# Study of spontaneous bacterial peritonitis in patients of cirrhosis with ascites

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**ABSTRACT**

**Introduction :** Spontaneous bacterial peritonitis (SBP) is a common complication of cirrhosis. It is defined as presence of > 250 polymorphonuclear cells (PMN) / $mm^3$ in ascites in the absence of an intrabdominal source of infection or malignancy[1]. This Hospital based cross sectional study was conducted in the medical college hospital from Central India.

**Aims and Objective :** To study rate of occurrence, clinical and laboratory profile of SBP and its variants in-patient of cirrhosis and correlate it's occurrence with severity of disease.

**Material and Methods :** After taking approval from Institutes' Ethics committee, 100 successive patients of cirrhosis with ascites fulfilling inclusion and exclusion criteria were enrolled. Clinical and laboratory profile of these patients were noted. Abdominal paracentesis was done and ascitic fluid was sent for culture sensitivity, routine biochemical and cytological examination. All the clinical, biochemical and microbiologic profile was compared in SBP and non-SBP groups.

**Results :** SBP was found in 42% of cases. Amongst these classical SBP was present in 16 (38.09%) followed by Culture negative neutrocytic ascites and Bacterascites. Escherichia coli was commonest organism found followed by pseudomonas and Klebsiella pneumonia. The common mode of presentation of SBP was abdominal tenderness followed by hepatic encephalopathy, abdominal pain and fever, distention of abdomen, hematemesis and melena. Statistical significant association was seen with hyponatremia, asctic fluid protein and MELD score.

**Conclusion :** SBP is a frequent complication of cirrhosis found in 42% of cirrhotic patients. It has heterogeneous clinical presentation or patient may be asymptomatic. Hence Ascitic fluid should be analyzed routinely in all cases of cirrhosis during first presentation and subsequently.

**Key words :** ascites, cirrhosis, and spontaneous bacterial peritonitis

## Introduction :

Spontaneous bacterial peritonitis (SBP) is the most frequent and life-threatening infection in patients with liver cirrhosis requiring prompt recognition and treatment[1]. In last few decades, a large body of knowledge has accumulated regarding the clinical presentation, diagnosis, pathogenesis, treatment and prevention of SBP, and the prognosis of the patients who develop this infection. SBP episodes develop in patients with advanced cirrhosis as a manifestation of severe derangement of hepatic function. Ascitic fluid infection is the most frequent infectious complication among patients with cirrhosis and ascites, comprising 31% of all bacterial infections.[2]

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The cause of SBP has not been established definitively but is believed to involve hematogenous spread of organisms in a patient in whom a diseased liver and altered portal circulation result in a defect in the usual filtration function.[3]

Fever, abdominal pain, increased distention of abdomen or associated complications like hepatic encephalopathy, hepatorenal syndrome are the common modes of presentation in SBP, but the absence of any of these features does not exclude SBP.[4] A diagnostic paracentesis is mandatory in all patients with cirrhosis requiring hospital admission. Risk of paracentesis is small despite almost invariable impairment of clotting in these patients.[5]

Cultures of the ascitic fluid are helpful in identifying the organism and are best performed by bedside inoculation of ascitic fluid in culture bottles.[6]

In hospitalized patients with cirrhosis, 10% to 25% will have an episode of SBP with a mortality rate of 17% to 50%[7]. With early recognition and prompt treatment mortality related to SBP can be minimized to great extent.

In view of the high rate of morbidity and mortality, which is associated with SBP, this study was carried out to find out frequency of spontaneous bacterial peritonitis in patients with liver cirrhosis with ascites.

**Materials and Methods :**

The present **cross sectional study** was conducted in a tertiary care hospital for two years between September 2011 and August 2013. Study was initiated after taking approval from Institutional Ethics committee. All newly diagnosed adult subjects with decompensated cirrhosis of liver who gave consent for study, were included and those who have received antibiotic therapy in the preceding 1 week, having secondary ascitic fluid infection or tuberculous or malignant ascites or those patients with cardiac cirrhosis were excluded from study. Hundred patients of cirrhosis of liver with ascites or its complications, fulfilling inclusion and exclusion criteria were enrolled in study after taking written consent. Cirrhosis of liver was diagnosed on the basis of clinical examination, and ultrasonography. Complete history was noted and thorough clinical examination was done. They were looked for clinical signs of hepatocellular failure. All patients were subjected to biochemical and hematological investigations like complete blood count, kidney function test, liver function test and special test like HIV and HBSAg, prothrombin, INR and ultrasonography. All subjects underwent paracentesis within 24 hours of admission, before giving any antibiotics. About 20 ml of ascitic fluid was tapped in each patient with aseptic precautions. 10 ml of ascitic fluid was immediately inoculated bedside in the blood culture bottles for microbiological analysis[8]. 10 ml of ascitic fluid was sent for biochemical and cytological examination. Gram's staining was done in all cases. Ascitic fluid was cultured to know the presence of pathogenic organisms and SBP was diagnosed by following criteria[9].

Ascitic fluid neutrophil (PMN) count greater than 250 cells / $mm^3$

& / or

Positive ascitic fluid culture

And

Absence of any primary source of infection in abdomen.

**Variants of SBP were also hold**

(i) Classic SBP : ascitic fluid PMN counts > 250 / $mm^3$ and positive culture.

(ii) Culture negative neutrocytic ascites (CNNA) : ascitic fluid PMN counts > 250 / $mm^3$ and negative culture

(iii) Monomicrobial Nonneutrocytic Bacterascites (MNB) : a culture positive ascitic fluid in the presence of PMN counts < 250 / $mm^3$.

Severity of cirrhosis was objectively measured by MELD score. MELD score was calculated by using the following formula :

**MELD = 9.57 × loge (Cr mg/dl) + 3.78 × loge (TBil mg/dl) + 11.20 × loge (INR) + 6.43.**

Patients were categorized in two groups

1. With SBP or it's variant
2. Without SBP. All parameters were compared in these 2 groups.

***Statistical Analysis :*** The results of the study were analyzed by the unpaired "t" test and chi square test. P values less than 0.05 were considered to be statistically significant irrespective of age and gender.

**Results :**

In this cross-sectional study 128 cirrhotic patients were screened. 18 patients were excluded as they gave history of receiving antibiotics in preceding week. 5 patients did not gave consent for abdominal paracentesis while 3 patients were diagnosed to have tuberculous peritonitis. Thus 100 patients of cirrhosis with ascites fulfilling inclusion criteria were enrolled in study.

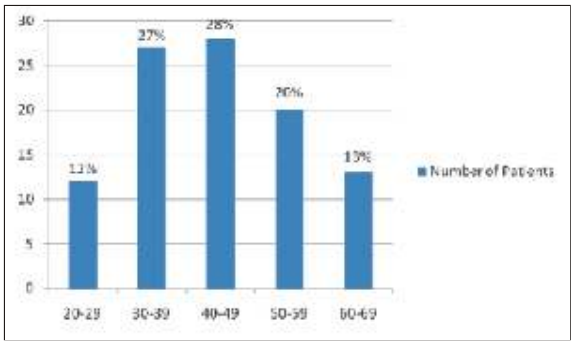


***Fig. 1 :*** **bar diagram showing distribution of study population as per age**

Out of 100 patients with cirrhosis with ascites majority of the patients were between 40-59 years of age ***(Fig. 1).*** Majority of the subjects were males with male : female ratio 19:1

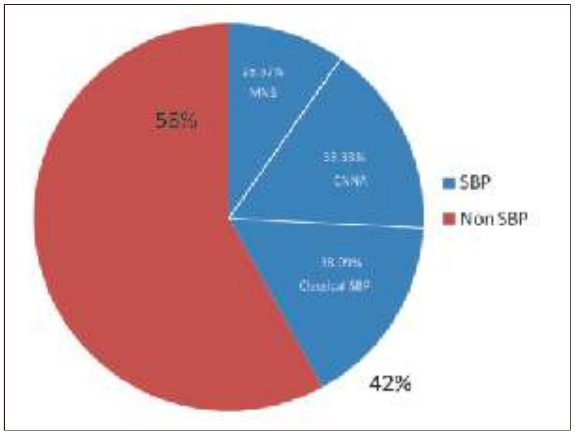


***Figure 2 :*** **Distribution of study population as per presence of classical SBP and its variants**

Spontaneous bacterial peritonitis was present in 42% patients. Out of total 42 cases of SBP, classical SBP was present in 16 (38.09 %), Culture negative neutrocytic ascites (CNNA) in 14 (33.33%) patients and monomicrobial nonneutrocytic bacterascites (MNB) in 12 (28.57%) patients.

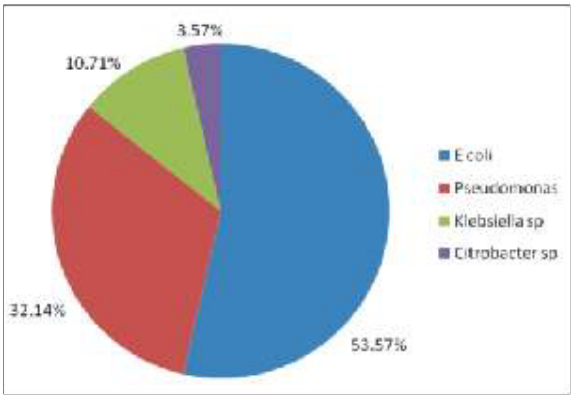


***Figure 3 :*** **Pie chart showing organisms causing SBP**

*E. Coli* was the most frequently cultured organism isolated in 15 (53.57%) cases, followed by pseudomonas in 9 (32.14%), klebsiella species in 3 (10.71%) and citrobacter species in 1 (3.57%) patient.

For the subsequent analysis of other parameters patients were divided into two groups in which one group consisted of patients with SBP and the other group with patients not having SBP.

***Table 1 :*** **Distribution of study population as per clinical features**

| Clinical features | SBP | | | Total SBP X=42 (%) | NON SBP Y=58 (%) | TOTAL N=100 | Z SCORE | P VALUE |
|---|---|---|---|---|---|---|---|---|
| | C-SBP | CNNA | MNB | | | | | |
| **Jaundice** | 13 | 14 | 9 | 36 (41.86%) | 50 (58.13%) | 86 | 0.02 | 0.97 |
| **Abdominal tenderness** | 9 | 4 | 4 | 17 (65.38%) | 9 (34.61%) | 26 | 2.14 | 0.01 |
| **Hematemesis / melena** | 3 | 4 | 2 | 9 (42.85%) | 12 (57.14%) | 21 | 0.65 | 0.51 |
| **Abdominal pain** | 4 | 4 | 2 | 10 (50%) | 10 (50%) | 20 | 0.72 | 0.46 |
| **Altered level of Consciousness** | 5 | 3 | 2 | 10 (58.82%) | 7 (41.17%) | 17 | 1.40 | 0.16 |
| **Fever** | 4 | 2 | 1 | 7 (46.66%) | 8 (53.33%) | 15 | 0.36 | 0.71 |
| **Asymptomatic** | 4 | 1 | 2 | 7 (46.66%) | 8 (53.33%) | 15 | 0.36 | 0.71 |
| **Hypotension** | 5 | 3 | 0 | 8 (61.53%) | 5 (38.46%) | 13 | 1.43 | 0.15 |

The common mode of presentation in our series was jaundice, which was seen in almost 86% patients however it was also commonest mode of presentation in Non SBP patients. Abdominal tenderness was next common presentation, which was significantly associated with SBP. None of the other features showed statistically significant association with SBP

***Table 2 :*** **Distribution of patients as per laboratory parameters**

| Investigation | SBP (mean±SD) | NON SBP (mean±SD) | t value | P value |
|---|---|---|---|---|
| Hemoglobin (gm/dl) | 8.37±2.42 | 8.29±1.92 | 0.177 | 0.10 |
| T.L.C (/cumm) | 13002±17537 | 9107±5482 | 1.39 | 0.001 |
| Platelet (/cumm) | 1.86±1.06 | 1.91±1.17 | 0.22 | 0.51 |
| Total bilirubin (mg/dl) | 7.36±9.88 | 10.32±11.44 | 1.40 | 0.43 |
| SGOT (U/L) | 94.95±71.64 | 109±84.88 | 0.89 | 0.25 |
| SGPT (U/L) | 57.94±38.78 | 57.95±40.33 | 0.001 | 0.80 |
| Alkaline phosphatase (units/L) | 323±178.63 | 399±213.71 | 1.93 | 0.22 |
| Total proteins (gm/dl) | 6.26±0.76 | 6.63±0.97 | 2.13 | 0.10 |
| Serum albumin (gm/dl) | 2.98±0.41 | 3±0.67 | 0.18 | 0.001 |
| Urea (mg/dl) | 54.81±39.825 | 42.95±34.92 | 1.54 | 0.35 |
| Creatinine (mg/dl) | 1.52±1.11 | 1±1.30 | 2.1 | 0.28 |
| Prothrombin Time (Sec) | 19.82±6.47 | 20.12±6.12 | 0.23 | 0.68 |

Amongst all the laboratory parameters only leucocytosis and low serum albumin were found to be significantly associated with occurrence of SBP. In none of the parameters there was statistically significant difference between two groups.

***Table 3 :*** **Ascitic fluid analysis**

| Content | SBP (mean±SD) | NON SBP (mean±SD) | t test | P value |
|---|---|---|---|---|
| AF albumin (g/dl) | 0.47±0.220 | .55±0.34 | 1.33 | 0.002 |
| TLC (/mm3) | 1289±1688 | 233±295 | 4 | 0.001 |
| PMN counts (/mm3) | 739±1208 | 60±64 | 3.63 | 0.001 |

In ascitic fluid analysis ascitic fluid albumin was low and TLC and PMN count were high in SBP group as compared to non-SBP group. These differences in all parameters were statistically significant

***Table 4 :*** **Correlation of SBP with S. Sodium Level**

| | | Total SBP% | NON-SBP% | |
|---|---|---|---|---|
| Sodium | ≤130 | 25(53.19) | 22(46.8) | 47 |
| | 131-135 | 16 (45.71) | 19 (54.28) | 35 |
| | ≥136 | 1 (5.55) | 17 (94.44) | 18 |
| Total | | 42 | 58 | 100 |

**Chi Square = 4.56; p = 0.03**

Amongst the biochemical parameters risk of occurrence of SBP was correlated with s. Sodium concentration. Mean S Na was low in SBP group as compared to Non SBP group. Risk of SBP was found to be significantly high when S Na was ≤ 130 meq/li as compared to patients with ≥ 130 meq/li.

***Table 5 :*** **Correlation of SBP with ascitic fluid protein**

| | | Total SBP% | NON-SBP% | |
|---|---|---|---|---|
| AF protein | <1 | 20 (52.63) | 18 (47.36) | 38 |
| | 1-2.5 | 20 (40) | 30 (60) | 50 |
| | >2.5 | 2 (16.66) | 10 (83.33) | 12 |
| Total | | 42 | 58 | 100 |

**Chi Square = 2.84; p= 0.049**

Analysis of ascitic fluid for protein showed 38% patient had protein < 1g/dl. Among them 52.63% patients had SBP. Only 16.66% patients with ascitic fluid protein > 2.5g/dl had SBP which clearly indicate association between low ascitic fluid protein and SBP

In this study, in all patients severity of disease was evaluated objectively by calculating MELD score. Mean and standard deviation of MELD score was calculated in each group. The difference of mean in various groups was calculated with F value (ANOVA), and it was found to be statistically significant with p value of 0.041. Mean value of MELD score in SBP group was17.43 and in NON SBP group 15.28.

***Table 6 :*** **Association between MELD SCORE and SBP**

| Type (SBP) | Mean | Std. Deviation |
|---|---|---|
| C-SBP | 21.06 | 9.916 |
| CNNA | 18.07 | 10.073 |
| MNB | 13.17 | 3.762 |
| NON SBP | 15.28 | 7.931 |
| Total SBP | **17.43** | **8.48** |

F value (ANOVA)=2.86 p=0.041

**TABLE 12: SBP AND MELD SCORE**

**Discussion :**

SBP is one of the most frequently encountered bacterial infections in patients with cirrhosis. The risk of developing SBP is greater in those with a coexistent gastrointestinal bleed, high serum bilirubin, a previous episode of SBP, or low ascitic fluid protein concentration (less than 1gm/dl). Its mortality has been decreased from 80 to 30% due to prompt diagnosis and early initiation of adequate treatment.

The frequency of SBP in our study was 42 %. As per studies conducted in different parts of world frequency of SBP found to be ranging 10% to 38.2%[10-15]. Great difference between prevalence might be because of late referral to tertiary hospitals and also difference in culture technique.

In our series relative frequency of variants of SBP classical SBP in 38.09 %, Culture negative CNNA 33.33% and MNB in 28.57% patients. Zaman A etal[16] in their study found classic SBP in 39.2% cases, CNNA in 57.14% and MNB in 3.57%. while Nepal N et al[17] found it to be 38.9%, 50% and 11% respectively. So frequency of classical SBC in our series was consistent with other series as well.

E. coli was commonest organism cultured in our series followed by pseudomonas, Klebsiella and Citobacter. Similar results were seen by Zaman A et al[16], Fu F[18] and Syed VA et al[19] also found E.coli as commonest organism grown. E. coli is commonest community acquired organisms seen in SBP , Pseudomonas, Klebsiella are most probably hospital acquired pathogens.

Amongst clinical features only abdominal tenderness was significantly associated with occurrence of SBP in our study while Syed VA et al found only abdominal pain to be significant clinical feature. Gill AS et al[4] also found comparable clinical features in SBP and non SBP group.

Only lab parameters found to be statistically significant in our study were TLC and low S albumin and low S sodium. Gill AS et al[4] found platelet count, S creatinine and INR as significant parameters while Syed VA et al found none of the blood parameters statistically significant. In our series all the ascitic fluid parameters were found to be statistically significant while Syed VA et al[19] found ascitic fluid TLC and PMN count significant but ascitic fluid protein to be non significant. Gill AS saw similar results. Schwabl P et al[20] also found significant correlation between low S. Sodium and occurrence of SBP. Ascitic fluid protein < 1gm% was found to

be significantly associated with SBP. Khan Z et al and Nepal N et al found similar results.

In our study MELD score was found to be predictive of SBP. Our results are consistent with observations done by Gayatri AA et al[21] and Schwabl P[20].

**Conclusion :**

SBP is commonly encountered complication of liver cirrhosis with ascites accounting for 42% of cirrhotic patients. Many patients can have variants of SBP hence culture of ascitic fluid should be done to detect SBP. None of the clinical feature consistently predicts occurrence of SBP and many patients remain asymptomatic; hence high index of suspicion is important for early diagnosis. E coli is the commonest organism responsible for SBP. S Sodium < 130 mg%, Ascitic fluid protein < 1 gm% and MELD score are significantly associated with occurrence of SBP. As occurrence of SBP can initiate downhill course in natural history of cirrhosis, all admitted patients should be screened for SBP.

**References :**


1. Wiest R, Krag A, Gerbes A. Spontaneous Bacterial Peritonitis Recent Guidelines and Beyond:Gut. 2012;61(2):297-310.
2. Wong F L, Blendis L: Ascites and spontaneous bacterial peritonitis. First principles of Gastroenterology; Chapter 14, p 531-535.
3. Guarner C, Soriano G: Bacterial translocation and its consequences in patients with cirrhosis. European Journal of Gastroenterology and Hepatology 2005 Jan; 17(1): 27-31.
4. Gill AS, Singh A, Matreja PS etal. Spontaneous bacterial peritonitis in alcoholic cirrhosis: an Indian Perspective. Euroasian J of Hepato-Gastroenterology, January- June 2012; 2(1): 14-19.
5. Jose Such, Bruce A Runyon: Spontaneous bacterial peritonitis, Clinical infectious diseases 1998; 27 : 669-76.
6. Cholongitas E, Papatheodoridis GV, Lahanas A, et al: Increasing frequency of Gram-positive bacteria in spontaneous bacterial peritonitis. Liver International 2005 Feb; 25(1): 57-61.
7. Gines P, Arroyo V, Rodes J. Therapy of ascites and spontaneous bacterial peritonitis. In: Cohen S, Davis GL, Gianella RA, et al., editors. Therapy of Digestive Disorders: A Companion to Sleisenger and Fortran's Gastrointestinal and Liver Disease. Philadelphia: WB Saunders; 2000. pp. 373-384.
8. Enomoto H, Inoue S, Matsuhisa A etal "Diagnosis of Spontaneous Bacterial Peritonitis and an In Situ Hybridization Approach to Detect an "Unidentified" Pathogen," International Journal of Hepatology, vol. 2014, 7 pages, 2014. doi:10.1155/2014/634617.
9. Rimola A, Garcia-Tsao G, Navasa M, et al. Diagnosis, treatment, and prophylaxis of spontaneous bacterial peritonitis: a consensus document. International Ascites Club. J Hepatol 2000; 32:142-153.
10. Evans, LT, Kim, R, Poterucha, JJ, Kamath, PS. Spontaneous bacterial peritonitis in asymptomatic outpatients with cirrhotic ascites. Hepatology 2003; 37: 897.
11. Iqbal S, Iman N, Alam N, Rahman S. Incidence of Spontaneous Bacterial Peritonitis in liver cirrhosis, the causative organisms and antibiotic sensitivity. JPMI 2004; 18:614-9.
12. Sarwar S, Alam A, Izhar M, khan AA, But AK, et al. Bedside diagnosis of spontaneous bacterial peritonitis using reagent strips. J Coll Physicians Surg Pak 2005; 15:418-21.
13. Imran M, Hashmi SN, Altaf A, Rashid H, Hussain T. Spontaneous Bacterial Peritonitis. Professional Med J Jun 2006; 13:201-5.
14. Lata J, Fejfar T, Krechler T, Musil T, Husová L, et al. Spontaneous bacterial peritonitis in the Czech Republic: prevalence and aetiology. Eur J Gastroenterol Hepatol 2003; 15:739-43.
15. Puri AS, Puri J, Ghoshal UC, Sharma BC, Saraswat VA, et al. Frequency, microbial spectrum and outcome of spontaneous bacterial peritonitis in north India. Indian J Gastroenterol. 1996 Jul; 15:86-9.
16. Nepal N, Pande PR, Pande R etal . Study of frequency of SBP in patients with alcoholic liver cirrhosis with ascites. Postgraduate Medical Journal of NAMS July-December 2009: 9(2)
17. Zaman A, Kareem R, Mahmood R, Hameed K, Khan EM. Frequency of microbial spectrum of spontaneous bacterial peritonitis in established cirrhosis liver. JAMC 2011; 23:15-7.
18. Fu F, Wang Y, Tao JL etal .Spontaneous ascitic fluid infection of patients with liver cirrhosis : culture negative neutrocytic ascites vs spontaneous bacterial peritonitis in Huai'an, China _ Int J Clin Exp Pathol 2017;10(2):2135-2141
19. Syed VA, Ansari JA, Karki P, Regmi M, Khanal B. Spontaneous bacterial peritonitis (SBP) in cirrhotic ascites: A prospective study in a tertiary care hospital, Nepal. Kathmandu University Medical Journal (2007), Vol. 5, No. 1, Issue 17, 48-59
20. Schwabl P, Bucsics T, Soucek K and etal. Risk factors for development of spontaneous bacterial peritonitis and subsequent mortality in cirrhotic patients with ascites. Liver Int. 2015 Sep;35(9):2121-8. doi: 10.1111/liv.12795. Epub 2015 Feb 18.
21. Gayatri AA, Suryadharma IG, Purwadi N. The relationship between a model of end stage liver disease score (MELD score) and the occurrence of spontaneous bacterial peritonitis in liver cirrhotic patients.Acta Med Indones. 2007 Apr-Jun;39(2):75-8.