Original Article

Risk Factors for Carbapenem-resistant *Klebsiella pneumoniae* Infection and Mortality of *Klebsiella pneumoniae* Infection

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Abstract

Background: *Klebsiella pneumoniae* (KP) is a pathogen commonly causing nosocomial infection. Carbapenem-resistant KP (CRKP) is more resistant to multiple antimicrobial drugs than carbapenem-susceptible KP (CSKP) isolates. The aim of the present study was to identify the risk factors for CRKP infection and the predictors of mortality among KP-infected adult patients.
Methods: Patients with CRKP and CSKP infection were categorized as the case group and control group, respectively, and we conducted a 1:1 ratio case-control study on these groups. The CRKP isolates collected were tested for antimicrobial susceptibility and presence of KP carbapenemase (KPC) gene. Clinical data were collected to identify risk factors for CRKP infection and mortality of KP infection. Risk factors were analyzed under univariable and multivariable logistic regression model.
Results: The independent risk factors for CRKP infection were admission to Intensive Care Unit (odds ratio [*OR*]: 15.486, 95% confidence interval [*CI*]: 3.175–75.541, $P < 0.001$); use of β-lactams and β-lactamase inhibitor combination (*OR*: 4.765, 95% *CI*: 1.508–15.055, $P = 0.008$); use of cephalosporins (*OR*: 8.033, 95% *CI*: 1.623–39.763, $P = 0.011$); fluoroquinolones (*OR*: 6.090, 95% *CI*: 1.343–27.613, $P = 0.019$); and indwelling of urethral catheter (*OR*: 6.164, 95% *CI*: 1.847–20.578, $P = 0.003$). However, older age (*OR*: 1.079, 95% *CI*: 1.005–1.158, $P = 0.036$), Charlson comorbidity index (*OR*: 4.690, 95% *CI*: 2.094–10.504, $P = 0.000$), and aminoglycoside use (*OR*: 670.252, 95% *CI*: 6.577–68,307.730, $P = 0.006$) were identified as independent risk factors for patient deaths with KP infection. The mortality of CRKP group was higher than that of the CSKP group. KPC gene did not play a role in the CRKP group. CRKP mortality was high.
Conclusion: Implementation of infection control measures and protection of the immunefunction are crucial.

Key words: Infection; *Klebsiella pneumonia*; Logistic Regression; Mortality; Risk Factors

Introduction

Klebsiella pneumoniae (KP) is a pathogen commonly causing nosocomial infection, which is the culprit of hospital-acquired infections including pneumoniae, bloodstream infection, urinary tract infection, and hepatic abscess, especially among immunocompromised people.[1-3] The usage of carbapenems is increasing dramatically in Chinese hospitals. Carbapenem-resistant KP (CRKP) is more resistant to multiple antimicrobial drugs than carbapenem-susceptible KP (CSKP) isolates. These resistant strains have been the source of hospital-acquired infections among severely ill patients, which exhibits apparently higher mortality than the infections with CSKP.[4]

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As the consequence of this, identifying the patients at risk of fatal infection is of crucial importance to the selection and efficacy of the therapies. Additionally, this knowledge is of importance for the design and the implementation of interventions aiming to prevent the spread of antimicrobial resistance.[5]

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The aim of the present study was to identify risk factors for CRKP infections and predictors of mortality among KP-infected adult patients.

Methods

Ethical approval

The retrospective study was approved by the Ethics Committee of Peking University First Hospital. All patients waived to sign the informed content.

Study design

To identify the risk factors for CRKP infections, we conducted a retrospective case-control study at Beijing University First Hospital, China, a tertiary care teaching hospital with 1600 beds. All the adult inpatients (age ≥18 years) with positive cultures of KP (48 h after admission) were selected from the medical records in the hospital's computerized microbiology laboratory database, dated between January 1, 2010, and December 31, 2014. The first positive sample of each patient was analyzed in the study.

Patients with CRKP were categorized as the case group, while patients with only CSKP were categorized as the control group. The controls were selected randomly from the source population admitted to the same department during the same time period. To identify the risk factors associated with infections caused by CRKP, clinical variables of the case group were compared with those of the control group. Based on the outcome, all the patients infected with KP were divided into the death group and the survival group.

Antimicrobial susceptibility test

Antimicrobial susceptibilities to various antimicrobial agents, including amikacin, imipenem, meropenem, cefoperazone-sulbactam, cefepime, moxifloxacin, levofloxacin, tigecycline, ceftriaxone, ertapenem, ceftazidime, and piperacillin-tazobactam, were determined by minimum inhibitory concentration (MIC) using the E-test. The results were interpreted according to the criteria recommended by the 2012 Clinical and Laboratory Standards Institute. CRKP was defined as an isolate with ertapenem (MICs ≥2 μg/ml), or imipenem and/or meropenem (MICs ≥4 μg/ml). The KP isolates susceptible to ertapenem, imipenem, and meropenem were considered as CSKP.

Detection of *Klebsiella pneumoniae* carbapenemase gene

All the CRKP isolates were subjected to detection of KPC gene using polymerase chain reaction methods as previously described by Tsai *et al*.[6]

Data collection

All the data in this study came from medical records, which were reviewed and collected if identified as KP positive 48 h after admission. The following data were retrieved from medical records of each patient: demographics (age and sex), comorbidities and underlying diseases (cardiovascular, pulmonary, renal, hepatic, central nervous system disease, diabetes mellitus, solid tumor or hematological malignancy, and immunocompromised), severity of illness classified by the Charlson comorbidity score, Intensive Care Unit (ICU) stay prior to KP isolation, history of hospitalization within the previous 6 months, antibiotic therapy administered in the 30 days prior to the positive culture, recent (≤1 month) surgical procedures, special treatments (corticosteroids, chemotherapy, and blood products), and recent (≤7 days) invasive procedures (central venous, urinary or gastric catheterization intubation, parenteral nutrition, mechanical ventilation, hemodialysis, and biopsy puncture). Time at risk was defined as the length of stay prior to a positive culture for the two groups and the total length of hospitalization for the control group.

Statistical analysis

Described and compared indicators of population groups' index were between different groups. Continuous variables were described as mean ± standard deviation (SD), which was compared using the Student's *t*-test. They were compared with the Mann-Whitney *U*-test if their distributions were not normal. Ranked data using the median (interquartile spacing) description are compared between the groups using Wilcoxon signed-rank test and inspection. Categorical variables were compared with a Pearson's Chi-square test or a Chi-square test with a continuity correction if the frequency is <5. Two sets of data from the two groups of participants were compared using independent samples *t*-test.

We established a univariable logistic regression model to explore the relationship between disease and research indicators. Multiple stepwise regression analysis was used to match multivariable logistic regression model. Stepwise regression analysis values of which standard $P \leq 0.05$ were included, excluding those of which standard $P > 0.05$. The area under receiver operating characteristic curve was evaluated under multivariable logistic regression model with prediction effect. We calculated the odds ratios (*OR*s) and the 95% confidence intervals (*CI*s) for the dichotomous categorical variables with CRKP or CSKP infection as the dependent variable. To identify the independent risk factors, variables with $P < 0.05$ in the univariable analysis were included in multivariable logistic regression model and analyzed using backward step-wise regression. We also calculated Hosmer-Lemeshow goodness-of-fit statistics. Null hypothesis was rejected if a type of *Klebsiella* was included in the model as an independent factor. Two-tailed $P \leq 0.05$ was considered statistically significant. The difference of inspection level was set to 5%, the *F*-test level was set to 10%, and the *CI* credibility was set as 95%. All statistical analyses were performed with STATA 13.0 (Stata Corp, College Station, Texas, USA) software for Windows.

Results

Forty-eight CRKP strains were isolated from the department of respiratory (15 strains), geriatric (14 strains), cardiovascular surgery, general surgery, blood and marrow transplantation and rheumatism (3 strains for each), hematology (2 strains), infectious disease, nephrology, neurology, orthopedics, and urology (1 strain for each). The specimens were collected from sputum (22 strains), urine (11 strains), blood (7 strains),

bronchoalveolar lavage fluid (3 strains), drainage liquid (2 strains), venous catheter (1 strain), and gastric juice (2 strains). The CSKP specimens were collected from departments and sites in one-to-one correspondence with those in CRKP group.

Risk factors associated with carbapenem-resistant *Klebsiella pneumoniae* infection

We reviewed the medical records of 96 index patients, whose mean age was 65.4 years, with a male-to-female ratio of 2.6:1. In univariable analysis, we have found the association of CRKP infection with Charlson comorbidity index, renal dysfunction, cardiovascular disease, ICU stay at the time of the positive culture, previous antibiotic use, use of β-lactams and β-lactamase inhibitor combinations, use of cephalosporins, carbapenems, fluoroquinolones, and antifungal agents, receipt of mechanical ventilation, indwelling of urethral catheter and gastric tube, hemodialysis, blood products' use, and Charlson comorbidity index [Table 1].

In multivariable logistic analysis, exposure to β-lactams and β-lactamase inhibitor combinations, cephalosporins, fluoroquinolones, ICU stay, and indwelling of urethral catheter tube were identified as risk factors for acquiring CRKP isolates [Table 2].

Table 1: Comparison of clinical characteristics of CSKP and CRKP

Parameters	CRKP (n = 48)	CSKP (n = 48)	$F/t/\chi^2$	P
Age (years), mean ± SD	67.7 ± 19.5	63.1 ± 17.8	1.08	0.230‡
Male, *n* (%)	35 (72.9)	34 (70.8)	1.65	0.821*
Concomitant diseases, *n* (%)				
Lung disease	6 (12.5)	6 (12.5)	0.86	>0.050*
Cardiovascular disease	34 (70.8)	23 (47.9)	4.89	0.024*
Hepatobiliary disease	11 (22.9)	11 (22.9)	2.34	>0.050
Renal dysfunction	21 (43.8)	11 (22.9)	0.68	0.033*
Diabetes mellitus	18 (37.5)	15 (31.3)	2.45	0.520*
Autoimmune disease	6 (12.5)	2 (4.2)	2.33	0.159*
Neurologic disease	22 (45.8)	13 (27.1)	3.29	0.059*
Tumor	13 (27.1)	18 (37.5)	1.66	0.277*
Hospitalization within the past half year, *n* (%)	33 (68.8)	25 (52.1)	2.03	0.097*
Previous surgery, *n* (%)	10 (20.8)	16 (33.3)	1.67	0.171*
ICU stay, *n* (%)	25 (52.1)	3 (6.3)	20.34	<0.001*
Previous antibiotic use within the past 1 month, *n* (%)	45 (93.8)	22 (45.8)	23.46	<0.001*
Exposure to any antibiotic, *n* (%)				
β-lactams and β-lactamase inhibitor combinations	29 (60.4)	12 (25.0)	30.45	0.001*
Cephalosporins	15 (31.3)	5 (10.4)	13.43	0.016*
Carbapenems	16 (33.3)	3 (6.3)	12.34	0.003*
Fluoroquinolones	14 (29.2)	6 (12.5)	3.85	0.050*
Aminoglycosides	2 (4.2)	2 (4.2)	0.81	>0.050*
Antifungal agents	4 (29.2)	4 (8.3)	8.65	0.014*
Metronidazole	6 (12.5)	5 (10.4)	1.23	0.749*
Fosfomycin	2 (4.2)	1 (2.1)	2.44	0.565*
Glycopeptides	9 (18.8)	3 (6.3)	3.11	0.077*
Aztreonam	7 (14.6)	2 (4.2)	2.56	0.099*
Others	9 (188)	4 (8.3)	2.44	0.145*
Invasive procedures, *n* (%)				
Deep venous catheterization	13 (27.1)	8 (16.7)	2.78	0.221*
Mechanical ventilation	26 (54.2)	11 (22.9)	18.90	0.002*
Indwelling of urethral catheter	33 (68.8)	14 (29.2)	27.89	0.000*
Indwelling of gastric tube	34 (70.8)	15 (31.3)	28.86	0.000*
Parenteral nutrition	4 (8.3)	7 (14.6)	2.11	0.342*
Hemodialysis	12 (25.0)	4 (8.3)	4.56	0.036*
Puncture	9 (18.8)	16 (33.3)	2.34	0.063*
Use of systemic steroids, *n* (%)	16 (33.3)	15 (31.3)	1.34	0.827*
Use of blood products, *n* (%)	27 (56.3)	15 (31.3)	8.89	0.015*
Chemotherapy, *n* (%)	4 (8.3)	8 (16.7)	3.41	0.225*
Hospital stay (days), median (25^{th} percentile–75^{th} percentile)	84 (41–188)	33 (21–60)	2.33	0.097†
Charlson comorbidity index, median (25^{th} percentile–75^{th} percentile)	4.0 (3.0–5.5)	3 (2.0–3.0)	14.45	0.001†
Time at risk (days), median (25^{th} percentile–75^{th} percentile)	46 (20–129)	12 (7–20)	2.34	0.263†
Mortality, *n* (%)	23 (47.9)	2 (4.2)	9.83	0.030*

*Chi-squared test with continuity correction; †Mann-Whitney *U*-test; ‡Student's *t*-test. KP: *Klebsiella pneumoniae*; SD: Standard deviation; CSKP: Carbapenem-susceptible KP; CRKP: Carbapenem-resistant KP; ICU: Intensive Care Unit.

Risk factors associated with mortality caused by *Klebsiella pneumoniae*

Among the 48 patients enrolled with CRKP infection, 23 (47.9%) patients died, while 2 (4.2%) patients died in the CSKP infection group. Among the total 25 deaths, most of the infections were concentrated in lower respiratory tract infection (21/25, 84.0%), followed by urinary tract infection (4/25, 16.0%). Mortality of KP infections was the same in concomitant diseases and invasive procedures as shown in the result of univariable analysis, presented in Table 3. The result from multivariable analysis indicated that older age, Charlson comorbidity index, and aminoglycosides use were independent risk factors for mortality. However, carbapenems' use was not found to be associated with mortality [Table 4].

The minimum inhibitory concentration of antimicrobial in *Klebsiella pneumoniae* carbapenemase-producing carbapenem-resistant *Klebsiella pneumoniae* isolates

As shown in Table 5, the antimicrobial susceptibilities between 31 KPC gene-positive CRKP isolates and 17 KPC gene-negative CRKP isolates were compared, and the MIC of the carbapenems, levofloxacin, β-lactams, and β-lactamase inhibitor combinations between the two groups was found to be significantly different. Fourteen of 31 KPC-gene positive isolates were separated from death group patients, with the 17 isolates of the rest from survival group. There was no significant difference for MIC between the death and the survival groups.

Discussion

CRKP is resistant to almost all antimicrobial agents, hence it poses a serious threat to public health.[7] Previously reported outbreaks have been associated with the plasmid-encoded KPC.[8] CRKP isolates harboring KPC gene are susceptible only to polymyxins, tigecycline, and few remaining aminoglycosides.[9] CRKP strains contain various drug resistance genes and they have exhibited relatively high resistance to ethyl alcohol, chlorhexidine acetate, and iodophor.[10] There has been a remarkable increase in CRKP cases reported in China since 2010. ST11 is the major clone in China.[11,12] In terms of clinical practice, we believe that more attention should be paid to risk factors associated with CRKP infection and KP-induced death.

Table 2: Multivariate analysis of risk factors for CRKP infections

Items	*OR* (95% *CI*)	*P*
β-lactams and β-lactamase inhibitor combinations	4.765 (1.508–15.055)	0.008
Cephalosporins	8.033 (1.623–39.763)	0.011
Fluoroquinolones	6.090 (1.343–27.613)	0.019
ICU stay	15.486 (3.175–75.541)	0.001
Indwelling of urethral catheter	6.164 (1.847–20.578)	0.003

KP: *Klebsiella pneumoniae*; CRKP: Carbapenem-resistant KP; ICU: Intensive Care Unit; *OR*: Odds ratio; *CI*: Confidence interval.

In our retrospective analysis, we found that a few independent risk factors were associated with infection and death. The use of any antibiotic within the past 1 month and exposure to β-lactams and β-lactamase inhibitor combinations, cephalosporins, and fluoroquinolones, rather than the carbapenems, were associated with CRKP infections. The result of our study is consistent with those of several earlier studies in which different kinds of antibiotic administration prior to CRKP infection were risk factors.[13-16] It remains a question how exposure to fluoroquinolones predisposes carbapenems' resistance among CRKP.

One of the other studies suggests that plasmid-encoded quinolone resistance determinant gene causing low-level fluoroquinolone resistance was located on KP plasmids encoding KPC genes.[13] Another study suggests that fluoroquinolones led to upregulation of the multidrug efflux pump MexEF-OprN and reduced levels of OprD porin,[17] with supervenient resistance to both fluoroquinolone and carbapenems.[18] The significance of these findings is not clear, but they have indicated that restricting the inappropriate use of antibacterial agents will decrease the chance of spreading CRKP.

Our study also suggested that ICU stay was associated with CRKP infection, which was consistent with some other studies.[4,19] The airborne and contact transmission of resistant bacteria in the ICU environment probably led to nosocomial infection on most patients admitted to the ICU,[13] especially for the critically ill patients with prolonged ICU stay who may undergo more invasive procedures and be treated with more broad-spectrum antibiotics. We also found in our study that indwelling of urethral catheter was an independent risk factor associated with CRKP infection, due to its close contact with the mucosal surface. Frequent invasive operations and tube indwelling could cause mucosal barrier injury, which eventually leads to further decline of body resistance and increase in the possibility of CRKP infection. Similarly, the studies conducted by Jiao *et al.*[13] and Tuon *et al.*[20] had shown that tracheotomy and mechanical ventilation were the independent risk factors associated with CRKP infection, respectively.

As indicated in our data, the mortality of CRKP infection patients was 47.9%, which was considerably higher than that of control group (4.2%, $P < 0.05$). The number of CRKP isolates detected from the death group was 23, 92% of all deaths, among them 14 KPC-gene positive isolates accounted for 60.8%. Nonetheless, the number of CRKP isolates detected from the survivals was 25, 35.2% among them, 17 KPC-gene positive isolates accounted for 68%. There was no significant difference between two groups on KPC gene carriage; however, there was a significant difference on the MIC of three kinds of antibiotics which were carbapenems, β-lactams/β-lactamase inhibitor combinations, and fluoroquinolone. There was no statistically significant difference of MIC between death group and survival group in KPC-gene positive isolates. It appears that the KPC was irrelevant to the patients with KPC gene-positive CRKP

Table 3: Analysis of risk factors associated with KP infection-induced death

Clinical characteristic	Death (n = 25)	Survival (n = 71)	$F/t/\chi^2$	P
Age (years), mean ± SD	74.2 ± 16.54	62.34 ± 18.61	30.67	0.006‡
Male, *n* (%)	22 (88.0)	47 (66.2)	8.76	0.037*
Concomitant diseases, *n* (%)				
Lung disease	3 (12.0)	9 (12.7)	2.34	0.930*
Cardiovascular disease	20 (80.0)	37 (52.1)	9.88	0.019*
Hepatobiliary disease	6 (24.0)	16 (22.5)	1.56	0.881*
Renal dysfunction	17 (68.0)	15 (21.1)	40.56	<0.001*
Diabetes mellitus	12 (48.0)	21 (29.6)	2.44	0.099*
Autoimmune disease	2 (8.0)	6 (8.5)	1.09	0.944*
Neurologic disease	12 (48.0)	23 (32.4)	2.34	0.166*
Tumor	11 (44.0)	20 (28.2)	2.13	0.149*
Hospitalization within the past half year, *n* (%)	19 (76.0)	39 (54.9)	3.12	0.069*
Previous surgery, *n* (%)	3 (12.0)	23 (32.4)	3.82	0.059*
ICU stay	15 (60.0)	13 (18.3)	20.45	<0.001*
Receipt of antibiotics, *n* (%)				
β-lactams and β-lactamase inhibitor combinations	15 (60.0)	33 (46.5)	2.11	0.248*
Cephalosporins	7 (28.0)	14 (19.7)	2.01	0.391*
Fluoroquinolones	9 (36.0)	17 (23.9)	2.33	0.247*
Aminoglycosides	12 (48.0)	3 (4.2)	20.12	<0.001*
Carbapenems	13 (52.0)	27 (38.0)	1.34	0.226*
Glycopeptides	5 (20.0)	11 (15.5)	1.86	0.604*
Metronidazole	2 (8.0)	8 (11.3)	1.78	0.647*
Fosfomycin	3 (12.0)	4 (5.6)	2.56	0.303*
Antifungal agents	10 (40.0)	9 (12.7)	20.45	0.005*
Others	9 (36.0)	13 (18.3)	2.88	0.075*
Site of infection, *n* (%)				
Respiratory tract	15 (60.0)	31 (43.7)	1.23	0.163*
Urinary tract	3 (12.0)	14 (19.7)	1.35	0.390*
Blood	4 (16.0)	15 (21.1)	1.67	0.581*
Others	3 (12.0)	11 (15.5)	1.58	0.671*
Invasive procedures, *n* (%)				
Deep venous catheterization	8 (32.0)	13 (18.3)	2.32	0.159*
Mechanical ventilation	19 (76.0)	18 (25.4)	40.12	<0.001*
Indwelling urethral catheter	18 (72.0)	29 (40.8)	32.11	0.009*
Indwelling gastric tube	20 (80.0)	29 (40.8)	34.56	0.002*
Parenteral nutrition	3 (12.0)	8 (11.3)	1.24	0.921*
Hemodialysis	10 (40.0)	6 (8.5)	24.56	0.001*
Puncture	4 (16.0)	20 (28.2)	1.67	0.233*
Use of systemic steroids, *n* (%)	8 (32.0)	23 (32.4)	1.76	0.971*
Use of blood products, *n* (%)	20 (80.0)	22 (31.0)	22.27	<0.001*
Chemotherapy, *n* (%)	2 (8.0)	10 (14.1)	2.67	0.435*
Hospital stay (days), median (25^{th} percentile–75^{th} percentile)	148 (71–225)	37 (22–71)	32.89	<0.001†
Charlson comorbidity index, median (25^{th} percentile–75^{th} percentile)	87.0 (42.0–152)	15.0 (7.0–33.0)	34.43	<0.001†
Time at risk (days), median (25^{th} percentile–75^{th} percentile)	6 (5–7)	3 (2–3)	28.89	<0.001†

*Chi-squared test with continuity correction; †Mann -Whitney *U*-test; ‡Student's *t*-test. *n*: Number of participants; SD: Standard deviation; KP: *Klebsiella pneumoniae*; ICU: Intensive Care Unit.

Table 4: Multivariate analysis of risk factors for KP infection-induced death

Items	*OR* (95% *CI*)	*P*
Charlson comorbidity index	4.690 (2.094–10.504)	0.000
Aminoglycosides	670.252 (6.577–68307.730)	0.006
Age	1.079 (1.005–1.158)	0.036

KP: *Klebsiella pneumoniae*; *OR*: Odds ratio; *CI*: Confidence interval.

mortality. Some studies suggested that KPC-producing KP gut colonization and infection appears to be an important risk factor for mortality. Further investigation remains to be performed.[21,22]

Charlson *et al*.'s weighted index of comorbidities is a rating system which is based on the underlying diseases.[23] Our data also identified that the median of Charlson comorbidity index of the death was 87, which was higher than the survival's (15).

Table 5: The comparison of antimicrobial MIC between KPC gene-positive and KPC gene-negative CRKP isolates

Items	AK	IP	MP	ETP	CPS	PTc	PM	MX	LE	TGC	CRO	TZ
*P**	0.501	0.126	0.880	0.370	0.697	0.373	0.375	0.143	0.449	0.309	0.091	0.961
P†	0.620	0.001	0.001	0.038	0.034	0.016	0.348	0.059	0.035	0.301	0.180	0.126

*The MIC difference between death group and survival group in KPC-gene positive isolates; †The MIC difference between KPC-gene positive group and negative group. AK: Amikacin; IP: Imipenem; MP: Meropenem; ETP: Ertapenem; CPS: Cefoperazone-sulbactam; PTc: Piperacillin-tazobactam; PM: Cefepime; MX: Moxifloxacin; LE: Levofloxacin; TGC: Tigecycline; CRO: Ceftriaxone; TZ: Ceftazidime; MIC: Minimum inhibitory concentration; KP: *Klebsiella pneumoniae*; KPC: KP carbapenemase; CRKP: Carbapenem-resistant KP.

Older age and high Charlson comorbidity index were independent risk factors for mortality of KP-infected patients. Meanwhile, several studies have found higher mortality rates related to patients' comorbidity.[24,25] The other study showed that the only risk factor independently associated with 30-day mortality was an elevated SOFA score on the 1st day of infection.[26] Some of the present clinical studies[27,28] focus on using antimicrobials to treat CRKP-infected patients to reduce mortality. Our study showed that more extensive use of aminoglycosides was also an independent risk factor. Whether the toxicity of the aminoglycosides induces the death of the hosts, which needs further research.

Apparently, ages, severe accompanying diseases, and inadequate antibiotic treatment would impair the immunity and increase the risk of infection and even death.

Our study had several limitations: first, the sample size was not large, which might lead to deviation in statistical analysis; second, this study was only conducted in one tertiary care teaching hospital in Beijing, China, the situation may differ in other cities and countries. Multisite study should be performed to have more reliable results.

In conclusion, mortality rate of CRKP infections is high, a high score of Charlson comorbidity index is the representative relevant risk factor in KP infection-caused deaths, which often occur in elderly frail patients with aminoglycoside use. Independent risk factors for CRKP infection were admission to ICU, antimicrobial use, and invasive operation. Therefore, it is of crucial importance to implement infection control measures and protect the immune function of the patients.

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Conflicts of interest

There are no conflicts of interest.

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