Gastroenterology & Hepatology Journal (GHJ)

HENDUN RESEARCH ACCESS

Case Report

Predictors of Mortality in Patients with Cirrhosis Admitted at Intensive Care Unit at Cardinal Santos Medical Center (Retrospective Analytical)

Kenji M Sato[1*], Jennielyn C Agcaoili[2], Diana A Payawal[3]

[1] Internal Medicine Resident, Year 3, Cardinal Santos Medical Center, Greenhills, San Juan Metro Manila, Philippines

[2] Adult Gastroenterology/Endoscopy, Cardinal Santos Medical Center, Greenhills San Juan, Metro Manila, Philippines

[3] Adult Gastroenterology/Endoscopy/Liver Diseases, Room 258 2/F Medical Arts Building, Cardinal Santos Medical Center, Green hills San Juan, Metro Manila, Philippines

Abstract

Cirrhotic patients who need critical care support show high morbidity and mortality rates compared with other critically ill patients. Their prognosis is, in fact, influenced by both the severity of the underlying hepatic disease and the worsening of extrahepatic organ function. Patients with cirrhosis are admitted to intensive care units (ICUs) for complications of portal hypertension such as variceal bleeding, hepatic encephalopathy or sepsis culminating in multiple organ failure in a large portion of patients. The objective of the study is to identify predictors of mortality in a retrospective analysis of patients with cirrhosis admitted to ICU of Cardinal Santos Medical Center and to compare these predictors to that established liver specific (Child-Pugh Score, MELD and MELD-Na) prognostic models. A total of 51 cirrhotic patients were admitted at the Cardinal Santos Medical Center Medical Intensive Care Unit between June 1, 2009 to June 30, 2015. The results are presented as means with ± standard deviations and confidence intervals of 95% for quantitative variables and as percentages for categorical variables. It was found that cirrhosis is more frequent in males and usually at their fifth and sixth decades of life and Hepatits B is the most common cause of cirrhosis. Although Child-Pugh score indicates the severity of underlying liver disease it cannot be considered as the best tool for predicting mortality in cirrhotic patients. Among patients admitted in the ICU, encephalopathy is a complication involving low survival. Among the clinical parameters, the use of mechanical ventilator, the need for inotropic support, the need for renal replacement therapy are associated with increased mortality rate. Among the laboratory parameters, lower venous pH and bicarbonate values in cirrhotic patients are significantly associated with mortality.

Hence, the prognosis for cirrhotic patients admitted to the ICU is poor.

Introduction

Cirrhosis is the final pathway for wide variety of chronic liver diseases. In 1978, World Health Organization (WHO) defined cirrhosis as a diffuse process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules [1]. In the evolution of many chronic diseases, cirrhosis is the stage that is considered irreversible. Cirrhosis has been a significant source of morbidity and mortality. According to the latest WHO data published in April 2011, liver disease deaths in Philippines reached 1.72% of total deaths [2].

Liver cirrhosis is the final stage of all chronic liver diseases. Patients progress from a compensated phase with no clinical complications to a decompensated phase, in which patients present the main clinical events in liver cirrhosis: variceal bleeding, ascites, renal failure, encephalopathy and hepatocellular carcinoma [3].

Patients with cirrhosis are admitted to intensive care units (ICUs) for complications of portal hypertension such as variceal bleeding, hepatic encephalopathy or sepsis culminating in multiple organ failure in a large portion of patients. Despite recent evidence suggesting improving outcomes in acutely ill patients with cirrhosis, in part due to better understanding of disease processes and improving ICU care, the over-all prognosis for patients with cirrhosis admitted to ICU remains poor with mortality rates ranging from 44 to 81%. Considering the high cost of adjunctive treatment modalities and the limited availability of ICU beds, the task of identifying patients who are most likely to benefit from aggressive treatment is imperative and poses great challenge for the clinicians involved in the care of these patients. Unfortunately, the quest for an accurate prognostic score applicable to these patients in clinical practice has remained elusive [4].

Many clinical and biochemical parameters have been suggested in order to predict more accurately the prognosis of cirrhotic patients and correctly asses their survival rate. They are important because of application of adequate therapy and prioritization of transplantation lists [5]. The Child Pugh score is still considered the cornerstone in prognostic evaluation of cirrhotic patients although it was formulated more than 30 years ago. Nevertheless, it has some drawbacks such as subjectivity of clinical parameters and limited discriminatory ability [6]. Recently, the Model for End-stage Liver disease (MELD) was introduced as a tool for predicting mortality risk and to assess

Corresponding author: Kenji M Sato, Internal Medicine Resident, Year 3, Cardinal Santos Medical Center, Greenhills, San Juan Metro Manila, Philippines, Tel: 0917-8091004; Fax: (02) 353-1145; E-mail: kenji.sato07@gmail.com

Received: January 13, 2017; **Accepted:** January 20, 2017; **Published:** January 26, 2017

the severity of the disease in patients with liver cirrhosis, as well as to determine organ allocation priorities [7].

The objective of the study is to identify predictors of mortality in a retrospective cross-sectional of patients with cirrhosis admitted to ICU and to compare these predictors to that established liver specific (Child-Pugh Score, MELD and MELD-Na) prognostic models.

Methodology

This is a retrospective study of patients with cirrhosis admitted at medical intensive care unit (ICU) at Cardinal Santos Medical Center (CSMC) between June 1, 2009 to June 30, 2015. The diagnosis for cirrhosis was established by presence of signs of portal hypertension e.g. ascites, esophageal varices, hepatic encephalopathy and liver imaging studies. Patients who presented with cholangiocarcinoma or other malignancies, post-liver transplantation or other post-operative hepatobilliary admissions to the ICU were excluded. All patients received optimal treatment according to the local ICU guidelines.

Data on age, gender, etiology of liver disease, number of years diagnosed with cirrhosis, indication for ICU admission, length of ICU stay were recorded. Laboratory parameters recorded during ICU admission were platelet count, blood urea nitrogen, Creatinine, sodium, AST, ALT, total bilirubin, INR and albumin. Laboratory parameters recorded during ICU stay arterial bicarbonate, pH, partial arterial pressure of oxygen (PaO_2) and inspired oxygen concentration (FiO_2). The severity of liver disease was graded by the Child Pugh, MELD and MELD-Na scores using parameters recorded on the day of admission.

Statistical Analysis

The results are presented as means with ± standard deviations and confidence intervals of 95% for quantitative variables and as percentages for categorical variables. We compared survivors with non-survivors with regards to demographic, clinical and laboratory variables as well as liver prognostic scores. For comparison of continuous variables the t test comparison of independent means and chi-square test to compare categorical variables was used. The data were processed using Statistical Package for Social Sciences version 20 (SPSS 20.0) for Windows.

Results

Baseline characteristics

A total of 51 cirrhotic patients were admitted at the Cardinal Santos Medical Center Medical Intensive Care Unit between June 1, 2009 to June 30, 2015. Majority were male (68.63%) and the mean age was 61.6 years. Hepatitis B virus infection (47.06%) was the most common etiology of cirrhosis followed by Non-Alcoholic Fatty Liver Disease (33.33%), Hepatitis C (9.80%) and alcoholic liver disease (9.80%). The indications for ICU admission were identified as Encephalopathy (43.14%), sepsis (25.49%) variceal bleed (19.61%) and acute respiratory failure (9.80%). The mean number of days for the ICU stay of the patients was between four to five. The overall mortality rate in the ICU was 39.22% in which the common cause of death was multi-organ failure (45%). Mean MELD, MELD-Na and Child Pugh scores were 42, 24 and 11 respectively.

Table 1

Predictors of mortality

Non-survivors were slightly younger than survivors (median age 61 vs. 64) and their most common etiology of cirrhosis was hepatitis B followed by NAFLD (Table 1). Non-survivors had higher incidence of encephalopathy (23.53% vs. 19.61%) while survivors had a higher incidence of sepsis (13.73% vs. 11.76%) variceal bleed (17.65% vs. 1.96%) and acute respiratory failure (5.88% vs. 3.92%) as shown in Table 2. However, there were no significant difference between survivors and non-survivors in terms of their age, gender, no. of years diagnosed with cirrhosis and the indication for ICU admission and length of ICU stay (Table 1).

Table 1: Baseline Characteristics of survivors and non-survivors.

Characteristics	Survivors	Non-survivor	p-value
Age	64.84 15.82	61.75 ± 20.235	0.545
Gender			0.43
Male	20 (39.22%)	15 (29.41%)	
Female	11 (21.57%)	5 (9.80%)	
Liver disease			
Hepatitis B	14 (27.45%)	10 (19.61%)	
NAFLD	10 (19.615%)	7 (13.73%)	
Alcoholic liver disease	3 (5.88%)	2 (3.92%)	
Hepatitis C	4 (7.84%)	1 (1.96%)	
Number of years diagnosed with cirrhosis	2.75	1.45	0.29
MELD	33.52 ± 12.315	42.2 ± 8.806	0.009*
MELD-Na	34 ±	44	0.009*
Child-Pugh Score			0.279
B	14 (27.45%)	6 (11.76%)	
C	17 (33.33%)	14 (27.45%)	

Non-survivors had significantly higher MELD and MELD-Na scores compared with survivors (Table 1).

Non-survivors had significantly used a mechanical ventilator (35.29%), needed an inotropic support (31.37%) and had undergone renal replacement therapy (25.49%) during their ICU stay compared to the survivors (Table 2).

The mean platelet of the survivors was 105.35 while for the non-survivors it was 59.681; with a p value of 0.776 the result of the platelet was interpreted as non-significant. The mean BUN of the survivors was 29.75 while for the non-survivors it was 48.385; with a p value of 0.451, the result of the mean BUN was interpreted as non-significant. The mean creatinine of the survivors was 174.2135 while for the non-survivors it was 259.247; with a p value of 0.057, the result of the mean creatinine was interpreted as non-significant. The mean sodium of the survivors was 135.55 while for the non-survivors it was 129.91; with

Table 2: Clinical characteristics of survivors and non-survivors.

Characteristics	Survivors	Non-survivors	p-value
Indication for ICU			0.182
Acute Respiratory Failure	3 (5.88%)	2 (3.92%)	
Sepsis	7 (13.73%)	6 (11.76%)	
Hepatorenal Syndrome	0 (0.00%)	1 (1.96%)	
Variceal Bleed	9 (17.65%)	1 (1.96%)	
Encephalopathy	10 (19.61%)	12 (23.53%)	
Length of Stay in the ICU	4.07	4.5	0.799
GI Bleeding			0.389
No	18 (35.29%)	14 (27.45%)	
Yes	13 (25.49%)	6 (11.76%)	
Mechanical Ventilation Support			0.009*
No	16 (31.37%)	3 (5.88%)	
Yes	14 (27.45%)	18 (35.29%)	
Inotropic Support			0.002*
No	20 (39.22%)	4 (7.84%)	
Yes	11 (21.57%)	16 (31.37%)	
Renal replacement therapy			0.026*
No	28 (54.90%)	13 (25.49%)	
Yes	3 (5.88%)	7 (13.73%)	

a p value of 0.193, the result of the mean sodium was interpreted as non-significant. The mean AST of the survivors was 196.42 while for the non-survivors was 656.45; with a p value of 0.18, the result of the mean AST was interpreted as non-significant. The mean ALT of the survivors was 105.79 while for the non-survivors it was 178.25; with a p value of 0.121, the result of the mean ALT was interpreted as non-significant. The mean total bilirubin of the survivors was 115.76 while for the non-survivors it was 141.1; with a p value of 0.418, the result of the mean bilirubin was interpreted as non-significant. The mean INR of the survivors was 2.8806 while for the non-survivors it was 1.904; with a p value of 0.59, the result of the mean INR was interpreted as non-significant. The mean PT Activity of the survivors was 180.97 while for the non-survivors it was 36.08; with a p value of 0.391, the result of the mean PT Activity was interpreted as non-significant. The mean albumin of the survivors was 23.77 while for the non-survivors it was 21; with a p value of 0.102, the result of the mean albumin was interpreted as non-significant. The mean pH of the survivors was 7.3098 while for the non-survivors it was 7.13229; with a p value of 0.004, the result of the mean pH was interpreted as significant. The mean HCO_3 of the survivors was 21.728 while for the non-survivors it was 14.856; with a p value of 0.018, the result of the mean HCO_3 was interpreted as significant. The mean PaO_2 of the survivors was 118.01 while for the non-survivors it was 111.312; with a p value of 0.811, the result of the mean PaO_2 was interpreted as not significant. The mean FiO_2 of the survivors was 1.1211 while for the non-survivors it was 4.1606; with a p value of 0.194, the result of the mean FiO_2 was interpreted as not significant.

Laboratory findings showed that non-survivors had significantly lower venous pH and bicarbonate values than the survivors.

Table 3

Discussion

This study investigated the predictive factors of mortality in cirrhotic patients admitted at ICU. As well known, cirrhosis is more frequent in males and usually at their fifth and sixth decades of life [8]. This study demonstrated that the common cause of cirrhosis in ICU setting was hepatitis B infection followed by NAFLD. This was different to that seen in Western countries. However, most studies from countries in eastern Asia like China have reported mainly hepatitis B virus as cause of chronic liver disease. The in-hospital mortality was 39.2% in the total cohort of 51 cirrhotic patients admitted at ICU which was higher in other published reports [7].

Many factors have been studied in predicting mortality of patients with liver cirrhosis as well as to improve the prognostic models. In the study by D'Amico [9], it was reported that the Child-Pugh was the best predictor of mortality in cirrhosis, followed by the five components measured individually. Surprisingly, Child Pugh class was not significantly different in the survivors and non-survivor patients. In study by Poolja in 2012, MELD was associated with lower survival of the five variables of Child-Pugh, bilirubin, albumin, INR, ascites and encephalopathy. It was also consistent with reports by other investigators in both MICU and non-MICU settings suggesting that the Child-Pugh score indicates the severity of underlying liver disease but is not the best tool for predicting mortality in cirrhotic patients [8].

Table 3: Laboratory characteristics of survivors and non-survivors.

Characteristics	Survivors	Non-survivors	p-value
Platelet ($x10^9$/l)	105.35 ± 111.58	59.681 ± 96.19	0.776
BUN (mmol/l)	29.75 ± 57.8596	48.385 ± 116.6559	0.451
Creatinine (mmol/l)	174.2135 ± 108.9115	259.247 ± 202.2374	0.057
Sodium (mmol/l)	137.55 ± 5.667	129.91 ± 31.579	0.193
AST (mmol/l)	196.42 ± 161.943	656.45 ± 1884.185	0.18
ALT (mmol/l)	105.79 ± 90.152	178.25 ± 230.555	0.121
Total Bilirubin (mmol/l)	115.76 ± 115.747	141.1 ± 95.342	0.418
INR	2.8806 ± 7.99806	1.904 ± 0.77919	0.59
PT Activity (%)	180.97 ± 746.22	36.08 ± 16.50	0.391
Albumin (g/l)	23.77 ± 5.988	21 ± 5.468	0.102
pH	7.3098 ± 0.161791	7.13229 ± 0.193736	0.004*
HCO3	21.728 ± 8.9163	14.856 ± 7.7075	0.018*
PaO2 (kPa)	118.01 ± 71.9731	111.312 ± 96.8625	0.811
FiO2	1.1211 ± 2.27033	4.1606 ± 9.70776	0.194
All values are expressed as mean with standard deviation.			

The results of this study presented the predominance of encephalopathy as the cause for indication of ICU admission is consistent with several studies [10]. A study by Bustamante concluded encephalopathy is a complication involving low survival. They followed for 17 months 111 patients with cirrhosis who had a first episode of acute encephalopathy, and found that 74% died during follow-up, with a survival rate of 42% per year [10].

Among the clinical parameters, the use of mechanical ventilator, the need for inotropic support, the need for renal replacement therapy are associated with increased mortality rate. Similarly, this was also evident in the study made by Levesque in which the result showed the need for other organ support therapy at ICU admission were significantly associated with ICU mortality [8]. This emphasizes the importance of multisystem organ failure over the preexisting co-morbid conditions in predicting mortality in cirrhotic patients admitted at ICU [8].

Among the laboratory parameters, lower venous pH and bicarbonate values in cirrhotic patients are significantly associated with mortality. Additionally, laboratory and clinical parameters of liver disease such as albumin, prothrombin time, bilirubin, platelet are not predictors of mortality.

In conclusion, this study confirms that the prognosis for cirrhotic patients admitted to the ICU is poor. We have clarified the predictors that are independently associated with mortality in these patients.

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