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Introduction and Objectives: It has been shown that DNA methylation patterns and miRNA levels are effective markers for distinguishing different stages of liver fibrosis in European patients. A liquid biopsy allows the evaluation of ccfDNA methylation levels from hepatocytes damaged by necrosis/apoptosis, releasing degraded genomic DNA into the circulatory system, which reflects the gene changes present in hepatocytes. This study aimed to evaluate the potential association of specific miRNAs and the percentage of DNA methylation of genes linked with fibrosis in liver tissue and liquid biopsy from MEXICAN patients with various degrees of liver fibrosis and its severity.

Materials and Methods: Transjugular liver biopsies and liquid biopsies were collected from 23 patients with sustained viral response to HCV and residual fibrosis. The percentage of methylation in CpG islands of PPARα, gamma and δ gene promoters, as well as TGFβ1 and PDGFα, will be determined by pyrosequencing in DNA extracted from the liver and ccfDNA. Fibrosis was stratified according to Metavir. miR-21, miR-34, miR-122, miR181b, miR192, and miR-200a/b expression was evaluated.

Results: Higher methylation percentages were detected in antifibrotic gene promoters (PPARα and gamma) in patients with more severe degrees of fibrosis (F4), both in tissue and in liquid biopsy. TGFβ1 and PDGFα, profibrogenic genes, showed significant hypomethylation in their promoter regions, indicating hyperactivation. In addition, the overexpression of miRNAs evaluated was associated with the degree of fibrosis and severity.

Conclusions: Epigenetic mechanisms (DNA methylation and microRNA expression) regulate the expression of multiple genes and their measurement can be a biomarker associated with the degree of fibrosis. Liquid biopsy is an effective and accessible method for evaluating the degree of fibrosis in Mexican subjects and for monitoring clinical protocols.

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P- 78 DIETHYINITROSAMINE AND 2-ACETYLAMINOFLUORENE CHRONIC ADMINISTRATION LEADS TO BIOCHEMICAL, HISTOLOGIC AND GENETIC CHANGES RELATED TO HEPATOCELLULAR CARCINOMA IN WISTAR RATS

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Introduction and Objectives: Hepatocellular carcinoma (HCC) is one of the neoplasms with the highest mortality worldwide. The causes of the development of HCC have been related to hepatitis B virus and exposure to aflatoxin B1; however, chronic alcohol use, nonalcoholic fatty liver disease, and hepatitis C virus infection are the most important risk factors for developing HCC. The establishment of animal models of HCC is crucial for both basic and translational studies of hepatocellular carcinoma and is a valuable tool to identify alterations during the progression of the disease. This study aimed to analyze the biochemical, histological, and gene expression alterations produced in a model of chemical hepatocarcinogenesis by the chronic administration of diethylnitrosamine (DEN) and 2-acetylaminofluorene (2-AAF) in Wistar rats.

Materials and Methods: Twelve Wistar rats weighing 180 to 200 g were divided into control and damage groups: rats were treated with DEN (50 mg/kg/wk) i.p and an intragastric dose of 2-AAF (25 mg/kg/wk) for 18 weeks. Serum clinical biochemistry was performed on VITROS Chemistry System 350® equipment. Masson's trichrome and Hematoxylin-Eosin stains were performed on the liver tissue. Relative gene expression was performed by RT-qPCR in LightCycler®96.

Results: The damage group had significant increases in total cholesterol, HDL-C, AST, ALT, ALKP, and GGT. Furthermore, histological analysis showed the loss of normal liver architecture with nuclear pleomorphism in the hepatocytes, atypical mitosis, and fibrous septa distributed between portal triads and collagen fibers through the hepatic sinusoids. The expression of *TGFb1* was significantly increased ($p<0.05$); on the contrary, *ALB*, *CAT* and, *PPARα* were downregulated ($P<0.05$), *CPT1A* was downregulated too but without significance.

Conclusions: Chronic administration of DEN and 2-AAF induces characteristic alterations of hepatocellular carcinoma in Wistar rats. The uncontrolled proliferation of malignant cells requires a constant supply of energy and macromolecules. In this work, cancer cells reprogrammed their fatty acid oxidation pathway by downregulation of *PPARα* and *CPT1A*.

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P- 79 LIVER TRANSPLANTATION FOR HEPATOCELLULAR, LOOKING FOR THE BETTER SELECTION CRITERIA. RESULTS FROM THE URUGUAYAN LIVER TRANSPLANT PROGRAM

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Introduction and Objectives: Liver transplantation (LT) is an established therapeutic in hepatocellular carcinoma (HCC). Since 90' Milan's criteria have been the gold standard for the selection of the best candidate. In the last decade, new expanded criteria have been developed, like UCSF, Up to 7 and AFP Model, with the purpose of achieving a better selection of liver transplant candidates. This study aimed to describe the results of LT for HCC in our center, evaluate different selection criteria, and assess survival.

Materials and Methods: Retrospective analysis of adult patients transplanted with HCC in the National Liver Transplant Program of Uruguay (07/2009-06/2022).

Results: Of 259 LT performed, 63 (23,9%) had HCC. Study Population: Age:57 ± 7 years, 82% males. Etiology: 32% hepatitis C, 32% alcohol, 13% NASH, 9% Autoimmune Hepatitis, 5% hepatitis B, 9% others. The median waiting list time is 68 days. At listing: median serum AFP 56 ± 160 ng/L, real MELD-Na 13 points, assigned supplementary 22 points in all diagnosed cases. 48.3% had locoregional treatments before transplant, 22.5% as downstaging and 25.8% as bridging therapy. Milán in= 81% (including effective downstaging), Beyond Milan and UCSF in = 6% and beyond UCSF= 2%. Incidentals=11%. In the explanted liver: non-confirmed HCC 3,3%, beyond Up to 7 criteria 25%, microvascular invasion 16,7 %, macrovascular invasion 6,7%. Imaging accuracy showed that 20% of the patients clinically within Milan criteria exceeded them on pathology. Considering AFP Model, 80% were in criteria. Recurrence-free survival at 1, 3, and 5 years: 94%, 86% and 86%, respectively. Overall Survival at 1, 3 and 5 years: 90%, 75% and 73%, respectively.

HCC-related and non-related deaths were 38% (n=7) and 61% (n=11), respectively.

Conclusions: Our results are similar when compared to other regional and international data. The AFP model seems to be a good patient selection tool in our setting.

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P- 80 DIFFERENTIAL EXPRESSION OF MATRIX METALLOPROTEINASE 7 IN CHRONIC LIVER DISEASES

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Introduction and Objectives: We recently published that in the serum of patients with chronic Hepatitis C, there are high concentrations of inactive Matrix Metalloproteinases (MMP). However, the MMP has not been studied in other liver diseases. This study aimed to evaluate serum concentrations of MMP-7 in different hepatic etiologies and according to fibrosis stage.

Materials and Methods: A cross-sectional and multicenter study was carried out, including subjects with alcoholism (WHO criteria), without (OH) and with liver injury (cirrhosis, CiOH); diagnosed by clinical, biochemical data, non-alcoholic fatty liver (NAFLD) and chronic Hepatitis C (CHC). Transitional elastography (Fibroscan) was performed in NAFLD and CHC, considering mild fibrosis (MF: F0, F1, F2) and advanced fibrosis (AF: F3, F4). As controls, subjects without alcohol consumption (CT) were recruited. For the quantification of MMP-7, Multiplex-MERCK© was used. Statistical analysis was performed using SPSS V.22 using Mann Whitney U, $p<0.05$.

Results: It included 99 subjects (OH); 45 (CiOH); 48 (CHC, FL); 54 (CHC, FA); 27 (NAFLD, FL); 36 (NAFLD, AF) and 131 CT. MMP-7 was found to be elevated in CHC (FL and FA) vs. CT; and decreased in OH, CiOH, NAFLD (FL and FA) vs. CT, plus there are significant differences between all etiologies, $p<0.001$. MMP-7 is a matrilysin that degrades extracellular matrix products (proteoglycans); it increases significantly in subjects with CHC compared to CT, while in other pathologies with stages, even in advanced fibrosis, the levels are decreased compared to CT.

Conclusions: The increased MMP-7 in serum of chronic Hepatitis C and decrease in alcoholism and non-alcoholic fatty liver patients suggests that, according to the etiology, the levels can be useful to make a differential diagnosis. We considered that it is a potential non-invasive biomarker.

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P- 81 PREVALENCE OF HEV INFECTION IN HIV CARRIERS, PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND CIRRHOTIC PATIENTS

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Introduction and Objectives: Hepatitis E is a neglected disease in Brazil. Hepatitis E virus (HEV) can cause chronic illness in immunocompromised patients. This study aimed to determine the seroprevalence and prevalence of HEV infection in different populations: HIV carriers, patients with inflammatory bowel disease (IBD) and cirrhotic patients.

Materials and Methods: The study design was cross-sectional. Participants were recruited from the HIV/AIDS and hepatology outpatient clinic and from the hepatology ward of the University Complex Hospital Professor Edgar Santos (HUPES, UFBA). The proposed sample size was 150 HIV carriers, 100 IBD patients and 50 cirrhotic patients (data and samples collection are in progress). Data were collected through interviews and a review of medical records, and a blood sample was collected for the investigation of anti-HEV IgM and IgG antibodies (Wantai), measurement of serum transaminases AST and ALT (Wiener lab) and detection of HEV -RNA (RealStar® HEV RT-PCR Kit 2.0, Altona).

Results: To date, 214 volunteers have been recruited, 143 of whom have HIV, 38 have IBD and 33 have cirrhosis. Serological tests