OXIDATIVE DAMAGE MARKERS IN ALCOHOLIC HEPATITIS

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Introduction and objective: Alcohol hepatitis (AH) is a clinical syndrome in patients with excessive and chronic alcohol consumption. Ethanol metabolism produces free radicals: reactive oxygen species (ROS) and reactive nitrogen species (RNS). This contributes to cellular damage in AH. The malondialdehyde (MDA) and carbonylated proteins are markers of oxidative damage in lipids and proteins. Our objective is to evaluate the levels of serum MDA and carbonylated proteins in AH patients with.

Materials and methods: This transversal study included 147 individuals divided into two groups: the control group (n=100), which consists of individuals with alcohol consumption ≤ 10 g/day and AUDIT score ≤ 7, and the group with AH patients (n=47). We measured the serum levels of MDA (thiobarbituric acid method) and carbonylated proteins (DNPH reaction). The statistical analysis was performed by the Windows SPSS v22 software. Data were expressed as mean values ± SEM. Comparisons were carried out by analysis of variance (ANOVA). A p-value <0.05 was considered statistically significant.

Results: The control group (CT), with a mean of 30.47±0.52 years old, had a consumption of 2.32±0.21g of alcohol daily (gOH/day) and an AUDIT score of 2.24±0.10. The AH patients, with a mean of 41.68± 1.3 years old, had a consumption of 354.25±39.54 gOH/day and an AUDIT score of 30±1.45. The AST, ALT, GGT, total and indirect bilirubin serum levels were higher in AH compared to CT (p<0.0001), with a ratio of AST/ALT ≥2. The albumin serum levels were lower (p<0.0001) in AH vs. CT. The carbonylated proteins serum levels were higher in patients with AH compared to CT (p<0.0001). No differences in MDA serum levels were found between both groups.

Discussion: We reported greater MDA serum levels (p=0.001) in alcoholic liver cirrhosis patients when compared to the control group; and an insignificant difference in carbonylated proteins serum level between both participant groups. The alcoholic hepatitis patients have an increase in carbonylated proteins oxidative damage while there is no lipidic damage.

Conclusions: Our results suggest that carbonylated proteins may a damage oxidative marker in the AH Mexican population. This damage may increase the risk of malnutrition, susceptibility to infections and sepsis, deficient coagulation factors production, gastrointestinal bleeding, among other complications that increase mortality. It is necessary to counteract oxidative damage to improve and complement the actual treatment in alcoholic hepatitis.

Competing interests. The authors declare they have no competing interests.

This work was partially financed by CONACyT SALUD-2016-272579 and PAPIIT- UNAM TA200515

https://doi.org/10.1016/j.aohep.2021.100642

TOTAL CHOLESTEROL / HIGH DENSITY LIPOPROTEIN CHOLESTEROL RATIO, TRIGLYCERIDES / HIGH DENSITY LIPOPROTEIN CHOLESTEROL WITH THE CONTROLLED ATTENUATION PARAMETER (CAP) IN NON-ALCOHOLIC FATTY LIVER

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Introduction and Objectives: Non-Alcoholic Fatty Liver Disease (NAFLD) is a global public health problem. The ratio of Total Cholesterol (TC) to High Density Lipoprotein Cholesterol (HDL) and Ultrasensitive C-Reactive Protein have been a biomarker of cardiovascular risk. In a study of the Chinese population, the CT/HDL ratio was established as a predictor of metabolic syndrome and NAFLD >3.8 The optimal cut-off level to predict NAFLD according to the ratio triglycerides (TG)/HDL was established in women >0.9 and in men > 1.4, with sensitivity and specificity of 78 and 77.3% respectively. There are optimal cut-off values of CT/HDL and TG/HDL to predict NAFLD[4]. However, they have not been associated with the degree of hepatic fat infiltration using Transient Elastography (FibroScan®) study by CAP, with a sensitivity of 82% and specificity of 91%. Objective: To describe the relationship CT/HDL, TG/HDL with the controlled attenuation parameter in patients diagnosed with non-alcoholic fatty liver.

Material and Methods: Retrospective study in patients registered in the database of the Gastroenterology outpatient clinic of the Juárez Hospital in Mexico, with a diagnosis of NAFLD, from January 1, 2017 to April 30, 2019, who underwent Fibroscan. The data were obtained from the records of the outpatient clinic and clinical record, it was analyzed in the statistical program Jamovi 1.1.9, to obtain means, medians and percentages. Chi-square test was used for analysis of categorical variables and unidirectional analysis of variance (ANOVA) for continuous variables, establishing a $p<0.05$ as significant.

Results: In total 48 patients, middle age 49 years (20-76), female 38 (79.2%), with no previous history 29 (60.4%) metabolic syndrome 33 (68.8%) diabetic 19 (39.6%) obesity 27 (56.3%) The CAP for steatosis evaluation: S1, 4 (8.3%) S2, 20 (41.7%) and S3, 24 (50%), for degree of liver fibrosis in Fibroscan: F0, 33 (68.8%) and F1, 14 (29.2%) and by FIB4 scale (<1.30) with NAFLD scale indeterminate fibrosis. The median CT/HDL ratio is not higher with the degree of CAP per FibroScan, being S1, 3.9 (3.1- 4.1) S2, 3.8 (2.3- 6.8) S3, 4.5 (3.1-7.2), (p 0.076). The higher the median TG/HDL ratio, the higher the degree of CAP per FibroScan, being S1, 2.3 (1.6- 2.7) S2, 3.8 (0.9- 7.9) S3, 4.6 (2-16.9) p value 0.008. It was associated that the higher the degree of CAP per Fibroscan, the higher the triglyceride levels above the normal upper value and the greater the association of presenting metabolic syndrome with a p value of 0.009 and 0.003 respectively. (see table)

Discussion: Higher levels of the TG/HDL ratio, elevated triglyceride levels, and the presence of metabolic syndrome increase the degree of CAP in this group of NAFLD patients. This study the largest population was female (79.2%) so it cannot be inferred that the TG/HDL ratio and degree of CAP is relevant for male sex, so more studies should be carried out and these variables determined. This study has as a limitation that it was carried out in a single hospital center so the cohort sample should be increased and carried out prospectively to really determine whether or not it has utility CT/ HDL relationship in NAFLD, since in this study a result was obtained without statistical significance.

Conclusions: The CT/HDL ratio was not associated with the degree of CAP by Fibroscan. It was determined that the higher the median TG/HDL ratio, the higher the degree of CAP in Fibroscan. However, it is necessary to consider this study in patients with high

body mass index lowers its sensitivity and specificity, so it should be performed with other advanced imaging modalities.

The authors declare that there is no conflict of interest.

Table
Relationship of CT/HDL, TG/HDL, lipid profile and metabolic syndrome with the degree of CAP by FibroScan

Parameters	Degree of CAP by FibroScan			P-value
	S1	S2	S3	
Triglycerides[a]	111.5 (14.82)	178.75 (64.5)	236.41 (113.10)	0.009
HDL cholesterol[a]	51.02(9.09)	46.49(10.17)	41(9.24)	0.068
LDL cholesterol[a]	126.75 (29.47)	113.72 (31.55)	115.94 (27.08)	0.331
Total cholesterol[a]	193 (48.10)	180.95(40.5)	188(38.68)	0.781
CT/HDL Ratio[b]	3.9 (3.1-4.1)	3.8(2.3-6.8)	4.5(3.1-7.2)	0.076
TG/HDL Ratio[b]	2.3 (1.6-2.7)	3.8 (0.9-7.9	4.6 (2-16.9)	0.008
Metabolic syndrome[c]				
Yes	1 (2.9)	13 (38.2)	20 (58.82)	0.003
No	3 (21.42)	7 (50)	4 (28.5)	

a: mean (standard deviation) b: median (ranges) c: number (percentage)
LDL: Low Density Lipoprotein HDL: High Density Lipoprotein

https://doi.org/10.1016/j.aohep.2021.100643

DIFFERENTIAL PROFILE OF PRO-INFLAMMATSORY / ANTI-INFLAMMATORY CYTOKINES AND MALONDIALDEHYDE IN PATIENTS WITH ALCOtHOL-INDUCED OR OBESITY OR MIXED INJURY

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Introduction and Objectives: Dysregulation of pro-inflammatory/anti-inflammatory cytokines and oxidative stress markers has been reported in Non-Alcoholic Steatohepatitis (NASH) and alcoholic steatohepatitis (ASH); however, in the disease recently known, as Both Alcoholic and Non-Alcoholic SteatoHepatitis (BASH) that meets the criteria of ASH and NASH have not been described. The objective was to evaluate the influence of alcohol and obesity on a differential profile of cytokines and malondialdehyde (MDA) in patients with these etiologies.

Material and methods: Cross-sectional, prospective, observational study. Patients from the "Dr. José E. González" from March 2019-March 2020, with a diagnosis of ASH (alcohol consumption ≥ 5 years, 30 g/day for men and 20 g/day for women), NASH (demonstrated by ultrasound, FibroScan or FibroMax) and BASH (ASH and NASH criteria). The serum cytokines interleukin-8 (IL-8), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-α), interleukin-1β (IL-1β), interleukin-10 (IL-10) and malondialdehyde (MDA) were determined. The protocol was approved by the ethics committee with registration MI19-000016.One-way analysis of variance was performed with Kruskal-Wallis and Dunn's post hoc. The results were expressed as median (interquartile range). The analysis was performed using Graph Pad Prism (v. 7.04, San Diego, CA, USA). A value of $p<0.05$ was considered significant.

Results: The patients were: 34 BASH, 43 NASH and 35 ASH. The severity of the patients with respect to clinical and biochemical parameters in increasing order was NASH <BASH <ASH. It was observed in increasing order that the levels of the cytokines IL-8, IL-6, IL-10 were: NASH <BASH <ASH; TNF-α levels were: BASH <NASH <ASH; IL-1β levels show no significant difference between groups (Figure). The BASH group showed higher concentration levels of MDA [20.00 (9.00-30.50) pg/mL] with significant difference (p = 0.0434) compared to NASH [14.00 (3.00-19.00) pg/mL], but not with ASH (Figure). Serum levels of IL-6 (A; p <0.0001), TNF-α (B; p=0.0014), IL-8 (C; p<0.0001), IL-10 (D; p<0.0001) and IL-1β (E; Not significant) in the different study groups.

Discussion: In ASH and NASH, common pathogenetic mechanisms mediated by pro-inflammatory.

The authors declare that there is no conflict of interest.

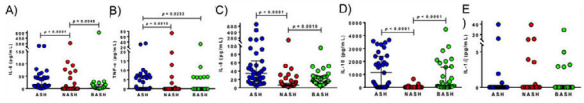

Figure. Serum levels of IL-6 (A; p <0.0001), TNF (B; p= 0.0014), IL-8 (C; p<0.0001), IL-10 (D; p<0.0001) and IL-1β (E; NS) in the different study groups. The values were expressed as median (interquartile range). NS: not significant.

https://doi.org/10.1016/j.aohep.2021.100644

PROFILE OF PRO AND ANTI-INFLAMMATORY CYTOKINES IN PATIENTS WITH CHRONIC LIVER DISEASE IN THE COMPENSATION, INFLAMMATION AND IMMUNOSUPPRESSION PHASES

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Introduction and objectives: Decompensated cirrhosis is defined by the onset of complications and is associated with immune dysfunction. This is the result of two processes: systemic inflammation and damage made by the immune system. Our objective was to determine the profile of pro and anti inflammatory cytokines in patients with chronic liver disease: alcoholic (OH), non-alcoholic steatohepatitis (NASH), autoimmune liver disease (AILD) and hepatitis C (HCV), in the phases of compensation, inflammation and immunosuppression, based on functional classifications and prognosis with the CHILD- PUGH, MELD and D'Amico scales.

Methods and materials: Prospective, observational, and cross-sectional study, made in the University Hospital, Dr. Jose E. Gonzalez during 2019-2020. A total of 108 patients were included: 28 OH, 27 NASH, 25 HCV and 27 AILD. The diagnosis and functional classification was made according to international guidelines. Inclusion criteria: over 18 years of age, signed informed consent. Exclusion criteria: hepatocellular carcinoma, other autoimmune pathologies. Blood samples (10 ml) were collected to quantify TNF-a, IL-8, IL-10, IL-1, IL-6. The protocol was approved by the ethics committee with registration MI20-0002. A one-way ANOVA was used to determine the differences between groups and stages

Results: In OH, there is an increase in IL-6 and IL-8 in the decompensation phase, Child-Pugh stage C, D'amico stage 5 and MELD from 25 to 34 points. NASH patients had an increase in IL-8 in the inflammation phase as assessed by Child-Pugh B and D'amico 3 and 4. There was an increase in IL-6 in the immunosuppression phase. In patients