Original Article

Clinical characteristics and risk factors for *Klebsiella pneumoniae* bloodstream infection in 152 immunocompetent patients

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Abstract

Objective: To investigate the clinical characteristics and prognostic risk factors for *Klebsiella pneumoniae* bloodstream infections in immunocompetent patients.

Methods: The study included patients with *K. pneumoniae* bloodstream infection treated in Zhongda Hospital from June 2016 to June 2021. Clinical data and antibiotic susceptibility test results were retrospectively collected and analyzed. Independent risk factors for mortality were screened using the chi-square test and multivariate logistic regression.

Results: A total of 152 patients were included in the analysis. In our cohort, 77.6% of patients were older than 60 years, and 80.9% of them had community-acquired infections. The most common complications were type 2 diabetes, hypertension, and stroke sequelae. The proportion of patients with septic shock or abscesses was 34.9% and 25.7%, respectively. There were significant differences in the site of infection, septic shock, and serum levels of procalcitonin, hypersensitive C-reactive protein, D-dimer, creatinine, and lactic acid between survivors and non-survivors (p < 0.05). Multivariate regression analysis showed that hospital-acquired infections, septic shock, length of hospital stay, and creatinine levels were independent risk factors for mortality. Antibiotic susceptibility test results indicated that clinical outcomes varied depending on bacterial sensitivity to ampicillin/sulbactam.

Discussion: *Klebsiella pneumoniae* is a common community-acquired and hospital-acquired bacteria and usually infects older people with complications such as diabetes. Nosocomial infections, length of stay, septic shock, and renal insufficiency are potentially associated with poor prognosis. Bacterial susceptibility to ampicillin/sulbactam affects prognosis.

Key words: Klebsiella pneumoniae; bloodstream infection; clinical features; antibiotic resistance; risk factors.

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Introduction

Klebsiella pneumoniae (KP) is a common pathogenic bacillus that causes infections in community and hospital settings. The 2019 China Antimicrobial Surveillance Network (CHINET) report revealed that the rate of isolation of KP in respiratory specimens was 20.6%, higher than that of all other bacterial species [1]. The detection rate of KP in blood samples was 16.5%, second to Escherichia coli. KP is classified into hypervirulent and classic according to virulence. Hypervirulent KP (hvKP) is characterized by high invasiveness and potential migration to the liver, lung, kidney, and eyeball [2,3]. The mortality rate from KP infections complicated with septic shock was 50-77% in the United States [4]. According to the European Antimicrobial Resistance Surveillance Network, the number of deaths caused by carbapenem-resistant KP (CRKP) increased six-fold from 2007 to 2015 [5], representing the highest increase in the rate of mortality among all drug-resistant bacterial infections. Since then, CRKP infections have become a global public health problem. To provide clinical evidence for the rational use of antibiotics and reduce mortality and bacterial resistance to antibiotics, this study retrospectively analyzed clinical characteristics and risk factors associated with KP bloodstream infections in a cohort admitted to our hospital from June 2016 to June 2021.

Methods

General information

This study was conducted from June 2016 to June 2021 in Zhongda Hospital of Southeast University, Jiangsu Province, China. The inclusion criteria were patients older than 18 years with positive blood cultures of KP and symptoms of infection (fever and abnormal leukocyte count). The exclusion criteria were (1) patients with incomplete medical or follow-up records, (2) patients with hematological diseases within 3 months before enrollment, (3) patients undergoing

chemotherapy due to cancer, (4) patients with acquired immune deficiency syndrome, and (5) patients with asymptomatic bacteremia. This study was approved by the Research Ethics Committee of Zhongda Hospital of Southeast University (Approval Number 2018ZDSYLL092-P01) and was registered in the Chinese Clinical Trial Registry (Registration Number ChiCTR1800019036).

Diagnostic criteria for bloodstream infections [6]

KP was isolated from blood cultures of patients with any of the following symptoms or signs: (1) body temperature > 38 °C or < 36 °C accompanied by chills; (2) invasion of the portal system or disseminated infections; (3) systemic infection but no detectable infection foci; (4) systolic blood pressure < 90 mmHg

 Table 1. General data and clinical characteristics of 152

 Klebsiella pneumoniae patients.

Klebsiella pneumoniae patients.	
Clinical and demographic characteristics	n (%)
Sample size	152 (100)
Gender	
Male	100 (65.8)
Female	52 (34.2)
Age (years)	
< 60	34 (22.4)
≥ 60	118 (77.6)
Onset place	
Community acquired	123 (80.9)
Hospital acquired	29 (19.1)
Initial lesion of infection	
Digestive system	61 (40.1)
Urinary system	36 (23.7)
Respiratory system	31 (20.4)
Skin soft tissue	6 (3.9)
Musculoskeletal system	4 (2.6)
Catheter-related	3 (2.0)
Neurological infection	3 (2.0)
Peritoneal cavity infection	2 (1.3)
Unknown location	7 (4.6)
Underlying disease	
Diabetes	65 (42.8)
Hypertension	63 (41.4)
Sequelae of stroke	29 (19.1)
Coronary heart disease	21 (13.8)
Malignant solid tumor	15 (9.9)
Renal insufficiency	12 (7.9)
Hematological diseases	9 (5.9)
Autoimmunity diseases	7 (4.6)
Admission Department	
Emergency ward	42 (27.6)
Intensive care unit	33 (21.7)
Department of general practice	15 (9.9)
Geriatric department	13 (8.6)
Intervention department	11 (7.2)
Department of Gastroenterology	10 (6.6)
Department of general surgery	10 (6.6)
Department of urological surgery	7 (4.6)
Department of nephrology	5 (3.3)
Other department	6 (3.9)
Viscera abscess	39 (25.7)
Septic shock	53 (34.9)
Prognosis after 28 days	
Survival	121 (79.6)
Fatal	31 (20.4)

(1 mmHg = 0.133 kPa) or more than 40 mmHg lower than the systolic blood pressure before admission in patients with septic shock.

Antibiotic susceptibility tests

Bacterial culture and identification were carried out in accordance with National Clinical Examination Procedures (fourth edition). Pathogenic bacteria were identified using the BioMérieux Vitek 2 Compact automatic bacterial identification and drug sensitivity analysis system. The results were interpreted according to the 30th edition of the Clinical and Laboratory Standards Institute (CISI-M100) [7].

Data collection

Clinical and laboratory data of patients with positive blood culture for KP were collected, including (1) general information: gender, age, underlying diseases, initial infection site, other sites of infection, length of hospital stay, complications, and prognosis; (2) laboratory examinations: leukocyte count, platelet count, procalcitonin (PCT), hypersensitive C-reactive protein (hs-CRP), prothrombin time, activated partial thrombin time. D-dimer. albumin. alanine aminotransferase, aspartate aminotransferase, total bilirubin, and creatinine; (4) antibiotic susceptibility test results. The cohort was divided into two groupssurvivors and non-survivors-according to 28-day mortality.

Statistical analysis

All statistical analyses were performed using SPSS version 22.0. Normally distributed and non-normally distributed continuous variables were described as means and standard deviations or medians and interquartile ranges, respectively. Non-normally distributed continuous variables were compared using Student's *t*-test or Mann–Whitney U test. Categorical variables were compared using the chi-square test and expressed as numbers and percentages. The baseline characteristics of survivors and non-survivors at admission were compared by one-way repeated-measures analysis of variance. Independent risk factors were identified by multiple logistic regression. A p value of less than 0.05 was considered statistically significant.

Results

General information

A total of 152 patients (100 males [65.8%] and 52 females [34.2%]) with KP bloodstream infections were included in the study. The age of the cohort ranged from

21 to 96 years, 118 (77.6%) patients were older than 60 years, and 123 (80.9%) of these patients acquired infections from community settings. The most common complications were type 2 diabetes (65, 42.8%), hypertension (63, 41.4%), and stroke sequelae (29, 19.1%). Infections were more common in the digestive system (61, 40.1%), urinary tract (36, 23.7%), respiratory tract (31, 20.4%), biliary tract (26, 17.1%), and gastrointestinal tract (3, 2.0%). Affected patients were admitted to emergency departments (42, 27.6%), intensive care units (33, 21.7%), or general practice departments (15, 9.9%). Fifty-three patients (34.9%) had septic shock. Thirty-nine patients (25.7%) had abscesses in different organs, including the liver (32

Table 2. Comparison of risk factors in survival and death groups.

cases), liver and lung (two cases), liver and brain (one case), lung and brain (one case), lung and kidney (one case), liver + lung + prostate (one case), and liver + lung + eyes (one case). Only 18 (11.8%) patients with abscesses underwent surgery or interventional therapy. The number of survivors and non-survivors was 121 and 31, respectively, with a 28-day mortality rate of 20.4%. The demographic and clinical characteristics of our patients are shown in Table 1.

Prognosis of infections by the chi-square test

Clinical outcomes varied depending on the site of infection ($\chi^2 = 4.381$, p = 0.036) and the development of septic shock ($\chi^2 = 7.914$, p = 0.005). Furthermore, the

	Survival			
Age (years)	71.77 ± 16.16	73.23 ± 12.14	<u>χ²/z</u> 0.172	<u>p</u> 0.864
Length of stay	17.66 ± 12.01	6.1 ± 9.53	5.999	0.000
Gender			0.464	0.496
Male	78 (78.0%)	22 (22.0%)		
Female	43 (82.7%)	9 (17.3%)		
Onset place			4.381	0.036
Community	102 (83.0%)	21 (17.1%)		
Hospital	19 (67.9%)	10 (32.1%)		
Initial lesion of infection			7.002	0.587
Digestive system	50 (82.0%)	11 (18.0%)		
Urinary system	31 (86.1%)	5 (13.9%)		
Respiratory system	23 (74.2%)	8 (25.8%)		
Skin soft tissue	4 (66.7%)	2 (33.3%)		
Musculoskeletal system	4 (100.0%)	0 (0.0%)		
Catheter-related	3 (75.0%)	1 (25.0%)		
Neurological infection	2 (66.7%)	1 (33.3%)		
Peritoneal cavity infection	2 (100.0%)	0 (0.0%)		
Multiple abscess	5 (71.4%)	2 (28.6%)		
inknown location	5 (71.4%)	2 (28.6%)		
Underlying disease		_ ()		
Diabetes	56 (86.2%)	9 (13.8%)	3.000	0.083
Sequelae of stroke	21 (72.4%)	8 (27.6%)	1.142	0.285
Malignant solid tumor	11 (73.3%)	4 (26.7%)	0.089	0.766
Hypertension	51 (81.0%)	12 (19.0%)	0.120	0.729
Coronary heart disease	17 (81.0%)	4 (19.0%)	0.027	0.869
Renal insufficiency	9 (75.0%)	3 (25.0%)	0.002	0.969
Hematological diseases	5 (55.6%)	4 (44.4%)	2.015	0.156
Autoimmunity diseases	5 (71.4%)	2 (28.6%)	0.005	0.845
Septic shock	34 (66.7%)	17 (33.3)	7.914	0.005
MDR KP	19 (82.6%)	4 (17.4%)	0.068	0.795
Lab examination	19 (02.070)	. (1,1,1,3)	0.000	0.795
WBC	11.5 (7.32~15.68)	11.12 (5.53~14.16)	0.718	0.473
PCT	10.53 (2.74~30.52)	26.0 (5.9~54.0)	2.054	0.040
CRP	165.2 (115.9~226.5)	107.2 (11.84~247)	2.115	0.034
IL-6	102 (58.5~153.5)	348 (308~368)	7.628	0.000
PLT	145 (91.5~192.5)	125 (50~196)	1.125	0.261
PT	13.7 (12.25~14.9)	14.9 (12.4~18.8)	2.124	0.034
APTT	29.6 (27.5~32.5)	30.7 (27.4~35.6)	1.441	0.150
D-Dimer	1171 (612~3145)	2286 (909~6749)	1.962	0.049
Cr	88 (69~128.5)	117 (78~181)	2.387	0.049
Lac	2.4 (1.5~3.55)	3.2 (1.8~6.8)	2.116	0.034
Lac Fbil	16.8 (9.95~27.35)	16.4 (9.2~50.5)	0.494	0.621
ALT	37 (21.5~87)	38 (27~106)	0.494	0.382
ALT	43 (28.5~95.5)	47 (32~187)	1.107	0.382
ALB	· · · · · · · · · · · · · · · · · · ·	$\frac{47(32 - 187)}{32.8(29.3 - 37.1)}$	1.630	0.208
	35.5 (31.5~38.2)			
Glu	9.1 (7.29~13.68)	8.18 (6.6~13.67)	0.844	0.399

WBC: white blood cell; PCT: procalcitonin; CRP: C-reactive protein; IL-6: interleukin-6; PLT: platelet; PT: prothrombin time; APTT: activated partial thromboplastin time; Cr: creatinine; Lac: lactic acid; Tbil: total bilirubin; ALT: glutamic-pyruvic transaminase; AST: glutamic oxalacetic transaminase; ALB: albumin; Glu: glucose.

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I able 5. Multiple logistic ana	llysis of risk factors of fatal	outcome.		
Risk factor	В	S.E	Wals	ŀ
Sentic shock	1 836	0.585	9 865	0.0

Risk factor	В	S.E	Wals	р	OR	95% (CI)
Septic shock	1.836	0.585	9.865	0.002	6.27	1.99~19.73
Hospital acquired infection	1.483	0.668	4.933	0.026	4.405	1.19~16.30
Length of stay	-0.198	0.044	20.489	0.000	0.82	0.75~0.89
Creatinine	0.004	0.002	3.970	0.046	1.004	$1.00 \sim 1.008$

levels of PCT ($\chi^2 = 2.054$, p = 0.004), hs-CRP ($\chi^2 =$ 2.115, p = 0.034), D-dimer ($\gamma^2 = 1.962$, p = 0.049), creatinine ($\chi^2 = 2.387$, p = 0.017), and lactic acid ($\chi^2 =$ 2.116, p = 0.034) differed significantly between survivors and non-survivors (Table 2).

Prognosis of infections by regression analysis

The parameters with statistical significance in the univariate analysis were included in the multivariate logistic regression model. Independent risk factors for mortality in KP bloodstream infections were septic shock (OR: 6.27, 95% CI: 1.99-19.73), hospitalacquired infections (OR: 4.405, 95% CI: 1.19-16.30), and creatinine levels (OR: 1.004, 95% CI: 1.00-1.008). Length of hospital stay (OR: 0.82, 95% CI: 0.75-0.89) might be a protective factor (Table 3 and Figure 1).

Antibiotic susceptibility test results

Among 152 strains, 15 (9.9%) were extendedspectrum β -lactamase (ESBL) producers, 23 (15.1%) multidrug-resistant, (10.5%)were 16 were carbapenem-resistant, and 10 (6.6%) were panresistant. These strains were completely resistant to ampicillin. The rate of resistance to cefazolin, furantoin, and ampicillin/sulbactam was 25.9%, 23.3%, and 22.6%, respectively. The rate of resistance to cotrimoxazole, aztreonam, ceftriaxone, ceftazidime, ciprofloxacin, and levofloxacin ranged from 15% to 20%. The rate of resistance to piperacillin/tazobactam, cefotetan, cefepime, gentamicin, tobramycin, and imipenem/cilastatin was approximately 10%.

Figure 1. Multiple logistic analysis of risk factors of fatal outcome.

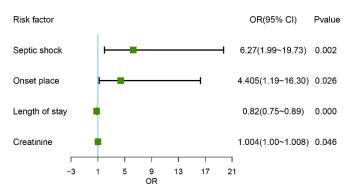


Figure 2. Antibiotics resistance and sensitivity of 152 strains of Klebsiella pneumoniae.

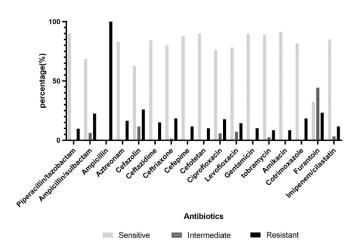


Table 4. Antibiotical resistance and sensitivity of 152 strains of *Klebsiella nneumoniae*

Antibiotics	S (%)	I (%)	R (%)	
Piperacillin/tazobactam	137 (90.1)	0 (0)	15 (9.9)	103
Ampicillin/sulbactam	104 (68.4)	9 (6.2)	33 (22.6)	84
Ampicillin	0 (0)	0 (0)	147 (100)	
Aztreonam	126 (82.9)	0 (0)	25 (16.6)	96
Cefazolin	70 (62.5)	13 (11.6)	29 (25.9)	103
Ceftazidime	128 (84.3)	1 (0.6)	23 (15.1)	75
Ceftriaxone	117 (80.1)	2 (1.4)	27 (18.5)	106
Cefepime	133 (87.5)	1 (0.6)	18 (11.8)	103
Cefotetan	132 (89.8)	0 (0)	15 (10.2)	78
Ciprofloxacin	116 (76.3)	9 (5.9)	27 (17.8)	58
Levofloxacin	119 (78.3)	11 (7.2)	22 (14.5)	12
Gentamicin	131 (89.7)	0(0)	15 (10.3)	69
Tobramycin	135 (88.8)	4 (2.6)	13 (8.6)	19
Amikacin	139 (91.4)	0 (0)	13 (8.6)	32
Cotrimoxazole	124 (81.6)	0 (0)	28 (18.4)	
Furantoin	43 (32.3)	59 (44.4)	31 (23.3)	17
Imipenem/cilastatin	129 (84.9)	5 (3.3)	18 (11.8)	16

The rate of resistance to amikacin and tobramycin was 8.6% (Table 4 and Figure 2). Univariate analysis showed that clinical outcomes varied depending on bacterial susceptibility to ampicillin/sulbactam ($\chi^2 = 12.151$, p = 0.002) but not to other antibiotics (Table 5).

Discussion

KP is a Gram-negative bacillus commonly found in clinical infection. The infection of pathogenic

enterobacteria causes pneumonia, liver abscesses, urinary and bloodstream infections, and other infectious diseases in community and hospital settings. The Blood Bacterial Resistant Investigation Collaborative System (BRICS) reported that the rate of detection of KP increased from 9.9% in 2014 to 18.4% in 2020 [8]. A systematic review showed that the rate of mortality from bloodstream infections due to KP was 54.30% [9], much higher than that reported in our study (23%).

Table 5. Comparison of antibiotics sensitivity in survival and death groups.

		Survival	Fatal	χ^2/z	р
	S	113	26	2.858	0.091
mikacin	Ι	0	0		
	R	8	5		
	S	110	27	0.403	0.525
Piperacillin/Tazobactam	Ι	0	0		
•	R	11	4		
	S	92	16	12.151	0.002
Ampicillin/Sulbactam	Ι	4	6		
•	R	25	7		
	S	103	24	1.066	0.302
Aztreonam	Ι	0	0		
	R	18	7		
	S	103	25	0.774	0.679
Ceftazidime	Ι	1	0		
	R	17	6		
	S	88	21	0.121	0.941
Cefazolin	Ι	10	3		
	R	23	6		
	S	94	22	0.673	0.714
Ciprofloxacin	Ι	7	2		
	R	20	7		
	S	98	23	0.632	0.729
Ceftriaxone	Ι	2	0		
	R	21	6		
	S	110	26	0.484	0.487
Cefotetan	Ι	0	0		
	R	11	4		
	S	43	8	0.95	0.622
Macrodantin	Ι	53	13		
	R	25	8		
	S	107	26	0.919	0.632
Cefepime	Ι	1	0		
1.	R	13	5		
	S	110	24	1.631	0.202
Gentamicin	Ι	0	0		
	R	11	5		
	S	110	26	1.94	0.379
mipenem	Ι	1	0		
•	R	10	5		
	S	95	24	0.111	0.946
Levofloxacin	Ī	9	2		
	R	17	5		
	S	99	25	0.023	0.881
Cotrimoxazole	I	0	0		
	R	22	6		
	S	108	27	1.9	0.387
Fobramycin	Ĩ	4	0		
	R	9	4		
	S	109	26	1.525	0.467
Ertapenem	I	1	0	1.020	0.107
	R	11	5		
	S	0	0	NA	NA
Ampicillin/sulbactam	I	0	0	1 12 1	1 12 1
in prenim suroueum	R	121	30		

S: sensitive; I: intermediate; R: resistant; p: p value.

Moreover, mortality increased two-fold in patients receiving inappropriate empirical treatment (95% CI: 1.1-3.4, p = 0.02) [10]. Therefore, clinicians should pay attention to bloodstream infections due to KP because of the high morbidity and mortality.

In our study, 77.6% of patients were older than 60 years, and the major sites of infection were the digestive and urinary systems. Thirty-one patients (20.4%) had liver abscesses, leading to infections in distant tissues and organs, including the brain, eye, and lung. In addition, the prevalence of underlying diseases such as diabetes, stroke sequelae, and malignant tumors was high in these patients, consistent with previous findings [11]. Older patients are more likely to have poor nutritional status, immune dysfunctions. and comorbidities. Moreover, invasive surgeries involving indwelling gastric tube and catheter placement require the use of broad-spectrum antibiotics, increasing susceptibility to KP infections [12]. The processes by which KP enters the bloodstream are unclear. Some studies have shown that KP colonizes the intestinal tract and invades the bloodstream by gastrointestinal translocation through the endothelial and intestinal barrier [13,14]. In our cohort, diabetes was the most common complication, accounting for 42.8% of cases, and the prevalence of diabetes was significantly higher in survivors than in non-survivors; nonetheless, there was no significant intergroup difference in this variable in the univariate analysis (p = 0.083). It was shown that 50.0% of patients with bloodstream infections due to HvKP had diabetes, and 77.8% of patients with septic shock had diabetes [15]. Clinical studies have demonstrated that capsular polysaccharide (CPS) is an important virulence factor of KP, and environmental glucose may increase the biosynthesis of CPS [16,17]. High glucose levels due to poor glycemic control stimulate CPS biosynthesis and CPS gene expression in hvKP, increasing resistance to phagocytosis and contributing to the development of invasive syndrome. Therefore, diabetes may be a risk factor for the development of bloodstream infections caused by hvKP isolates.

Patients with KP bloodstream infections were divided into survivors and non-survivors according to 28-day mortality. The results of multivariate analysis showed that hospital-acquired infection, septic shock, length of hospital stay, and creatinine level were independent risk factors for bloodstream infections. The proportion of patients older than 60 years was 77.6%, most of whom had multiple underlying diseases. Moreover, most patients with hospital-acquired infections were in critical condition and had received appropriate treatment before outpatient and emergency treatment, especially the long-term use of antibiotics, resulting in the emergence of multidrug- and pandrugresistant strains [18,19]. Septic shock is an independent risk factor for acute kidney injury (AKI) [20]. The prevalence of AKI is proportional to the severity of infection; for instance, the prevalence of AKI in patients with severe infection or septic shock was approximately 23% and 51%, respectively [21]. Moreover, the advanced AKI stages are associated with worse prognosis [22]. Our results showed that the incidence of septic shock was high in patients with KP bloodstream infections, and AKI increased the risk of death. Therefore, more attention should be paid to the occurrence of AKI in patients with hospital-acquired bloodstream infections due to KP.

The prevalence of drug-resistant KP, especially carbapenem-resistant strains, is increasing with the widespread use of antibiotics. Previous literature suggested that the hypervirulence and antibiotic resistance of KP would not overlap [23]. Nonetheless, nosocomial carbapenem-resistant hvKP strains were isolated in a tertiary hospital in Beijing, reducing the efficacy of treatment [24]. CHINET showed that resistance rate of KP strains to imipenem increased from 14.1% in 2014 to 24.2% in 2020 [25]. However, resistance to commonly used antibiotics in our samples was low, and the rate of resistance to imipenem was 11.8%, significantly lower than that reported by CHINET. This discrepancy may be related to two reasons: first, 87.7% of KP strains evaluated by CHINET were isolated from inpatients, and the incidence of CRKP in ICU patients was 23.0%. In turn, 82.2% of KP infections in our cohort were communityacquired, resulting in lower carbapenem selective pressure; second, the samples analyzed in CHINET were obtained from respiratory secretions (36.2%), urine (20.8%), and blood (15.0%). In contrast, all our samples were obtained from blood, and the rate of contamination was low.

In China, the BRICS 2018-2019 showed that the resistance rate of KP isolates to cephalosporins (first, second, and third generations), quinolones, and sulfamethoxazole was higher than 30%, that to cefepime, cefoxitin, piperacillin, and tazobactam was 20-30%, and that to amikacin was 14.6%; in turn, these isolates were highly sensitive to polymyxin and tigecycline [26]. Our antibiotic susceptibility results were similar to those of BRICS; however, antibiotic resistance rates were significantly lower than those reported by BRICS. These rates were lower than 20% for all evaluated antibiotics, except for cefazolin,

furantoin, and ampicillin/sulbactam, and the resistance to amikacin was the lowest. This result may be because most patients in our cohort had community-acquired infections. Moreover, the small sample size may lead to sampling errors.

Our results showed that the susceptibility of KP to carbapenem, cefepime, cefotetan, piperacillintazobactam, and amikacin was 84.2%, 87.3%, 89.5%, 89.5%, and 91.4%. KP produces ESBLs, AmpC βlactamases, and carbapenemases through drug resistance genes to hydrolyze β -lactams. In this respect, the KPC-producing enzyme was resistant to carbapenem and other β -lactams [27,28]. Although serotyping was not conducted in this study, the resistance rate to imipenem/cilastatin was higher than that to piperacillin/tazobactam, probably because of the excessive use of carbapenem in patients with nosocomial infections, underscoring the need to limit the excessive use of this antimicrobial agent.

Conclusions

KP is highly prevalent and causes severe infections, reducing treatment efficacy. KP bloodstream infections are particularly concerning, especially in older patients with diabetes complicated by liver abscesses. Septic shock and elevated serum creatinine levels were independent risk factors for KP bloodstream infections and mortality. Carbapenems, enzyme inhibitors, fourthgeneration cephalosporins, and aminoglycosides should be rationally used as first-line antibiotics for empirical treatment based on drug resistance data. Moreover, drug susceptibility testing is essential to adjust treatment and reduce antibiotic exposure, antimicrobial resistance, and mortality.

Ethical Approval

This research was approved by the Research Ethics Committee of Zhongda Hospital, Southeast University.

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Authors' contributions

Qun Zhang designed and conceptualized the study and wrote the manuscript. Pan Wang and Menghuan Shen collected and analyzed data and wrote the manuscript. Chun Shan collected and analyzed data. All authors approved the final version of the manuscript.

Availability of data and materials

The datasets used or analyzed in this study are available from the corresponding author upon reasonable request.

References

- Hu F, Guo Y, Yang Y, Zheng Y, Wu S, Jiang X, Zhu D, Wang F; China Antimicrobial Surveillance Network (CHINET) Study Group (2019) Resistance reported from China antimicrobial surveillance network (CHINET) in 2018. Eur J Clin Microbiol Infect Dis 38: 2275-2281. doi: 10.1007/s10096-019-03673-1.
- Chrystle M, Vishak A, Sindhu K, Jane M (2021) Primary lung abscess due to multidrug-resistant *Klebsiella pneumoniae*. BMJ Case Rep 14: e244759. doi: 10.1136/bcr-2021-244759.
- Huang HL, Lu PL, Lin CY, Chen YH, Kuo CH, Lin WR (2013) *Klebsiella pneumoniae* bacteremia and renosplenic abscesses without intestinal symptoms as the initial manifestations of non-steroidal anti-inflammatory drug-induced colitis: a rare case report. BMC Gastroenterol 13: 139. doi: 10.1186/1471-230X-13-139.
- 4. Solomon SL, Oliver KB (2014) Antibiotic resistance threats in the United States: stepping back from the brink. Am Fam Physician 89: 938-941. doi: 10.1016/j.medcli.2013.11.008.
- 5. Cassini A, Högberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS, Colomb-Cotinat M, Kretzschmar ME, Devleesschauwer B, Cecchini M, Ouakrim DA, Oliveira TC, Struelens MJ, Suetens C, Monnet DL, Burden of AMR Collaborative Group (2019) Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modeling analysis. Lancet Infect Dis 19: 56-66. doi: 10.1016/S1473-3099(18)30605-4.
- Ministry of Health of the People's Republic of China (2001) Diagnostic criteria for nosocomial infections (proposed). Natl Med J China 81: 314-320. doi: 10.3760/j.issn.0376-2491.2001.05.027.
- Humphries R, Bobenchik AM, Hindler JA, Schuetz AN (2021) Overview of changes to the clinical and laboratory standards institute performance standards for antimicrobial susceptibility testing, M100, 31st Edition. J Clin Microbiol 59: e0021321. doi: 10.1128/JCM.00213-21.
- Chen YB, Ji JR, Ying CQ, Liu ZY, Yang Q, Kong HS, Dai YY, Wang JL, Mao HF, Ding H, Liu YY, Zhou YZ, Lu H, Yin YD, Jin Y, Xu HY, Zhang LX, Wang L, Dong HX, Yang ZH, Chen FH, Huang DH, Liao GL, Tian PP, Liu D, Geng Y, Man SJ, Zhang BH, Huang Y, Guo L, Cao JM, Gu BQ, Li YH, Hu HX, Luan L, Hu SY, Zheng L, Li AY, Xu R, Liang KP, Li Z, Liu DH, Quan B, Liu Q, Shen JL, Liao YQ, Chen H, Bai QQ, Xia XS, Wang SF, Liang JH, Zhang LP, Dong YQ, Qi XY, Wang JZ, Hu XF, Yan XP, Qiao DY, Meng L, Xiao YH (2021) BRICS report of 2020: the bacterial composition and antimicrobial resistance profile of clinical isolates from bloodstream infections in China. Chin J Clin Infect Dis 14: 413-426. doi: 10.3760/cma.j.issn.1674-2397.2021.06.002.
- Xu L, Sun X, Ma X (2017) Systematic review and metaanalysis of mortality of patients infected with carbapenemresistant *Klebsiella pneumoniae*. Ann Clin Microbiol Antimicrob 16: 18. doi: 10.1186/s12941-017-0191-3.
- Girometti N, Lewis RE, Giannella M, Ambretti S, Bartoletti M, Tedeschi S, Tumietto F, Cristini F, Trapani F, Gaibani P, Viale P (2014) *Klebsiella pneumoniae* bloodstream infection: epidemiology and impact of inappropriate empirical therapy. Medicine (Baltimore). 93: 298-309. doi: 10.1097/MD.00000000000111.
- 11. Tsai SS, Huang JC, Chen ST, Sun JH, Wang CC, Lin SF, Hsu BR, Lin JD, Huang SY, Huang YY (2010) Characteristics of *Klebsiella pneumoniae* bacteremia in community-acquired and

nosocomial infections in diabetic patients. Chang Gung Med J 33: 532-539.

- Jiao Y, Qin Y, Liu J, Li Q, Dong Y, Shang Y, Huang Y, Liu R (2015) Risk factors for carbapenem-resistant *Klebsiella pneumoniae* infection/colonization and predictors of mortality: a retrospective study. Pathog Glob Health 109: 68-74. doi: 10.1179/2047773215Y.0000000004.
- Shon AS, Bajwa RP, Russo TA (2013) Hypervirulent (hypermucoviscous) *Klebsiella pneumoniae*: a new and dangerous breed. Virulence 4: 107-118. doi: 10.4161/viru.22718.
- 14. Desta K, Woldeamanuel Y, Azazh A, Mohammod H, Desalegn D, Shimelis D, Gulilat D, Lamisso B, Makonnen E, Worku A, Mannerqvist K, Struwe J, Aspevall O, Aklillu E (2016) high gastrointestinal colonization rate with extended-spectrum β-lactamase-producing enterobacteriaceae in hospitalized patients: emergence of carbapenemase-producing *K. pneumoniae* in Ethiopia. PLoS One 11: e0161685. doi: 10.1371/journal.pone.0161685.
- Ma R, Wang XD, Nie DP (2018) Clinical features of hypervirulent *Klebsiella pneumoniae* bloodstream infection. Chinese Journal of Infection Control 17(1):26-30. doi: 10.3969j.issn.1671-9638.2018.01.006. [Article in Chinese]
- 16. Xu Q, Yang X, Chan EWC, Chen S (2021) The hypermucoviscosity of hypervirulent *K. pneumoniae* confers the ability to evade neutrophil-mediated phagocytosis. Virulence 12: 2050-2059. doi: 10.1080/21505594.2021.1960101.
- Lee CH, Chen IL, Chuah SK, Tai WC, Chang CC, Chen FJ, Chen JF (2016) Impact of glycemic control on capsular polysaccharide biosynthesis and opsonophagocytosis of *Klebsiella pneumoniae*: Implications for invasive syndrome in patients with diabetes mellitus. Virulence 7: 770-778. doi: 10.1080/21505594.2016.1186315.
- Junyan Q, Mei K, Yang L, Jiayuan Q, Xiaoju L (2017) The clinical characteristics and risk factors of mortality in adult patients with carbapenem resistant Gram-negative bacteria blood infections. Chinese Journal of Antibiotics 42: 212-217. doi:10.3969/j.issn.1001-8689.2017.03.009. [Article in Chinese]
- Zhang L, Liu ZY, Xu YC, Li TS, Yang QW, Wang AX (2012) Clinical analysis of adult primary bloodstream infection. Natl Med J China 92: 894-898. doi:10.3760/cma.j.issn.0376-2491.2012.13.009.
- de Maio Carrilho CM, de Oliveira LM, Gaudereto J, Perozin JS, Urbano MR, Camargo CH, Grion CM, Levin AS, Costa SF (2016) A prospective study of treatment of carbapenemresistant *Enterobacteriaceae* infections and risk factors associated with outcome. BMC Infect Dis 16: 629. doi: 10.1186/s12879-016-1979-z.
- Bagshaw SM, Lapinsky S, Dial S, Arabi Y, Dodek P, Wood G, Ellis P, Guzman J, Marshall J, Parrillo JE, Skrobik Y, Kumar A; Cooperative Antimicrobial Therapy of Septic Shock (CATSS) Database Research Group (2009) Acute kidney injury in septic shock: clinical outcomes and impact of duration of hypotension prior to initiation of antimicrobial therapy. Intensive Care Med 35: 871-881. doi: 10.1007/s00134-008-1367-2.
- Chen DJ, Mai Y (2018) Risk factors and prognosis of acute kidney injury in patients with septic shock. International Journal of Laboratory Medicine 39: 2112-2115. doi: 10.3969/j.issn.1673-4130.2018.17.010. [Article in Chinese]

- Hennequin C, Robin F (2016) Correlation between antimicrobial resistance and virulence in *Klebsiella pneumoniae*. Eur J Clin Microbiol Infect Dis 35: 333-341. doi: 10.1007/s10096-015-2559-7.
- 24. Yao B, Xiao X, Wang F, Zhou L, Zhang X, Zhang J (2015) Clinical and molecular characteristics of multi-clone carbapenem-resistant hypervirulent (hypermucoviscous) *Klebsiella pneumoniae* isolates in a tertiary hospital in Beijing, China. Int J Infect Dis 37: 107-112. doi: 10.1016/j.ijid.2015.06.023.
- 25. Hu FP, Guo Y, Zhu DM, Wang F, Jiang XF, Xu YC, Zhang XJ, Zhang ZX, Ji P, Xie Y, Kang M, Wang CQ, Wang AM, Xu YH, Huang Y, Sun ZY, Chen ZJ, Ni YX, Sun JY, Chu YZ, Tian SF, Hu ZD, Li J, Yu YS, Lin J, Shan B, Du Yan, Guo Sufang, Wei Lianhua, Zou Fengmei, Zhang H, Wang C, Hu YJ, Ai XM, Zhuo C, Su DH, Guo DW, Zhao JY, Yu H, Huang XN, Liu WE, Li YM, Jin Y, Shao CH, Xu XS, Yan C, Wang SM, Chu YF, Zhang LX, Ma J, Zhou SP, Zhou Y, Zhu L, Meng JH, Dong F, Zheng HY, Hu FF, Shen H, Zhou WQ, Jia W, Li G, Wu JS, Lu YM, Li JH, Duan JJ, Kang JB, Ma XB, Zheng YP, Guo RY, Zhu Y, Chen YS, Meng O, Wang SF, Hu XF, Shen JL, Wang RZ, Fang Hua, YU Bixia, ZHAO Yong, GONG Ping, WEN Kaizhen, ZHANG Yirong, LIU Jiangshan, LIAO LF, Gu HQ, Jiang L, He W, Xu SH, Feng J, Dou R, Yue CL (2021) CHINET surveillance of bacterial resistance across China: report of the results in 2020. Chinese Journal of Infection and Chemotherapy 21: 377-387. doi. 10.16718/j.1009-7708.2021.04.001. [Article in Chinese]
- 26. Chen YB, Ji JR, Ying CQ, Wang PP, Liu ZY, Yang Q, Kong HS, Ding H, Liu YY, Mao HF, Huang Y, Yang ZH, Dai YY, Liao GL, Zhu L, Zhang LP, Li YH, Xu HY, Cao JM, Zhang BH, Guo L, Dong HX, Hu SY, Man SJ, Wang L, Liao ZX, Xu R, Liu D, Jin Y, Zhou YZ, Liao YQ, Chen FH, Gu BQ, Wang JL, Liang JH, Zheng L, Li AY, Shen JL, Dong YQ, Zhang LX, Hu HX, Quan B, Zhu WC, Liang KP, Liu Q, Wang SF, Yan XP, Kang JB, Xia XS, Ma L, Sun L, Luan L, Wang JZ, Li Z, Qiao DY, Zhang L, Li LJ, Xiao YH (2021) BRICS report of 2018-2019: the distribution and antimicrobial resistance profile of clinical isolates from blood culture in China. Chinese Journal of Clinical Infectious Diseases 14: 32-45. doi:10.3760/cma.j.issn.1674-2397.2021.01.007. [Article in Chinese]
- Paterson DL (2006) Resistance in gram-negative bacteria: *Enterobacteriaceae*. Am J Med 119: S20-8. doi: 10.1016/j.amjmed.2006.03.013.
- Denisuik AJ, Lagacé-Wiens PR, Pitout JD, Mulvey MR, Simner PJ, Tailor F, Karlowsky JA, Hoban DJ, Adam HJ, Zhanel GG, Canadian Antimicrobial Resistance Alliance (2013) Molecular epidemiology of extended-spectrum βlactamase-, AmpC β-lactamase- and carbapenemaseproducing *Escherichia coli* and *Klebsiella pneumoniae* isolated from Canadian hospitals over a 5 year period: CANWARD 2007-11. J Antimicrob Chemother 68: i57-65. doi: 10.1093/jac/dkt027.

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