



Research Article

**PREVALENCE OF SPONTANEOUS BACTERIAL PERITONITIS IN PATIENTS OF LIVER CIRRHOSIS AND ITS ROLE IN PREDICTING 30 DAY IN HOSPITAL MORTALITY AND FUTURE HOSPITALIZATION**

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**ABSTRACT**

**Background and objectives:** Spontaneous bacterial peritonitis (SBP) is the infection of a previously sterile ascitic fluid, with no apparent intra-abdominal source of infection. Spontaneous bacterial peritonitis is a common complication in cirrhotic patients. The objectives of this study was to evaluate the prevalence, clinical profile, course, microbiology, response to treatment and outcome of SBP.

**Materials and methods:** The study was conducted at Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow. Two hundred sixteen patients of cirrhosis of liver with ascites were taken for study. The duration of study was six months (January 2018 – June 2018). Diagnosis of cirrhosis of liver was made on basis of clinical presentation, routine biochemical and hematological blood investigations and ultrasound abdomen. Both old and newly diagnosed admitted cases of cirrhosis of liver with ascites were taken up for this study. Ascitic fluid analysis was done for all patients of cirrhosis at the time of admission. All patients of SBP who survived were put on prophylactic norfloxacin 400mg once daily therapy on discharge. Ascitic fluid analysis was repeated on all subsequent admissions.

**Results:** The prevalence of SBP in our admitted patients with cirrhosis and ascites was 18.52%. Only 6.6% of patients developed second episode of SBP on norfloxacin prophylaxis. The 30 day in hospital mortality attributable to SBP was 25%. Median survival of those who died were 11 days. Among patients who survived first episode of SBP and started on norfloxacin prophylaxis 70% required repeat hospitalization due to complications of cirrhosis within six months of first admission.

**Conclusion:** The present study showed that SBP is a common complication of Cirrhosis with ascites. Norfloxacin prophylaxis is associated with reduced recurrences of spontaneous bacterial peritonitis. Patients having SBP have poor survival and require repeated admission because of poor liver functions.

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**INTRODUCTION**

Spontaneous bacterial peritonitis the term was coined by Correia & Conn in 1985. The term was coined to distinguish this form of infection from surgical peritonitis. Although many patients with SBP have a focus of infection (e.g. - urinary tract infection or pneumonia), they are labeled as having SBP unless the focus requires surgical intervention (e.g. - ruptured viscus). The diagnosis of SBP is made when there is a positive ascitic fluid culture and/or elevated ascitic fluid absolute polymorphonuclear cell count > 250 cells/mm<sup>3</sup> without an evident intra-abdominal surgically treatable source of infection<sup>1</sup>.

Most patients with SBP have symptoms and / or signs clearly suggestive of peritoneal infection especially abdominal pain,

fever and alterations in gastrointestinal motility<sup>2,3,4</sup>. In other patients the development of SBP may be clinically manifested by impairment of liver function like development of hepatic encephalopathy or renal failure as the predominant or only feature<sup>1</sup>.

E Coli, Streptococci & Klebsiella cause most episodes of SBP and mono-microbial bacterascites<sup>5</sup>. Although earlier studies report approximately 6% prevalence of anaerobes among SBP flora, this is probably a reflection of the presence of unrecognized cases of Secondary Bacterial peritonitis. In a recent series, anaerobes caused approximately 1% of SBP.<sup>11,12</sup> Empirical antibiotic treatment is indicated in all cases of clinically compatible ascitic fluid infection with ascitic fluid PMN counts equal to or higher than cells/mm<sup>3</sup>.<sup>1</sup> Because SBP is a good marker of end stage liver disease, it has been proposed as an indication for liver transplantation<sup>6,7</sup>.

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Survival after SBP: Survival expectancy after one episode of SBP has been reported to be very short, with a one year and 2 year probability of survival of 30 - 50% & 25 - 30% respectively.<sup>8,9</sup> Since survival expectancy after liver transplantation is currently much higher patients recovering from an episode of SBP should be considered as potential candidates for liver transplantation.

In the past 48% to 95% of patients with spontaneous ascitic fluid infection died during the hospitalization in which the diagnosis was made, despite antibiotic treatment. Now a reduction in mortality has been attributed to early detection and treatment of infection as well as avoidance of nephrotoxic antibiotics. The mortality showed a strong correlation with age and intensive care unit stay.<sup>13,14</sup>

**Aim**

1. To evaluate the prevalence of SBP.
2. To evaluate its clinical profile, clinical course and microbiology
3. To evaluate its response to treatment, re-hospitalization and assess its short – term outcome (30 day in hospital mortality).

**MATERIAL AND METHODS**

216 patients of cirrhosis of liver of varied etiology with ascites admitted in Gastromedicine ward of Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow (U.P.) during the period from January 2018 to June2018 were included in study. A through history was taken and physical examination performed. Ascitic fluid analysis was done in every case irrespective of symptoms.

10 ml of ascitic fluid was inoculated into brain heart infusion bottle and 5 ml in a sterile test tube at bedside and sent to laboratory for routine analysis and culture-sensitivity. The diagnosis of SBP was based on neutrophil count in ascitic fluid  $\geq 250$  cells/mm<sup>3</sup> and/or positive ascitic fluid culture. If ascitic fluid cultures were positive and the neutrophils count was  $> 250$  cells/mm<sup>3</sup>, patients were diagnosed as having culture-positive neutrocytic ascites. If ascitic fluid cultures were negative in the presence of neutrophils  $> 250$  cells/mm<sup>3</sup>, 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 monobacterial bacterascites (MNB). Ascitic fluid analysis was repeated after 5 days to look for course of SBP. After discharge, patients with SBP were put on oral norfloxacin 400 mg once daily for prophylaxis. All patients included in study were followed for 6 months. Ascitic fluid analysis was repeated on all subsequent admissions.

**Inclusion Criteria**

All patients of cirrhosis of liver of varied etiology with ascites above 15 years of age.

**Exclusion criteria**

1. Patients who already received treatment (antibiotics) before admission into hospital.
2. Patients of ascites with surgical source of infection intra-abdominally e.g. - perforation of intestine, traumatic causes of peritonitis.
3. Patients who had undergone large volume paracentesis within 10 days prior to admission into hospital.

4. Patients with malignancy

A complete physical examination was made to look for the various stigmata and signs of complications of cirrhosis. All the patients then underwent following investigations.

**Blood Investigations:** CBC, LFT, S. Protein/Albumin, RBS, PT/INR, RFT, AFP, HBsAg, Anti-HCV, HIV I & II

**Radiological Investigations:** X-Ray Chest PA view, Ultrasound / CT Abdomen, ECG,

**Ascitic fluid analysis**

- Cytology :Total Count, PMN Count, Malignant Cells
- Biochemistry :Total Proteins, Albumin, ADA level
- Culture : Conventional Method, Modified Method

**RESULTS**

Statistical analysis of 216 cases of cirrhosis with ascites which were admitted in Gastromedicine ward of Dr. Ram Manohar Lohia Institute of Medical sciences, Lucknow, (U.P.) during the period from January 2018 to June2018 was done.

**Table 1** Age incidence

Age in Years	Number of Patients	Percentage
15 – 24	12	5.56
25 – 34	36	16.67
35 – 44	46	21.30
45 – 54	58	26.85
55 – 64	44	20.37
65 – 74	16	7.40
75 – 84	4	1.85
<b>Total</b>	<b>216</b>	<b>100</b>

The younger patient was 18 years old. The oldest patient was 77 years old (table 1). Out of 216 patients 152 were male and 64 were female. Male to Female ratio was 2.375:1 (table2).

**Table 2** Sex Incidence

Sex Incidence	Number of Patients	Percentage
Females	64	29.63
Males	152	70.37

**Table 3** Clinical Signs

Sign	No. of Patients	Percentage
Ascites	216	100
Pedal Edema	128	59.26
Dilated Abdominal Veins	68	31.48
Splenomegaly	156	72.22
Icterus	71	32.87
Pallor	110	50.93
Clubbing	10	4.63
Hepatomegaly	67	31.02

**Laboratory Data**

Hemoglobin  $<6$  gm% was found in 56 patients, blood urea values  $>40$ mg% found in 22 patients and serum creatinine  $>1.5$  mg% found in 20 patients. Most common etiology of liver cirrhosis was ethanol-induced (36.57%) followed by cryptogenic/non-alcoholic fatty liver disease-NAFLD (24.07%). Hepatitis B and C virus related cirrhosis constituted 21.83% and 17.12% respectively. Only 1.38% patients were of Auto-immune liver disease. None of the patients were having SOL in liver. On ultrasound examination liver was shrunken in 62.96% of patients. Upper G.I. endoscopy revealed Grade-I esophageal varices in 19.9%, Grade-II in 26.85%, Grade-III-IV in 37.96% patients. Thirty three patients had no varices. Ascitic fluid culture showed E. coli to be the most common

organism (Table -4). No organism could be isolated in culture in 52.5% of patients and diagnosis was established by increased polymorphonuclear cell count (>250 cells/mm<sup>3</sup>).

**Table 4** Ascitic fluid cultures in patients of SBP

Organism	No. of Patients	Percentage
E.Coli	11	27.5%
Klebsiella	3	7.5%
Proteus	2	5%
S. Aureus	2	5%
Pseudomonas	1	2.5%
No Organism (CNNA)	21	52.5%
Total	40	100%

Twenty two patients had SBP during their first admission. Out of 22 patients, 6 died and remaining 16 were put on oral norfloxacin prophylaxis 400mg once daily at discharge and followed up for 6 months. Out of 6 patients who died on first admission because of SBP, 5 had renal dysfunction.

194 patients not having SBP on first admission and not on norfloxacin prophylaxis were followed for 6 months. Out of 194 patients, 4 were lost to follow up. 18 patients developed SBP on subsequent admission. Out of 18 patients who developed SBP, 4 patients died. Out of 4 patients who died, 3 had renal dysfunction as well.

The prevalence of SBP in our admitted patients with cirrhosis and ascites was 18.52%. Only 6.6% of patients developed second episode of SBP on norfloxacin prophylaxis. The 30 day in hospital mortality attributable to SBP was 25%. Median survival of those who died were 11 days. Among patients who survived first episode of SBP and started on norfloxacin prophylaxis 70% required repeat hospitalization due to complications of cirrhosis within six months of first admission.

## DISCUSSION

The current study reports the prospective evaluation of SBP in liver cirrhosis and provides information on the role of SBP in predicting mortality and subsequent hospitalization in cirrhotic patients. In the present study cirrhosis is more common in 45-54 years age group which is similar to reports by Bhatia *et al*<sup>15</sup>. Male predominance was seen in our cirrhotic population with a ratio of 2.375:1. It is in keeping with reports by Mukherjee *et al* 3.5:1.<sup>20</sup> This is likely secondary to frequent alcohol abuse in men than women. Among the symptoms, fever was the most common symptom (41.67 %), similar to that quoted by Mihas A.A. *et al* (54%)<sup>10</sup>. Renal dysfunction was seen in 80% patients of SBP who died during hospital stay similar to that stated by Mihas *et al* (87%)<sup>10</sup>. 30 day in hospital mortality in our patients of SBP was 25% in contrast to 43.11% in study of Bhatia *et al*<sup>15</sup>. This is likely due to lesser number of renal failure patients in our study as against study by Bhatia *et al* in which very sick patients who had prior history of antibiotic use requiring ICU hospitalization were recruited. Among the 10 patients who died in hospital all were culture positive and having ascitic fluid PMN count > 1000 cells/mm<sup>3</sup>. There were no deaths in CNNA group. Among the 30 patients who received oral norfloxacin prophylaxis, two patients (6.67%) developed recurrence of SBP over 6 months follow up. The one year recurrence rate of SBP in patients on long term norfloxacin prophylaxis range from 1.8% (Novella *et al*<sup>18</sup>) to 20% (Marciano *et al*<sup>16</sup>) in literature. This recurrence was seen with gram positive organism (S. aureus) in our two patients on

norfloxacin prophylaxis. The study by Marciano *et al* had confirmed the preponderance of Gram positive organism in recurrences of SBP on oral Norfloxacin prophylaxis. Recurrence rate in patients on Norfloxacin prophylaxis (6.6%) was quite less compared to cirrhotics who were on no prophylaxis (18.52%). in our study. Similarly, dramatic reduction in SBP recurrence rate from 35 to 12 % was seen in placebo and norfloxacin group with prior history of SBP in the study conducted Pere Gines *et al*<sup>17</sup>. Seventy percent patients with prior history of SBP required repeat hospitalization due to complications of cirrhosis within six months of first admission in this study. Three months re-admissions rate of 53% was reported in large series of 1353 cirrhotic patients admitted for non-elective indications.<sup>19</sup>

## CONCLUSION

SBP, a common complication of cirrhosis is associated with increased mortality. Mortality rate is higher in presence of renal dysfunction. Incidence of SBP decreases with antibiotic prophylaxis in patients with previous history of SBP. Recurrent SBP is seen in gram positive infection inspite of norfloxacin prophylaxis. High re-admission rate in patients of SBP reflect poor liver functions and high incidence of other complications in patients of SBP.

## References

- Guarner C, Soriano G. Spontaneous Bacterial Peritonitis. *Semin Liver Dis.* 1997;17 (3):203-17.
- Toledo C, Salmeron JM, Rimola A, Navasa M, Arroyo V, Llach J *et al*. Spontaneous Bacterial Peritonitis in cirrhosis: predictive factors of infection resolution and survival in patients treated with Cefotaxime. *Hepatology* 1993; 17:251-7.
- Llovet JM, Planas R, Morillas R, Quer JC, Cabre E, Boix J, *et al*. Short term prognosis of cirrhotics with spontaneous bacterial peritonitis: multivariate study. *Am J Gastroenterology* 1993; 88:388-92.
- Hoefs JC, Runyon B.A. Spontaneous Bacterial Peritonitis Disease-a-month 1985; 31:1-48.
- Rimola A. Infections in liver disease. In: Mcintyre N, Benhamou JP, Bircher J, Rizzetto M, Rodes J, editors, *Oxford Textbook of Clinical Hepatology.* Oxford University Press 1991; p.1272-84.
- Klipe VE, Krakauer H, Wren RE, Analysis of liver transplant experience from 37 transplant centers as reported to Medicare. *Transplantation* 1993; 56:554-61.
- European liver transplant Registry Data analysis 05/1968 - 06/1997. Hospital Paul Brousse, Villejuif, France.
- Tito L, Rimola A, Gines P, Llach J, Arroyo V, Rodes J. Recurrence of SBP in cirrhosis : frequency and predictive factors. *Hepatology* 1988;8:27-31.
- Silvain C, Mannant PR, Ingrand P, Fort E, Besson I, Beuchant M. Recidive de l'infection spontanee du liquide d'ascite au cours de la cirrhose. *Gastroenterol Clin Biol* 1991;15:106-9.
- Mihis AA, Toussaint J, HSU, Dotherow P, Achord JL. SBP in Cirrhosis clinical and laboratory features, survival and prognostic indicators. *Hepato Gastroenterology* 1992;39(6):520-522.
- Runyon BA, Canawati HN, Akriviadis EA. Optimization of ascitic fluid culture technique.

- Gastroenterology 1988;95(5):1351-5
12. Runyon BA. Monomicrobial non-neutrocytic bacterascites: A variant of spontaneous bacterial peritonitis. *Hepatology* 1990;12 (4 Pt 1):710-5.
  13. Runyon BA, AASLD Practice Guidelines Committee. Management of adult patients with ascites due to cirrhosis: An update. *Hepatology* 2009; 49(6):2087-107.
  14. Runyon BA. Approach to the patient with ascites. In: Yamada T, Alpers DH, Laine L, *et al*, editors. *Textbook of gastroenterology*. 3rd ed. Philadelphia: Lippincott Williams& Wilkins; 1999.
  15. Chinmaya Kumar Bal, Ripu Daman, Vikram Bhatia *et al*. Predictors of fifty days in hospital mortality in decompensated cirrhosis patients with spontaneous bacterial peritonitis. *World J Hepatol* 2016 April 28; 8(12): 566-572
  16. Sebastián Marciano *et al*. Spontaneous bacterial peritonitis recurrence in patients with cirrhosis receiving secondary prophylaxis with norfloxacin. *Eur J Gastroenterol Hepatol*. 2019;31 (4):540-546.
  17. Pere Ginés *et al*. Norfloxacin prevents spontaneous bacterial peritonitis recurrence in cirrhosis: Results of a double blind, placebo controlled trial. *Hepatology* 1990;12 (4 Pt1):716-24.
  18. Novella *et al*. Continuous Versus Inpatient Prophylaxis of the First Episode of Spontaneous Bacterial Peritonitis with Norfloxacin. *Hepatology* 1997;25 (3):532-6.
  19. JS Bajaj *et al*. The Three-Month Readmission Rate Remains Unacceptably High in a Large North American Cohort of Cirrhotic Patients. *Hepatology* 2016; 64(1):200–208.
  20. Mukherjee PS, Vishnubhatla S, Amrapurkar DN *et al* (2017): Etiology and mode of presentation of chronic liver diseases in India: A multi centric study: *PLoS ONE* 12(10): e0187033

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