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### Original Article

## Spontaneous bacterial peritonitis in cirrhosis of liver with ascites-a cross sectional study.

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#### ABSTRACT

**BACKGROUND:** Spontaneous bacterial peritonitis (SBP) is a common and potentially fatal complication of cirrhosis of liver with ascites, both in alcoholic and non-alcoholic liver disease, although more common in former case. **AIMS :** To determine the prevalence of spontaneous bacterial peritonitis (SBP) and its clinical profiles in patients of cirrhosis of liver with ascites. **STUDY DESIGN :** A cross sectional study. **PATIENTS :** A total of 50 patients of cirrhosis of liver with ascites. **METHODS :** These patients were diagnosed on the basis of clinical evaluation, biochemical investigation, ultrasonography of the abdomen, ascitic fluid examination for protein, PMN count, and bacterial culture using conventional method. **RESULTS :** Prevalence of SBP in these patients was 18%. The commonest clinical variant of SBP observed was Culture Negative Neutrocytic Ascites (CNNA), present in 77.78% of patients. 11.11% had Mono microbial Non neutrocytic Bacterascites (MNBA), and remaining 11.11% of patients had Classic Spontaneous Bacterial Peritonitis (C-SBP). 88.89% of the patients showed one or the other clinical manifestation and 11.11% were asymptomatic. In symptomatic patients, chief clinical features observed were abdominal pain, fever, hepatic encephalopathy and rebound tenderness. Among laboratory parameters, mean serum bilirubin was 6.48mg/dl, serum albumin was 2.41gm/dl, SPTR was 7.6 sec and mean ascitic fluid protein concentration was 93gm/dl. Ascitic fluid culture was positive in 22.22% of cases. Organisms isolated were E-coli in C-SBP patient and *S.aureus* in MNBA patient. 88.89% of patients who had SBP were in Child-Pugh's class 'C' server liver disease. 22.22% patients with SBP expired during the hospital stay. **CONCLUSION:** With these observations, it can be concluded that, SBP is one of the common complication of cirrhosis of liver with ascites. As a proportion of these patients remain asymptomatic, high degree of clinical suspicion, backed by relevant laboratory investigation are key for its accurate diagnosis and subsequent effective treatment, nevertheless, death can be an inevitable outcome.

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### 1. Introduction

Spontaneous bacterial peritonitis (SBP) is by definition an infection of the previously sterile ascitic fluid, without any apparent intra-abdominal source of infection.<sup>1</sup>

Ascites remains the commonest of the three major

complications of advanced or decompensated cirrhosis (along with hepatic encephalopathy and variceal haemorrhage). Cirrhotic patients with ascites are particularly susceptible to SBP due to altered gut permeability, suppression of the reticuloendothelial system and bacterial over growth.<sup>1,2</sup> Cirrhotics with ascites have, over a one-year period, 10% probability of developing the first episode of spontaneous bacterial peritonitis (SBP).<sup>3</sup>

SBP is a serious complication of cirrhotic ascites. SBP is the most frequent bacterial infection in cirrhosis, accounting for 10-30% of all reported bacterial infections in hospitalised

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The long term prognosis remains extremely poor among survivors of an episode of SBP, a manifestation of severe liver disease. Probability of survival of 1-2 years are in the range of 30% and 20% respectively.<sup>5</sup>

Hence the current study was undertaken to determine the prevalence of spontaneous bacterial peritonitis (SBP) and its clinical profiles in patients of cirrhosis of liver with ascites.

## 2. Material and Methods

The present cross sectional study was carried out for a period of one year in a tertiary health care centre. The research protocol was approved by the institutional research committee. Fifty patients of cirrhosis of liver with ascites admitted under Department of Medicine and Department of Gastroenterology were enrolled in the present study.

All patients with cirrhosis of liver with ascites diagnosed on the basis of clinical evaluation, biochemical investigation, ultrasonography, were included in the study. Patients who had antibiotics within two weeks prior to admission, patients classified having secondary peritonitis, ascites due to causes like tuberculosis, malignancy, renal or cardiac diseases were excluded from the study.

All the patients were subjected for routine investigations like complete blood count, urine analysis, blood sugar, renal function tests, chest X-ray and also special investigations like liver function tests, including prothrombin time and ultrasonography of abdomen. Serological tests for Hepatitis B and Hepatitis C were performed by spot method. Positive results were confirmed by ELISA.

After obtaining an informed and a written consent from the patient a diagnostic abdominal paracentesis was performed within 24 hours of admission.

Ascitic fluid was aspirated and sent for cell count and typing, biochemical analysis for estimation of sugar, proteins, and albumin, Gram's stain, ZN stain for AFB, malignant cytology and culture and sensitivity.

Based on the results of ascitic fluid analysis patients were grouped under following categories :

### 1. Classic - Spontaneous Bacterial Peritonitis (C-SBP)

- Ascitic fluid neutrophil count is equal to or more than 250 cells /ml.
- Ascitic fluid culture grows a single type of pathogenic organism.
- No surgically treatable intra abdominal source of infection.

### 2. Mono-microbial Non-neutrocytic Bacterascites (MNBA)

- Ascitic fluid neutrophil count is less than 250 cells / ml
- Ascitic fluid culture grows a single type of pathogenic organism.
- No surgically treatable intra abdominal source of infection.

- Ascitic fluid neutrophil count is equal to or more than 250 cells/ml
- Ascitic fluid culture is sterile.
- No surgically treatable intraabdominal source of infection.

**Statistical analysis :** Statistical analysis was done using mean value for all clinical and laboratory parameters of SBP and its variants.

## Observation and Results

A total of fifty cases of cirrhosis of liver with ascites were studied These patients were screened for Spontaneous Bacterial Peritonitis (SBP).

There were nine patients of SBP in our study.

SBP was more common in 5th and 6th decades with 3 patients in each age group. The mean age was 54.44(± 11) years. (Table-1)

8 patients were males and 1 patient was female. Male to female ratio was 8:1

Out of 9 patients, 6 patients (66.67%) had alcoholic cirrhosis, in 2 patients aetiology was not found (cryptogenic), 1 patient (11.11%) had hepatitis-B associated cirrhosis, and no patient had hepatitis-C associated cirrhosis.

Out of 9 cases of SBP, 7(77.78%) were of culture negative neutrocytic ascites (CNNA), followed by 1(11.11%) each of classic-spontaneous bacterial peritonitis (C-SBP) and mono-microbial non-neutrocytic bacterascites (MNBA). Thus CNNA was the commonest clinical variant.

In symptomatic SBP patients, abdominal pain was seen in 7(77.78%) patients, fever was seen in 6(66.67%) patients, hepatic encephalopathy in 6(66.67%) patients, rebound tenderness in 5(55.55%) patients, absent bowel sounds in 3(33.33%) patients, upper G.I. bleeding in 3(33.33%) patients, and hypotension in 2(22.22%) patients. Combination of various symptoms were present in our study, and we found that most of our patients were having more than one symptom.(Table-2)

Mean serum bilirubin level was 6.48 ± 4.2mg/dl, mean serum albumin was 2.41 ± 0.39gm/dl, Mean value of SPTR was 7.6 ± 1.80 sec..(Table-3)

Highest concentration of protein in ascitic fluid observed in our study was 1.9gm/dl and lowest was 0.40gm/dl. Mean ascitic fluid concentration was 0.93 ± 0.44gm/dl.

Ascitic fluid culture was positive in 2 patients (22.22%), with gram-negative bacteria, E. coli being responsible for one case and gram-positive cocci, Staphylococcus aureus for the other. (Table-4)

Out of 9 patients of SBP and its variants, 8 (88.89%) patients were in Child Pugh's Class C and only 1 (11.11%) case was in Child Pugh's Class B. (Table-5)

Resolution of SBP was achieved in 7 patients (77.78%) during the hospital stay and 2 patients expired during the episode, mortality rate being 22.22%.

**Table-1. Age distribution of patients with SBP**

Age group in years	No of patients
20-29	0
30-39	1
40-49	2
50-59	3
60-69	3
70	0
Total	9

**Table-2. Salient clinical features in patients of SBP**

Clinical features	C-SBP	MNBA	CNNA							Total (%)
			1	2	3	4	5	6	7	
Abdominal pain	+	-	+	+	+	+	-	+	+	7 (77.78)
Fever	+	-	+	+	+	-	+	+	-	6 (66.67)
Upper G.I	+	-	-	-	-	+	-	+	-	3 (33.33)
Rebound tenderness	-	-	+	+	+	-	+	-	+	5 (55.56)
Hypotension	+	-	-	-	-	+	-	-	-	2 (22.22)
Absent bowel sounds	+	-	-	+	-	+	-	-	-	3 (33.33)
Hepatic-encephalopathy	+	-	-	-	+	+	+	+	+	6 (66.67)

**Table-3. LABORATORY PARAMETERS IN SBP**

Groups	SERUM BILIRUBIN (mg/dl)	SERUM ALBUMIN (gm/dl)	SERUM PROTHROMBIN TIMERISE (sec)
C-SBP	12.4	2.0	8.2
MNBA	2.3	2.3	6.2
CNNA	9.0	2.5	5.8
	2.2	3.2	4.9
	1.8	1.9	7.4
	13.0	2.5	6.5
	6.2	2.7	7.0
	5.2	2.5	7.3
	6.2	2.1	11.2
Meant SD	6.484.2	2.410.39	7.61.8

**Table-4. Ascitic fluid culture**

Type of SBP	Organism detected
C-SBP, n=1	<i>E. coli</i>
MNBA, n=1	<i>S. aureus</i>
CNNA, n=7	*NOG

\*No Organism Grown

**Table-5. Severity of cirrhosis of liver in sbp**

Groups	Pugh score	Pugh grading
C-SBP	15	C
MNBA	11	C
CNNA	10	C
	9	B
	11	C
	15	C
	12	C
	14	C
	13	C

**3. Discussion**

50 patients of cirrhosis of liver with ascites, secondary to various aetiologies, diagnosed on the basis of history, physical findings of chronic liver disease and portal hypertension, abnormal findings of liver function tests and ultrasonography of abdomen were enrolled in our study, amongst which 9 were diagnosed to be SBP (One C-SBP, One MNBA, and Seven CNNA), as per the inclusion criteria described previously. Hence overall prevalence of SBP was 18%. Our findings are consistent with some of the studies conducted at other centers in India. Venkataswami et al., in their study of 100 patients, have reported 23.3% prevalence of SBP.<sup>6</sup> Patnaik et al., in their study of 120 patients, have diagnosed 24 cases of SBP, giving an overall prevalence of 20%.<sup>7</sup> The results of our study are in contrast with some of the studies like that of Lata J et al, who in their study of 99 patients, have reported the SBP prevalence of 35.5%.<sup>8</sup> Jain AP et al, in their series of 63 patients, have reported SBP prevalence of 34.92%.<sup>9</sup> The difference between the results of these two studies and present study may be due to the difference in culture positivity of ascitic fluid. Lata J et al, have reported 11 culture positive cases<sup>8</sup> while Jain AP et al, have reported 18 culture positive cases<sup>9</sup> in contrast to 2 culture positive cases in present study. The higher culture positivity in their studies may be the reason for the higher prevalence rate.

In present study, out of 9 cases of SBP, 7 were of CNNA (77.78%) and 1 (11.11%) was C-SBP and the other was MNBA (11.11%). Thus, CNNA was the commonest type of SBP in our study. These findings are contradictory to many studies, where C-SBP is the most common variant. Patnaik et al, reported 16 C-SBP cases and 6 cases of CNNA among 24 cases of SBP<sup>7</sup>. In another study by Almadal TP et al, out of 14 cases of SBP, 8 were C-SBP, 4 were MNBA and only 2 were CNNA<sup>10</sup>. The higher frequency of CNNA observed in our study might be due to use of conventional culture method of ascitic fluid. Various studies have proved that modified method of ascitic fluid culture in blood culture bottle is far superior to conventional one<sup>11</sup>. The other factors that may have contributed to culture negativity are, delay in transportation, not processing the sample for anaerobic organisms routinely.

In the present study, out of 9 patients of SBP 6 had alcoholism as the underlying cause of cirrhosis (66.67%). In 2 patients, the cause was not found (22.22%) and one case was positive for HbsAg (11.11%). But in the study by Amarapurkar et al, HbsAg positivity was the commonest predisposing factor. In their study of 31 patients of cirrhosis, 12 were HbsAg positive.<sup>12</sup> This higher HbsAg positivity in their study can be explained by geographical variation in seropositivity of HBsAg or can be a mere incidental finding.

In present study of 9 patients, youngest was 34 years old and the eldest was 68 years old. The mean age of patients with SBP was 54.44 years. Our findings are consistent with the findings of Lata J et al, and Boxieda et al, whose studies have reported the mean age of SBP cases to be 59.69 years and 56.67 years respectively<sup>8,13</sup>. However, in the study by Amarapurkar et al, mean age of SBP cases was significantly lower i.e., 42 years. This difference may be due to relatively younger patients in their study.<sup>12</sup>

Out of 9 patients, in the present study of SBP, 8 were males and only one was female, thus the M:F ratio was 8:1. Studies by Boxieda et al, and Lata J et al, also show male predominance. The male to female ratio in their study was 3.6:1 and 1.6:1 respectively<sup>8,13</sup>. Male predominance in our study and that of Boxieda et al and Lata J et al may be because of higher frequency of alcoholic cirrhosis in the male subjects studied. However, study by Venkataswamy et al, at Tirupati reports female predominance with M:F ratio 2:3. This fact is apparently unexplainable<sup>6</sup>.

In present study of 9 patients, 1 was asymptomatic (11.11%), while remaining 8 patients presented with various symptoms of the disease. Our findings correlate well with the studies by Runyon BA et al and Weinstein MP et al.<sup>14,15</sup> In Runyon BA et al study of 246 patients, 22 were asymptomatic (9%), while in Weinstein's study of 28 patients, 2 were asymptomatic (7%). Boxeida et al, have reported much smaller percentage of asymptomatic SBP (3.43%)<sup>13</sup>.

Abdominal pain was commonest clinical feature being present in 7 out of 9 patients of SBP (77.78%) in the present study. Fever and hepatic encephalopathy were next most common clinical features

being present in 6 patients each (66.67%). Rebound tenderness was third most common clinical feature which was present in 5 patients (55.56%). Upper Gastrointestinal (G.I) bleed and absent bowel sounds were seen in 3 patients each (33.33%). Hypotension was seen in 2 patients (22.22%). In Runyon BA et al study, similar observations were seen with abdominal pain in 60% cases. Fever and hepatic encephalopathy in 67% and 57% of cases respectively. Rebound tenderness and absent bowel sounds were seen in 42% of cases, hypotension was seen in 27% of cases.<sup>14</sup> In another study, Venkataswamy et al, have reported abdominal pain as the commonest clinical presentation in 67% of the cases, fever and rebound tenderness in only 19% of the cases, upper G.I bleeding in 14% of the cases. None of the cases had hepatic encephalopathy, absent bowel sounds and hypotension.<sup>6</sup> Study conducted by Weinstein M.P et al, has reported abdominal pain in 79%, fever in 68%, hepatic encephalopathy and absent bowel sounds in 54%, rebound tenderness in 42% of the cases, hypotension in 14% of cases as the presenting symptom.<sup>15</sup> In comparison with the above studies our observations were similar. In contrast to our study, Thanopoulou AC et al, have reported abdominal pain in 42% of cases, fever in 45%, hepatic encephalopathy in 8.6% of cases and no case with hypotension and rebound tenderness in their study.<sup>16</sup> This difference was probably due to inclusion of less severe liver disease patients.

Various biochemical parameters considered in our study were serum bilirubin, serum albumin, serum prothrombin time rise (SPTR) and ascitic fluid protein concentration. The mean serum bilirubin of patients with SBP in our study was 6.48 39 mg/dl and is similar to the study done by Liach et al, which has reported serum bilirubin of 6mg/dl<sup>17</sup> but is less compared to other studies done by Weinstein et al (11.8mg/dl)<sup>15</sup> and Correia JP et al (10.6mg/dl).<sup>18</sup>

The mean serum prothrombin time rise (SPTR) in our patients was 7.6 1.80 sec, which is similar to a study done by Weinstein et al (7.1 second)<sup>15</sup> but is higher than reported by Liach et al (4.20 second)<sup>17</sup> which probably reflects more advanced liver disease in our patients.

The mean serum albumin in our study was 2.41 0.39g/dl and it is similar to the study done by Venkataswamy et al (2.38g/dl), and Weinstein M.P et al (2.30g/dl).<sup>6,15</sup>

The mean ascitic fluid protein concentration in our study was 0.93 0.44g/dl and is similar to the findings of the study done by Runyon BA et al (1.0gm/dl).<sup>19</sup> In contrast to our study, Jain AP et al, have reported an ascitic fluid protein concentration in the range of 1-2 g/dl.<sup>9</sup> This may probably be due to more number of cases of cirrhosis of non-alcoholic aetiology in their study when compared to present study which included more number of alcoholic cirrhosis patients.

In our study, out of 9 patients, 2 were culture positive patients accounting for 22.22%. The organisms isolated from ascitic fluid were *E.coli* in one patient and *Staphylococcus aureus* in other

patient. Similar observations were reported in a study by Thanopoulou AC et al with ascitic fluid culture positive in 24.7% of cases and *E.coli* in 60% of cases.<sup>16</sup> However in a study, Jain AP et al, have reported *Staphylococcus aureus* (44.44%) as the commonest organism followed by *E-coli* (22.22%).<sup>9</sup>

In our study of 9 patients with SBP, eight had Child Pugh's Class-C severe liver disease and one was in Child Pugh's Class B. Similar observations were observed in a study by Amarpurkar D. N. et al, who reported 6 out of 7 cases in Child Pugh's Class-C severe liver disease and only 1 case in Class B.<sup>12</sup>

In hospital mortality of SBP in our study was 22.22% which is high compared to studies done by Venkataswamy et al (11%),<sup>6</sup> Thanopoulou AC et al (10%)<sup>16</sup> This may probably be because of 2 reasons. Firstly, most of our patients with SBP had Class C severe underlying liver disease; secondly, late arrival of the patients to the hospital. However, Jain AP et al, have reported, inhospital mortality rate of 27.2% which is similar to the present study.<sup>9</sup> Weinstein et al, in 1978 have reported even much higher mortality rate of 57%<sup>15</sup>. Franca et al, in their prognostic study of 47 SBP patients have reported that, 67% of the patients improved of which 44% had recurrence. Morality rate at 1 month was 32% and was 69% at 6 months.<sup>20</sup>

#### 4. Conclusion

With these observations, it can be concluded that, SBP is one of the common complication of cirrhosis of liver with ascites. As a proportion of these patients remain asymptomatic, high degree of clinical suspicion, backed by relevant laboratory investigation are key for its accurate diagnosis and subsequent effective treatment, nevertheless, death can be an inevitable outcome.

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