



Original Article



Bacterial Peritonitis among Chronic Liver Disease Patients—A Cross-sectional Study from Northeast India

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ABSTRACT

Background: In the present era of increasing antimicrobial resistance in multiple infections, many studies have shown that even with spontaneous bacterial peritonitis (SBP), the bacteriological and resistance patterns have changed over the years with regional variations. This study was conducted to determine the bacteriological profile of peritonitis patients among the group of cirrhotic patients and their outcomes.

Methodology: This was a one-year cross-sectional observational study in which cirrhotic patients with ascites were evaluated for SBP. Cytological analysis, biochemical tests (albumin, protein, glucose, lactate dehydrogenase), and culture and sensitivity on the ascitic fluid were carried out.

Results: 120 cirrhotic patients with ascites were included in the study. Thirty-eight (31.99%) patients had SBP. Classical SBP was present in 13 patients (34.21%), bacterascites in 7 patients (18.42%) and culture-negative neutrocytic ascites (CNNA) in 18 patients (47.36%). *Escherichia coli* was the most common organism (50%, n=10), followed by *Acinetobacter* spp. (15%, n=3), *Klebsiella pneumoniae*, *Enterobacter* spp. and *Enterococcus* spp. (10%, n=2 each), and methicillin-sensitive *Staphylococcus aureus* (MSSA) (5%, n=1). The mortality among the SBP patients was higher than that among the non-SBP patients (42.10% vs. 15.85%, p=0.0013). Sepsis (with or without septic shock) and renal failure were the most common causes of mortality in these SBP patients.

Conclusion: The present study showed that culture-positive SBP in cirrhotic patients was mainly attributed to gram-negative bacterial infections. The resistance among common bacterial isolates was high against third-generation cephalosporins and fluoroquinolones. Patients with multidrug-resistant infections had poor outcomes.

KEYWORDS: Antimicrobial resistance; Culture-negative neutrocytic ascites; Liver cirrhosis; Multidrug-resistant infections; Peritonitis

INTRODUCTION

Spontaneous bacterial peritonitis (SBP) is a life-threatening infection with a significant impact on short-term mortality in patients with chronic liver

disease (CLD). Therefore, it requires prompt recognition and treatment.¹ The development of SBP in advanced cirrhosis is an indication for liver transplantation.² Third-generation cephalosporins, mainly cefotaxime, are recommended as the first-line

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antibiotic for treating SBP.³ However, due to the irrational use of antibiotics, which is evident in the human medical field and poultry, there has been an increased incidence of multidrug-resistant (MDR) infections in humans that were not apparent in the previous century. There is an increase in extended-spectrum β -lactamase (ESBL)-producing gram-negative bacteria and methicillin-resistant *Staphylococcus aureus* (MRSA), which pose a new challenge in treating SBP.^{1,4}

As MDR is directly related to the mortality of patients, the only factors modifiable in the present condition are a timely diagnosis and effective first-line treatment. With many antibiotic-resistant strains in the current era, the local antibiogram is a must, as it will guide choosing the best empirical antibiotic therapy at the right time to prevent higher mortality.

Considering all these factors and with the limited data in Northeast India, the investigators carried out this study to determine the burden of peritonitis patients with decompensated CLD and the bacteriological profile, clinical spectrum, associated diseases, and complications among both SBP and non-SBP patients.

METHODOLOGY

Study design and center

It was a cross-sectional observational study of one-year duration conducted in North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, a tertiary care referral hospital in Shillong, Meghalaya, India.

Inclusion and exclusion criteria

Patients with CLD and ascites were included and evaluated for SBP. Patients who had antibiotic therapy before admission and those with ascites due to other causes were excluded.

Laboratory investigations

Ascitic fluid samples were aseptically collected from patients by ascitic tap (diagnostic paracentesis) from the patient's abdomen. Cytological analysis, biochemical tests (albumin, protein, glucose, lactate dehydrogenase), and culture and sensitivity on the ascitic fluid were carried out per standard guidelines. The bacteriological profile of the ascitic fluid culture and the respective antibiotic sensitivity of the bacterial isolates were analyzed.

Definitions and outcome variables

SBP was defined if the ascitic fluid sent for analysis had ≥ 250 polymorphonuclear (PMN) cells/mm³ or if the ascitic fluid bacterial culture was positive without an

intra-abdominal source of infection or a malignancy.³ The outcome of the patients and response to antibiotic therapy were assessed in terms of resolution, defined as the disappearance of clinical signs of infection and $>25\%$ decrease in the ascitic fluid neutrophil count of the initial value when repeated after 48 hrs.

Statistical analysis

The data were entered in Microsoft Excel 2016. SPSS version 26 was used to perform the statistical analysis. Categorical variables are displayed as percentages, and continuous variables are expressed as the mean and median. A comparative study using the Chi-square test was performed for categorical variables, and the Student's t-test was used to compare continuous variables between the patients with SBP and those without SBP. A p-value of <0.05 was considered significant.

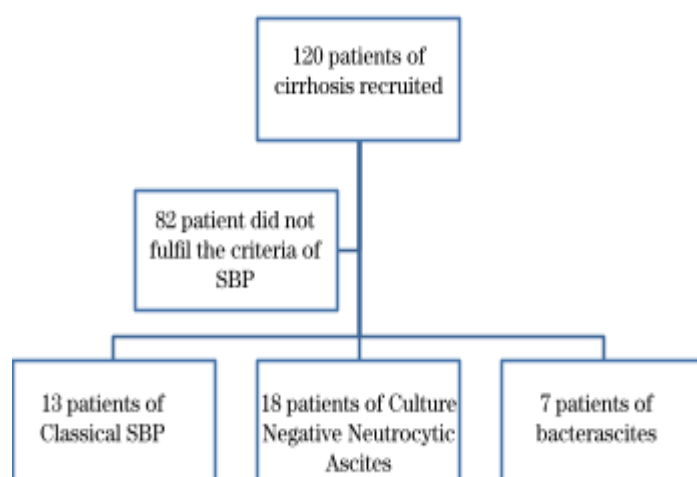
Ethical statement

The study was approved by the Institute Ethical Committee of North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya (Ref: T11/17/11 IEC NEIGRIHMS). Written informed consent was collected from all patients before their inclusion in the study.

RESULTS

A total of 120 cirrhotic patients with ascites were included in the study. SBP was detected in 38 patients (31.99%) (Figure 1).

Figure 1: STROBE flow chart



Classical SBP was present in 13 patients, bacterascites SBP in 7 patients and culture-negative neutrocytic ascites (CNNA) in 18 patients.

Table 1. Demographic profile and laboratory parameters of the SBP and non-SBP patients

	Total (N= 120)	Spontaneous bacterial peritonitis (n=38)	Non-spontaneous bacterial peritonitis (n=82)	p-value
Age (mean)	45.59 ± 10.98	45.81±13.19	45.48±9.87	
Sex				
Male	96 (80%)	28(78%)	68(82%)	
Female	24 (20%)	10(26%)	14(36%)	
Causes of liver cirrhosis				
Alcohol consumption	91(75.80%)	28(78%)	63(76%)	0.715
Nonalcoholic steatohepatitis	5(4.16%)	1(2%)	4(4%)	0.557
Hepatitis B	2(1.66%)	1(2%)	1(1%)	0.534
Hepatitis C	3(2.50%)	0	3(3%)	0.233
Drug-induced	2(1.66%)	2(5%)	0	0.029
Hepatitis B and alcohol	3(2.50%)	1(2%)	2(2%)	0.002
Hepatitis C and alcohol	1(0.83%)	0	1(1%)	0.511
Idiopathic	13(10.83%)	5(13%)	8(9%)	0.569
Child-Pugh Score				
A		0	0	
B	36 (30%)	10 (26%)	26(31%)	
C	84 (70%)	28 (73%)	56(68%)	
Clinical presentation				
Abdominal tenderness	31	26(68.42%)	5(6.09%)	<0.001
Jaundice	76	25(65.78%)	51(62.19%)	0.7
Pain abdomen	37	17(44.73%)	20(24.39%)	0.024
Fever	23	16(42.10%)	17(20.73%)	0.014
Hepatic Encephalopathy	37	13(34.21%)	24(29.26%)	0.581
Shortness of breath	66	11(28.94%)	51(62.19%)	0.001
UGI Bleeding	22	11(28.94%)	11(13.41%)	0.041
Vomiting	16	5(13.15%)	11(13.41%)	0.954
Constipation	19	4(10.52%)	15(18.29%)	0.282
Diarrhoea	4	1(2.63%)	3(3.65%)	0.746
Laboratory parameters		Mean (SD)	Mean (SD)	p-value
Haemoglobin(gm/dl)		9.46 (2.76)	8.79(2.17)	0.1525
Total leucocyte counts		17572.63 (25757.35)	10914.63 (7948.17)	0.0344
Platelets		168815.8 (67529.32)	199573.2 (196367.4)	0.35
INR		1.99 (0.91)	1.86 (0.63)	0.3657
Total Bilirubin (mg/dl)		8.24 (9.4)	6.49 (7.29)	0.2679
Aspartate aminotransferase(U/l)		78.94 (54.7)	84.95 (59.26)	0.5976
Alanine transaminase(U/l)		52.8 (36.59)	62.26 (79.31)	0.4879
Serum albumin (mg/dl)		2.39 (0.62)	2.38 (0.55)	0.9293
Urea (mg/dl)		77.08 (66.9)	48.81 (47.8)	0.0093
Creatinine (mg/dl)		2.05 (1.53)	1.67 (1.66)	0.2345
Sodium (mmol/dl)		137.96 (4.74)	136.49 (16.38)	0.5890
Potassium (mmol/dl)		4.26 (0.82)	4.08 (0.78)	0.2496
Ascitic fluid analysis		Mean (SD)	Mean (SD)	
Total count		1701.31(1651.37)	192.13(255.37)	<0.0001
Glucose		112.76(39.16)	130.72(37.28)	0.0172
Total Protein		1.31(0.9)	1.23(0.9)	0.6514
Albumin		0.47(0.44)	0.42(0.45)	0.5697
SAAG		1.93(0.55)	1.97(0.44)	0.6701

Descriptive characteristics

The demographic profile and laboratory parameters of all patients are depicted in Table 1.

80% of all participants were males. Consumption of alcohol was the predisposing factor of cirrhosis in the majority (75.80%) of cases. Most patients in the present

study group fell under CHILD-PUGH class C (70%), followed by class B (30%). Abdominal tenderness (68.42%), jaundice (65.78%), and abdominal pain (44.73%) were the common presentations of patients with SBP, whereas non-SBP patients presented mostly with jaundice (62.19%), and shortness of breath (62.19%).

Comparative analysis between SBP and non-SBP groups of patients

There were no statistically significant differences with respect to gender, causes of liver cirrhosis (except for drug-induced and combined hepatitis B and alcohol consumption), Child-Pugh Score, jaundice, hepatic encephalopathy, vomiting, abdominal pain, fever, constipation, and diarrhea between the SBP and non-SBP groups except for the presence of abdominal tenderness and shortness of breath in the SBP group.

The mean values of the total leucocyte count and urea were significantly higher in the SBP group than in the non-SBP group. Although not significant, serum creatinine was also higher among the SBP group than the non-SBP group.

Bacteriological and susceptibility profile

Out of the 20 culture-positive cases of SBP (13 classical SBP and seven bacterascites), the majority could be attributed to Gram-negative bacterial infections (n=17; 85%), whereas Gram-positive bacterial infections contributed only 15% (n=3) of the culture-positive SBP cases. *E. coli* was the most common organism (n=10, 50%), followed by *Acinetobacter* spp. (n=3, 15%), *K. pneumoniae*, *Enterobacter* spp., *Enterococcus* spp. (n=2, 10% each) and methicillin-sensitive *Staphylococcus aureus* (MSSA) (n=1, 5%), respectively. The susceptibility profile of the Gram-negative isolates varied across species. *E. coli* isolates (n=10) were mostly resistant to cefotaxime (80%) and ciprofloxacin (60%), followed by piperacillin-tazobactam (40%) and meropenem (40%), respectively. The second most common isolate, *Acinetobacter* spp (n=3), was totally resistant to third-generation cephalosporin, piperacillin-tazobactam, and meropenem.

On the other hand, all Gram-positive isolates (*Enterococcus* spp.=2 and MSSA=1) were susceptible to linezolid (100%), vancomycin (100%), and gentamicin (100%). Both isolates of enterococci were resistant to ciprofloxacin.

Overall, 60% of all bacterial isolates were resistant to at least one antibiotic in three or more antibiotic classes and were classified as multidrug-resistant (MDR).

The outcome of patients

Out of 38 SBP patients, 16 (43.10%) expired. The mortality among the SBP patients (42.10%) was significantly higher than that among the non-SBP patients (15.85%). Among the 16 SBP patients who expired, sepsis and renal failure were the most common causes of mortality (6; 37.50% each), whereas two patients (12.50%) died due to upper gastrointestinal bleeding. Aspiration pneumonia and hepatic encephalopathy were responsible for the death of one patient (6.25%) each. The culture-negative SBP patients had a poorer prognosis in terms of mortality than the culture-positive patients (44.44% vs. 40%), but the difference was not statistically significant. Moreover, cases with MDR bacterial infections had a higher mortality rate than those with non-MDR bacterial infections (41.66% vs. 37.5%).

DISCUSSION

Spontaneous bacterial peritonitis (SBP) is a severe complication of cirrhosis, and its treatment involves the use of antibiotics and the prophylactic use of fluoroquinolones. Antimicrobial resistance has emerged as one of the most critical health issues in the 21st century. A systematic review recently revealed that the global burden of antimicrobial resistance (AMR) was 4.95 million deaths in 2019, and 1.27 million of these deaths were from bacterial AMR.⁵ A risk of AMR development in cirrhotic patients was previously attributed to antibiotic prophylaxis with fluoroquinolones;⁶ however, a randomized control trial by Moreau et al. on 291 cirrhotic patients found that prophylactic antibiotic therapy was not associated with an increased incidence of MDR infections.⁷

In the present study, the ascitic fluid culture was positive in 52.63% of the SBP-diagnosed cases. In a recent study by Ding et al. on 748 patients with SBP, 44.7% had culture-positive SBP.¹ Other studies have shown that culture positivity may range from 35% to as high as 65%.^{8,9}

In the current study, gram-negative organisms were isolated in 85% of the culture-positive SBP cases, with *E. coli* being the most common organism (50%). This finding is similar a retrospective cohort study on 236 patients with SBP by Cheong et al. where 72.9% of SBP cases were due to gram-negative bacteria and 43.2% were due to *E. coli*.¹⁰ This is consistent with a recent review by Wang et al. on gut microbiota and bacterial translocation, showing that gram-negative organisms are predominant.¹¹ Few studies reported gram-positive bacteria as the predominant cause of SBP.¹²⁻¹⁵ But the present study did not support the latter finding, with

Enterococcus spp and MSSA contributing to only 15% of all culture-positive SBP cases.

This study found a high proportion of MDR organisms (60%) in culture-positive SBP cases. A recent retrospective study by Olivera et al. on 113 monobacterial SBP cases found MDR bacteria in 46.9% of cases.¹⁶ The present study found that *E. coli* was the most common among the gram-negative isolates, with 80% isolates resistant to third-generation cephalosporins and 60% isolates resistant to fluoroquinolones. Previous studies have shown that cephalosporin resistance was 16-25%, and quinolone resistance was seen in 25.7%-70% of the isolates.¹⁶⁻¹⁹ These findings of this study are worrisome since third-generation cephalosporins are the drug of choice for treating SBP, and fluoroquinolones are used as prophylactic medication.

Cases with MDR bacterial infections had a higher mortality rate compared to cases with non-MDR bacterial infections (41.66% vs. 37.5%). Similar results were also obtained in a Spanish study by Fernandez et al., who showed that developing infections by resistant bacteria is associated with higher mortality rates.²⁰ Merli et al. also mentioned in their research that the hospital mortality rate related to drug-resistant organisms was twice as high as that associated with other organisms.²¹

There were a few limitations in the present study. The present study had a small sample size, and included only 38 SBP cases. The study was conducted in a single tertiary care hospital. Future multi-centric studies with more participants may be planned based on the findings of the present study.

CONCLUSION

The present study showed that culture-positive SBP in cirrhotic patients was mainly attributed to Gram-negative bacterial infections, particularly *E. coli*. The resistance among common bacterial isolates was high against third-generation cephalosporins and fluoroquinolones. Patients with MDR infections had poor outcomes. Thus, in the present era of AMR, the local antibiogram is critical in dictating empirical therapy for patients with SBP, and there is a need for good antibiotic stewardship in all hospital settings.

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CONFLICT OF INTERESTS STATEMENT

The authors declare no conflict of interest

SOURCE OF FUNDING

None

ETHICS STATEMENT INCLUDING PATIENT CONSENT

Not applicable

AUTHORS' CONTRIBUTIONS

IT: Gave Concept

AM: Design

KGL: Collected data

PKB: Analysed

CJL: Review & editing; Supervision; Validation

GRBT: Review & editing; Supervision; Validation

ML: Review & editing; Supervision; Validation

GW: Reviewed the draft with final approval of article

AI DECLARATION

No AI tool was used to generate research data, perform data analysis, interpret findings, formulate scientific conclusions, or make editorial decisions. All AI-assisted content was critically reviewed, verified, and revised by the authors. The authors take full responsibility for the accuracy, originality, integrity, and final content of the manuscript.

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