P. Cordero-Pérez[3], L. Muñoz-Espinoza[3], J. Córdova-Gallardo[4], D. Kershenobich[1,5], G. Gutiérrez-Reyes[1]

[1] *Laboratorio de Hígado, Páncreas y Motilidad (HIPAM). Unidad de Medicina Experimental, UNAM. Ciudad de México, México*
[2] *Hospital General de México "Dr. Eduardo Liceaga". Ciudad de México, México*
[3] *Hospital Universitario, Facultad de Medicina, UANL. Nuevo León, México*
[4] *Hospital General Dr. Manuel Gea González. Ciudad de México, México*
[5] *Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán". Ciudad de México, México*

**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-$\alpha$ have been reported in cirrhosis and have been associated with progression to hepatocellular carcinoma. While TNF-$\alpha$ 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-$\alpha$ 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-$\alpha$ 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-$\alpha$ 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-$\alpha$ in patients with HA, it is related to the severity of HA and mortality[1]. Also, there are reports about high levels of TNF-$\alpha$ in patients with CHC[2], that contrast with our data, this may be because TNF-$\alpha$ acts differently in a chronic stage. The low concentration of TNF-$\alpha$ 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-$\alpha$ in HA compared to CiOH indicates that the inflammatory process actively participates in the acute damage induced by excessive alcohol consumption.

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## DETERMINATION OF LEUKOCYTE PROFILE IN CHRONIC ALCOHOL CONSUMPTION

E.A. Alamo-Capula[1], M. Hernandez Santillan[1], A. Hernandez-Barragan[1], S. Sánchez-Valle[1], I. Altamirano-Mendoza[1], Z. Medina-Avila[1], M. Martínez-Castillo[1], D. Santana-Vargas[1], Y. Bejar[2], F. Higuera de la Tijera[2], J.L. Pérez-Hernández[2], D. Kershenobich[1], G. Gutiérrez-Reyes[1]

[1] *Laboratorio Hígado, Páncreas y Motilidad (HIPAM). Unidad de Investigación en Medicina Experimental, UNAM. Ciudad de México, México*
[2] *Hospital General de México "Dr. Eduardo Liceaga". Ciudad de México, México*

**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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**Table 1**
Leukocyte profile of patients with different types of alcohol-related liver damage

| | Control (n=300) | Alcoholism (n=102) | Cirrhosis (n=121) | Alcoholic Hepatitis (n=47) |
|---|---|---|---|---|
| Leukocytes (miles/mm$^3$) | 6.7 (7.7, 5.8) | 6.7 (7.8, 5.8) | 6.1 (9, 4.4) | 15 (20, 11) c*,e*,f* |
| Lymphocytes (miles/mm$^3$) | 2.2 (2.7, 1.8) | 1.9 (2.3, 1.7) a€ | 1.4 (2, 1)d* | 1.7 (4.9, 1) |
| Monocytes (miles/mm$^3$) | 0.4 (0.5, 0.27) | 0.4 (0.5, 0.3) a€ | 0.5 (0.7, 0.4) | 0.8 (1.2, 0.5) c+,e+,f€ |
| Neutrophils (miles/mm$^3$) | 3.6 (4.7, 2.9) | 4.1 (5, 3.3)a+ | 3.3 (5.7, 2.2) d€ | 12 (19, 7)c*, e*,f* |

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## SERUM DETERMINATION OF MMP-2 AND MMP-9 ACCORDING TO THE PATTERN OF ALCOHOL CONSUMPTION AND IN ALCOHOLIC HEPATIC DISEASE

A. Hernandez-Barragan[1], M. Martinez-Castillo[1], J.L. Pérez-Hernández[2], F. Higuera-De la Tijera[2], D. Santana-Vargas[1], D. Kershenobich[3], G. Gutiérrez-Reyes[1]

[1] *Liver, Pancreas and Motility laboratory, Unit of Experimental Medicine, School of Medicine, National Autonomous University of Mexico (UNAM), General Hospital of Mexico, Mexico City, Mexico*
[2] *General Hospital of México Dr. Eduardo Liceaga. México City, México*
[3] *National Institute of Medical Sciences and Nutrition "Salvador Zubirán", México City, México*

**Introduction and Objectives:** The damage caused by alcohol consumption generates liver fibrosis, which is characterized by the accumulation of extracellular matrix (ECM); To limit the liver damage, MMP-2 and MMP-9 gelatinases are produced as mediators to degrade ECM products. Their importance in liver damage proposes them as possible markers and target molecules in the diagnosis of alcohol consumption, as well as in alcoholic liver disease [1]. The objective of this work is to evaluate the serum concentrations of MMP-2 and MMP-9 gelatinases in subjects with different patterns of alcohol consumption and in alcoholic liver disease patients.

**Materials and methods:** A cross-sectional study was carried out in which subjects with different patterns of alcohol consumption were included. The inclusion was according to the AUDIT, DSM-IV, and clinical and biochemical data of liver disease: risk (Ri), abuse (Ab), dependence (OH), cirrhosis due to alcohol (CiOH) and alcoholic hepatitis (HA). A group without alcohol consumption (TC) was also included for comparison. For the quantification of MMP-2 and MMP-9, a multiple suspension assay (Milliplex®-MERCK ©) was used. Statistical analysis was performed using SPSS V.22 software using Mann Whitney U. P <0.05 was considered statistically significant; values were expressed as mean ± standard error.

**Discussion:** In 2015 Prystupa, A. et al. used MMP-2 and MMP-9 as markers of progression of damage in alcohol cirrhosis; however, there are no more related studies so far. Our data shows that the synthesis of MMP-2 and MMP-9 in consumption patterns and in liver disease are decreased from risky consumption, promoting the accumulation of ECM in liver tissue.

**Conclusion:** Serum levels of MMP-2 and MMP-9 gelatinases are affected by alcohol consumption, even in a risk pattern. MMP-2 and MMP-9 can be used as markers of alcohol-induced damage in early stages.

Conflict of interests: The authors declare that there is no conflict of interest.

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## COMPARISON OF CXCL-8 and IFN-γ PRODUCTION IN ACUTE AND CHRONIC STAGES OF LIVER DISEASE

I. Altamirano-Mendoza[1], M. Martínez-Castillo[1], Z. Medina-Avila[1], L. García-Islas[1], J.L. Pérez-Hernández[2], F. Higuera-De la Tijera[2], D. Santana-Vargas[2], J. Cordova-Gallardo[3], D. Kershenobich[4], G. Gutiérrez-Reyes[1]

[1] *Laboratorio de Hígado, Páncreas y Motilidad (HIPAM). Unidad de Investigación en Medicina Experimental, Facultad de Medicina, UNAM. México City, México*
[2] *Hospital General de México "Dr. Eduardo Liceaga". México City, México*
[3] *Hospital General Dr. Manuel Gea González. México City, México*
[4] *Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán". México City, México*

**Introduction and objective:** Hepatitis C virus and alcoholism are the main causes of Chronic Liver Disease. (1) The increase of CXCL-8 has been correlated with mortality in alcoholic hepatitis (AH), while in Chronic Hepatitis C (CHC) with the disease severity. (2) The IFN-$\gamma$ has an anti-viral and anti-fibrotic function. There are few comparative studies in patients regarding the production of these mediators and their possible implication in liver damage. The objective is to evaluate the concentrations of CXCL-8 and IFN-$\gamma$ in the serum of AH, alcoholic cirrhosis (CiOH) and CHC patients.

**Materials and methods:** A multicenter cross-sectional study was carried out. Four participant groups were included: AH, CiOH, CHC and control group (CT). For the quantification of CXCL-8 and IFN-$\gamma$ a multiple suspension array assay (Milliplex®-MERCK©) was used. Statistical analysis was performed by the SPSS V.22 software using Mann-Whitney-U-test. A p-value<0.05 was considered statistically significant. Values were expressed as median (Q3, Q1).

**Results:** 110 individuals were included: AH (10), CiOH (25), CHC (25) and CT (50). In CXCL-8 quantification, significant differences were detected in AH vs. CT, CiOH vs. CT, CHC vs. CT, CiOH vs. AH and CHC vs. AH ($p \leq 0.001$). While in IFN-$\gamma$, the differences were detected in AH vs. CT, CiOH vs. CT, CHC vs. CT, CiOH vs. AH and CHC vs. AH ($p \leq 0.001$).

**Discussion:** Differences were detected in both molecules when comparing the chronic stages (CiOH and CHC) with the acute stage (HA), while no differences were found when comparing both chronic stages. The highest CXCL-8 concentration corresponds to AH, reflecting its importance in prognosis and mortality. (2) The increase of IFN-$\gamma$ in CiOH and CHC may have a role in the regulation of fibrogenesis because of its anti-fibrotic function.

**Conclusion:** The deregulation of mediators such as IL-8 and IFN-$\gamma$ promotes systemic inflammation in both acute and chronic stages, being greater in AH. This may indicate an association with the susceptibility to persistent respiratory and gastrointestinal diseases.

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