

Spontaneous Bacterial Peritonitis in Alcoholic Cirrhosis: An Indian Perspective

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ABSTRACT

Background: Spontaneous bacterial peritonitis (SBP) is commonly associated with cirrhosis of liver, and has been associated with high mortality. Model for end-stage liver disease (MELD) scoring system has been applied as a marker of disease severity and predictor of mortality in patients with alcoholic cirrhosis. Recent studies have estimated a prevalence of 10 to 30% SBP in cirrhotic patients with ascites admitted to hospitals but the data is lacking on Indian population. Hence, the present study was designed to evaluate the profile of SBP in patients with alcoholic cirrhosis in North India according to MELD score.

Materials and methods: The prospective study was conducted in patients admitted in the department of medicine. A total of 100 patients suffering from alcoholic cirrhosis with ascites were enrolled in the study. All subjects underwent the following test for biochemical parameters, abdominal ultrasonography, chest X-ray, endoscopic findings and paracentesis was performed and analyzed. MELD score was calculated for all the patients.

Results: Out of total patients, 24% reported with SBP. Patients suffering from SBP had statistically significant ($p < 0.05$) higher MELD score, International normalized ratio (INR) and serum creatinine levels. Also, the patients with SBP had significantly ($p < 0.05$) lower platelet count as compared to patients without SBP. All the other parameters were comparable in both the groups.

Conclusion: SBP is a common complication of alcoholic cirrhosis of Indian patients and measures should be taken for their containment.

Abbreviations: SBP: Spontaneous bacterial peritonitis; MELD: Model for end-stage liver disease; INR: International normalized ratio; TIPS: Transjugular intrahepatic portosystemic shunt; ICH-GCP: International conference on harmonization-good clinical practice; AFB: Acid fast bacilli; CNNA: Culture negative neutrocytic ascites; MNB: Monobacterial bacterascites; AST: Aspartate transaminase; ALT: Alanine transaminase; SAAG: Serum ascites albumin-gradient.

Keywords: Spontaneous bacterial peritonitis, Cirrhosis, Ascites, MELD score.

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INTRODUCTION

Spontaneous bacterial peritonitis (SBP) occurs commonly in conjunction with cirrhosis of liver, frequently the result

of alcoholism.¹ It has been associated with high mortality. Early reports suggested a mortality rate of approximately 95% in patients with SBP.^{2,3} There has been a decline in 1-year mortality of 50 to 70% in hospitalized patients.⁴ A higher mortality was seen in patients with a serum bilirubin >8 mg/dl or serum creatinine >2.5 mg/dl.⁵ There was a high probability of recurrence of SBP of 70% at 1-year and with each episode of SBP the probability of survival becomes significantly lower.⁶

The cause of SBP is believed to involve hematogenous spread of organisms with a diseased liver and altered portal circulation results in a defect in the usual filtration function. Organisms are able to multiply in ascitic fluid. Proteins of the complement cascade have lower levels in cirrhotic patients and the opsonic and phagocytic properties of neutrophils are decreased in patients with cirrhosis.^{7,8}

In approximately 50 to 60% of cases, the organism responsible is isolated in ascitic fluid or in blood cultures, the remaining are variants of SBP.⁹⁻¹¹ More than 92% of cases of SBP are monomicrobial, with aerobic Gram-negative bacilli; being responsible for more than two-third of all cases with *Escherichia coli* being the most common followed by *Klebsiella species*.¹² Almost 25% of cases are caused by Gram-positive organisms, with streptococcal species being most common followed by *Staphylococcus aureus*.^{12,13} Anaerobe causes nearly 1% of SBP and monobacterial ascites.^{14,15}

The clinical features of SBP are variable and range from typical picture of fever, icterus, hepatic encephalopathy, generalized abdominal pain, abdominal tenderness, and decreased bowel sounds to a totally asymptomatic SBP, which occurs in approximately 10 to 32% of cases.^{5,16} Since, classic clinical features are not present in all patients it is important to do diagnostic paracentesis for cell count and cultures in any patient with onset of ascites or any cirrhotic patient with ascites who develops a compatible symptom (i.e. symptoms suggestive of SBP), including unexplained encephalopathy, and any patient with stable ascites who deteriorates suddenly.¹⁷

The model for end-stage liver disease (MELD) scoring system was originally designed for the assessment of short-term prognosis in patients with liver cirrhosis undergoing a transjugular intrahepatic portosystemic shunt (TIPS) to

alleviate portal hypertension.¹⁸ Subsequently, it has been applied as a marker of disease severity and predictor of mortality in patients with alcoholic cirrhosis. The individual components of the MELD score have been described as individual predictors of mortality from alcoholic hepatitis in various studies.¹⁹

Recent studies using newer diagnostic criteria and improved culture techniques have estimated a prevalence of SBP in 10 to 30% of cirrhotic patients with ascites admitted to hospitals.²⁰ Indian data is scanty regarding the incidence of SBP in alcoholic cirrhosis. The present study evaluates the profile of SBP in patients of alcoholic cirrhosis in North India according to MELD score.

MATERIALS AND METHODS

Patients

The prospective study was conducted in patients admitted in the Department of Medicine, Dayanand Medical College and Hospital, Ludhiana, India. The duration of study was 1 year from April 2004 to March 2005. A total of 100 patients suffering from alcoholic cirrhosis with ascites and admitted in hospital were enrolled in the study after they signed an informed written consent. Patients of both the sexes above the age of 18 years were included in the study. The study was approved by the Institutional Ethics Committee of Dayanand Medical College and Hospital, Ludhiana and was conducted in accordance with Helsinki declaration of 1975, as revised in 1983 and as per ICH-GCP guidelines.

Patients were screened at the beginning of the study. A detailed medical and drug history was obtained. Patients with secondary bacterial peritonitis, hepatitis C virus infection, hepatitis B virus infection, HIV infection, tubercular peritonitis, congestive heart failure or nephrotic syndrome were excluded from the study on the basis of appropriate investigations. Patients who qualified the exclusion and inclusion criteria were enrolled in the study.

Diagnosis

The diagnosis of cirrhosis was established on the basis of following investigations: Biochemical parameters-liver function test, complete blood count, INR ratio, viral markers, renal function test, abdominal ultrasonography, chest X-ray and endoscopic findings.

All subjects underwent paracentesis within 24 hours of admission under aseptic conditions. Ascitic fluid analysis was done which included cytology, Gram's staining, AFB staining by Ziehl-Neelson staining, fungal smear examination, ascitic fluid culture sensitivity, ascitic fluid

biochemical analysis, blood culture, total serum proteins, serum albumin and cytology for malignant cells.

Cytological Measurements

According to ascitic fluid culture and cytology reports, the SBP was classified as:

1. *Classic spontaneous bacterial peritonitis*: The diagnosis of spontaneous bacterial peritonitis was considered, if the ascitic fluid polymorphonuclear cell count was $\geq 250/\text{mm}^3$, culture of ascitic fluid was positive in the absence of intra-abdominal source of infection.
2. *Culture negative neutrocytic ascites (CNNA)*: The diagnosis of culture negative neutrocytic ascites was considered if ascitic fluid polymorphonuclear cell count was $>250/\text{mm}^3$, negative ascitic fluid culture, no previous antibiotic treatment within 30 days and no intra-abdominal source of infection.
3. *Monobacterial bacterascites (MNB)*: The diagnosis of monobacterial bacterascites was considered if ascitic fluid polymorphonuclear cell count $< 250/\text{mm}^3$, culture of ascitic fluid positive, no intra-abdominal local source of infection.

Severity and Grading

The severity of cirrhosis was assessed by model for end-stage liver disease (MELD). http://www.unos.org/resources/MELD_calculator.²¹

SBP was diagnosed using standard criteria, namely, an absolute neutrophil count of ≥ 250 cells/ mm^3 , that is neutrocytic ascites, in the absence of an intra-abdominal source of infection. If ascitic fluid cultures were positive and the neutrophil count was ≥ 250 cells/ mm^3 , such patients were diagnosed as having culture-positive neutrocytic ascites. If ascitic fluid cultures were negative in the presence of neutrocytic ascites, these patients were characterized as having culture-negative neutrocytic ascites (CNNA). Patients with positive cultures on ascitic fluid but without neutrocytic ascites were classified as having bacterascites.²²

Statistical Analysis

The data was tabulated as mean \pm standard deviation (SD). Results were analyzed using nonparametric tests (Chi-square test, Wilcoxon sign ranked test and Mann Whitney U-test) and parametric tests (two tailed student t-test). A $p < 0.05$ was considered statistically significant. Nominal variables were compared with Chi-square analysis. The student t-test was used for comparison of group means for normally distributed data and the Mann-Whitney U-test/ Wilcoxon sign rank test was used for nonnormally distributed data.

RESULTS

A total of 250 patients with alcoholic cirrhosis admitted in Dayanand Medical College and Hospital, Ludhiana, India were screened for primary assessment. One hundred patients of the total 250 had accompanying ascites and were enrolled in the study. All the 100 patients in the age group of 18 to 90 years underwent all the laboratory investigation as per the study protocol. Twenty-four of them (24%) were diagnose as SBP.

The demographic and clinical presentation of patients suffering from SBP were comparable to patients without SBP (Table 1) except for MELD score which was significantly higher in patients with SBP compared to that with non-SBP (19 ± 2.42 vs 15 ± 3.93 , $p < 0.05$).

Liver Function Test

Serum bilirubin, AST, ALT, AST/ALT ratio and serum albumin levels were seen in all the patients (Fig. 1 and Table 2). All the parameters were comparable in both the groups. Although the serum bilirubin levels were slightly higher in patients without SBP but it was not statistically significant.

Other Biochemical Parameters

All the patients also underwent complete blood count, INR ratio and serum creatinine estimation (Table 2). The INR was significantly higher in SBP patients compared to non-SBP (2.98 ± 1.4 vs 2.43 ± 0.93 , $p < 0.05$). Also, the levels of serum creatinine were significantly higher in patients with

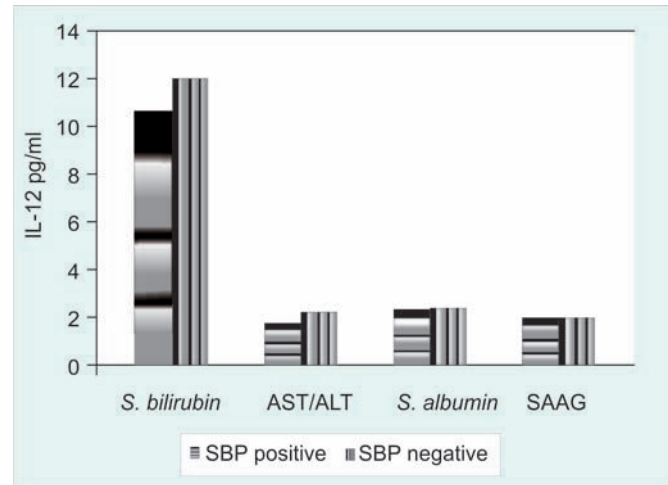


Fig. 1: Liver function test (LFT) in both the groups

SBP compared to those in non-SBP patients (2.44 ± 0.84 vs 1.8 ± 1.35 , $p < 0.05$). Similarly, the patients with SBP had significantly lower platelet count as compared to patients without SBP (112 ± 50.66 vs 157.3 ± 92.63 lac/mm³, $p < 0.05$).

MELD Score

MELD score was interpreted for prognosis in patients with cirrhosis. The MELD score was classified as score range between 0 to 5, 6 and 10, 11 and 15, 16 and 20, 21 and 25 and >26 (Fig. 2). The score range of patients with SBP was from 15 to 25 while those without SBP had a score range from 6 to 25. There was no patient in both the groups that had a score range of 0 to 5. Patients with SBP had a significantly higher ($p < 0.05$) number in the score range of

Table 1: Demographic and clinical presentation of the patients

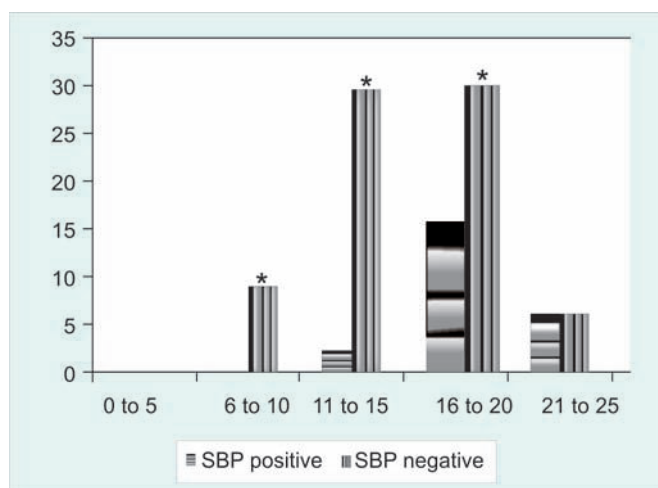
Characteristics	Spontaneous bacterial peritonitis positive	Spontaneous bacterial peritonitis negative	p-value
Age (years) (mean \pm SD)	48.75 \pm 11.49	49.32 \pm 11.37	0.83**
MELD score (mean \pm SD)	19 \pm 2.42	15 \pm 3.93*	< 0.05**
Jaundice (%)	20 (83.3)	54 (71.1)	0.40***
Fever (%)	15 (62.5)	33 (43.4)	0.18***
Encephalopathy (%)	14 (58.3)	45 (59.2)	0.89***
Upper gastrointestinal blood (%)	3 (12.5)	19 (25)	0.30***

* $p < 0.05$ as compared to the other group; **Using unpaired student t-test; ***Using Chi-square test

Table 2: Biochemical parameters

Characteristics	Spontaneous bacterial peritonitis positive	Spontaneous bacterial peritonitis negative	p-value
Total leukocyte count (mean \pm SD)	12.95 \pm 8.18	11.72 \pm 6.31	0.44**
Hemoglobin (mean \pm SD)	9.84 \pm 1.89	10.15 \pm 1.91	0.48**
Platelet count (mean \pm SD)	112 \pm 50.66	157.27 \pm 92.63*	< 0.05**
Serum creatinine (mean \pm SD)	2.44 \pm 0.84	1.80 \pm 1.35*	< 0.05**
AST (mean \pm SD)	121.42 \pm 50.26	117.88 \pm 73.54	0.83**
ALT (mean \pm SD)	68.75 \pm 30.34	64.71 \pm 67.52	0.79**
INR (mean \pm SD)	3.22 \pm 1.24	2.43 \pm 0.92*	< 0.05**
Ascitic albumin (mean \pm SD)	0.36 \pm 0.32	0.467 \pm 0.35	< 0.18**

* $p < 0.05$ as compared to the other group; **Using unpaired student t-test



*p < 0.05 as compared to other group

Fig. 2: Model for end-stage liver disease (MELD) in both groups

>16 (22 vs 36) whereas the patients without SBP mostly had a score <15 (39 vs 2).

Bacteriological Report

All the patients enrolled in the study underwent abdominal paracentesis within 24 hours of admission and the ascitic fluid was sent for estimation. Three patients had blood culture positive belonging to the group of patients with SBP. Acid fast bacilli staining and fungal smear was negative in all the patients.

The report of ascitic fluid analysis of patients with SBP is presented in Table 3. All the 24 patients with SBP underwent ascitic fluid culture sensitivity and 50% had positive culture report. *E. coli* was the predominant organism seen in patients with positive culture report. The majority of patients had CNNA variant of SBP and most of the patients had a polymorph nuclear count of >250/mm³.

Table 3: Bacterial report of spontaneous bacterial peritonitis positive patients

Characteristics	Number of patients (%)
Bacteremia	
Positive	3 (12.5)
Negative	21 (87.5)
Variants	
Classic SBP	6 (25)
CNNA	14 (58.3)
MNB	4 (16.7)
PMN count	
>250	20 (83.3)
<250	4 (16.7)
Ascitic fluid culture sensitivity	
Positive	12 (50)
Negative	12 (50)
Bacteriological data	
<i>E. coli</i>	5 (20.8)
<i>Acinetobacter</i>	1 (4.2)
<i>Staphylococcus aureus</i>	4 (16.7)
<i>Staphylococcus epidermidis</i>	2 (8.3)

DISCUSSION

Spontaneous bacterial peritonitis is a frequent and serious complication of cirrhosis (alcoholic cirrhosis) and carries a high mortality, if goes undetected and untreated, hence sensitive and specific measures are required for its early diagnosis.

All the patients in our study were male because of cultural reasons as women do not indulge in alcohol drinking in Punjab.

The age of the patients in our study ranged between 18 and 90 years. The mean age was 49.06 ± 11.35 years. Most of the patients were in fourth and fifth decade of their life. The mean age of all patients in a study conducted by Filik L et al was 49.91 ± 15.01 (17-90 years) (n = 214).²³ The most common clinical presentation was jaundice (83%), followed by fever (63%), encephalopathy (58%) and upper gastrointestinal tract bleeding (UGIB) (13%). The results were consistent with the study conducted by Runyon BA et al¹⁶ in which fever was the most common feature (67%) followed by abdominal pain (60%), abdominal tenderness (42%), encephalopathy (57%).^{2,16,24,25} In other study, jaundice was present in 54.5% patients, hepatic encephalopathy in 50.7%, abdominal pain in 44.4% and fever in 38.8% patients.²³

In our study on 100 patients of alcoholic cirrhosis with ascites, SBP was diagnosed in 24 patients. This was consistent with study conducted by Caly et al that revealed a prevalence of 10 to 30% of SBP in cirrhotic patients with ascites admitted to hospitals.²⁰ In a study conducted by Figueireda et al, SBP was prevalent in 20% of cirrhotic patients with ascites.²⁶

Out of 24 patients of SBP, six were of classic SBP type, 14 were of CNNA type and four were of monobacterial bacterascites. This was earlier proven in study conducted by Runyon et al that the incidence of CNNA variant of SBP ranges from 7 to 44% of total SBP patients.¹⁴

Monobacterial bacterascites constitute 1/3rd of total patients with culture positive spontaneous infected ascites^{5,17,27} and also in our study, it constitute 1/3rd of total culture positive cases (4 out of 12 culture positive cases).

In a study conducted by Figueiredo et al classic SBP, CNNA and MNB were present in 24, 66 and 10% of alcoholic cirrhotic patients respectively.²⁶

In a study conducted in medical ward of Khyber Teaching Hospital, Peshawar in 2003, out of which 200 cirrhotic patients, SBP was present in 102 patients. Classic SBP was present in 38.23%, CNNA in 57.84% while MNB was in 3.92% of patients.²⁸

The mean MELD score²⁹ in the group of patients with SBP was 19 in our study which was slightly more than the

scores reported by Evan et al and lower than that reported by Malinchoc et al.³⁰ The patients in our study who had reported with and without SBP did not have any significant difference in serum albumin and serum bilirubin and the results of our study were quite similar to those reported by Evans et al.^{22,30} The patients in our study with SBP had significantly higher serum creatinine and INR as compared to patients without SBP and differed from study from Evans et al.^{22,30}

In the study conducted by Filik et al it was found that of all the factors analyzed in patients with chronic liver disease, fatigue, hepatitis, hepatic encephalopathy, leukocytosis, renal dysfunction (creatinine >2 mg/dl), coagulopathy (PTI >2.5 INR) and low ascitic protein level (<1gm/dl) were statistically correlated with poor prognosis ($p < 0.05$).²³

In approximately 50 to 60% of cases, the organism responsible is isolated in ascitic fluid or in blood culture.⁹⁻¹¹ Studies have shown that bedside inoculation of the ascitic fluid into blood culture bottles has significantly increased the detection rate for the responsible organism.³¹ More than 92% cases of SBP are monomicrobial, with aerobic Gram-negative bacilli; being responsible for more than 2/3rd of all cases. Almost 25% of cases are caused by Gram-positive organism, with streptococcal species being most common.¹³ The most common organisms being *Escherichia coli*, *Klebsiella*, *Streptococcus viridans*, *Staphylococcus aureus*, other Gram-negative and Gram-positive organisms.¹² In our study out of 24 patients with SBP, 12 were ascitic fluid culture positive. Out of which *Escherichia coli* was present in five patients, *Staphylococcus aureus* in four patients, *Staphylococcus epidermidis* in two patients and *Acinetobacter* in one patient. Study conducted in Khyber Teaching Hospital, Peshawar in 2003, showed *E. coli* was isolated in 58.13%, *Streptococcus pneumoniae* in 18.60%, *Staphylococcus aureus* in 9.13%, *Klebsiella* in 9.13% and *Acinetobacter* in 4.63%.²⁸

In a prospective study conducted by Pawar et al, *E. coli* was present in 60% of cases. There was a significantly greater ($p < 0.001$) ascitic fluid culture positivity with direct inoculation into blood culture bottles, i.e. 66.7% compared to 31.1% by conventional method.³²

To conclude the present study on patients with alcoholic cirrhosis with ascites, we found that 24% patients reported with SBP, the mean MELD score in this group of patients was significantly more as compared to other cirrhotic patients. Using the appropriate diagnostic criteria, the classic SBP was the most common presentation in SBP.

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