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Conflict of interest: No

Introduction and Objectives: A high density of liver mast cell is associated to liver damage progression in chronic liver diseases. Emerging evidence have suggested that MC degranulation play a crucial role in liver fibrosis induced by hepatic stellate cells (HSCs) activation. However, the contribution of neuroimmune activation of MC by stress related neuropeptide Substance P(SP)remains unexplored. *Objective:* To evaluate the impact of SP-dependent MC activation in HSCs transdifferentiation.

Patients / Materials and Methods: In vitro studies were performed by using Human mast cell line (HMC-1), stimulated with SP (30min), and HSCs cell line (LX-2), subsequently stimulated by 24h with supernatants of SP-MC activated. Supernatants of unstimulated (ns) MC and MC stimulated with 48/80 compound, as well as a direct LX-2 SP (dSP) stimulation were considered as experimental control. Western blotting was performed to measure alfa-smooth muscle actine (α-SMA) expression level, a HSCs transdifferentiation marker, and GADPH, as loading control. A direct stimulation of HSCs by tryptase for 24h and subsequent α-SMA immunostaining by indirect immunofluorescent was performed for qualitative assessment of HSC morphology. Statistical analyses: ANOVA test in experimental replicates (N=3), by using GraphPad Prisma. Significance was set at $p<0.05$.

Results and Discussion: Despite not statistically differences were observed infold change α-SMA/GADPH level expression among SP stimulated MC and other experimental groups (ns MC, 0.394 ± 0.08; 48/80 MC, 0.256 ± 0.130; SP MC, 0.274 ± 0.120; dSP, 0.621 ± 0.524) p=0.544, morphological changes of HSCs associated to cell transdifferentiation were observed after 24h of tryptase stimulation.

Conclusions: Our results shown that MC tryptase can induce HSCs transdifferentiaton. Short-term effect of SP-MC activation fail to achieve in HSCs activation, suggesting long term MC stimulation need to be explored to evaluate SP-MC impact in HSCs transdifferentiaton. Funding OAIC n°13022.

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P-22 URINARY BIOMARKER NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (NGAL) FOR IDENTIFYING ACUTE KIDNEY INJURY IN PATIENTS WITH SEVERE ALCOHOLIC HEPATITIS AND CIRRHOSIS

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Conflict of interest: No

Introduction and Objectives: Patients with hepatic cirrhosis (HC) and severe alcoholic hepatitis (AH) are at risk of developing acute kidney injury (AKI) due to multiple factors. The main phenotypes of AKI include hypovolemic, acute tubular necrosis (ATN), hepatorenal syndrome (HRS), and miscellaneous types. The urinary biomarker Neutrophil Gelatinase-Associated Lipocalin (NGAL) may be useful for differential diagnosis, as it is an early-produced protein at the renal tubular level.

The objective of this study is to establish the correlation between urinary biomarker NGAL levels and the phenotype of acute kidney injury in cirrhotic patients with severe alcoholic hepatitis.

Patients / Materials and Methods: Descriptive, retrospective, and analytical study of patients with a diagnosis of severe alcoholic hepatitis with cirrhosis, acute kidney injury classified by AKI-ICA (Acute Kidney Injury Criteria-International Club of Ascites), and urinary NGAL values. Three groups were compared: one with hypovolemic AKI, the second group with ATN-type AKI, and a control group of 55 patients with non-alcoholic cirrhosis and ATN-type AKI. *Statistical analysis:* Data are presented as Mean $\pm$ SD or Median (IQR 25-75). Univariate analysis was conducted to compare AKI phenotypes (hypovolemic, ATN, and non-alcoholic etiology ATN with a cohort of 55 patients) with MELD and Child-Pugh as cofactors; significance was considered at ≤ 0.05.

Results and Discussion: A total of 102 patients were included with an average age of 45 (39.7-51) years; 93 (91.17%) were men and 9 (8.82%) were women. Cirrhosis was classified as Child-Pugh A: 4 (3.92%), B: 5 (4.9%), and C: 93 (91.17%). Severe Alcoholic Hepatitis had a MELD score of 32 (26-39) points, a modified Maddrey score of 58.9 (44.9-102.2) points, an ABIC (Age-Bilirubin-INR-Creatinine) score of 8.5 ± 1.4 points, and a Glasgow score of 9 (8-10) points. Acute kidney injury was present in 74.5% (n=76) of cases with the following AKI-ICA grades: 1A: 9 (8.82%), 1B: 9 (8.82%), 2: 17 (16.66%), and 3: 41 (40.19%). The phenotypes were: Hypovolemic AKI: 50 (65.78%), Acute Tubular Necrosis (ATN): 23 (30.26%), and Hepatorenal Syndrome: 3 (3.94%).

The mean NGAL levels for the acute kidney injury phenotypes were hypovolemic 79.64 ± 61.73, ATN 857.79 ± 914.95, and non-alcoholic etiology ATN 743.09 ± 971.39. Significant differences were found between groups $F(74,1)=30.54$ $p\leq.001$; comparisons between groups were important for hypovolemic acute kidney injury vs. ATN $p\leq.001$; hypovolemic acute kidney injury vs. non-alcoholic ATN $p\leq.001$, and not significant between ATN groups p=0.806 (Figure 1).

Conclusions: There is a relationship between urinary biomarker NGAL values and the hypovolemic acute kidney injury phenotype compared to ATN in cirrhotic patients with severe alcoholic hepatitis and ATN of other etiologies; it is an early biomarker of renal damage useful for establishing severity and prognosis.

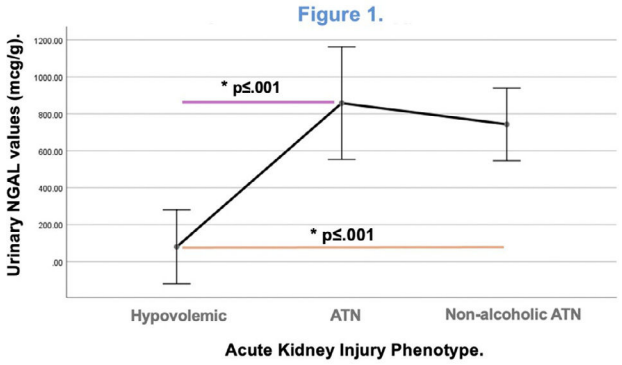

Figure 1. Univariate analysis of AKI phenotypes (hypovolemic, ATN, and Non-alcoholic ATN etiology) with NGAL values.

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P-23 PORTAL VEIN THROMBOSIS IS ASSOCIATED WITH HEPATIC DECOMPENSATIONS WITHOUT LIVER STIFFNESS INCREASE IN HEPATOSPLENIC SCHISTOSOMIASIS

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Conflict of interest: No

Introduction and Objectives: Hepatosplenic schistosomiasis (HSS) is one of the main causes of non-cirrhotic presinusoidal portal hypertension. Although liver stiffness in HSS is typically lower than in cirrhosis, it is still unknown if over the years liver injury related to periportal fibrosis, to metabolic disease or vascular complications can alter liver stiffness and impact in serious hepatic events. This study aims to determine whether metabolic factors, portal vein thrombosis (PVT), or changes in liver stiffness over time are associated with serious hepatic events (SHE) in HSS patients.

Patients / Materials and Methods: In this prospective study, adults with laboratory and radiologically confirmed HSS, without concurrent cirrhosis or other liver diseases, were included. All participants underwent initial transient elastography, followed by a second assessment after at least 3 years. The primary outcome was the occurrence of SHE, defined as upper variceal bleeding and/or ascites.

Results and Discussion: Among the 26 patients studied, 65.4% were male, with a mean age of 55 ± 9 years. The main metabolic comorbidities were obesity (27%), hypertriglyceridemia (8%), low HDL-c (4%), and diabetes (13%). Baseline liver stiffness measurement (LSM) was 9.9 kPa (±3.9) and the controlled attenuation parameter (CAP) was 238 dB/m (IQR 121-270). After a median follow-up of 59 months (IQR 51-64), serious hepatic events occurred in 46% of the patients. There was a non-significant median absolute increase in LSM of 1.4 kPa (IQR -1.5 to +3.6) and a median relative increase of +14% (IQR -17% to +50%), with no statistically significant differences in paired analysis (p = 0.140). No metabolic or anthropometric factors were associated with changes in liver stiffness. PVT occurred in 7 patients (26.9%) and was the only factor significantly associated with the occurrence of serious hepatic events (p = 0.026), although it did not significantly interfere with LSM (p = 0.842).

Conclusions: LSM remained relatively stable in HSS patients over a median follow-up of almost 5 years, proving to be a useful tool in distinguishing HSS from cirrhosis. SHE were primarily associated with PVT, which may further elevate portal pressure.

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P-24 DESCRIPTION OF SERUM MICRORNAS EXPRESSION AMONG INDIVIDUALS WITH VIRAL HEPATITIS AND LONG COVID

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Conflict of interest: No

Introduction and Objectives: Long COVID syndrome affects millions of people and is characterized by the permanence of signs and symptoms after 90 days of SARS-CoV-2 infection. MicroRNAs (miRNAs) are small non-coding RNAs that are related to different conditions and can characterize profiles including liver disease. OBJECTIVES: Characterize the serum expression of miRNAs in relation to viral hepatitis B and C and Long COVID.

Patients / Materials and Methods: Serums were obtained from 69 individuals from 4 groups: (i) only Long COVID (n=18); (ii) Viral Hepatitis/Long COVID (n=21); (iii) only Viral Hepatitis (n=10) and (iv) control individuals (n=20). MiRNAs were isolated using a commercial extraction kit and miR-122, miR-143 and miR-223 were evaluated using quantitative real-time PCR. The expression of the examined genes was calculated from the formula RQ = 2-ΔΔCT. Statistical analysis was carried out using GraphPad Prism 9.5.1 software.

Results and Discussion: The upregulation of the miRNAs analyzed was observed in the groups with diseases compared to the control, all with statistical significance (p<0.05). Of the groups with diseases, the Viral Hepatitis/Long COVID group showed the highest expression of all three miRNAs analyzed. For miR-122, the Viral Hepatitis/Long COVID and only Viral Hepatitis groups were up-regulated with mean RQ of 100.38 ± 122.06 and 80.72 ± 173.16, respectively, compared to the control 3.20 ± 8.75 (p<0.05). For miR-143 and mir-223, the highest expression was in the Hepatitis/Long COVID (mean RQ: 316.36 ± 572.96 and 270.45 ± 558.55, respectively) followed by the only Long COVID group (mean RQ: 158.12 ± 262.42 and 115.65 ± 191.30, respectively), both with statistical significance when compared to the control (mean RQ: 4.12 ± 5.37 and 3.78 ± 8.5, respectively).

Conclusions: The presence of disease affects the expression of these miRNAs when compared to healthy individuals. The description of these targets will contribute to the understanding of Long COVID and its association with other diseases.

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