

ORIGINAL ARTICLE

Clinical and Microbiological Characteristics of Bloodstream Infections due to CRKP

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ABSTRACT

Background: Bloodstream infections caused by carbapenem-resistant *Klebsiella pneumoniae* (CRKP) often result in high mortality rates. This study aimed to explore the local epidemiology and risk factors of CRKP bloodstream infections, characterize the resistance and virulence genes of CRKP isolates in this region of China, and identify the circulating hypervirulent *Klebsiella pneumoniae* strains locally.

Methods: In a case-controlled retrospective study, we examined the prevalence, patient background, and risk factors for CRKP BSIs.

Results: The overall CRKP BSI incidence was 2.2 (54/2,420,826) per 100,000 patient-days. Acute operation ($p = 0.012$), being a resident in a long-term-care facility ($p = 0.019$), transfer to ICU within 30 days ($p = 0.014$), pulmonary diseases ($p = 0.022$), renal diseases ($p = 0.004$), liver diseases ($p = 0.008$), abdominal infections ($p = 0.005$), gastric tube ($p = 0.011$), quinolone use ($p = 0.029$), carbapenem use ($p = 0.001$), and antifungal agent use prior to culture within 30 days ($p = 0.001$) were risk factors for CRKP BSIs. In total, 88.9% (48/54) isolates were detected with KPC carbapenemase, followed by NDM carbapenemase at 7.4% (4/54). *YcfM*, *wabG*, and *entB* were present in all strains. The following four virulence genes had a positivity rate of over 90%: *fimH* (98.15%), *mrkD* (96.30%), *uge* (92.60%), and *kpn* (92.60%).

Conclusions: Acute operation, being a resident in a long-term-care facility, transfer to ICU within 30 days, pulmonary diseases, renal diseases, liver diseases, abdominal infections, gastric tube, quinolone use, carbapenem use, and antifungal agent use prior to culture within 30 days were risk factors for CRKP BSIs. KPC carbapenemase ranked first in isolates of CRKP BSIs. Virulence genes were widely present.

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Supplementary Data

Table S1. Carbapenemase genes and virulence genes of *Klebsiella pneumonia*.

Primer	Primer sequence (5' - 3')	Product size (bp)
Carbapenemase genes		
KPC	F: TGTCACTGTATCGCCGTC	900
	R: CTCAGTGCTCTACAGAAAACC	
NDM	F: GCAGCTTGTCGGCCATGCGGGC	782
	R: GGTCGCGAAGCTGAGCACC GCAT	
IMP	F: GAAGGCGTTTATGTTTCATAC	587
	R: GTACGTTTCAAGAGTGATGC	
VIM	F: GTTTGGTCGCATATCGCAAC	389
	R: AATGCGCAGCACCAGGATAG	
OXA48-like	F: GCGTGGTTAAGGATGAACAC	438
	R: CATCAAGTTCAACCCAACCG	
Virulence genes		
rmpA	F: ACTGGGCTACCTCTGCTTCA	516
	R: CTTGCATGAGCCATCTTTCA	
wcaG	F: GGTGGKTCAGCAATCGTA	169
	R: ACTATCCGCCAACTTTTGC	
uge	F: TCTTCACGCCTTCCTTCACT	534
	R: GATCATCCGGTCTCCCTGTA	
fimH	F: TGCTGCTGGGCTGGTCGATG	688
	R: GGGAGGGTGACGGTGACATC	
mrkD	F: CCACCAACTATTCCCTCGAA	226
	R: ATGGAACCCACATCGACATT	
ycfM	F: ATCAGCAGTCGGGTCAGC	160
	R: CTTCTCCAGCATTCAGCG	
entB	F: ATTCCTCAACTTCTGGGGC	371
	R: AGCATCGGTGGCGGTGGTCA	
iutA	F: GGCTGGACATCATGGGAAGTGG	300
	R: CGTCGGGAACGGGTAGAATCG	
k2A	F: CAACCATGGTGGTCGATTAG	543
	R: TGGTAGCCATATCCCTTTGG	
PEG-344	F: CTTGAAACTATCCCTCCAGTC	508
	R: CCAGCGAAAGAATAACCCC	
kpn	F: GTATGACTCGGGGAAGATTA	626
	R: CAGAAGCAGCCACCACACG	
magA	F: GGTGCTCTTTACATCATTGC	1,282
	R: GCAATGGCCATTTGCGTTAG	
wabG	F: ACCATCGGCCATTTGATAGA	169
	R: CGGACTGGCAGATCCATATC	
iroN	F: AAGTCAAAGCAGGGGTTGCCCG	665
	R: GACGCCGACATTAAGACGCAG	
allS	F: CCGAAACATTACGCACCTTT	508
	R: ATCACGAAGAGCCAGGTCAC	

Table S2. Comparison of patient characteristics between CRKP and CSKP groups.

Characteristic ^a	CRKP group ^b (n = 54) n, %	CSKP group ^b (n = 108) n, %	p-value
Age (median years, range)	69 (0 - 94)	69 (0 - 93)	0.925
0 - 15	2 (3.7)	4 (3.7)	
16 - 30	0 (0.0)	0 (0.0)	
31 - 40	3 (5.6)	6 (5.6)	
41 - 50	8 (14.8)	14 (13.0)	
51 - 60	3 (5.6)	8 (7.4)	
61 - 70	14 (25.9)	29 (26.9)	
71 - 80	14 (25.9)	25 (23.1)	
81 - 90	8 (14.8)	19 (17.6)	
91 - 100	2 (3.7)	3 (2.8)	
Gender			
Male	36 (66.7)	72 (66.7)	1.000
Female	18 (33.3)	36 (33.3)	
Health care exposure during prior year			
Acute care hospitalization	24 (44.4)	52 (48.1)	0.656
Acute operation	12 (22.2)	10 (9.3)	0.023
Dialysis	4 (7.4)	2 (1.9)	0.186
Residency in a long-term-care facility	13 (24.1)	1 (0.9)	< 0.001
Transfer to ICU within 30 days	34 (63.0)	14 (13.0)	< 0.001
Receipt of corticosteroids	4 (7.4)	3 (2.8)	0.339
Underlying conditions			
Diabetes mellitus	11 (20.4)	23 (21.3)	0.891
Hypertension	19 (35.2)	39 (36.1)	0.908
Cancer ^c	21 (38.9)	60 (55.6)	0.046
Neurological diseases ^d	16 (29.6)	11 (10.2)	0.002
Blood diseases ^e	13 (24.1)	12 (11.1)	0.031
Pulmonary diseases ^f	33 (61.1)	36 (33.3)	0.001
Renal diseases ^g	21 (38.9)	17 (15.7)	0.001
Liver diseases ^h	27 (50.0)	36 (33.3)	0.040
Heart diseases ⁱ	17 (31.5)	20 (18.5)	0.064
Abdominal infections	17 (31.5)	9 (8.3)	< 0.001
Skin infections	5 (9.3)	3 (2.8)	0.158
Body temperature prior to culture > 38.0°C	29 (53.7)	52 (48.1)	0.505
Smoking	11 (20.4)	24 (22.2)	0.787
Drinking	8 (14.8)	19 (17.6)	0.655
Blood transfusion	35 (64.8)	34 (31.5)	< 0.001
Chemoradiotherapy	4 (7.4)	18 (16.7)	0.168
Indwelling devices prior to culture			
Central venous catheter	39 (72.2)	40 (37.0)	< 0.001
Gastric tube	40 (74.1)	18 (16.7)	< 0.001
Tracheal cannula	25 (46.3)	14 (13.0)	< 0.001
Urinary catheter	44 (81.5)	42 (38.9)	< 0.001

Table S2. Comparison of patient characteristics between CRKP and CSKP groups (continued).

Characteristic ^a	CRKP group ^b (n = 54) n, %	CSKP group ^b (n = 108) n, %	p-value
Laboratory findings			
White blood cells/mm³			
Median (IQR)	10,945 (7,143 - 14,128)	8,060 (4,760 - 12,653)	
Subgroup			
< 4,000	3 (5.6)	14 (13.0)	0.239
> 10,000	30 (55.6)	40 (37.0)	0.025
Platelets < 100 × 10 ⁹ /L	6 (11.1)	27 (25.0)	0.039
C-reactive protein > 10 mg/L	43 (79.6)	74 (68.5)	0.137
Procalcitonin			
0.5 to 2 ng/mL	10 (18.5)	15 (13.9)	0.442
> 2 ng/mL	22 (40.7)	36 (33.3)	0.354
Total protein < 60g/L	18 (33.3)	41 (38.0)	0.564
Albumin < 35g/L	33 (61.1)	67 (62.0)	0.909
Antimicrobial use prior to culture within 30 days			
Quinolone use	26 (48.1)	33 (30.6)	0.028
Cephalosporin use	37 (68.5)	44 (40.7)	0.001
Carbapenem use	50 (92.6)	78 (72.2)	0.005
Tetracycline use	11 (20.4)	4 (3.7)	0.002
Oxazolidinone use	24 (44.4)	17 (15.7)	< 0.001
Glycopeptides use	15 (27.8)	6 (5.6)	< 0.001
Clistin use	6 (11.1)	1 (0.9)	0.009
Metronidazole use	5 (9.3)	9 (8.3)	0.843
Aminoglycosides use	6 (11.1)	2 (1.9)	0.029
Macrolides use	5 (9.3)	1 (0.9)	0.027
Trimethoprim-sulfamethoxazole use	2 (3.7)	2 (1.9)	0.858
Antifungal agent use prior to culture within 30 days	29(18.5)	15 (13.9)	< 0.001
Length of stay (Median (IQR)) ^j	34 (20 - 57)	17 (10 - 30)	< 0.001
Discharge disposition			
Recovery and improvement	34 (63.0)	90 (83.3)	0.003
Patient transfer to another hospital	8 (14.8)	9 (8.3)	
Functional status deterioration	11 (20.4)	8 (7.4)	
In-hospital mortality	1 (1.9)	1 (0.9)	
Medical expense for admission ^j (Mean ± SD, RMB)	257,914.5 ± 29,861.5	82,766.8 ± 121,097.1	< 0.001

CRKP: carbapenem-resistant *Klebsiella pneumoniae*, CSKP: carbapenem-sensitive *Klebsiella pneumoniae*.

a: IQR, interquartile range.

b: Data are presented as the number/total number (%), unless otherwise indicated.

c: Cancer includes malignancy of the lung, digestive tract, gynecology, hematological system, and neurological system.

d: Neurological diseases include stroke, transient ischemic attack, cerebral palsy, and meningitis.

e: Blood diseases include disorders of red blood cells, disorders of white blood cells, disorders of plasma cells, disorders of the lymphatic system, hemorrhagic, and thrombotic disorders.

f: Pulmonary diseases include chronic obstructive pulmonary disease (COPD), asthma, interstitial lung disease, history of pneumonia and tuberculosis, emphysema, respiratory failure, and infection.

g: Renal diseases include azotemia and chronic kidney disease.

h: Liver diseases include cirrhosis, hepatitis, liver abscess, hepatic adiposum (i.e. fatty liver), and hepatic injury.

i: Heart diseases include congestive heart failure, coronary heart disease, valve replacement, and congenital heart disease.

j: Only patients admitted to hospital were evaluated.

Table S3. Comparison of antibiotic susceptibility between CRKP and CSKP groups.

Antimicrobial agent	CRKP group n = 54 (%)	CSKP group n = 108 (%)	p-value
Meropenem	0 (0.0)	108 (100.0)	< 0.001
Imipenem	1 (1.85)	108 (100.0)	< 0.001
Ertapenem	0 (0.0)	108 (100.0)	< 0.001
Doripenem	0 (0.0)	108 (100.0)	< 0.001
Cefepime	1 (1.85)	104 (96.3)	< 0.001
Ceftazidime	0 (0.0)	96(88.9)	< 0.001
Cefotaxime	0 (0.0)	79(73.1)	< 0.001
Ceftriaxone	0 (0.0)	77 (71.3)	< 0.001
Piperacillin/Tazobactam	0 (0.0)	94 (87.0)	< 0.001
Amikacin	12 (22.2)	96 (88.9)	< 0.001
Tobramycin	8 (14.8)	90 (83.3)	< 0.001
Gentamycin	6 (11.1)	89 (82.4)	< 0.001
Ciprofloxacin	1 (1.85)	88 (81.5)	< 0.001
Levofloxacin	1 (1.85)	92 (85.2)	< 0.001
Trimethopri-sulfamethoxazole	12 (22.2)	92 (85.2)	< 0.001
Aztreonam	1 (1.85)	91 (84.3)	< 0.001
Tigecycline	54 (100.0)	108 (100.0)	1.000
Clistin-polymyxin-B	100 (100.0)	108 (100.0)	1.000
Ceftazidime/Avibactam	48 (88.9)	108 (100.0)	0.002

CRKP: carbapenem-resistant *Klebsiella pneumoniae*, CSKP: carbapem-sensitive *Klebsiella pneumoniae*.