suterella cluster. The Proteobacteria/Firmicutes ratio as a potential marker of dysbiosis, was significantly elevated in ACLF patients. Serum levels of hs-CRP and IL-6 were potentially increased in ACLF, in comparison to CD and CS. hs-CRP correlated positively with IL-6 and the Proteobacteria/Firmicutes ratio and negatively with α-diversity. IL-6 levels were positively correlated with MELD-Na. Finally, ROC curve analyses showed that hs-CRP allows discrimination of infections in patients with CD with a cut-off point >70.7 mg/L (AUROC: 0.75, with 90% sensitivity and 68.9% specificity). IL-6 allows discrimination of hepatic encephalopathy (HE) in patients with CD and ACLF with a cut-off point >7051.1 pg/mL (AUROC: 0.67, with 81.4% sensitivity and 45.8% specificity).

Conclusions: The dysbiotic/proinflammatory profile of IM in ACLF correlated with the potential increase in systemic inflammation. The bacterial cluster "Prevotella, Bacteroides and Suterella" represents a hallmark of mortality within 7 and 90 days. IL-6 and hs-CRP allow discrimination of HE and infections in patients with alcohol-associated cirrhosis.

Ethical statement: The study was conducted in accordance with the latest update of the Declaration of Helsinki and the Regulations on Human Studies in Health Matters of the Mexican Republic.

The protocol was approved by the ethics committees of the Civil Hospitals of Guadalajara (010/20 and 00012) and the Ethics, Research and Biosafety Committee of the University Center for Health Sciences of the University of Guadalajara (22-96).

Declaration of interests: None.

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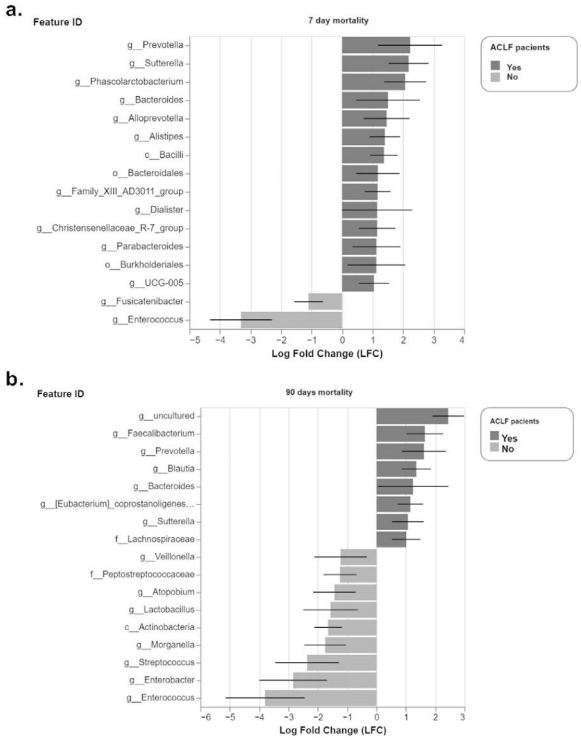
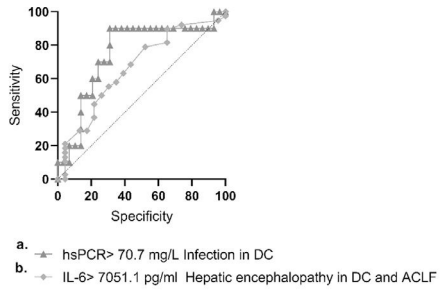


Figure 1. ***Analysis of fecal microbiota from patients with ACLF and its association with mortality.*** a) and b) Differential bacterial

taxonomy (at the level of bacterial family and genera) at 7 and 90 days of patients who died, compared to those who did not die. The bars represent the log-fold change (LFC) between both groups. The blue bars indicate the characteristic taxa of the group that died, while the brown bars represent the survivor group. A cut-off of $p<0.05$ and $q<0.05$ was used. Analyzed by means of ANCOM-BC algorithm (Analysis of Compositions of Microbiomes with Bias Correction).



	AUROC	p	Sensitivity (%)	Specificity (%)
Infection in DC (hsPCR>70.7 mg/L)	0.75	0.009	90	68.97
HE in DC and ACLF (IL-6>7051.17 pg/ml)	0.67	0.014	81.4	45.8

Figure 2. ***High-sensitivity C-reactive protein (hs-CRP) and interleukin 6 (IL-6): biomarkers associated with bacterial infections and the presence of hepatic encephalopathy.*** a) ROC curve of hs-CRP, which demonstrates the prediction of bacterial infections in patients with decompensated cirrhosis without ACLF (cut-off point >70.7 mg/L (AUROC: 0.75, with 90% sensitivity and 68.9% specificity); b) ROC curve of IL-6, that demonstrates the prediction of hepatic encephalopathy in patients with decompensated cirrhosis with ACLF and without ACLF (cut-off point >7051.1 pg/ml (AUROC: 0.67, with 81.4% sensitivity and 45.8% specificity).

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IGFBPs in chronic liver diseases: Are they potential biomarkers?

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Introduction and objectives: Liver diseases are caused by alcohol consumption, Hepatitis C virus, and metabolic dysfunction. There are few studies on insulin-like growth factor binding proteins (IGFBPs), also IGFBP-1 being involved in regulating glucose and lipid metabolism but its relation with liver diseases has not been fully clarified yet. To evaluate serum levels of IGFBPs 1,2,3 and 7 in subjects with alcoholic liver cirrhosis, alcoholic hepatitis, chronic hepatitis C, and Metabolic Dysfunction-Associated Steatotic Liver Disease.

Materials and patients: Prospective, cross-sectional, and multicenter study; approved by the research and ethics commission at UNAM, and the Hospital General de México, which included subjects with clinical and biochemical data of alcohol-related liver damage, defining two groups: alcoholic liver cirrhosis (OHCi) and alcoholic hepatitis (AH). Another group with Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). The last group was defined with a diagnosis of chronic hepatitis C (HepC). FibroScan Testing, and/or Fibrotest were realized. All study groups were compared with healthy subjects called the control group (CT). IGFBPs were quantified in serum using a multiplex suspension array. The data were analyzed and compared between groups. For statistical analysis, Kruskal-Wallis and Mann-Whitney U tests were used.

Results: The serum concentrations of IGFBPs 1, 2, and 7 in Hepatitis C were elevated compared to all groups. In the case of HA, IGFBP-2, 3, and 7 decreased compared to the CT group, while IGFBP-1 was higher compared to CT. For IGFBP-3, all groups were decreased compared to the CT group. In the MASLD and CiOH groups, low concentrations of IGFBPs 1, 2, 3, and 7 were observed when compared with HepC, AH, and CT groups.

Conclusions: The serum levels of IGFBPs highlight have the relevance in the diverse liver diseases, it's evident in Hepatitis C are synthesized in higher concentration, while in MASLD and alcohol-related liver disease the concentration is lower, these proteins can be used as differential serum markers in liver diseases. It's necessary to conduct studies that would allow us to find new mechanisms involved in lipid metabolism and its relationship with liver disease.

Ethical statement: The protocol was approved by the Ethics and Research Committees of the "Dr. Eduardo Liceaga" General Hospital of Mexico (HG/DI/16/107/03/082), and the Faculty of Medicine of UNAM (FMD/DI/15/2015).

Declaration of interests: None.

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Clinical and epidemiologic characteristics of pregnant women with liver disease in a tertiary hospital.

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Introduction and Objectives: It has been demonstrated that approximately 3% of pregnant women are affected by some type of liver disorder. The aim of this study is to determine the clinical and epidemiological characteristics of pregnant patients who developed liver disease during their pregnancy or liver pathology unrelated to pregnancy.

Materials and Patients: The study is a retrospective and observational analysis of a cohort composed of 72 pregnant women