Commentary | Open Access

Hepatoma Research

Gkoufa *et al. Hepatoma Res.* 2026;12:45 **DOI:**10.20517/2394-5079.2026.59

Evolving epidemiology and antimicrobial resistance in cirrhosis: time for a region-specific approach

Aikaterini Gkoufa[1], Vasileios Lekakis[2], Dimitrios Basoulis[3], Evangelos Cholongitas[1]

Citation: Gkoufa A, Lekakis V, Basoulis D, Cholongitas E. Evolving epidemiology and antimicrobial resistance in cirrhosis: time for a region-specific approach. *Hepatoma Res.* 2026;12:45. https://dx.doi.org/10.20517/2394-5079.2026.59

Received: 7 May 2026
First Decision: 9 Jul 2026
Revised: 18 Jul 2026
Accepted: 29 Jul 2026
Published: 6 Aug 2026

Academic Editor: Nan Li
Copy Editor: Ting-Ting Hu
Production Editor: Ting-Ting Hu

Cirrhosis is well recognized as a condition associated with a markedly increased susceptibility to infections, and although overall mortality from cirrhosis-related complications has declined over time, mortality attributable to sepsis remains disproportionately high[1]. Beyond being a frequent complication, infections play a pivotal role in liver disease progression, often acting as triggers for acute decompensation or acute-on-chronic liver failure. Pathophysiological evidence suggests that this heightened vulnerability arises from a combination of impaired innate and adaptive immune responses due to hepatic dysfunction, alongside increased bacterial translocation and alterations in gut microbiota composition[2,3]. Importantly, as infectious episodes are strongly associated with adverse outcomes in patients with cirrhosis, this burden is further exacerbated in the current era of antimicrobial resistance, where therapeutic options are increasingly limited. In this context, studies such as the recent work by Cai *et al.* are particularly important, offering valuable insights into the evolving global landscape of infections in cirrhosis[4].

In their comprehensive systematic review and meta-analysis, Cai *et al.* examined the evolving epidemiology of infections among patients with cirrhosis globally[4]. The authors explored temporal trends alongside geographical variability, providing a detailed assessment of differences in pathogen distribution and antimicrobial resistance patterns across regions. Their analysis underscores substantial geographical and temporal variation in the microbiological landscape of infections in cirrhosis, while the pattern of infection sites remains relatively stable, with spontaneous bacterial peritonitis and urinary tract infections consistently representing the most common clinical entities. Gram-negative bacteria remain predominant in low- and lower-middle-income settings, particularly in South-East Asia, whereas Gram-positive pathogens are more frequently encountered in

[1]First Department of Internal Medicine, Laiko General Hospital, Medical School, National and Kapodistrian University of Athens, Athens 11527, Greece.
[2]Department of Gastroenterology, General Hospital of Athens Georgios Gennimatas, Athens 11527, Greece.
[3]Department of Pathophysiology, Laiko General Hospital, Medical School of National and Kapodistrian University of Athens, Athens 11527, Greece.

Correspondence to: Dr. Evangelos Cholongitas, First Department of Internal Medicine, Laiko General Hospital, Medical School, National and Kapodistrian University of Athens, Athens 11527, Greece. E-mail: cholongitas@yahoo.gr

high-income regions, especially in Europe, with their relative contribution increasing over time. This divergence likely reflects differences in healthcare exposure. In high-income settings, easier access to medical care is associated with more frequent hospitalizations and invasive procedures - such as central venous catheterization, transjugular intrahepatic portosystemic shunt placement, and repeated paracentesis - which may predispose patients to infections caused by Gram-positive bacteria. Additional factors may further contribute to the rising prevalence and resistance of these pathogens. The widespread use of quinolones for prophylaxis may exert selective pressure favoring Gram-positive bacteria, while emerging evidence suggests that rifaximin use in cirrhosis could be linked to cross-resistance to daptomycin in vancomycin-resistant *Enterococcus faecium*[5]. In this context, it is not surprising that over time, the effectiveness of commonly used antibiotics such as quinolones and third-generation cephalosporins has declined, as also highlighted in the present meta-analysis.

Nevertheless, based on this study[4], there is a global rise in antimicrobial resistance among both Gram-positive and Gram-negative organisms, with multidrug-resistant pathogens accounting for roughly one-third of all positive cultures in their meta-analysis. Notably, this burden is unequally distributed, with a disproportionate impact on resource-limited regions. A plausible explanation for this finding may be related to the fact that in response to the growing threat of antimicrobial resistance, structured efforts to optimize antimicrobial use have been developed since the early 21st century, mostly through the implementation of antimicrobial stewardship programs[6]. These programs represent coordinated, multidisciplinary initiatives typically involving infectious diseases specialists, clinical pharmacists with relevant expertise, microbiologists, infection control professionals, epidemiologists, and information systems support[7]. Their primary goal is to promote the judicious use of antimicrobials through appropriate selection, dosage, route, and duration of therapy, particularly in vulnerable populations such as critically ill or immunocompromised patients. However, the successful implementation of such strategies depends on the availability of adequate human, financial, and technical resources, which are more readily accessible in high-income settings. Additionally, infrastructural limitations in lower-income countries constrain access to advanced diagnostic tools, such as molecular techniques and next-generation sequencing, despite these approaches not yet being considered standard-of-care strategies in cirrhosis management. As a result, timely identification of pathogens and antimicrobial susceptibility testing may be challenging, limiting the ability to implement targeted therapy and complicating practices such as antimicrobial de-escalation. In such circumstances, prolonged use of empiric broad-spectrum antibiotic therapy may become necessary, which in turn exerts selective pressure and contributes to the emergence of antimicrobial resistance. Collectively, these factors may contribute to the higher prevalence of multidrug-resistant pathogens observed in Asian regions.

A major strength of the study by Cai *et al.*, lies in its large pooled sample and its broad global scope, enabling the assessment of temporal trends and regional variation in infection characteristics, microbiological profiles, antimicrobial resistance patterns, and clinical outcomes in patients with cirrhosis[4]. Nevertheless, as the authors also acknowledge, these findings should be interpreted with caution. The observed differences are likely shaped by multiple underlying factors, and a careful appraisal of potential sources of heterogeneity is essential when considering their clinical applicability. Beyond the well-recognized disparities in healthcare access and infrastructure between low- and high-income regions, another limitation is the unequal representation of many geographical areas (e.g., only three of the 169 included studies were from Africa). Regions with limited research capacity and/or scientific activity may be underrepresented, whereas data from more resource-rich settings are more readily available, potentially introducing bias into global estimates. Consequently, the disproportionate contribution of studies from high-income countries, particularly Europe, may limit the generalizability of these findings to regions with distinct epidemiological profiles and healthcare infrastructures. Furthermore, the inclusion of studies across a wide temporal range adds another layer of complexity. Over time, shifts in antimicrobial resistance patterns, evolving diagnostic technologies,

and changes in microbiological methods and susceptibility testing standards may affect the comparability of results. In addition, variability in the definitions of infections and multidrug-resistant organisms across included studies, along with differences in antimicrobial susceptibility testing methodologies, may further contribute to heterogeneity and limit the consistency of pooled estimates. Overall, as a considerable proportion of the included studies were published more than two decades ago, preceding major advances in culture techniques, susceptibility testing methodologies, diagnostic standards, and the definitions of antimicrobial resistance, part of the observed heterogeneity may reflect methodological evolution rather than true changes in the epidemiology of infections and antimicrobial resistance.

In parallel, variations in local and national treatment guidelines across different healthcare systems further limit the extent to which findings can be generalized across settings.

Another notable finding of this meta-analysis is the increase in in-hospital mortality among patients with community-acquired infections over time, despite a simultaneous decline in 30-day mortality for both community-acquired and nosocomial infections. This apparent discrepancy likely reflects changes in patient characteristics and evolving healthcare practices. Individuals presenting with community-acquired infections may now have more advanced liver disease and a higher burden of comorbidities, which could contribute to increased early mortality during hospitalization. Conversely, improvements in post-discharge management and follow-up care may help explain the reduction in 30-day mortality. Furthermore, the growing prevalence of antimicrobial resistance may negatively impact the effectiveness of initial empirical therapy, particularly in community-acquired infections, thereby influencing in-hospital outcomes.

In summary, even though reported findings by Cai *et al.* should be interpreted as broad descriptive estimates rather than precise epidemiological rates, this comprehensive analysis underscores the need for continuous reassessment of empirical antibiotic strategies and prophylactic approaches in patients with cirrhosis, in light of the dynamic and evolving microbial landscape, both in terms of pathogen distribution and resistance patterns[4]. Three key implications emerge from these findings. First, sustained, high-quality epidemiological surveillance is essential to characterize regional variations in antimicrobial resistance and guide locally adapted prevention and treatment strategies, particularly in settings with heterogeneous healthcare resources. Second, healthcare institutions should establish dedicated antimicrobial stewardship programs involving multidisciplinary teams responsible for implementing targeted interventions, including risk-based screening for colonization with multidrug-resistant organisms, appropriate cohorting or infection-control measures for colonized patients, systematic monitoring of antibiotic consumption, and timely optimization of antimicrobial therapy through microbiologically guided de-escalation strategies. Third, incorporating colonization status and local resistance patterns into clinical decision-making may improve risk stratification, enhance the appropriateness of empirical therapy, and reduce unnecessary antimicrobial exposure. Together, these measures represent essential components of a proactive approach to balancing effective infection management in cirrhosis with the urgent need to limit the further emergence of antimicrobial resistance[8]. Nevertheless, even with optimal antimicrobial management, infection-related morbidity and mortality are unlikely to be fully eliminated in cirrhotic patients, reflecting the underlying vulnerability and complexity of this population.

DECLARATIONS

Authors' contributions

Manuscript writing: Gkoufa A
Research design: Gkoufa A, Lekakis V, Basoulis D
Review and editing of the manuscript: Cholongitas E, Lekakis V, Basoulis D
All authors read and approved the final manuscript.

Availability of data and materials

Not applicable.

AI and AI-assisted tools statement

Not applicable.

Financial support and sponsorship

None.

Conflicts of interest

Cholongitas E is an Editorial Board Member of the journal *Hepatoma Research*. Cholongitas E was not involved in any steps of editorial processing, notably including reviewers' selection, manuscript handling and decision making. The other authors declare that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCES

1. Piano S, Bunchorntavakul C, Marciano S, Rajender Reddy K. Infections in cirrhosis. *Lancet Gastroenterol Hepatol.* 2024;9:745-57. DOI PubMed
2. Cullaro G, Sharma R, Trebicka J, Cárdenas A, Verna EC. Precipitants of acute-on-chronic liver failure: an opportunity for preventative measures to improve outcomes. *Liver Transpl.* 2020;26:283-93. DOI PubMed PMC
3. Albillos A, Lario M, Álvarez-Mon M. Cirrhosis-associated immune dysfunction: distinctive features and clinical relevance. *J Hepatol.* 2014;61:1385-96. DOI PubMed
4. Cai J, Yip TC, Wong GL, et al. Global epidemiology of bacterial infections in patients with cirrhosis: a systematic review and meta-analysis. *J Hepatol.* 2026;84:1089-101. DOI PubMed
5. Turner AM, Li L, Monk IR, et al. Rifaximin prophylaxis causes resistance to the last-resort antibiotic daptomycin. *Nature.* 2024;635:969-77. DOI PubMed PMC
6. Deresinski S. Principles of antibiotic therapy in severe infections: optimizing the therapeutic approach by use of laboratory and clinical data. *Clin Infect Dis.* 2007;45:S177-83. DOI PubMed
7. Giamarellou H, Galani L, Karavasilis T, Ioannidis K, Karaiskos I. Antimicrobial stewardship in the hospital setting: a narrative review. *Antibiotics.* 2023;12:1557. DOI PubMed PMC
8. Paintsil EK, Adu-Asiamah CK, Kronsten VT, Ntuli Y, Shawcross DL. Global trends in antimicrobial resistance among cirrhosis patients with bacteremia: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol.* 2026;24:69-80. DOI PubMed