Bacterial infections in cirrhotic patients

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Cirrhosis is the most common cause of mortality and morbidity worldwide, and bacterial infections are very common in patients with cirrhosis, often leading to mortality (1,2). In patients with cirrhosis, there is an increased risk of dying from sepsis compared with that from other complications (3). Multiple-drug-resistant (MDR) bacteria are more common because of antimicrobial resistance.

A multicenter, prospective, intercontinental study entitled "Epidemiology and Effects of Bacterial Infections in Patients With Cirrhosis Worldwide" by Piano et al assessing the prevalence and outcomes of bacterial and fungal infection in patients with cirrhosis was published in *Gastroenterology* in 2019. The primary end point of the study was the prevalence of MDR and extensive-drug-resistant (XDR) infections. Secondary end points were in-hospital mortality, 28-day mortality, development of acute-on-chronic liver failure, septic shock, transfer to the intensive care unit (ICU), and need for organ support during hospitalization. In this study, demographic, clinical, microbiological, and treatment data of 1302 hospitalized patients with cirrhosis and bacterial or fungal infection at 46 centers (15 in Asia, 15 in Europe, 11 in South America, and 5 in North America) were collected and patients were followed until death, liver transplantation, or discharge.

During the study period, 1302 patients were enrolled, comprising 565 (43%) from Europe, 416 (32%) from Asia, and 321 (25%) from North and South America. Most patients were men (69%), and their mean age was 57±13 years. Alcohol was the most common cause of cirrhosis, followed by hepatitis C infection and nonalcoholic steatohepatitis. Patients had advanced liver disease, as indicated by the high prevalence of ascites (77%), hepatic encephalopathy (38%), mean model of end-stage liver disease (MELD) score (21±8), MELD sodium (MELD-Na) score (24±8), and Child-Turcotte-Pugh score (10±2). Notably, 35% of patients had ACLF at the time of diagnosis of infection. The most common infections were spontaneous bacterial peritonitis (SBP; 27%), urinary tract infection (UTI; 22%), and pneumonia (19%). At the time of diagnosis, 174 patients (14%) had septic shock. Microbiological cultures were positive for 57% of patients, and 959 bacterial strains were isolated in total. Gram-negative bacteria were the most common isolates (57%), and gram-positive bacteria accounted for 38% of positive cultures. MDR bacteria were isolated in 34% of patients with a positive culture. Seventy-three XDR bacteria were isolated in 62 patients. MDR bacterial infections were very common in Indian centers, and the prevalence of XDR infections was strikingly higher in Indian centers.

Infections caused by MDR bacteria were more common in young patients, men, and those with poor liver function according to MELD-Na and Child-Turcotte-Pugh scores. Use of systemic antibiotics for the treatment of bacterial infection for at least 5 days during the previous 3 months, invasive procedures during the previous month, and exposure to healthcare were among the known risk factors for MDR bacteria. Previous administration of an antibiotic prophylaxis for SBP with quinolones was not found to be more frequent in patients with MDR bacterial infection. Analysis of predictors of XDR bacteria yielded similar results.

The main aim of this study was to provide a global view of the epidemiology of bacterial infections in patients with cirrhosis. The authors found that acquired infections were more common than healthcare-associated or nosocomial infections in all continents However, in almost 50% of patients, the bacterial infection developed after exposure to healthcare facilities. In this study, the global prevalence of infections sustained by MDR bacteria was 34%, which is quite higher than that reported in previous studies (4,5-8).

Furthermore, large differences were found in the prevalence of infections sustained by MDR and XDR bacteria

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among different geographic areas, with the highest rate reported in Indian centers (73% and 33%, respectively) and the lowest in North American centers (18% and 2%, respectively); this is because India was the world's largest consumer of antibiotics. SBP prophylaxis with quinolones was not among the predictors of MDR bacterial infections. However, this is disputable because most previous studies concluded that quinolone prophylaxis is the one of the primary drivers of the spread of MDR infections in cirrhosis (4,6,7)

Additionally, their results are in parallel with the findings of a randomized controlled trial that compared norfloxacin with placebo in 291 patients with decompensated cirrhosis, indicating that the risk of developing infections from MDR bacteria was not higher in patients receiving norfloxacin than in those who received placebo, thereby concluding that quinolones should be used for primary or secondary SBP prophylaxis (9). In other studies, the efficacy of empirical antibiotic treatment was found to be an independent predictor of in-hospital and 28-day mortality and a strong independent predictor of mortality beyond age, degree of inflammation, MELD-Na score, presence of ACLF, and new qSOFA score (2,10). As expected following the large-scale use of antibiotics, a study at a tertiary university hospital in Turkey showed that in 114 hospitalized patients with cirrhotic infections, half of the cultures were determined to be positive for resistant bacteria, which is associated with the use of oral prophylactic antibiotics, extended duration of hospitalization, and frequent transfer to the ICU. Daily lactulose usage appears to decrease resistant bacterial infections in hospitalized patients with cirrhosis (11).

This study is the largest and first global study to assess the epidemiology and clinical impact of infections in patients with cirrhosis. However, it has some limitations, such as not including centers from Africa or other geographic areas, such as Turkey. The study showed that the spread of MDR and XDR bacterial infections is a relevant threat to the health of patients with cirrhosis. Considering the large differences in the prevalence of MDR and XDR infections across different geographical regions, empirical antibiotic treatment needs to be adapted to national, regional, or even local microbiological epidemiology.

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