Participation of the immune response and oxidative stress in alcoholism and liver cirrhosis due to alcohol

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Introduction and Objectives: The spectrum of alcoholic liver disease (ALD) includes steatosis, steatohepatitis, alcoholic hepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma. The pathophysiology of liver damage due to chronic alcohol consumption is complex. It is partly a result of reactive oxygen species (ROS) and reactive nitrogen species (RNS), products of oxidative stress, which is one of the mechanisms that will activate the immune system creating a pro-inflammatory state, increasing the levels of several cytokines (TNF-α, IL-1, IL-6, IL-8, MCP-1 and TGF-1).

Objective: To study oxidative stress and the production of proinflammatory cytokines that intervene in the different stages of liver damage due to alcohol (alcoholism, alcohol-related liver cirrhosis, and alcoholic hepatitis).

Material and Patients: A cross-sectional, prospective, and analytical study that included patients from the Gastroenterology service and donors from the Blood Bank. Patients at different stages of the disease and a control group of healthy subjects (blood bank donors) were included. They were divided into 4 groups: Alcoholism (OH), alcoholic liver cirrhosis (CiOH), alcoholic hepatitis (HA), and healthy controls (CT). From each participant, 20 ml of peripheral blood was obtained for the relevant determinations. Normally distributed data were obtained and ANOVA and orthogonal analyses were performed to detect group differences. A U-Mann Whitney test was used. $P < 0.05$ was taken as a significant difference.

Results: 236 subjects were included: 67 patients in OH group; 40 patients with CiOH; 39 patients with Alcoholic Hepatitis (AH), and 90 subjects CT. The gender distribution in patients with ALD (CiOH, and HA) was 77.5% men and 22.5% women. The average alcohol consumption was 376.6±151.6 grams. The CiOH and HA groups presented alterations in platelets, bilirubin, and cytolysis markers at the expense of AST with a significant difference ($p<0.05$). Regarding oxidative stress, lipoperoxidation was greater in patients with chronic disease (CiOH) and protein damage (protein carbonyls) was greater in HA with $p<0.05$. Regarding cytokines and chemokines, TNF-α presented a higher level in CiOH and HA ($p<0.5$), IL-6 presented an elevation in CiOH and HA ($p<0.05$); IL-10 was elevated in OH, CiOH and HA, MCP-1 and IL-8 showed greater elevation in HA, $p<0.05$.

Conclusions: Oxidative stress and the elevation of proinflammatory cytokines and chemokines have different behaviors in the various stages of alcohol liver disease, which influences the progression and prognosis of the disease. These findings could be considered as possible therapeutic targets.

Ethical statement: Each patient has explained the research in detail. Those who decided to participate signed the informed consent letter.

Declaration of interests: None.

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Table 1
Demographic and biochemical characterization of the study groups.

	OH (67)	CiOH (40)	AH (39)	CT (90	P*
Gener (n) (%)					
Female	21(31)	2(5)	2(5)	28(26)	
Male	46 (69)	38(95)	37(95)	62(74)	b*, c*
Age	46 ±10	47±8	38±7	38±10	a*, b*, e*
BMI	27±7	27±7	27±5	28±4	
gr OH/day	320±125	350±130	460±200	1.3±2	a*, b*, c*
Hb (gr/dL)	14±4	12±3	11.2±0.5	17±1	a*, b*, c*
Platelets (1000 × 3)	205±95	138±90	93±36	268±65	b*, c*
BT (mg/dL)	2.3±1.1	3±0.4	18.8±2.4	0.8±0.03	a*, b*, c*, f*
BD (mg/dL)	1.4±0.5	1.8±0.2	8.6±1.9	0.7±0.03	a*, b*, c*
AST (U/L)	39±10	63±6	142±17.9	30±1	b*, c*, f*
ALT (U/L)	31±5	37±3	57.1±5.4	28±2	b*, c*, f*
GGT (U/L)	70.8±21.9	206±48.8	254±74.8	29.6±2.8	a*, b*, c*, e*

(OH= Alcoholic, CiOH= alcohol cirrhosis, AH= Alcoholic hepatitis, CT= control). Statistical differences: **a**. OH vs CT, **b**. CiOH vs CT, **c**. HA vs CT, **d**. OH vs CiOH, **e**. OH vs HA y **f**. CiOH vs HA. *p < 0.05

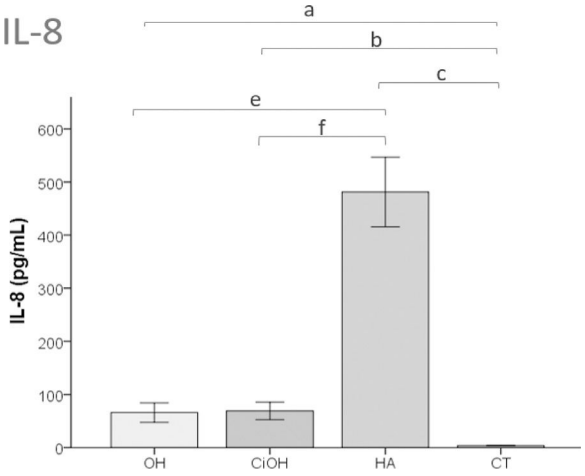

Figure 1. Interleukin IL-8.
(OH= Alcoholic, CiOH= alcohol cirrhosis, HA= Alcoholic hepatitis, CT= control). Statistical differences: a. OH vs CT, b. CiOH vs CT, c. HA vs CT, d. OH vs CiOH, e. OH vs HA y f. CiOH vs HA. *p < 0.05

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Patterns of antimicrobial resistance and susceptibility in patients with spontaneous bacterial peritonitis at the General Hospital of Mexico "Dr. Eduardo Liceaga"

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Introduction and Objectives: Spontaneous bacterial peritonitis (SBP) is a serious complication in cirrhotic patients, with high morbidity and mortality. Antimicrobial resistance complicates treatment and increases complications. This study aims to determine resistance patterns in microorganisms in SBP to improve treatment efficacy.

Materials and Patients: A descriptive, observational, and retrospective study on patterns of antimicrobial resistance and

susceptibility in patients with spontaneous bacterial peritonitis was conducted at the General Hospital of Mexico "Dr. Eduardo Liceaga" between January 2022 and January 2024. Clinical information was collected from the records of the Gastroenterology Service. Microbiological results were obtained from reports from the Microbiology Service. Patients diagnosed with hepatic cirrhosis and meeting the criteria for SBP were included. Clinical and microbiological data were collected, analyzing variables such as age, sex, etiology of liver disease, and associated decompensations, such as gastrointestinal bleeding and hepatic encephalopathy. Antimicrobial resistance patterns, as well as clinical and microbiological characteristics of patients with SBP, were examined. This analysis aims to contribute to the optimal management of SBP and the development of more effective antimicrobial treatment strategies.

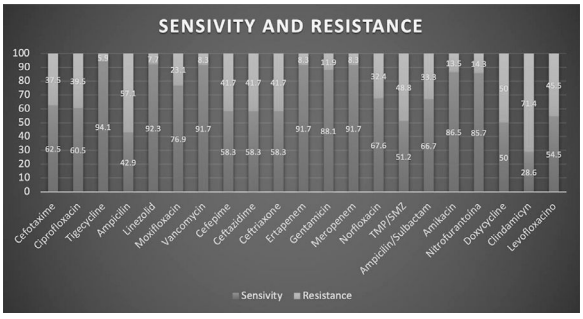
Results: A total of 48 patients were included, 52.1% were men, with a mean age of 52.4 ± 12.7 years. The predominant etiology of cirrhosis was alcohol, present in 56.3% of cases. Among the isolated bacteria, Escherichia coli (56.25%), Klebsiella pneumoniae (12.5%), Enterococcus faecalis (6.25%), Streptococcus spp. (6.25%), Staphylococcus epidermidis (4.16%), Staphylococcus aureus (4.16%), Enterococcus gallinarum (4.16%), Staphylococcus marcescens (2.08%), Acinetobacter sobria (2.08%), and Staphylococcus haemolyticus (2.08%) were prominent. The sensitivity and resistance table to different antimicrobials are presented in Graph 1.

Conclusions: Antimicrobial resistance is increasing in patients with SBP, leaving few effective alternatives, where cephalosporins and quinolones, recommended treatments, are no longer sufficiently useful, which is dangerous in the context of empirical therapy given the high risk of therapeutic response failure.

Ethical statement: This study was reviewed and approved by the ethics committee.

Conflict of Interest: None.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.



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Ceftriaxone versus cefotaxime in the treatment of spontaneous bacterial peritonitis

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Introduction and Objectives: Infections in cirrhotic patients occur in one-third of hospitalized patients. Spontaneous infections (spontaneous bacteremia, spontaneous bacterial peritonitis (SBP), and spontaneous empyema) are the most common and their management with third-generation cephalosporins (cefotaxime or ceftriaxone) is recommended. The effect of albumin on in vitro antimicrobial activity is greater for cefotaxime.

Materials and Patients: This is a retrospective, observational, and analytical study. We included clinical records of patients admitted to the Gastroenterology service of the Hospital General de México "Dr. Eduardo Liceaga" from March 2021 to February 2024 with a diagnosis of SBP ≥ 250 polymorphonuclears (PMN), comparing two different treatments (cefotaxime 2gr c/12 hours vs ceftrixone 1 or 2gr/day) and follow-up one year after the event. We evaluated the response to treatment with a second paracentesis with 48 hours of antibiotic therapy. We determined the recurrence at 12 months and the relationship with serum albumin levels in treated patients. We excluded patients with secondary bacterial peritonitis, tuberculosis or carcinomatosis, and previous antibiotic use (except rifaximin). Qualitative variables were expressed as frequencies and percentages; numerical variables as means and standard deviation. We used X2, Student's t-test, and Mann-Whitney U to compare the variables. To compare the percentages of deaths per treatment, response rate, and recurrences at one year, we used the Z test for contingency tables. The log-rank test and the Kaplan-Meier survival curve were used to evaluate survival per treatment at 30 days. A value of $P < 0.05$ was considered statistically significant.

Results: Out of 950 hospitalized cirrhotic, 6.42% (61) presented SBP. 63.9% were male and aged 52±11.9 years. Etiology of cirrhosis, 39.3% alcohol, 26.2% unfiliated, 14.8% MASLD, and 8.2% autoimmune hepatitis. Comparing groups, 29 patients with cefotaxime and 32 with ceftriaxone, with no differences concerning Child-Pugh, MELD score (23 vs 31, p=0.07), acute on chronic liver failure (ACLF) (56.5% vs 43. 5%, p=0.79), ACFL points (55 vs 53, p=0.52), leukocytes, PMN and DHL levels in ascites fluid (p=0.55, p=0.45 and p=0.52), and serum albumin (2.32g/dl vs 2.26gr/dl, p=0.71). An equal response rate was observed at 28/32 (87.5%) for cefotaxime and 26/29(89.7%) for ceftriaxone with no statistical differences between groups. The recurrence rate was similar with 3 cases for each group with no differences between them. The mortality rate was 14/61(23%); 4/32(12.5%) for cefotaxime and 10/29(34.5%) for ceftriaxone with statistical differences between groups. At 30 days total mortality was 9/61(14.8%) with 2/32(6.2%) for cefotaxime and 7/29 (24.13%) for ceftriaxone with no difference between groups Log-Rank(1) = 3.75 p=0.053.

Conclusions: The ceftriaxone or cefotaxime is equally effective in patients with SBP, with no difference in ACLF, serum albumin level, or ceftriaxone dose(1-2gr/day). The recurrence rate was similar between both treatments, with a tendency towards higher mortality for ceftriaxone without differences in terms of etiology, ACLF, or the severity of cirrhosis.

Ethical Statement: Retrospective study, the identity of the patients was kept secret at all times.

Declaration of interests: None.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

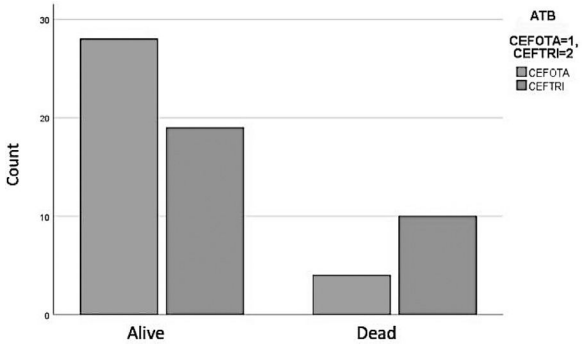

Figure 1. Bars expressing patients who survived or died with respect to type of antibiotic.

Source: Data extracted from records of the Gastroenterology service of the Hospital General de México "Dr. Eduardo Liceaga".