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ORIGINAL PAPER

Bacterial infections in cirrhosis of liver: a hospital based study

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ABSTRACT

Introduction: *Bacterial infections represents one of the most important precipitating event for acute decompensation and mortality in a case of cirrhosis of liver. Patients with cirrhosis are highly susceptible for bacterial infections and their severe courses. Infections occur more often in advanced stage of liver disease, impair hepatic function, trigger the onset of complications, and are significant factors of mortality as well. Gastrointestinal hemorrhage confers a higher risk for infections and infections play important role in provoking of variceal bleeding episodes and can also be associated with the failure to control bleeding. The incidence and severity of infection in cirrhosis is greater than in the population without cirrhosis. Infection with multi resistant organisms is common in cirrhosis and its occurrence is associated with higher mortality rates than in patients without cirrhosis. The end-organ damaging effect of bacterial infection is greater in patients with cirrhosis due to altered sensitivity, which often culminates in acute-on-chronic liver failure. Delays in the diagnosis and start of treatment results in higher mortality particularly in hypotensive patients with cirrhosis.* ***Materials and methods***: *This was a hospital based observational, descriptive study to find data on bacterial infection in 123 cirrhotic patients.* ***Results***: *Bacterial infection was present in 41(33.33%) patients of study population. SBP was the most common (39.02%) bacterial infection documented. In hospital mortality was highest with Child Pugh Class C (50%).* ***Conclusion***: *With increase in Child Pugh Class, bacterial infections and in hospital mortality increases.*

Keywords: *Child pugh score; culture isolates; in hospital mortality.*

INTRODUCTION

Cirrhosis of Liver is considered as an immunocompromised state that leads to a variety of infections which then accounts for an approximately 30% mortality.[1] Bacterial infections occur in 32% to 34% of admitted patients with cirrhosis[2] and in 45% of those with gastrointestinal hemorrhage.[3]

In cirrhosis, bacterial infection is defined as a pathological process caused by invasion of normally sterile tissue, fluid or cavity by pathogenic or potentially pathogenic bacteria. Approximately one-third of bacterial infections are community acquired, one-third health care associated and one-third nosocomial.[4]

Infections are increasingly recognized as a major trigger of systemic inflammation and organ failure in advanced cirrhosis leading to a fourfold increased mortality.[5]

Decompensated liver cirrhosis predisposes to delayed intestinal transit time, increased intestinal permeability and disturbed expression of intestinal antimicrobial peptides thereby facilitating the translocation of bacteria and bacterial products from the gastrointestinal lumen through the lamina propria into the mesenteric lymph nodes, ascitic fluid and systemic circulation.[6] Gram negative enteric bacilli translocate more easily than gram positive bacteria and obligate anaerobes.[7]

The most common bacterial infections encountered in clinical practice in cirrhosis are spontaneous bacterial peritonitis (25%-31%), urinary tract infections (20%-25%), pneumonia

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(15%-21%), and soft tissue infections (11%).[8]

Infection leads to accelerated deterioration of liver function and is the most common identifiable extra hepatic trigger of acute-on-chronic liver failure (ACLF), which is characterized by organ failure and extremely poor survival (28-day mortality rate 30–40%).[9] Systemic inflammation triggered by infection may cause ACLF through complex mechanisms including an exaggerated inflammatory response and systemic oxidative stress via pathogen-or danger/damage-associated molecular patterns and/or alteration of tissue homeostasis as a consequence of inflammation. These features may induce tissue damage (cell dysfunction, apoptosis, or necrosis), organ failure, and even death. Thus, understanding characteristics of infection in patients with ACLF is important.

MATERIALS AND METHODS

This was a hospital based observational, descriptive study carried out in Department of Medicine, in Gauhati Medical College and Hospital, Guwahati during a period of one year. Patients above 12 years of age and belonging to either sex who were cirrhotic were included in the study. Patients aged less than 12 years, not willing to give consent and patients on antibiotic therapy during admission were excluded from the study. A scheme of case taking or proforma was filled up meticulously for every patient included in the study by interviewing patients/attendants, thorough clinical examination and relevant investigations.

The case of clinical cirrhosis of the liver will be defined as a patient having at least one clinical sign of hepato cellular failure and one of the portal hypertension along with at least three USG findings suggestive of cirrhosis of liver.[10,11]

The diagnosis of Spontaneous Bacterial Peritonitis (SBP) was made by >250 neutrocytes in ascitic fluid and/or positive culture for a certain germ and exclusion of other secondary causes of peritonitis. Urinary Tract Infection (UTI) diagnosis was made by clinical symptoms and signs (dysuria, fever), >10 leucocytes in urinalysis and/or positive blood culture (>10,000 CFU/ml). The diagnosis of Respiratory Tract Infection (RTI) was made by clinical symptoms and signs (fever, cough, expectoration, pulmonary sound); positive radiological signs (patchy alveolar opacities); and/or positive bacteriological examination (sputum). Skin and soft tissue infections (SSTI) were diagnosed by fever, local signs (blush, tumefaction and pain), leukocytosis with neutrophilia, positive cultures of wound secretions.[12,13]

Statistical analysis was done with Windows Excel 2013 and Graph Pad prism 7.02. Fischer's Exact Test was used to calculate p value.

RESULTS

Out of 123 cirrhotic patients,41(33.33%) had bacterial infection. Apart from upper GI bleeding, patients without infections 82(66.66%) were admitted due to other reasons like uncomplicated ascites, various stages of hepatic encephalopathy, electrolyte imbalance and hepatoma. Total number of male patients were 92(74.79%) and 31(25.20%) were female patients. Maximum number of patients in the study group were between 55-64 years of age (34.95%). The most common cause of cirrhosis was alcohol (79.67%) followed by Cryptogenic, Hepatitis B, Hepatitis C, Hepatits B + Alcohol and Hepatitis C + Alcohol. Majority of the study population belonged to Child Pugh Class C (58.3%) (**Figure 1**).

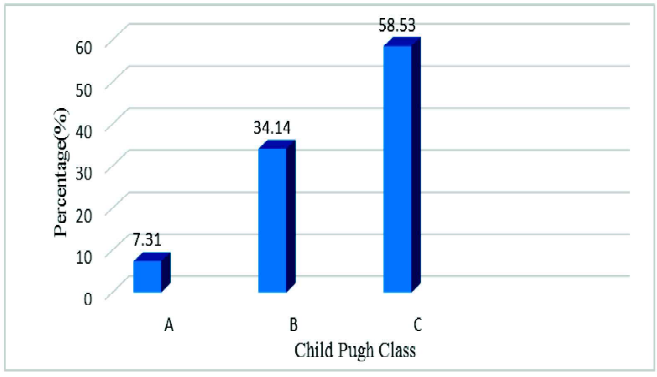

Figure 1 Distribution of Child Pugh Class

The most common type of infection in the study group was Spontaneous Bacterial Peritonitis (36.58%) followed by Urinary Tract Infection (26.82%), Skin and soft tissue infection (19.51%) and Pneumonia (17.07%) (**Figure 2**).

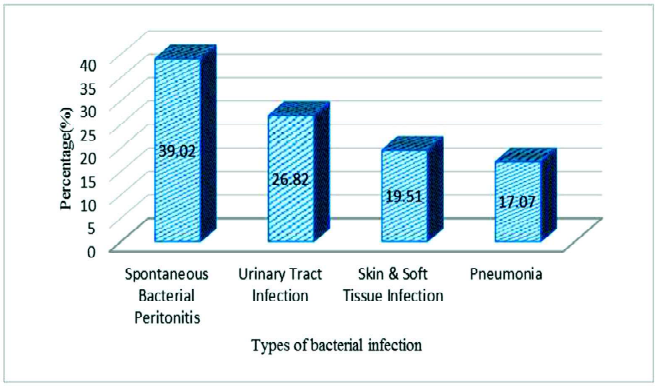

Figure 2 Frequency of Infection Types

Ascitic fluid culture was positive in 26.67% of cases. E coli was the most common (20%) bacterial isolate followed by Klebsiella (6.67%). Urine culture was positive in 81.82% of cases with E coli being the most common (54.54%) bacterial isolate followed by Enterococcus (18.18%) and Klebsiella (9.09%). Culture positivity in cases of pneumonia were 71.32% with Streptococcus pneumonia being the most common bacterial isolate (57.14%) followed by Klebsiella pneumonia (14.28%). Culture were positive in 37.5% cases of skin and soft tissue infection. Most common bacterial isolate from swab culture was Staphylococcus aureus in 25% cases followed by E coli in 12.5%. Frequency of bacterial infection (41.67%) (**Figure 3**) and in hospital mortality (30%) (**Figure 4**) were significantly ($p<0.05$) higher in Child Pugh Class C than Child Pugh Class A-B.

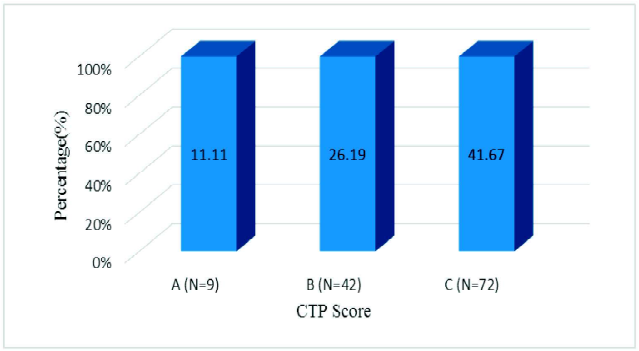

Figure 3 Bacterial Infection in relation to CTP

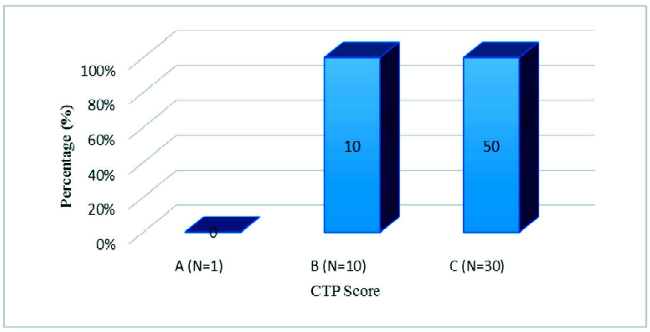

Figure 4 Hospital Mortality in patients with bacterial infection

In hospital mortality was seen highest with Spontaneous Bacterial Peritonitis (37.5%) followed by Pneumoniae (25%). Both UTI and Skin & Soft Tissue Infection were associated with in hospital mortality in 18.75% of cases (**Figure 5**).

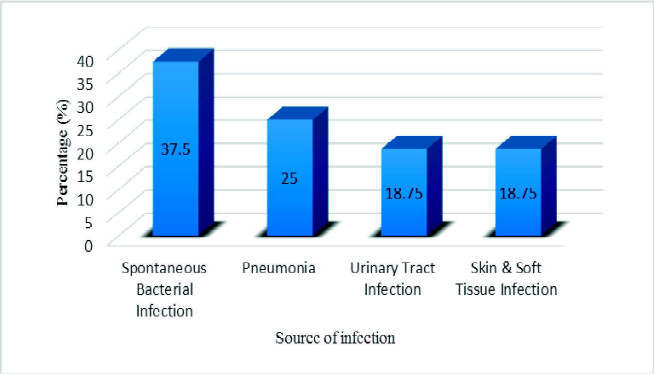

Figure 5 Hospital Mortality in relation to source of infection

DISCUSSION

In the current study the mean age of presentation was 53.5 years and males constituted the majority of the cases 74.79%. In a meta analysis conducted by Aravanti et al in 2010, mean age of bacterial infection in cirrhotic patients was 56 years and majority of them were males 68.3%.[14]

In the present study, alcohol was identified as the commonest cause of cirrhosis in 79.67% cases followed by cryptogenic in 12.19%; Hepatitis B in 4.06% and Hepatitis C in 1.62% cases. Karki et al in 2014 reported 84% alcoholic cirrhosis 12% Hepatitis C related and 8.2% Hepatitis B related.[15] In the current study upper GI bleed was present in 34.95% of the patients which is comparable with findings of Park et al 2015 where upper Gastro-intestinal bleed in alcoholic cirrhosis with bacterial infection was reported in 33.8% cases.[16]

In our study 33.33% of patients were found to have bacterial infections which was comparable with Fernandez et al 2012 study that reported 25% to 35% patients develop bacterial infection in cirrhosis at the time of admission or after hospitalization.[17] In the present study SBP was reported as the most common type of bacterial infection in patients with cirrhosis, 39.02%. Ascitic Fluid culture was positive in 26.65% of cases with E-coli being the most common bacterial isolate. Purohit 2015 has reported 43.80% cases of SBP in patients with cirrhosis where culture positive cases were 43.6% with E-coli as the most common isolate.[18] The low proportion of positive Ascitic fluid culture in our study is probably due to the relatively low concentration of bacteria in Ascitic fluid.

UTI was the second most common bacterial infection in the current study is 26.82% with 81.81% of the cases being culture positive where E coli was the most common isolate from urine. Lee et al in 2015 reported that in cirrhotic patients 80% of UTI is culture positive with the large majority being gram negative bacilli (76%) and E coli being the commonest.[19]

In the present study frequency of pneumonia was 17.07% with 71.32% culture positive cases. Streptococcus pneumonia was isolated in 57. 145 cases and Klebsiella pneumonia from 14.28% cases. Fernandez et al in 2002 reported 15% cases of pneumonia in their study.[20] Sunil K et al in 2011 found 70% sputum culture positive cases in cirrhotics.[12] Gustot et al 2012 also reported that the most common bacterial isolate was Streptococcus pneumonia in cirrhotic patients with pneumonia.[21]

In our study skin and soft tissue infection was present in 19.51% of cases. Most common bacterial isolate was Staphylococcus aureus 25% followed by E coli 12.25%. Mohan et al in 2010 showed the prevalence of cellulitis in cirrhotic between 10.5%- 12.5% with E coli as the commonest isolate.[22] Hamaza et al in 2014 also reported Klebsiella, Pseudomonas, Staphylococcus and E coli as common bacterial isolates from cellulitis in cirrhosis.[23]

In the present study in-hospital mortality was seen mostly with Child Pugh Class C i.e., 50%. With Child Pugh Class B morality was 10%. No mortality was seen with Child Pugh Class A. Maximum mortality was seen with SBP 37.50% followed by Pneumoniae 25% and UTI and SSTI both 18.75%. Our study is comparable to study by Scott et al 2013 where worsening liver disease correlated with increased mortality:3.1% Class A,23.6% Class B and 32.8% Class C.[24] Bal et al in 2016 in-hospital mortality rates attributable to SBP 43.11%.[25] Tsao et al in 2004 reported mortality for first episode of SBP ranges from 10% to 25%.[26] Ghaliony et al in 2015 reported mortality of 15% in cirrhotics with pneumonia.[27]

Fernandez et al in 2012 reported in-hospital mortality between 10% to 18% in Cirrhotics with UTI.[28] Mortality of 19% was seen in cirrhotics with SSTI as reported by Mohan et al in 2011.[22] Probably the higher rates of mortality in the present study may be due to lack of proper health care facilities and patients presenting late in decompensated stages.

CONCLUSION

Cirrhosis of liver is a condition with varied manifestations. Unfortunately, in this part of the country, patient presents with advanced stage of the disease. Alcohol is the most common etiological factor for cirrhosis followed by cryptogenic with ascites being the most common presentation. As cirrhosis is considered as an immunocompromised state it leads to a variety of infections. The most common bacterial infection in patients of cirrhosis in order of frequency is spontaneous bacterial peritonitis followed by urinary tract infection, skin and soft tissue infection and pneumonia . Most common bacterial isolates from spontaneous bacterial peritonitis and urinary tract infection was gram negative bacilli whereas gram positive cocci was the most common isolate in cases of pneumonia and skin and soft tissue infection. In hospital mortality and distribution of bacterial infection in Child Pugh Class C was significantly higher ($p<0.0285$) than Child Pugh Class A-B. Bacterial infection most frequently associated with in hospital mortality is Spontaneous Bacterial Peritonitis. Although small in number, this group of patients falls into the category of Bacterial Infection in Cirrhosis. However, prospective studies with larger sample sizes are necessary to arrive at a definite conclusion.

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