Systemic Inflammatory Response Syndrome and MELD Score in Hospital Outcome of Patients with Liver Cirrhosis

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ABSTRACT

BACKGROUND

The evidence saying that the rate of Systemic Inflammatory Response Syndrome (SIRS) is high in patients with advanced cirrhosis and portal hypertension, this could have negative outcome on patients prognosis.

METHODS

This prospective study included 109 cirrhotic patients who were admitted to Imam Khomeini Hospital, affiliated with Orumieh University of Medical Sciences, during 2011-2012. The presence of SIRS and the model for end stage liver disease (MELD) were assessed on admission and during the hospital stay. SIRS was considered positive if patients had two or more of the following: temperature of >38ºC or <36ºC; heart rate >90 beats/min; respiratory rate >20/min or PaCO2 <32 mmHg or the use of mechanical ventilation; WBC >12000/mm^3 or <4000/mm^3 or more than 10% immature neutrophil count. MELD was calculated as: MELD = 3.8 [Ln serum bilirubin (mg/dl)] +11.2 [Ln INR] +9.6 [Ln serum creatinine (mg/dl)] +6.4. Hospital outcome was defined as death or hospital discharge.

RESULTS

A total of 109 cirrhotic patients between the ages of 14 to 84 (mean: 54.6 ±18.4) years were included. There were 65 (59%) male patients. Of the 109 patients, 76 (69.8%) were SIRS-negative and 33 (30.2%) were SIRS-positive. The mean calculated MELD score for all patients was 15.5. There was a correlation noted between SIRS and high serum creatinine levels (p=0.01) and between SIRS and a high MELD score (p=0.00). During follow-up 19 (17.4%) patients died. SIRS was correlated with death (p<0.00) on multivariate analysis, SIRS was independently associated with hospital death.

CONCLUSION

SIRS is a relatively frequent event in cirrhotic patients admitted to referral centers. It is closely related to the severity of liver disease as shown by the MELD score. SIRS independently and adversely affects the in-hospital outcome in patients with liver cirrhosis.

KEYWORDS

SIRS; Cirrhosis; MELD; Hospital outcome

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Received: 10 May 2012
Accepted: 25 Jun. 2012

Please cite this paper as:
Behroozian R, Bayazidchi M, Rasooli J. Systemic Inflammatory Response Syndrome and MELD Score in Hospital Outcome of Patients with Liver Cirrhosis. *Middle East J Dig Dis* 2012;4:168-72.

INTRODUCTION

The evidence saying that the rate of Systemic Inflammatory Response Syndrome (SIRS) is high in patients with advanced cirrhosis and portal hypertension. This could have negative outcome on patients prognosis.[1] In cirrhotic patients inflammation has been shown to cause serious complications such as variceal bleeding, encephalopathy and worsening of previous liver failure.[2] Except for hepatocellular carcinoma (HCC) as a cause of death, liver and/or renal dysfunction is the main factors that determine patient's in-hospital outcome in advanced cirrhosis.[3,4]

Systemic inflammatory response syndrome (SIRS) is according to the recommendation of the American Collage of Chest Physicians/Society of Critical Care Medicine Consensus Conference.[5]

This complication can severely impact the model for end stage liver disease (MELD) score as it may cause acute or chronic liver failure, acute renal damage, clotting dysfunction, elevation in creatinine and INR levels, and might be associated with increased mortality.[1,6-10] MELD is a scoring system to predict patient survival based on the patient's bilirubin, creatinine and INR levels. We have hypothesized that the degree of chronic liver disease or cirrhosis and the level of liver function may also be affected by the incidence of SIRS in these patients.

In this study we aim to determine (i) the prevalence of systemic inflammation in an outcome of cirrhotic patients randomly admitted to our tertiary referral hospital, (ii) correlation of MELD scores to the presence or absence of SIRS, and (iii) their relationship with in-hospital outcome. The main endpoint was in-hospital death.

MATERIALS AND METHODS

This was a prospective study conducted in Imam Khomeini Hospital, affiliated with Orumieh University of Medical Sciences during 2011-2012. Approval for the study was granted by the Ethical Committee of Orumieh University were informed consents signed by patients for participating in the study.

A check list was used to collect data to calculate the MELD score, the presence of SIRS, and demographic characteristics of subjects that included age; sex; etiology and duration of cirrhosis; body temperature; WBC count; respiratory and heart rates; as well as INR, creatinine and bilirubin levels.

In this study we considered a patient cirrhotic if the liver biopsy result showed cirrhotic changes or if there was evidence of clinical signs of portal hypertension and impaired coagulation and/or ascites.

The MELD score was calculated using an online calculator (www.uptodate.com/contents/model-for-end-stage-liver-disease-meld) where:

MELD = 3.8 [Ln serum bilirubin (mg/dl)] + 11.2 [Ln INR] + 9.6 [Ln serum creatinine (mg/dl)] + 6.4

SIRS was set according to recommendations by the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference as the presence of at least two of the following: temperature of >38ºC or <36ºC; heart rate >90 beats/min; respiratory rate >20/min or PaCO2 <32 mmHg or the use of mechanical ventilation; WBC >12000/mm^3 or <4000/mm^3 or more than 10% immature neutrophil count. We calculated SIRS on the first day of admission.

The outcome was defined as death or discharge following admission.

We have reported the data as means ± standard error and we used Mann–Whitney U tests to compare patients with and without SIRS. We also used Univariate analysis to correlate variables.

Logistic regression models were performed with multivariate analyses for identifying variables that were independently associated with outcome. All statistical analyses were performed using SPSS 16.

RESULTS

There were 109 cirrhotic patients between the ages of 14 to 84 (mean: 54.6 ± 18.4) years. Of these, 65 (59.6%) were male and 44 (40.4%) were female. The etiologies of cirrhosis were reported as hepatitis B (31.2%), cryptogenic (47.7%), hepatitis C (6.4%), autoimmune (6.4%), progressive sclerosing cholangitis (4%), Budd-Chiari syndrome (2.8%), and Wilson disease (1.8%). Main reasons for hospital admission were gastrointestinal bleeding (34.2%), ascites

(31.6%), and hepatic encephalopathy (6.6%). There were 78 (71.55%) patients who were SIRS-negative and 31 (28.44%) SIRS-positive upon hospital admission. Per physical examinations, 39 (35.8%) had evidence of icterus and 74 (68.5%) had ascites. Mean systolic BP was 111 mmHg, mean pulse was 84 beats/min and mean respiratory rate was 18.45/min. Mean MELD score of all patients was 15.5, mean bilirubin was 3.7 mg/dl and mean serum creatinine level was 1.25 mg/dl. The overall mean hospitalization period was 7.9 days. However, the mean hospitalization period was 7.8 ± 4.9 days for SIRS-positive patients, whereas it was 8.2 ± 4.1 days for SIRS-negative patients.

There were no significant differences in terms of age and gender according to SIRS status there were 63.6% male SIRS-positive patients whose mean age was 51.6 years, compared with 59% males that had a mean age of 57.95 years for SIRS-negative patients. There was a significant difference in outcome as SIRS-positive patients had a survival of 61.2% compared with SIRS-negative patients whose survival was 91.0% (p=0.0001). There was an association between MELD score in SIRS-positive (14.03 ± 5.6) and SIRS-negative [(8.8 ± 7.6) p=0.0001]. The odds ratio for MELD and SIRS showed that SIRS was independently associated with hospital outcome.

Table 1: **MELD score and laboratory data according to SIRS status.**

Variants	SIRS-negative	SIRS-positive	p-value
MELD score	8.8 ± 7.6	14.03 ± 5.6	0.00
Laboratory Analyses			
Bilirubin	3.27 ± 4.39	4.84 ± 6.05	0.133
Creatinine	0.99 ± 0.47	1.86 ± 2.0	0.01
INR	1.46 ± 0.47	1.64 ± 0.53	0.94

DISCUSSION

There are growing evidences that in a population with advanced liver disease and renal failure, systemic inflammation is quite frequent and might be associated with a negative outcome.[1]

In a study by Cazzaniga et al.,16 out of 141 cirrhotic patients died during follow up, which included 24% SIRS-positive and 4% SIRS-negative patients.[10] In our study the mortality rate was 19 out of 109 cirrhotic patients, of which 38% were SIRS-positive and 8% were SIRS-negative. The higher mortality rate in our study might have been attributed to the unavailability of advanced medical treatment, such as liver transplants in our center.

One of the most important finding of the present study was the close correlation between SIRS and death in the hospital. This is to confirm that the death predication by SIRS is independent of the of liver disease severity which was estimated by MELD score. This is to suggest that SIRS has poor prognosis and increases patient's mortality risk.

Thus SIRS possibly caused a decline in the

Table 2: **Factors independently associate with patients' outcome in 109 cirrhotic patients**

Outcome	Odds ratio	95% confidence interval
SIRS	10.64	3.34-32.7
MELD	2.68	0.61-8.49

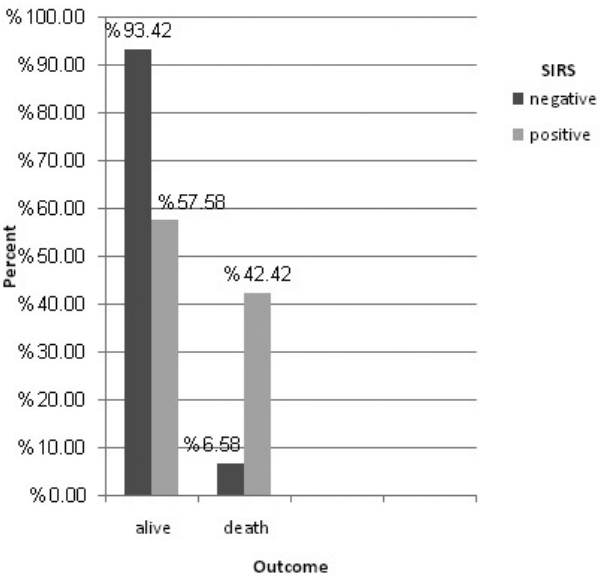

Fig1: **Outcome in SIRS positive and SIRS negative patients.**

patient's condition, increasing the risk of death.

In a study by Thabut et al.,[1] which was performed in cirrhotic patients that had renal failure, all patients who died either presented with SIRS on admission or developed SIRS during hospitalization. In our study, only 5 (9%) patients without SIRS died. In another study by Yuasa et al., the mortality rate in SIRS-positive (50%) patients was significantly higher than in those who were SIRS-negative (8%; $p<0.01$). Their study also concluded that SIRS was independently associated with death in patients with cirrhosis and gastrointestinal bleeding.[6]

In the present study there was a close correlation between SIRS and MELD scores. This confirmed that SIRS occurs in patients with advanced cirrhosis who have signs of liver and/or renal failure. According to a study by Leithead et al., there were 78% of patients with renal dysfunction who had SIRS and 53% of those without renal dysfunction who were SIRS-positive ($p=0.017$).[8] According to these researchers, SIRS was considered to be a risk factor for renal dysfunction in patients with liver failure. This was confirmed by the finding that serum creatinine levels correlated with the presence of SIRS. Whether the impairment of liver and renal functions causes systemic inflammation or, conversely, the development of an inflammatory process causes organ dysfunction is unclear, but both phenomena are probably operative in cirrhosis. Thabut et al. also demonstrated a correlation between SIRS and acute renal failure.[1]

It should always consider a warning when patients admitted to hospital with cirrhosis develop SIRS. Also whether or not treat the systemic inflammation in this patient and whether it will be beneficial needs further investigation.[12,13]

In conclusion, study shows that; SIRS is a relatively common in admitted patients with complicated cirrhosis. SIRS is closely related to severity of liver disease in cirrhotic patients as is shown by its relationship with MELD score. SIRS independently and adversely affects in-hospital survival of patients with cirrhosis.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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