International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2016): 79.57 | Impact Factor (2017): 7.296

Is SIRS a Predictive Factor of Mortality in Cirrhotic Patients?

A. Benayad[1], S. Oubaha[2], K. Krati[3], Z. Semlani[4]

Hepato-Gastroenterology Department, Mohamed VI University Hospital , Marrakech, Morocco

Abstract: ***Introduction: Systemic inflammatory response syndrome (SIRS) is a common condition in patients with cirrhosis of the liver. This condition predisposes to deterioration of liver function and serious effects on the course of the disease with significant morbidity and mortality. Patients and methods: This is a retrospective study performed in the hepatogastroenterology department of Mohamed VI University Hospital of Marrakech over a 2-year period from 2016 to December 2017, including all cirrhotic patients whose diagnosis was was established on clinico-biological, endoscopic and morphological criteria, and who were hospitalized for decompensation of cirrhosis, the analysis was made on the data of their last hospitalization. The Child-Pugh and MELD scores were calculated, systemic inflammatory response syndrome (SIRS) was systematically sought, the statistical analysis was performed by the FISHER software in uni-varied and multi-variate analysis. Results: 188 patients were cirrhotic in decompensation, of which 56 presented the SIRS (30%) the overall mortality rate was 11% or 18 patients, 15 of them met the criteria of SIRS. SIRS patients had a high bacterial infection prevalence (p = 0.008), and a higher prevalence of jaundice (p <0.001), SIRS was also associated with low hemoglobin <9g / dl (p = 0.004), elevated serum creatinine in a unified analysis; mortality rate was associated with infection (p = 0.003), association with hepatocellular carcinoma (p = 0.0018), gastrointestinal bleeding (p = 0.0028), hepatic encephalopathy (p = 0) , 001), ethylism (p = 0.05); age> 80years (p = 0.032). Conclusion: in our experience, SIRIS was the most important predictor of hospital mortality in our cirrhotic patients***

Keywords: cirrhosis, SIRIS, infection, hospital mortality, prognosis

1. Introduction

Systemic Inflammatory Response Syndrome (SIRS) is a common condition in patients with cirrhosis of the liver, it can further impair liver functions and have serious effects on the course of the disease with significant morbidity and mortality. [1,2]. This increase in mortality can reach 4 times in cirrhotic patients: 30% of patients die in the month following infection and 30% die within one year [2,4]. The most common serious effects on the course of cirrhosis of the liver are hypertensive bleeding and hepatic encephalopathy [3].

Purpose: The purpose of this study was to determine the prevalence of systemic inflammatory response syndrome in patients with liver cirrhosis and its impact on liver and kidney function

2. Patients and methods

It is a retrospective study carried out at the hepato-gastroenterology department of Mohamed VI University Hospital of Marrakech over a period of 3 years from 2015 to February 2018; we included before all cirrhotic patients whose diagnosis was established on clinico-biological, endoscopic and morphological criteria, and who were hospitalized for decompensation of cirrhosis and excluded all the patients having other comorbidity which can explain the mortality in particular terminal extra-hepatic diseases (pulmonary or cardiac decompensation, metastatic cancer)

The prognostic scores used were the Child-Pugh score and the MELD score

Depending on the type of decompensation and the triggering factors, the therapeutic management was carried out according to the recommendations of the European scholarly society (EASL), the American society (AASLD) and the BAVENO VI consensus, in fact in case of suspicion of a factor or a Infectious focus and according to the sign of call an infectious assessment was systematically made made of a thorax radio; cyto-bacteriological examination of the urine, ascitic fluid and a vaginal sample; in case of febrile peak (T °> 38.5) blood cultures were performed; in the case of gastrointestinal bleeding, management was based on the administration of vasoactive agents as medical treatment, and endoscopic treatment consisting of ligation of oesophageal varices or filling with biological glue and antibiotic prophylaxis, blood transfusion was discussed. according to the clinico-biological tolerance of the patient; in patients with hepatic encephalopathy patients were on oral lactulose and rifaximin; infection of the ascitic fluid was treated with antibiotic therapy with cyclosporine 3 rd generation and albumin infusion to prevent hepatorenal syndrome.

The SRIS was defined according to recommendations of the American College of Thoracic Doctors / Society of Critical Care Medicine Consensus Conference [6] by the presence of at least two of the following clinical or biological signs: temperature> 38.8C or <36 8C; heart rate> 90 / min, respiratory rate> 20 / min and / or PaCO2 <32 mm Hg; leukocytosis> 12,000 or <4,000 / mm3 or presence of more than 10% circulating immature forms. These parameters were systematically sought at admission and during the hospitalization of the patient.

The statistical analysis was performed by the SAS software in uni-varied and multi-variate analysis

3. Results

During the period of our studies; We could collect 188 cirrhotic decompensated and hospitalized in our department, the male sex was predominant with a sex ratio (M / f) at 1.6 the average age was 69 years with extremes ranging from 45 years to 89 years. years, 15 patients had a history of chronic hypertension (hypertension) under treatment a patient was followed for heart failure with atrial fibrillation cardiac arrhythmia (ACFA), three patients were followed for dysthyroidism, 13 patients were diabetic type I and 22 patients diabetic type II. The main risk factors for hepatic viral transmission in our patients involved informal dental care in 38 patients with scarification in 22 patients and unprotected sex in 16 patients.

The etiology of cirrhosis was predominated by viral etiology; autoimmune pathology, alcoholic steatosis, nonalcoholic steatosis; respectively 45% of cases (HVB in 32%, HCV in 44%, HCV infection-HVC 12%), 6%, 11%; 2%, 3% and in 30% of patients the etiology was not determined following an incomplete etiological assessment due to the urgency of hospitalization.

Cirrhosis was ranked C in 34% of patients, score B in 38% and score A in 28% of cases; the mean MELD score was estimated at 18.9 [6- 42].

The most common decompensation that led to hospitalization was gastrointestinal bleeding associated with rupture of oesophageal varices and gastric (71%), ascites decompensation including ascites fluid infection (ISLA) (32%), hepatic encephalopathy (6%) and jaundice decompensation in 19%, the infectious focus isolated outside the ISLA was pulmonary, urinary, cutaneous, gynecological infection respectively 3.2%, 2%, 1%; the identified germs was klebsiella pneumonia n = 3, Escheichia coli n = 1

The duration of hospitalization was estimated at 6 days (1 - 10 days), transfer to intensive care was carried out in 71% of cases the overall mortality rate was 11%

56 patients responded to at least two of the SIRS diagnostic criteria as recommended by the American College of Thoracic Doctors / Society of Critical Care Medicine Consensus Conference [6].

Demographic, clinical, and biochemical data for patients with and without SIRS are shown in Table I. In fact, 56 patients with SIRS had a prevalence of high bacterial infection requiring hospitalization ($p = 0.008$), and a higher prevalence of jaundice ($p < 0.001$), SIRS was also associated with a low hemoglobin level <9g / dl ($p = 0.004$), elevated serum creatinine, elevated serum potassium, alanine aminotransferase (ALT), higher serum bilirubin levels, and a CRP> 20mg / l were also associated with SIRS with a statistically highly significant correlation ($p < 0.001$)

In our study, 83% of patients with SIRS died, the infection was associated with high mortality, in fact, patients with sepsis or septic shock and having a high white blood cell, high CRP, had a high high risk of mortality compared to uninfected patient, in a uni-variety analysis; the mortality rate was associated with the following variants with statistically significant values: the association with hepatocellular carcinoma ($p = 0.0018$), gastrointestinal bleeding ($p = 0.0028$), hepatic encephalopathy ($p = 0$, 001), ethylism ($p = 0.05$); age> 80 years ($p = 0.032$) (Table II)

The multi-varied analysis showed that the SIRS AND MELD are predictors of hospital mortality with odds ratios of 6.5 and 3.9 respectively

4. Discussion

We found that SIRS is a common complication rather than an association in patients with cirrhosis of the liver. It is associated with the onset of portal hypertension and negatively affects survival in patients with advanced cirrhosis. In support of these findings, Arvaniti et al. [4] concluded that mortality increases in patients with 38% infection: 30.3% at 1 month and 63% at 12 months [4]. In a recent study, Hong Zhao et al collected 222 cirrhotic, 40 deaths were recorded at the 28th day after the revelation of infection, male sex, circulatory failure, pulmonary insufficiency, bacterial infection were identified as factors independent mortality risk in cirrhotic patients with bacteremia. [5]

Although we have reported a significant correlation between SIRS and bacterial infection, many cirrhotic patients have been diagnosed with SIRS in the absence of a proven bacterial infection. Many explanations have been correlated to this hypothesis: intestinal bacterial proliferation and altered intestinal permeability in cirrhotic patients that lead to increased translocation of bacteria and endotoxin secretion in the portal circulation [6]. The altered phagocytic function of the reticuloendothelial system and the systemic porto shunt make it possible to reach high concentrations of endotoxin which are found in cirrhotic patients even without obvious infection [7]. Endotoxin activates monocytes and promotes the release of pro-inflammatory cytokines. Indeed, serum levels of interleukin-1 (IL-1), interleukin-6 (IL-6), tumor necrosis factor-a (TNFa), and interferon-c are elevated in patients with cirrhosis. proportion with the severity of liver disease.

Several evidence suggests that endotoxemia plays a central role in stimulating nitric nitric acid (NO) production or indirectly by the cytokine cascade, and is correlated with the concentration of NO of metabolites in cirrhosis [8] , 9].

Our results and many studies suggest that SIRS is correlated with acute renal failure [2,10]. This can be explained by the synthesis and release of cytokines in the case of SIRS leading to a systemic and renal hemodynamic disturbance and a hepatorenal syndrome. [11,12].

Several ongoing studies that the presence of SRIS is common during cirrhotic haemorrhage, are life-threatening [14, 15]. In addition, Cazzaniga et al. found a significant association between the occurrence of portal-related gastrointestinal bleeding and the presence of SRIS (18% vs. 0%, $p = 0.001$) [13]

SRIS favors hepatic encephalopathy, indeed in a single-centric prospective study, Rolando et al. [15], included over a period of 11 years and 887 patients hospitalized for acute liver failure. Patients with SIRI were hospitalized, infected, and at increased risk of severe hepatic encephalopathy (77% vs. 68%, p = 0.003). In ten cirrhotic patients, Shawcross et al. [16] by inducing hyperammonemia by administering an amino acid solution mimicking the composition of hemoglobin found a significant deterioration of neuropsychological tests, but only ... SRIS was already present. This can be explained by the influence of pro-inflammatory cytokines on the diffusion of ammonium into endothelial cells of the central nervous system and by the inhibition of glutamate uptake by astrocytes via nitric oxide to alter the glutamatergic neurotransmission; alterations in vascular permeability, described in both SRIS and cirrhosis, have favored hepatic encephalopathy by reducing cerebral blood flow [17,13]

We also noticed an association between SIRS and the Child-Pugh score, this finding is corroborated by the significant correlation between SIRS and serum bilirubin increase. In our study, 18 patients died during hospitalization, 15 of them had SIRS while the other patients died without SIRS. Again, consistent with this hypothesis, other investigators have shown that SIRS is independently associated with death in patients with advanced cirrhosis and gastrointestinal bleeding [6,18]. Our study also showed that by combining SIRS and the Child-Pugh score as two independent variables, it is possible to specify a patient sector with a high probability of mortality in the hospital.

5. Conclusion:

In current practice, SIRS research can assess the prognosis of cirrhotic patients, it is also important to look for infections in all hospitalized cirrhotic, as a result, this group of patients should be thoroughly examined, studied and closely monitored for infections to predict, prevent, diagnose early and treat this disease, broad-spectrum probabilistic antibiotic therapy may be warranted in subgroups of patients with SIRS even in the absence of documented infection at the risk of misdiagnosing an occult bacterial infection

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Table I: Demographic and Clinical Characteristics of Cirrhotic Patients with and without SIRS

	SIRS +	SIRS -	P
Age	46[27-89]	32[16-96]	0.07
Sexe H/F	0.58	0.7	NS
The etiology of cirrhosis			
-virale:	22	63	0.078
-dysummunitaire	2	9	NS
-éthylique	2	10	NS
- NASH	0	4	NS
-syndrome de budd –chiari	1	5	NS
Carcinome hépatocellulaire	26	52	0.089
The type of decompensation of cirrhosis:			
-ascitique	22	70	NS
-hémorragique	32	101	0.047
-ictérique	21	12	<0.001
-l'encéphalopathie hépatique	12	4	0.026
hépato - rénalSyndrome	42	21	0.0015
Isolatedinfectious :			
-ISLA	34	12	0.025
- Pulmonary infection	4	2	NS
-urinary-gynecological infection	3	1	NS
-skin infection	2	1	NS
- multiple sites of infections	11	4	<0.001
CRP (mg/l)	41 [16-92]	21 [2-32]	0.028
Biological elements:			
-hémoglobine(g/dl)	7.8 [4.4-12]	10.4 [8-16]	<0.001
-plaquette (10e/mm3)	109 [6-320]	199[143-387]	NS
-white blood cells(e/mm3)	7234.3[1120-24000]	11.274[4.000-13.000]	NS
-prothrombine (%)	52[17-92%]	39[7-72%]	NS
-bilirubine	21[3-249]	72[23-365]	<0.001
-ASAT (UI/L)	48[12-183]	46[12-102]	NS
-ALAT (UI/L)	31[12-206]	93[9-109]	<0.001
-albuminé (g/l)	22.5[21-37]	31.1[24-41]	<0.001
-créatine (mg/l)	11.1[12-62]	19.6[4-39]	<0.001
-NA+(mEq/l)	134.5[112-146]	130.7[117-147]	0.098
- K+ (mEq/l)	4.3[2.9-9.8]	4.9[2.6-6.8]	<0.001
CHILD Score:			
-A	2	41	NS
-B	14	25	0.045
-C	38	22	0.0018
MELD Score	16.5[6-36]	25[11-42]	0.0019

Table II: Predictors of Hospital Mortality by Univariate Analysis of 188 Patients

	Vivants(n=140)	Décès (n=18)	P
Age	56 [16-84]	82.9[52-89]	0.032
Sexe H/F	0.68	0.82	NS
The etiology of cirrhosis			
-virale	74	11	0.25
-dysummunitaire	10	2	0.098
-éthylique	20	1	0.05
- NASH	4	0	NS
-syndrome de budd –chiari	4	1	NS
Carcinome hépatocellulaire	63	15	0.018
The type of decompensation of cirrhosis:			
-ascitique	65	3	0.95
-hémorragique	119	11	0.028
-ictérique	22	15	0.058
-l'encéphalopathie hépatique	4	16	0.0017
hépatO – rénalSyndrome	47	15	0.0018
Isolated infectious :			
-ISLA	36	2	NS
- Pulmonary infection	5	1	NS
-urinary-gynecological infection	2	2	NS
-skin infection	3	0	NS
- multiple sites of infections	5	7	0.036

CRP	22[2-42]	48[18-92]	0.084
SIRS	9	15	<0.001
Sepsis	1	13	<0.001
Septicshock	0	9	<0.001
Biologicalelements:			
-hémoglobine(g/dl)	9.4 [4.6-16.3]	8.8 [4.8-13.6]	NS
-plaquette (10e/mm3)	133 [211-281]	116.10 [7-340]	0.06
-white blood cells (10e/mm3)	9.286[4.000-12.369]	23000[11200-24000]	0.04
-prothrombine (%)	56 [17-94%]	41 [7-83%]	0.08
-bilirubinE	83.0 [21-365]	31.3 [9-263]	0.035
-ASAT (UI/L)	95.8 [19-182]	32 [12-156]	NS
-ALAT (UI/L)	84 [24-206]	36 [9-190]	NS
-albumiNe (g/l)	23 [21-31]	38 [31-41]	NS
-créatinE (mg/l)	28 [9-62]	12 [4-49]	0.08
-NA+ (mEq/l)	128[110-139]	135[119-147]	NS
-K+ (mEq/l)	4 .9[2.5-6.9]	5.2[3.1-9.8]	NS
child Score:			
-A	51	0	0.001
-B	66	7	
-C	30	11	
MELD Score	15.1 [6-34]	25[12-42]	<0.0001