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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-α have been reported in cirrhosis and have been associated with progression to hepatocellular carcinoma. While TNF-α 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-α 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-α 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-α 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-α in patients with HA, it is related to the severity of HA and mortality[1]. Also, there are reports about high levels of TNF-α in patients with CHC[2], that contrast with our data, this may be because TNF-α acts differently in a chronic stage. The low concentration of TNF-α 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-α 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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