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Bacterial Infections In Hospitalized Patients With Liver Cirrhosis In A Tertiary Care Hospital

Manoj Kumar Sahu[1], Ayaskanta Singh[1], Kanishka Uthansingh[1], Debasmita Behera[2], Girish Kumar Pati[1]*

[1]Department of Gastroenterology, IMS & SUM Hospital, Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar, Odisha, India

[2]Department of Skin & VD, IMS & SUM Hospital, Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar, Odisha, India

Correspondence Author: Girish Kumar Pati, Department of Gastroenterology, IMS & SUM Hospital, Siksha 'O' Anusandhan (Deemed to be University), Bhubaneswar, Odisha- 751003

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Abstract

Background And Aim: Patients with liver cirrhosis have a high risk of developing bacterial infections. The prevalence of bacterial infections is about 25-39% in hospitalized cirrhotic patients. There is scarcity of reports on the epidemiology of bacterial infections in cirrhotics from this region. Therefore this study was carried out with an aim to evaluate the prevalence, type and etiology of bacterial infections and pattern of antibiotic resistance in cirrhotics.

Result: Consecutive 60 cirrhotics patients with bacterial infections were included in the study. Male outnumbered the females (Male: Female – 3:1). Mean age of presentation was 49.73±11.59 years. Most common cause of underlying cirrhosis was alcohol related (60%). Baseline CTP and MELD were 8.5±1.7 and 17.75±9.23 respectively. Mean duration of hospitalization was 12.38±9.73 days. 53.33% patients had severe hypoalbuminemia (< 2.5 gm%) and received albumin infusion. 66.66% patients had ascites. Most common bacterial infection was urinary tract infection (66.66%) with most common isolate as *Klebsiella pneumoniae* (40%) followed by *E.coli* (26.66%). Antibiotic resistance was found most commonly with cephalosporin (80%) followed by amoxicillin-clavulanic acid (60%) and quinolones (60%). Antibiotic resistance was least commonly found with tigecycline (0%), and vancomycin (0%) followed by linezolid (0.06%). Most common antibiotic prescribed was piperacillin-tazobactum (40%). All the patients responded to the antibiotics.

Conclusion: Most common bacterial infection was urinary tract infection with *Klebsiella pneumoniae* as the most common isolate with zero resistance to tigecycline and vancomycin in the hospitalized cirrhotic patients from our region.

Key Words: Antibiotic resistance, ascites, bacterial infection, cirrhosis

Introduction

Cirrhotic patients were more prone to suffer from bacterial infections, sepsis and sepsis-related death compared to non cirrhotic cases [1, 2]. Around 1/3rd cirrhotic cases present with infection at hospital admission or develop

infection during hospitalization [3]. As cirrhotic patients remain in a more immunocompromised state compared to non cirrhotic cases due to altered body defense mechanisms and increased bacterial translocation through the gut because of increased permeability, therefore they are more prone to suffer from various bacterial infections [4, 5]. Usually the prevalence of bacterial infections parallels the severity of liver dysfunction [5]. Bacterial infections in cirrhotics may culminate in multiple organ failure leading to high morbidity and mortality [6]. However, the diagnosis of bacterial infection in cirrhotics is often difficult, as they usually present with signs of nonspecific clinical deterioration and rarely with the classical clinical characteristics of systemic inflammation, such as fever and raised white blood cell (WBC) count. Also the presence of portal hypertension, hepatic encephalopathy and the effect of β-blockers might modify the clinical pictures and biochemical parameters of systemic inflammatory response syndrome (SIRS) resulting in too much difficulty to arrive at a conclusive diagnosis of bacterial infection and sepsis [7]. Therefore the cirrhotics are more prone to suffer from increased complication of infections and sepsis, due to delay in the appropriate diagnosis, which can be largely prevented by prompt initiation of appropriate empirical antibiotics after sending the blood, urinary or, ascitic fluid sample for culture and sensitivity [8].

As there is scarcity of published reports on the epidemiology of bacterial infections in cirrhotics from this region, therefore this study was carried out with an aim to evaluate the type and etiology of bacterial infections and pattern of antibiotic resistance in these infections in hospitalized cirrhotic cases.

Materials And Methods

Consecutive hospitalized cirrhotic patients with bacterial infection in the department of Gastroenterology, IMS & SUM Hospital, Bhubaneswar in-between November 2017 and April 2018 were enrolled in the study and prospectively evaluated. The patients with incomplete medical records, history of liver or, solid organ transplantation, variceal bleeding at the time of admission, infection with human immunodeficiency virus, evidence of hepatocellular carcinoma or other solid tumors, current use of antibiotics were excluded from the study.

The diagnosis of cirrhosis was established by a combination of clinical, biochemical and ultrasonographic imaging data. Liver failure severity was assessed by the Child Turcotte Pugh (CTP) Score and the model for end-stage liver disease (MELD) scores [9,10].

On the day of admission all the patients with cirrhosis were evaluated by a battery of tests for early diagnosis of infection, which included Complete blood count (CBC), urine (Routine & microscopic), chest radiograph, blood and urine culture, ascitic fluid biochemical and cytological assay including culture and sensitivity.

The diagnosis of spontaneous bacterial peritonitis (SBP) in patients with cirrhosis was suspected when ascitic fluid total neutrophil cell counts was >250/mm3 regardless of the result of the ascitic fluid culture [11]. Urinary tract infection was diagnosed with microscopic examination of urine and positive culture of $>10^5$ colonies/mL urine, with isolation of no more than 2 species of organisms, along with one of the following symptoms: fever >38°C, dysuria or suprapubic tenderness. Patients were suspected to suffer from pulmonary infections if they had breathlessness or cough and finding of a new radiographic infiltrate for which a nonbacterial or noninfectious cause may not be attributable. Pulmonary bacterial infection was clearly documented when a bacterial pathogen was isolated in sputum, bronchial aspirate, bronchoalveolar lavage fluid, or pleural fluid. Bacteremia was defined when blood cultures were positive and clinical signs or symptoms of infection were present. In all patients demographic and clinical data were

collected together with routine laboratory data on the first day after admission.

Statistical Analysis

Data were analyzed using SPSS version 21, presented as the mean ± standard deviation. Continuous variables were analyzed using the Student's *t*-test. Categorical values using the chi-square test. Two-tailed P-values <0.05 were considered to be statistically significant.

The study was conducted in compliance with the Declaration of Helsinki and was approved by the hospital's ethics committee.

Results

One hundred twenty Consecutive cirrhotic patients with bacterial infections were evaluated. Male outnumbered the female [Male: Female-3:1]. 30% patients with cirrhosis in our centre were found to suffer from bacterial infections. Mean age of presentation was 49.73±11.59 years. Most common cause of underlying cirrhosis was alcohol related (60%). 26.66% had hepatitis B virus (HBV) related cirrhosis. 6.66% with hepatitis C (HCV) related cirrhosis. Cryptogenic cirrhosis was suspected in 6.66% cases. Baseline total leukocyte counts (TLC) and INR (PT) at the time of admission was 6701.93±1774.28 and 2±1.89 respectively. Serum bilirubin, creatinine and sodium at the time of admission were 6.56±3.96, 1.55±1.46 and 134.2±8.7 meq/L respectively. Baseline CTP and MELD at the time of admission were 8.5±1.7 and 17.75±9.23 respectively. 53.33% patients had severe hypoalbuminemia (< 2.5 gm%) and received albumin infusion. 66.66% patients had ascites. Most common bacterial infection was urinary tract infection (66.66%) with most common isolate as *Klebsiella pneumoniae* (40%) followed by *E.coli* (26.66%). Different sites of bacterial infection were described in table 1. Organisms isolated described in table 2. Antibiotic resistance was found most commonly with cephalosporin (80%) followed by amoxicillin-clavulanic acid (60%) and quinolones (60%). Antibiotic resistance was least commonly found with tigecycline (0%), and vancomycin (0%) followed by linezolid (0.06%). The spectrum about different antibiotic resistance was highlighted in table 3. Most common antibiotic prescribed in our centre was piperacillin-tazobactum (40%). The details about first line empiric use of different antibiotics in our centre were described in table 4. 20% cases developed acute renal failure and needed dose modification. 6.66% patients had cardiac insufficiency and treated with inodilators. Mean duration of hospitalization was 12.38±9.73 days. 20% patients needed regular vital status assessment during hospitalization and therefore treated in intensive care unit (ICU).The in-hospital mortality was 8% in our centre.

Table 1: Sites of bacterial infection

Sites of infection	% cases affected
Urinary Tract	66.66
Blood	7.66
Peritoneum (SBP)	6.66
Joints	6.62
Lung	6.3
Skin	6.1

SBP: Spontaneous Bacterial Peritonitis

Table 2: Different isolated microbial organisms

Isolated Organisms	% cases found
Klebsiella pneumoniae	40
E. coli	26.66
Staphylococcus uureus	13.33
Acinetobacter	13.33
Providentia rettgeri	6.66

Table 3: Spectrum of antibiotic resistance

Antibiotics	% cases having resistance
Tigecycline	0
Vancomycine	0
Linezolid	6.66

Methicillin + Oxacillin	13.33
Aminoglycoside	40
Meropenam	46.66
Quinolones	60
Amoxycillin + Clavulamic acid	60
Cephalosporin	80

Table 4: Different first line antibiotics prescribed in our centre empirically

Antibiotics used	% cases prescribed
Piperacillin + Tazobactum	40
Amikacin	13.33
Piperacillin + Tazobactum + Clarithromycin	6.68
Amikacin + Cefalosporin	6.66
Cefalosporin + Sulbactum	6.66
Clarithromycin	6.66
Linezolid	6.66
Levofloxacin + Nitrofurantoin	6.64

Discussion

Bacterial infections in cirrhotics represent a major cause of hospitalization and may lead to significant morbidity and mortality [12,13,14]. Immediate treatment initiation is required, but clear clinical and laboratory data supporting the diagnosis are lacking. Usually the rate of bacterial infections was 5–7% in the general hospital population, whereas this rate was much higher at 32–34% among hospitalized cirrhotics [15–20]. We have also got similar frequencies of increased infection risk in our hospitalized cirrhotics. 30% cirrhotics patients in our centre were found to suffer from bacterial infection as similarly found in the previous studies [15–20]. In our region most of the cirrhotics had UTI as the most common infection as similarly observed in the previous study by Singhal A *et al* [15]. Of the various infections, prevalence rates of UTI and skin infection were 15–18% and 6–10% in hospitalised cirrhotic cases [21–24]. In our study 66.66% had UTI, which was quite high compared to previous reports [21,24]. Whether the trend for increasing prevalence of UTI over time is because of rampant use of urinary catheterization could not be answered from our study because of so many limitations. 6.66% patients had skin infection which was similarly found in the previous study [22, 23]. Female gender is a known risk factor for UTI in cirrhosis [5, 21, 24]. In this study also 80% females had UTI. SBP was observed in 6.66% cases which was in consistent with previous studies [1,18]. In our study 6.66% patients had blood culture positivity for bacterial growth, as similarly found in the study by Singhal A et al [15]. Previous studies reported around 15–30% in-hospital mortality rate among infected cirrhotics compared to 6–8% in uninfected cirrhotics [1, 25]. The in hospital mortality in our study was 8%, which is relatively less compared to previous studies [1, 25]. In this study patients with sepsis had mortality rate of 40% which was similarly found in the previously studies with reported mortality rate of 26–44% [5, 26]. Most of the patients had WBC report within normal ranges which may be explained in the context of increased occurrence of hypersplenism in the cirrhotics, may falsely reveal normal or low values of WBC report despite of “relative” increase in WBC count. In our study most of the isolated bacteria were sensitive to higher generation of broad spectrum antibiotics. In previous studies from Asia and USA, around half of cirrhotic cases had antibiotic bacterial resistance [27,28]. High levels of multiresistance were found among cirrhotic patients, as well as among other patients, suggesting that the current high prevalence of these bacteria is mainly related to an epidemiological change in hospital infections, which is often not dependent on the patient’s underlying disease. Nosocomial infections, long-term antibiotic prophylaxis with norfloxacin, infection by multiresistant bacteria in the past six months, and use of

beta-lactam antibiotics in the last three months were proven to be risk factors for the occurrence of infections by multiresistant bacteria in cirrhotic patients [20]. In our study most of the isolated bacteria were gram-negative. Amongst the gram-negative bacteria, the most common one was *Klebsiella pneumonia*, where as amongst the gram-positive bacteria the most frequent one was coagulase-negative Staphylococcus species. These results are in agreement with previous studies [20,27,29]. In our region most of the cirrhotics (80%) had antibiotic resistance against cephalosporin as similarly found in the previous studies because of rampant use of third-generation cephalosporins as the first choice empirical antibiotics against SBP and other infections [30,31]. The Special Conference on Bacterial Infections held by the European Association for the Study of the Liver (EASL) established new guidelines for the empirical treatment of infections in cirrhotic patients [32]. In general, third-generation cephalosporins continued to be recommended as the empirical therapy for community-acquired infections; whereas, carbapenams, should be used in nosocomial infections. Healthcare-associated pneumonia taking place in ICU should ideally be treated as nosocomial infections, whereas the treatment of healthcare-associated cellulitis and spontaneous infections should be based on the severity of the infection and on local pattern of bacterial resistance.

Limitations

Our studies had some limitations. We had not stratified the occurrence of bacterial infections as per their underlying cause of chronic liver disease (CLD) and CLD status. We have not done comparative analysis of mortality rate among the cirrhotic cases basing on their pattern of bacterial infections, CLD status and bacterial resistance. Associated confounding factors such as presence of cardiopulmonary compromise, diabetes which may adversely affect the prognosis in cirrhotics with infection. We have not searched for multiple bacterial resistances basing on the isolated organisms in the culture and sensitivity study.

Conclusion

To conclude, in our region most of the cirrhotics had UTI as the most common bacterial infection which was relatively higher in the female gender. Our patients had not too much broad antibiotics resistance. Despite of resource constraint region and limited health care facility in our region, cirrhotic cases with bacterial infection had relatively less mortality in comparison to Western studies which indicates possibly our cirrhotic cases were less immunocompromised compared to Western cirrhotic populations. Therefore higher generation of broad spectrum antibiotics was seldom required in our region as most cases may respond to lower to medium generation of antibiotics. Early and effective antimicrobial treatment is essential in the management of cirrhotic patients with bacterial infections. The choice of the empirical therapy should be based not only on the severity and the origin of the infection, but also on the local microbiological profile for better outcome. Long term prospective studies with a better study design overcoming our study limitations are suggested to identify patients at risk of infection, to develop strategies to prevent hospital acquired infections and to evaluate the role of prophylactic interventions for better patient care and outcome in future.

Conflict Of Interest

All authors read the manuscript and there is no conflict of interest in author sequence

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