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ORIGINAL RESEARCH

Risk Factors for Carbapenem-Resistant *Klebsiella pneumoniae* Bloodstream Infections and Outcomes

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Purpose: The incidence of carbapenem-resistant *Klebsiella pneumoniae* (CRKP) bloodstream infections (BSIs) is increasing globally; however, little has been reported on the risk factors and outcomes of CRKP BSIs in central China. This study aimed to determine the clinical risk factors for CRKP BSIs and the outcomes of CRKP BSIs.

Patients and Methods: We performed a case-control study of 239 patients with *K. pneumoniae* BSIs who were treated at Henan Provincial People's Hospital between July 2017 and July 2018. The cases (n=98, 41%) had CRKP BSIs, and the controls (n=141, 59%) had non-carbapenem-resistant *K. pneumoniae* (non-CRKP) BSIs. Antimicrobial sensitivity was determined using automated broth microdilution and an agar disk diffusion method. Data were obtained from clinical and laboratory records. Multivariate logistic regression and Pearson chi-square tests were used to identify clinical factors and outcomes associated with carbapenem resistance.

Results: Risk factors for carbapenem resistance included recent carbapenem use (odds ratio [OR]: 9.98, 95% confidence interval [CI]: 5.2–17.1, $P<0.001$), invasive procedures (OR: 11.1, 95% CI: 3.3–37.7, $P<0.001$), and pre-existing diseases of the digestive system (OR: 8.22, 95% CI: 1.73–39.2, $P=0.008$). Treatment failure was more frequent in the cases (84.7%) than in the controls (32.6%).

Conclusion: Exposure to antibiotics, especially carbapenems, and invasive procedures were the major risk factors for carbapenem resistance among patients with *K. pneumoniae* BSIs. Strict control measures should be implemented to prevent the emergence and spread of CRKP.

Keywords: antimicrobial resistance, bacteremia, digestive system diseases, treatment failure

Introduction

With the increasing use of carbapenems in hospitals worldwide, carbapenem-resistant *Klebsiella pneumoniae* (CRKP) has become an important threat to public health, and its management and treatment pose a challenge for clinicians.[1] *K. pneumoniae* is a major opportunistic pathogen that can lead to hospital-acquired infections,[2] and the lower respiratory tract and blood are most common sites of infection.[3] CRKP was first reported in 1997, and an increasing number of CRKP cases have been reported throughout the world, including in the United States, Europe, and Asia.[4–6] However, little has been reported about the risk factors and outcomes of CRKP in persons with bloodstream infections (BSIs) in central China. Therefore, the present study aimed to determine the risk factors for CRKP, and the outcomes of CRKP among people living in Henan Province, China.

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Materials and Methods

Study Subjects

This cross-sectional case-control study used clinical and microbiological data of patients who had been treated for *K. pneumoniae* BSIs in the Henan provincial hospital, a tertiary care teaching hospital with 5000 beds, between July 2017 and July 2018. Henan Province has the second highest population in China with about 100 million people, and the hospital has 13 intensive care unit (ICU) wards with about 300 beds that provide care to about 7000 inpatients annually. The ICUs are staffed by 100 professional doctors and 300 nurses. The study group comprised all patients with a first episode of CRKP BSI diagnosed during the study period. Accordingly, the patients in the control group were recruited from among non-CRKP patients of the same age and from the same source population, following the principle of matching, in a simple and random manner. Calculation of the sample size is based on analysis of the difference in incidence between patients with and those without CRKP BSIs.

Definition of Cases and Controls

The Infectious Diseases Working Party of the European Society for Blood and Marrow Transplantation (EBMT),[7,8] defined a *K. pneumoniae* BSI as the presence of at least one positive blood culture with concomitant signs and symptoms of infection. Patients with *K. pneumoniae* BSIs were identified from the microbiology laboratory database. CRKP was defined as minimal inhibition concentration (MIC) for imipenem or meropenem ≥4 μg/mL. Patients with CRKP BSIs were assigned to the case group, and patients with non-carbapenem-resistant *K. pneumoniae* (non-CRKP) BSIs were randomly assigned to the control group.

Definition of Outcomes

The EBMT defines successful treatment of CRKP BSIs as recovery from BSI following treatment, with resolution of patients with CRKP BSI who remained alive or therapy patients without the signs of infection.[7,8] Treatment failure is defined as either death or a recurrence of *K. pneumoniae* infection before discharge from the hospital. However, we were unable to ascertain all *K. pneumoniae*-related deaths because some patients were discharged from the hospital without completing treatment. In accordance with Chinese tradition, especially in some rural areas, family members are not willing to let patients die outside of their homes, and seriously ill patients sometimes request to be discharged from the hospital and to discontinue treatment so that they can die at home. Therefore, we extended the definition of treatment failure to include patients who were discharged from the hospital without completing the treatment.

K. pneumoniae BSI-related death or recurrence was defined as follows: BSI was considered as the primary cause of death or recurrence if the patient died after admission, within 120 hrs after the last positive blood culture and *K. pneumonia* was identified as the cause of death, with no other cause (including underlying disease, persistent neutropenia, other infections, and hemorrhage). *K. pneumoniae* BSI was considered an associated cause of death or recurrence when another cause was also present (uncontrolled underlying disease, persistent neutropenia, and/or graft versus host disease). Deaths or recurrences that were not related to *K. pneumoniae* BSI were defined as such when *K. pneumoniae* BSI had cleared by the time of death (as indicated by an absence of signs of infection or a positive culture).

Variables

Clinical data were collected from medical charts and/or hospital computer system databases. The following data were collected on each patient: age, sex, inpatient time, admission diagnosis, hospitalization, ICU admission, antibiotic use, intravascular catheter use, number of previous transfers between hospitals and departments, and history of blood transfusion. Data on the length of hospitalization, microbiological data, antimicrobial therapies, and outcomes were also collected.

The definition of admission diagnosis was based on the patient's diagnosis on admission, classified according to the International Classification of Diseases-11 (ICD-11).[9]

Ethical Approval

The Ethics Committee of the Henan Provincial People's Hospital approved this study. The requirement for informed consent was waived because this was a retrospective study that used routinely collected data and inclusion of these data in the study was not associated with any risks to the patients. Additionally, we stated to confirm the patient data confidentiality.

Microbiological Methods

The Vitek 2 system (bioMérieux, Marcy l'Étoile, France) and the Phoenix100 automated system (Becton Dickinson Co., Sparks, MD, USA) were used for *K pneumoniae* isolate identification. Matrix-assisted lasers desorption/ionization

time-of-flight mass spectrometry (MALDI-TOF-MS) (Bruker Corporation, Karlsruhe, Germany) was used to confirm the identity of the isolate. MIC values for antimicrobial agents were determined by an automated broth microdilution method (Becton Dickinson Co., Sparks, MD, USA). Antibiotic susceptibility testing results were compared using the agar disk diffusion method (Becton Dickenson Co., Sparks, MD, USA), in accordance with the Clinical and Laboratory Standards Institute (CLSI) breakpoints. Results were interpreted according to CLSI criteria (CLSI2018).[10,11]

Statistical Analyses

Categorical variables were reported as frequencies and percentages, and continuous variables were reported as means and standard deviations (SDs) if they were normally distributed or as medians and interquartile ranges (IQRs) if they were non-normally distributed. Categorical variables were compared using chi-square or Fisher's exact tests, and continuous variables were compared using Student's *t* test or the Mann–Whitney *U*-test, according to their distribution. For univariate analyses, results were reported as odds ratios (ORs) with 95% confidence intervals (CIs) and *P* values. Variables with *P* values<0.1 in the univariate analyses were selected for possible inclusion in multivariate logistic regression. We used backward stepwise logistic regression to select variables for inclusion in the final multivariate logistic regression model to evaluate risk factors for CRKP BSIs. The discrimination ability of the logistic regression model was assessed by estimating the area under the receiver operating characteristic (ROC) curve. Model calibration was assessed using the Hosmer–Lemeshow test for goodness of fit. Five hundred-day survival curves were constructed using the Kaplan–Meier method. Log-rank tests were performed with Prism7.0 (GraphPad) software. Other statistical analyses were performed with SPSS 20.0 software (IBM Corporation, Armonk, NY, USA). Two-tailed *P* values <0.05 were considered statistically significant.

Results

Characteristics of Study Participants

We identified 239 patients who were diagnosed with *K. pneumoniae* BSIs during the study period. Of the 239 patients, 98 had CRKP BSIs (cases), and 141 had Non-CRKP BSIs (controls). Patient characteristics are shown in Table 1. The mean ages of the cases and controls were 55±17 years and 56±17 years, respectively (*P*=0.66). The mean length of hospital stay was also similar in cases and controls (55±7 days and 51±5 days, respectively; *P*=0.67). As shown in Figure 1, the main admission diagnoses were infectious diseases, diseases of the digestive system, hematologic diseases, and tumors. As shown in Figure 2, the largest number of study patients were from the ICU, the surgical department, and the hematology department.

Risk Factors for Carbapenem-Resistant *Klebsiella pneumoniae* Bloodstream Infections

The results of the univariate analysis to identify risk factors associated with CRKP BSIs are shown in Table 1. The following factors were found to be associated with CRKP BSIs: underlying disease, injury, prior presence of intravascular catheter, number of previous transfers between hospitals and departments, blood transfusion, and hospitalization in ICUs. Prior exposure to cephalosporin, carbapenem, beta-lactam-beta-lactamase inhibitors, antifungal drugs and other antibiotics were also significant risk factors.

The results of the multivariate analysis are shown in Table 2. The independent risk factors for CRKP BSIs were diseases of the digestive system, diagnostic punctures, transfer between departments, and carbapenem exposure.

Comparison of the Incidence of Treatment Failure Among the Cases and the Controls

Of the 98 cases, 7 died, 76 discontinued treatment or asked to be discharged from the hospital, and 15 were cured. Of the 141 controls, 2 died, 44 discontinued treatment or asked to be discharged from the hospital, and 95 were cured. The rate of treatment failure among cases (84.7%) was considerably higher than that among controls (32.6%). The survival curve analysis confirmed that the cases had a lower survival rate than the controls (Figure 3).

Risk Factors for Treatment Failure

The results of the univariate analysis are shown in Table 3, Patients with treatment failure were hospitalized for a significantly shorter period than those with treatment success (mean: 44±5 days versus 62±1 days; p=0.01). In the univariate analysis, the following variables were identified as risk factors for treatment failure: underlying diseases, such as cardiovascular or respiratory diseases;

Table 1 Univariate Analysis of Risk Factors for Carbapenem-Resistant *Klebsiella pneumoniae* Bloodstream Infections

Variables	CRKP (N=98) n (%)	Non-CRKP (N=141) n (%)	OR (95% CI)	*P*
Basic Information				
Male	76 (77.6)	88 (62.4)	2.1 (1.2–3.7)	0.013
Admission to an ICU	82 (83.7)	44 (31.2)	11.3 (5.9–21.5)	<0.001
History of hospital transfers	78 (79.6)	54 (38.3)	6.7 (3.5–12.3)	<0.001
History of department transfers	74 (75.5)	35 (24.8)	9.9 (5.2–16.7)	<0.001
Admission Diagnosis				
Diabetes, hypertension	30 (30.6)	42 (29.8)	1.0 (0.6–1.7)	0.89
Cardiovascular diseases	26 (26.5)	11 (7.8)	4.1 (2.0–10.0)	<0.001
Respiratory diseases	51 (52.0)	20 (14.12)	6.7 (3.5–12.3)	<0.001
Neurological diseases	28 (28.6)	14 (9.9)	3.8 (1.8–7.9)	<0.001
Hematological diseases	17 (17.4)	22 (15.6)	0.9 (0.4–1.7)	0.69
Digestive diseases	36 (36.7)	31 (22.0)	2.2 (1.4–3.9)	0.008
Chronic liver diseases	22 (22.5)	23 (16.3)	0.7 (0.4–1.3)	0.23
Chronic nephrosis	23 (23.5)	8 (5.7)	5.3 (2.1–12.2)	<0.001
Malignancy	11 (11.2)	34 (24.1)	2.5 (1.2–5.2)	0.013
Infections and allergic diseases	63 (64.3)	42 (29.8)	4.6 (2.6–8.3)	<0.001
Trauma	10 (10.2)	3 (2.13)	5.1 (1.6–21.1)	0.004
Invasive Procedures				
Diagnostic punctures	56 (57.1)	37 (26.2)	3.9 (2.2–6.7)	<0.001
Organ and stem cell transplants	3 (3.01)	5 (3.6)	1.2 (0.3–5.0)	0.84
Chemotherapy	16 (16.3)	30 (21.3)	1.4 (0.7–2.7)	0.34
Surgery within the past 3 months	80 (81.6)	40 (28.4)	11.2 (6.7–21.5)	<0.001
CVC	58 (59.2)	28 (19.9)	5.9 (3.3–11.2)	<0.001
Hemodialysis and plasma exchange	25 (25.5)	10 (7.1)	4.4 (2.2–9.9)	<0.001
Catheter	73 (74.5)	27 (19.2)	12.3 (6.7–22.5)	<0.001
Tracheal intubation	73 (74.5)	31 (22.0)	11.3 (5.9–19.9)	<0.001
Gastric tube	70 (71.4)	32 (22.7)	9.8 (4.9–16.7)	<0.001
History of repeat transfusions	73 (74.5)	56 (39.7)	4.4 (2.5–7.8)	<0.001
Antibiotic Exposure				
Penicillin	12 (12.2)	18 (12.8)	0.9 (0.4–2.0)	0.83
Cephalosporin	30 (30.6)	16 (11.4)	3.4 (1.7–7.1)	<0.001
Carbapenem	79 (80.6)	45 (31.9)	10.0 (5.2–17.1)	<0.001
Aztreonam	1 (1.0)	10 (7.1)	7.4 (0.9–58.8)	0.06
Beta-lactam-beta-lactamase inhibitors	51 (52.0)	14 (9.9)	9.9 (5.0–19.9)	<0.001
Aminoglycosides	11 (12.2)	11 (7.8)	0.7 (0.61–3.8)	0.37
Quinolone	15 (15.3)	20 (14.2)	0.9 (0.44–1.9)	0.81
Sulfonamides	3 (3.1)	5 (3.6)	1.2 (0.3–5.0)	0.84
Anaerobic antibiotics	2 (2.0)	9 (6.4)	3.3 (0.7–15.6)	0.11
Linezolid	19 (19.34)	4 (2.8)	8.8 (2.7–25.0)	<0.001
Antifungals	21 (21.4)	6 (4.3)	6.7 (2.4–16.5)	<0.001
Teicoplanin	13 (13.3)	10 (7.1)	0.5 (0.2–1.2)	0.11
Vancomycin	8 (8.2)	2 (1.4)	6.7 (1.3–33.3)	0.03

Abbreviations: CI, confidence interval; CRKP, carbapenem-resistant *Klebsiella pneumoniae*; CVC, central venous catheterization; ICU, intensive care unit; OR, odds ratio.

days in hospital; prior presence of intravascular catheter; number of previous transfers between hospitals and departments; blood transfusion; and hospitalization in ICUs. Prior use of carbapenem, linezolid, antifungal agents, vancomycin, and beta-lactam-beta-lactamase inhibitors were also significant risk factors. Independent risk factors for CRKP treatment failure included malignancy, diagnostic punctures, tracheal intubation, transfer between hospital departments, and prolonged hospitalization (Table 4).

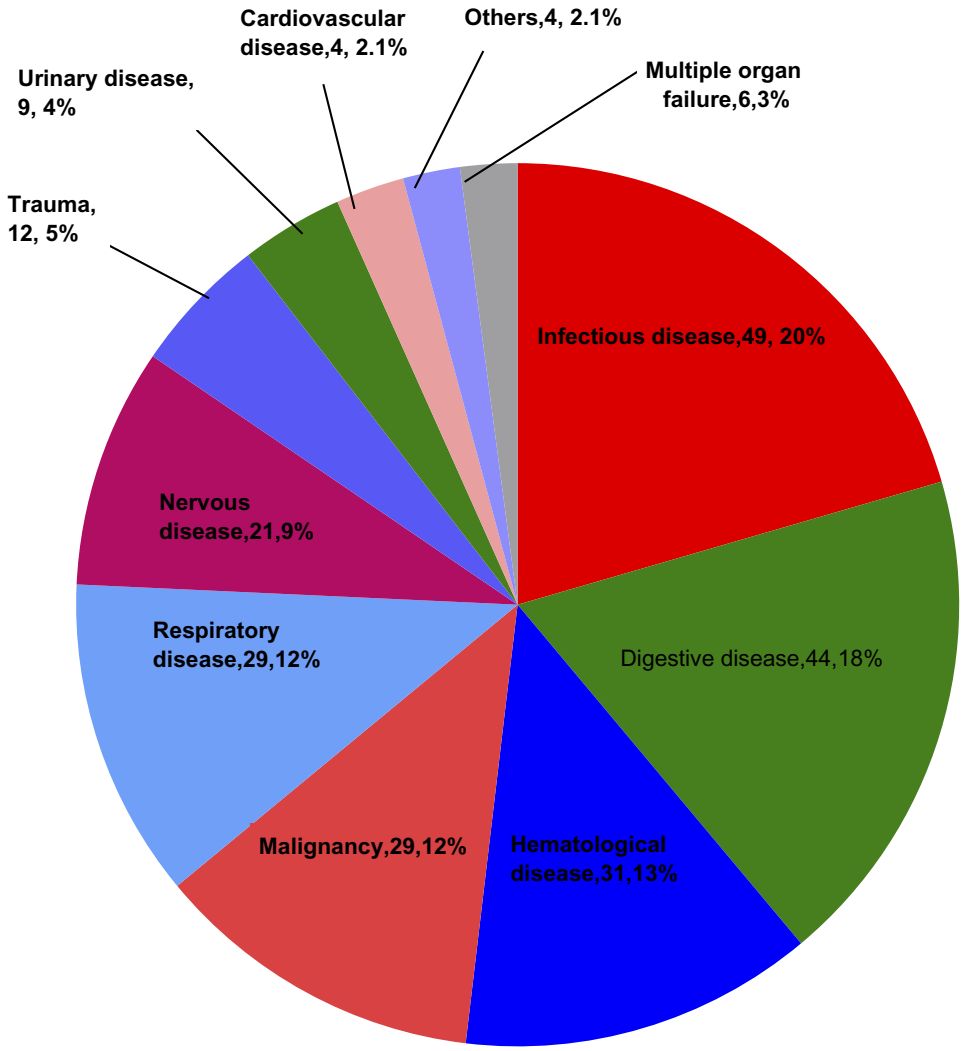

Figure 1 Admission diagnoses among patients with *Klebsiella pneumoniae* bloodstream infections. Infectious diseases and digestive diseases were the major admission diagnoses among patients with *Klebsiella pneumoniae* bloodstream infections. "Others" includes an assortment of admission diagnoses that were grouped because the frequencies of the individual diagnoses were too small to display separately.

Discussion

Among the 239 patients with *K. pneumoniae* BSIs, 98 were infected with CRKP. The risk factors for CRKP BSIs and treatment failure included the prior use of antibiotics, invasive procedures, and digestive system diseases. This study is the first to report these risk factors for CRKP BSIs.

K. pneumoniae is one of the most common Gram-negative bacterial infections, and it is associated with serious BSIs.[12] In hospitals, BSIs caused by *K. pneumoniae* rank second among Gram-negative bacterial infections and are associated with serious conditions and a poor prognosis.[13,14] CRKP BSIs are common among hospital inpatients but are especially common among patients admitted to ICUs.[15] This may be because of several factors. Patients in ICUs might have received multiple antibiotics, have had severe primary diseases, have undergone major surgery, or have experienced trauma. In addition, patients in ICUs are subjected to a variety of invasive surgical procedures. In our hospital, the emergence of CRKP BSIs is a challenge for medical staff. The high frequency of CRKP BSIs in the general surgery department is likely to be largely due to the high frequency of invasive procedures such as catheter insertion.

Previously published reviews have reported several risk factors for CRKP, including severe underlying diseases, use of broad-spectrum antibiotics, use of carbapenem antibiotics, a long hospitalization period,

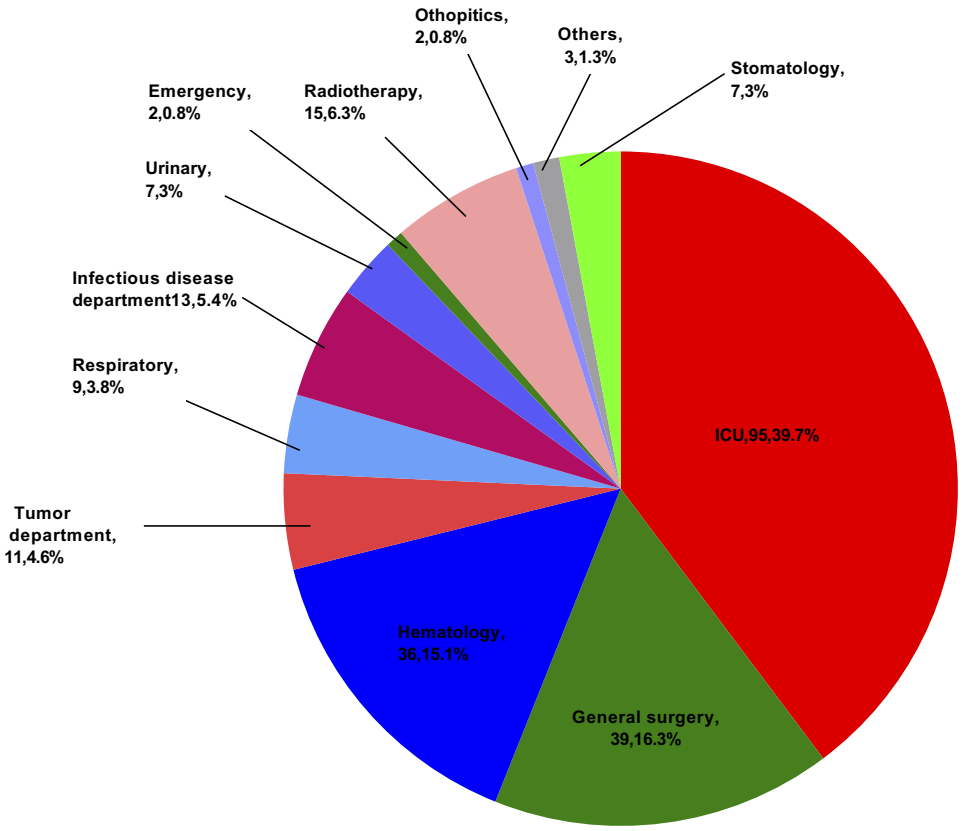

Figure 2 Frequency distribution of hospital departments among patients with *Klebsiella pneumoniae* bloodstream infections. Intensive care units and general surgery were the most common departments among patients with *Klebsiella pneumoniae* bloodstream infections. "Others" includes an assortment of departments that were grouped because the numbers of patients admitted to each department were too small to display separately.

malignancies, hematopoietic stem cell transplantation, tracheotomy, mechanical ventilation, and indwelling catheters.[5,16,17] In our study, univariate analysis results showed that ICU admission, respiratory disease, cardiovascular disease, nervous system disease, digestive disease, invasive operations, and carbapenem exposure were all risk factors for CRKP BSIs. These results are similar to those of previous studies in other parts of the world.[18] Multivariate regression analysis showed that digestive disease, invasive procedures, and the length of hospitalization were independent risk factors for CRKP BSIs. Notably, in the present study, digestive diseases were found to be a risk factor for CRKP BSIs. Digestive diseases have not been reported as a risk factor for CRKP BSIs in published

Table 2 Multivariate Analysis of Factors Associated with Carbapenem Resistance Among Patients with *Klebsiella pneumonia* Bloodstream Infections

Factor	*P*	OR (95% CI)
Digestive diseases	0.008	8.2 (1.7–39.2)
Diagnostic punctures	0.02	3.8 (1.2–11.6)
Carbapenem exposure	0.002	5.2 (1.8–14.9)
Departments transfer	0.04	3.6 (1.1–12.0)

Abbreviations: CI, confidence interval; OR, odds ratio.

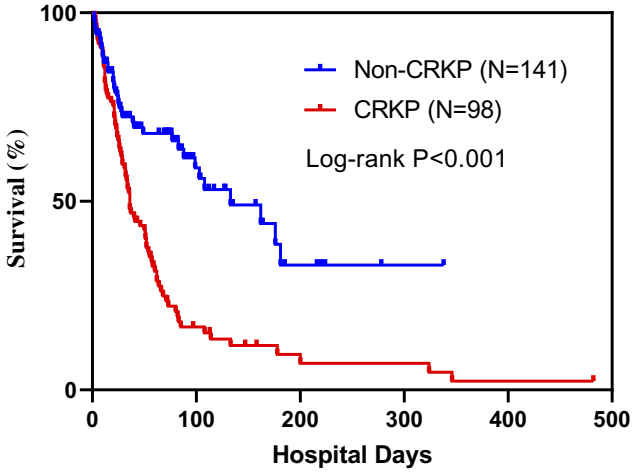

Figure 3 Survival curves comparing survival among patients with carbapenem-resistant and non- carbapenem-resistant *Klebsiella pneumoniae* bloodstream infections. Patients with carbapenem-resistant *Klebsiella pneumoniae* bloodstream infections had a lower survival than patients with non-carbapenem-resistant *K. pneumoniae* bloodstream infections (*P*<0.001).

Table 3 Univariate Analysis of Risk Factors for Treatment Failure of *Klebsiella pneumonia* Bloodstream Infections

Variables	Treatment Success (N=110) n (%)	Treatment Failure (N=129) n (%)	OR (95% CI)	*P*
Basic Information				
CRKP	15 (13.6)	83 (64.3)	11.4 (6.0–21.7)	<0.001
Age ≥50 years	75 (68.2)	82 (63.6)	1.2 (0.7–2.1)	0.45
Male	71 (64.5)	93 (72.1)	0.7 (0.4–1.2)	0.21
ICU patient	21(19.1)	74(57.4)	5.9(3.4–11.1)	<0.001
Admitted to ICU	82 (74.5)	31 (24.0)	9.9 (5.1–16.6)	<0.001
Transferred between hospitals	42 (38.2)	90 (69.8)	3.7 (2.2–6.4)	<0.001
Transferred between departments	34 (30.9)	75 (58.1)	3.1 (1.8–5.3)	<0.001
Admission Diagnosis				
Cardiovascular diseases	10 (9.1)	27(20.9)	2.65 (1.2–5.8)	0.01
Respiratory diseases	16 (14.5)	55 (42.6)	4.4 (2.3–8.2)	<0.001
Neurological diseases	9 (8.2)	33 (25.6)	3.9 (1.8–8.7)	<0.001
Hematological diseases	15 (13.6)	24 (18.6)	1.5 (0.7–3.0)	0.29
Digestive diseases	32 (29.1)	35 (27.1)	0.9 (0.5–1.7)	0.82
Chronic liver diseases	19 (17.3)	26 (20.2)	1.2 (0.6–2.3)	0.57
Chronic nephrosis	9 (8.2)	22 (17.1)	2.3 (1.0–5.2)	0.04
Malignancy	24 (21.8)	21 (16.3)	0.7 (0.4–1.4)	0.29
Infections and allergic diseases	32 (29.1)	73 (56.6)	3.3 (1.9–5.7)	<0.001
Trauma	3 (2.7)	10 (7.8)	3.2 (0.9–11.8)	0.07
Invasive Procedures				
Diagnostic punctures	34 (30.9)	59 (45.7)	1.9 (1.1–3.2)	0.02
Organ or stem cell transplants	7 (6.4)	1 (0.8)	8.9 (1.1–9.9)	0.04
Chemotherapy	22 (20)	24 (18.6)	0.9 (0.5–1.7)	0.79
Surgery within the previous 3 months	35 (31.8)	85 (65.9)	4.1(2.4–7.1)	<0.001
Catheter	22 (20)	78 (60.5)	6.1 (3.4–10.9)	<0.001
Gastric tube	22 (20)	80 (62.0)	6.5 (3.6–11.8)	<0.001
History of repeat transfusions	46 (41.8)	83 (64.3)	2.5 (1.6–4.2)	<0.001
CVC	15 (13.6)	71 (55.0)	8.3 (4.3–15.9)	<0.001
Hemodialysis and plasma exchange	7 (6.4)	28 (21.7)	4.1 (1.7–9.8)	0.001
Antibiotic Exposure				
Penicillin	13 (11.8)	15 (11.6)	1.0 (0.5–2.2)	0.96
Cephalosporin	18 (16.4)	28 (21.7)	1.4 (0.7–2.7)	0.30
Carbapenem	35 (31.8)	90 (69.8)	5.0 (2.9–8.6)	<0.001
Aztreonam	9 (8.2)	2 (1.6)	0.2 (0.04–0.8)	0.02
Beta lactam-beta-lactamase inhibitors	11 (10)	54 (41.9)	6.5 (3.2–13.2)	<0.001
Aminoglycosides	12 (10.9)	10 (7.8)	0.7 (0.3–1.7)	0.40
Quinolone	16 (14.5)	19 (14.7)	1.0 (0.5–2.1)	0.97
Sulfonamides	6 (5.5)	2 (1.6)	0.2 (0.1–1.4)	0.09
Anaerobic antibiotics	5(4.5)	6 (4.7)	1.0(0.3–3.4)	0.98
Linezolid	4 (3.6)	19 (14.7)	4.6 (1.5–13.9)	0.004
Antifungals	5 (4.5)	22 (17.1)	4.3 (1.6–11.8)	0.002
Teicoplanin	6 (5.5)	17 (13.2)	2.6 (1–6.93)	0.04
Vancomycin	1 (0.9)	9 (7.0)	8.2 (1.0–65.6)	0.02

Abbreviations: CI, confidence interval; CRKP, carbapenem-resistant; CVC, Central venous catheter; ICU, Intensive care unit; OR, odds ratio.

studies and thus is an important finding with clinical implications. *K. pneumoniae* is part of the normal commensal flora of the digestive tract. If digestive system diseases such as bleeding within the digestive tract, gastric ulcer, and pancreatitis occur, *K. pneumoniae* may enter the bloodstream and cause BSIs, including CRKP BSIs.

Table 4 Multivariate Analysis of Risk Factors for Treatment Failure Among Patients with *Klebsiella pneumonia* Bloodstream Infections

Factor	*P*	OR (95% CI)
Malignancy	0.04	2.7 (1.7–6.9)
Diagnostic punctures	0.04	3.1 (1.0–9.3)
Admission to an ICU	0.048	5.8 (1.0–32.7)
Tracheal intubation	<0.001	11.1 (3.3–37.7)
Interdepartmental transfers	0.03	4.3 (1.1–16.6)
Days of hospitalization	0.002	11.9 (2.6–56.1)

Abbreviations: CI, confidence interval; ICU, intensive care unit; OR, odds ratio.

The overuse of broad-spectrum antimicrobial agents and invasive procedures has led to an increase in the prevalence of drug-resistant *K. pneumoniae* and in the incidence of CRKP infection.[19,20] Our findings are consistent with those of other studies, which have reported a strong association between exposure to carbapenem agents and CRKP infection.[21,22] Carbapenem use may cause selective pressure on resistant microorganisms, thereby increasing the risk of infection. Although a few studies have shown that avoiding unnecessary changes in the use of antimicrobials can reduce the incidence of CRKP infections,[23] the results of our study suggest that the use of carbapenems should be minimized. Moreover, the control measures for hospital infection include appropriate and strict isolation precautions, such as hand hygiene of medical staff and isolation of each patient in a separate, walled room, and surgery for only CRKP infection should be implemented to prevent the emergence and spread of CRKP.

This study showed that risk factors for CRKP include repeated, long-term hospitalization, and multiple hospital and department transfers during hospitalization. These results are similar to those of other studies.[18,24] More attention should be given to the risks posed by these factors in hospital settings.

However, it should be noted that this study has several limitations. First, the retrospective study design could have led to information and selection biases. Results of the multivariate analysis showed that baseline disease aggravates CRKP BSIs. This has not been reported previously[25,26] and may be because of sampling bias caused by the small number of patients with underlying diseases in this study. Second, being a retrospective study, it also does not provide sufficient strength of evidence to establish a causal relationship between possible risk factors for CRKP infection. Additionally, there may have been unmeasured confounders associated with CRKP infection. Third, we did not measure the overall incidence of CRKP BSIs and thus the patients in our study may not represent the range of severity of CRKP, and this may be a source of bias.[27]

In conclusion, our results confirm that CRKP BSIs are relatively common in hospital settings, which poses an important challenge to clinicians. This retrospective analysis of risk factors for CRKP infection suggests that the misuse of antibiotics such as carbapenems as well as invasive procedures contribute to the spread of CRKP. Therefore, clinicians should strictly monitor antibiotic application and ensure rational use of carbapenems.

Ethics Approval and Informed Consent

The Ethics Committee of the Henan Provincial People's Hospital approved this study. Informed consent was waived because it was a retrospective study that used routinely collected data and inclusion in the study was not associated with any risk for patients. Additionally, we stated to confirm patient data confidentiality.

Data Sharing Statement

The datasets generated for this study are available from the corresponding author on request.

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Disclosure

The authors declare no conflicts of interest in this work.

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