STUDY OF PREVALENCE OF SPONTANEOUS BACTERIAL PERITONITIS IN CIRRHOSIS OF LIVER WITH ASCITES

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ABSTRACT

BACKGROUND

Cirrhosis of Liver is the common hepatological disorder in clinical practice. The development of Ascites is a marker of Prognosis. Spontaneous Bacterial Peritonitis is responsible for the deterioration of the condition. Without prompt diagnosis, the diagnosis and treatment of infected Ascites may be delayed, leading to death. Study was conducted in 50 patients of Govt. General Hospital, Anantapuramu, to determine the prevalence of spontaneous bacterial peritonitis in Cirrhosis of liver with Ascites patients. Of these 50 patients, 9 patients (18%) showed features of SBP, 7 patient's (77.7%) PMN count was >250/mm³, 2 patient's (22.3%) culture was positive for E. coli. All cases with abdominal pain, tenderness and altered sensorium were having features of SBP. Study showed SBP more common in advanced liver disease. Presence of Jaundice had no significance, but the degree of Jaundice is an indicator of SBP. Study shown Cirrhotic patients with constitution of symptoms should be screened for SBP and started on Antibiotic therapy so that mortality can be reduced.

KEYWORDS

Spontaneous Bacterial Peritonitis; Cirrhosis, Ascites.

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INTRODUCTION

Cirrhosis of Liver is the common hepatological disorder seen in clinical practice. Ascites is the consequence of portal hypertension, which is a 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

One of the predisposing factors which is responsible for hepatic encephalopathy and subsequent deterioration in the condition of cirrhosis patient is appearance of Spontaneous Bacterial Peritonitis (SBP). The terminal event in these patients is Hepatic encephalopathy.

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 SBP and MNB in patients who are not receiving selective intestinal decontaminants.

Patients with cirrhosis are unusually predisposed to Bacterial infection because of multiple defects in Immune defense. Low ascitic fluid total protein concentrations as well as the phagocytic dysfunction associated with cirrhosis are risk factors for bacterial infection. Paracentesis itself has been proposed as a risk factor for ascitic fluid infection.⁴

Gastrointestinal haemorrhage and Urinary Tract Infection are under-recognized risk factors for SBP.⁵

Clinical deterioration, especially fever or abdominal pain in a patient with ascites should raise the suspicion of infection and prompt a paracentesis.⁵

SBP is statistically more likely to be diagnosed on the first paracentesis than on subsequent taps.⁵

So unexplained fever, hypothermia, hypotension, encephalopathy, abdominal pain or simply unexplained clinical deterioration should be considered as indicators for diagnostic paracentesis in cirrhotics for the diagnosis of SBP.^{6,7,8,9,10,11} SBP is caused by enteric group of organisms in about 75% and the remainder by non-enteric group of organisms including anaerobes.^{12,13}

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 ascetic 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.¹⁴ 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 aetiological causes, so that early diagnosis will help in early initiation of treatment of SBP leading to improvement of clinical state.

AIMS AND OBJECTIVES OF STUDY

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

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MATERIALS AND METHODS

Source of Data

This study was carried out on patients admitted to Government General Hospital, Anantapur, Govt. Medical College, Anantapur.

Study Subjects

Patients admitted for cirrhosis of liver with ascites or its complications were studied during the period from January 2015 to June 2015. All patients who were confirmed of hepatic cirrhosis with ascites by ultrasound were screened for SBP. Liver size, caudate/right lobe ratio, liver surface, echogenicity, portal vein diameter, portal vein mean flow velocity and spleen size were variables used in diagnosing cirrhosis. Total of 50 patients were studied thoroughly with regards to both history and clinical examination as per Proforma, which is attached in Annexure.

METHODS

SBP was diagnosed by following criteria.^{15,16} 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. 10 mL of ascitic fluid was immediately inoculated into blood culture bottles at the bed side for microbiological analysis.
2. 10 mL of ascitic fluid was sent to the laboratory in sterile test tubes for conventional culture.
3. 10 mL of ascitic fluid was utilized for biochemical and cytological examination.

Ascitic fluid of all patients were analysed 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 total of 20 mL of ascetic fluid was inoculated, 10 mL was inoculated in blood broth. The broth bottle was incubated under aerobic conditions at 35°C for 7 days. Blind subcultures on sheep blood agar and MacConkey agar (Incubated in aerobic conditions) and in phenylethyl alcohol agar (Incubated in anaerobic conditions) were performed at 48 and 72 h. The final report will be made after 72 hours. Both plates and broth were examined daily for visible growth. When turbidity was detected, additional subcultures were performed. On isolation the organisms were characterized by standard protocol and antibiotic sensitivity evaluated. The method adopted for statistical analysis is "t-test" using GraphPad calculator.

Inclusion Criteria

Cirrhosis of liver was diagnosed on the basis of clinical features suggestive of chronic liver disease. Biochemical features (Modestly raised 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 and portal hypertension. Upper gastrointestinal endoscopy showing evidence of portal hypertension. Liver biopsy (Wherever possible) showing features of cirrhosis.

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 and persistent localized abdominal pain and tenderness
 - b. Presence of following
3. Ascitic fluid lactic dehydrogenase concentration more than 225 mg/dL.
4. Ascitic fluid glucose concentration less than 50 mg/dL.
 - a. Isolation of more than one micro-organism in the ascitic fluid culture.
 - b. An evidence of an intra-abdominal surgically treatable source of infection.
5. Tuberculosis abdomen with ascites.
6. Malignancy with ascites.

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.

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 1: Details of Symptoms

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 and drowsiness. Vomiting was the presenting complaint in 2% of patients.

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

Table 2: 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. Asterixis 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. Ascitic fluid was aspirated for diagnostic purpose in all subjects for evaluation of the cause and presence of SBP. A total of 20 mL of ascetic fluid was inoculated, 10 mL in Glucose broth at bedside and another 10 mL was inoculated in Blood broth. Remaining fluid was utilized for cytological and biochemical tests and the results are tabulated below.

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 3: Prevalence 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 4: 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 in 8 patients had SBP (66%), 7 patients had PMN count >250/mm³ (CNNA) and 1 was culture positive (MNB).

Three patients presented with altered sensorium; all the 3 patients were positive for SBP. Among these 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. Similarly, Ascites had no significance to the occurrence.

Signs	No. of Patients	Positive SBP	PMN >250/mm 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 5: Clinical Signs in Correlation with SBP

Investigations	Outcome				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 6: Comparison of Investigations between the Patients of SBP and Patients without SBP					

* Significant, ** Highly Significant

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) and Ascitic fluid protein (0.0260) which are highly statistically significant.

DISCUSSION

18% of Ascitic subjects had Spontaneous Bacterial Peritonitis out of 50 Cirrhotic Ascitic cases presently studied. In these 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 72 hrs.

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%.^{17,18,19,20,21,22,23} Andreu et al reported a prevalence of 28%, while Amarapurkar et al found it to be 22.5%.

In a study involving 169 cirrhotic patients, Jarcuska et al found evidence of SBP by first paracentesis in 27 (16.0%). Romney et al in a study involving 67 cirrhotic patients found no case of CNNA and only 10 of MNB.²⁴

Obstein KL²⁵ 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.

MP Agarwal et al from Delhi studied 41 patients of cirrhotic ascites, among them 14 patients diagnosed to have SBP or one of its variants. A prevalence of 34.14%.

Study Series	Prevalence (%)
Andreu et al	28%
Amarapurkar et al	22.5%
Jarcuska et al	16%
Romney et al	14.9%
MP Agarwal et al	34.14%
Obstein K et al	26.12%
Present Study	18%

Table 7: Study Series

Study Series	Mihas AA Toussaint J	Present Study
Fever	69%	66%
Abdominal pain	59%	100%
Abdominal Tenderness	49%	100%
Hepatic Encephalopathy (Altered sensorium)	54%	100%

Table 8: Study of Symptoms

In present study all the cases with abdominal pain, abdominal tenderness, altered sensorium were having SBP.

SUMMARY

18% of Ascitic subjects had Spontaneous Bacterial Peritonitis out of 50 Cirrhotic Ascitic cases presently studied. In this, 7 patients had only PMN count $>250/\text{mm}^3$, but culture negative for any organisms. Only 2 subjects were culture positive and isolated *E. coli* organism on culture by 72 hrs. 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%. Andreu et al reported a prevalence of 28%, while Amarapurkar et al found it to be 22.5%.

Mean age of the patients were 50.7 and mean age of patients diagnosed for SBP was 53.22. Dr. Dilshad Muhammad et al study showed mean age of whole of the population was found to be 51 ± 12.49 years.

In present study all the cases with abdominal pain, abdominal tenderness, altered sensorium were having SBP. So it is better to screen for ascitic fluid analysis in patients of cirrhosis with above complaints.

In present study, 87.5% of the 9 patients in the SBP group belonged to Child-Pugh class C and 6.25% to class B. This finding supports the view that SBP is more common in patients with advanced liver disease. In a study by Amarapurkar et al had found that 6 of the 7 patients detected to have SBP belonged to class C (87.71%).

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%. Ascitic fluid protein plays an important role in developing SBP in these patients.

In Runyon BA series, the patients with ascitic fluid protein $<1 \text{ gm/dL}$ were more predisposed to development of SBP. Present study patients with ascitic fluid protein $<1 \text{ gm/dL}$ are

frequently predisposed to SBP as in the other series cited above.

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 ascetic 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 aetiological causes, so that early diagnosis will help in early initiation of treatment of SBP leading to improvement of clinical state.

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