CULTURE-BASED IDENTIFICATION OF CAUSATIVE ORGANISMS IN ASCITIC FLUIDS OF PATIENTS WITH SPONTANEOUS BACTERIAL PERITONITIS SECONDARY TO DECOMPENSATED LIVER DISEASE AND THEIR SENSITIVITIES TO CEFTRIAXONE AS AN EMPIRIC THERAPY

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ABSTRACT

OBJECTIVES

To identify the pathogens in the ascitic fluids of patients with spontaneous bacterial peritonitis and then to determine their sensitivity pattern to ceftriaxone.

METHODOLOGY

The cross-sectional study was conducted at the Medical Unit-A, Department of Medicine, Hayatabad Medical Complex, Peshawar, from November 2021 to April 2022. Before ceftriaxone treatment was started, a minimum of 10 ml of ascitic fluid was introduced into a blood culture vial. Only patients with a positive culture were registered, and their information was gathered using a proforma. For statistical analysis, SPSS version 23 was used.

RESULTS

A total of 96 patients were enrolled in our study. There were 62 (59.52%) male and 34 (40.48%) female patients. Based on the isolation and identification of bacteria, the most prevalent bacteria isolated was Escherichia coli in 36 (37.5%) patients, followed by Acinetobacter Spp in 13 (13.54%) patients, Streptococcus spp in 14 (14.58%), Enterococcus spp in 11 (11.45%), Staphylococcus aureus in 9 (9.39%), MRSA in 8(8.33%) and K. Pneumonia in 5(5.21%) patients. The overall sensitivity of ceftriaxone to gram-positive bacteria was observed in 12 (42.85%) isolates, whereas the overall sensitivity of ceftriaxone to gram-negative bacteria was observed in 25 (36.76%) isolates. (p=0.091) (Figure 6).

CONCLUSION

Our study concludes that gram-negative bacteria were more prevalent than gram-positive bacteria in ascitic fluids of patients with spontaneous bacterial peritonitis. The most common isolated pathogen was E.coli. Gram-negative was more resistant to ceftriaxone as compared to gram-positive bacteria.

KEYWORDS: *Pathogen, Bacterial Peritonitis, Liver Disease, Ceftriaxone*

INTRODUCTION

Decompensated liver cirrhotic patients are at risk for the alarming but curable complication known as spontaneous bacterial peritonitis (SBP), which has a reported fatality rate of up to 90% if left untreated.[1] SBP is characterized as an ascitic fluid infection with a polymorphonuclear cell count of at least 250 cells/ml, having one bacterial cell growth and no intra-abdominal or extra-abdominal source of infection. There are two types of SBP: Bacteriascites (BA) and Culture Negative Neutrocytic Ascites (CNNA).[2] SBP nearly primarily affects those with portal hypertension, often due to liver cirrhosis. Typically, the source of the infectious agent is difficult to identify.[3] Symptoms such as high body temperature, chills, vomiting, nausea, stomach pain, soreness, and general malaise are seen in patients. It is unclear how the SBP pathophysiology works. Possible causes of SBP include bacteremia from the respiratory tract or urinary tract, iatrogenic causes such as endoscopic treatment of gastric varices or esophageal varices and the growth of bacteria and associated endotoxins from the gastrointestinal tract (GIT) to the peritoneal cavity as a result of compromised defensive systems in cirrhosis.[3] Hospitalized liver cirrhosis patients have a 10–30% risk of developing SBP.[4] A diagnosis accuracy of up to 80% for culture-positive SBP may be attained using the blood culture bottle technique at the bedside.[5] The majority of the microorganisms that are accountable for SBP belong to

the family Enterobacteriaceae. In 60% of instances, Escherichia coli is the primary offender, trailed by Klebsiella pneumoniae in 14% of cases, while gram-positive bacteria in ascitic fluid culture are documented in up to 24% of cases.[6] Ceftriaxone is the most frequently prescribed empiric antibiotic for SBP, and it is helpful against Escherichia coli in 71.4% of cases, Klebsiella pneumoniae in 66.6% of cases, and Gram-positive bacteria Staphylococcus aureus in 66.6% of cases.[7] Due to various invasive procedures and selective gut cleansing of gram-negative bacteria by antibiotic prophylaxis for SBP, there is a growing tendency of gram-positive organisms found in the culture of ascitic fluid.[8] Research from Copenhagen backs this observation, demonstrating an increase in the prevalence of gram-positive cocci to 45.9% and a total antibiotic coverage of 57% with ceftriaxone and taking into account the fact that, as was already mentioned, gram-positive bacteria are developed in ascites fluid cultures from patients SBP patients with liver cirrhosis and have a poor reactivity to ceftriaxone as an initial treatment, and that gram-negative bacteria have significant resistance to ceftriaxone in various settings.[9] There is insufficient data that the microbial distribution in ascitic fluid from our nation has changed in this way. In our setting, ceftriaxone is often used as an empiric treatment, thus it is crucial to search for current trends in the SBP-causing organisms and their response to ceftriaxone. A combination of empiric treatment or monotherapy with a wide range of antibiotics would be recommended if the alteration described above occurs.

METHODOLOGY

The cross-sectional study was conducted at the Medical Unit –A, Department of Medicine, Hayatabad medical complex, Peshawar. Our study lasted six months, from November 2021 to April 2022. The sample size was 96 based on the WHO calculator for sample size, taking a confidence interval of 95%, absolute precision of 7 %, and anticipated population proportion of 14%.[6] The ethical committee of the hospital gave the study approval. All the cirrhotic ascites patients with bacterial peritonitis, of all ages and either gender, having growth of microbes on the culture media were included. In contrast, all the patients with ascites like Malignant ascites, Tuberculous ascites and patients unwilling to participate were excluded from the current study. After obtaining the participants informed agreement, 96 patients, including inpatients and outpatients, who met the inclusion and exclusion criteria, were recruited for the study. To aspirate ascitic fluid, a complete aseptic procedure was used. Before ceftriaxone treatment was started, a minimum of 10 ml of ascitic fluid was introduced into a blood culture vial. If necessary, imaging help was obtained. The microbiology department and hospital database system were used to monitor the results of these samples. Only patients with a positive culture were registered, and their information was gathered using a proforma. To do the statistical analysis, SPSS version 23 was used. Calculations of frequency and percentages were made for gram-positive and gram-negative organisms and ceftriaxone sensitivity, and the mean and standard deviation were computed for the age of patients. The sensitivity of ceftriaxone against gram-positive and gram-negative bacteria was compared using the Chi-square test. P values under 0.05 were considered significant.

RESULTS

A total of 96 patients were enrolled in our study. There were 62 (59.52%) male and 34 (40.48%) female patients. Our study's mean (±SD) age was 39 (±4.2) years. In the current study, 7 (7.29%) patients were 30-45 years old, 48 (50%) patients were 46-55 years old, 36 (37.5%) patients were 56-65 years old, whereas 5 (5.21%) were age group more than 66 years.

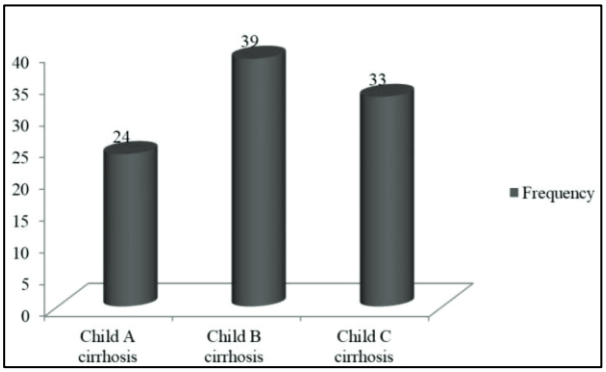

Figure 1: Frequency of Patients Based on Child Class of Cirrhosis

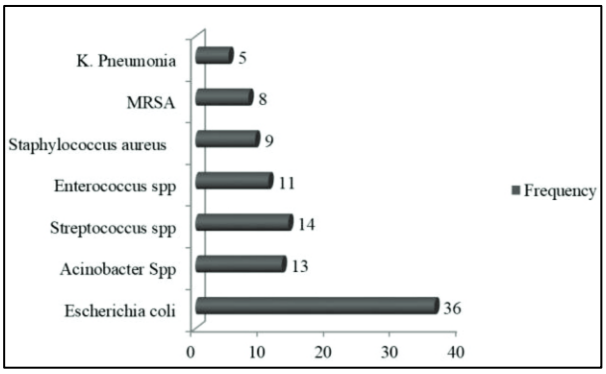

Figure 2: Frequency of Patients Based on Isolation of Causative Organisms

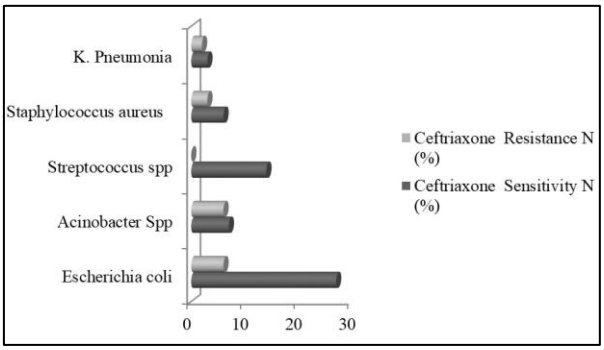

Figure 3: Resistance and Sensitivity Pattern of Ceftriaxone against the Different Causative Pathogens

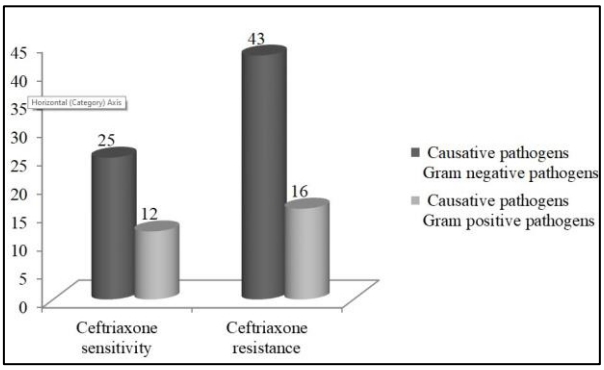

Figure 4: Resistance and Sensitivity Pattern of Ceftriaxone against Gram-Negative and Gram-Positive Bacteria

DISCUSSION

Spontaneous bacterial peritonitis (SBP) is an infection of the normally sterile ascitic fluid that develops without a known infectious source inside the abdomen.[10] A positive culture of ascitic fluid or the detection of more than 500/cm leukocytes or more than 250/cm neutrophils in the ascitic fluid serve as the diagnostic criterion for SBP. One of the frequent side effects of cirrhosis, occurring between 7% and 23% of the time, is spontaneous bacterial peritonitis.[11,12] Ascites have a variety of causes across the globe, which is mostly owing to the varying incidence of liver cirrhosis, alcohol usage, and other disorders. Hepatitis C and B-related liver cirrhosis is our nation's most frequent cause of ascites, although alcohol is the most frequent cause in Western populations. Patients with hepatic cirrhosis often develop spontaneous bacterial peritonitis. It has a high death and morbidity rate. Early diagnosis and therapy are the gold standard strategy in managing people with SBP. In our study, a total of 96 patients were enrolled. There were 62 (59.52%) male and 34 (40.48%) female patients. Our study's mean (±SD) age was 39 (±4.2) years. In the current study, 7 (7.29%) patients were 30-45 years old, 48 (50%) patients were 46-55 years old, 36 (37.5%) patients were 56-65 years old, whereas 5 (5.21%) were age group more than 66 years. Based on child class, Child A cirrhosis, Child B cirrhosis and Child C cirrhosis were observed in 24 (25%), 39 (40.63%) and 33 (34.38%) patients, respectively. Based on the isolation and identification of bacteria, the most prevalent bacteria isolated was Escherichia coli in 36 (37.5%) patients followed by Acinobacter Spp in 13 (13.54%) patients, Streptococcus spp in 14 (14.58%), Enterococcus spp in 11 (11.45%), Staphylococcus aureus in 9 (9.39%), MRSA in 8(8.33%) and K. Pneumonia in 5(5.21%) patients. In our study, ceftriaxone was sensitive in 27 (75%) isolates of Escherichia coli, 14 (100%) isolates of Streptococcus spp, 3 (60%) isolates of K. Pneumonia, 6 (66.67%) isolates of Staphylococcus aureus, in 7 (53.85%) isolates of Acinobacter Spp. The overall sensitivity of ceftriaxone to gram-positive bacteria was observed in 12 (42.85%) isolates, whereas the overall sensitivity of ceftriaxone to gram-negative bacteria was observed in 25 (36.76%) isolates (p=0.091). A similar study was done by Mukhtar Ahmad et al. in Pakistan. They reported almost similar results to our study. They reported that the most common bacteria isolated in their study was E.coli, observed in 36% of the samples. The other reported organisms were Streptococcus spp, Staphylococcus aureus, Acinobacter Spp and K. Pneumoniae. They also reported more gram-negative isolates as compared to gram-positive isolates.[7] Another similar study was conducted by Mohsin Raza et al., who found that Escherichia coli was present in 49 patients (31.2%), Acinobacter Spp was found in 24 patients (15.3%), Streptococcus was found in 21 patients (13.4%), Enterococcus was found in 19 patients (12.1%), Staphylococcus aureus was found in 18 patients (11.4%), MRSA was found in 17 patients (10.8%), and K. pneumonia was observed in 9 (5.7%) patients. Ceftriaxone was observed as sensitive in 69 (43.9%) isolates found in their study.[13] In their study, Haider et al. found that gram-negative organisms made up 60% of the infections, whereas gram-positive species made up up to 30% of SBP infections.[6] Another study carried out by Anwar Ali et al. also reported comparable results to our study. They reported that the most common bacteria isolated in their study was E.coli, followed by Streptococcus spp, Staphylococcus aureus, Acinobacter Spp and K. Pneumoniae. They also reported more gram-negative isolates as compared to gram-positive isolates.[14] Globally, there is increasing evidence that people with liver cirrhosis are becoming resistant to ceftriaxone against several SBP bacteria. In particular, in individuals with a high risk of developing cephalosporin resistance, we require additional study to determine the broad spectrum antibiotics for SBP patients. This would aid in lowering SBP patients death

rates, which are a significant side effect of liver cirrhosis. The investigation provides valuable insights into the culture-based identification of bacteria in ascitic fluids from patients with spontaneous bacterial peritonitis. The study's male preponderance aligns with the higher prevalence of cirrhosis in males. The age distribution, with most patients falling within the middle-age range, corresponds to the typical occurrence of liver disease and its complications during these years. The classification of cirrhosis severity based on Child-Pugh criteria is consistent with the advanced liver disease state, as indicated by a notable proportion of patients classified as Child B and Child C. Identifying the organisms responsible for infection is pivotal in guiding effective antibiotic treatment. Escherichia coli emerged as the dominant pathogen among the isolated bacteria from ascitic fluids. This finding aligns with previous research indicating its prevalence in SBP cases.[15,16] The presence of other bacterial strains, such as Acinetobacter spp, Streptococcus spp, Enterococcus spp, and Staphylococcus aureus, underscores the polymicrobial nature of ascitic fluid infections. The presence of methicillin-resistant Staphylococcus aureus (MRSA) is of particular significance, highlighting the potential impact of antibiotic-resistant strains in driving infections. Gram-positive organisms were predominantly isolated in our study, which aligns with findings from different countries across the globe.[17,18] The frequencies of these bacterial isolates offer insights into local epidemiology and have implications for choosing empirical antibiotic therapies. Ceftriaxone, a third-generation cephalosporin with broad-spectrum activity, demonstrated noteworthy sensitivity against diverse isolates. Notably, the most prevalent pathogen, Escherichia coli, exhibited significant sensitivity to ceftriaxone, reinforcing its role as a viable choice for empirical treatment. The high sensitivity shown by Streptococcus spp, along with the fair sensitivity in cases of K. pneumoniae and Acinetobacter spp, indicates the potential utility of ceftriaxone as an initial therapeutic option in cases where the gram-positive infection is suspected; however, the empiric use of ceftriaxone might be discouraged in cases where there is a high suspicion of gram-negative infections. Similar studies demonstrated a poor sensitivity of gram-negative pathogens towards ceftriaxone and other cephalosporins.[19,20,21,22] The observation that ceftriaxone sensitivity was relatively lower in gram-negative bacteria compared to their gram-positive counterparts introduces intriguing considerations. This discrepancy could stem from various factors, including differences in cell wall structures and mechanisms of resistance. Importantly, the lack of statistical significance in the sensitivity difference between gram-positive and gram-negative bacteria underscores that ceftriaxone maintains reasonable efficacy across both categories. However, this finding underscores the need to consistently monitor local resistance patterns and account for additional factors, such as patient comorbidities and prior antibiotic exposure, when determining the most appropriate empirical antibiotic strategy. This study contributes to understanding the microbiological characteristics and antibiotic sensitivity trends of causative agents in SBP. The prevalence of distinct bacterial species, their responses to ceftriaxone, and the absence of statistically significant sensitivity differences between gram-positive and gram-negative bacteria offer valuable guidance for shaping empirical antibiotic therapies. With antibiotic resistance remaining a pressing concern, continuous monitoring of local resistance patterns and ongoing research endeavours are imperative for making evidence-based clinical decisions and optimizing patient outcomes.

LIMITATIONS

The study's findings are important for understanding the microbiology and antibiotic sensitivity profiles of ascitic fluid infections in SBP patients. However, certain limitations should be acknowledged. The study's sample size is relatively modest, which may temper the broader applicability of its results. Additionally, the study examined ceftriaxone sensitivity without delving into wider antibiotic resistance patterns. Future investigations might consider exploring alternative antibiotic options and their respective sensitivities.

CONCLUSIONS

Our study concludes that gram-negative bacteria were more prevalent than gram-positive bacteria in ascitic fluids of patients with spontaneous bacterial peritonitis. The most common isolated pathogen was E.coli. Gram-negative was more resistant to ceftriaxone as compared to gram-positive bacteria. There is a growing problem with bacteria becoming resistant to ceftriaxone. Thus it has to be replaced with a different broad-spectrum antibiotic. When selecting the proper antibiotics, information on the ascetic fluid pathogenic organisms in a particular population is crucial.

CONFLICT OF INTEREST: None

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