

FREQUENCY, MICROBIAL SPECTRUM, CLINICAL AND BIOCHEMICAL FEATURES OF SPONTANEOUS BACTERIAL PERITONITIS AND ITS VARIANTS

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ABSTRACT: Cirrhotic patients with ascites presenting at Chandka Medical College Hospital, Larkana, from May 1997 to June 1998 were included in the study to see the frequency, bacterial spectrum, clinical and biochemical features of spontaneous bacterial peritonitis (SBP). Ninety cases (63 males and 27 females) of liver cirrhosis with ascites were selected for analysis. SBP was found in 29 (32.2%) of cases. The breakup of SBP into its subtypes was, classic SBP found in 10 (34.5%) of cases, the bacterascites (BA) was found in 1 (3.4%) and that of culture negative neutrocyte ascites (CNNA) was found among 18 (62.1%) of cases. The frequency of organisms found in culture of ascitic fluid was; *E. coli* was found in 7 (63.64%) cases, pneumococcus in 2 (18.18%) cases, Klebsiella in 1 (9.09%) and Staphylococcus in 1 (9.09%). Mortality rate in patients with SBP was 31.03%

KEY WORDS: Peritonitis Liver Cirrhosis Microbiology

INTRODUCTION

Spontaneous Bacterial Peritonitis (SBP) is defined as bacterial infection of the ascitic fluid, without any intra-abdominal surgically treatable source of infection¹. The pathogenesis of spontaneous ascitic fluid infection appears to involve translocation of bacteria from the gut to the mesenteric lymph nodes, depressed reticuloendothelial phagocytic activity and deficient ascitic fluid antibacterial activity². The criteria for diagnosis of SBP is the presence of $\geq 500/\text{mm}^3$ of leukocytes or presence of ≥ 250 neutrophils in the ascitic fluid³⁻⁵. Depending on the cell count and culture of ascitic fluid, it has been further classified into its variants^{1,6-8}.

- **Bacterascites (BA):** defined as ascitic fluid leucocyte count $< 500/\text{mm}^3$ or neutrophil count $< 250/\text{mm}^3$ with positive blood culture.

- **Culture negative neutrocytic ascites (CNNA):** defined as ascitic fluid leucocyte count $\geq 500/\text{mm}^3$ or neutrophil count $\geq 250/\text{mm}^3$ with negative culture.

SBP is an often-overlooked fatal complication of cirrhosis. It carries a high morbidity and mortality⁹ and needs further exploration for better understanding and documentation of its frequency. Local data on this important issue is scanty¹⁰. The study was conducted to document:

- Frequency of SBP
- Frequency of the variants of SBP
- Causative organisms in these patients.

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- Compare the clinical features and biochemical profile of patients with and without SBP.

MATERIAL AND METHOD

Informed oral consent was obtained from all patients selected for the study. Consecutive patients of established diagnosis of cirrhosis with ascites presenting at Chandka Medical College Hospital (CMCH) Larkana from May 1997 to June 1998 were included in the study. The diagnosis of cirrhosis was made on evaluation of history, clinical examination, reduced liver span on ultrasound and ascites. Patients were segregated into the different variants of SBP based on the cell count and culture of ascitic fluid. Frequency of different variants was estimated and statistical analysis was carried out for significance by calculating 'p' value and 'X²' tests.

Exclusion criteria

- Patients having secondary peritonitis due to appendicitis, gastrointestinal perforation, abdominal tuberculosis, septicemia, intestinal obstruction, traumas etc.
- History of antibiotic therapy during past ten days.

Instruments

All selected patients were examined clinically and details were recorded in a proforma. Patients were classified into class A, B and C according to Child-Pugh's Criteria and scoring was done¹¹.

All patients were subjected to the following investigations.

- Complete Blood Counts (Sysmex K4500), urine routine examination, X-ray chest PA view, plain X-Ray abdomen, Pan abdomen ultrasound.

- HBsAg (Acon, Acon Laboratories, Inc. Allentown USA).
- Prothrombin time (Thromboplastin with calcium, BioMerieux Vitek, Inc. Hazelwood, USA).
- Ascitic fluid routine examination, culture and sensitivity: The ascitic fluid of every patient was aspirated under aseptic measure from left flank before initiation of therapy. Twenty ml of ascitic fluid was aspirated in a heparinized disposable syringe out of which 10 ml was immediately inoculated into blood broth bottle (Microsystem-01, Biosanrahx) and 10 ml, was sent to the laboratory for routine examination and cytology. After 48 hours, the subsequent subcultures on agar media were taken for further 24 hours.

Statistical analysis

All results for continuous variables are expressed as mean \pm SD. The Mann-Whitney U test and t-test were used to compare continuous variables between different groups. The p values for comparisons of categorical variables were generated by the chi-square test for proportions with appropriate degrees of freedom and p values of less than 0.05 according to the two sided McNemar test were considered to indicate statistical significance. All calculations were done with SPSS 7.5 (Statistical Package for Social Sciences, Chicago).

RESULTS

One hundred six patients presenting with ascites due to cirrhosis were inducted. Out of them 16 cases not fulfilling the inclusion criteria were excluded. Three patients expired before subjecting to investigation, 5 refused for undergoing series of investigations and 8 were already taking antibiotics at the time of presentation.

Ninety cases of the liver cirrhosis with ascites fulfilling the inclusion criteria were selected for analysis. These included 63 males and 27 females, their mean age \pm SD was 43.14 \pm 16.89 years for males and 44.03 \pm 18.47 years for females. No significant difference was present between the mean age of two sexes (p=0.8, 95% C.I. -8.83 to 7.04).

Among 90 cases assessed, SBP was found in 29 (32.2%) of cases. The breakup of SBP into its subtypes was, the classic SBP was found in 10 (34.5%) of cases, BA in one (3.4%) and CNNA was found among 18(62.1%) of cases.

Signs and symptoms at presentation

At the time of presentation pain was abdominal, present in 48 (53.3%), abdominal tenderness was noted in 86 (95.6%), jaundice was observed in 47 (52.2%), fever was present in 69 (76.7%) and abdominal rigidity was found among 17 (18.9%) of cases. The break-up of clinical features according to SBP and Non-SBP group is given in Table I. Statistically significant difference was observed only in the frequency of abdominal rigidity between the two groups (p = 0.02).

Grading for hepatic encephalopathy at presentation¹¹

Grading for hepatic encephalopathy was also done at the time of presentation which showed that 64 (71.1%) of cases were in grade-0, 17 (18.9%) of cases were in grade-I, 3 (3.3%) of cases were in Grade-II, 4 (4.4%) of cases were in grade-III and 2 (2.2%) cases were in grade-IV. Details according to the Non-SBP and SBP groups is given in Table II. The p-value of difference of hepatic encephalopathy in the two groups was 0.02.

TABLE I Clinical features at presentation in SBP and Non-SBP groups

Clinical Features	Non-SBP (n=61)	SBP (n=29)	P value
Abdominal pain	29 (47.5%)	19 (65.5%)	0.12
Abdominal tenderness	57 (93.4%)	29 (100%)	0.3
Abdominal rigidity	07 (41.2%)	10 (58.8%)	0.02*
Fever	47 (77.0%)	22 (75.9%)	1.0
Jaundice	33 (54.1%)	14 (48.3%)	0.66

* Statistically significant (p < 0.05)

TABLE II Grading of hepatic encephalopathy in SBP and Non-SBP groups

Encep. Grade	Non-SBP (n=61)	SBP (n=29)	Total
Grade-0	46 (75.4%)	18 (62.1%)	64 (71.1%)
Grade-I	12 (19.7%)	5 (17.2%)	17 (18.9%)
Grade-II	1 (1.6%)	2 (6.9%)	3 (03.3%)
Grade-III	0	4 (13.8%)	4 (04.4%)
Grade-IV	2 (3.3%)	0	2 (02.2%)

Child-Pugh's grading for severity of liver disease¹¹

At the time of presentation 1(1.1%) patient was in Class-A, 38 (42.2%) were in Class-B and 51 (56.7%) were in Class-C according to the Child-Pugh's grading. The P value calculated by Mann-Whitney U test was 0.04; showing a significant difference between Child-Pugh's grading in SBP and non-SBP groups. The mean of Child-Pugh's score of SBP group was 10.03 \pm 1.89 and that of non-SBP was 9.67 \pm 1.67. The P value was equal to 0.36, 95% C.I. -1.14 to 0.42. This shows no significant difference in Child-Pugh's score between SBP and non-SBP groups.

Bio-chemical examination

Details of bio-chemical examination done in the studied patients are given in Table III.

Out of 90 cases, HbsAg was found positive among 64(71.01%) of cases. The frequency of organisms found in culture of ascitic fluid was; E. coli in 7 (63.64%) cases, pneumococcus in 2 (18.18%) cases, Klebsiella in 1(9.09%) and Staphylococcus in 1 (9.09%).

In our study 17 (18.9%) patients expired during their hospital stay. Out of them 9 (31.03%) expired from SBP group and 8 (13.1%) expired from non-SBP group.

DISCUSSION

Spontaneous bacterial peritonitis (SBP) is a common and potentially fatal complication of liver cirrhosis with ascites. In our study SBP was present in 32.2% in hospitalized patients of cirrhosis. Our figure correlates with figures reported from other studies conducted in Pakistan, i.e. 33% from Aga Khan University Hospital (AKUH) Karachi¹² and 32.9% from Rawalpindi General Hospital (RGH) Rawalpindi¹³. Only one study from Nawabshah has reported a very high prevalence of SBP of 64%¹⁰ at their center and their results don't match with ours and other studies conducted in the region. Studies from foreign countries report the frequency of SBP from 7-25%^{14,15} which is less than found in Pakistan. This is attributed to poor hygienic conditions and high prevalence of infectious diseases in Pakistan as compared to foreign countries.

TABLE III Biochemical comparison in SBP and Non-SBP Groups

Biochemistry	SBP (mean±SD)	Non-SBP (mean±SD)	P value
Haemoglobin (gm/dl)	9.54±2.31	9.90±0.90	0.44
Bilirubin (mg/dl)	5.75±6.23	3.30±0.45	< 0.01*
ALT (IU/L)	150.17±263.94	72.55±54.11	< 0.02*
S. Protein (gm/dl)	6.44±0.79	6.54±0.88	0.6
S. Albumin (gm/dl)	2.44±0.4	2.64±0.28	< 0.001*
P.T. (sec.)	5.86±7.54	2.96±0.29	< 0.01*
Ascitic fluid TLC (cells/mm ³)	2734.83±2204.71	231.91 ±191.2	< 0.001*
Ascitic fluid neutrophils (cells/mm ³)	1919.55±1788.4	27.21 ±67.37	<0.001*
Ascitic fluid lymphocytes (cells/mm ³)	714.48±516.0	96.47 ±136.37	< 0.001*
Ascitic albumin (gm/dl)	0.89±0.24	1.39 ±0.4	< 0.001*

*Statistically Significant p < 0.05

SBP has two variants, bacterascites (BA) and culture negative neutrocytic ascites (CNNA). In our study frequency of BA was 3.5% and that of CNNA was 20.0%. In a study conducted at Civil Hospital Karachi¹⁶, the BA was found in 11.12% and CNNA was found in 44.44% of patients of SBP. The frequency of BA and CNNA as reported from Rawalpindi are 0.0% and 66.7% respectively in SBP. The difference in frequency could be attributed to host of factors like immune and general health status, causative organisms and small number of patients in these studies.

We used blood culture bottles for the culture of ascitic fluid as the positive yield is higher in blood culture bottle as that on agar plate and its sensitivity has been reported to be as high as 91%¹⁷. Recently Ortiz J et al¹⁸ used an automated calorimetric, microbial detection system Bact/ALERT. This method gives an earlier result with similar sensitivity.

Cell criteria in ascitic fluid appears to be a better method for the diagnosis of SBP, as it can provide an early diagnosis and hence early antibiotic therapy can be started, preventing serious complications. In our study we found abdominal pain in 65.5% and tenderness in 100% of SBP cases. Other studies have shown pain in 80% and tenderness in 51.5% to 53.33% cases respectively^{19,20}. Various studies from western countries have reported fever in 67.5-75.0% of patients of SBP. In our series, we found fever in 75.8% cases of SBP.

Infection anywhere in the body, including SBP can precipitate hepatic encephalopathy and it is therefore expected that clinical features of hepatic encephalopathy will be more in patients having SBP. Patients with jaundice due to advanced liver cell dysfunction are more prone to various infections like SBP, and SBP itself can cause further deterioration of liver function and deepening of jaundice. Jaundice was observed in 48.0% in SBP group in our study, whereas this figure was 79% in study conducted at Rawalpindi¹³.

Patients with upper GI hemorrhage are also prone to develop SBP and its variants²¹. As this increases the translocation of gut flora to mesenteric lymph nodes and due to loss of blood, the hypovolemia impairs the phagocytic activity of the reticuloendothelial system. Ascitic fluid is a walking media in cirrhotic patients. Due to low opsonic activity of its protein, the cirrhotic patients are more prone to develop SBP. In our study we also found low ascitic protein concentration, i.e. 0.89 gm/dl in SBP group. The microorganisms of SBP are usually of gut flora mostly *E. coli*. We found *E. coli* in 63.64% of cases. In another study conducted at Jinnah Postgraduate Medical Centre (JPMC), the *E. coli* was found in 50% of cases. The difference in the frequency might be due to the small number of patients in JPMC study.

The mean total leukocyte count (TLC) in ascitic fluid in JPMC study was 1304/mm³, while that in AKUH it study was 4812/mm³. The mean total leukocyte count (TLC) in ascitic fluid of our series was 2735/mm³ in SBP group. HBsAg was found positive among 22 (24.4%) of cases in our series, while that of at JPMC series was found positive in 9 (60.0%) of cases respectively. In our series we found statistically significant differences in serum bilirubin, ALT, serum albumin, prothrombin time, ascitic fluid TLC, neutrophils, lymphocytes and ascitic fluid albumin among the SBP and Non-SBP groups. These are detailed in Table III.

The hospital mortality rate varies from 20-40%. In our study mortality rate in SBP group was 31.03%.

CONCLUSION

Spontaneous bacterial peritonitis is common complication of cirrhosis of liver in our setting. Its risk increases with the decrease in ascitic albumin. *E. Coli* was found to be the commonest causative organism of SBP. Early diagnosis and prompt treatment is necessary to decrease morbidity and mortality of SBP.

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