Correlation between Connective Tissue Growth Factor and the degree of fibrosis in patients with cholestasis.

Cristian Y. Sánchez-Sánchez[1],
Diego F. Abendaño-Rivera[1],
Viridiana López-Ladrón de Guevara[1],
María A. Diaz-Castro[1], Fátima Higuera-De La Tijera[1],
Carolina Guzmán-Arriaga[2],
Ángel D. Santana-Vargas[3], José L. Pérez-Hernández[1]

[1] *Department of Gastroenterology and Hepatology General Hospital of Mexico "Dr. Eduardo Liceaga," Mexico City, Mexico*
[2] *Liver, Pancreas, and Motility Laboratory, Experimental Medicine Unit General Hospital of Mexico "Dr. Eduardo Liceaga," Mexico City, Mexico*
[3] *Research Department General Hospital of Mexico "Dr. Eduardo Liceaga," Mexico City, Mexico*

Introduction and Objectives: The Connective Tissue Growth Factor (CTGF) is a multifunctional protein recognized as an important mediator in fibrogenic pathways in liver diseases. We aimed to establish the correlation between serum CTGF levels using Enzyme-Linked ImmunoSorbent Assay (ELISA) and the degree of hepatic fibrosis measured by transient elastography in patients with cholestasis diagnosed with Primary Biliary Cholangitis (PBC).

Materials and Patients: Prospective, analytical, experimental study. Three groups were recruited: the first group comprised patients with cholestasis, the second group comprised patients with cirrhosis due to Hepatitis C Virus (HCV), and the third group comprised healthy subjects. Anthropometric and biochemical data were collected. A blood sample was collected to quantify serum levels of CTGF using ELISA. The degree of fibrosis was determined by transient elastography. Statistical analysis: Data are presented as Mean±SD or Median (IQR 25-75). They were analyzed by one-way ANOVA with Tukey's post-hoc test or Kruskal-Wallis with Dunn's post-hoc test. The following parameters were calculated: Sensitivity (S), Specificity (E), Positive Predictive Values (PPV), Negative Predictive Values (NPV), and the area under the ROC curve (AUROC). A p-value <0.05 was considered significant.

Results: Thirty patients with cholestasis diagnosed with PBC were included, along with a group of subjects with cirrhosis due to Hepatitis C Virus (VHC-F4, n=6), and a control group without liver disease (C, n=17). It was observed that there is a positive correlation between CTGF levels and the degree of fibrosis in patients with cholestasis (PBC), but not in patients with cirrhosis due to HCV. Using a cutoff point of 630 pg/mL, a sensitivity (S) of 0.93, specificity (E) of 0.91, positive predictive value (PPV) of 0.93, negative predictive value (NPV) of 0.91, and an area under the ROC curve (AUROC) of 0.97 with a Youden index of 0.85 were obtained (Figure 1). With a serum CTGF value of 520 pg/mL in patients with PBC without fibrosis or with moderate fibrosis compared to controls and HCV-F4, a sensitivity (S) of 0.75, specificity (E) of 0.87, and AUROC of 0.88 for F0, and a sensitivity (S) of 0.91, specificity (E) of 0.87, and AUROC of 0.94 for F2 were identified (Figure 1). Regarding the degree of fibrosis, CTGF was significantly higher in F4 compared to F0 in patients with PBC. In the case of the VHC-F4 group, there were no differences compared to the group without liver disease, suggesting a specificity of CTGF for fibrosis due to cholestatic disease (Figure 2).

Conclusions: There is a direct correlation between serum levels of CTGF in patients with cholestasis and the degrees of fibrosis measured by transient elastography, as well as specific cutoff points for discrimination with and without fibrosis for PBC.

Ethical statement: This protocol was approved by the Research Ethics Committee of the General Hospital of Mexico " Dr. Eduardo Liceaga" Mexico City, Mexico (CEI-HGM) with the number (DI/12/UME/05/21).

Declaration of interests: None.

Funding: This work was partially funded by CONACYT (CB-221137).

Figure 1.

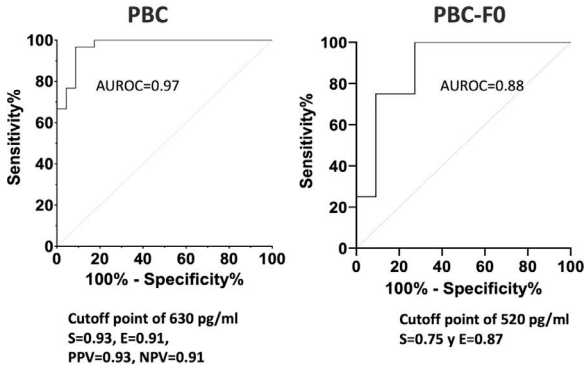
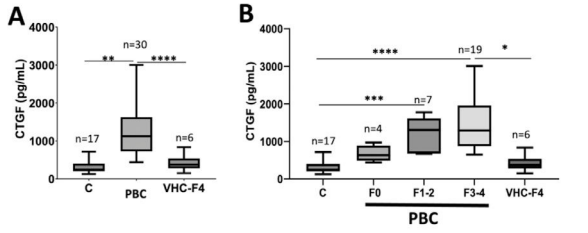


Figure 2.



Median (RIC). Kruskal-Wallis con post-hoc de Dunn. *p<0.05, **p<0.01, ***p<0.005, ****p<0.001

https://doi.org/10.1016/j.aohep.2025.101807

Evaluation of the effect of HCV Core protein on the epithelial-mesenchymal transition (EMT) process in non-tumorigenic immortalized hepatocytes

Verónica Alvarado-Martínez,
Tania G. Heredia-Torres, Sonia A. Lozano-Sepúlveda,
Ana M. Rivas-Estilla

Center for Research and Innovation in Medical Virology. Department of Biochemistry and Molecular Medicine. Faculty of Medicine. UANL. Mexico

Introduction and Objectives: The HCV Core protein is involved in metabolic remodeling and, energy reprogramming through enzymatic changes and redistribution of energy resources, promoting epithelial-mesenchymal transition (EMT) and liver disease. This study addressed the metabolic changes involved in EMT by evaluating the expression of Vimentin and E-cadherin in a non-cancerous cell model.

Materials and Patients: An expression plasmid for the HCV Core protein genotype 1b (p-Core) was designed. Transient transfection was performed in the THLE-2 cell line, characterized by a morphology similar to non-tumorigenic human hepatocytes and the expression of differentiated hepatocyte markers, making it ideal for metabolic assays due to its ability to express and regulate proteins involved in metabolism more effectively than primary hepatocyte cultures. For the transfection, p-Core concentrations of 0.5 - 2.0 μg were used, and the cells were cultured for 72 hours. Subsequently, total proteins were extracted and quantified using PKR buffer. The expression levels of Core, Vimentin, and E-cadherin proteins were evaluated by Western Blot, using 40 μg of protein. The relative expression of the

proteins was calculated in relation to the endogenous expression of GAPDH using ImageJ software, and the analysis was performed in triplicate.

Results: The expression of the viral Core protein (21 kDa) was detected in THLE-2 cells transfected with the p-Core plasmid at 72 hours. It was observed that the expression of the E-cadherin protein (120 kDa) decreased by 80% (in cells transfected with 0.5 μg) and by 25% in cells transfected with 2.0 μg of p-Core. Lastly, an increase in the expression levels of the Vimentin protein (57 kDa) was observed in relation to the concentration of p-Core, doubling with 0.5 μg and increasing sixfold with 2.0 μg of p-Core.

Conclusions: The expression of the viral Core protein modulates the translational expression levels of E-cadherin and Vimentin in THLE-2 cells, suggesting its possible involvement in cell adhesion, mobility, and metabolism by HCV. However, detailed studies of the implicated metabolic pathways are required to establish the activation pathways involved.

Ethical statement: This work is original and has not been previously published.

Declaration of interests: None.

Funding: The resources used in this study were funded by the Center for Research and Innovation in Medical Virology of the Faculty of Medicine at UANL without additional funding

https://doi.org/10.1016/j.aohep.2025.101808

Degrees of Liver Stiffness and Steatosis as Predictors of Preeclampsia Complications

Andrés T. Flores-y-Flores[1],
Orestes de J. Cobos-Quevedo[2],
José L. Perez-Hernández[2], Jesús C. Briones-Garduño[3],
Daniel Santana-Vargas[4]

[1] *Obstetrics and Gynecology, High Specialty South Central Hospital, Mexico*
[2] *Division of Hepatology, General Hospital of Mexico, Mexico*
[3] *Obstetrics and Gynecology Department, General Hospital of Mexico, Mexico*
[4] *Research Department, General Hospital of Mexico, Mexico*

Introduction and Objectives: Liver damage in preeclampsia is caused by antiangiogenic factors such as soluble tyrosine kinase, placental growth factor, and soluble endoglin. These induce endothelial injury and fibrin deposits in the hepatic microcirculation, thus modifying the physical characteristics of the liver parenchyma and its stiffness. This study aims to evaluate the correlation between the degree of liver stiffness and the severity of patients with preeclampsia.

Materials and Patients: An observational, analytical, cross-sectional, and prospective study. Pregnant women from week 20 of gestation were included, and divided into 3 groups: normal pregnancy, pre-eclampsia, and pre-eclampsia with severity features; They were recruited from February 2023 to August 2023 in Mexicoś City General Hospital, Obstetrics department. Transient elastography was performed on all of them. Pregnant women with chronic systemic arterial hypertension and pre-existing liver diseases were excluded. Descriptive statistics measures of central tendency were performed, and univariate analysis was carried out considering kilopascals (kPa) as a dependent univariable and the group (without preeclampsia, preeclampsia, and preeclampsia with severity criteria) as fixed factors and BMI as a covariate.

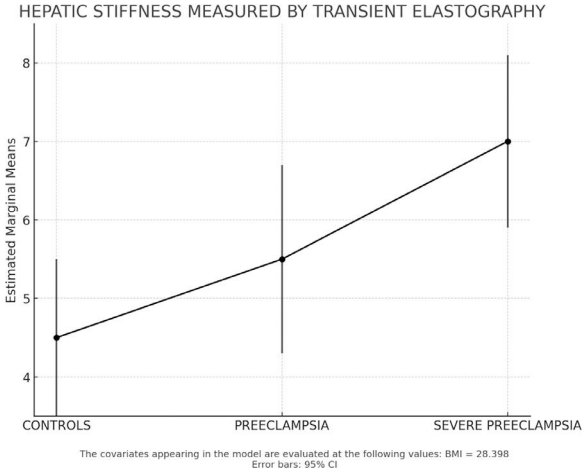
Results: 34 patients were included, 9 in the control group, 12 in the preeclampsia group and 13 in the preeclampsia with severity features group. The mean gestational age was 32 $\pm$ 5.8 weeks. The mean age was 27.26 $\pm$ 7.73 years. The mean BMI was 28.88 $\pm$ 4.83. The mean kPa in the control group was 4.35 $\pm$ 0.98, in the preeclampsia without severity features group 5.05 $\pm$ 0.87, and in the preeclampsia with severity features group 6.67 $\pm$ 1.84. The mean control group CAP was 202.82 $\pm$ 21.26 db/m2, in the preeclampsia without severity features group was 227.81 $\pm$ 47.81 db/m2, and in the preeclampsia with severity features group was 215.28 $\pm$ 37.41 db/m2. Univariate contrasts were significant for preeclampsia with severity criteria features versus preeclampsia F (2 of 23) = 7.679, p = 0.011. Preeclampsia with severity features versus control F (2 of 22) = 11.134, p = 0.003

Conclusions: Liver stiffness significantly increases in patients with preeclampsia and preeclampsia with severity features measured by transient elastography. This increase is due to intrahepatic fibrin deposition, but not by fibrosis (collagen) itself. Transient elastography could be useful as a predictor of severity in patients with preeclampsia.

Ethical statement: Study approved by the research ethics committee of the General Hospital of Mexico registration key DI/23/310-E/03/37.

Declaration of interests: None.

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



https://doi.org/10.1016/j.aohep.2025.101809

Portal cholangiopathy secondary to cavernomatous transformation of the portal vein. Case report

Karla J. Arroyo García, Luis A. Esquivel-Pacheco,
Alexis V. Hinostroza-Pezo, Adolfo Gamiño-Morfín,
Alejandro D. Mendoza-Rea, Luis R. Alvarez-Martín,
Carlos A. Galvan-Castro

Internal medicine / Gastroenterology department, High Specialty Regional Hospital, Yucatan, Mexico

Introduction and Objectives: Portal cholangitis is a set of alterations that appear in the bile duct secondary to portal hypertension (PH). It is extremely rare and its main etiology is cavernomatous transformation of the portal vein (CPVT). The objective is to present the case of a patient with portal cholangiopathy secondary to TCVP.

Materials and Patients: A 17-year-old man with no relevant history began with hemorrhoidal bleeding, requiring hemorrhoidectomy. After 3 weeks, he presented abdominal pain and constipation. Abdominal computed tomography revealed free abdominal fluid, splenomegaly, and portal dilation. A diagnostic paracentesis was performed with GASA 3.1 and liver Doppler ultrasound with a 9mm portal vein, collateral veins, thrombosis and portal cavernomatosis.