Original article

Clinical features, management and outcome in patients admitted with liver cirrhosis to the ICU - A retrospective study

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Abstract

Background: Hepatic cirrhosis is an important cause of morbidity and mortality in the intensive care unit (ICU). **Objective**: To determine the precipitating factors, presenting complaints, course of the disease and predictors of mortality in patients with liver cirrhosis admitted to the ICU. **Methods:** This retrospective study was conducted at Multidisciplinary ICU at tertiary care hospital from April 2013 to March 2014. A total of 107 patients diagnosed with liver cirrhosis were admitted to the ICU. Of these, 17 were discharged against medical advice. The remaining 90 patients were included in the study. Their case notes were examined for data such as severity of disease, precipitating events and their course in the ICU. The survivors were followed up telephonically to assess survival at six months. **Results**: There were 30 survivors and 60 nonsurvivors. The stage of cirrhosis (based on modified Child-Pugh criteria) had significant association with hospital mortality and disease outcome. Mortality was significantly higher in patients presenting with sepsis and septic shock (P=0.022) and hepatic encephalopathy (P=0.007). Interventions such as mechanical ventilatory support (P=0.002), inotropes (P=0.001) and vasopressors (P=0.048), variceal banding (P=0.005), need for transfusion of fresh frozen plasma (P=0.001) and packed cell transfusion (P=0.036) showed significant association with clinical outcome. **Conclusion**: Overall mortality rate of patients admitted in the ICU with liver cirrhosis is high (66.7%). Mortality rate is higher in those with Stage C cirrhosis, sepsis and septic shock and hepatic failure. Among the patients who survive, one third may not survive beyond six months after hospital discharge.

Keywords: Cirrhosis, Fibrosis, Hepatic, Portal hypertension, Sepsis

Introduction

Hepatic cirrhosis is characterised by diffuse hepatic fibrosis and nodule formation. It has significant morbidity and causes premature death. Chronic viral hepatitis and excessive alcohol consumption are the most common causes of cirrhosis and portal hypertension.

Critically ill patients with chronic liver diseases admitted to the ICU have high mortality rates ranging from 50-100%, especially in those with multiorgan dysfunction and septic shock.[1-6] The Child-Turcotte classification,[7] and its subsequent modification by Pugh,[8] is usually used to grade the severity of cirrhosis. The Acute Physiology and Chronic Health Evaluation (APACHE) II,[9] is a widely used severity-of-illness scale to predict hospital mortality in critically ill patients of all disease categories including cirrhosis admitted to the intensive care units. Cirrhotic patients often require ICU admission when they present with massive gastrointestinal bleed, sepsis and septic

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shock, respiratory and hepatic failure. This study was aimed at studying the clinical profile of cirrhotic patients admitted to the ICU of a tertiary hospital in South India.

Methods

This was a retrospective survey, conducted at Multidisciplinary Intensive Care Units at a tertiary hospital in South India. The study was approved by the hospital Research and Ethics Committee.

All adult patients diagnosed with liver cirrhosis (of any aetiology) requiring admission to the ICU (for any reason) between April 2013 and March 2014 were included. Patients below the age of 18 years, those with concurrent malignancy, HIV infection and patients posted for liver transplantation as also those patients who were discharged against medical advice (DAMA) were excluded.

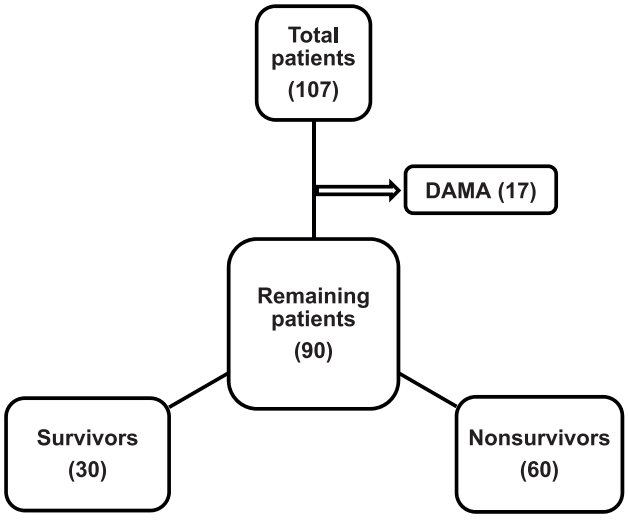

Figure 1: Flowchart of the study

The case files of all patients included in the study were examined for the following: demographic data (age, gender), cause of cirrhosis of liver, stage of the disease modified Child-Pugh criteria, duration of the disease (as known to the patient), co-morbidities, APACHE II score, reason for admission to the hospital, any previous admissions to hospital and/or ICU, reason for admission to the ICU, precipitating factors for admission to ICU, clinical features at admission to ICU, course in ICU: whether respiratory support was required (type and duration), requirement of inotropes (type and duration), renal dysfunction, requirement of dialysis, blood and blood product transfusions, outcome: duration of ICU stay and duration of hospital stay, survival to ICU discharge, survival to hospital discharge and six-month survival. In the case of readmission to ICU during the same hospitalisation, only the last admission to ICU was analysed. All information was noted down in a proforma and data was analysed after completion of the data collection. Any contact telephone numbers, if available, were noted down to evaluate for six-month survival and present condition in those patients who survived to hospital discharge.

Statistical analysis

Data were analysed using SPSS Statistics 22 (SPSS Inc. Chicago, IL). Descriptive statistics are expressed as mean ± SD unless otherwise stated. The primary analysis compared hospital survivors with nonsurvivors. Independent samples t-test was used for comparison of the means of continuous variables and normally distributed data. Categorical data were tested using the chi square statistic. All statistical tests were 2-tailed, and a significance level of $P = .05$ or less was used.

Results

A total of 107 patients admitted to ICU with cirrhosis of liver were enrolled in this study. Out of 107 patients, 17 patients were excluded as they were discharged against medical advice (DAMA). Remaining 90 patients were classified into survivors and nonsurvivors to hospital discharge. The two groups were then compared based on clinical characteristics, reasons for hospital and ICU admissions, therapeutic interventions, overall disease progression and clinical outcome.

Demographic data and clinical characteristics including age, gender, APACHE II score, causes and stage of cirrhosis, comorbidities and duration of disease (as known to the patient) are given in *Table 1*. There were more male patients (86.7% and 88.3%) than female in both groups. Mean APACHE II score was a little higher in non-survivors group (15.167 in survivors and 20.117 in nonsurvivors group).

Table 1: Demographic and clinical characteristics

	Survivors (n = 30)	Nonsurvivors (n = 60)	*P value*
Age (mean ± SD)*	50.80 ± 9.189	50.45 ± 11.538	0.232
Male n (%)*	26 (86.7)	53 (88.3)	0.820
APACHE II Score (mean ± SD)	15.167 ± 6.148	20.12 ± 7.8	0.150
Cause of cirrhosis n (%)*			0.484
Alcoholic liver disease	23 (76.7)	45 (75)	
HCV	6 (20)	9 (15)	
Cryptogenic	1 (3.3)	6 (10)	
Stage of cirrhosis n (%)*			0.001
A	6 (20)	5 (8.3)	
B	13 (43.3)	8 (13.3)	
C	11 (36.7)	47 (78.3)	
Co-morbidities n (%)*			
DM	9 (30)	14 (23.3)	0.494
HTN	6 (20)	8 (13.3)	0.411

*Values given as mean ± SD, or number (%). Abbreviations: APACHE II = Acute Physiology, Age, and Chronic Health Evaluation; HCV = Hepatitis C Virus; DM = Diabetes Mellitus; HTN = Hypertension. # $P < .05$ by X^2 test and independent samples t-test.

Alcoholic liver disease (ALD) was the major cause of cirrhosis (a total of 58 out of 90 patients, 23 in survivors and 45 in non-survivors group) followed by hepatitis C-related cirrhosis and cryptogenic cirrhosis. Both groups exhibited similar baseline characteristics and their frequencies were not significantly statistically different. From clinical characteristics, only the stage of cirrhosis (based on modified Child-Pugh criteria) had a significant association ($P = .001$) with hospital mortality and disease outcome. Among patients who survived, 20% were in Stage A, 43.3% were in Stage B whereas 36.7% were in Stage C. Among patients who did not survive; 8.3% were in Stage A, 13.3% were in Stage B whereas 78.3% were in Stage C. While the mortality was not different in Stage A and B (8.3 and 13.3%), patients in Stage C Cirrhosis had a very high mortality.

The main precipitating factors and reasons for hospital and ICU admission are listed in *Table 2*. The six most common reasons for hospital admission were abdominal distension, haematemesis, melaena, jaundice, altered sensorium and pedal oedema. It was noted that none of the above reasons had statistically significant association to clinical outcome in both the groups. The six most common reasons or precipitating factors for ICU admission were sepsis with septic shock, multiorgan dysfunction syndrome (MODS), acute renal failure (ARF), massive gastrointestinal bleeding, hepatic encephalopathy and grade III oesophageal varices. Among the precipitating factors leading to ICU admission, it was noted that mortality was significantly higher in patients presenting with sepsis and septic shock ($P = .022$) and even higher in patients presenting with hepatic encephalopathy ($P = 0.007$).

Table 2: Precipitating factors and reasons for ICU and hospital admission

	Survivors *(n = 30)*	Non-survivors *(n = 60)*	*P value*
Reason for hospital admission n (%)*			
Abdominal distension	16 (53.3)	41 (68.3)	0.164
Haematemesis	13 (43.3)	19 (31.7)	0.276
Melaena	7 (23.3)	18 (30)	0.506
Jaundice	3 (10)	15 (25)	0.094
Altered sensorium	11 (36.7)	24 (40)	0.760
Pedal oedema	9 (30)	19 (31.7)	0.872
Reason for ICU admission n (%)*			
Sepsis with septic shock	7 (23.3)	29 (48.3)	0.022
MODS	3 (10)	14 (23.3)	0.128
ARF	11 (36.7)	21 (35)	0.876
Massive GI bleed	7 (23.3)	18 (30)	0.506
Hepatic encephalopathy	7 (23.3)	32 (53.3)	0.007
Grade 3 oesophageal varices	15 (50)	30 (50)	1.00

*Values given as number (%).

Abbreviations: MODS = Multiorgan Dysfunction Syndrome; ARF = Acute Renal Failure

# $P < .05$ by X^2 test (chi-square)

The basic therapeutic interventions and resources used in treatment and management of patients with liver cirrhosis in both groups are given in *Table 3*. No patient received noninvasive mechanical ventilation as they did not meet the criteria for it. Based on the analysis of this study, from the above therapies and interventions used specifically in the management of cirrhotic patients, the need for mechanical ventilatory support ($P = .002$) in case of respiratory failure, use of inotropes ($P = .001$) and vasopressors ($P = .048$), variceal banding ($P = .005$), need for FFP ($P = .001$) and PRBC ($P = .036$) transfusions were significantly associated with mortality.

Table 3: Therapeutic interventions in patients admitted with liver cirrhosis

	Survivors *(n = 30)*	Nonsurvivors *(n = 60)*	*P value*
Invasive MV n (%)	8 (26.7)	37 (61.7)	.002
MV duration (days)	3.50 ± 1.69	3.76 ± 2.80	.148
Drugs n (%)			
Inotropes	7 (23.3)	38 (63.3)	.001
Vasopressors	1 (3.3)	11 (18.3)	.048
Other treatment n (%)			
Variceal banding n (%)	11 (36.7)	7 (11.7)	.005
Octreotide infusion	8 (26.7)	21 (35)	.425
Control of hepatic failure	15 (50)	41 (68.3)	.091
Dialysis n (%)	7 (23.3)	17 (28.3)	.613
Blood & blood products n (%)			
FFP	6 (20)	38 (63.3)	.001
PRBC	12 (40)	38 (63.3)	.036
Platelet	5 (16.7)	16 (26.7)	.290

* Values given as mean ± SD or number (%).
Abbreviations: MV = Mechanical Ventilation; FFP = Fresh Frozen Plasma; PRBC = Packed Red Blood Cells
# P < .05 by Chi-square test and independent samples t-test

The total duration of ICU and hospital stay and overall clinical prognosis of patients were included in *Table 4*. The five main components assessed for the outcome of patients were length of ICU stay, length of hospital stay, survival to ICU discharge and 6 month survival post-hospital discharge. It was noted, the duration of ICU ($P = .018$) and hospital ($P = .016$) stays had statistically significant association with outcome. Out of 30 patients who survived to hospital discharge (survivor group), 19 patients were alive at 6 months post-hospital discharge.

Table 4: Duration of ICU and hospital length of stay and outcome

	Survivors *(n = 30)*	Nonsurvivors *(n = 60)*	*P value*
Duration of ICU stay (mean ± SD)	5.77 ± 2.712	6.60 ± 4.48	.018
Duration of hospital stay (mean ± SD)	9.80 ± 5.189	10.33 ± 8.03	.061
Survival to ICU discharge n (%)	30 (100)	15 (25)	.001
Survival at 6 months n (%)	19 (63.3)		

* Values given as mean ± SD or number (%); ICU = Intensive Care Unit **(independent t test**

Discussion

Patients with cirrhosis of liver (irrespective of the baseline aetiology of cirrhosis) admitted in intensive care that required organ support, clinical management including extensive interventions and therapies are expected to have a poor prognosis. Overall mortality rates of 43-100% have been reported.[2,3,5,9-11] This study was done to observe the clinical features, management and outcome of patients admitted with cirrhosis to our ICU.

Wehler *et al* have shown that the Sequential Organ Failure Assessment (SOFA) is an excellent prognostic system for predicting in-hospital mortality in critically ill patients with liver cirrhosis. They have reported the overall predictive accuracy of the SOFA as 15% and 17% greater than that of the APACHE II and Child-Pugh systems, respectively.[3]

Constantinos *et al* have conducted a prospective study on 147 cirrhotic patients to compare the Child-Pugh, APACHE II and APACHE III scoring systems in predicting hospital mortality of patients with live cirrhosis.[5] Their results indicated that between the three scores, Child-Pugh score had the least statistically significant discrepancy between predicted and observed mortality. Our study also showed that APACHE II score was not an accurate clinical predictor for hospital mortality. However, the Child-Pugh score was calculated for each patient and Stage C of cirrhosis had a statistically significant association with mortality.

Our study was a retrospective analysis from a single institution. All the workup, diagnosis, and treatment were done by the physicians. All prognostic systems (APACHE II and Child-Pugh scores) are not readily applicable to individual patients because of the fact that scoring systems are developed to predict group outcomes. Patients who were discharged against medical advice were excluded from our study.

However, in the light of international literature and findings of our own study, it can reasonably safely stated that requirement of admission in a cirrhotic patient, particularly Stage C, requiring respiratory or cardiovascular support or have had a bleed

needing transfusion of blood products carries a poor prognosis and the expected mortality rates are very high.

Conclusion

The overall mortality rate of patients admitted in the ICU with liver cirrhosis is high (66.7%). Mortality rate is higher in those who present with Stage C cirrhosis, sepsis and septic shock, hepatic failure, who require invasive mechanical ventilation and inotropes. There is no correlation between mortality and those patients who have undergo variceal banding, required octreotide infusion or required dialysis. Among patients who survive to hospital discharge, one third may not survive beyond six months after discharge.

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