

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

Results: HSC-LX2 co-cultured with transfected Huh7 showed an 8.3, 6.7 and 4-fold increase in collagen1, TGFB1 and timp1 expression respectively induced by NS5A and a 6.5, 1.8 and 6.2-fold increase respectively induced by Core, all these compared to HSC-LX2 co-cultured with untransfected Huh7. We detected 28 overexpressed genes in Huh7 (NS5A+) and 46 differentially expressed genes in Huh7 (Core +) in co-culture with HSC-LX2, compared to untransfected Huh7 in co-culture with HSC-LX2. Analysis of the expression profile showed that the TGF β 1, the ECM regulation, and growth factors pathways are the molecular mechanisms involved during the co-culture of Huh7 transfected with NS5A or Core with HSC-LX2.

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

Ethical statement

The protocol was registered and approved by the Ethics Committee.

Declaration of interests

None

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

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

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

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

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

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

Ethical statement

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

Declaration of interests

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

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

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

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

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

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

Ethical statement

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

Declaration of interests

None

Funding

None

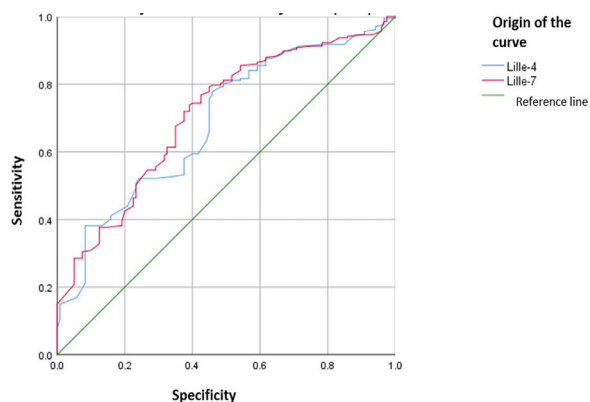


Figure 1. Area Under the Receiver Operating Characteristic Curve (AUROC) of Lille-4 and Lille-7 for predicting 28-day mortality.

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Hepatic injury biomarkers in COVID-19

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

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

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

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

Ethical statement

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

Declaration of interests

None

Funding

None

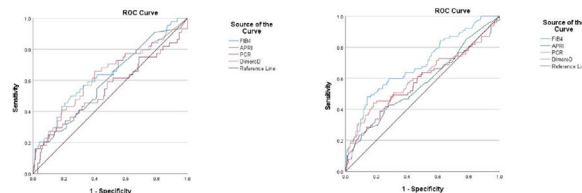


Figure 1: ROC curves.

Table 1

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

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

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