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Original Article

Clinical, Microbiological, and Antibiotic Treatment Characteristics of Bacterial Infections in Patients with Liver Cirrhosis in China: A Multicenter Study

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Abstract

Background and Aims: Epidemiological data on bacterial infections in cirrhosis in China remain limited. Therefore, we aimed to conduct a multicenter study to investigate the characteristics and outcomes of patients with cirrhosis and bacterial infections in China. ***Methods:*** We retrospectively enrolled 1,438 hospitalized adult patients with cirrhosis and bacterial or fungal infections from 24 hospitals across China between January 2018 and September 2024. Data on demographics, clinical features, microbiology, treatment, and outcomes were collected. ***Results:*** A total of 1,783 infection episodes were recorded, including 1,668 first infections and 115 second infections. Most infections were community-acquired (86.6%). Pneumonia was the most common infection type (26.7%), followed by spontaneous bacterial peritonitis (19.5%) and spontaneous bacteremia (14.1%). Among 754 pathogens isolated from 620 patients, Klebsiella pneumoniae

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(20.1%) was nearly as common as *Escherichia coli* (21.7%). Multidrug-resistant (MDR) organisms accounted for 41.0% of all isolates, with extended-spectrum β-lactamase-producing *Escherichia coli* being the most prevalent MDR strain (8.9% of patients). Adherence to empirical antibiotic treatment guidelines from the European Association for the Study of the Liver was significantly lower in this cohort compared to the global study (21.5% vs. 61.2%, $P < 0.001$), accompanied by a lower clinical resolution rate (63.5% vs. 79.8%, $P < 0.001$). ***Conclusions:*** The clinical and microbiological characteristics of bacterial infections in patients with cirrhosis in China differ substantially from those reported in other regions. These findings highlight the need for region-specific management and prevention strategies, particularly in light of the changing microbiological landscape, high MDR prevalence, and suboptimal antibiotic practices.

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Introduction

Liver cirrhosis represents the end stage of chronic liver disease, regardless of its etiology. Globally, complications of cirrhosis account for more than one million deaths annually.[1,2] Patients with cirrhosis, particularly those with decompensated disease, are highly susceptible to bacterial infections, with an incidence ranging from 25% to 46% among hospitalized patients.[3–7] These infections often lead to severe clinical consequences, including a fourfold increase in mortality among patients with decompensated cirrhosis,[8] as well as a detrimental impact on long-term outcomes even in those with compensated disease.[9] Moreover, bacterial infection is the most common trigger of acute-on-chronic liver failure (ACLF), resulting in a more severe clinical course and poorer outcomes compared to ACLF precipitated by other causes.[4]

Accurate epidemiological data on bacterial infections in patients with cirrhosis are critical for optimizing prevention, clinical management, and public health strategies, particularly in the context of increasing multidrug-resistant (MDR) bacteria.[3,5,10–13] Furthermore, substantial geographic variability in infection profiles and treatment practices underscores the need for region-specific data, as emphasized by two recent global studies.[3,14] However, such data remain scarce in China.

To address this gap, we conducted a multicenter cohort study to investigate the demographic, clinical, microbiological, and antibiotic treatment characteristics of patients with cirrhosis and bacterial infections in China. We also compared these findings with international data to identify potential region-specific differences.

Methods

Patient

This multicenter, retrospective study consecutively enrolled 1,438 hospitalized adult patients with cirrhosis and bacterial or fungal infections across 24 hospitals in China between January 2018 and September 2024. A detailed flowchart of patient selection is presented in Supplementary Figure 1. Patients were excluded if they met any of the following criteria: (1) hepatocellular carcinoma; (2) extrahepatic malignancy; (3) severe extrahepatic comorbidities, including congestive heart failure (New York Heart Association class ≥ III), chronic obstructive pulmonary disease (Global Initiative for Chronic Obstructive Lung Disease stage ≥ III), or chronic kidney disease requiring renal replacement therapy; (4) history of solid organ transplantation; (5) human immunodeficiency virus infection; or (6) use of immunosuppressive agents (excluding corticosteroids for liver-related indications) within one month prior to admission.

The study adhered to the Declaration of Helsinki and was approved by the Ethics Committee of the First Affiliated Hospital, School of Medicine, Zhejiang University (IIT20230123B-R1). Written informed consent was waived by the Ethics Committee.

Data collection and follow-up

Demographic, clinical, laboratory, microbiological, and treatment-related data at the time of infection diagnosis were retrieved from the electronic medical record systems of each participating hospital using a standardized, pre-specified data collection form. Additional in-hospital data included the occurrence of new bacterial or fungal infections, development of septic shock, ACLF, transfer to the intensive care unit (ICU), use of vasopressors, mechanical ventilation, and renal replacement therapy. For patients who developed a second infection during hospitalization, repeat microbiological cultures and antibiotic susceptibility testing were performed using previously described approaches.[15,16]

Pre-admission data were also collected, including: (1) antibiotic use within the preceding three months; (2) recent use of medications such as rifaximin, β-blockers, proton pump inhibitors (PPIs), or quinolone prophylaxis within the past month; (3) history of invasive procedures (e.g., surgery, central venous catheterization, indwelling urinary catheter, or paracentesis) in the prior three months; (4) ICU admission within the past week; and (5) any infection occurring within three months prior to index hospitalization. Patients were followed until death, liver transplantation, or their last available visit within 90 days of admission, whichever occurred first.

Definitions

Cirrhosis was diagnosed based on radiological evidence of a nodular liver contour, endoscopic signs of portal hypertension, or clinical evidence of hepatic decompensation.[17] ACLF was defined according to the European Association for the Study of the Liver (EASL)–Chronic Liver Failure Consortium criteria.[18]

Diagnostic criteria for each type of infection are provided in Supplementary Table 1. A second infection was defined as a new nosocomial infection occurring after the initial infection during the same hospitalization.[14,19] The diagnostic criteria were applied consistently across infection episodes.

A positive quick Sequential Organ Failure Assessment score was defined by the presence of at least two of the following: (1) altered mental status; (2) respiratory rate ≥ 22 breaths/m; and (3) systolic blood pressure ≤ 100 mmHg.[20] Systemic inflammatory response syndrome was defined by the presence of at least two of the following: (1) body temperature < 36°C or > 38°C; (2) heart rate > 90 beats/m; (3) respiratory rate > 20 breaths/m; (4) white blood cell count < 4,000/mm^3 or > 12,000/mm^3; or (5) immature neutrophil count > 10%.[21] Septic shock was diagnosed as sepsis with hypotension requiring vasopressors.[22]

MDR bacteria were defined as isolates resistant to at least one agent in three or more antimicrobial classes.[10] Extensively drug-resistant (XDR) bacteria were defined as isolates susceptible to only one or two antimicrobial classes, while pan-drug-resistant bacteria were resistant to all currently

available antibiotics.[10]

Empirical antibiotic regimens were categorized into two strategies: (1) classical strategies, including first- to third-generation cephalosporins, amoxicillin-clavulanic acid, cloxacillin, or quinolones; and (2) MDR-covered strategies, including piperacillin-tazobactam, carbapenems, or ceftazidime/cefepime with or without glycopeptides (or linezolid/daptomycin).[23] Clinical response to empirical therapy was assessed by the treating physician based on symptom resolution, laboratory improvement, and microbiological results. Antibiotic regimens were considered "adherent" to EASL guidelines[24] if at least one recommended antibiotic was used (Supplementary Table 2). Non-adherent regimens were further classified as "weaker" (narrower spectrum than recommended) or "broader" (wider spectrum than recommended). Antibiotic escalation was defined as the addition of at least one new agent or a switch to a broader-spectrum agent within five days. De-escalation was defined as a reduction in the number of antibiotics or a switch to a narrower-spectrum regimen within the same timeframe.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation or median (IQR), and compared using Student's t test, one-way ANOVA, or the Kruskal–Wallis test, as appropriate. Categorical variables were expressed as counts (percentages) and compared using Pearson's chi-square test or Fisher's exact test.

Multivariate Cox proportional hazards models were used to identify independent factors associated with in-hospital, 28-day, and 90-day mortality.[25] Candidate variables included: age, sex (female as reference), diabetes, hypertension, cirrhosis etiology (hepatitis B virus as reference), recent infection, prior transjugular intrahepatic portosystemic shunt (TIPS), recent medication use, prior antibiotic exposure, recent invasive procedures, ICU admission, presence of ascites, hepatic encephalopathy (HE), model for end-stage liver disease (MELD) score, culture positivity (vs. negative), MDR isolates (vs. non-MDR), and empirical antibiotic strategy.

All statistical tests were two-tailed, and *P*-values < 0.05 were considered significant. Statistical analyses were performed using SPSS 26.0 (Chicago, IL) and R 4.3.1 (Vienna, Austria).

Results

Characteristics of the patients

A total of 1,438 patients with cirrhosis and bacterial or fungal infections were enrolled across 24 centers (Supplementary Fig. 2). As shown in Table 1, the median age was 61.0 years (IQR, 52.0–72.0), and 63.6% were male. A total of 362 (25.2%) and 377 (26.2%) patients had diabetes mellitus and hypertension, respectively. Hepatitis B virus was the predominant etiology of cirrhosis (44.6%), followed by alcohol-related liver disease (17.9%). Overall, 529 patients (36.8%) had recent infections, and 3.8% had a history of TIPS. The median hospital stay was 11.0 (IQR, 8.0–17.0) days. ACLF was diagnosed in 288 patients (20.0%). The median MELD and MELD-Na scores were 14.0 (IQR, 9.0–19.0) and 16.0 (IQR, 10.0–23.0), respectively. A total of 22 (1.5%), 142 (9.9%), and 230 (16.0%) patients died during hospitalization, at 28-day, and 90-day follow-up, respectively.

Characteristics of the first infection

Among the first documented infections (Table 2), 86.6% were community-acquired and 13.4% were nosocomial. Pneumonia was the most prevalent infection (26.7%), followed by spontaneous bacterial peritonitis (SBP, 19.5%) and spontaneous bacteremia (14.1%). At diagnosis, 54.2% of patients met the criteria for systemic inflammatory response syndrome, 7.2% had a quick Sequential Organ Failure Assessment score ≥ 2, and 8.1% presented with septic shock.

Culture tests identified 754 microorganisms from 620 patients, with more than one species isolated in 7.9% of cases. Detailed isolate data by center are provided in Supplementary Table 3. Overall, gram-negative bacteria were the most common (58.5%), followed by gram-positive bacteria (28.1%), and fungi accounted for approximately 13%. The most frequent isolates were *Escherichia coli* (21.7%), *Klebsiella pneumoniae* (20.1%), and *Staphylococcus aureus* (8.9%). The prevalence of MDR and XDR isolates was 41.0% and 2.5%, respectively.

Initial empirical antibiotic regimens included MDR coverage in 65.9% of cases, while 34.1% received classical regimens. During treatment, 61.7% of patients remained on the initial regimen, 30.0% required escalation, and 8.4% underwent de-escalation. The clinical resolution rate was 63.5%.

The 24 participating centers were categorized into three tiers: central, regional, and county-level hospitals (Supplementary Table 4). Among them, central hospitals had the highest rate of positive cultures (47.7%), followed by regional (40.0%) and county-level hospitals (37.4%). Despite differences in culture positivity, the prevalence of MDR and XDR organisms did not significantly differ across hospital tiers.

Characteristics of the second infection

A total of 115 second infection episodes occurred in 99 patients (6.9%) (Supplementary Table 5). The most common types were pneumonia (21.7%), urinary tract infection (UTI, 19.1%), and spontaneous bacteremia (19.1%). The culture positivity rate was 69.7%, with polymicrobial infections identified in 17.2% of cases. The most frequently isolated pathogens included *Enterococcus faecium* (20.1%), *Klebsiella pneumoniae* (19.0%), and *Escherichia coli* (11.4%). MDR bacteria were detected in 51.9% of cases, and XDR bacteria in 5.1%. Notably, pan-drug-resistant bacteria were identified in 97 cases of second infections.

Prevalence and types of MDR/XDR bacteria

A total of 284 MDR and XDR bacterial isolates were identified from 259 patients across 284 infection episodes (Table 3). Among gram-negative organisms, extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli* was the most frequently detected MDR pathogen, accounting for 7.7% of all isolates, 8.9% of patients, and 8.5% of infection episodes. This was followed by ESBL-producing *Klebsiella pneumoniae*, which represented 2.3% of isolates, 2.7% of patients, and 2.6% of episodes. Among gram-positive organisms, *vancomycin-susceptible enterococci* and *methicillin-resistant Staphylococcus aureus* (MRSA) were the most common. *Vancomycin-susceptible enterococci* was identified in 26 isolates (4.0%), affecting 26 patients (4.6%) and corresponding to 26 infection episodes (4.2%). MRSA was found in 20 isolates (3.1%), involving 20 patients (3.6%) and 22 infection episodes (3.5%).

Factors associated with mortality

A total of 22, 142, and 230 deaths occurred during hospitalization and at 28-day and 90-day follow-up, respectively. In the multivariable Cox regression analysis (Table 4), the following were independently associated with in-hospital mortality: hypertension (adjusted hazard ratio [aHR], 3.888;

Table 1. Baseline characteristics of the overall cohort of the first infection

Characteristics	n = 1,438
Age (y)	61.0 (52.0–72.0)
Sex, n (%)	
Male	914 (63.6)
Female	524 (36.4)
Diabetes mellitus, n (%)	362 (25.2)
Hypertension, n (%)	377 (26.2)
Etiology, n (%)	
HBV	641 (44.6)
Alcohol	257 (17.9)
MASLD	80 (5.6)
Cryptogenic	131 (9.1)
Others	329 (22.9)
Recent* infection, n (%)	529 (36.8)
History of TIPS, n (%)	54 (3.8)
Recent* medications, n (%)	
Rifaximin	24 (1.7)
β-blockers	65 (4.5)
PPIs	273 (19.0)
Quinolone prophylaxis	77 (5.4)
Recent* antibiotic use, n (%)	332 (23.1)
Invasive procedures, n (%)	226 (15.7)
Recent* ICU admission, n (%)	24 (1.7)
Length of hospital stay (day)	11.0 (8.0–17.0)
MAP (mmHg)	81.3 (72.7–92.0)
HR (bpm)	92.0 (83.0–105.0)
Body temperature (°C)	37.8 (37.1–38.6)
RR (breath/min)	20.0 (19.0–21.0)
SpO_2	97.0 (95.0–98.0)
Leukocytes (10^9/L)	6.2 (3.6–10.5)
NLR	5.0 (2.0–11.1)
C-reactive protein (mg/L)	29.1 (10.5–68.0)
Albumin (g/L)	28.5 (24.9–32.6)
TB (μmol/L)	40.7 (19.7–101.2)
Cr (μmol/L)	77.0 (60.0–110.4)
Serum sodium (mmol/L)	136.8 (133.0–139.8)
INR	1.4 (1.2–1.7)
Ascites, n (%)	658 (45.8)
Hepatic encephalopathy, n (%)	
Grades 1/2	147 (10.2)
Grades 3/4	133 (9.2)
Use of vasopressors, n (%)	162 (11.3)
Transfer to ICU, n (%)	140 (9.7)

(continued)

Table 1. *(continued)*

Characteristics	n = 1,438
Mechanical ventilation, n (%)	86 (6.0)
Renal replacement therapy, n (%)	40 (2.8)
ACLF, n (%)	288 (20.0)
MELD score	14.0 (9.0–19.0)
MELD-Na score	16.0 (10.0–23.0)
Second infection, n (%)	99 (6.9)
In-hospital mortality, n (%)	22 (1.5)
28-day mortality, n (%)	142 (9.9)
90-day mortality, n (%)	230 (16.0)

Data are presented as medians (IQR), or numbers (percent). Definition of recent: recent infection, history of infections; recent medications, in the previous month; recent antibiotic use, in the previous three months; recent ICU admission, in the previous week. HBV, hepatitis B virus; MASLD, metabolic dysfunction-associated steatotic liver disease; PBC, primary biliary cirrhosis; AIH, autoimmune hepatitis; TIPS, transjugular intrahepatic portosystemic shunt; PPIs, proton pump inhibitors; ICU, intensive care unit; MAP, mean arterial pressure; HR, heart rate; RR, respiratory rate; SpO_2, percutaneous arterial oxygen saturation; NLR, neutrophil-to-lymphocyte ratio; TB, total bilirubin; Cr, creatinine; INR, international normalized ratio; ACLF, acute-on-chronic liver failure; MELD, model for end-stage liver disease; MELD-Na, MELD plus serum sodium; SD, standard deviations; IQR, interquartile range.

95% CI, 1.403–10.770; *P* = 0.009), recent infection (aHR, 5.567; 95% CI, 1.689–18.346; *P* = 0.005), recent quinolone prophylaxis (aHR, 5.489; 95% CI, 1.045–28.837; *P* = 0.044), higher MELD score (aHR, 1.086; 95% CI, 1.048–1.126; *P* < 0.001), and HE grade 3/4 (aHR, 5.425; 95% CI, 1.890–15.565; *P* = 0.002).

Independent risk factors for 28-day mortality included: cryptogenic cirrhosis (aHR, 2.252; 95% CI, 1.258–4.030; *P* = 0.006), a history of TIPS (aHR, 2.193; 95% CI, 1.043–4.612; *P* = 0.038), recent use of PPIs (aHR, 0.586; 95% CI, 0.348–0.985; *P* = 0.044), HE grade 3/4 (aHR, 1.874; 95% CI, 1.102–3.186; *P* = 0.020), and MELD score (aHR, 1.092; 95% CI, 1.046–1.139; *P* < 0.001). At 90-day follow-up, independent predictors of mortality included: other cirrhosis etiologies (aHR, 1.483; 95% CI, 1.009–2.179; *P* = 0.045), a history of TIPS (aHR, 1.948; 95% CI, 1.104–3.563; *P* = 0.022), presence of minimal or no ascites (aHR, 0.535; 95% CI, 0.313–0.913; *P* = 0.022), HE (aHR, 2.138; 95% CI, 1.464–3.122; *P* < 0.001), MELD score (aHR, 1.076; 95% CI, 1.064–1.088; *P* < 0.001), and a positive microbiological culture result (aHR, 1.772; 95% CI, 1.002–3.134; *P* = 0.049).

Comparison of clinical and microbiological characteristics between culture-positive and culture-negative infections

Among the 1,188 patients who underwent culture testing, 620 (52.2%) had positive results. Supplementary Table 6 summarizes the clinical characteristics of patients with culture-positive versus culture-negative infections at the time of their first documented infection. Compared to those with culture-negative results, culture-positive patients had a higher prevalence of diabetes mellitus (29.2% vs. 22.0%, *P* = 0.005), more frequent recent infections (41.8% vs. 34.3%, *P* = 0.008), and a greater history of prior antibiotic exposure (26.3% vs. 20.6%, *P* = 0.021). In terms of infection severity, culture-positive patients were more likely to present with ACLF (25.7% vs. 15.8%, *P* < 0.001) and had significantly higher MELD and MELD-Na scores.

As shown in Supplementary Table 7, community-acquired infections were more common among culture-negative patients (88.2% vs. 83.4%, *P* = 0.018), who also had a significantly lower incidence of septic shock compared to those with positive cultures (5.1% vs. 16.6%, *P* < 0.001). Although empirical antibiotic strategies at baseline did not differ significantly between groups, patients with culture-positive infections were more likely to undergo antibiotic escalation (38.8% vs. 25.8%, *P* < 0.05), and their clinical resolution rates were notably lower (53.5% vs. 70.1%, *P* < 0.001).

Patients with positive cultures had significantly higher in-hospital mortality (2.6% vs. 0.7%, *P* = 0.012). Similarly, culture-negative patients demonstrated improved survival at both 28-day and 90-day follow-up (Supplementary Fig. 3B and C).

Comparison of clinical and microbiological characteristics of bacterial infections: Chinese versus global cohorts

As shown in Table 5, the proportion of community-acquired infections in the Chinese cohort was significantly higher than that reported in the global study (86.6% vs. 74.0%, *P* < 0.001). Compared with patients in the global cohort, Chinese patients were more likely to present with pneumonia (28.7% vs. 18.9%, *P* < 0.05) and spontaneous bacteremia (15.2% vs. 7.8%, *P* < 0.05), but were less likely to develop SBP (21.0% vs. 27.6%, *P* < 0.05) or urinary tract infections (8.6% vs. 22.5%, *P* < 0.05). Culture-positive infections were significantly less frequent in the Chinese cohort (43.1% vs. 56.8%, *P* < 0.001). *Klebsiella pneumoniae* was more commonly isolated in China (20.1% vs. 15.5%, *P* < 0.05), while *Escherichia coli* (21.7% vs. 28.9%, *P* < 0.05) and *Enterococcus faecalis* (2.1% vs. 5.6%, *P* < 0.05) were less frequently detected.

Although the overall prevalence of MDR bacteria was higher in China (41.0% vs. 35.0%, *P* = 0.014), the incidence of XDR organisms was significantly lower (2.5% vs. 7.9%, *P* < 0.05). Regarding specific resistance patterns, *carbapenem-resistant Enterobacteriaceae* and *vancomycin-resistant enterococci* were less common in China, whereas MRSA was more frequently isolated.

A detailed comparison across geographic regions—including China, the United States, Asia (excluding China), and Europe—is presented in Supplementary Table 8 and yielded consistent findings regarding the epidemiological characteristics of Chinese patients.

Comparison of antibiotic treatment practices: Chinese versus global cohorts

As shown in Table 6, adherence to the EASL guidelines for

Table 2. Clinical and microbiological characteristics of the first infection

Characteristics	n = 1,438
Type of infection, n (%)	
Community acquired	1,245 (86.6)
Nosocomial	193 (13.4)
Site of infection per infection, n (number of infections/%)	
SBP	326 (19.5)
Pneumonia	445 (26.7)
UTI	134 (8.0)
Spontaneous bacteremia	236 (14.1)
Skin and soft tissue	96 (5.8)
Bacterial entero-colitis	44 (2.6)
Cholangitis	118 (7.1)
Others	154 (9.3)
Unproven bacterial infection	115 (6.9)
Severity of infection, n (%)	
SIRS	780 (54.2)
qSOFA	104 (7.2)
Septic shock	117 (8.1)
Patients with positive cultures, n (%)	620 (43.1)
Isolates per patient, n (%)	
1	506 (35.2)
>1	114 (7.9)
Type of strains isolated, n (%)[†]	
Gram-negative	441 (58.5)
Gram-positive	212 (28.1)
Fungi	101 (13.4)
Most frequently isolated bacteria, n (%)[‡]	
Escherichia coli	142 (21.7)
Klebsiella pneumoniae	131 (20.1)
Staphylococcus aureus	58 (8.9)
Acinetobacter baumannii	31 (4.7)
Enterococcus faecium	28 (4.3)
Pseudomonas aeruginosa	22 (3.4)
Enterococcus faecalis	14 (2.1)
MDR, n (%)[‡]	268 (41.0)
XDR, n (%)[‡]	16 (2.5)
Type of empirical antibiotic strategies, n (%)[§]	
Classical	484 (34.1)
MDR coverage	936 (65.9)
Change of antibiotic treatment, n (%)	
Escalation	426 (30.0)
De-escalation	119 (8.4)
No change	877 (61.7)
Clinical resolution, n (%)	913 (63.5)

Data are presented as numbers (percent). [†]In 754 isolates; [‡]In 653 isolates; [§]Available in 1,420 patients. SBP, spontaneous bacterial peritonitis; UTI, urinary tract infection; SIRS, systemic inflammatory response syndrome; qSOFA, quick sepsis-related organ failure assessment; MDR, multidrug-resistant; XDR, extensively drug-resistant.

Table 3. Prevalence of MDR/XDR bacteria and specific types

Strains	Number of isolates	Number of patients	Number of episodes of infections	Incidence (%)		
				Per isolate (n = 653)	Per patient (n = 560)	Per episode (n = 627)
Total	284	259	284	43.5	46.3	45.3
MDR	268	243	265	41.0	43.4	42.3
ESBL-E	50	50	53	7.7	8.9	8.5
ESBL-KP	15	15	16	2.3	2.7	2.6
CRKP	5	5	5	0.8	0.9	0.8
CRPA	4	4	4	0.6	0.7	0.6
CRE	6	6	6	0.9	1.1	1.0
CRAB	4	4	4	0.6	0.7	0.6
MRSA	20	20	22	3.1	3.6	3.5
VSE	26	26	26	4.0	4.6	4.2
XDR	16	16	19	2.5	2.9	3.0

Data are presented as numbers or percentages. MDR, multidrug-resistant; ESBL-E, extended-spectrum β-lactamase *Escherichia coli*; ESBL-KP, extended-spectrum β-lactamase *Klebsiella pneumoniae*; CRKP, carbapenem-resistant *Klebsiella pneumoniae*; CRPA, carbapenem-resistant *Pseudomonas aeruginosa*; CRE, carbapenem-resistant *Enterobacteriaceae*; CRAB, carbapenem-resistant *Acinetobacter baumannii*; MRSA, methicillin-resistant *Staphylococcus aureus*; VSE, vancomycin-susceptible *enterococci*; XDR, extensively drug-resistant.

empirical antibiotic therapy was significantly lower in the Chinese cohort compared with the global cohort (21.5% vs. 61.2%, $P < 0.001$). Adherence rates were highest in the United States (65.0%) and Europe (64.0%) (Supplementary Table 9). Chinese patients were more likely to receive broader-spectrum empirical antibiotics beyond guideline recommendations (75.1% vs. 35.5%, $P < 0.001$). Specifically, β-lactamase inhibitors such as piperacillin–tazobactam

Table 4. Factors associated with in-hospital/28-day/90-day death in patients with cirrhosis and infection

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
In-hospital						
Hypertension	2.373	1.024–5.497	0.044	3.888	1.403–10.770	0.009
Recent infection	3.523	1.436–8.644	0.006	5.567	1.689–18.346	0.005
Recent quinolone prophylaxis	2.355	0.692–8.018	0.170	5.489	1.045–28.837	0.044
Recent antibiotic use	1.533	0.639–3.679	0.338	0.229	0.059–0.885	0.033
HE grade 3/4	5.863	2.344–14.665	<0.001	5.425	1.890–15.565	0.002
MELDs	1.081	1.048–1.116	<0.001	1.086	1.048–1.126	<0.001
28-day						
Cryptogenic etiology	1.480	0.887–2.469	0.134	2.252	1.258–4.030	0.006
History of TIPS	1.627	0.797–3.321	0.181	2.193	1.043–4.612	0.038
Recent use of PPIs	0.808	0.517–1.263	0.349	0.586	0.348–0.985	0.044
HE	1.914	1.144–3.202	0.013	1.874	1.102–3.186	0.020
MELDs	1.082	1.071–1.093	<0.001	1.092	1.046–1.139	<0.001
90-day						
Other etiology	1.078	0.777–1.497	0.652	1.483	1.009–2.179	0.045
History of TIPS	1.681	0.961–2.943	0.069	1.984	1.104–3.563	0.022
Little or no ascites	0.471	0.280–0.793	0.005	0.535	0.313–0.913	0.022
HE	2.395	1.661–3.455	<0.001	2.138	1.464–3.122	<0.001
MELDs	1.070	1.061–1.080	<0.001	1.076	1.064–1.088	<0.001
Positive cultures	1.720	1.167–2.534	0.006	1.772	1.002–3.134	0.049

Statistical analysis was performed using the Cox proportional hazards model. HRs and 95% CIs were adjusted for age, sex, diabetes mellitus, hypertension, etiology of cirrhosis, recent infection, history of TIPS, recent medications, recent antibiotic use, recent ICU admission, ascites, HE, MELD score, positive cultures, MDR, and empirical antibiotic treatment. HR, hazard ratio; CI, confidence interval; HE, hepatic encephalopathy; MELD, model for end-stage liver disease; TIPS, transjugular intrahepatic portosystemic shunt; PPIs, proton pump inhibitors.

Table 5. Comparison of the characteristics of infections between patients in the study and those in the global study

Characteristics	China (n = 1,438)	Global (n = 1,302)[†]	*P*-value
Type of infection, n (%)			<0.001
Community acquired	1,245 (86.6)	964 (74.0)	
Nosocomial	193 (13.4)	338 (26.0)	
Site of infection, n (%)			<0.001
Unproven bacterial infection	115 (6.9)	20 (1.5)	
Proven site	1,553 (93.1)	1,282 (98.5)	
SBP	326 (21.0)	354 (27.6)	<0.05
Pneumonia	445 (28.7)	242 (18.9)	<0.05
UTI	134 (8.6)	289 (22.5)	<0.05
Spontaneous bacteremia	236 (15.2)	100 (7.8)	<0.05
Skin and soft tissue	96 (6.2)	101 (7.9)	>0.05
Bacterial entero-colitis	44 (2.8)	31 (2.4)	>0.05
Cholangitis	118 (7.6)	37 (2.9)	<0.05
Others	154 (9.9)	128 (10.0)	>0.05
Severity of infection, n (%)			
SIRS	780 (54.2)	405 (36.2)	<0.001
qSOFA	104 (7.2)	255 (22.8)	<0.001
Septic shock	117 (8.1)	174 (13.4)	<0.001
Patients with positive cultures, n (%)	620 (43.1)	740 (56.8)	<0.001
Isolates per patient, n (%)			<0.001
1	506 (35.2)	592 (45.5)	
>1	114 (7.9)	148 (11.4)	
Type of strains isolated, n (%)			
Gram-negative	441 (58.5)	561 (58.5)	>0.05
Gram-positive	212 (28.1)	360 (37.5)	<0.05
Fungi	101 (13.4)	38 (4.0)	<0.05
Most frequently isolated bacteria, n (%)			
Escherichia coli	142 (21.7)	266 (28.9)	<0.05
Klebsiella pneumoniae	131 (20.1)	143 (15.5)	<0.05
Staphylococcus aureus	58 (8.9)	78 (8.5)	>0.05
Enterococcus faecalis	14 (2.1)	52 (5.6)	<0.05
Enterococcus faecium	28 (4.3)	53 (5.8)	>0.05
MDR bacteria, n (%)	268 (41.0)	322 (35.0)	0.014
ESBL- *Enterobacteriaceae*	50 (18.7)	89 (27.6)	<0.05
CRE	6 (2.2)	35 (10.9)	<0.05
Acinetobacter baumannii	7 (2.6)	19 (5.9)	>0.05
MRSA	20 (7.5)	14 (4.3)	>0.05
VRE	0 (0.0)	16 (5.0)	<0.05
XDR bacteria, n (%)	16 (2.5)	73 (7.9)	<0.05

Data are presented as numbers (percent). Statistical analysis was performed using the Chi-squared test or Fisher's exact test. [†]Data were extracted from a global study [Piano S, Singh V, Caraceni P, Maiwall R, Alessandria C, Fernandez J, *et al*. Epidemiology and Effects of Bacterial Infections in Patients With Cirrhosis Worldwide. Gastroenterology 2019;156(5):1368–1380.e1310]. SBP, spontaneous bacterial peritonitis; UTI, urinary tract infection; SIRS, systemic inflammatory response syndrome; qSOFA, quick sepsis-related organ failure assessment; MDR, multidrug-resistant; ESBL, extended-spectrum β-lactamase; CRE, carbapenem-resistant *Enterobacteriaceae*; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant *enterococci*; XDR, extensively drug-resistant.

Table 6. Comparison of antibiotic treatment practices in Chinese patients with cirrhosis versus those in the global study

Characteristics	China (n = 1,438)	Global (n = 1,302)†	*P*-value
In vitro susceptibility to empirical antibiotic treatment, n (%)			0.008
Susceptible	400 (76.8)	500 (69.9)	
Non-susceptible	121 (23.2)	215 (30.1)	
Adherence to the EASL empirical antibiotic treatment recommendations, n (%)			
Adherence	267 (21.5)	796 (61.2)	<0.001
Non-adherence	976 (78.5)	504 (38.8)	<0.001
Weaker	243 (24.9)	325 (64.5)	<0.001
Broader	733 (75.1)	179 (35.5)	<0.001
Change of antibiotic treatment, n (%)			
Escalation	426 (30.0)	477 (36.6)	<0.05
De-escalation	119 (8.4)	102 (7.8)	>0.05
No change	877 (61.7)	(55.5)	<0.05
Clinical resolution, n (%)	913 (63.5)	1,038 (79.8)	<0.001

Data are presented as numbers (percent). Statistical analysis was performed using the Chi-squared test or Fisher's exact test. †Data were extracted from a global study [Piano S, Singh V, Caraceni P, Maiwall R, Alessandria C, Fernandez J, *et al*. Epidemiology and Effects of Bacterial Infections in Patients With Cirrhosis Worldwide. Gastroenterology 2019;156(5):1368–1380.e1310]. EASL, European Association for the Study of the Liver.

and cefoperazone–sulbactam (39.6%) and carbapenems (17.6%) were more frequently used in China. In contrast, classical β-lactamases/β-lactamase inhibitor combinations (e.g., amoxicillin–clavulanic acid or ampicillin–sulbactam, 5.5%) and third-generation cephalosporins (19.7%) were prescribed less commonly (Supplementary Table 10). Notably, the clinical resolution rate was significantly lower in the Chinese cohort compared to the global population (63.5% vs. 79.8%, $P < 0.001$).

Discussion

In this large, multicenter cohort study, we characterized the demographic, clinical, and microbiological profiles of patients with cirrhosis and bacterial infections in China and compared these findings with global data to highlight regional disparities. Patients in the Chinese cohort exhibited a high prevalence of community-acquired infections, with non-SBP infections being the predominant type. Notably, the emergence of *Klebsiella pneumoniae* as a leading pathogen and the high rate of MDR isolates (41.0%) were concerning trends. Even more alarming was the low adherence to clinical practice guidelines for empirical antibiotic therapy, which was associated with a suboptimal clinical resolution rate. These findings underscore the urgent need for region-specific strategies for infection prevention and treatment optimization.

Compared to the global cohort, Chinese patients were more likely to develop pneumonia, a trend also observed in other Asian populations when data were stratified by region.[26] This higher incidence aligns with previous studies[3,14,26,27] and may be attributed to factors such as high population density, environmental or climatic conditions, and lifestyle behaviors like smoking.[14,26] Additionally, Chinese patients had a significantly higher proportion of spontaneous bacteremia compared to other regions, a concerning finding given the strong association between bloodstream infections and poor outcomes in patients with cirrhosis.[28] In contrast, UTIs were markedly less frequent in this cohort, a trend consistent with prior Chinese studies.[27] This may be partly explained by fewer ICU admissions and, consequently, less frequent use of indwelling urinary catheters, a known risk factor for UTIs, especially in Western countries.[6,27]

Several microbiological trends warrant attention. Gram-negative bacteria were the most common pathogens, with *Enterobacteriaceae* being the predominant isolate, consistent with global data. Notably, *Klebsiella pneumoniae* emerged as the second most frequent isolate, nearly as common as *Escherichia coli*. Infections caused by *Klebsiella pneumoniae* are associated with increased mortality, prolonged hospital stays, and higher healthcare costs due to its virulence, resistance, and transmissibility.[29–31] Of particular concern is the emergence of carbapenem-resistant hypervirulent *Klebsiella pneumoniae*, which is both MDR and highly transmissible.[32–36] This poses a significant public health threat, especially for cirrhotic patients who are inherently more susceptible to severe infections.

Timely surveillance and targeted intervention strategies are urgently needed to curb its spread.

Another major concern was the high prevalence of MDR bacteria, which reached 41.0%, exceeding global estimates, despite the predominance of community-acquired infections in our cohort. Among second infections, exclusively nosocomial, MDR isolates accounted for 51.9% of cases. This likely contributes to the substantial negative impact of secondary infections on survival among cirrhotic patients.[19] Regarding resistance patterns, ESBL-producing *Enterobacteriaceae* remained the most common, consistent with global data. However, we also observed a significantly higher proportion of MRSA isolates in our study population. The increasing prevalence of *Staphylococcus aureus* has been linked to the widespread use of invasive medical procedures and exogenous sources of infection.[37] This is particularly concerning given MRSA's broad array of virulence factors, its ability to acquire resistance, and its potential to generate novel clones.[38] A prior study has shown that MRSA infections are associated with significantly higher mortality in patients with cirrhosis compared to infections caused by other bacterial species.[39]

Our findings also highlighted important gaps in clinical practice. Adherence to EASL guidelines for empirical antibiotic therapy was substantially lower in the Chinese cohort,

with a strong preference for broader-spectrum agents. Paradoxically, this more aggressive antibiotic approach did not translate into improved clinical outcomes, as evidenced by a significantly lower clinical resolution rate compared to the global cohort. While this discrepancy may reflect differences in patient characteristics or definitions of clinical resolution, it nonetheless underscores the urgent need to optimize empirical antibiotic strategies. For example, the antibiotic piperacillin–tazobactam, which was frequently used in our cohort, is known to be suboptimal against ESBL-producing *Enterobacteriaceae*,[40] the most common MDR bacteria identified. Second, the culture-positive rate in our cohort was 43.1%, which was lower than that reported in the global study. This discrepancy may be attributed to differences in infection types. For instance, compared with the global cohort, our study included a lower proportion of UTIs and a higher proportion of pneumonia and unproven infections—conditions that are often diagnosed clinically without a confirmed microbiological culture. Third, the widespread use of PPIs, which has been associated with an increased risk of bacterial infections,[41,42] along with the underutilization of rifaximin, β-blockers, and quinolone prophylaxis, which are known to reduce microbial translocation and the risk of bacterial infections,[43–46] may have contributed to the high infection rate observed in this predominantly community-acquired setting.

This study has several limitations. First, its retrospective design may introduce selection bias. Additionally, heterogeneity in diagnostic and therapeutic practices across participating centers, along with the absence of centralized microbiological testing, could have led to misclassification of infection sources and inconsistencies in sample quality and clinical management.[47] Second, the lack of long-term follow-up data limits our ability to evaluate extended outcomes. This is particularly relevant given prior evidence indicating that up to 63% of cirrhotic patients with infections may die within one year.[8] Third, we did not adjust for potential confounders such as age, sex, and liver disease etiology when comparing the epidemiological patterns in our cohort to those in the global study. Lastly, variations in local healthcare infrastructure, resource availability, and prescribing practices across different countries and hospitals may influence adherence to international guidelines. Furthermore, the local epidemiology of infections may influence empirical antibiotic choices, which could confound the interpretation of guideline adherence.

Conclusions

This study reveals a distinct epidemiological pattern of bacterial infections in patients with cirrhosis in China compared to other regions worldwide. Non-SBP infections predominated, with pneumonia emerging as the most common infection type. The rising prevalence of *Klebsiella pneumoniae*, the substantial burden of MDR organisms, and the suboptimal adherence to clinical guidelines underscore critical challenges in infection management. These findings call for increased awareness and coordinated efforts among clinicians, infection control specialists, and public health authorities to develop region-specific strategies aimed at improving outcomes for this vulnerable population.

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Conflict of interest

YS has been an Editorial Board Member of *Journal of Clinical and Translational Hepatology* since 2022. The other authors have no conflict of interests related to this publication.

Author contributions

Study design, data analysis (XZ, YS, JS, QY), manuscript drafting (XZ, YS), study concept, and study supervision (YS). All authors contribute to data collection, data interpretation, manuscript editing. All authors have approved the final version and publication of the manuscript.

Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2024) and was approved by the Ethics Committee of the First Affiliated Hospital, School of Medicine, Zhejiang University (IIT20230123B-R1). Written informed consent was waived by the Ethics Committee.

Data sharing statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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