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ORIGINAL ARTICLE

Prediction of In-Hospital Mortality in Spontaneous Bacterial Peritonitis Patients with Advanced Liver Disease

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ABSTRACT

Introduction: Bacterial infections are known reason for morbidity and mortality in hospitalized patients with cirrhosis among which Spontaneous bacterial peritonitis (SBP) is most common, accounts for around 20% to 30% mortality rate.
Objective: To evaluate the frequency of in-hospital mortality in SBP patients.
Study Design: Descriptive case series.
Setting: Asian Institute of Medical Sciences Hospital Hyderabad.
Duration: From 1st January 2019 to 30th June 2019.
Material and Methods: Adult patients diagnosed to have spontaneous bacterial peritonitis and followed for outcome.
Results: 223 patients of spontaneous bacterial peritonitis I,e 165 (74%) male and 58 (26%) female fulfilling the inclusion criteria were enrolled in study. Mean age obtained was 47.56 ± 13.069 years and Hepatitis C with most common etiology for CLD was 128 (57.4%) followed by Hepatitis B 26 (11.7%), Hepatitis B + D 30 (13.5 %) and Alcohol 8 (3.6 %). Hepatocellular carcinoma in 70 (31.4 %) only. CTP (Child-Turcot-Pugh) score and MELD (Model for End-stage Liver Disease) score used to access stage of cirrhosis. 38 (17 %) patients with CTP class B and 185 (83 %) with CTP class C. The mean MELD score of all patients found to be 23.09 ± 15.686. Among 223 patients, in-hospital mortality was observed in 61 (27.4%), 115 (51.6%) were discharged with improvement and rest 47 (21.1%) discharged with no improvement.
Practical Implication: This study's findings underscore the need for early detection and aggressive management of Spontaneous Bacterial Peritonitis in patients with advanced liver disease, especially those with CTP Class C and high MELD scores, to reduce the high in-hospital mortality rate.
Conclusion: Significantly high in-hospital mortality was found to be associated with SBP, with CTP Class C, High MELD Score, increased creatinine, bilirubin, PT, INR and decreased albumin especially in females.
Keywords: Cirrhosis; In-hospital mortality; Spontaneous bacterial peritonitis

INTRODUCTION

The advanced chronic liver disease (ACLD) is characterised by a transition from a clinically compensated state (cACLD) to a symptomatic decompensated state with increased risk for mortality. Whereas ACLD patients are more prone to develop acute-on-chronic liver failure (ACLF), a systemic inflammatory syndrome associated with multi-organ dysfunction. [1] Bacterial infections are commonest cause of morbidity and mortality in hospitalized patients with cirrhosis. Main pathophysiological mechanism of SI involves abnormal translocation of bacteria and pathogen-associated molecular patterns from the intestinal lumen into the portal and systemic circulation is considered the cirrhosis, highlighting the central role of the gut–liver axis.[2] Spontaneous bacterial peritonitis (SBP) defined as the presence of >250 polymorphonuclear cells (PMN)/mm^3 in ascites in the absence of an intra-abdominal source of infection or malignancy.[3] SBP incident varies between 7% to 30% per annum and mortality of SBP is around 20% to 30% I,e most frequent and life-threatening infection in patients with liver cirrhosis requiring urgnet diagnosis and therapy.[4-5]

Ascites the first and foremost common sign of hepatic decompensation, developing in ~50% of compensated cirrhotic patients within 10 years.[6-7] Ascites is a Greek word (askos) that means a bag or a sac. Ascites is the collection of pathologic fluid within the peritoneal cavity. The ascitic fluid represents a state of total-body sodium and water excess, but the event that initiates the unbalance is unclear. Many pathogenic processes have been implicated about 75% likely occur as a result of portal hypertension in liver cirrhosis, remainder due to infective, inflammatory, infiltrative conditions, Hypoalbuminemia and low plasma oncotic pressure favour the extravasation of fluid from the plasma to the peritoneal fluid. [10] Currently Child-Pugh and model for end-stage liver disease (MELD) scores are used for assessing prognosis of liver dysfunction[8-9]. Patients with ascites face a poor outcome, especially with concominant spontaneous bacterial peritonitis (SBP) infection, having high recurrence chances, poor prognosis and mortality rate.[11]

While there's a substantial amount of literature investigating the morbidity and mortality rates among patients with Spontaneous Bacterial Peritonitis (SBP) in the context of cirrhosis, fewer studies have specifically examined in-hospital mortality in these patients in the local context. There is a particularly noticeable gap in understanding how variables such as CTP class, MELD scores, and certain biochemical parameters influence the outcomes in these patients. This study is significant as it attempts to fill this gap by investigating the frequency of in-hospital mortality in SBP patients, thereby providing valuable insights into the factors influencing mortality. Such understanding can drive improved strategies for the clinical management of SBP patients with advanced liver disease, potentially leading to improved patient outcomes and reduced mortality rates.

MATERIALS AND METHODS

Study design and setting: Cross-sectional study was conducted from 1st January 2019 to 30th June 2019 at Asian Institute of Medical Science, Hyderabad.
Population and sample size: Total 223 patients, 165 (74%) male and 58 (26%) female with spontaneous bacterial peritonitis filling the inclusion criteria were enrolled. Mean age was 47.56 ± 13.069 years. Cirrhosis was diagnosed by clinical, laboratory, imaging, and/or histologic criteria within 24 h of hospital admission.
Data collection: Data included patient age, sex, etiology of liver disease, severity of ascites, grade of hepatic encephalopathy, serum creatinine, total serum bilirubin, serum albumin, prothrombin time with international normalized ratio (INR), and ascitic fluid analysis. Biochemical evaluations was done in hospital laboratory. CTP score was determined on the basis of severity of ascites, hepatic encephalopathy, prolongation of prothrombin time, total serum bilirubin and albumin level. MELD score was calculated with serum creatinine, bilirubin and INR. Patients would be observed in hospital and will be assessed for 72 hours for death or discharge.
Reliability and Validity: This study's reliability is bolstered by the standardized methods used in diagnosing Spontaneous Bacterial Peritonitis (SBP) and the use of accepted scoring systems like

Child-Turcot-Pugh (CTP) and Model for End-stage Liver Disease (MELD), allowing consistent data collection and result comparability. The validity of the study is substantiated by the diverse patient sample, increasing the generalizability of the findings. However, potential confounding variables in this observational study might impact internal validity, and the single-center design may limit external validity. Future multi-center studies can enhance validity. Despite these limitations, the study's reliability and validity are robust, adding valuable insights into SBP in advanced liver disease.

Data analysis: The data was analysed by researcher on SPSS (version 20.0) and. A descriptive analysis was done for demographic features, presented as mean ± standard deviation for quantitative and qualitative variables. Number and percentage of outcome (in-hospital mortality) will be calculated, stratified and to control the effect modifier by chi-square test. The statistical level will be considered significant at $p < 0.05$.

RESULTS

A total of 223 patients diagnosed with Spontaneous Bacterial Peritonitis (SBP) were enrolled in the study. The baseline characteristics, as displayed in Table 1, indicated a higher proportion of male (74%) than female (26%) participants, with a mean age of 47.56 ± 13.069 years. Hepatitis C emerged as the most prevalent etiology for chronic liver disease (CLD), accounting for 57.4% of cases, followed by Hepatitis B (11.7%), Hepatitis B + D (13.5%), non-alcoholic non-viral liver disease (9%), and alcohol-induced liver disease (3.6%). Notably, Hepatocellular carcinoma was detected in 31.4% of patients. The severity of cirrhosis was assessed using Child-Turcot-Pugh (CTP) and Model for End-stage Liver Disease (MELD) scores. Majority of patients were classified as CTP Class C (83%), indicative of more advanced disease. The mean MELD score across all patients was 23.09 ± 15.686, suggesting a significant disease burden.

Key laboratory parameters for participants at baseline are shown in Table 2, with mean total bilirubin levels of 5.88 ± 7.53 mg/dl, mean albumin levels of 2.378 ± 0.514 g/dl, and mean prothrombin time of 21.77 ± 8.654 seconds, highlighting a state of impaired liver function and coagulation.

Regarding the study outcomes presented in Table 3, in-hospital mortality was recorded for 27.4% of patients, while 51.6% were discharged with an improvement in their condition, and 21.1% showed no improvement. When stratified by gender (Table 4), the in-hospital mortality rate was higher among females (33%) compared to males (25%), although this difference was not statistically significant (p=0.283). A significant difference (p=0.001) was observed when mortality was stratified by CTP class (Table 5), with a higher mortality rate among Class C patients (32%) compared to Class B (5%).

Tables 6-11 indicate a positive correlation between in-hospital mortality and higher MELD scores, increased bilirubin and creatinine levels, reduced albumin levels, and prolonged prothrombin time and INR. Specifically, a MELD score above 35 was associated with a 53% mortality rate, underscoring the prognostic utility of these markers in predicting mortality outcomes in patients with SBP.

Table 1: Baseline characteristics of the patients

Variable	Frequency (%)
Age (Mean –years)	47.56 ± 13.069
Gender Male Female	 165 (74%) 58 (26%)
CLD etiology Hepatitis C Hepatitis B Hepatitis B + C Hepatitis B + D NBNC Alcohol	 128 (57.4%) 26 (11.7%) 11 (4.9 %) 30 (13.5 %) 20 (9 %) 8 (3.6 %)
CTP Class Class B Class C	 38 (17 %) 185 (83 %)

Table 2: Laboratory Parameters

Variable	Mean ± SD
Creatinine (mg/dl)	1.909 ± 1.413
Total bilirubin (mg/dl)	5.88 ± 7.53
Albumin (g/dl)	2.378 ± 0.514
Platelets (10^3/uL)	105.41 ± 73.856
Prothrombin time (seconds)	21.77 ± 8.654

Table 3: Outcome of patients

Outcome	Frequency (%)
In-hospital mortality	61 (27.4%)
Discharged with improvement	115 (51.6%)
Discharged with same condition	47 (21.1%)

Table 4: Frequency of in-hospital mortality stratified by gender.

		Outcome		P Value
Gender		In-Hospital Death	Discharged	
Male	N	42	123	0.283
	%	25%	75%	
Female	N	19	39	
	%	33%	67%	

Table 5: Frequency of in-hospital mortality stratified by CTP class.

		Outcome		P Value
CTP		In-Hospital Death	Discharged	
B	N	2	36	0.001
	%	5%	95%	
C	N	59	126	
	%	32%	68%	

Table 6: Frequency of in-hospital mortality stratified by MELD.

		Outcome		P Value
Meld Group		In-Hospital Death	Discharged	
<15	n	2	51	<0.001
	%	4%	96%	
16-25	n	22	69	
	%	24%	76%	
26-30	n	17	24	
	%	41%	59%	
>30	n	20	18	
	%	53%	47%	

Table 7: Frequency of in-hospital mortality stratified by Bilirubin.

		Outcome		P Value
Billiburin Group		In-Hospital Death	Discharged	
1-3.0	n	16	83	0.004
	%	16%	84%	
3.1 - 5	n	20	37	
	%	35%	65%	
>5	n	25	42	
	%	37%	63%	

Table 8: Frequency of in-hospital mortality stratified by Album

Albumin Group		Outcome		P Value
		In-Hospital Death	Discharged	
<2.0	n	28	30	<0.001
	%	48%	52%	
2.1 - 3.0	n	31	118	
	%	21%	79%	
>3.0	n	2	14	
	%	13%	88%	

Table 9: Frequency of in-hospital mortality stratified by PT (Prothrombin Time).

PT Group		Outcome		P Value
		In-Hospital Death	Discharged	
12-18	n	18	87	0.004
	%	17%	83%	
19-24	n	18	37	
	%	33%	67%	
>24	n	25	38	
	%	40%	60%	

Table 10: Frequency of in-hospital mortality stratified by INR (International Normalized Ratio).

INR Group		Outcome		P Value
		In-Hospital Death	Discharged	
<1.5	n	11	62	0.002
	%	15%	85%	
1.5-2.0	n	23	63	
	%	27%	73%	
>2.0	n	27	37	
	%	42%	58%	

Table 11: Frequency of in-hospital mortality stratified by Creatinine.

Creatinine Group		Outcome		P Value
		In-Hospital Death	Discharged	
<1.5	n	14	91	<0.001
	%	13%	87%	
1.5-2.0	n	17	31	
	%	35%	65%	
2.1-3.0	n	14	19	
	%	42%	58%	
>3.0	n	16	21	
	%	43%	57%	

DISCUSSION

High in-hospital mortality is seen in this study population as compared to similar studies done in developed countries population. Further, high in-hospital mortality was found to be associated with female gender, Child Class C, High MELD Score, high creatinine, bilirubin, PT, INR and low albumin.

Liach et al , reported the occurrence of the first episode of SBP in cirrhotic patients with ascites followed for a long period of time was relatively low at 11% after one year and 15% after 3years of follow up. This variation in comparison to our study are due to that they included patients with only moderately advance liver disease, as 80% of patients were with CTP class A and B only while in our study 85% of patients were in CTP Class C. They also included patients who were on oral non-absorbable antibiotics during UGI bleeding which on follow up may have reduced the risk of SBP in their patients.[12] Luke T Evan et al, reported the prevalence of SBP was 3.5% in the population of 427 cirrhotic outpatients. SBP in outpatients is less frequent and may have better outcome than in hospitalized patients with SBP.[10]

In Various cohort studies of in-hospital mortality associated with SBP through the last few decades I,e from 1984 to 1989, the Liver Unit at the University of Barcelona Hospital Clinic reported 38% in-hospital mortality in 185 cirrhotic patients with SBP.[13] In a study using the Maryland Health Services Cost Review database of all patients admitted to Maryland hospitals with SBP as a diagnosis from 1988 to 1998, the rate of in-hospital mortality was 32.6%.[11] Whereas, from 1998 to 2007, in-hospital mortality associated with SBP using the National Inpatient Sample (NIS) appears to have lowered to 20.2%. In another study in the United States from 2006 to 2014 the overall in-hospital mortality was 17.6% for patients with SBP. Which is lower than the rate reported by several previous cohort studies in the United States and abroad examining in-hospital mortality of patients with SBP from 1984 to 1989 (38%), 1988 to 1998 (32.6%), and 1998 to 2007 (20.2%).[11,13,14]

In our study, the overall in-hospital mortality was 27.4% for patients with SBP, almost equal to the rate reported by several previous cohort studies. High in-hospital death were found to be in Female (33%) gender as compared to male (25%). Baseline liver diseases were analysed according to mortality outcome. CTP-C (32%) has highest mortality as compared to CTP-B (5%). Bilirubin >8mg/dl, INR > 2 minutes, PT > 24 seconds, creatinine > 2.4mg/dl and MELD > 30 is associated with high in-hospital mortality. Results of this study coincide with those of Thuluvath et al. from 2001 in that in-hospital mortality was 32.6% and older age was associated with high in-hospital death while race was not a assessed for SBP mortality in our study[15]. However, in contrast to Thuluvath et al. we also found an increased mortality in advanced liver disease (CTP-C and MELD >30). [11]

Our study revealed a high prevalence of Hepatitis C as an underlying etiology for chronic liver disease in SBP patients, which aligns with the global burden of Hepatitis C, particularly in regions like Asia. However, it's worth noting that a substantial proportion of patients had hepatocellular carcinoma, highlighting the frequent co-occurrence of these conditions and the increased risk they pose to patient mortality [16-17].

CONCLUSION

In end stage liver disease due to cirrhosis with ascites, any risk factor like SBP is sufficient to alter the balance and affect the sequence of consequences leading to mortality. Patients with other risk factors like fever, UGI bleed and hepatic encephalopathy are found to be aggravating factors for developing SBP. SBP is easy to diagnose and treate hence clinicians should have a high index of suspicion and low threshold for diagnosis. Early diagnosed cases of SBP can be treated with very good success rate up to 73%. Gram-negative organism are predominantely found in most SBP infections now a days. Neutrophilia in ascitic fluid should be taken as sufficient criteria to treat the patient as culture positivity is low.

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