

Infections in Liver Disease



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KEYWORDS

- Infections • Cirrhosis • Sepsis • Acute on chronic liver failure • Septic shock
- Cirrhosis-associated immune dysfunction • Antibiotics • Acute kidney injury

KEY POINTS

- Infections are common in end-stage liver disease and the incidence is much higher than in the general population.
- Infectious insults are frequent precipitators of decompensated cirrhosis and acute on chronic liver failure.
- Cirrhosis is a state of systemic inflammation and immune dysfunction leading to enhanced susceptibility to infections.
- Spontaneous bacterial peritonitis and urinary tract infections are the most common infections in cirrhosis.
- The spectrum of microorganisms is shifting with the emergence of resistant organisms and this has important implications for therapy and prophylaxis.

INTRODUCTION

Infectious complications in end-stage liver disease (ESLD) are the leading cause of mortality, morbidity,^{1,2} and the development of acute on chronic liver failure (ACLF). Once infection occurs, the host with cirrhosis is vulnerable to further infections and complications, such as acute kidney injury (AKI), de-listing from liver transplantation, prolonged hospital stays, and multiple organ failure. In this review, we discuss the importance of changing spectrum of infections in liver disease, new diagnostic modalities with their limitations, and current management strategies for a focused approach in treatment.

EPIDEMIOLOGY OF INFECTIONS IN LIVER DISEASE

Despite better understanding of the mechanisms of increased susceptibility to infection in chronic liver disease and advances in treatment, occurrence of infection is still

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associated with major morbidity and mortality. Between 25% and 35% of patients with cirrhosis either have infection at admission or acquire an infection during their hospitalization. The incidence of infections in patients with cirrhosis is 4 to 5 times greater than in the general population.

Incidence/Prevalence

According to one study, approximately 30% of bacterial infections in patients with cirrhosis were community acquired, 30% were health care associated (HCA; infections that occurred in the first 2 days of admission in patients in contact with the health care environment in the past 3 months), and 40% were nosocomial. Fernandez and colleagues^{3,4} prospectively studied bacterial infections among hospitalized patients with cirrhosis and found that among 1567 admissions for decompensated cirrhosis, 507 admissions (32%) had infections on admission or during hospitalization. A follow-up study of 1578 admissions between 2005 and 2007 for complications of cirrhosis reported that 390 admissions (25%) had infections. Merli and colleagues⁵ reported a prevalence of 36% in the study of 150 patients with cirrhosis, and Borzio and colleagues⁶ in their prospective study of 450 patients reported a similar prevalence of 34%.

Significance of Infectious Insult in Liver Disease

It is well established that infections contribute to a high morbidity and mortality in patients with liver disease. The natural history of cirrhosis is characterized by an asymptomatic phase, referred to as “compensated cirrhosis,” followed by a progressive phase marked by the development of complications of portal hypertension and/or liver dysfunction, designated “decompensated cirrhosis.” Progression of the decompensated disease may be accelerated by the development of other complications, such as bleeding, renal impairment, and sepsis.⁷ Arvaniti and colleagues,⁸ in a large meta-analysis, found a fourfold increase in mortality for patients with cirrhosis with infection compared with similar patients with cirrhosis who were not infected.

In nonalcoholic fatty liver disease (NAFLD), progression to nonalcoholic steatohepatitis (NASH) and advanced disease has been linked to endotoxemia.⁹ Impaired immune function in acute liver failure leads to an increased incidence of bacterial and fungal infections.^{10,11} These infections are associated with increasing severity of complications, such as worsening hepatic encephalopathy but interestingly do not seem to adversely influence outcomes.^{12,13} This may be due to increased surveillance and heightened alertness for bacterial infection as well as early (preemptive) therapy with effective antimicrobials.¹⁴ Similarly, patients with liver failure awaiting transplantation are at increased risk of infections, and although infections before transplantation may not affect mortality, in the posttransplant period early bacterial infections are a major cause of mortality.^{15,16}

Major Risk Factors of Infection in Liver Disease

Merli and colleagues⁵ prospectively studied outcomes of 150 patients with cirrhosis and examined putative risk factors for infections. On multivariate analysis, a history of previous infection in the past 12 months, a model for end-stage liver disease (MELD) score of 15 or greater, and a diagnosis of protein malnutrition were independent predictors for infections and sepsis.

In other studies, prior history of gastrointestinal bleeding, high Child-Pugh scores, low albumin ascites, and prior history of spontaneous bacterial peritonitis emerged as some other risk factors associated with increased risk of infection. Further, the spectrum of infections in liver disease has gradually shifted toward the emergence of multidrug-resistant bacterial isolates. Fernandez and colleagues⁴ found that

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