The pattern of microbial flora in Spontaneous bacterial peritonitis in Cirrhotic patients
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Abstract

Introduction: Spontaneous bacterial peritonitis (SBP) is the bacterial infection of ascitic fluid in the absence of other apparent causes. It is the most prevalent and serious infection in cirrhosis and leads to significant morbidity and mortality. The frequency of SBP in hospitalized patients with cirrhosis varies from 7 to 23% in the west and it is around 33% in Pakistan. Our study aim was to determine the frequency of microbial organisms isolated from spontaneous bacterial peritonitis in cirrhotic patients.

Materials and Methods: We did a cross-sectional study at the Department of Medicine, Fauji Foundation Hospital Rawalpindi for 6 months. Cirrhosis was diagnosed on the bases of clinical, biochemical and ultrasonography findings. Peripheral blood samples were obtained for the evaluation of complete blood cell count, polymorphonuclear leukocyte count, albumin and coagulation parameters. At the same time, the patients underwent paracentesis and a 20ml ascitic fluid sample was taken for culture sensitivity along with routine biochemical examination from the pathology department lab at our hospital.

Results: A total of 150 patients were enrolled according to the inclusion criteria of the study. The mean age (yrs) of patients was 32.3±9.31. The frequency and percentages of male and female patients were 70 (46.7) and 80 (53.3) respectively. Frequency and percentages of E Coli and streptococcal pneumonia were 94 (62.7) and 34 (22.7) respectively, whereas frequency and percentages of staph aureus and Klebsiella were 22 (14.7).

Conclusion: SBP is quite common in patients with cirrhosis. It should be suspected in all such cases presenting with typical or atypical features. E Coli was the most common causative organisms in our study but gram-positive organisms were quite frequent as well.

Keywords: SBP, Cirrhosis, Peritonitis.
**Introduction**

Spontaneous bacterial peritonitis (SBP) is an infection of ascitic fluid without any other measurable cause. It contributes to significant morbidity and mortality in cirrhotic patients as it also leads to renal and hepatic impairment. In hospitalized patients with cirrhosis, its prevalence ranges from 7 to 23% in world-wide and around 33% in Pakistan. The in-hospital mortality rate can reach between 20%-40% despite infection control strategies. Recent studies have shown that the prevalence of multidrug-resistant bacteria is increasing in these patients.

Pathogenesis of spontaneous bacterial peritonitis involves the translocation of the normal flora of the gut into the mesenteric lymph nodes and then ascitic fluid. In one study it is assumed that the etiology of spontaneous bacterial peritonitis is changing which is supported by frequent failure of cefotaxime previously considered as a treatment of choice for this disease. In Literature the most common organisms causing spontaneous bacterial peritonitis are Gram-negative rods including E Coli and Klebsiella. In some studies, gram-positive rods are considered the most common organisms and examples are Enterococcus Faecalis and Strep Viridens. In another study, the frequency of occurrence of E Coli is 66 %, Streptococcal Pneumonia 16.0%, Staph aureus, and Klebsiella was 8% respectively.

Recent studies suggest that antibiotic resistance of gram-negative bacteria is on the rise along with an increased prevalence of gram-positive bacteria in SBP, so importance must be given to this change in order to improve clinical outcomes in such patients. Previously gram-negative bacteria especially enterobacteriaceae were the most common organisms causing spontaneous bacterial peritonitis but some studies report gram-positive cocci to be the most common bacteria in culture-positive SBP and a variety of other drug-resistant microorganisms have also emerged. As a result of high rates of changing organisms in SBP, the choice of optimal antibiotic therapy is vital in individual patients. The explanations of antibiotic resistance to different organisms in SBP are the exposure of patients to the hospital environment, invasive diagnosis maneuvers and the use of prophylactic antibiotic therapy. In order to decrease mortality in SBP, it is important to administer appropriate antibiotics as soon as possible after determining the microbial organism in ascitic fluid culture report.

Spontaneous bacterial peritonitis is a serious complication of cirrhosis of the liver and needs to be addressed as early as possible. In order to start an empirical antibiotic, it is important to know the spectrum of pathogens involved in this disease as soon as possible. The prognosis of these patients is related to accurate diagnosis and appropriate treatment as it decreases the mortality rate. This study will determine the frequency of occurrence of different organisms in the pathogenesis of spontaneous bacterial peritonitis and thus increase our information in order to use empirical antibiotics as this will help to decrease the SBP associated mortality.

**Materials and Methods**

It was a Cross-sectional study done at the Department of Medicine, Fauji Foundation Hospital Rawalpindi for six months. The study was aimed to determine the frequency of microbial organisms isolated from patients with spontaneous bacterial peritonitis having chronic liver disease. Cirrhosis of liver was defined by characteristic ultrasonographic findings, shrunken liver, nodular regeneration, portal hypertension (portal vein diameter greater than 11 mm) and splenomegaly (size greater than 11 cm) done by an expert Radiologist. Spontaneous bacterial peritonitis was defined on ascites fluid routine examination having WBC count >250/mm and positive ascitic fluid gram stain and culture. The sample size was calculated using the WHO sample size calculator with a confidence interval of 95%, and a sample of 165 patients was calculated for the study. Patients were taken through non-probability consecutive sampling and all patients with liver cirrhosis, ascites and SBP irrespective of gender and age were recruited. Patients already taking antibiotics within 10 days, patients with a history of an abdominal surgical procedure in the preceding month and patient with other causes of increased polymorphonuclear leukocyte count in the ascitic fluid such as tuberculosis, pancreatitis, peritoneal carcinomatosis, and malignancy were excluded based on previous history and medical record.

Patients were included after taking informed consent for using their data in this research. Peripheral blood samples were obtained for the evaluation of complete blood cell count, polymorphonuclear leukocyte count, biochemical markers for example albumin and coagulation. At the same time, the patients underwent paracentesis and a 20ml ascitic fluid sample was taken, out of which 10ml was inoculated into a blood culture.
bottle and send for culture sensitivity along with the remaining 10ml for routine biochemical examination to pathology department lab at our hospital. The organism was grown within 72 hours and the growth of the organism in gram stain report was verified by a pathologist at the hospital lab. All the data were analyzed using the software SPSS version 17. Values of continuous variables like age, polymorph nuclear cell count were expressed as mean ±SD. Categorical variables like gender and frequency of microbial organisms were expressed as percentages.

Results

Out of 165 recruited patients, data of 150 patients was available for final analysis. The rest of the 15 patient’s data was excluded due to various reasons like withdrawal of consent, contaminated samples and loss of follow up of patients. In our study, the mean age of patients was 32.3±9.31years with ranges from 25 to 70 years. The frequency and percentages of male patients were 70 (46.7), whereas the frequency and percentages of female patients were 80 (53.3). Frequency and percentages of E Coli and streptococcal pneumonia were 94 (62.7) and 34 (22.7) respectively, whereas frequency and percentages of Staph aureus and Klebsiella were 22 (14.7), as shown in Table 1.

Effect modifier like Age (yrs) was stratified and compared with types of microbial organisms. In patients with age ranges from 25 – 45 years, frequency and percentages of E coli and streptococcal pneumonia were 54 (57.4), 23 (67.6) and 8 (36.4) respectively, whereas frequency and percentages of Staph aureus and Klebsiella were 11 (36.2) and 8 (36.4) respectively. The post-stratification comparison was done as shown in Table 2. Effect modifier like gender was stratified and compared with types of microbial organisms. In male patients, frequency and percentages of Ecoli, Streptococcal Pneumonia, Staphylococcus, and Klebsiella were 46 (48.9), 16 (47.1) and 08 (36.4) respectively. Similarly in female patients, frequency and percentages of Ecoli, Streptococcal Pneumonia, Staphylococcus and Klebsiella were 48 (51.1), 18 (52.9) and 14 (63.3) respectively. Post-stratification was done by applying the chi-square test which was statistically significant (p-value 0.567), as shown in Table 3.

Discussion

Liver cirrhosis constitutes a remarkable contributor to mortality worldwide. Portal hypertension is the main causative factor for most of the complications of cirrhosis. 50% of patients of compensated cirrhosis
develop ascites within 10 years; which is mostly the earliest sign of portal hypertension.13 Cirrhotic patients with portal hypertension have poor prognosis without transplantation and development of spontaneous bacterial peritonitis (SBP) further accelerates the disease progression14 and mortality of the condition.15 Despite an improvement in patient care, mortality after a single episode of SBP is estimated to be 32.5% at 1 month and 66.2% after 1 year.16 Without prophylactic antibiotics; two-thirds of these patients have recurrences of infection within 12 months.17 Patients of cirrhosis with higher serum bilirubin, Child-Pugh stage C, and thrombocytopenia are more likely to develop SBP.18 Primary prevention for SBP is endorsed in patients with ascites if ascitic fluid protein concentration is low, or there is renal dysfunction, as characterized by serum creatinine of >1.2mg/dL, BUN>25mg/dL, or serum sodium ≤130mEq/L.19 Norfloxacin is preferably the recommended primary prophylaxis agent for patients with a previous episode of SBP.20,21 It is defined as a bacterial infection of the ascitic fluid without a recognizable intra-abdominal source. The Worldwide incidence of spontaneous bacterial peritonitis in hospitalized patients with cirrhosis is 7–23%, while in Pakistan it is reported to be 33%.22 Translocation of bacteria from the intestinal lumen to extra-intestinal sites or mesenteric nodes is the main pathophysiological mechanism. This is due to increased permeability of gut in cirrhotic patients; which is brought about by defective local as well as systemic immunity in the backdrop of altered gut flora in patients with portal hypertension.23 Gram-negative bacteria are the most common culprit when they leak into the blood after overwhelming the quarantine of mesenteric nodes.24 Subsequently, they settle in the ascitic fluid and lead to spontaneous bacterial peritonitis.25 Thus most causative organisms belong to intestinal flora26, most commonly E. Coli or a Klebsiella is involved.27 Recognition of pathogens is very important for the choice of antibiotic treatment.28 But microbial cultures take time; considering the high mortality risk of SBP, antibiotics should be commenced before culture results. This is mostly guided by the prior knowledge of the microbial spectrum in these patient groups.29 In our study, the mean age of patients was 32.3±9.31 with ranges from 25 to 70 years similar to a study done by D’Amico G et al30 where the mean age of patients was 50.20±14.39 years. In our study, male patients were 70 (46.7%), whereas 80 (53.3%) were females. In our study frequency and percentages of Ecoli and Streptococcal Pneumonia were 94 (62.7) and 34 (22.7) respectively, whereas frequency and percentages of staph. Aureus and Klebsiella were 22 (14.7). Similarly in a study by Shizuma et al frequency and percentages of Ecoli and Streptococcal Pneumonia was 8(66.6) and 2(16.6) respectively, whereas frequency and percentages of Klebsiella were 1(8.33).31 Recognition of risk factors can determine the patients requiring the primary prophylaxis.32 In addition to the conventional risk factors mentioned above, increased ascetic fluid polymorph (PMN) count is also considered a risk factor for SBP32. Recently, C-Reactive protein (CRP) is also being investigated as a prognostic factor in cirrhotic patients with SBP.33 Literature suggests higher 1-month mortality in patients with SBP who have positive bacterial cultures.34 SBP is frequently followed by sepsis, renal dysfunction, and encephalopathy; all of which further pave the path for worse outcomes.35 This emphasizes the need for vigilance on the part of clinicians for early diagnosis and prompt treatment of this condition in order to improve the short and long term mortality. With the help of our study and new emerging data, we can identify risk factors for SBP development and pattern of microbial flora under current circumstances which will help in early aggressive treatment to decrease mortality. However, our study has some limitations, such as the limited sample size and some possible recruiting bias at a tertiary care hospital.

**Conclusion**

The study concludes that the frequency of spontaneous bacterial peritonitis is substantially high in cirrhotic patients. It may present with typical or atypical features so, a high index of suspicion should be maintained for its timely diagnosis and treatment. Knowledge of the microbial spectrum in this condition can help achieve this goal.

**References**

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