Pakistan J. Zool., vol. 57(3), pp 1083-1090, 2025 DOI: https://dx.doi.org/10.17582/journal.pjz/20230725182234

Drug Resistance of Bloodstream Infection with *Klebsiella pneumoniae* and Detection of drug resistance Genes

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ABSTRACT

Klebsiella pneumoniae (KP) bacteria are usually present on mucous membranes in animals or in the environment (e.g., water and soil). This work investigated the drug resistance (DR) of bloodstream infection (BSI) KP and the risk factors of infection and prognosis of KP. One hundred and fifty KP strains in our hospital were selected and rolled into a survival group (63 cases) and a death group (87 cases) according to clinical outcomes. According to the type of DR, the strains were rolled into a carbapenem-sensitive KP (CSKP) group (n = 93) and a carbapenem-resistant KP (CRKP) group (n = 57). The DR and resistance genes of KP were analyzed. Logistic regression analysis (LRA) was utilized to explore the risk factors of KP infection and its prognosis. Strains in this work showed DR to most antibiotics, with TEM (20.7%), CTX (14%), and SHV (33.3%) being the main components. Logistic multivariate analysis (LMA) showed that hyperglycemia and history of immune diseases were independent risk factors (IRFs) for CRKP infection (P<0.05), and advanced age, septic shock, bacteremia, and organ failure were IRFs for predicting the death of patients (P<0.05). To conclude KP BSI strains (TEM, CTX, and SHV strains) showed DR to most antibiotics. Hyperglycemia and history of immune diseases were IRFs for CRKP infection; while advanced age, septic shock, bacteremia, and organ failure were IRFs for predicting death.

Article Information
Received 25 May 2023
Revised 28 September 2023
Accepted 08 October 2023
Available online 29 December 2023 (early access)
Published 21 April 2025

Authors' Contribution
JL and XZ collected the samples. JL analysed the data. XZ conducted the experiments and analysed the results. All authors discussed the results and wrote the manuscript.

Key words
Bloodstream infection, *Klebsiella pneumoniae*, Drug resistance, Infection, Risk factors

INTRODUCTION

Klebsiella pneumonia (KP) bacteria are usually present on mucous membranes in animals or in the environment (e.g., water and soil). In human body, KP bacteria are mainly located in the gastrointestinal tract and a few in the nasopharynx. When the body's immunity is low, KP bacteria can enter the blood circulation or other tissues through mucous membranes and cause infection (Shen *et al*., 2020). KP bacteria have become a major cause of nosocomial infection, as well as a risk factor for serious community-acquired infection, which can cause lung, blood, skin tissue, urinary system and other infections (Whang *et al*., 2020). Carbapenem is stable for AmpC beta-lactamases or extended spectrum B-lactamases (ESBLs) because its antibacterial profile covers many Gram-negative and Gram-positive bacteria well, and carbapenem is widely and widely used (Taherikalani *et al*., 2013). However, after a carbapenem-resistant *Klebsiella pneumoniae* (CRKP) strain of *Klebsiella pneumoniae* (KPC) was firstly reported in the United States, a large number of carbapenem-resistant Enterobacteriaceae (CRE) strains have been gradually reported worldwide, seriously threatening global public health security (Durante-Mangoni *et al*., 2019). However, the bloodstream infection (BSI) of bacteria gets into the bloodstream has a very high mortality rate and is prone to metastatic infection and nosocomial infection as well as antibiotic resistance, which increases the difficulty of clinical treatment and brings more challenges to clinicians (Hsu *et al*., 2021).

BSI is a serious clinical syndrome caused by bacteria, which can lead to shock, multiple organ failure, etc. (Huang *et al*., 2022). KP BSI has become a global problem, with drug-resistant outbreaks occurring in some countries or regions. Most cases have been reported in southern Europe (Italy, Athens, etc.), Asia (Korea, China, etc.), USA, etc. A multicenter retrospective study in China showed that the overall incidence of BSI of KP bacteria was 20.5%, while a multicenter retrospective study in Italy showed that the incidence of BSI caused by drug-resistant strains could be as high as 67.6%. BSI is often significantly associated with higher mortality, and is one of the IRFs of KP infection

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0030-9923/2025/0003-1083 $ 9.00/00

death (Moraes *et al*., 2022). The mortality rate of BSI caused by antibiotic-resistant strains was significantly higher than that caused by antibiotic-sensitive strains. Most studies show that there is a wide range of factors affecting death in patients with KP bacteria BSI (Reis *et al*., 2022; Long *et al*., 2022), including advanced age, septic shock, mechanical ventilation, central venous catheter, and insensitive empirical anti-infection treatment. However, there is still some controversy. A few studies have shown that insensitive empiric anti-infective therapy has no significant correlation with clinical outcome.

Broad-spectrum cephalosporins and quinolones are commonly used in the treatment of KP bacteria (Shin *et al*., 2022). However, the widespread use of such drugs has accelerated the emergence of quinolone resistance and EsBL-producing *E. coli* and KP bacteria, which have become epidemic trends in many parts of the world. Due to the decreased activity of the above antibacterial drugs, more and more clinicians choose carbapenem antibiotics for related infections, accelerating the emergence of CRE and forming an outbreak trend in recent years (Chiotos *et al*., 2020). The drug resistance rate of BSI KP bacteria is between 30% and 65%, and even higher in some areas. KPC can effectively hydrolyze all cephalosporins, monocycloβlactam, carbapenem drugs, and even β-lactamase inhibitors, forcing people to increase the use of some second-line drugs, such as tigacycline, colistin, and gentamicin (Hu *et al*., 2021). Over time, more and more studies found that the resistance rate of bacteria to colistin gradually increased, from the initial 20% to 59%, which may be related to the increased use of this drug in recent years. The outbreak of drug-resistant bacteria brings new challenges to anti-infective treatment.

Therefore, in order to clarify the drug resistance characteristics of KP, the sensitivity of KP to antibiotics, drug resistance (DR) and related genes were analyzed in this work. Furthermore, logistic multivariate analysis (LMA) was performed on the data of different patients, and logistic regression analysis (LRA) was conducted for the indicators with significant differences to explore the risk factors of KP infection and the risk factors affecting its prognosis, to give a reference for the control of KP bacteria in clinic.

MATERIALS AND METHODS

Subjects

One hundred and fifty strains of KP isolated from our hospital from 2021 to 2023 were collected as study specimens. All-cause mortality was calculated within 30 days of positive blood culture, and patients were divided into a survival group (63 cases) and a death group (87 cases) according to the final outcomes. The strains were divided into 93 carbapenem-sensitive (CSKP) and 57 carbapenem-resistant *Klebsiella pneumoniae* (CRKP) groups.

The patients were enrolled if they satisfied the two conditions: Firstly, the patients showed at least one CRKP positive blood culture meeting the diagnostic criteria of BSI, that is, body temperature > 38℃ or < 36℃, accompanied by chills, combined with one of the following conditions such as presence of (i) invasion portals or migration lesions; (ii) symptoms of systemic poisoning without obvious infection; (iii) rash or hemorrhagic spots, hepatosplenomegaly, blood neutrophilia with left shift of nucleus, and no other explanation; (iv) systolic blood pressure was < 90 mmHg or decreased by 40 mmHg from the original systolic blood pressure; and (v) blood culture isolated pathogenic microorganisms or antigenic substances of pathogens detected in blood. Secondly, all the obtained KP strains can be detected by standard microbiology methods and Phoenix System-L00BD automated Microbiology System (BD Diagnostics, USA), and confirmed as KP bacteria.

The patients were excluded if they had any of the following conditions: (1) KP BSI patients without clinical records; (2) those with repeated detection and combination of other bacterial/viral infections; (3) patients who died within 24 h after the onset of BSI; and (5) those with anti-infective treatment <48 h.

Antimicrobial susceptibility test

The strain was inoculated on LB medium and cultured overnight. The next day, the Phoenix ix system - l00 BD automation microbial system measured its antimicrobial sensitivity. Antibiotics mainly first-generation cephalosporins (cefazolin), the second-generation cephalosporins (cefuroxime), the third-generation cephalosporins (ceftriaxone, ceftazidime, and cefotaxime), fourth-generation of cephalosporins (cefepime), monocyclic β-lacamides (amtronam), cephalomycin (cefoxitin) β-lactam antibiotic compound preparations (amoxicillin/clavulanic acid, cefotaxime/clavulanic acid, ceftazidime/clavulanic acid, piperacillin/tazobactam, and ampicillin/sulbactam), sulfanilamide antimicrobial drugs (compound neosumine), sminoglycosides (amikacin, gentamicin, ciprofloxacin, and levofloxacin), penicillin (piperacillin and ampicillin), carbapenem antibiotics (meropenem and imipenem), Tetracycline; Chloramphenicol. The results of drug sensitivity were interpreted according to the recommendations of the American Institute of Clinical and Laboratory Standards.

Detection of drug resistance genes

Detection of drug resistance genes 133 genomic DNA of 153 strains was extracted by boiling method as amplification template. PCR was 134 used to amplify ESBLs encoding genes (*blacTx, blaTEM,* and *blasHv*) and carbapenem enzyme 135 encoding genes (*blakpc, blanDM, blamp, blavIM,* and *blaoxA-48*). The amplified DNA was detected by 136 agarose gel electrophoresis. The PCR products of the PCR positive strains weresent to Shanghai 137 Bioengineering Technology Co., Ltd. for sequencing, and the sequencing results were compared.

Primers of drug resistance genes and virulence genes were designed based on the principle of primer specificity. Primers were synthesized by Sangon Bioengineering (Shanghai) Co., LTD. The sequence of drug resistance gene primers was shown in Table I.

The PCR cycle conditions were as follows: Predenaturation at 90°C for 10 min, denaturation at 95°C for 30 sec, annealing at 60°C for 30 sec, extension at 72°C for 60 sec, with 35 cycles in total. It was extended for 5 min at 72°C. The amplified product was subjected to agarose nucleic acid gel electrophoresis with a voltage of 100 V and a concentration of 1% for 45 min.

Assessment indicators of risk factors

For assessment of risk factors of KP infection the basic clinical information of patients, including age, gender, previous disease history (lung, liver, and gallbladder disease, etc.), complications (hyperglycemia, hypertension, liver abscess, etc.), acute physiological and chronic health (APACHE II) score (Kumar and Griwan, 2018), and organ failure estimated score (SOFA score) (Zhang *et al*., 2022) were recoded. In addition to preoperative basic data, the length of hospital stays (LOS), and invasive procedures (central venous catheter PICC inserted into peripheral vein, mechanical ventilation, gastroscopy, endoscopic retrograde cholangiopanchography ERCP, bronchoscopy, blood purification, central venous catheter CVC indent, and indent catheter) received after admission were collected, APACHE II scores, and SOFA scores were also recoded.

Statistical analysis

SPSS 23.0 was utilized for statistical analysis. The measurement data consistent with normal distribution were represented by mean ± standard deviation (x ± s). Independent sample T test was utilized for comparison between the two groups, and Mann-Whitney U test was employed for analysis of non-normal distribution. Count data were expressed in frequency and percentile and analyzed using Chi-square test or Fisher's exact probability method. The risk factors of infection or death were analyzed by binary logistic regression. $P<0.05$ was considered to be statistically significant.

Table I. Sequence of primers of drug-resistant genes.

Genes	Primer (5'→3')	Amplification length (bp)
bla_{NDM-1}	F GGGCAGTCGCTTCCAACGGT	475
	R GTAGTGCTCAGTGTCGGCAT	
bla_{VIM}	F GATGGTGTTTGGTCGCATA	390
	R CGAATGCGCAGCACCAG	
bla_{KPC}	F CGTCTAGTTCTGCTGTCTTG	798
	R CTTGTCATCCTTGTTAGGCG	
bla_{IMP}	F GGAATAGAGTGGCTTAAYTCTC	232
	R CCAAACYACTASGTTATCT	
bla_{OXA-48}	F GCGTGGTTAAGGATGAACAC	438
	R CATCAAGTTCAACCCAACCG	
bla_{TEM}	F TCGCCGCATACACTATTCTCAGAATGA	445
	R ACGCTCACCGGCTCCAGATTTAT	
bla_{SHV}	F ATG CGT TATATT CGC CTG TG	747
	R TGC TTT GTT ATT CGG GCC AA	
bla_{CTX-M}	F ATGTGCAGYACCAGTAARGTKATGGC	593
	R TGGGTRAARTARGTSACCAGAAYCAGCGG	

RESULTS

Analysis of DR characteristics of KP bacteria

Table II shows the DR rates of different antobiotics used in this study.

Table II. Results of antimicrobial susceptibility test.

Type	R	General	S
Ceftriaxone	36 (24.0)	22 (14.7)	92 (61.3)
Cefuroxime	51 (34.0)	16 (10.7)	83 (55.3)
Cefazolin	74 (49.3)	13 (8.7)	63 (42.0)
Cefepime	33 (22.0)	8 (5.3)	107 (71.3)
Ceftazidime	41 (27.3)	10 (6.7)	99 (66.0)
Cefotaxime	51 (34.0)	14 (9.3)	85 (56.7)
Cefoxitin	24 (16.0)	16 (10.7)	110 (73.3)
Amtriannan	46 (30.7)	4 (2.7)	100 (66.7)
Cefotaxime/clavulanic acid	27 (18.0)	35 (23.3)	88 (58.7)
Ceftazidime/clavulanic acid	31 (20.7)	52 (34.7)	96 (64.0)
Ampicillin/sulbactam	52 (34.7)	12 (8.0)	86 (57.3)
Amoxicillin/clavulanic acid	32 (21.3)	15 (10.0)	106 (70.7)
Piperacillin/tazobactam	30 (20.0)	9 (6.0)	111 (74.0)
Cotrimoxazole	44 (29.3)	0 (0.0)	140 (93.3)
Ciprofloxacin	32 (21.3)	10 (6.7)	108 (72.0)
Amikacin	5 (3.3)	1 (0.7)	144 (96.0)
Gentamicin	29 (19.3)	0 (0.0)	121 (80.7)
Levofloxacin	30 (20.0)	7 (4.7)	113 (75.3)
Ampicillin	147(98.0)	2 (1.3)	1 (0.7)
Piperacillin	60 (40.0)	4 (2.7)	86 (57.3)
Imipenem	7 (4.7)	0 (0.0)	143 (95.3)
Meropenem	5 (3.3)	1 (0.7)	144 (96.0)
Chloramphenicol	41 (27.3)	2 (1.3)	107 (71.3)
Tetracycline	50 (33.3)	6 (4.0)	94 (62.7)

R, resistant; S, sensitive.

The results shown in Figure 1 demosntrated that strains of the genes *blaIMP, blaOXA-48,* and *blaNDM* tested positive. Strains expressing *blaVIM, blaKPC, blaTEM, blaSHV,* and *blaCTX* accounted for 1.3%, 4.7%, 20.7%, 33.3%, and 14%, respectively. Meanwhile, those co-expressing *blaTEM+blaSHV, blaCTX+blaSHV,* and *blaTEM+blaSHV+blaCTX* accounted for 12%, 6.7%, and 4.7%, respectively.

Analysis of risk factors of KP infection

Univariate analysis disclosed that 9 patients in the CRKP group were complicated with liver abscess, 21 patients were with hyperglycemia, and 3 patients had a history of immune diseases, showing great differences to those in the CSKP group (P<0.05). However, no obvious difference was observed in other indicators (P>0.05), as shown in Table III.

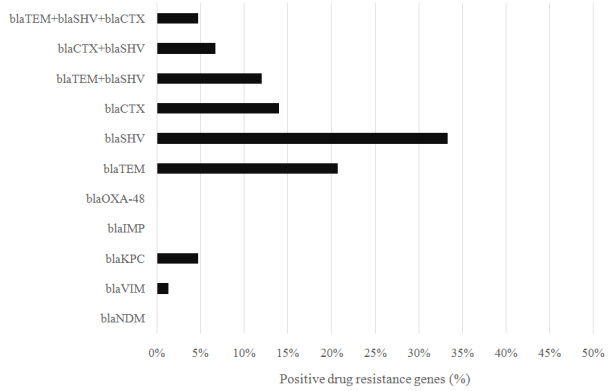

Fig. 1. Results of drug resistance gene detection.

Table III. Results of univariate analysis of infection factors.

Indicators	CRKP group (n = 57)	CSKP group (n = 93)	x^2	P
Age (years old)	48.3±6.2	47.5±6.6	0.836	0.217
Sex (cases)			0.463	0.509
Males	35	59		
Females	22	34		
Complications (cases)				
Liver abscess [a]	9	3	7.164	0.007
Organ failure	2	5	0.177	1.936
Hyperglycemia [a]	21	14	9.636	0.002
Hypertension	13	28	0.537	0.498
Hydrothorax	3	6	0.106	1.985
Bacteremia	9	14	0.268	0.579
Septic shock	8	14	0.274	0.586
History of diseases (cases)				
Respiratory disease	5	9	0.359	0.762
Hepatobiliary diseases	12	20	1.839	0.273
Gastrointestinal diseases	8	15	0.036	3.845
Diseases of urinary system	2	2	0.937	0.209
Cardiovascular and cerebrovascular diseases	11	19	0.088	2.094
Neuropathy	2	1	3.928	0.124
Immune disease [a]	3	15	13.874	0.000
Neoplastic diseases	5	8	1.447	0.259
Others				
SOFA score	7.3±2.4	7.8±3.1	3.614	0.852
APACHE II score	15.7±6.3	16.5±7.1	2.742	0.186

[a] indicated an observable difference with P<0.05 based on the CSKP group. APACHE, acute physiology and chronic health; CRKP, carbapenem-resistant *Klebsiella pneumoniae;* CSKP, carbapenem-sensitive *Klebsiella pneumoniae;* SOFA, Organ failure estimated score.

In this case, LMA was further performed (Table IV), which revealed that the history of diabetes and history of immune diseases were IRFs of CRKP infection.

Table IV. LMA results of risk factors.

Influencing factors	β	S.E.	Wald	OR	P	95% CI	
						Upper limit	Lower limit
Liver abscess	0.208	0.603	0.084	6.174	0.287	0.928	26.643
Hyperglycemia	3.937	0.417	32.491	13.103	<0.01	2.938	13.268
History of immune diseases	1.727	0.826	4.584	9.995	<0.01	2.306	10.891

Related risk factors affecting prognosis

Analysis of prognostic factors showed that the mean age of patients in the survival group was (44.3±5.8) years and the mean LOS was 22.4±4.7 days. There were 2 patients with organ failure, 6 patients with septic shock, 21 patients with mechanical ventilation, 9 patients with endoscopic retrograde cholangiopancreatography (ERCP), 13 patients with blood purification, 14 patients with central venous catheter (CVC), and 28 patients with catheter. Besides, the average APACHE II score was 13.5±5.8. All these indicators exhibited obvious differences with the values in the death group (P<0.05). Table V listed the above results data.

Based on this, LMA was further applied to these factors and disclosed that advanced age, septic shock, organ failure, and bacteremia were IRFs to predict the death of the patient (Table VI).

DISCUSSION

KP bacteria belong to Enterobacteriaceae, Gram-negative bacilli, strong resistance to the outside world, can exist in human skin, respiratory tract, intestinal tract, and urogenital tract. Generally, it does not cause disease, but can cause BSI, pneumonia and urinary tract infection when the body's resistance decreases. With the widespread use of broad-spectrum antibiotics, especially carbapenem, invasive procedures, glucocorticoids and immunosuppressants, and the increase in organ transplantation, carbapenem resistant infections are becoming more prominent, especially the increasing incidence of KP BSI worldwide. It has become one of the difficult problems in clinical anti-infection treatment (Falcone et al., 2021). In addition, the overall resistance rate of various antibacterial agents to KP

Table V. Results of univariate analysis of prognostic factors.

Indicators	Survival group (n = 63)	Death group (n = 87)	x^2	P
Age (years old) [a]	44.3±5.8	50.2±6.1	7.092	0.008
LOS (d) [a]	22.4±4.7	31.8±5.2	1.148	0.035
Sex (cases)			1.093	0.632
Males	38	51		
Females	25	36		
Complications (cases)				
Liver abscess	16	19	4.902	0.927
Organ failure [a]	18	20	5.471	0.781
Hyperglycemia	5	7	4.829	0.537
Hypertension	2	5	6.311	0.044
Hydrothorax	5	4	2.958	0.498
Bacteremia [a]	10	24	7.529	0.001
Septic shock [a]	6	16	1.154	0.001
History of diseases (cases)				
Respiratory disease	8	6	7.482	0.705
Hepatobiliary diseases	11	15	4.992	0.558
Gastrointestinal diseases	10	13	3.091	0.691
Diseases of urinary system	1	3	6.853	0.825
Cardiovascular and cerebrovascular diseases	16	14	5.104	0.384
Neuropathy	1	2	9.685	1.006
Immune disease [a]	4	4	8.626	1.532
Neoplastic diseases	5	7	5.287	0.207
Invasive operation (cases)				
PICC[a]	10	31	7.185	0.008
Mechanical ventilation [a]	21	54	9.738	0.002
Gastroscope	15	15	4.216	0.594
ERCP[a]	9	3	8.099	0.008
Bronchoscope	18	22	1.093	0.707
Blood purification [a]	13	46	9.517	0.001
CVC [a]	14	37	6.291	0.002
Indwelling catheter	28	40	2.642	0.264
Mode of administration				
Simple drug	30	42	3.628	0.717
Combination of drugs	33	45	4.653	0.536
Others				
SOFA score	5.5±3.1	8.3±4.2	7.901	0.457
APACHE II score [a]	13.5±5.8	18.2±6.4	1.862	0.024

[a] indicated an observable difference with P<0.05 based on the death group. ERCP, endoscopic retrograde cholangiopancreatography; CVC, central venous catheter; PICC, peripherally inserted central catheter; LOS, length of stay. For other abbreviation, see Table III.

Table VI. LMA regression results of prognostic factors.

Influencing factors	β	S.E.	Wald	OR	P	95% CI	
						Upper limit	Lower limit
Advanced age	0.182	0.007	7.458	2.125	< 0.05	1.001	2.073
LOS	3.385	1.462	6.298	4.291	0.583	0.976	6.185
Organ failure	4.635	2.859	9.748	55.841	< 0.05	4.729	75.582
Septic shock	-2.005	0.483	8.473	2.103	< 0.01	1.494	5.394
Bacteremia	-0.183	0.034	7.394	0.505	< 0.05	2.094	0.287
PICC	0.205	0.592	0.039	1.086	0.726	3.173	0.952
Mechanical ventilation	-0.447	0.198	0.381	8.088	0.615	0.584	3.121
ERCP	4.162	2.409	8.411	52.427	3.194	3.455	100.136
Blood purification	-0.596	0.542	1.883	0.686	1.394	0.125	4.287
CVC	1.466	0.805	0.757	1.436	0.318	0.743	11.839
APACHE II score	3.348	2.187	8.492	32.574	0.159	1.084	3.426

For other abbreviation, see Table III.

was increasing, as was the detection rate of CRKP. In this study, we analyzed the drug resistance characteristics of CRKP. It was found that strains in this work show DR for most antibiotics, but the DR rates of cefoxetine, cefotaxime/clavulanate, amicacin, gentamicin, meropenem, and imipenem were relatively low (< 20%), so these drugs may be given priority in clinical treatment. However, Cienfuegos-Gallet *et al*. (2019) have suggested that daily use of meropenem (OR =1.18, 95% CI =1.10-1.28) and cefepime (OR = 1.22, 95% CI = 1.03-1.49) would increase the risk of carbapenem resistance. Therefore, the specific use needs to be confirmed by large sample clinical trials.

In addition, drug resistance genes were also analyzed, and the results showed that TEM, CTX, and SHV producing strains were the main strains in our hospital, accounting for 20.7%, 14%, and 33.3%, respectively. In a study by Jin *et al*. (2021), it was revealed that the key drug-resistant genes in *Klebsiella pneumoniae* (KP) include ramR, lon, pmrB, phoQ, and mgrB. According to Yu *et al*. (2019) blaKPC-2 was identified as the primary drug-resistant gene carried by clinical KP isolates in their hospital. Miryala *et al*. (2020) observed in KP that the SHV-11 gene, along with its functional partner genes *gyrA, parC, glsA, osmE, yjhA, yhdT, rimL,* and *pepB*, exhibited drug-resistant mechanisms. In a study conducted in South Africa (Madni *et al*., 2021), whole-genome sequencing was used to analyze KP strains isolated from an intensive care unit in a public hospital. The study revealed that the major drug-resistant genes present were BLAOXA-1, blaCTX-M-15, and blaTEM-1B. It's evident that drug-resistant gene profiles can vary across different regions and hospitals. Our study might only reflect the characteristics of strains within our institution.

After analyzing KP infection and its prognostic risk factors, it was observed that hyperglycemia and history of immune diseases were IRFs of CRKP infection. Advanced age, septic shock, bacteremia, and organ failure were the IRFs that predicted death. According to the studies of Xie *et al*. (2020), hyperglycemia, hypoproteinemia, critical illness, and multi-drug resistant bacterial infection are the risk factors for CR-BSI death. Cao *et al*. (2022) showed that patients with septic shock, mechanical ventilation and platelet deficiency were more likely to have poor prognosis. Wang *et al*. (2022) found that advanced age, renal insufficiency, tracheotomy and ICU hospitalization were the IRFs of death in patients with CRKP infection. Panda *et al*. (2022) have shown that invasive mechanical ventilation is the IRFs of death in patients with CRKP. In the past, there were a large number of similar studies, but the results were different. This may be because our data came from a single department in a single center, which was easy to cause selection bias, and could not represent the overall situation of the region, which may have nothing to do with other patient groups.

In conclusion, BSI KP bacteria in our hospital are resistant to third-generation cephalosporins, monocycloβ-lactam antibiotics and even carbapenem antibiotics, which brings great difficulties to clinical treatment. The history of diabetes and hepatobiliary diseases was IRFs infected with CRKP. Age, septic shock, organ failure, and APACHE II score are IRFs that predict patient death. However, the sample included in this work was from a single source and the sample size was small. Although it had tried to collect and analyze as much clinical data as possible, it still failed to represent KP BSI patients from other regions and hospitals. Even some data are insufficient and some

variables cannot be explored. Finally, a method was adopted herein to determine whether the combination of new drugs (such as cephalosporin and meropenem) will improve the efficacy and prognosis of patients, which may be a new direction for future research.

CONCLUSION

This work revealed that KP BSI strains showed DR To most antibiotics, and TEM, CTX, and SHV strains were dominant. Cefoxitin, cefotaxime/clavulanate, amicacin, gentamicin, meropenem, and imipenem had relatively low DR rates and may be given priority in future clinical treatment. Hyperglycemia and history of immune diseases were IRFs for CRKP infection; advanced age, septic shock, bacteremia, and organ failure were the IRFs that predicted death. The subjects included were from a single source and with a small sample size, and some variables could not be included, so that the results obtained could not represent KP BSI patients in other regions or hospitals. Therefore, in the future, further research involving a larger patient population, including both in-hospital and out-patient cases, patients from different hospitals and regions, will be necessary to delve deeper into the antibiotic resistance of Klebsiella pneumoniae and the utilization of relevant medications.

ACKNOWLEDGEMENT

The authors are grateful for the support received from The First Affiliated Hospital of Chongqing Medical University (Jinshan Campus).

Funding

The study received no external funding.

IRB approval

This research was carried out with the approval of Research Guidance Workshop Committee (The First Affiliated Hospital of Chongqing Medical University).

Ethical statement

All applicable international, national, and/or institutional guidelines for the care and use of animals were followed.

Statement of conflict of interest

The authors have declared no conflict of interest.

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