



THE BACTERIAL SPECTRUM OF SPONTANEOUS BACTERIAL PERITONITIS IN PATIENTS WITH CIRRHOSIS OF LIVER.

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Article received on:

27/09/2019

Accepted for publication:

03/02/2020

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ABSTRACT... Objectives: To identify the bacterial spectrum of SBP in patients with cirrhosis of liver. **Study Design:** Descriptive Cross-sectional study. **Setting:** Department of Gastroenterology and Hepatology, Madina Teaching Hospital, Faisalabad. **Period:** 1st November, 2018 – 30th June, 2019. **Material & Methods:** Two hundred and fifty cirrhotic patients having ascites and clinical symptoms and signs of SBP, consecutively admitted in the ward or presented to OPD were included in the study. **Results:** A total of 250 patients included in this study. SBP was diagnosed according to the predetermined criteria in 140 patients. The culture-negative ascites was found in 77 (55%) and culture-positive ascites was found in 63 (45%) patients. The most common organism was E.Coli 28 (47.45%) followed by Enterococcus 10 (16.94%), Klebsiella Pneumoniae 6 (10.17%), Streptococcal Pneumoniae 5 (8.47%), S.aureus 5 (8.47%), Acinetobacter 3 (5.08%) and miscellaneous 2 (3.38%). **Conclusion:** The percentage of SBP is quite high among patients having cirrhosis and ascites and the Gram-negative bacterial spectrum is still much common in our region.

Key words: Ascites, Bacterial Spectrum, Cirrhosis, Spontaneous Bacterial Peritonitis (SBP).

Article Citation: Babar AN, Rasool S, Azhar S, Komal J, Hanif S. The bacterial spectrum of spontaneous bacterial peritonitis in patients with cirrhosis of liver. Professional Med J 2020; 27(10):2099-2103.
DOI: 10.29309/TPMJ/2020.27.10.4200

INTRODUCTION

Ascites is a frequent and serious complication developing in about 50% of patients having compensated cirrhosis over the period of 10years.¹ This intraperitoneal fluid is susceptible to infection signifying poor outcome. Spontaneous Bacterial Peritonitis (SBP) is defined as the infection of ascitic fluid, without any identifiable intra-abdominal source of infection.

SBP is the most common infection in patients of liver cirrhosis; it contributes about 10-30% of all bacterial infections in this patient population.² The prevalence of SBP is low in outpatients without symptoms ranging up to 3.5%, but its prevalence is much higher in admitted patients, which is 8%-36%.²

In cirrhosis of liver infection of ascetic fluid is contributed both by poor local immune response of the ascetic fluid and inadequate systemic immune response. Patients with SBP may present

in different ways with wide range of symptoms, like fever, chills, pain abdomen, signs of sever peritonitis like ileus and shock are rare. The diagnosis may be missed unless paracentesis is performed. That's the reason a diagnostic paracentesis is recommended in all the patients admitted in hospital with ascites irrespective of the clinical symptoms of SBP.

Based on diagnostic criteria SBP can be classified into following three types;

- A) Classical SBP: Patients having typical signs and symptoms of SBP, polymorphonuclear (PMN) cell count in ascitic fluid > 250 cells/mm³ and positive gram stain and culture.
- B) Culture negative neutrocytic ascites (CNNA): Patients having minimum clinical symptoms but PMN cell count in ascetic fluid > 500 cells / mm³ and culture is negative plus negative gram staining.
- C) Bacterascites: Patients having few clinical symptoms, PMN cell count in ascetic fluid

< 250 / mm³ and gram stain plus bacterial culture positive.

Studies have reported one year mortality rate after first episode of SBP in these patients as 31% and 93%. But this mortality rate has been decreased to 20% in admitted patients due to early diagnosis and prompt treatment.³ Factors responsible for poor prognosis of SBP in cirrhosis that are reported in different studies are age, child score, intensive care admission, nosocomial origin, hepatic encephalopathy, high serum values of creatinine and bilirubin, culture positivity, bacteremia and CARD15/NOD2 variants were identified as risk factor on genetic level.⁴

The Bacterial Translocation (BT) is known as the most common cause of SBP.⁵ BT on a limited scale to mesenteric lymph nodes (MLN) is considered physiological, but more severe BT is considered pathological. Some intestinal bacteria are able to make their way into the MLN like *Escherichia coli*, *Klebsiella pneumoniae* and other *Enterobacteriaceae*. These are the most common organism causing SBP and studies on DNA sequencing revealed the identity of bacteria genotypically in MLN and ascites.^{5,6}

Three factors are identified in causing BT in cirrhosis of liver;⁴

- Alteration in microbiota of the gut.
- Increased permeability of the intestinal mucosa.
- Impaired immune system.

In liver cirrhosis the fecal microbial composition changes and the prevalence of potentially fatal bacteria like *Enterobacteriaceae* increases.⁵ In cirrhosis of liver increased number of colonies in gut and changes in their composition is secondary to decrease in paneth cell defenses, reduced motility of the intestine as well as reduced secretions from pancreatobiliary system and portal hypertension enteropathy.⁴

The most common causative organisms for SBP are aerobic Gram-negative bacteria belonging to the family of *Enterobacteriaceae* and non-enterococcal *Streptococcus* species. However

severe infection with gram positive infections are emerging.⁷ The current bacterial profile for causing SBP and its antibiotic sensitivity needs to be redefined at regular intervals. Identifying the type of bacteria in patients having SBP can permit starting early and targeted therapies and ultimately reducing mortality of SBP.

To identify the bacterial spectrum of SBP in patients with cirrhosis of liver.

MATERIAL & METHODS

It is a Descriptive cross sectional study conducted of Gastroenterology & Hepatology Department Madina Teaching Hospital, Faisalabad from 1st November: 2018 – 30th June: 2019

CIRRHOSIS: Cirrhosis is defined as evident on histopathological specimen obtained from biopsy and/or collective information of laboratory, imaging characteristics or clinical parameters.⁶

1. Stage 4 fibrosis on biopsy.
2. Combination of any two or more of the following; platelets count <140 000 per μ l, oesophageal varices presence on endoscopy, imaging studies showing evidence of cirrhosis and/or portal hypertension and/or ascites, FibroSure and elastography suggestive of stage 4 fibrosis.

Spontaneous Bacterial Peritonitis

The diagnosis of SBP is made when there is an increased ascitic fluid absolute PMN count (i.e., >250 cells/mm³ [0.25 _ 109/L]) with or without positive bacterial culture of ascitic fluid, with no evidence of intra-abdominal, surgically treatable infection source.⁸

Inclusion Criteria

All cirrhotic patients having ascites with/without clinical symptoms and signs of SBP, consecutively admitted in ward or presented to OPD were enrolled in the study.

Exclusion Criteria

Patients with following conditions were excluded from the study

1. with Hepatocellular Carcinoma (HCC)

2. On antibiotics for SBP prophylaxis.
3. Who received antibiotics for any reason in the last 7 days.
4. Having history of gastrointestinal bleed in past 7 days.
5. Having infection in any other part of the body
6. With known source of abdominal pain or localized tenderness.

In all the study participants a detailed medical history was taken and a complete physical exam was done. The routine laboratory tests including full blood count, prothrombin time, international normalization ratio and biochemical tests including serum electrolytes, renal and liver function tests were carried out in all patients before administering the first dose of antibiotic. Imaging studies including radiographs of the chest and abdomen and an abdominal ultrasound was also done. The liver disease severity was calculated by using the Child-Pugh scoring system.

Under aseptic measure a diagnostic paracentesis from left lower quadrant was performed without ultrasound guidance. The ascitic fluid analysis comprised of following tests: total and differential cell counts; total fluid protein, albumin, glucose, lactate dehydrogenase and pH of the fluid. The bacterial cultures were also sent of all patients. Ten milliliters of ascitic fluid was inoculated into blood culture bottles (aerobic and anaerobic). All these tests were performed in the central pathology laboratory in Madina Teaching Hospital, Faisalabad.

RESULTS

The demographic features of the patients found in this study are given in Table-I. Total 250 patients included in this study have a mean age of 56.3 ± 8.7 (SD). Out of these 250 patients 140 (56%) were male and 110 (44%) were female. In these patients Hepatitis C 127 (50.8%) was most prevalent as the causes of cirrhosis of liver followed by hepatitis B 77 (30.8%) and others 46 (18.4%). Most of the patients had advanced stage liver disease child class C 155 (62%).

SBP was diagnosed according to the above mentioned criteria in 140 patients. The culture

negative ascites was found in 77 (55%) and culture positive ascites was found in 63 (45%) patients. In culture positive ascites single organism was found in 59 (93.65%) and more than one organism was found in 4 (6.34%). Table-II. The microbacterial spectrum found in the ascitic fluid of different patients is shown in the Table-III. The most common organism was E.Coli 28 (47.45%) followed by Enterococcus 10 (16.94%), Klebsiella Pneumoniae 6 (10.17%), Streptococcal Pneumoniae 5 (8.47%), S.aureus 5 (8.47%), Acinetobacter 3 (5.08%) and miscellaneous 2 (3.38%).

Patients Demographics n= 250 (%)	
Age (years) mean \pm SD	56.3 \pm 8.7
Sex (Women : Men)	110 (44%): 140 (56%)
Causes of Cirrhosis (%)	
Hepatitis B	77 (30.8%)
Hepatitis C	127 (50.8%)
Others	46 (18.4%)
Child-Pugh Class (%)	
Child-Pugh Class A	22 (8.8%)
Child-Pugh Class B	73 (29.2%)
Child-Pugh Class C	155 (62%)
Ascitic Fluid, median (range)	
Protein (g/dl)	1.4 (0.41-3.18)
Albumin (g/dl)	0.83 (0.21-1.98)
Total leukocytic (count/mm ³)	725 (30-14,540)
Neutrophilic (count/mm ³)	305 (14-7,360)

Table-I. Demographic features of the patients.

Patients having SBP n=140	
Culture Negative ascites	77(55%)
Culture Positive ascites	63(45%)
Monomicrobial SBP	59(93.65%)
Polymicrobial SBP	4(6.34%)

Table-II. Culture in patients having SBP.

Microorganisms	Culture Positive Ascites n=59 (93.65%)
E.Coli	28 (47.45%)
Enterococcus	10 (16.94%)
Klebsiella Pneumoniae	6 (10.17%)
Streptococcal Pneumoniae	5 (8.47%)
S.aureus	5 (8.47%)
Acinetobacter	3 (5.08%)
Miscellaneous	2 (3.38%)

Table-III. Spectrum of Microorganisms isolated from the Ascitic Fluid of Patients with SBP.

DISCUSSION

We performed this study to focus attention on the current bacterial spectrum of SBP and help the clinician regarding the choice of antibiotic in our region. We used the Hoefs and Runton criteria⁸ to diagnose the SBP, according to this criteria patients with clinical symptoms and signs suggestive of peritonitis, Ascitic fluid polymorphonuclear cell count more than 250/mm³ and a positive bacterial culture. The other criteria used is the one Conn and Atterbury⁸, in this criteria the AFPMN count is greater than 500/mm³ and neutrophil count more than 250/mm³ with minimal clinical feature and bacterial culture. (CNNA).

In our study SBP was diagnosed in 140 (56%) patients Table 2. Other studies conducted locally reported SBP in 51%⁹ and 64%¹⁰ patients respectively; these results are comparable to our study. Studies from abroad have reported the SBP in 25-31% of cases.^{11,12} This high incidence of SBP in our population could be due to late referral of the patients to tertiary care hospital, poverty, lack of education, malnourishment and presentation at advance stage disease.

Out of 140 patients having SBP, 77 (55%) patients had culture negative ascites while 63 (45%) patients had culture positive ascites. Another local study has reported 57.84% patients with culture negative ascites and 42 % patients with culture positive ascites.¹¹ A study conducted in Turkey has reported 55.5% patients with culture negative ascites and 44.5% patients with culture positive ascites.¹² These results are identical to the findings we came across in our study.

Historically gram negative bacterial infection is the major cause of SBP in cirrhotic ascites. The culture report of our study revealed E.coli is the most prevalent organism in 28 (47.45%) followed by Enterococcus 10 (16.94%), Klebsiella Pneumoniae 6 (10.17%), Streptococcal Pneumoniae 5 (8.47%), S.aureus 5 (8.47%), Acinetobacter 3 (5.08%) and miscellaneous 2 (3.38%). Table-III. In a local study they isolated E.coli in 58.13%, streptococcus pneumoniae in 18.60%, Staphylococcus aureus in 9.30%, Klebsiella in 9.30% and Acinetobacter species in 4.65% of the patients.¹¹ A foreign study showed slightly different microbial spectrum with microorganism found, E.coli in 45.8%, Klebsiella ozytoca in 18.7%, Group D Streptococci in 14.6% and Staphylococcus in 36.7%.¹³ Another study from Denmark reported the prevalence of E.Coli 17%, Klebsiella spp: 6% and Staphylococcus 8%.¹⁴ These variations might be due to difference in geographical, demographic and etiological factors of the patients.

The examination report of ascitic fluid of the patients in our study revealed median value of protein 1.4 g/dl, albumin 0.83 g/dl, Total leukocyte 725 count/mm³ and Neutrophils 305 count/mm³. The median value of these parameters found in ascitic fluid of another study conducted in Turkey were as follows, total protein 1.1 g/dl, albumin 0.56 g/dl, total leukocytes 675 count/mm³, Neutrophils 320 count/mm³.^{3,12} While a Study from Poland reported median Total Leukocyte Count 571/mm³, median Neutrophil Count 145/mm³ and median total protein 1.85g/L.¹⁵

CONCLUSION

We concluded from this study that the percentage of SBP is quite high among patients having cirrhosis and ascites and the Gram negative bacterial spectrum is still prevalent in our region. The presentation of SBP may be typical or atypical. A diagnostic paracentesis must be performed quickly for culture sensitivity and complete examination and start the patient on empirical antibiotic covering the gram negative bacteria to reduce the mortality, while awaiting the culture sensitivity result.

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