

A CLINICAL STUDY OF SPONTANEOUS BACTERIAL PERITONITIS IN CIRRHOSIS OF LIVER WITH ASCITES IN TERTIARY CARE HOSPITAL

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ABSTRACT

Cirrhosis of Liver is the common hepatological disorder seen in clinical practice. Ascites is the Consequence of portal hypertension which is characteristic clinical feature of cirrhosis. One of the predisposing factors which is responsible for subsequent deterioration in the condition of cirrhosis patient is appearance of spontaneous bacterial peritonitis. Total of 50 patients who were confirmed of hepatic cirrhosis with ascites by ultra sound were screened for SBP and were studied thoroughly with regards to history, clinical examination, cytological, microbiological and biomedical tests. In present study the prevalence of Spontaneous Bacterial Peritonitis is found to be 18%. Among this 18%, 7 patients (77.7%) were Culture Negative Neutrocytic Ascites (CNNA) and 2 patients (22.3%) were Mono Bacterial Non Neutrocytic Bacterascitis. (MNB).

KEYWORDS

Cirrhosis of liver, Spontaneous Bacterial Peritonitis(SBP), Culture Negative Neutrocytic Ascites(CNNA), Mono Bacterial Non Neutrocytic Bacter Ascites. (MNB).

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INTRODUCTION: Cirrhosis is defined anatomically as a diffuse process with fibrosis and nodule formation of liver due to various causes. Ascites is the Consequence of portal hypertension which is characteristic clinical feature of cirrhosis. The development of ascites is a marker of prognosis in liver cirrhosis, as it indicates a reduction in 1- and 5-year survival rates by 15% and 23.5%, respectively.¹

The symptoms and signs of SBP are fever, abdominal pain, abdominal tenderness, rebound tenderness, altered mental status. Although 87% of patients with SBP are symptomatic, at the time the infection is diagnosed the symptoms and signs of infection are often subtle such as slight change in mental status.

Without prompt paracentesis the diagnosis and treatment of infected ascites may be delayed often resulting in death of the patient. A single organism usually, enteric group is cultured from the ascitic fluid in majority of cases.² Mild bacterial translocation to the mesenteric lymph nodes is a documented physiological event; however, only a few intestinal bacteria, including Escherichia coli, Klebsiella pneumoniae, and other Enterobacteriaceae, are able to efficiently translocate from the lumen of the gut to the mesenteric lymph nodes.³ E.coli, Streptococci and Klebsiella cause most episodes of Spontaneous Bacterial Peritonitis(SBP), Mono Bacterial Non Neutrocytic Bacter

Ascites (MNB) in patients who are not receiving selective intestinal decontaminants.

Type of infection	PMN cell count/ mm ³	Bacterial culture result
SBP	>250	Positive (Usually 1 organism)
Culture Negative Neutrocytic Ascites(CNNA)	>250	Negative
Mono Bacterial Non Neutrocytic Bacter Ascites(MNB)	<250	Positive (1 Organism)
Secondary Bacterial Peritonitis	250	Positive (Poly microbial)
Poly microbial Bacterascites	<250	Positive (Ploy microbial)

Table 1: Classification of ascitic fluid infection^{4,5,6}

AIMS & OBJECTIVES OF STUDY:

- To determine the Prevalence of spontaneous bacterial peritonitis & variants in patients of cirrhosis of liver with ascites.
- To study clinical profile of spontaneous bacterial peritonitis & its variants.

MATERIALS AND METHODS:

Source of Data: This Study was carried out on patients admitted to Government General Hospital, Kurnool Medical College, Kurnool.

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Study Subjects: Total of 50 patients who were confirmed of hepatic cirrhosis with ascites by ultra sound were screened for SBP and were studied thoroughly with regards to history, clinical examination, cytological, microbiological and biomedical tests.

METHODS: SBP was diagnosed by following criteria.^{7,8}

An ascitic fluid neutrophil count greater than 250 cells/mm³. Or A positive ascitic fluid culture, and an absence of a primary source of infection in abdomen.

Ascitic fluid for analysis was aspirated as soon as the patients were admitted, and diagnosed to be suffering from Cirrhosis of Liver, before giving any antibiotics. All patients underwent paracentesis within 24 hours of admission.

About 30 ml of ascitic fluid was tapped in each patient with aseptic precautions.

1. 10ml of ascitic fluid was immediately inoculated in to blood culture bottles at the bed side for microbiological analysis.
2. 10ml of ascitic fluid was sent to the laboratory in sterile test tubes for conventional culture.
3. 10ml of ascitic fluid was utilized for biochemical and cytological examination.

Ascitic fluid of all patients were analyzed for the type of cells and cell count. Gram's stain was done in all cases. Ascitic fluid was cultured to know the presence of pathogenic organisms.

Ascitic fluid was subjected to culture in blood culture bottles, Cytological and Biochemical examination including protein, albumin, glucose and pH.

A. Inclusion Criteria: Cirrhosis of liver was diagnosed on the basis of clinical features suggestive of chronic liver disease. Biochemical features (modestly elevated liver enzymes, Hypoalbuminemia, reversal of albumin to globulin ratio and prolonged prothrombin time) all suggestive of chronic liver disease ultrasound abdomen showing features of cirrhosis of liver & portal hypertension. Upper gastrointestinal endoscopy showing evidence of portal hypertension.

Liver biopsy (wherever possible) showing features of cirrhosis were included in present study.

B. Exclusion Criteria: The following patients were excluded from study:

1. Patient who had received antibiotic within 3 weeks prior to admission.
2. Patients classified as having secondary peritonitis which was diagnosed when one of the following features were present.
 - a) Selective & persistent localized abdominal pain & tenderness
 - b) Presence of following;
 1. Ascitic fluid lactic dehydrogenase concentration more than 225 mg/dL.
 2. Ascitic fluid glucose concentration less than 50 mg/dL.

- c) Isolation of more than one microorganism in the ascitic fluid culture.
 - d) An evidence of an intra-abdominal surgically treatable source of infection.
3. Tuberculosis abdomen with ascites.
 4. Malignancy with ascites.

Diagnostic Criteria:^{4,5,6,8}

1. An ascitic fluid neutrophil count greater than 250 cells/mm³.
Or
2. A positive ascitic fluid culture,
And
3. An absence of a primary source of infection.

Classification of AF infection have been described⁹

SBP: SBP has been defined as an Ascitic Fluid (AF) infection associated with a positive bacterial culture and an AF polymorphonuclear (PMN) cell count of >250/mm³, in the absence of a surgically treatable intraabdominal source of infection.

SBP was the first Ascitic Fluid infection described and is probably the most common variant. Because this infection is almost always monomicrobial, growth of more than one organism should raise a suspicion of secondary peritonitis.

Culture-negative Neutrocytic ascites (CNNA): This variant is diagnosed when cultures of AF is negative, a PMN cell count is >250/mm³, and when there is no surgically treatable intraabdominal source of infection. The clinical, prognostic, and therapeutic characteristics of CNNA are similar to that of SBP, and therefore both are treated in a similar fashion.

Mono microbial non neutrocytic bacterascites (MNB):

This variant is characterized by the isolation of bacteria in cultures of AF and a PMN cell count of < 250/mm³. Mono microbial non neutrocytic bacterascites may represent an early form of spontaneous bacterial peritonitis.

Secondary Bacterial Peritonitis: This entity is diagnosed in cases for which AF cultures are positive (usually polymicrobial), PMN cell counts are >250/mm³, and for which there is a surgically treatable intraabdominal source of infection.

Polymicrobial Bacterascites: Polymicrobial Bacterascites is diagnosed when gram staining or cultures of AF demonstrate multiple organisms and there is a PMN cell count of <250mm³. This variant usually occurs as a result of inadvertent puncture of the intestines during attempted paracentesis.

RESULTS AND ANALYSIS: Total 50 patients were studied thoroughly with regards to both history and clinical examination, cytological, microbiological and biomedical tests. The observations of the study are analysed.

Age in years	Number	Percentage
30-39	8	16%
40-49	17	34%
50-59	14	28%
60-69	10	20%
70-79	1	2%

Table 2: Age distribution of patients studied

Age distribution ranged widely with youngest patient being 30 years and oldest patient of 76 years. Mean age of the study population is 50.7 years. Maximum number of patients are found in age group of 40-69 years. Alcoholism is less in younger age group & prolonged consumption is required to cause Liver damage.

Elderly population were less in number constituting 20% of population, hence in the present study also number of elderly alcoholic are less in number, as in general population.

In the present study males are 86% and 14% of cirrhotics are females. Hence in the present study also there are more Male patients compared to female patients with a ratio of 6. Alcoholism is common in Male patients. Alcoholics are more prone to cirrhosis with Ascites. Alcoholism is less in females, but when they consume alcohol, more susceptible at lower levels due to low body mass index, because of stigma they may not disclose alcohol intake, duration, quantity of alcohol.

Sex	Number of patients	Percentage
Male	43	86%
Female	7	14%

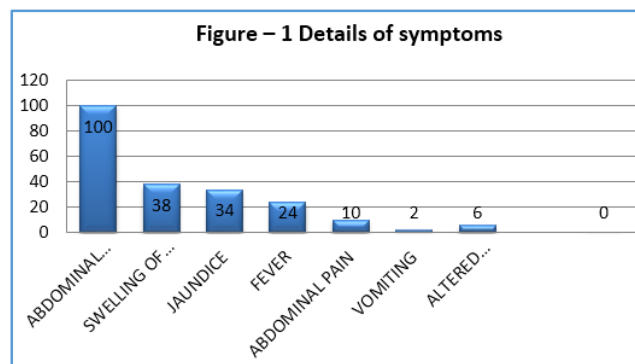
Table 3: Sex distribution of patients studied

Symptomatology: All study subjects had free fluid in abdomen which was mild to massive in degree. 24% of cases had fever it was mild to moderate in degree in 8 cases it was associated with chills. 10% had abdominal pain at the time of presentation, it was vague pain, distributed all over the abdomen, lasting throughout the day. There were no relieving factors.

34% patients had Jaundice as the presenting complaints, associated with yellow colouration of urine. While 6 % of cases were admitted with history of altered sensorium ranging from irritability, restlessness to drowsiness. Vomiting was the presenting complaint in 2% of patients.

Symptoms	Number of patients	Percentage
Abdominal distention	50	100%
Swelling of lower limbs	19	38%
Jaundice	17	34%
Fever	12	24%
Abdominal pain	5	10%
Vomiting	1	2%
Altered sensorium	3	6%

Table 4: Details of symptoms



Physical Signs: All (100%) the patients studied in this series had moderate to severe ascites, among them 18% of cases had tense ascites. Icterus was seen in 54% of cases. Bilirubin level ranged from 0.7–24.4 mg/dl. Pedal oedema was seen in 38% cases. Fever was seen in 24% of patients. Asterexis was seen in 10% of cases. Hepatomegaly was seen in 4% of cases only these patients were in early phase of cirrhosis and was having minimal ascites. Diffuse abdominal tenderness was seen in 10% of cases.

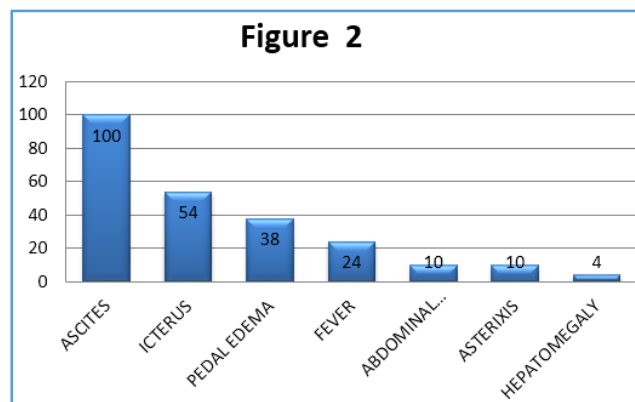
All the cases were investigated for evidence of portal hypertension by Ultrasonography.

Ascetic fluid was aspirated for diagnostic purpose in all subjects for evaluation of the cause & presence of SBP. A total of 20ml of ascetic fluid was inoculated, 10ml in Glucose broth at bed side and another 10ml was inoculated in Blood broth.

Remaining fluid was utilized for cytological and biochemical tests and the results are tabulated.

Signs	Number of patients	Percentage
Ascites	50	100%
Icterus	27	54%
Pedal edema	19	38%
Fever	12	24%
Abdominal tenderness	5	10%
Asterexis	5	10%
Hepatomegaly	2	4%

Table 5

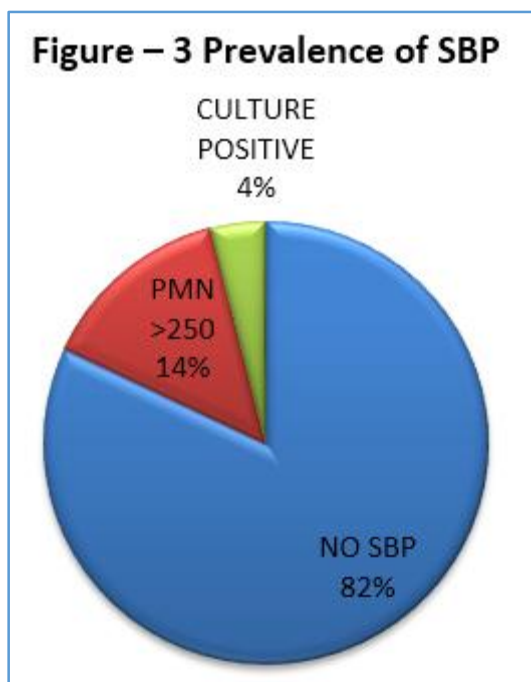


Prevalence of SBP: Among The 50 patients with cirrhotic ascites which was confirmed by Ultrasound Abdomen 9 patients were found positive for SBP, in this 7 patients had

only PMN count >250/mm³ but culture negative for any organism. Only 2 subjects were culture positive and isolated E.coli organism by 72hrs, by culture. All the positive cases were males. The mean age of positive patients -50.58years

Total no. of patients	Patients positive for SBP	Positive by PMN count >250/mm ³	Positive by culture	Males	Females
50	9	7	2	9	0

Table 6

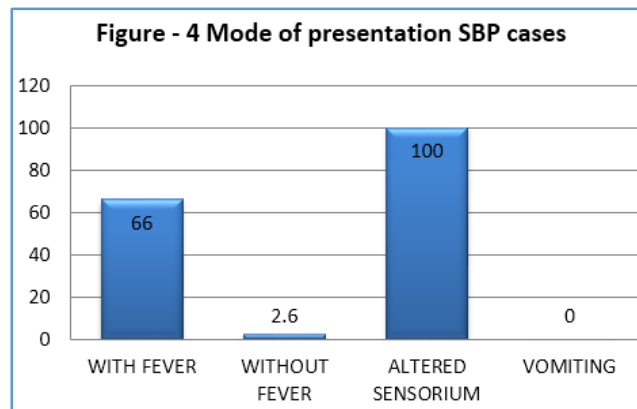


Mode of presentation SBP cases: Among the 50 patients studied 12 patients presented with fever, 1 presented with vomiting and 3 patients presented with altered sensorium. In 12 patients who presented with fever, 8 patients were had SBP (66%), 7 patients had PMN count >250/mm³ (CNNA) and 1 was culture positive (MNB).

3 patients presented with altered sensorium all the 3 patients was positive for SBP among this three positive cases one was culture positive (E.coli) MNB and the rest 2 had PMN count >250/mm³ (CNNA). Presence of Jaundice had no significance to SBP, but the degree of Jaundice is an indicator of SBP

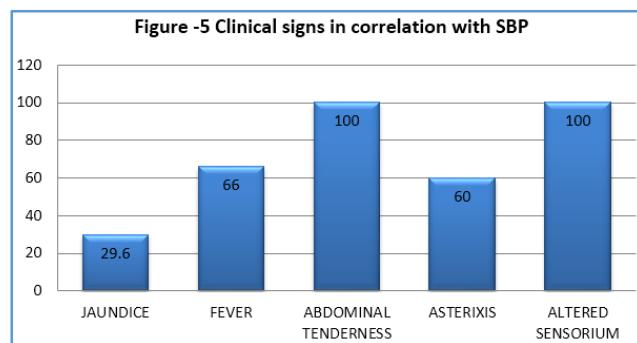
Mode of presentation	No. of cases	Positive for SBP	PMN count >250/mm ³	Culture positive	Percentage
With fever	12	8	7	1	66%
Without fever	38	1	Nil	Nil	2.6%
Altered sensorium	3	3	2	1	100%
Vomiting	1	Nil	Nil	Nil	0%

Table 7



Signs	No. of patients	Positive SBP	PMN >250/m ³	Culture positive	Percentage
Jaundice	27	8	7	1	29.6%
Fever	12	8	7	1	66%
Abdominal tenderness	5	5	4	1	100%
Asterixis	5	3	3	Nil	60%
Altered sensorium	3	3	2	1	100%

Table 8: clinical signs in correlation with SBP



Comparing signs and incidence of SBP 5 patients had abdominal tenderness all these 5 patients were positive for SBP. 4 patients had PMN count >250/mm³ (CNNA) and 1 were culture positive (MNB) On admission 5 patients had Asterexis, in these 5 patients 3 patients were positive for SBP and all the 3 were positive by PMN count >250/mm³ (CNNA). Among the 12 patients who had admitted with fever 8 were positive for SBP, 7 patients had PMN count>250/mm³ (CNNA) and 1 patient was culture positive (MNB). 27 patients had Jaundice in which only 8 were diagnosed SBP and 3 patients admitted with altered sensorium and all were positive for SBP.

All patients Presenting of Abdominal tenderness and altered sensorium had SBP. Presence of Fever had more chances of SBP, compared to Jaundice (29.6%).

Total Bilirubin In mg/dl	No. of cases	Positive cases	Percentage
0-1	0	0	0
1.1-2	19	2	10.52%

2.1-3	8	1	12.5%
3.1-4	11	2	18.18%
>4	12	4	33%

Table 9: Correlation of bilirubin with SBP

Serum bilirubin levels in patient's ranges from 1.1 to a maximum of 10.1mg/dl MEAN –6.30mg/dl with SD of +3.47.

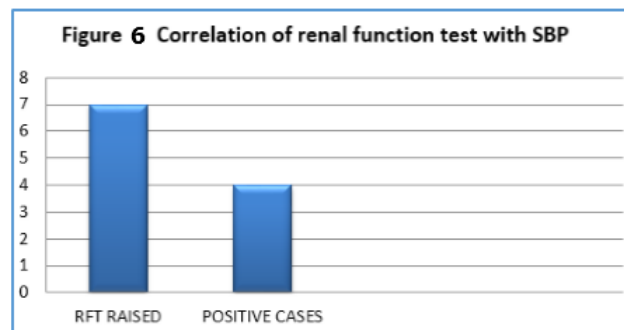
Maximum number of positive cases for SBP was seen in patients whose total bilirubin was more than 4mg/dl (33%).

Higher the derangement of Liver function, more the chances of SBP. Damaged liver is unable to detoxify the toxic organisms, leading to SBP.¹⁰

Correlation of renal function tests with SBP: Altered renal function was seen in 7 patients among them 4 patients were positive for SBP (57.14%). chances of SBP increases with severity of renal dysfunction.

RFT Raised	Positive Cases	Percentage
7	4	57.14%

Table 10



Comparison of investigations between the patients of SBP and patients without SBP: Comparison of investigations between the patients of SBP and Patients without SBP are studied using t test, which showed significant p value in Total count (<0.0001), Total Bilirubin (<0.0001), Serum Creatinine (<0.0001) and Ascitic Fluid cell count (<0.0001) Ascitic fluid protein (0.0260) which are highly statistically significant.

Investigations	Out come				P value
	Patients with SBP		Patients without SBP		
	Mean	SD	Mean	SD	
Total count	15061.11	422.71	8603	314.28	<0.0001**
Total bilirubin	6.30	3.47	2.91	1.38	<0.0001**
SGOT	182.67	31.56	175.44	28.51	0.5022
SGPT	155.44	11.93	153.98	22.34	0.8553
Serum creatinine	3.24	1.99	1.28	0.64	<0.0001**
AF protein	1.256	0.667	1.69	0.474	0.0260*
AF cell count	526.67	206.67	165.05	6.55	<0.0001**

Table 11

* Significant, ** Highly significant.

DISCUSSION: Spontaneous Bacterial Peritonitis (SBP) is by definition an infection of previously sterile ascitic fluid, without any apparent intra-abdominal source of infection. A polymorpho nuclear cell count of more than 250/mm³ in ascitic fluid is currently considered diagnostic of SBP and warrants the prompt start of antibiotic treatment.^{7,11}

The incidence of SBP in decompensated cirrhosis varies from 10 – 40% Specifically in Asia among Arab patients, it was reported that 10.4% of patients with cirrhotic ascites of non-alcoholic origin had culture-positive SBP, whereas 29.6% had culture-negative neutrocytic ascites (CNNA). Another report from northern India reported that 30% of hospitalized cirrhotic patients had SBP or its variants.

In present study 18% of Ascitic subjects had Spontaneous Bacterial Peritonitis out of 50 Cirrhotic Ascitic cases presently studied. In this 7 patients had only PMN count >250/mm³ but culture negative for any organisms. Only 2 subjects were culture positive and isolated E.coli organism on culture by 72hrs.

In present study the prevalence of SBP is found to be 18 %. Among this 18% (9 patients) 7 (77.7%) were CNNA and 2 (22.3%) were MNB. In various studies, routine

paracentesis has documented a prevalence of SBP of 10 - 27%^{12,13,14} Andreu et al reported a prevalence of 28% while Amarapurkar DN, Viswanathan, desai, found it to be 22.5%.⁴

Romney et al, in a study involving 67 cirrhotic patients found no case CNNA and only 10 of MNB. Obstein KL et al in a retrospective case control study of patients with cirrhosis and ascites found 29 (26.12%) of 111 patients with cirrhosis were found to have SBP.

Mean age of the patients was 50.7 and mean age of patients diagnosed for SBP was 53.22. SBP was seen in predominantly older age group, with most patients in 5th and 6th decade. Mean age at the time of diagnosis was 50.58 years. Mean age at the time of diagnosis in Filik L, Unal S was 49.9 years. 39 years in N Rawat, MK Bhatnagar¹⁵ series and 44 years in Mihas AA study.

In present study of 50 patients with cirrhotic ascites 43 (86%) were males, 7 were (14%) females. Dilshad Muhammad et al¹³ from Faisalabad studied 50 patients of cirrhosis with ascites of which 27 (54%) were males and 23 (46%) were females.

The common mode of presentation of SBP in present series was with fever, altered sensorium and abdominal

tenderness. Among 12 patients presented with fever 66% of cases had SBP. All the three patients presented with altered sensorium were positive for SBP. In Mihas AA, Toussaint J, study the clinical features were fever (69%) range and abdominal pain range (59%). include hepatic encephalopathy (54%), abdominal tenderness (49%), diarrhoea (32%).

In present study two MNB cases (22.22%) were positive for E.coli which isolated in first 72 hours. In the study by Runyon et al, E.coli was responsible for 27.3% of cases of SBP and Staphylococcus aureus for 6.8%. While Wilcox et al demonstrated Escherichia coli as the culprit in 45% cases and Staphylococcus aureus in 12% cases.

Ascitic fluid protein plays an important role in developing SBP in these patients. Present study Patients with ascitic fluid protein < 1 gm./ dl are frequently predisposed to SBP as in the other series cited above. In Runyon BA series the patients with ascitic fluid protein < 1 gm/dl were more predisposed to development of SBP.

CONCLUSIONS:

- Cirrhotic cases with constitutional symptoms must be compulsorily screened for SBP and started on Antibiotic therapy to reduce the mortality.
- SBP being the problem in cirrhosis with ascites, all cirrhotics should be screened for SBP with at least ascitic fluid analysis, PMN cell count and culture of ascitic fluid.
- To maximize survival it is important that paracentesis is performed in all patients with ascites at the time of hospitalization.
- So that infection can be detected and treated promptly. These patients must be treated with antibiotics aggressively as they have poor prognosis and high mortality if not treated early.

The present study is taken up to find SBP in cases of ascites and find its etiological causes, so that early diagnosis will help in early initiation of treatment of SBP leading to improvement of clinical state.

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