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Original Article

Global Prevalence, Temporal Trends, and Associated Mortality of Bacterial Infections in Patients with Liver Cirrhosis: A Meta-analysis

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Abstract

Background and Aims: Bacterial infections (BIs) are common and severe complications in patients with liver cirrhosis, but global data are limited. Here, we aimed to evaluate the global prevalence, temporal changes, and associated mortality risk of BIs in liver cirrhosis. ***Methods:*** We systematically searched PubMed, Embase, Web of Science, and the Cochrane Library for eligible studies published without language restrictions until 11 August 2025. A random-effects model was used for meta-analyses, meta-regression by study year, and pooling adjusted hazard ratios. ***Results:*** Fifty-nine studies, including 1,191,421 patients with cirrhosis, were analyzed. The pooled prevalence of BIs (33 studies) was 35.1% (95% confidence interval (CI): 29.2–41.4). The prevalence of *Escherichia coli* and *Streptococcus* spp. was 3.8% (95% CI: 2.5–5.2) and 1.5% (95% CI: 0.8–2.6), respectively. The pooled prevalence of multidrug-resistant bacteria was 6.8% (95% CI: 4.0–11.3). The most common BI sites were the gastrointestinal tract, ascites fluid, and urinary tract. The highest prevalence of BIs was reported in Europe (38.2%; 95% CI: 24.8–53.6), followed by South America (37.5%; 95% CI: 29.7–46.1) and Asia (22.8%; 95% CI: 16.3–30.9). Patients with acute-on-chronic liver failure showed the highest prevalence of BIs (44.2%; 95% CI: 29.7–59.8). A modest increasing trend in BIs prevalence was observed over time. BIs were associated with an increased risk of mortality in patients with cirrhosis (adjusted hazard ratios 2.22, 95% CI 1.33–3.71). ***Conclusions:*** BIs are prevalent in cirrhosis, especially in acute-on-chronic liver failure, with a modest upward trend and increased mortality risk.

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Introduction

Bacterial infections (BIs) pose a substantial threat to public health, with severe illnesses and increasing mortality rates caused by antibiotic-resistant strains.[1] These infections lead to serious complications, especially in vulnerable populations such as the elderly and immunocompromised individuals. Estimating hospital infection rates is difficult due to varying diagnostic criteria, under conditions ranging from the presence of asymptomatic cases to the complexity of healthcare settings. In addition, the Centers for Disease Control and Prevention in the United States and Europe have recommended different thresholds for the diagnosis of various BI infections.[2,3] Therefore, accurate assessment is essential for the effective control of infection and improved outcomes for infected patients.

Cirrhosis is the end stage of various chronic liver diseases, including fatty liver disease, alcoholic liver disease, and hepatitis virus infection. BIs are frequent and serious complications in patients with cirrhosis, creating significant clinical challenges due to their high morbidity, high short-term mortality, and detrimental impact on long-term prognosis.[4–7] Patients with cirrhosis are vulnerable to BIs due to various factors, including gut dysbiosis, compromised intestinal integrity, increased bacterial translocation across the gut wall, immune dysfunction associated with cirrhosis, and portal-systemic shunting.[5,8] BIs cause systemic inflammation that leads to organ failure and acute-on-chronic liver failure (ACLF), resulting in a high risk of short-term mortality and potentially increasing the mortality rate fourfold.[9] The diversity of bacterial pathogens and the variety of infection sites further complicate the management of these patients.[10,11] Furthermore, the prevalence and types of BIs in patients with cirrhosis vary substantially across different countries and regions, reflecting differences in healthcare infrastructure, antimicrobial stewardship, local microbial ecology, and resistance landscapes.[12] In addition, a major concern is the increasing prevalence of infections caused by multidrug-resistant (MDR) organisms. Patients infected with MDR bacteria present higher rates of septic shock, intensive care unit (ICU) admissions, mechanical ventilation, or renal replacement therapy compared with patients without MDR bacteria.[7,10,12] Understanding the regional and global epidemiology of these infections is crucial for improving the management and outcomes of patients with cirrhosis.

While previous studies have focused on local or regional estimates, global evidence remains fragmented. Here, we conducted a meta-analysis to estimate the global prevalence of BIs in patients with liver cirrhosis, investigate temporal trends using meta-regression, and assess their association with mortality.

Methods

Search strategy and selection criteria

This meta-analysis was conducted following the updated PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (2020),[13,14] and the protocol was registered on PROSPERO (CRD42024589916). We searched PubMed, Embase, Web of Science, and the Cochrane Library until August 11, 2025, without language restrictions, to identify relevant full-text studies reporting BIs in patients with cirrhosis. The search strategy included MeSH terms and keywords such as "Bacteria", "*Escherichia coli*", "*Staphylococcus*", "*Klebsiella*", "*Streptococcus*", "*Pseudomonas*", "*Enterococcus*", "*Acinetobacter*", "*Proteus*", and conditions like "bacteremia", "pneumonia", and "sepsis". These terms were combined with Boolean operators ("OR", "AND") and refined with liver cirrhosis-related terms such as "cirrhosis" and "cirrhotic" in the Keywords, Title, and Abstract fields. Supplementary Table 1 shows the search strategies for all included databases. We excluded letters, editorials, case reports, reviews, comments, and case series because of their insufficient methodology. Additionally, we searched for potential studies by manually reviewing the reference lists of the included studies and relevant reviews. Title and abstract screening for eligibility was independently conducted by TYX and WYP based on a predefined set of inclusion and exclusion criteria (Supplementary Table 2). Any discrepancies were resolved through consensus or by consulting ZJ or WBY.

Data extraction and quality assessment

A complete information list was extracted from the articles and entered into a Microsoft Excel worksheet. The following data were independently extracted by two reviewers (TYX and WYP): author names, publication year, period of conduct, study location, sample size, study design, sample characteristics, type of infection, infected sites, infected bacterial species, and prevalence estimates. In addition, for each study, we extracted the case definitions of BIs, including site-specific criteria and thresholds (Supplementary Table 3). For each included study, we extracted the ACLF definition that was explicitly stated or cited. We then classified each definition according to the European Association for the Study of the Liver (EASL)-Chronic Liver Failure Consortium (CLIF),[15] Asian-Pacific Association for the Study of the Liver (APASL),[16,17] Chinese Group on the Study of Severe Hepatitis B,[18] North American Consortium for the Study of End-Stage Liver Disease,[4] or other established criteria. When a study cited more than one set of criteria, the one designated as primary by the authors was used for classification. The authors were contacted to request additional data if the relevant data were not readily available. At least two authors independently evaluated the quality of the included studies (TYX, WYP, ZJ, and WBY) using the Joanna Briggs Institute's Critical Appraisal Checklist for Prevalence Studies.[19] Any disagreements were resolved by consensus or consultation with a third author (FYC).

Statistical analysis

The prevalence of BIs was calculated via a meta-analysis of single proportions by dividing the number of affected patients by the total study population.[20] Prior to pooling the data for meta-analysis, the original proportions and the logit transformations were tested for normality, and the method that best approximated a normal distribution was selected based on the results.[21] Quantitative variables are presented herein as the mean values ± standard deviations and median values with corresponding ranges. The significance level was set at 0.05, and differences with p-values below this threshold were considered statistically significant. A random-effects model was used for all analyses to account for between-study variability, as recommended in the Cochrane Handbook.[22] Subgroup analyses were performed based on study characteristics, including study location, country's economic status (categorized by the World Bank classification of high-, upper-middle-, and low-income countries),[23] study design, study period, and patient populations. The significance threshold for subgroup differences was set at $p < 0.05$, with values below this threshold indicating significance. Publication bias was assessed qualitatively by visually inspecting funnel plot symmetry. A symmetric funnel plot suggests minimal publication bias, while asymmetry may indicate potential publication bias, heterogeneity, or small-study effects.[21] We modeled temporal trends in BIs prevalence using random-effects meta-regression with the study mid-year as a continuous moderator, and results were visualized on the proportion scale via a bubble plot.[24] Adjusted hazard ratios (HRs) for mortality associated with BIs were pooled using a random-effects model. The analysis was conducted in R v4.2.3 via meta-packages and metaprop functions.[25]

Results

Of the 31,002 articles identified through the search, 59 studies were included in the review (Fig. 1). These included studies involved 1,191,421 patients. Table 1 shows the characteristics of each study.[4,6,7,10,12,26,27-79] These studies reported BIs in hospitalized, outpatient, ICU-admitted, and ACLF patients with cirrhosis. Thirty-three studies examined multiple BIs, and twenty-six studies examined specific BIs, such as bacteraemia, spontaneous bacterial peritonitis (SBP), and urinary tract infection (UTI). These studies were conducted in Asia (n = 24), Europe (n = 17), North America (n = 10), South America (n = 3), and Africa (n = 3), with two multicenter studies. Of the 59 studies, 30 were retrospective cohort studies, 22 were prospective cohort studies, five were case-control studies, and two were cross-sectional studies. The sample sizes of the included studies ranged from 45 to 742,391. According to the Joanna Briggs Institute's Critical Appraisal Checklist for Prevalence Studies, 46 studies were rated low risk of bias, whereas 13 were rated moderate risk of bias (Supplementary Table 4).

Sample attributes

In 49 studies, all cases of cirrhosis were included in the denominator, whereas ACLF was included in 10 studies. The criteria for diagnosing cirrhosis included clinical, biochemical, ultrasonographic, and endoscopic assessments. Histopathology was used in 29 studies, ICD coding in four studies, APASL-ACLF criteria in four studies, and EASL-ACLF criteria in five studies, while 17 studies did not specify their criteria. The etiology of cirrhosis varies, with alcohol, viral hepatitis, and nonalcoholic fatty liver disease being the most common causes.

Description of BIs

Among 1,191,421 patients (59 studies), 180,132 had BIs. *Escherichia coli* (*E. coli*) was reported in 301 out of 8,592

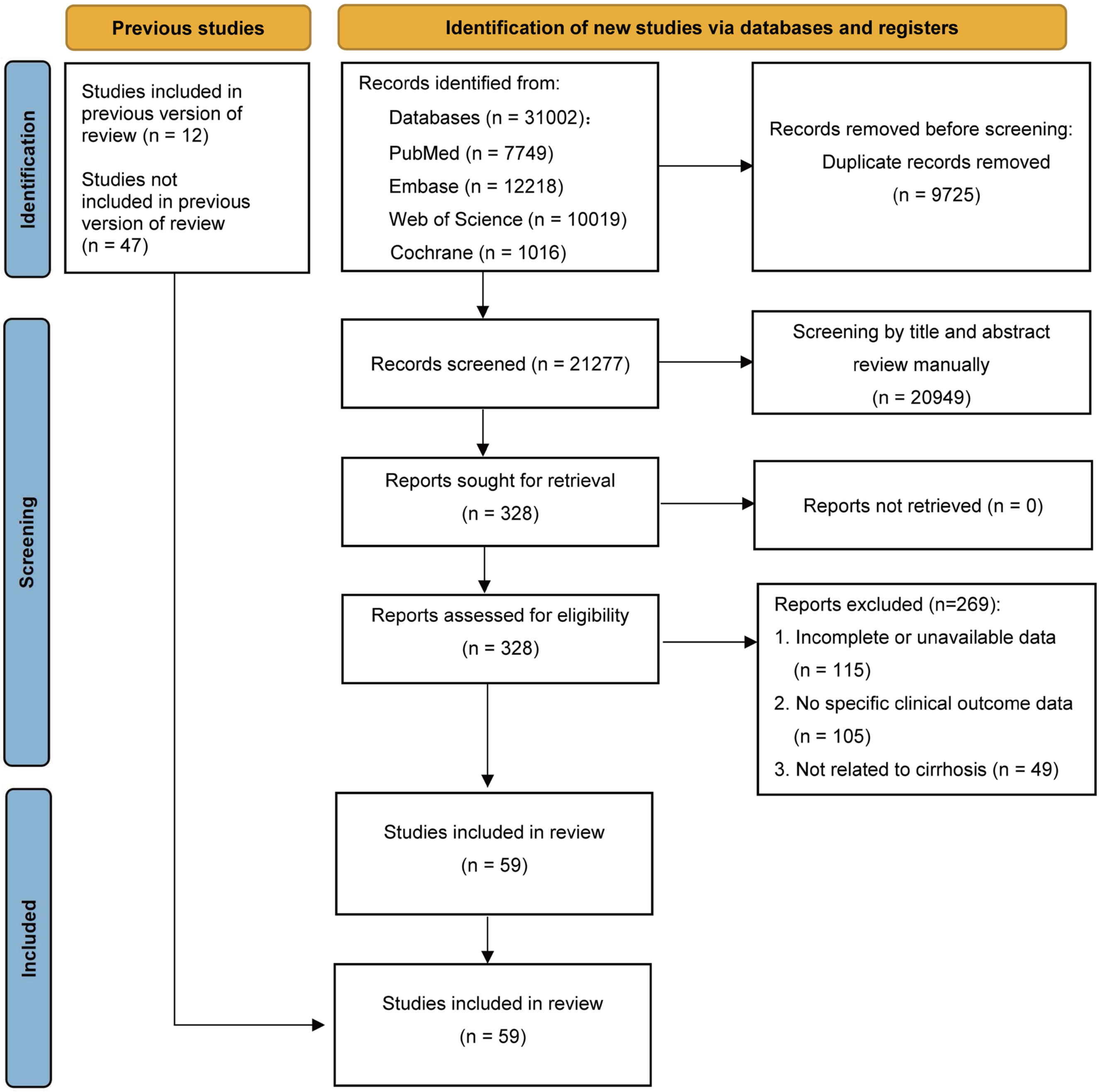

Fig. 1. PRISMA flow diagram of the search strategy.

patients (15 studies), *Streptococcus spp.* in 96 out of 8,709 patients (14 studies), *Klebsiella spp.* in 96 out of 8,484 patients (14 studies), *Staphylococcus spp.* in 124 out of 7,917 patients (13 studies), *Pseudomonas spp.* in 25 out of 8,002 patients (nine studies), *Enterococcus spp.* in 64 out of 5,964 patients (eight studies), *Acinetobacter spp.* in seven out of 798 patients (three studies), and *Proteus spp.* in seven out of 1,321 patients (three studies). Gram-negative bacteria were reported in 561 out of 9,253 patients (15 studies), and gram-positive bacteria were reported in 444 out of 9,253 patients (15 studies). The types of BIs included SBP, reported in 30 studies (3,853 out of 48,304 patients), UTI in 16 studies (1,211 out of 16,261 patients), bacteraemia in 16 studies (1,080 out of 24,622 patients), respiratory tract infection in 14 studies (996 out of 15,236 patients), skin and soft tissue infection in 10 studies (338 out of 10,508 patients), gastrointestinal infection (GII) in seven studies (324 out of 3,129 patients), pneumonia in six studies (284 out of 4,680 patients), spontaneous bacterial empyema in three studies (34 out of 1,767 patients), cellulitis in two studies (78 out of 2,324 patients), and sepsis in two studies (63 out of 1,678 patients).

Meta-analysis with subgroup analysis

On the basis of 59 studies that investigated both single and

Table 1. Characteristics of the studies included in this meta-analysis

Authors (year)	Country, period of conduct	Study design	No. of patients	BI evaluated and criteria	Prevalence of BI	Site, mode of infection	Bacteriological characteristics
Piano *et al*. 2019[12]	Multicenter, 2015–2016	Prospective cohort	1,302	Multiple BI	740/1,302	NS	MDR (n = 253)
Baijal *et al*. 2014[27]	India, 2013–2013	Prospective cohort	420	Multiple BI	93/420	SBP (n = 33)	*E. coli* (n = 18), *Staphylococcus spp.* (n = 15), *Streptococcus spp.* (n = 7), *Klebsiella spp.* (n = 6), *Pseudomonas spp.* (n = 2), MDR (n = 20)
Borzio *et al*. 2001[28]	Italy, 1995–1996	Prospective cohort	405	Multiple BI	150/405	UTI (n = 62), SBP (n = 34), bacteraemia (n = 32), RTI (n = 26), others (n = 19)	*E. coli* (n = 38), *S. aureus* (n = 19), *Enterococcus spp.* (n = 16), *Streptococcus spp.* (n = 12), *Pseudomonas spp.* (n = 5), *Klebsiella spp.* (n = 3), *Proteus spp.* (n = 2), others (n = 51)
Kremer *et al*. 2022[29]	Germany, 2019–2021	Prospective cohort	239	Multiple BI	151/239	NS	MDR (n = 7)
Mohan *et al*. 2011a[30]	India, 2007–2008	Case-control	200	SSTI	21/200	SSTI (n = 21)	*E. coli* (n = 11), *K. pneumoniae* (n = 4), *S. aureus* (n = 2)
Fernández *et al*. 2012[10]	Spain, 2005–2007	Prospective cohort	1,578	Multiple BI	390/1,578	SBP (n = 126), UTI (n = 98), cellulitis (n = 66), sepsis (n = 62), pneumonia (n = 46), bacteraemia (n = 30), purulent bronchitis (n = 27), catheter infection (n = 23), others (n = 29)	MDR (n = 92)
Bajaj *et al*. 2014[4]	USA, NS	Prospective cohort	507	Multiple BI	80/507	NS	NS
El-Amin *et al*. 2017[31]	Egypt, NS	Cross-sectional	100	Multiple BI	54/100	SBP (n = 24), UTI (n = 13), RTI (n = 12), GII (n = 3), SSTI (n = 1), sepsis (n = 1)	*Staphylococcus spp.* (n = 27), *Streptococcus spp.* (n = 6), *E. coli* (n = 4), *Enterococcus spp.* (n = 2), *Pseudomonas spp.* (n = 1), *Klebsiella spp.* (n = 1), others (n = 5)
Bajaj *et al*. 2018[32]	USA, NS	Prospective cohort	2,743	Multiple BI	918/2,743	UTI (n = 297), SBP (n = 227), RTI (n = 136), bacteraemia (n = 121), SSTI (n = 95), others (n = 146)	NS

(continued)

Table 1. *(continued)*

Authors (year)	Country, period of conduct	Study design	No. of patients	BI evaluated and criteria	Prevalence of BI	Site, mode of infection	Bacteriological characteristics
Bartoletti *et al*. 2014[33]	Italy, 2008–2012	Retrospective cohort	8,874	Bacteraemia	146/8,874	Bacteraemia (n = 146)	*E. coli* (n = 43), *Staphylococcus spp.* (n = 21), *K. pneumoniae* (n = 29), *E. faecium* (n = 15), *E. faecalis* (n = 12), *Pseudomonas spp.* (n = 10), *Acinetobacter spp.* (n = 10), *S. pneumoniae* (n = 4), others (n = 28)
Li *et al*. 2015a[34]	China, 2011–2013	Retrospective cohort	6,086	SBP	506/6,086	SBP (n = 506)	NS
Alexopoulou *et al*. 2013[35]	Greece, 2008–2011	Retrospective cohort	156	SBP	47/156	SBP (n = 47)	*Streptococcus spp.* (n = 10), *Enterococcus spp.* (n = 9), *E. coli* (n = 8), *Staphylococcus spp.* (n = 7), *Klebsiella spp.* (n = 5), *Pseudomonas spp.* (n = 2), MDR (n = 9), others (n = 6)
Dionigi *et al*. 2017[36]	USA, 2007–2008	Retrospective cohort	781	Multiple BI	200/781	Bacteraemia (n = 73), SBP (n = 71), UTI (n = 37), pleural fluid (n = 9), others (n = 69)	MDR (n = 46), GNB (n = 100), GPB (n = 139)
Bajaj *et al*. 2019[37]	USA, 2013–2014	Prospective cohort	2,864	Multiple BI	998/2,864	UTI (n = 256), SBP (n = 218), RTI (n = 132), bacteraemia (n = 110), SSTI (n = 89)	*C. difficile* (n = 65)
Caly *et al*. 1993[38]	Brazil, 1987–1990	Prospective cohort	170	Multiple BI	80/170	SBP (n = 32), UTI (n = 26), pneumonia (n = 22), SSTI (n = 12), bacteraemia (n = 4), others (n = 7)	*E. coli* (n = 12), *Streptococcus spp.* (n = 10), *S. aureus* (n = 8), *K. pneumoniae* (n = 4), *Proteus spp.* (n = 3), others (n = 10)
Santoiemma *et al*. 2020[39]	USA, 2006–2016	Retrospective cohort	2,159	SBP	314/2,159	SBP (n = 314)	NS
Evans *et al*. 2003[40]	USA, 1994–2000	Prospective cohort	427	SBP	23/427	SBP (n = 23)	*S. viridans* (n = 4), *S. aureus* (n = 3), *Pseudomonas spp.* (n = 1), others (n = 6)
Hung *et al*. 2015[41]	China, 2004–2004	Retrospective cohort	16,992	SBP	451/16,992	SBP (n = 451)	NS
D'Oliveira *et al*. 2022[42]	Brazil, 2012–2018	Retrospective cohort	784	Multiple BI	285/784	NS	NS
Tang *et al*. 2022[43]	China, 2020–2022	Retrospective cohort	1,271	Multiple BI	480/1,271	SBP (n = 292), RTI (n = 82), UTI (n = 12), GII (n = 9), SSTI (n = 3), others (n = 83)	NS

(continued)

Table 1. *(continued)*

Authors (year)	Country, period of conduct	Study design	No. of patients	BI evaluated and criteria	Prevalence of BI	Site, mode of infection	Bacteriological characteristics
Liu *et al*. 2020[44]	China, 2016–2018	Retrospective cohort	974	Multiple BI	203/974	SBP (n = 76), RTI (n = 54), UTI (n = 28), bacteraemia (n = 18), GII (n = 12), SSTI (n = 3), others (n = 12)	NS
Cheng *et al*. 2017[45]	China, 2013–2016	Retrospective cohort	1,043	Bacteraemia	112/1,043	Bacteraemia (n = 112)	NS
Li *et al*. 2015b[46]	China, 2010–2013	Retrospective cohort	419	SBP	82/419	SBP (n = 82)	NS
Choudhuri *et al*. 2018[47]	India, 2015–2017	Retrospective cohort	106	Multiple BI	23/106	NS	MDR (n = 23)
Ponzetto *et al*. 2000[48]	Italy, NS	Case-control	45	GII	40/45	GII (n = 40)	NS
Rahimkhani *et al*. 2008[49]	Pakistan, 2006–2008	Case-control	60	GII	39/60	GII (n = 39)	NS
TANDON *et al*. 2012[7]	USA, 2009–2010	Retrospective cohort	746	Multiple BI	115/746	UTI (n = 37), SBP (n = 28), pneumonia (n = 22), bacteraemia (n = 10), cellulitis (n = 12), SBEM (n = 2), others (n = 4)	*E. coli* (n = 15), *K. pneumoniae* (n = 16), *S. aureus* (n = 10), *Streptococcus spp.* (n = 4), *P. aeruginosa* (n = 2), *P. mirabilis* (n = 2), others (n = 21)
Siringo *et al*. 1997[50]	Italy, NS	Case-control	153	GII	117/153	GII (n = 117)	NS
Angeloni *et al*. 2008[51]	Italy, 2004–2006	Retrospective cohort	228	SBP	38	SBP (n = 38)	*E. coli* (n = 2), *K. pneumoniae* (n = 2), *Enterococcus spp.* (n = 2), *S. aureus* (n = 1), others (n = 2)
Chen *et al*. 2019[52]	China, 2015–2015	Prospective cohort	526	GII	104/526	GII (n = 104)	*C. difficile* (n = 104)
Zhao *et al*. 2018[53]	China, 2011–2017	Retrospective cohort	1,465	Multiple BI	635/1,465	Bacteraemia (n = 199), RTI (n = 193), SBP (n = 191), UTI (n = 42), others (n = 10)	MDR (n = 280)
Fernández *et al*. 2019[54]	Europe, 2011–2011	Prospective cohort	1,146	Multiple BI	455/1,146	SBP (n = 130), UTI (n = 111), pneumonia (n = 85), SSTI (n = 44), bacteraemia (n = 28), others (n = 122)	NS

(continued)

Table 1. *(continued)*

Authors (year)	Country, period of conduct	Study design	No. of patients	BI evaluated and criteria	Prevalence of BI	Site, mode of infection	Bacteriological characteristics
Sargenti *et al*. 2015[6]	Sweden, 2001–2010	Retrospective cohort	633	Multiple BI	241/633	UTI (n = 76), SBP (n = 61), pneumonia (n = 55), SSTI (n = 51), bacteraemia (n = 48), mixed infection (n = 19), others (n = 88)	NS
Gunjača *et al*. 2010[55]	Croatia, 2006–2007	Prospective cohort	108	SBP	23/108	SBP (n = 23)	*E. coli* (n = 7), MRSA (n = 2), *Acinetobacter spp.* (n = 2), *S. aureus* (n = 1), *Streptococcus spp.* (n = 1), *S.epidermidis* (n = 1), *E. faecalis* (n = 1)
Singal *et al*. 2014[56]	USA, 1998–2007	Retrospective cohort	742,391	Multiple BI	168,654/742,391	NS	NS
Chu *et al*. 1995[57]	China, 1992–1992	Retrospective cohort	443	SBP	140/443	SBP (n = 140)	NS
Mohan *et al*. 2011b[58]	USA, 2008–2009	Prospective cohort	110	SBP	7/110	SBP (n = 7)	*E. coli* (n = 1), *Klebsiella spp.* (n = 1), *S. aureus* (n = 1)
Cadranel *et al*. 1999[59]	France, 1994–1994	Case-control	244	UTI	38/244	UTI (n = 38)	NS
Zhu *et al*. 2012[60]	China, 2007–2010	Retrospective cohort	240	Multiple BI	60/240	NS	NS
Xing *et al*. 2014[61]	China, 2011–2013	Retrospective cohort	734	Multiple BI	79/734	RTI (n = 50), UTI (n = 26), others (n = 4)	NS
Makhlouf *et al*. 2012[62]	Egypt, 2010–2011	Cross-sectional	901	SBEM	16/901	SBEM (n = 16)	*E. coli* (n = 6), *K. pneumoniae* (n = 2), *Streptococcus spp.* (n = 2), *P. aeruginosa* (n = 1)
Xiol *et al*. 1996[63]	USA, 1988–1992	Prospective cohort	120	SBEM	16/120	SBEM (n = 16)	*E. coli* (n = 8), *Streptococcus spp.* (n = 5), *Enterococcus spp.* (n = 2), *K. pneumoniae* (n = 2), *P. stutzeri* (n = 1)
Syed *et al*. 2007[64]	Nepal, NS	Prospective cohort	81	SBP	20/81	SBP (n = 20)	*E. coli* (n = 3), *S. pneumoniae* (n = 2), *P. aeruginosa* (n = 1), *Acinetobacter spp.* (n = 1)
Abu-Freha *et al*. 2021[65]	Israel, 1996–2020	Retrospective cohort	1,035	SBP	173/1,035	SBP (n = 173)	NS
Dia *et al*. 2014[66]	Senegal, 2010–2010	Prospective cohort	55	SBP	15/55	SBP (n = 15)	NS
Rubinstein *et al*. 2001[67]	Uruguay, 1998–2000	Prospective cohort	64	SBP	17/64	SBP (n = 17)	NS

Table 1. *(continued)*

Authors (year)	Country, period of conduct	Study design	No. of patients	BI evaluated and criteria	Prevalence of BI	Site, mode of infection	Bacteriological characteristics
Karvellas *et al*. 2010[68]	United Kingdom, 2003–2005	Retrospective cohort	184	Bacteraemia	67/184	Bacteraemia (n = 67)	NS
Mücke *et al*. 2018[69]	Germany, 2008–2015	Retrospective cohort	173	Multiple BI	80/173	NS	NS
Fernández *et al*. 2017[26]	Spain, NS	Prospective cohort	407	Multiple BI	269/407	SBP (n = 63), UTI (n = 52), pneumonia (n = 54), SSTI (n = 19), bacteraemia (n = 19), others (n = 62)	NS
Katoonizadeh *et al*. 2010[70]	Belgium, 2002–2007	Prospective cohort	53	Multiple BI	31/53	NS	NS
Su *et al*. 2021[71]	China, 2014–2015	Retrospective cohort	609	Bacteraemia	63/609	Bacteraemia (n = 63)	*E. coli* (n = 23), *Klebsiella spp.* (n = 14), *Acinetobacter spp.* (n = 4), *S. epidermidis* (n = 4), *Streptococcus spp.* (n = 4), *S. aureus* (n = 3), *Pseudomonas spp.* (n = 1), *E. faecium* (n = 1), *S. hominis* (n = 1), MDR (n = 25), others (n = 8)
Moreau *et al*. 2013[72]	Europe, 2011–2011	Prospective cohort	303	Multiple BI	154/303	NS	NS
Shalimar *et al*. 2018[73]	India, 2011–2017	Retrospective cohort	417	Multiple BI	320/417	NS	NS
Cai *et al*. 2017[74]	China, 2008–2014	Retrospective cohort	389	Multiple BI	266/389	NS	NS
Cao *et al*. 2024[75]	Multicenter, 2021–2022	Prospective cohort	1,293	Multiple BI	1,293/4,238	SBP (n = 391)	*E.coli* (n = 145), *K. pneumoniae* (n = 35), *Enterococcus spp.*(n = 31), *S. aureus*(n = 22), *Streptococcus spp.*(n = 28), *Pseudomonas spp.*(n = 10), *C.difficile* (n = 8), MDR (n = 74)
Nakayama *et al*. 2018[76]	Japan , 2011–2014	Retrospective cohort	102	Multiple BI	26/102	NS	NS
Jeong *et al*. 2025[77]	South Korea 2009–2021	Retrospective cohort	381,691	Multiple BI	65,122/381,691	NS	NS
Hoshi *et al*. 2021[78]	Japan, 2012–2019	Retrospective cohort	285	Multiple BI	57/285	NS	NS
Park *et al*. 2015[79]	South Korea 2010-2012	Retrospective cohort	442	Multiple BI	110/442	NS	NS

C. difficile, Clostridioides difficile; E. coli, Escherichia coli; E. faecalis, Enterococcus faecalis; E. faecium, Enterococcus faecium; GNB, gram-negative bacteria; GPB, gram-positive bacteria; *K. pneumoniae, Klebsiella pneumoniae;* MDR, Multidrug-resistant; MRSA, methicillin-resistant *Staphylococcus aureus;* NS, not stated; *P. aeruginosa, Pseudomonas aeruginosa; P. mirabilis, Proteus mirabilis; P. stutzeri, Pseudomonas stutzeri;* RTI, respiratory tract infection; *S. aureus, Staphylococcus aureus; S. epidermidis, Staphylococcus epidermidis; S. hominis, Staphylococcus hominis; S. pneumoniae, Streptococcus pneumoniae; S. viridans, Streptococcus viridans;* SBEM, spontaneous bacterial empyema; SBP, spontaneous bacteria peritonitis; SSTI, skin and soft tissue infection; UTI, urinary tract infection.

multiple BIs, the pooled overall prevalence of BIs in cirrhosis patients was 26.3% (95% confidence interval (CI): 20.9–32.5) (Fig. 2). This prevalence increased to 35.1% (95% CI: 29.2–41.4) when only the 33 studies focused on multiple BIs were pooled (Supplementary Fig. 1). Subgroup analysis revealed that the main sources of variation in overall BI estimates were the population studied, the geographic location, the study design, the country's economic status, and the decade in which the study was conducted. Higher overall BI estimates were observed in studies that included patients with ACLF, patients admitted to the ICU, or outpatients as the denominator than in those involving all hospitalized patients (44.2%, 29.8%, 34.3%, and 21.7%, respectively; $p = 0.0232$) (Fig. 3). Furthermore, in a prespecified subgroup analysis stratified by ACLF definition, the pooled BI prevalence was 51.9% (95% CI: 33.4–69.8) for EASL-CLIF and 32.0% (95% CI: 14.2–57.2) for APASL. The unspecified definition category contained only one study, yielding 58.5% (95% CI: 44.1–71.9) (Supplementary Fig. 2). The prevalence of BIs varied across different regions of the world. The estimates from Europe (38.2%) were higher than those from South America (37.5%), Asia (22.8%), North America (17.0%), and Africa (16.4%), $p = 0.0007$ (Fig. 4). The studies with the highest prevalence pooled were from Pakistan (65.0%), Belgium (58.5%), and Germany (55.1%), $p < 0.01$ (Supplementary Fig. 3). Moreover, the prevalence in tropical zones (28.3%) was higher than in temperate zones (25.1%) (Supplementary Fig. 4). Additionally, estimates from lower-middle-income countries (27.2%) were higher than those from high-income (26.3%) and upper-middle-income countries (21.8%), $p = 0.7479$ (Supplementary Fig. 5). An increasing trend in the pooled estimates of overall BIs was observed over the last ten years, rising from 20.9% (95% CI: 15.4–27.6) to 30.5% (95% CI: 21.7–40.9), $p = 0.0895$ (Supplementary Fig. 6). Furthermore, the prevalence varied by study design, with case-control studies showing the highest prevalence at 49.9% (Supplementary Fig. 7).

Types of BIs

The pooled prevalence of *E. coli* in patients with cirrhosis was 3.8% (95% CI: 2.5–5.2), that of *Streptococcus* spp. was 1.5% (95% CI: 0.8–2.6), that of *Klebsiella* spp. was 1.3% (95% CI: 0.9–1.8), that of *Staphylococcus* spp. was 2.0% (95% CI: 1.0–4.0), that of *Pseudomonas* spp. was 0.3% (95% CI: 0.2–0.6), that of *Enterococcus* spp. was 1.3% (95% CI: 0.6–2.8), that of *Acinetobacter* spp. was 0.9% (95% CI: 0.4–1.8), that of *Proteus* spp. was 0.6% (95% CI: 0.2–1.4), and the overall prevalence of gram-negative bacteria was 6.4% (95% CI: 4.3–9.3), that of gram-positive bacteria was 4.2% (95% CI: 2.1–8.3), and that of MDR bacteria was 6.8% (95% CI: 4.0–11.3) (Supplementary Figs. 8–19).

Sites of BIs

The site-specific pooled prevalence of BIs was highest for GII (18.4%), followed by SBP (12.4%), UTI (7.0%), respiratory tract infection (7.0%), bacteraemia (5.1%), skin and soft tissue infection (2.6%), and spontaneous bacterial empyema (1.9%) (Supplementary Figs. 20–26).

The temporal trends of BIs

After excluding studies without reported study years, 52 studies remained, spanning study mid-years 1988–2022. Random-effects meta-regression showed an upward temporal trend ($\beta_1 = 0.0176$, SE 0.0221; $p = 0.426$), corresponding to an annual percent change of 1.78% (95% CI: −2.54–6.29). Predicted prevalence increased from 17.9% (95% CI: 7.8–36.1) in 1988 to 28.5% (95% CI: 16.9–43.8) in 2022 (Fig. 5).

Association between BIs and mortality

Across six studies reporting adjusted HRs for mortality, BIs were associated with a higher risk of death, with pooled adjusted HRs of 2.22 (95% CI: 1.33–3.71). Between-study heterogeneity was extreme ($I^2 = 99.4\%$, $\tau^2 = 0.233$), and the 95% prediction interval was 0.58–8.55, indicating substantial variation in the true effects across settings (Fig. 6).

Risk of bias

The funnel plot showed symmetry, indicating no significant evidence of publication bias (Supplementary Fig. 27).[80] However, heterogeneity or small-study effects cannot be completely excluded. The substantial heterogeneity observed among individual studies was accounted for by applying a random-effects model to all calculations. Additionally, subgroup analyses were performed on the basis of various criteria, including the study location, study design, country's economic status, and other characteristics.

Discussion

This review, which synthesizes studies from 21 countries across five continents, estimates the pooled prevalence of BIs in cirrhosis patients to be 35.1% (ranging from 29.2% to 41.4%). These studies focus on different patient populations, including hospitalized patients, ICU-admitted patients, ACLF patients, and outpatients, highlighting the significant burden and prevalence of BIs in these groups. This high prevalence translates into a significant annual burden on healthcare systems with respect to patient numbers and associated costs.[81] These infections often lead to prolonged hospital stays, an increased need for intensive care, and a higher likelihood of complications, including sepsis and organ failure, all of which escalate healthcare costs.[4,5] Furthermore, the recurrent nature of these infections contributes to repeated admissions and increased resource utilization, placing a considerable strain on healthcare systems.[82]

The meta-analysis revealed significant variations in BI prevalence across different sites in patients with cirrhosis. The most prevalent infections in patients with cirrhosis are GII (18.4%), SBP (12.4%), and UTI (7.0%). *E. coli* was the most prevalent pathogen, with an overall pooled prevalence of 3.8% (95% CI: 2.5–5.2, $I^2 = 87.5\%$). MDR bacteria (6.8%, 95% CI: 4.0–11.3, $I^2 = 98.5\%$) were particularly concerning, showing considerable variability across regions. Among gram-negative bacteria, *Klebsiella* spp. had a prevalence of 1.3% (95% CI: 0.9–1.8), whereas *Pseudomonas* spp. and *Proteus* spp. had lower prevalence rates of 0.3% and 0.6%, respectively. Gram-positive bacteria such as *Staphylococcus* spp. (2.0%, 95% CI: 1.0–4.0), with *S. aureus* (1.2%, 95% CI: 0.7–2.2) as the prominent species, also showed a notable presence. Overall, gram-negative bacteria (6.4%) were more prevalent than gram-positive bacteria (4.2%), reflecting the dominance of gram-negative pathogens. This may be attributable to intestinal dysbiosis, loss of gut-barrier integrity, increased bacterial translocation, immune dysfunction, and portosystemic shunting in cirrhosis, all of which promote the passage of enteric gram-negative bacteria and the development of infection.[5,8] These findings emphasize the necessity of targeted antimicrobial strategies, especially given the high prevalence and resistance patterns of MDR organisms.[12] The overall pooled prevalence may have been underestimated due to low bacterial culture positivity in pa-

Study	Events	Total	Proportion	95%−CI
Piano 2019	740	1302	0.568	[0.541; 0.595]
Baijal 2014	93	420	0.221	[0.183; 0.264]
Borzio 2001	150	405	0.370	[0.323; 0.419]
Kremer 2001	151	239	0.632	[0.567; 0.693]
Mohan 2011a	21	200	0.105	[0.066; 0.156]
Fernandez 2012	390	1578	0.247	[0.226; 0.269]
Bajaj 2014	80	507	0.158	[0.127; 0.192]
El−Amin 2017	54	100	0.540	[0.437; 0.640]
Bajaj 2018	918	2743	0.335	[0.317; 0.353]
Bartoletti 2014	146	8874	0.016	[0.014; 0.019]
Li 2015a	506	6086	0.083	[0.076; 0.090]
Alexopoulou 2013	47	156	0.301	[0.231; 0.380]
Dionigi 2017	200	781	0.256	[0.226; 0.288]
Bajaj 2019	998	2864	0.348	[0.331; 0.366]
Caly 1993	80	170	0.471	[0.394; 0.549]
Santoiemma 2020	314	2159	0.145	[0.131; 0.161]
Evans 2003	23	427	0.054	[0.034; 0.080]
Hung 2015	451	16992	0.027	[0.024; 0.029]
D'Oliveira 2022	285	784	0.364	[0.330; 0.398]
Tang 2022	480	1271	0.378	[0.351; 0.405]
Liu 2020	203	974	0.208	[0.183; 0.235]
Cheng 2017	112	1043	0.107	[0.089; 0.128]
Li 2015b	82	419	0.196	[0.159; 0.237]
Choudhuri 2018	23	106	0.217	[0.143; 0.308]
Ponzetto 2000	40	45	0.889	[0.759; 0.963]
Rahimkhani 2008	39	60	0.650	[0.516; 0.769]
TANDON 2012	115	746	0.154	[0.129; 0.182]
Siringo 1997	117	153	0.765	[0.689; 0.829]
Angeloni 2008	38	228	0.167	[0.121; 0.222]
Chen 2019	104	526	0.198	[0.165; 0.234]
Zhao 2018	635	1465	0.433	[0.408; 0.459]
Fernandez 2019	455	1146	0.397	[0.369; 0.426]
Sargenti 2015	241	633	0.381	[0.343; 0.420]
Gunjaca 2010	23	108	0.213	[0.140; 0.302]
Singal 2014	168654	742391	0.227	[0.226; 0.228]
Chu 1995	140	443	0.316	[0.273; 0.362]
Mohan 2011b	7	110	0.064	[0.026; 0.127]
Cadranel 1999	38	244	0.156	[0.113; 0.207]
Zhu 2012	60	240	0.250	[0.197; 0.310]
Xing 2014	79	734	0.108	[0.086; 0.132]
Makhlouf 2012	16	901	0.018	[0.010; 0.029]
Xiol 1996	16	120	0.133	[0.078; 0.207]
Syed 2007	20	81	0.247	[0.158; 0.355]
Abu−Freha 2021	173	1035	0.167	[0.145; 0.191]
Dia 2014	15	55	0.273	[0.161; 0.410]
Rubinstein 2001	17	64	0.266	[0.163; 0.391]
Karvellas 2010	67	184	0.364	[0.295; 0.438]
Mucke 2018	80	173	0.462	[0.386; 0.540]
Fernandez 2017	269	407	0.661	[0.613; 0.707]
Katoonizadeh 2010	31	53	0.585	[0.441; 0.719]
Su 2021	63	609	0.103	[0.080; 0.130]
Moreau 2013	154	303	0.508	[0.450; 0.566]
Shalimar 2018	320	417	0.767	[0.724; 0.807]
Cai 2017	266	389	0.684	[0.635; 0.730]
Cao 2024	1293	4238	0.305	[0.291; 0.319]
Nakayama 2018	26	102	0.255	[0.174; 0.351]
Jeong 2025	65122	381691	0.171	[0.169; 0.172]
Hoshi 2021	57	285	0.200	[0.155; 0.251]
Park 2015	110	442	0.249	[0.209; 0.292]
Random effects model		**1191421**	**0.263**	**[0.209; 0.325]**

Heterogeneity: $I^2 = 99.6\%$, $\tau^2 = 1.3639$, $p = 0$

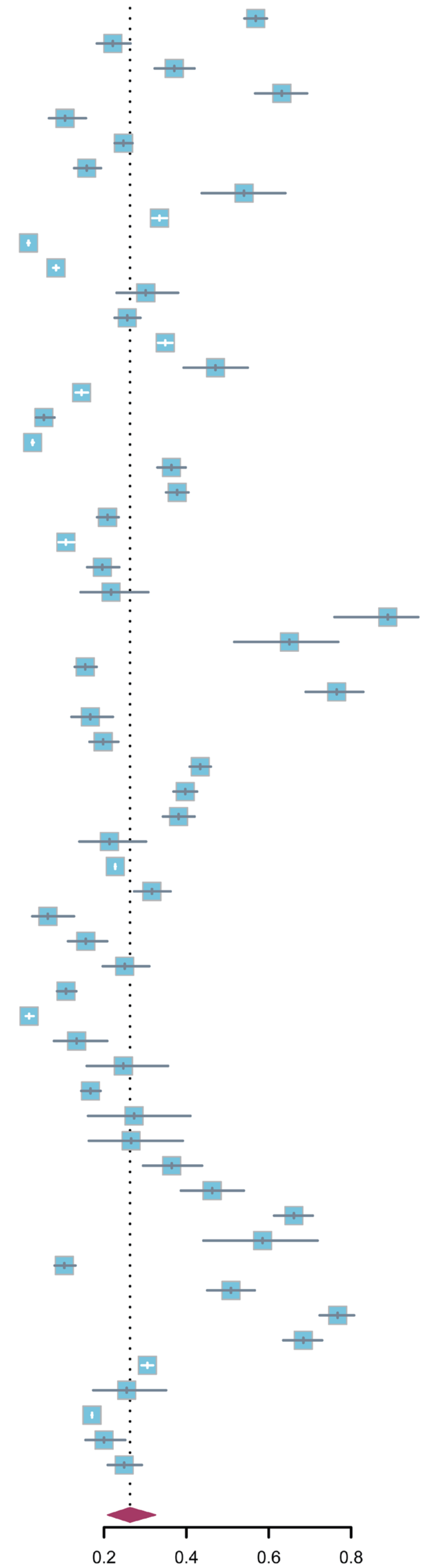

Fig. 2. Pooled overall prevalence of BIs in patients with cirrhosis in the included studies. BIs, bacterial infections.

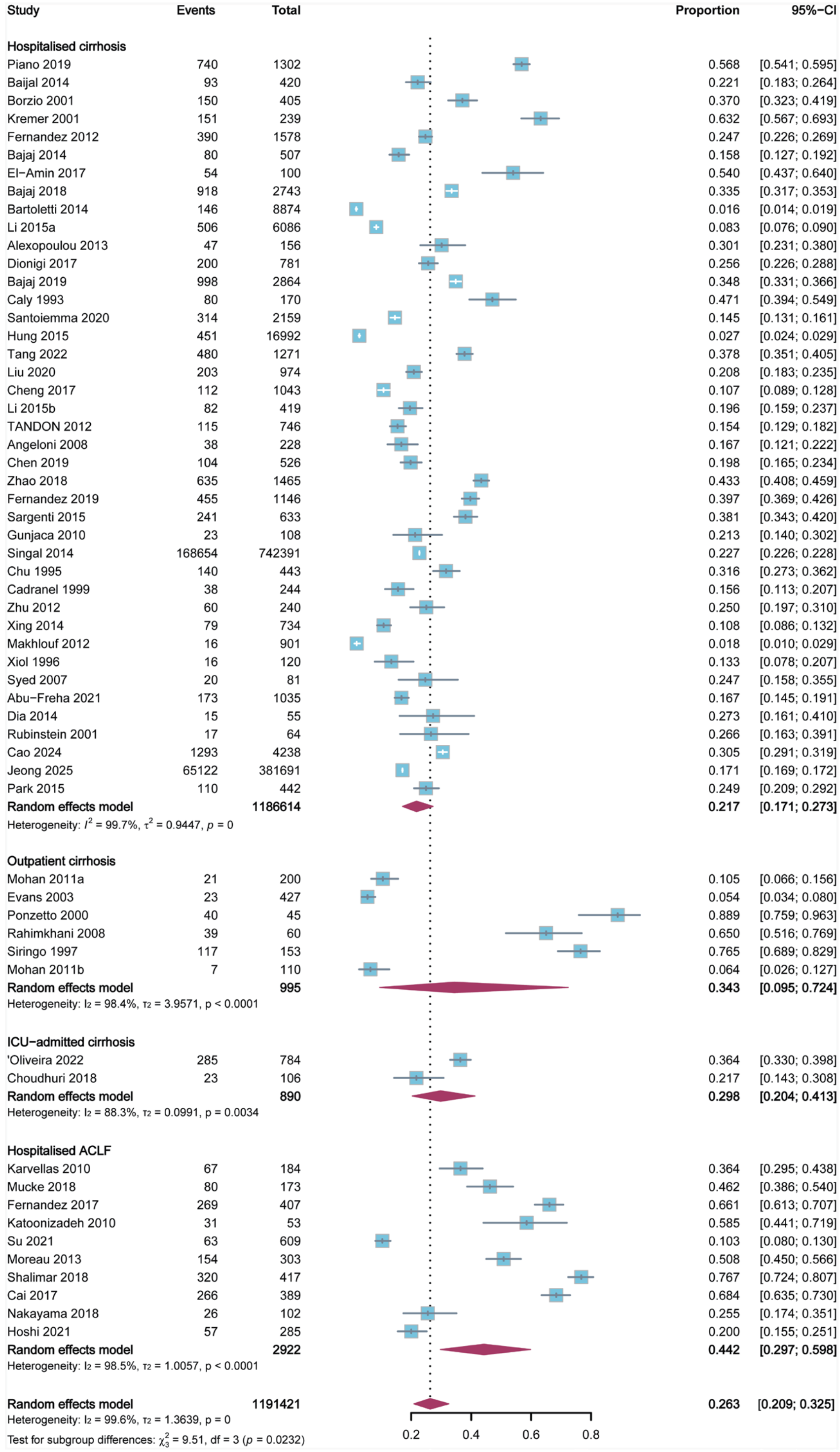

Fig. 3. Forest plot demonstrating the pooled prevalence of BIs in patients with cirrhosis by subgroup: Clinical status. BIs, bacterial infections.

tients with cirrhosis.[8] This limitation, especially in cases involving fastidious organisms or prior antibiotic use, could have led to underreporting and obscuring of the true infection burden, potentially biasing the meta-analysis results.[83] For instance, the relatively low pooled prevalence of *E. coli* (3.8%, 95% CI: 2.5–5.2) and other pathogens such as *Klebsiella spp.* (1.3%, 95% CI: 0.9–1.8) could reflect these diagnostic gaps. Moreover, variations in diagnostic criteria across studies, including differences in sampling methods, patient settings (e.g., ICU vs. non-ICU), and laboratory techniques, contribute to significant heterogeneity. Improved diagnostic techniques are essential to address this issue in future stud-

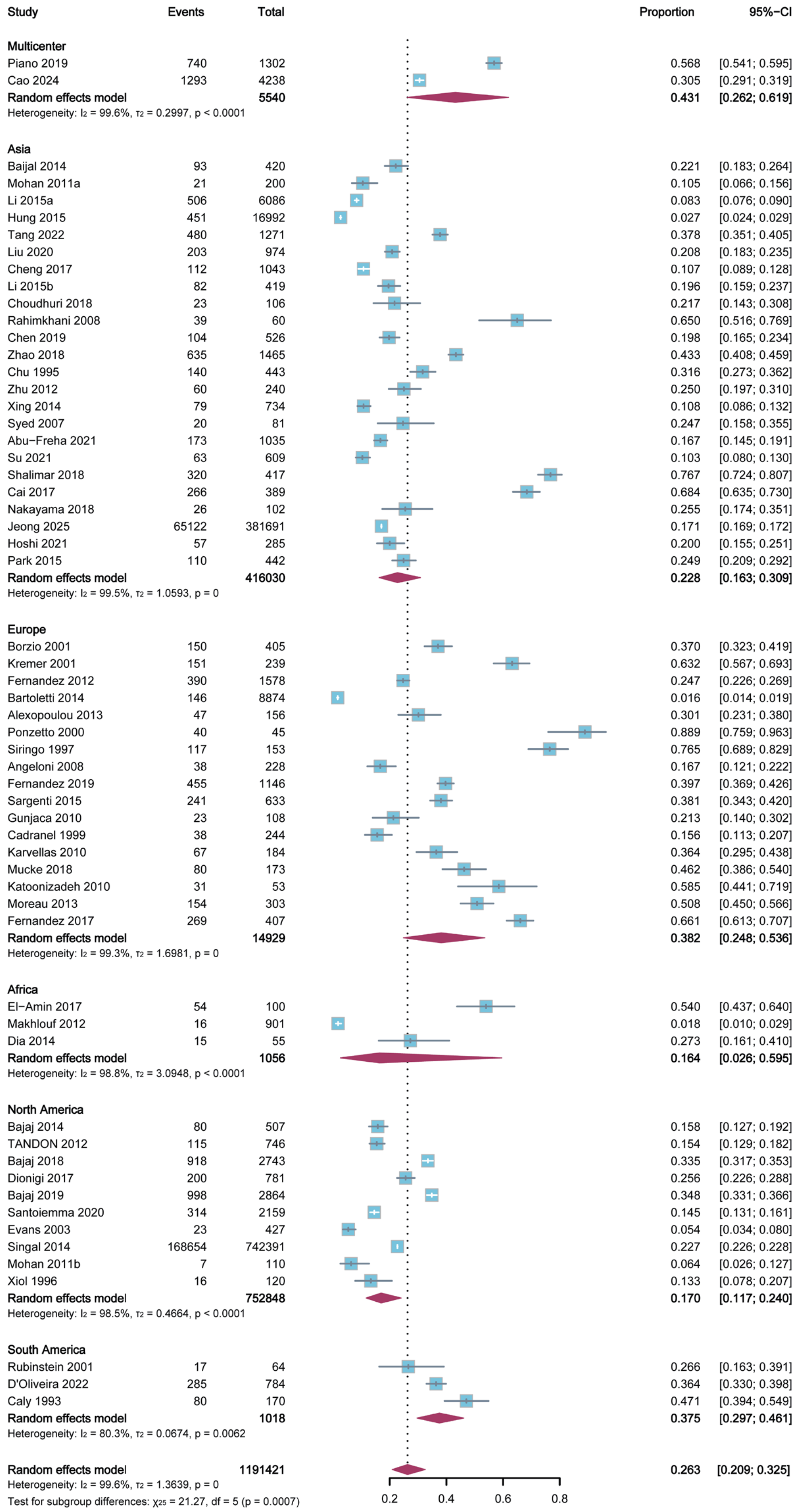

Fig. 4. Forest plot demonstrating the pooled prevalence of BIs in patients with cirrhosis by subgroup: Continent. BIs, bacterial infections.

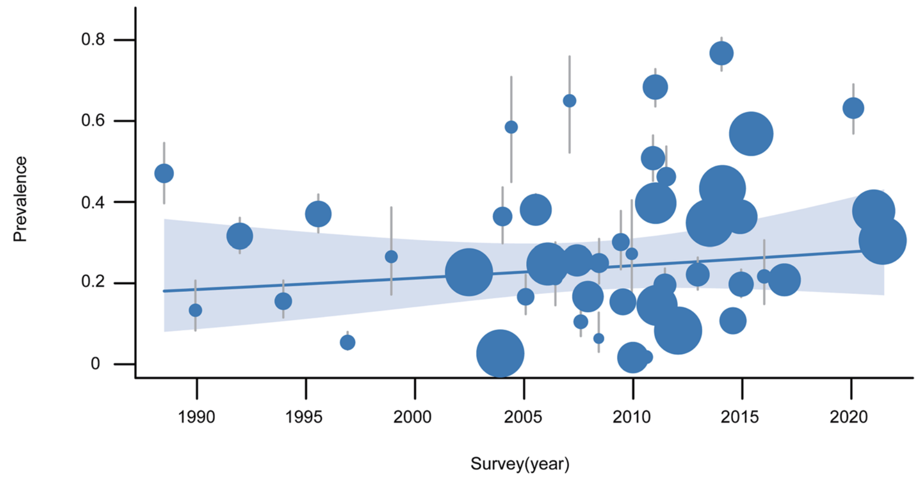

Fig. 5. The temporal trends of BIs in patients with cirrhosis from 1988 to 2022. BIs, bacterial infections.

ies.

Europe ranks high in terms of the pooled prevalence of BIs among patients with cirrhosis (38.2%), which is comparable to that in South America (37.5%). This finding indicates that even in regions with well-developed healthcare systems, patients with cirrhosis remain susceptible to BIs. The wide CI (95% CI: 24.8–53.6) indicates significant variability between studies, reflecting the various study designs, patient populations, and healthcare settings across the different European countries. The pooled prevalence of BIs in patients with cirrhosis in North America is 17%, which is a moderate level. Countries such as the United States benefit from advanced healthcare systems, which allow for better infection control measures, timely diagnoses, and effective treatments. Notably, the pooled prevalence of BIs in cirrhosis patients in Africa was 16.4% (95% CI: 2.6–59.5), although the wide CI suggested considerable variability among the included studies. The lower overall infection rate might have been due to underreporting or smaller sample sizes, as well as the variability in healthcare access across different African countries. Asia has a moderately high pooled prevalence of BIs in cirrhosis, at 22.8% (95% CI: 16.3–30.9), which varies significantly among different countries, particularly between India (32.8%) and China (23.7%). The regional heterogeneity in Asia, with varying healthcare quality and practices, likely contributes to this rate.[84] Countries with more advanced healthcare systems may have better infection control, whereas developing countries may still face significant challenges.[85] The substantial regional variation observed in BI prevalence may be attributable to differences in case mix, patterns of healthcare exposure, antimicrobial usage, and methods of diagnosis. European cohorts often include a larger share of alcohol-related and more decompensated cirrhosis, which is associated with immune dysfunction and bacterial translocation, whereas many Asian cohorts include more hepatitis B-related disease with different risk profiles. Exposure to invasive procedures and devices, ICU admission, and a higher nosocomial proportion can also raise infection risk. Patterns of antibiotic prophylaxis and treatment, together with regional resistance ecology, may further shift observed prevalence.[86] Finally, diagnostic intensity and access to culture and imaging vary across settings, which can inflate detection in well-resourced systems and depress it where testing is limited. Overall, these continental contrasts reflect biology and differences in diagnosis and testing, rather than geography alone.

In this meta-analysis, we showed that cirrhosis patients with ACLF (44.2%), as well as those in ICU (29.8%) or outpatient (34.3%) settings, present a significantly higher prevalence of BIs. Infections are key triggers for ACLF and are the most common cause. Among these, BIs are the main reason, with the resulting systemic inflammatory response syndrome leading to acute decompensation, multi-organ dysfunction, and failure in patients with cirrhosis. This chain reaction disrupts the balance of the immune system, worsens organ damage, and accelerates disease progression, ultimately

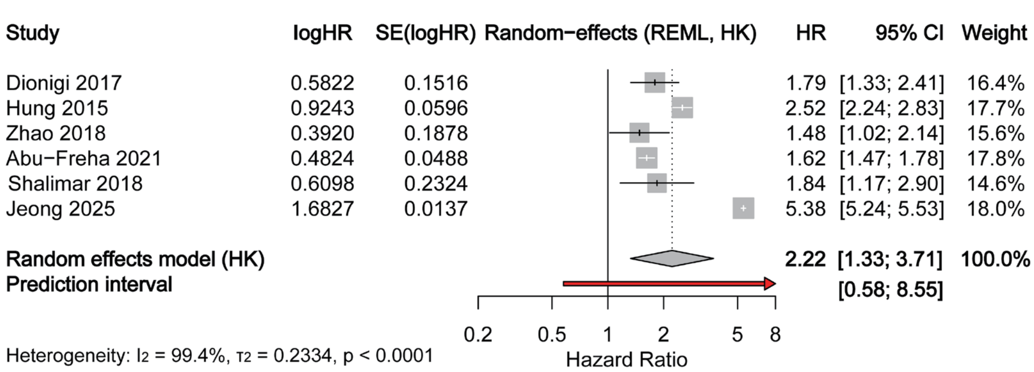

Fig. 6. Forest plot for adjusted HRs for mortality associated with BIs in patients with cirrhosis. BIs, bacterial infections; HR, hazard ratio.

increasing the risk of mortality in ACLF. Conversely, ACLF patients may exhibit an excessive systemic inflammatory response that leads to immune paralysis, thus increasing their risk for early infections.[87] We further evaluated whether the high BI prevalence in ACLF varied by the definition used. In subgroup analyses stratified by ACLF definition, the pooled BI prevalence was 51.9% (95% CI, 33.4–69.8) in studies based on the EASL-CLIF criteria and 32.0% (95% CI, 14.2–57.2) in those based on the APASL criteria; one study with an unspecified definition reported 58.5% (95% CI, 44.1–71.9). Although between-definition differences were not statistically significant (p = 0.189), the higher point estimate with EASL-CLIF may reflect enrichment for extrahepatic organ failures and a more severely ill case mix. These observations underscore the need for consensus ACLF definitions in future epidemiological studies, given the impact of definitional choices on case selection, prevalence estimates, and generalizability.[88] For patients with cirrhosis admitted to ICUs for care, BIs represent a serious clinical challenge due to various risk factors.[26] These include invasive devices, immunosuppression, broad-spectrum antibiotics, and fungal colonization, which increase the risk of cross-infection and subsequent secondary infections.[89] The compromised immunity, muscle weakness, and limited mobilization of patients with cirrhosis increase their susceptibility to infections.[89] Treatment delays, environmental exposure, and limited preventive strategies are likely contributors to the higher infection rates among outpatients with cirrhosis.[26] The difference in BI prevalence between ICU and outpatient settings warrants further consideration. ICU-based studies often focus on more severe infections, potentially underestimating the total burden of infections by excluding mild or subclinical cases. Furthermore, ICU settings typically have rigorous infection control measures, including strict hygiene protocols and early infection management, which may reduce the prevalence of infections compared to outpatient settings. In contrast, the higher prevalence of infections in outpatient settings may be influenced by underdiagnosis and delayed treatment. Outpatient populations may also include undiagnosed or poorly managed decompensated cirrhosis cases, increasing susceptibility to infections.

Interestingly, there appears to be a modest upward trend in the prevalence of BIs in patients with cirrhosis. Our meta-regression analysis revealed a rising pattern in predicted prevalence from 17.9% in 1988 to 28.5% in 2022. Subgroup analysis also suggested a higher prevalence of BIs in the last 10 years (30.5%) compared to earlier periods (20.9%). Several factors may underlie this temporal increase. Advances in the medical management of chronic liver disease have prolonged the survival of cirrhotic patients, inadvertently increasing their cumulative exposure to healthcare environments where nosocomial infections are more likely to occur, particularly in high-risk settings such as the ICU.[83] Furthermore, the more frequent use of invasive procedures, including paracentesis, endoscopy, and catheterization, increases the degree of risk.[90]

Furthermore, our pooled analysis showed that BIs were significantly associated with increased mortality risk in patients with cirrhosis, with pooled HRs of 2.22 (95% CI: 1.33–3.71). This result highlights that infections not only occur frequently but also have a major impact on patient outcomes. The immunocompromised state of cirrhosis may predispose patients to rapid clinical decline following infection, often culminating in organ failure or the development of ACLF. These findings emphasize the critical need for early recognition, prompt antimicrobial intervention, and robust infection prevention strategies to reduce infection-related mortality in this vulnerable population.

The strengths of this review include its comprehensive analysis of global epidemiological trends in BIs among patients with cirrhosis and its investigation of variations in prevalence estimates. Although this meta-analysis provides valuable insights into the infection prevalence in patients with cirrhosis, several limitations should be considered. The heterogeneity observed across studies, in terms of population characteristics, diagnostic methods, and study quality, limits the generalizability of these results. The variability in infection prevalence may be influenced by differences in study quality, including sample size, methodological rigor, and consistency in reporting criteria. Additionally, the retrospective design of many studies may introduce selection bias, and the absence of standardized infection criteria may affect the reliability of pooled estimates. Furthermore, the variability in regional healthcare settings, including access to diagnostic tools and antimicrobial treatments, likely contributes to the underreporting of infection rates, particularly in lower-resource settings. Not all countries were represented, and several regions were informed by only a small number of studies, which limits geographic coverage and reduces the precision of regional estimates. A further methodological limitation arises from heterogeneous diagnostic criteria. A detailed inspection of the extracted criteria (Supplementary Table 3) confirms that the definition of each infection site varied across studies. For SBP, most studies defined cases by an ascitic polymorphonuclear neutrophil count of at least 250 cells/mm^3, regardless of culture. However, some used 500 cells/mm^3 or higher, and a few required a positive ascitic culture. For UTI, most studies combined compatible symptoms with pyuria, for example, more than 10–15 white blood cells per high-power field or more than 10 leukocytes per microliter, and/or a positive urine Gram stain or culture. Some studies explicitly required culture positivity, whereas a few accepted symptoms with pyuria without a mandatory culture. These definitional differences can bias prevalence in opposite directions because culture-dependent definitions tend to underestimate infections when prior antibiotics reduce yield or when the inoculum is low, whereas clinical or composite criteria may overestimate by capturing noninfectious presentations. The pooled estimates should therefore be read as averages across nonidentical constructs, which highlights the need for standardized site-specific definitions and transparent microbiological reporting to improve comparability and external validity. A recent multicenter study in China reported substantial differences in the clinical and microbiological profiles of BIs compared with global data, including a notably high prevalence of MDR organisms and a lower adherence to empirical antibiotic guidelines. These findings underscore the impact of regional practice variations on both diagnostic yield and treatment outcomes, reinforcing the necessity of internationally harmonized criteria and reporting standards.[91] Another limitation is the insufficient data on clinical characteristics, such as decompensated versus compensated cirrhosis or cirrhosis etiology, limiting specific subgroup analyses. Moreover, our review did not specifically address the potential relationship between MDR and antibiotic usage (for instance, in hepatic encephalopathy or prophylaxis against SBP), which needs further investigation. Future studies should address these gaps to better understand infection risks and improve the applicability of findings. These findings underscore the need for improved diagnostic protocols, standardized infection criteria, and more uniform study designs in future research to provide clearer guidance for the clinical management of patients with cirrhosis.

Conclusions

BIs are common in patients with liver cirrhosis and show a modest upward trend over time, with the highest burdens observed in ACLF and notable regional variation. Gastrointestinal infections, SBP and UTI predominate, gram-negative organisms are more frequent than gram-positive organisms, and MDR pathogens are significant. Importantly, infections are associated with a higher mortality, underscoring the need for improved diagnostic approaches and standardized research frameworks to deliver clearer guidance for the clinical management of patients with liver cirrhosis.

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Conflict of interest

YCF has been an Associate Editor of *Journal of Clinical and Translational Hepatology* since 2013. The other authors have no conflict of interests related to this publication.

Author contributions

Data analysis and interpretation, drafting of the manuscript (YXT, YPW), data collection (YXT, YPW, BYW, JZ, QA), critical comments and reading (YHY), study conception and design, revision of the manuscript, and leadership responsibility for the research (YCF). All authors have approved the final version and publication of the manuscript.

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