*Original Article*

# The Predictive Factors for Recurrence of Spontaneous Bacterial Peritonitis

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## Summary

**Background and objectives:** *Spontaneous bacterial peritonitis (SBP) is a common and critical complication of cirrhosis. The aim of this work is to find the possible predictive factors for recurrence of SBP in decompensated cirrhotic patients.* **Patients and methods:** *This study included one hundred and thirty-four cirrhotic ascitic patients who were diagnosed with SBP. The diagnosis of SBP was based on ascitic polymorph-onuclear leukocytes (PMN) counts ≥250 cells/mm3. The studied patients were classified into two groups; group 1 included sixty-ninth patients with recurrent SBP and group 2; included sixty-five patients with non-recurrent SPB.* **Results:** *A significant difference was found between both studied groups as regards the presence of fever, HRS (hepatorenal syndrome, the serum albumin and the ascitic fluid PMN in ascitic cirrhotic patients (P= 0.010, p= 0.001, p=0.021, p= 0.045 respectively). Furthermore, a multivariate analysis revealed that the presence of fever, hepatorenal syndrome, and increased ascitic fluid PMN represent independent variables predict the recurrence of SBP in cirrhotic ascetic patients (p= 0.001 for all).* **Conclusion:** *Our study revealed that the presence of fever, HRS, and increased PMN count in ascitic fluid were independent predictors of recurrence of SBP in cirrhotic ascetic patients..*

**Keywords:** *SBP; recurrence; hypoalbuminemia; PMN count and hepatorenal syndrome (HRS).*

## Introduction

SBP has been considered a life-threatening infection that requires a prompt diagnosis and treatment. Its incidence in hospitalized patients varies from 10%-30%[1]. The diagnosis of SBP is based on PMN cell count of more than 250/ µL in the ascitic fluid which is not associated with an intra-abdominal origin of infection or surgery in patients with liver cirrhosis[2]. The recurrence rate is also high and one-year mortality rate after the first episode of SBP has been estimated to be between 31% and 93%[3]. Further adding to the inherent morbidity of SBP is its tendency for recurrence. After an episode of SBP has been successfully cleared with antibiotic therapy, recurrence rates ranged from 40% to 70% within the first year[4]. However, there are insufficient data on the factors responsible for the recurrence of SBP. Therefore, the aim of this study is to find the factors predicting the recurrence of SBP in cirrhotic patients with ascites.

## Patients and Methods

This prospective observational study was carried out at the Tropical and Internal Medicine Departments, Mansoura University, and Egyptian Liver Research Institute and Hospital (ELRIH), Sherbin, El-Mansoura, Egypt from August 2016 to July 2017. We recruited 651 patients with liver cirrhosis and ascites referred for paracentesis. All participants were subjected to the following assessments; complete history taking and physical examination, abdominal ultrasounography, laboratory assessment, including full blood count, liver profile, serum creatinine, and

ascitic fluid analysis (PMN count, protein, bacteriologic culture with antibiotic susceptibility testing, and pathological assessment). Ascitic fluid paracentesis was done for every patient with cirrhosis and ascites that was admitted to our department, as a conventional procedure. SBP diagnosis was based on the existence of ≥250 cells/mL ascitic fluid PMN, with or without the positive culture of ascitic fluid in the absenteeism of hemorrhagic ascites and secondary peritonitis.

### Exclusion criteria

Involved immunocompromised patients, and patients who had taken antibiotics prior to hospital admission or on prophylactic antibiotics for SBP. Moreover, patients with heart failure, renal failure, neoplastic disorders, hematological disorders, clinically evident autoimmune disorders were also excluded from this study.

### Sampling

1. Five ml of venous blood was withdrawn; one ml in polystyrene EDTA tube for CBC and four ml delivered in another tube and allowed to clot. Non-hemolyzed sera were separated by centrifugation and used for determination of CRP and liver functions [ALT, AST, albumin and bilirubin] and creatinine.
2. The ascitic fluid samples were aspirated, using paracentesis technique, under complete aseptic conditions, with the patient in the supine position, from a puncture site in the right or left lower quadrant. All samples for diagnostic investigations were instantly collected at the bedside and processed by laboratory staff without any delay.

### Methodology

1- Liver profile, blood glucose, and serum creat-enine concentrations were checked on a Dimension X-pand plus chemistry analyzer (Roche Diagnostics, Basel, Switzerland) usingan enzyme-based kit and commercially available reagents.

2- Blood picture was determined using CELL-DYN, Emerald cell counter (ABBOTT, Germany).

This study was performed with the approval of the Mansoura Faculty of Medicine Institutional Review Board "MFM-IRB". All patients provided written informed consent prior to participation in any protocol-specific procedures.

### Statistical analysis

All statistical analyses were performed with the SPSS version 17.0 software (Chicago, USA). Distribution of data was firstly tested by Kolmogorov-Smirnov test. Parametric data were expressed in mean and standard deviation (SD). The mean and SD of the differences with the limits of agreement determined as the mean ± 2 SD of the difference (95%CI). For inter-group comparisons, the unpaired t-test was used. Statistical significance was indicated in a P-value of less than 0.05. All hypothesis testing was two-tailed.

## Results

Out of 651 patients with liver cirrhosis and ascites, only one hundred and thirty-four patients with proven diagnosis of SBP were included in this study. The included patients were divided into group 1; included sixty-nine patients with recurrent SBP (53 males and 16 females) and group 2; included sixty-five patients with non-recurrent SPB (41 males and 24 females). The mean age of the patients in the recurrent group of SBP was (54.8 ± 6.9/year), while in non-recurrent SBP was (56.3 ± 9.7/year). No significant differences were raised between patients with and without recurrent SBP as regard, age, and sex. Moreover, a significant difference was found between both studied groups as regards the presence of fever and HRS (P= 0.001), tab. (1). A significant difference was found between both studied groups as regards the serum albumin and the ascitic fluid PMN (p=0.021, p= 0.045 respectively).No significant differences were found as regards, ALT, ASL, bilirubin, INR, serum creatinine, CRP, ascitic WBC, ascitic lymphocytes and the complete blood count(CBC), tab. (2). The multivariate analysis showed that the presence of fever, hepatorenal syndrome, and the ascitic fluid PMN represent independent variables predict the SBP recurrence in cirrhotic ascetic patients (p= 0.001 for each), tab. (3).

Table (1) Demographic and clinical characteristics of the studied groups

| Variable | Patients with recurrent SBP N=69 | Patients without recurrent SBP N=65 | p-value |
|---|---|---|---|
| **Age/year (mean±SD)** | 54.8 ± 6.9 | 56.3 ± 9.7 | 0.309 |
| **Sex:** Males, n (%) | 53 (76.8) | 41 (63.1) | 0.082 |
| Females, n (%) | 16 (23.2) | 24 (36.9) | |
| **Abdominal Pain:** | | | |
| No, n (%) | 24 (36.4) | 34 (52.3) | 0.066 |
| Yes, n (%) | 42 (63.6) | 31 (47.7) | |
| **Fever:** No, n (%) | 23 (33.3) | 36 (55.4) | 0.010 |
| Yes, n (%) | 46 (66.7) | 29 (44.6) | |
| **DM:** No, n (%) | 43 (62.3) | 48 (73.8) | 0.153 |
| Yes, n (%) | 26 (37.7) | 17 (26.2) | |
| **HBV:** No, n (%) | 57 (82.6) | 52 (80.0) | 0.698 |
| Yes, n (%) | 12 (17.4) | 13 (20.0) | |
| **HE:** No, n (%) | 14 (20.3) | 16 (24.6) | 0.548 |
| Yes, n (%) | 55 (79.7) | 49 (75.4) | |
| **ROV:** No, n (%) | 57 (82.6) | 47 (72.3) | 0.153 |
| Yes, n (%) | 12 (17.4) | 18 (27.7) | |
| **HRS:** No, n (%) | 44 (63.8) | 58 (89.2) | 0.001 |
| Yes, n (%) | 25 (36.2) | 7 (10.8) | |

***DM**, diabetes mellitus; **HBV**, hepatitis B virus; **HCV**, hepatitis C virus; **HE**, hepatic encephalopathy; **ROV**, rupture oesophageal varices; **HRS**; hepatorenal syndrome.*

Table (2) The laboratory findings in the studied groups

| Variable | Patients With Recurrence N=69 | Patients Without Recurrence N=65 | p-value |
|---|---|---|---|
| **Albumin, median (IQR)** | 2.4 (0.8) | 2.1 (0.9) | 0.021 |
| **AST, median (IQR)** | 61.0 (53.5) | 60.0 (74.3) | 0.174 |
| **ALT, median (IQR)** | 29.0 (19.5) | 34.0 (23.5) | 0.109 |
| **INR, median (IQR)** | 1.59 (0.70) | 1.51 (0.75) | 0.782 |
| **Bilirubin, median (IQR)** | 2.20 (4.15) | 4.50 (4.45) | 0.055 |
| **Creatinine, median (IQR)** | 1.4 (1.75) | 1.3 (1.2) | 0.079 |
| **CRP, median (IQR)** | 48.0 (24.0) | 44.0 (84.0) | 0.791 |
| **Ascitic WBC, median (IQR)** | 2300.0 (3800.0) | 1600.0 (2950.0) | 0.416 |
| **Ascitic PMN, median (IQR)** | 70.0 (23.0) | 64.0 (10.0) | 0.045 |
| **Ascitic Lymph, median (IQR)** | 36.0 (10.0) | 30.0 (23.0) | 0.061 |
| **Blood WBC, median (IQR)** | 8200.0 (5100.0) | 7300 (9160.0) | 0.596 |
| **Blood PMN, median (IQR)** | 72.0 (20.0) | 72.3 (15.8) | 0.757 |
| **Blood Lymph, median (IQR)** | 16.9 (8.8) | 15.7 (11.3) | 0.922 |
| **HB median (IQR)** | 9.5 (2.4) | 10.1 (2.3) | 0.113 |
| **Platelets, median (IQR)** | 79000 (93000) | 70000 (94400) | 0.432 |

***AST**, aspartate aminotransferase; **ALT**, alanine aminotransaminase; **INR**, international normalized ratio; **CRP**, C reactive protein; **WBC**, white blood cell; **PMN**, polymorphonuclear; **Hb**, hemoglobin.*

Table (3) Multivariate Analysis for predictors of SBP

| Variable | p-value | OROdds ratio | 95% CI |
|---|---|---|---|
| **Fever** | 0.001 | 10.885 | 3.560 - 33.286 |
| **HRS** | 0.001 | 8.637 | 2.529 - 29.484 |
| **Ascitic PMN** | 0.001 | 0.001 | 0.929 |

***HRS**, hepatorenal syndrome; **PMN**, polymorphonuclearlecocytes.*

## Discussion

Spontaneous bacterial peritonitis is a common and critical complication of cirrhotic ascitic patients[5]. Patients who have possessed an episode of SBP carried a one-year recurrence rate of 40% to 70% and a one-year mortality rate of 50% to 70%[6]. In this prospective observational study, which conducted on 134 patients with ascites and SBP, multiple logistic regression analysis showed that presence of fever, the presence of HRS and ascetic fluid PMN cell count, were all independent predictors of recurrence of SBP in patients with cirrhotic ascites. Although the serum albumin in the present study is significantly lower in patients with non-recurrent SBP versus the patients with recurrent SBP, the serum albumin was found to be significantly decreased in all studied patients. A result which is consistent with those demonstrated in the studies of Sandhu et al who found that the recurrence rate of SBP was 42.6% and the low serum albumin prior to discharge was power fully associated with SBP recurrence[7]. The liver cirrhosis is associated with hypoalbuminemia because of the mixed effects of the inadequate protein intake and inflammation. Also, in liver cirrhosis, there is an increased intestinal permeability and intestinal mucosal edema that encourages bacterial translocation where hypoalbuminemia is associated with these phenomena[8,9]. Furthermore, the hypoalbuminemia is related to lower serum complement levels, which may result in higher susceptibility to infections[10], and this can reveal the association between hypoalbuminemia and the occurrence and recurrence of SBP. One of the most frequent symptoms and signs in patients with SBP is pyrexia[11]. Another independent predictor of recurrence of SBP in our study is the presence of fever at the time of diagnosis of SPB, these results were consistent with the study conducted by Runyon et al who demonstrated that fever was the most common feature (67%) of SBP, followed by abdominal pain (60%), abdominal tenderness (42%) and encephalopathy (57%)[12]. In contrast, some authors report that about 30% of patients with paracentesis-proven SBP may be completely asymptomatic[13]. In this study, HRS is an independent predictive factor of recurrence of SBP. Sort et al demonstrated that renal function impairment occurs in almost 30% to 40% of patients with SBP and considered as one of the most significant predictors of death in SBP[14]. Also, it was demonstrated that the increased incidence of SBP associated with low protein in ascitic fluid, impaired renal function and liver cell failure (Child score > 9 and bilirubin > 3) [15]. An increased ascetic fluid PMN cell count considered as one of the most important independent predictors for recurrence of SBP in our study. On the other side, Ljubicic et al demonstrated that the recurrence of SBP was associated with increased ascitic fluid[16]. Also, few studies have been revealed that the failure of the PMN cell count to drop below 250/ml may result in higher mortality and higher recurrence rates of SBP[17-19].

## Conclusion

Our study revealed that the presence of fever, HRS, and increased ascitic PMN count in ascitic fluid were independent predictors of recurrence of SBP in cirrhotic ascetic patients. Thus, identification of risk factors for SBP recurrence is of critical relevance for trying to improve prognosis.

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