World Journal of Hepatology

Submit a Manuscript: https://www.f6publishing.com

World J Hepatol 2024 December 27; 16(12): 1441-1449

DOI: 10.4254/wjh.v16.i12.1441

ISSN 1948-5182 (online)

ORIGINAL ARTICLE

Retrospective Study

Clinical analysis of *Klebsiella pneumoniae* infection in patients with liver cirrhosis in Beijing

Yu Zhang, Hong Zhao, Shi-Bo Ji, Hui-Chun Xing

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade B
Novelty: Grade B
Creativity or Innovation: Grade B
Scientific Significance: Grade B

P-Reviewer: Babani SA

Received: June 4, 2024
Revised: October 7, 2024
Accepted: November 12, 2024
Published online: December 27, 2024
Processing time: 178 Days and 6.9 Hours

Yu Zhang, Shi-Bo Ji, Hui-Chun Xing, Center of Liver Diseases Division 3, Beijing Ditan Hospital, Capital Medical University, Peking University Ditan Teaching Hospital, Beijing 100015, China

Hong Zhao, Center of Liver Diseases Division 1, Beijing Ditan Hospital, Capital Medical University, Peking University Ditan Teaching Hospital, Beijing 100015, China

Corresponding author: Hui-Chun Xing, PhD, Professor, Center of Liver Diseases Division 3, Beijing Ditan Hospital, Capital Medical University, Peking University Ditan Teaching Hospital, No. 8 Jingshun East Street, Chaoyang District, Beijing 100015, China.
hchxing@sohu.com

Abstract

BACKGROUND

The incidence of *Klebsiella pneumoniae* (*K. pneumoniae*) infection in patients with cirrhosis has been increasing over recent years, posing certain difficulties in clinical treatment.

AIM

To analyze the clinical features of patients with liver cirrhosis and identify the risk factors to help the early diagnosis and treatment of these diseases.

METHODS

Clinical data and laboratory tests were collected from 72 patients with cirrhosis confirmed by secretion or blood culture of *K. pneumoniae* infection at Beijing Ditan Hospital, Capital Medical University, between May 2016 and October 2018. Data from hospitalized patients with liver cirrhosis and *K. pneumoniae* infections, including age, sex, antimicrobial use, length of stay, site of infection, distribution of pathogenic bacteria, complications, invasive operations, laboratory indicators, treatment, and clinical regression, were extracted and retrospectively analyzed. Clinical data and biochemical values were included in the multivariate logistic regression analysis.

RESULTS

A total of 52 men and 20 women, with an age range from 29 to 85 years and an average age of 57.7 ± 12.54, were analyzed. The incidence of hospital *K. pneumoniae* infection in patients with cirrhosis was approximately 19.44%. The most common the infection site was the bloodstream, followed by the respiratory tract,

abdominal cavity, and biliary tract. Risk factors for infection were old age, long hospital stays, gastrointestinal bleeding, and low serum albumin levels, while prophylactic antibiotics were protective factors. The multivariate analysis suggested that other infections, chronic diseases, and invasive procedures were independent factors.

CONCLUSION
In clinical practice, the length of hospital stays should be shortened as much as possible, invasive operations should be reduced, antibiotics should be rationally used, and the patients' liver function should be timely improved. This is of great significance for reducing the incidence of hospital infection.

Key Words: *Klebsiella pneumoniae*; Cirrhosis; Antibiotics; Logistic regression; Hospital infection

Core Tip: Patients with cirrhosis are susceptible to infections, particularly nosocomial infections, due to severe impairment of liver function and reduced immune function. The study profoundly expands our knowledge about the clinical feature of the Klebsiella pneumoniae (*K. pneumoniae*) infection with chronic liver disease. And this is the first study of its kind to be published in China on *K. pneumoniae* infection in individuals with liver cirrhosis. The findings of this investigation are reliable and show a considerable difference.

Citation: Zhang Y, Zhao H, Ji SB, Xing HC. Clinical analysis of *Klebsiella pneumoniae* infection in patients with liver cirrhosis in Beijing. *World J Hepatol* 2024; 16(12): 1441-1449
URL: https://www.wjgnet.com/1948-5182/full/v16/i12/1441.htm
DOI: https://dx.doi.org/10.4254/wjh.v16.i12.1441

INTRODUCTION

Cirrhosis is a late-stage liver disease. Patients with cirrhosis are susceptible to infections, particularly nosocomial infections, owing to severe impairment of liver function and reduced immune function[1]. Studies have shown that the mortality rate of patients with cirrhosis and nosocomial infections is 15%, significantly higher than the 7% mortality rate for uninfected patients[2,3]. Furthermore, nosocomial infections not only prolong the hospital stay of these patients but also significantly affect their prognosis[4]. *Klebsiella pneumoniae* (*K. pneumoniae*) is a major pathogen causing hospital-acquired infections, accounting for over 20% of all hospital-acquired infections with gram-negative bacilli[5-7]. In immunocompromised individuals, classical *K. pneumoniae* strains can cause serious infections, such as pneumonia, meningitis, liver abscesses, wound infections, and sepsis[8-10]. They can also increase drug resistance[11]. In 2017, the World Health Organization published a list of pathogens for which new antimicrobial treatments are urgently required. Within this list, "ESKAPE" (*Enterococcus faecalis*, *Staphylococcus aureus*, *K. pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*) were designated as having "priority status"[12,13]. The incidence of bacteremia in patients with cirrhosis has been increasing over recent years, posing certain difficulties in clinical treatment[13,14]. The current study summarized and analyzed the clinical and laboratory examination characteristics of patients with end-stage liver disease combined with *K. pneumoniae* infection to help with the early diagnosis and treatment of such diseases.

MATERIALS AND METHODS

Patients

Clinical data and laboratory tests were collected from 72 patients with cirrhosis confirmed by secretion or blood culture of *K. pneumoniae* infection at Beijing Ditan Hospital, Capital Medical University, from May 2016 to October 2018. All patients met the diagnostic criteria for cirrhosis, as diagnosed according to the viral hepatitis control program[8]. The laboratory confirmed the pathogenic diagnosis. Alcoholic cirrhosis was diagnosed according to the guidelines for the treatment of alcoholic liver disease[9], and primary biliary cirrhosis was diagnosed according to the consensus on the diagnosis and treatment of primary biliary cirrhosis (also known as primary biliary cholangitis)[10]. Finally, 52 men and 20 women were included in the analysis (age ranged from 29 to 85 years, with an average of 57.7 ± 12.54). Additionally, 12 deaths (16.67%) were observed. This study was approved by the Ethics Committee of the Beijing Ditan Hospital, Capital Medical University, and written informed consent was obtained from all participants.

Clinical information

Clinical information, including age, sex, antimicrobial use, length of stay, site of infection, distribution of pathogenic bacteria, complications, invasive operations, laboratory indicators, treatment, and clinical regression, were collected from all patients using the hospital's electronic medical record system.

Table 1 Comparison of the underlying information, *n* (%)

Variable	Group 1: Death group (*n* = 12)	Group 2: Improved group (*n* = 60)	χ^2	*P* value
Gender:Male	11 (91.7)	41 (68.3)	2.714	0.099
History of hypertension	3 (25)	18 (30)	0.121	0.728
History of diabetes mellitus	3 (25)	15 (25)	0.000	1.000
History of lung disease	2 (16.7)	4 (6.7)	1.309	0.253
History of heart disease	1 (8.3)	7 (11.7)	0.113	0.737
Chronic kidney disease	3 (25)	2 (3.3)	7.264	0.007[a]
Neurological	3 (25)	7 (11.7)	1.486	0.223
History of malignancy	2 (16.7)	9 (15)	0.021	0.884
Heavy alcohol consumption	7 (58.3)	14 (23.3)	5.929	0.015[a]
History of hospitalization within 30 days	4 (33.3)	15 (25)	0.357	0.550
History of antibiotic exposure within 15 days	1 (8.3)	6 (10)	0.032	0.859
Blood glucose > 7.8	4 (33.3)	22 (36.7)	0.048	0.826

[a]$P < 0.05$.

Statistical analysis

The data were collated using Excel 2003, and the comparison of the differences in the indicators was analyzed using SPSS 22.0. The measurement data were expressed as mean ± SD or median (interquartile range), and the count data were expressed as *n* (%). The comparison of normally distributed measurement data between the two groups was performed using the two independent sample *t*-test, while the comparison of count data between the two groups was performed using the χ^2 test. The analysis of influencing factors was performed using dichotomous logistics regression. A *P* value < 0.05 represented statistical significance.

RESULTS

Prevalence and site of nosocomial infections

Nosocomial infections occurred in 14 out of the 72 patients, with an incidence of 19.44%. The sites of infection were bloodstream in 36 cases (50.00%), respiratory tract in 13 cases (18.05%), chest in 11 cases (15.27%), abdomen in eight cases (11.11%), biliary tract in five cases (6.94%), and urinary tract in four cases (5.56%).

Single factor analysis affecting prognosis for improved discharge

The χ^2 test was used to compare the differences in gender, history of hypertension, history of diabetes, history of lung disease, history of heart disease, history of chronic kidney disease, history of neurological disease, history of malignancy, history of heavy alcohol consumption, history of hospitalization within 30 days, history of antibiotic exposure within 15 days, and blood glucose > 7.8 between the death group and the group discharged in good condition. Chronic kidney disease (25% *vs* 3.30%; $\chi^2 = 7.264$, $P = 0.007$) and a history of heavy drinking (58.3% *vs* 23.3%; $\chi^2 = 5.929$, $P = 0.015$) were significantly higher in the death group than in the well-discharge group (Table 1).

The χ^2 test was used to compare differences in the site of infection between the death and discharge groups. However, no differences were found between groups ($\chi^2 = 1.806$, $P = 0.771$). Nevertheless, the χ^2 analysis showed a higher carbapenem resistance (25% *vs* 1.7%; $\chi^2 = 10.376$, $P = 0.001$), a higher rate of co-infection with other bacteria (41.7% *vs* 8.3%; $\chi^2 = 9.290$, $P = 0.002$), and a higher incidence of liver failure (91.7% *vs* 18.3%; $\chi^2 = 25.344$, $P < 0.001$), but also lower occurrence of hepatic encephalopathy (33.3% *vs* 71.7%; $\chi^2 = 22.851$, $P = 0.001$) in the death group than in the well-discharge group (Table 2).

Moreover, the χ^2 test suggested a lower rate of non-admission to the intensive care unit, a higher rate of arteriovenous placement/tracheal intubation/catheterization, higher use of carbapenems and lower use of vancomycin in the death group than in the well-discharge group (Table 3).

A two-independent sample t-test was used to compare and analyze the differences in various measures between the death and the improved discharge groups. The results of the analysis showed significant differences in diastolic blood pressure ($t = -2.385$, $P = 0.020$), total bilirubin (TBIL) ($t = 5.013$, $P < 0.001$), direct bilirubin ($t = 4.287$, $P < 0.001$), albumin (ALB) ($t = -2.144$, $P = 0.035$), and International normalized ratio ($t = 5.365$, $P < 0.001$; Table 4).

Table 2 Comparison of the disease information, *n* (%)

Variable		Death group (*n* = 12)	Improved group (*n* = 60)	χ^2	*P* value
Site of infection	Lung	2 (16.7)	11 (18.3)	1.806	0.771
	Urinary tract	0 (0)	4 (6.7)		
	Blood	6 (50)	30 (50)		
	Ascites	1 (8.3)	7 (11.7)		
	Pleural fluid	3 (25)	8 (13.3)		
Carbapenem-resistant	Yes	3 (25)	1 (1.7)	10.376	0.001[b]
Co-infection with other bacteria	Yes	5 (41.7)	5 (8.3)	9.290	0.002[b]
Co-infection with fungal infections	Yes	3 (25)	7 (11.7)	1.486	0.223
Co-infection with viral infection	Yes	0 (0)	2 (3.3)	0.411	0.521
Nosocomial infection	Yes	4 (33.3)	10 (16.7)	1.773	0.183
Liver failure	Yes	11 (91.7)	11 (18.3)	25.344	0.000[b]
Liver cirrhosis	None	0 (0)	2 (3.3)	4.393	0.494
	HBV	5 (41.7)	30 (50)		
	HCV	1 (8.3)	5 (8.3)		
	Alcoholic	5 (41.7)	11 (18.3)		
	Autoimmune	0 (0)	7 (11.7)		
	Unknown	1 (8.3)	5 (8.3)		
Hepatocellular carcinoma	Yes	3 (25)	16 (26.7)	0.014	0.905
Hepatic encephalopathy	0	4 (33.3)	43 (71.7)	22.851	0.001[b]
	1	0 (0)	10 (16.7)		
	2	5 (41.7)	5 (8.3)		
	3	1 (0.08)	2 (0.03)		
	4	2 (0.17)	0 (0)		
Gastrointestinal hemorrhage	Yes	4 (33.3)	14 (23.3)	0.533	0.465

[b]$P < 0.01$.
HBV: Hepatitis C virus; HCV: Hepatitis C virus.

Logistic regression analysis affecting prognosis for improved discharge

Whether or not the prognosis was improved, discharge was used as the dependent variable Y (Y = 0, death; Y = 1, improved), and each variable that was significantly different between the two groups was used as the independent variable X. Dichotomous logistics regression was used to screen the influencing factors using stepwise regression, and the final analysis showed that chronic kidney disease [B = -4.060, odds ratio (OR) = 0.017], comorbid other bacterial infections (B = -2.715, OR = 0.066), liver failure, arterial-venous placement, and TBIL were the main factors affecting the prognosis for improvement. The results of the final analysis showed that chronic kidney disease (B = -4.060, OR = 0.017), co-infection with other bacteria (B = -2.715, OR = 0.066), liver failure (B = -3.705, OR = 0.025), and higher TBIL (B = -0.008, OR = 0.992) were the main factors affecting the prognosis for discharge (Table 5).

DISCUSSION

The number of patients with chronic liver disease in China is increasing, and many of these patients gradually progress to cirrhosis. Patients with cirrhosis are immunocompromised, and co-infection is one of the common complications in these patients, which can seriously affect their prognosis and increase the burden of medical costs. Statistical analysis shows that the most common pathogenic bacteria are gram-negative bacilli (59.7%), including *Escherichia coli* (*E. coli*) (31.09%) and *K. pneumoniae* (9.06%)[15]. *Klebsiella* spp. includes five species, among which *K. pneumoniae* is the most pathogenic to humans. It is 0.5-0.8 μm × 1-2 μm in size, with thick pods and hairs, without budding and flagella, and with O and K antigens. In recent years, *K. pneumoniae* has become a common pathogen causing hospital-acquired infections. This

Table 3 Comparison of the treatment information, *n* (%)

Variable		Death group (*n* = 12)	Improved group (*n* = 60)	χ^2	*P* value
ICU	No	8 (66.7)	59 (98.3)	21.278	0.001[b]
Arteriovenous catheterization	Yes	4 (33.3)	1 (1.7)	15.518	0.000[b]
Tracheal intubation	Yes	4 (33.3)	1 (1.7)	15.518	0.000[b]
Catheterization cannula	Yes	4 (33.3)	1 (1.7)	15.518	0.000[b]
No antibiotics	Yes	12 (100)	54 (90)	1.309	0.253
Quinolones	Yes	3 (25)	14 (23.3)	0.015	0.901
Carbapenems	Yes	10 (83.3)	25 (41.7)	6.950	0.008[b]
First and second generations of cephalosporin	Yes	1 (8.3)	11 (18.3)	0.720	0.396
Third-generation cephalosporin	Yes	0 (0)	10 (16.7)	2.134	0.144
Antibiotics with an enzyme inhibitor	Yes	5 (41.7)	22 (36.7)	0.107	0.744
Vancomycin	Yes	3 (25)	5 (8.3)		0.094

[b]$P < 0.01$.
ICU: Intensive care unit.

infection is often observed in patients with long hospital stays, severe underlying diseases, and immunocompromised patients using glucocorticoids or chemotherapy drugs. *K. pneumoniae* is found in the human respiratory and intestinal tracts. When the body's immunity decreases, it can cause multi-site infections, such as lung, intracranial, urinary tract, intestinal, and bloodstream infections. In severe cases, sepsis, shock, and multi-organ failure can endanger patients' lives [16,17].

In this study, 14 patients (19.44%) with *K. pneumoniae* sepsis had nosocomial infections. Therefore, focusing on reducing the incidence of nosocomial infections is an important preventive strategy to reduce *K. pneumoniae* infections. The data of the current study suggested that the incidence of nosocomial *K. pneumoniae* infection in patients with cirrhosis was approximately 19.44%, which is slightly lower than the approximately 30% reported in previous studies[18,19]. Patients with cirrhosis are at high risk of infection because they are at the end stage of liver disease owing to the development of hypersplenism and hypoproteinemia and reduced phagocytosis of liver macrophages, significantly reduced cellular and humoral immune function of the body, and the formation of portal hypertension, bruising, edema and increased permeability of the intestinal wall. This leads to dysbiosis of the intestinal flora and easier invasion of bacteria into the abdominal cavity through the intestinal wall[20,21]. In this study, the most common sites of complications of hospital-acquired infections in patients with cirrhosis were the bloodstream and respiratory tract, followed by the abdominal and biliary tract, which is consistent with relevant reports[22]. The study results suggest that the factors associated with hospital-acquired infections in patients with cirrhosis are complex, with older age, longer hospital stay, gastrointestinal bleeding, and low serum ALB levels being high-risk factors for infection, and prophylactic antibiotics being protective factors for infection. Longer hospital stays increase the risk of exposure to pathogenic bacteria[23-25] and cross-infection [26].

In recent years, with the extensive development of invasive procedures and with the widespread use of carbapenems, an increasing number of carbapenem-resistant *K. pneumoniae* have been reported worldwide, posing a serious threat to public health. The China Drug Resistance Surveillance Network showed that *K. pneumoniae* had the second highest isolation rate among gram-negative bacteria in 2021, making it the bloodstream infection pathogen after *E. coli*. Carbapenems are the last class of lactam drugs for the treatment of gram-negative bacteria and are the first-line antibiotics for treating multidrug-resistant *K. pneumoniae* infections[27]. Studies have shown that the resistance rate of *K. pneumoniae* to imipenem and meropenem has increased significantly. Its high virulence and the drug resistance have led to high morbidity and mortality, posing a serious threat to treatment and infection control. Hasan has isolated and identified gram-negative bacteria from 100 of 250 samples collected from burn patients (40%), of which 66 (66%) were carbapenem resistant[28]. Patients with decompensated cirrhosis have a higher risk of infection following the development of gastrointestinal bleeding that causes changes in pH and disrupts the micro-ecological balance in the gut, leading to an overgrowth of intestinal bacteria and dysbiosis of the intestinal flora and an increased risk of infection in patients[29]. Low serum ALB indicates poor liver function and a significantly reduced ability to fight pathogenic bacteria [29]. National and international opinions consider hypoproteinemia as a risk factor for complicating infections in cirrhosis, while prophylactic antibiotics may reduce the incidence of infection[30-32]. Multifactorial analysis suggests that co-infections, chronic diseases, and invasive operations are all independent factors. Since this research was conducted at a single center retrospectively, the external validation cohort was not accessible. Nonetheless, this is the first study of its kind to be published in China on *K. pneumoniae* infection in individuals with liver cirrhosis. The findings of this investigation are reliable and show a considerable difference. A multi-center prospective study with a larger sample size is now being conducted to thoroughly analyze this finding in the future.

Table 4 Comparison of the clinical index

Variable	Prognosis	mean ± SD	*t*	*P* value
Age	Death	60.67 ± 10.76	0.898	0.372
	Improved	57.1 ± 12.87		
Temperature	Death	37.61 ± 1.38	-1.530	0.131
	Improved	38.3 ± 1.44		
Pulse	Death	86.92 ± 15.7	-0.768	0.445
	Improved	90.95 ± 16.78		
Respiratory	Death	21.17 ± 4.53	1.828	0.072
	Improved	19.8 ± 1.68		
SBP	Death	111.5 ± 13.87	-1.136	0.260
	Improved	116.27 ± 13.15		
DBP	Death	64.5 ± 7.48	-2.385	0.020[a]
	Improved	71.63 ± 9.78		
WBC	Death	7 ± 3.01	-0.456	0.650
	Improved	7.81 ± 6.02		
Neutrophils%	Death	81.63 ± 8.36	1.049	0.298
	Improved	77.79 ± 12.05		
Neutrophils	Death	5.78 ± 2.86	-0.356	0.723
	Improved	6.39 ± 5.7		
Lymphocyte	Death	0.8 ± 0.62	-0.242	0.809
	Improved	0.85 ± 0.55		
Hb	Death	91.75 ± 25.5	-0.797	0.428
	Improved	98.61 ± 27.51		
PLT	Death	76.78 ± 45.91	-1.536	0.129
	Improved	129.2 ± 115.81		
ALT	Death	45.54 ± 44.39	-0.454	0.652
	Improved	57.55 ± 89.12		
AST	Death	64.54 ± 43.87	-0.367	0.715
	Improved	74.09 ± 87.51		
TBIL	Death	263.75 ± 183.22	5.013	0.000[b]
	Improved	69.57 ± 107.45		
DBIL	Death	177.75 ± 146.82	4.287	0.000[b]
	Improved	47.26 ± 83.51		
ALB	Death	70.15 ± 144.12	2.225	0.029[a]
	Improved	29.72 ± 6.59		
CHE	Death	1644.25 ± 579.51	-2.144	0.035[a]
	Improved	2710.68 ± 1694.73		
INR	Death	2.54 ± 1.05	5.365	0.000[b]
	Improved	1.53 ± 0.46		
Cr	Death	102.76 ± 58.45	1.520	0.133
	Improved	78.93 ± 47.74		
eGFR	Death	78.86 ± 34.63	-1.410	0.163

	Improved	92.42 ± 29.56		
CRP	Death	33.66 ± 37.7	-0.475	0.636
	Improved	162.16 ± 891.13		
PCT	Death	3.13 ± 5.23	-0.498	0.620
	Improved	6.03 ± 19.86		
CD4	Death	177.6 ± 106.5	-2.016	0.052
	Improved	434.76 ± 278.74		
Days of in-hospital	Death	24.17 ± 26.7	0.540	0.591
	Improved	21.25 ± 14.59		
Ascites	Death	49.09 ± 33.76	1.509	0.136
	Improved	31.81 ± 35.02		

[a]$P < 0.05$.
[b]$P < 0.01$.
SBP: Systolic blood pressure; DBP: Diastolic blood pressure; WBC: White blood cell; Hb: Hemoglobin; PLT: Platelet; ALT: Alanine transaminase; AST: Aspartate transaminase; TBIL: Total bilirubin; DBIL: Direct Bilirubin; ALB: Albumin; CHE: Cholinesterase; INR: International normalized ratio; Cr: Creatinine; eGFR: Glomerular filtration rate; CRP: C-reaction protein; PCT: Procalcitonin; CD4: Cluster of differentiation 4 cell.

Table 5 Logistics regression analysis of the influence on prognosis

Variable	B	SE	Wald	*P* value	OR	95%CI for OR
Chronic kidney disease	-4.060	2.099	3.742	0.053	0.017	0.000-1.055
Combined with other bacteria	-2.715	1.615	2.827	0.093	0.066	0.003-1.568
Liver failure	-3.705	1.455	6.481	0.011[a]	0.025	0.001-0.426
Arteriovenous catheterization	-2.873	1.589	3.268	0.071	0.057	0.003-1.274
TBIL	-0.008	0.004	4.397	0.036[a]	0.992	0.984-0.999
Contant	6.523	1.873	12.124	0.000[a]	680.624	-

[a]$P < 0.05$.
TBIL: Total bilirubin; OR: Odds ratio.

CONCLUSION

Therefore, patients' length of stay should be shortened, invasive operations should be reduced, antibacterial drugs should be applied, and liver function should be promptly improved in clinical practice, as this could significantly reduce the incidence of nosocomial infections in patients. Currently, drug resistance in *K. pneumoniae* has become an important health problem that cannot be ignored and requires more attention and research. This study has several limitations. First, because this study was performed in a single center and retrospectively, an external validation cohort was not available. Second, as a retrospective study, there is a lack of drug resistance test data of the included patients. A further multicenter prospective study with a larger sample size is currently in progress to validate our study results.

FOOTNOTES

Author contributions: Guarantor of the article Xing HC accepts full responsibility for the conduct of the study, has access to the data, and has control of the decision to publish; Zhang Y proposed the concept, contributed to the study design, wrote the manuscript, and performed statistical analysis; Zhao H contributed to the study design and performed statistical analysis, and data collection; Ji SB contributed to data collection.

Supported by the National Key R & D Program of China, No. 2021YFC2301800.

Institutional review board statement: The study was reviewed and approved by the Ethics Committee of the Beijing Ditan Hospital, No. JDLZ[2017]-001.

Informed consent statement: Written informed consent was obtained from all participants.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Data sharing statement: No additional data are available.

Country of origin: China

ORCID number: Yu Zhang 0000-0002-3469-152X; Hui-Chun Xing 0000-0002-9111-9669.

S-Editor: Li L
L-Editor: A
P-Editor: Zhao YQ

REFERENCES

1 **Yardeni D**, Ghany MG. Review article: hepatitis B-current and emerging therapies. *Aliment Pharmacol Ther* 2022; **55**: 805-819 [PMID: 35224760 DOI: 10.1111/apt.16828]
2 **Iriana S**, Sharma S, McDonough S, Zarate ER, Adler DG. Outcomes among inpatients with cirrhosis and Clostridioides difficile infection in the modern era: results from an analysis of the National Inpatient Sample. *Ann Gastroenterol* 2021; **34**: 721-727 [PMID: 34475744 DOI: 10.20524/aog.2021.0646]
3 **Wong F**, Piano S, Singh V, Bartoletti M, Maiwall R, Alessandria C, Fernandez J, Soares EC, Kim DJ, Kim SE, Marino M, Vorobioff J, Barea RCR, Merli M, Elkrief L, Vargas V, Krag A, Singh SP, Lesmana LA, Toledo C, Marciano S, Verhelst X, Intagliata N, Rabinowich L, Colombato L, Kim SG, Gerbes A, Durand F, Roblero JP, Bruns T, Yoon EL, Girala M, Pyrsopoulos NT, Kim TH, Yim SY, Juanola A, Gadano A, Angeli P; International Club of Ascites Global Study Group. Clinical features and evolution of bacterial infection-related acute-on-chronic liver failure. *J Hepatol* 2021; **74**: 330-339 [PMID: 32781201 DOI: 10.1016/j.jhep.2020.07.046]
4 **Onorato L**, Monari C, Capuano S, Grimaldi P, Coppola N. Prevalence and Therapeutic Management of Infections by Multi-Drug-Resistant Organisms (MDROs) in Patients with Liver Cirrhosis: A Narrative Review. *Antibiotics (Basel)* 2022; **11** [PMID: 35203834 DOI: 10.3390/antibiotics11020232]
5 **Di Tella D**, Tamburro M, Guerrizio G, Fanelli I, Sammarco ML, Ripabelli G. Molecular Epidemiological Insights into Colistin-Resistant and Carbapenemases-Producing Clinical Klebsiella pneumoniae Isolates. *Infect Drug Resist* 2019; **12**: 3783-3795 [PMID: 31819559 DOI: 10.2147/IDR.S226416]
6 **Cejas D**, Elena A, Guevara Nuñez D, Sevillano Platero P, De Paulis A, Magariños F, Alfonso C, Berger MA, Fernández-Canigia L, Gutkind G, Radice M. Changing epidemiology of KPC-producing Klebsiella pneumoniae in Argentina: Emergence of hypermucoviscous ST25 and high-risk clone ST307. *J Glob Antimicrob Resist* 2019; **18**: 238-242 [PMID: 31202977 DOI: 10.1016/j.jgar.2019.06.005]
7 **Zhang Z**, Sun Z, Tian L. Antimicrobial Resistance Among Pathogens Causing Bloodstream Infections: A Multicenter Surveillance Report Over 20 Years (1998-2017). *Infect Drug Resist* 2022; **15**: 249-260 [PMID: 35115793 DOI: 10.2147/IDR.S344875]
8 **Gonzalez-Ferrer S**, Peñaloza HF, Budnick JA, Bain WG, Nordstrom HR, Lee JS, Van Tyne D. Finding Order in the Chaos: Outstanding Questions in Klebsiella pneumoniae Pathogenesis. *Infect Immun* 2021; **89**: e00693-20 [PMID: 33558323 DOI: 10.1128/IAI.00693-20]
9 **Bengoechea JA**, Sa Pessoa J. Klebsiella pneumoniae infection biology: living to counteract host defences. *FEMS Microbiol Rev* 2019; **43**: 123-144 [PMID: 30452654 DOI: 10.1093/femsre/fuy043]
10 **Sá-Pessoa J**, Przybyszewska K, Vasconcelos FN, Dumigan A, Frank CG, Hobley L, Bengoechea JA. Klebsiella pneumoniae Reduces SUMOylation To Limit Host Defense Responses. *mBio* 2020; **11**: e01733-20 [PMID: 32994335 DOI: 10.1128/mBio.01733-20]
11 **Scholtz V**, Vaňková E, Kašparová P, Premanath R, Karunasagar I, Julák J. Non-thermal Plasma Treatment of ESKAPE Pathogens: A Review. *Front Microbiol* 2021; **12**: 737635 [PMID: 34712211 DOI: 10.3389/fmicb.2021.737635]
12 **Ghosh S**, Lahiri D, Nag M, Dey A, Pandit S, Sarkar T, Pati S, Abdul Kari Z, Ishak AR, Edinur HA, Ray RR. Phytocompound Mediated Blockage of Quorum Sensing Cascade in ESKAPE Pathogens. *Antibiotics (Basel)* 2022; **11**: 61 [PMID: 35052938 DOI: 10.3390/antibiotics11010061]
13 **Seleem NM**, Abd El Latif HK, Shaldam MA, El-Ganiny A. Drugs with new lease of life as quorum sensing inhibitors: for combating MDR Acinetobacter baumannii infections. *Eur J Clin Microbiol Infect Dis* 2020; **39**: 1687-1702 [PMID: 32328851 DOI: 10.1007/s10096-020-03882-z]
14 **Biondo C**. Bacterial Antibiotic Resistance: The Most Critical Pathogens. *Pathogens* 2023; **12**: 116 [PMID: 36678464 DOI: 10.3390/pathogens12010116]
15 **Hawser SP**, Badal RE, Bouchillon SK, Hoban DJ, Biedenbach DJ, Cantón R, Paterson DL. Monitoring the global in vitro activity of ertapenem against Escherichia coli from intra-abdominal infections: SMART 2002-2010. *Int J Antimicrob Agents* 2013; **41**: 224-228 [PMID: 23305657 DOI: 10.1016/j.ijantimicag.2012.10.014]
16 **Wang SJ**, Yin S, Gu WY, Zhang Y, Li H. Acute-on-chronic liver failure exists in patients with hepatitis B virus-related decompensated cirrhosis. *J Dig Dis* 2018; **19**: 614-625 [PMID: 30226019 DOI: 10.1111/1751-2980.12671]
17 **Cai Q**, Zhu M, Duan J, Wang H, Sheng J. Establishment of prognostic scoring models for different etiologies of acute decompensation in hospitalized patients with cirrhosis. *J Int Med Res* 2019; **47**: 4492-4504 [PMID: 31364441 DOI: 10.1177/0300060519862065]
18 **Morais R**, Liberal R, Santos A, Pita I, Coelho R, Gaspar R, Andrade A, Cardoso H, Rodrigues S, Macedo G. Another clinical unmet need in liver patients: Multidrug resistant bacteria in decompensated cirrhosis. *J Hepatol* 2019; **71**: 844-845 [PMID: 31362835 DOI: 10.1016/j.jhep.2019.06.010]

19 **Fernández J**, Prado V, Trebicka J, Amoros A, Gustot T, Wiest R, Deulofeu C, Garcia E, Acevedo J, Fuhrmann V, Durand F, Sánchez C, Papp M, Caraceni P, Vargas V, Bañares R, Piano S, Janicko M, Albillos A, Alessandria C, Soriano G, Welzel TM, Laleman W, Gerbes A, De Gottardi A, Merli M, Coenraad M, Saliba F, Pavesi M, Jalan R, Ginès P, Angeli P, Arroyo V; European Foundation for the Study of Chronic Liver Failure (EF-Clif). Multidrug-resistant bacterial infections in patients with decompensated cirrhosis and with acute-on-chronic liver failure in Europe. *J Hepatol* 2019; **70**: 398-411 [PMID: 30391380 DOI: 10.1016/j.jhep.2018.10.027]

20 **Philips CA**, Ahamed R, Abduljaleel JKP, Rajesh S, Augustine P. Identification and Analysis of Gut Microbiota and Functional Metabolism in Decompensated Cirrhosis with Infection. *J Clin Transl Hepatol* 2023; **11**: 15-25 [PMID: 36406325 DOI: 10.14218/JCTH.2021.00428]

21 **Singh V**, Singh A, Agarwal R. Midodrine and albumin in decompensated cirrhosis: Down but not out…. *J Hepatol* 2019; **70**: 811 [PMID: 30685125 DOI: 10.1016/j.jhep.2018.11.008]

22 **Ventura E**, Zeneroli ML. Concentration-reinfusion (CR) of ascitic of ascitic fluid in the treatment of decompensated liver cirrhosis with diuretic-resistant ascites. *Postgrad Med J* 1975; **51**: 577-580 [PMID: 1234346 DOI: 10.1136/pgmj.51.598.577]

23 **Levy S**, Samuel D. Prevention of decompensation in cirrhosis: a new youth for β blockers. *Lancet* 2019; **393**: 1571-1572 [PMID: 30910327 DOI: 10.1016/S0140-6736(19)30736-6]

24 **Korula J**. In compensated cirrhosis with portal hypertension, β-blockers reduced a composite of decompensation or death. *Ann Intern Med* 2019; **171**: JC21 [PMID: 31426064 DOI: 10.7326/ACPJ201908200-021]

25 **Villanueva C**, Albillos A, Genescà J, Abraldes JG, Calleja JL, Aracil C, Bañares R, Morillas R, Poca M, Peñas B, Augustin S, Garcia-Pagan JC, Pavel O, Bosch J. Development of hyperdynamic circulation and response to β-blockers in compensated cirrhosis with portal hypertension. *Hepatology* 2016; **63**: 197-206 [PMID: 26422126 DOI: 10.1002/hep.28264]

26 **Preda CM**, Popescu CP, Baicus C, Constantinescu I, Oproiu A, Voiosu T, Diculescu M, Negreanu L, Gheorghe L, Sporea I, Trifan A, Ceausu E, Proca D, Manuc M. Risk of hepatitis B virus reactivation in hepatitis B virus + hepatitis C virus-co-infected patients with compensated liver cirrhosis treated with ombitasvir, paritaprevir/r + dasabuvir + ribavirin. *J Viral Hepat* 2018; **25**: 834-841 [PMID: 29397016 DOI: 10.1111/jvh.12872]

27 **Livermore DM**. The impact of carbapenemases on antimicrobial development and therapy. *Curr Opin Investig Drugs* 2002; **3**: 218-224 [PMID: 12020049]

28 **Hasan SA**, Raoof WM, Ahmed KK. Antibacterial activity of deer musk and Ziziphus spina-christi against carbapebem resis-tant gram negative bacteria isolated from patients with burns and wounds. *Regul Mech Biosyst* 2024; **15**: 267-278 [DOI: 10.15421/022439]

29 **Zaccherini G**, Baldassarre M, Bartoletti M, Tufoni M, Berardi S, Tamè M, Napoli L, Siniscalchi A, Fabbri A, Marconi L, Antognoli A, Iannone G, Domenicali M, Viale P, Trevisani F, Bernardi M, Caraceni P. Prediction of nosocomial acute-on-chronic liver failure in patients with cirrhosis admitted to hospital with acute decompensation. *JHEP Rep* 2019; **1**: 270-277 [PMID: 32039378 DOI: 10.1016/j.jhepr.2019.07.005]

30 **Piano S**, Tonon M, Vettore E, Stanco M, Pilutti C, Romano A, Mareso S, Gambino C, Brocca A, Sticca A, Fasolato S, Angeli P. Incidence, predictors and outcomes of acute-on-chronic liver failure in outpatients with cirrhosis. *J Hepatol* 2017; **67**: 1177-1184 [PMID: 28733221 DOI: 10.1016/j.jhep.2017.07.008]

31 **Picon RV**, Bertol FS, Tovo CV, de Mattos ÂZ. Chronic liver failure-consortium acute-on-chronic liver failure and acute decompensation scores predict mortality in Brazilian cirrhotic patients. *World J Gastroenterol* 2017; **23**: 5237-5245 [PMID: 28811718 DOI: 10.3748/wjg.v23.i28.5237]

32 **Alexopoulou A**, Vasilieva L, Mani I, Agiasotelli D, Pantelidaki H, Dourakis SP. Single center validation of mortality scores in patients with acute decompensation of cirrhosis with and without acute-on-chronic liver failure. *Scand J Gastroenterol* 2017; **52**: 1385-1390 [PMID: 28851246 DOI: 10.1080/00365521.2017.1369560]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com