JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Shifts in hospital-associated pathogens and prevalence trends of carbapenem-resistant *Escherichia coli* infections, 2021–2023

Luyao Liu[1 #], Shihui Liu[1 #], Zhenghai Yang[1], Fan Wang[2], Huiwen Yuan[1], Hao Xu[1], Jinguan Chen[1], Xiaoning Li[1]

[1] Department of Laboratory Medicine, The First Affiliated Hospital of Wannan Medical College, Wuhu, Anhui, China
[2] Department of Dermatology, the First Affiliated Hospital of Wannan Medical College, Wuhu, Anhui, China

# Authors contributed equally to this work.

Abstract

Introduction: Carbapenem-resistant *Escherichia coli* (CREC) have emerged as a significant global health threat, particularly in hospital settings, due to their high resistance to critical antibiotics. This study aimed to evaluate the dynamics of pathogenic bacterial isolates in clinical specimens, characterize patients with CREC infections, and identify risk factors for co-infection; in order to strengthen surveillance and infection control measures.

Methodology: Clinical specimens were collected from patients at a tertiary hospital in southern Anhui Province between 2021 and 2023. Strain identification and antibiotic susceptibility testing were performed using a time-of-flight mass spectrometry analyzer and the VITEK-2 compact system. Demographic and clinical data were analyzed using rigorous statistical methods.

Results: The predominant bacterial species isolated included *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*. Notably, the prevalence of CREC increased from 10.10% in 2021 to 16.36% in 2023. The predominant carbapenem-resistant Enterobacteriaceae (CRE) species were *Enterobacter cloacae*, *Klebsiella pneumoniae*, and *Escherichia coli*; with the proportion of CREC increasing significantly from 10.10% in 2021 to 16.36% in 2023. Of the 81 patients with CREC, 65.43% were over 60 years old. The most common specimen types were urine and sputum, with the highest proportion of patients in the intensive care unit (ICU; 32.10%). Analysis of the co-infected population revealed that ICU patients with tracheal intubation were significant risk factors. Co-infection with carbapenem-resistant *Acinetobacter baumannii* (CRAB) showed a concerning annual rise.

Conclusions: There is urgent need for enhanced surveillance and stringent infection control measures to mitigate the spread of CREC and associated nosocomial infections.

Key words: *Escherichia coli*; carbapenem-resistance; clinical; epidemiology; coinfection.

J Infect Dev Ctries 2025; 19(7):1100-1107. doi:10.3855/jidc.20930

(Received 07 October 2024 – Accepted 23 April 2025)

Introduction

Since the first identification of carbapenem-resistant *Klebsiella pneumoniae* (CRKP) in 1997, carbapenem-resistant Enterobacteriaceae (CRE) have rapidly emerged as a global health threat [1]. The US Centers for Disease Control and Prevention (CDC) has classified CRE as an urgent public health concern. Among the CRE, carbapenem-resistant *Escherichia coli* (CREC) has gained particular prominence due to its rising infection rates in recent years [2]. CREC is characterized by high pathogenicity and substantial antibiotic resistance, making it especially dangerous for immunocompromised individuals and patients undergoing invasive procedures. These infections result in prolonged hospitalizations, increased healthcare costs, and elevated mortality rates; all of which pose significant risks to patient outcomes and healthcare systems [3]. The epidemiological landscape of CREC has been the subject of numerous regional and national studies; however, variations in environmental factors, economic conditions, and healthcare infrastructure contribute to discrepancies in bacterial distribution and resistance patterns [4,5]. Therefore, a comprehensive understanding of CREC's epidemiology and its associated clinical features is essential for the development of effective prevention and control strategies.

This study presents a retrospective analysis of the bacterial distribution and clinical characteristics of CREC infections, based on clinical specimens collected from a tertiary hospital in southern Anhui Province between 2021 and 2023. Additionally, the risk factors associated with co-infection in patients infected with CREC were investigated [6]. The findings aim to

provide a scientific foundation for the prevention and control of hospital-acquired infections and the transmission of CREC.

Methodology

Bacterial isolates

Clinical isolates were obtained from patient specimens collected at Yijishan Hospital of Wannan Medical College between January 2021 and December 2023. Bacterial identification was performed using a time-of-flight mass spectrometry analyzer (VITEK MS; BioMérieux, Marcy-l'Étoile, France) and the fully automated VITEK-2 Compact Microbial Identification System (BioMérieux, Marcy-l'Étoile, France). Antimicrobial susceptibility testing was conducted using the appropriate drug susceptibility cards. Duplicate isolates from the same site and from a single patient were excluded, and only the initial isolate was recorded.

Clinical data collection

Demographic and clinical data, including gender, age, and medical history, were collected for all patients. Clinical information included the diagnosis, specific therapeutic interventions, disease progression, and changes in the bacterial profile observed at various time points.

Statistical analysis

Data were compiled using Microsoft Excel and analyzed with SPSS version 27.0 (IBM Corp, Armonk, NY, USA). Group comparisons were performed using the Chi-squared test, with statistical significance defined as $p < 0.05$.

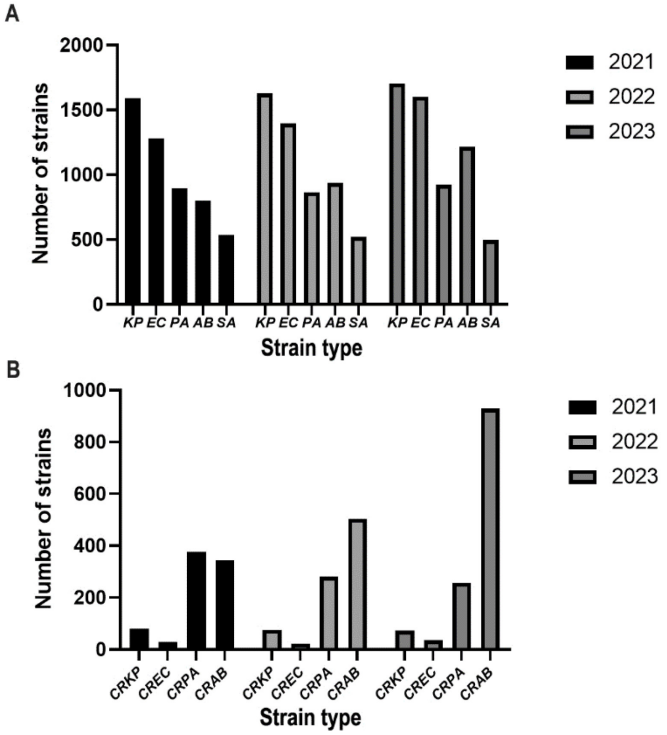
Results

Top 5 bacterial isolates cultured from clinical specimens, 2021–2023

The 5 most commonly isolated bacterial species from clinical specimens at the hospital between January 2021 and December 2023 were *K. pneumoniae*, *E. coli*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Staphylococcus aureus*; with the first 4 being Gram-negative bacilli (GNR) (Table 1, Figure 1). The number of *K. pneumoniae* cases increased from 1,591 in 2021 to 1,702 in 2023; while the proportion of CRKP among total *K. pneumoniae* cases rose from 2.09% in 2021 to 4.23% in 2023.

Similarly, the number of *E. coli* cases increased from 1,279 in 2021 to 1,601 in 2023. However, the proportion of CREC remained relatively stable,

Figure 1. Top five bacterial isolates cultured from clinical specimens, 2021–2023.



A. Histogram of the top five bacterial isolates; **B.** Histogram of the top four carbapenem-resistant Gram-negative bacteria. KP: *Klebsiella pneumoniae*; EC: *Escherichia coli*; PA: *Pseudomonas aeruginosa*; AB: *Acinetobacter baumannii*; SA: *Staphylococcus aureus*; CRKP: carbapenem-resistant *Klebsiella pneumoniae*; CREC: carbapenem-resistant *Escherichia coli*; CRPA: carbapenem-resistant *Pseudomonas aeruginosa*; CRAB: carbapenem-resistant *Acinetobacter baumannii*.

Table 1. Numbers and percentages of the top 5 bacterial isolates and carbapenem-resistant Gram-negative rods (CR-GNRs) cultured from clinical specimens, 2021–2023.

Bacteria	2021		2022		2023	
	GNR n = 4563	CR-GNR n = 830	GNR n = 4823	CR-GNR n = 883	GNR n = 5439	CR-GNR n = 1292
Klebsiella pneumoniae	1591 (31.21%）	81 (2.09%)	1626 (30.43%）	76 (4.67%)	1702 (28.67%)	72 (4.23%)
Escherichia coli	1279 (25.09%）	29 (2.27%)	1394 (26.09%）	23 (1.65%)	1601 (26.97%)	35 (2.19%)
Pseudomonas aeruginosa	894 (17.54%）	376 (42.06%)	866 (16.21%)	280 (32.33%)	922 (15.53%)	256 (27.77%)
Acinetobacter baumannii	799 (15.68%）	344 (43.05%)	937 (17.54%)	504 (53.79%)	1214 (20.45%)	929 (76.52%)
Staphylococcus aureus	534 (10.48%）	NA	520 (9.73%）	NA	497 (8.37%）	NA

Carbapenems are used to treat Gram-negative bacteria, while *S. aureus* is a Gram-positive coccus. Since no carbapenem-resistant drugs were identified, no statistical data were available for this group.

fluctuating slightly from 2.27% in 2021 to 2.19% in 2023. *P. aeruginosa* exhibited relative stability throughout the study period. However, the proportion of carbapenem-resistant *P. aeruginosa* (CRPA) declined significantly from 42.06% in 2021 to 27.77% in 2023. In contrast, the number of *A. baumannii* cases surged from 799 in 2021 to 1,214 in 2023; with the proportion of carbapenem-resistant *A. baumannii* (CRAB) increasing sharply from 43.05% in 2021 to 76.52% in 2023.

Changes in the composition ratios of CRE, 2021–2023

Among CRE, *K. pneumoniae*, *E. coli*, and *Aspergillus chimaera* were the most frequently encountered carbapenem-resistant pathogens in the clinical setting. The proportion of CREC among all CRE isolates over the 3-year period increased from 10.10% in 2021 to 12.17% in 2022, and further to 16.36% in 2023; indicating a clear upward trend (Table 2).

Characteristics of patients with CREC infections

A retrospective analysis of clinical data from 81 patients with CREC infections between 2021 and 2023 is summarized in Table 3. Among these patients, 50 (61.73%) were male and 31 (38.27%) were female. The age distribution was as follows: 1 patient (1.23%) was aged 0–20 years, 6 patients (7.41%) were aged 20–40 years, 21 patients (25.93%) were aged 40–60 years, 41 patients (50.62%) were aged 60–80 years, and 12 patients (14.81%) were aged 80 years or older.

In terms of the affected systems, 22 cases (27.16%) involved the urinary system, 13 cases (16.05%) involved the respiratory system, 12 cases (14.81%) involved the neurological system, and 10 cases (12.35%) involved the gastrointestinal system. Infections of other systems accounted for less than 10% each. Further analysis of the clinical isolates revealed that 32 cases (39.51%) were derived from urine, 29 cases (35.80%) from sputum, and the remaining sample sources represented less than 10% each.

The distribution of patients across departments showed that the highest proportion were in the intensive care unit (ICU) with 26 patients (32.10%), followed by 14 patients (17.28%) in urology, and 11 patients (13.58%) in neurology. Fewer than 10% of the patients were distributed across other departments. Among the cohort, 29 patients (35.80%) were tracheally intubated, while 52 patients (64.20%) were not.

For the purposes of this study, infection with CREC and simultaneous detection of pathogenic bacteria other than *E. coli* was defined as co-infection, detection of

Table 3. Demographic and clinical information of the 81 patients infected with carbapenem-resistant *Escherichia coli* (CREC).

Characteristic	n	%
Gender		
Male	50	61.73%
Female	31	38.27%
Age		
0–20 years	1	1.23%
20–40 years	6	7.41%
40–60 years	21	25.93%
60–80 years	41	50.62%
> 80 years	12	14.81%
Sample type		
Urine	32	39.51%
Sputum	29	35.80%
Secretions	7	8.64%
Blood	3	3.70%
Other	10	12.35%
Affected system		
Urinary system	22	27.16%
Nephrolithiasis	9	/
Respiratory system	13	16.05%
Pulmonary infection	12	/
Nervous system	12	14.81%
Intracranial lesions	8	/
Extra-cranial injuries	2	/
Digestive system	10	12.35%
Hematologic system	5	6.17%
Circulatory system	4	4.94%
Reproductive system	3	3.70%
Cardiovascular system	3	3.70%
Other	9	11.11%
Department		
Intensive care unit	26	32.10%
Urology	14	17.28%
Neurology	11	13.58%
Hematology	7	8.64%
Burn and plastic surgery	4	4.94%
Gynecology	3	3.70%
Other	16	19.75%
Endotracheal Intubation		
Yes	29	35.80%
No	52	64.20%
Co-infection		
Yes	45	55.56%
No	36	44.44%

Table 2. Variations in the composition ratios of carbapenem-resistant Enterobacteriaceae (CRE) over the years, 2021–2023.

Bacteria	2021 (n = 287)		2022 (n = 189)		2023 (n = 214)	
	n	%	n	%	n	%
Morganella morganii	107	37.28%	65	34.39%	81	37.85%
Klebsiella pneumoniae	81	28.22%	76	40.21%	72	33.64%
Escherichia coli	29	10.10%	23	12.17%	35	16.36%
Morganella morganii	25	8.71%	5	2.65%	6	2.80%
Enterobacter cloacae	22	7.67%	14	7.41%	18	8.41%
Citrobacter freundii	14	4.88%	3	1.59%	0	0.00%
Klebsiella oxytoca	9	3.14%	3	1.59%	2	0.93%

carbapenem-resistant bacteria other than *E. coli* was defined as CRB co-infection, and detection of CREC only was defined as simple infection. A total of 45 patients (55.56%) presented with co-infections, while 36 patients (44.44%) had simple infections.

Univariate analysis of co-infection with other bacterial infections in CREC patients

Co-infections in patients are often associated with increased clinical complexity, prolonged illness duration, and recurrent infections; highlighting the importance of identifying the risk factors contributing to these co-infections. In this study, the clinical characteristics of patients with co-infections were compared to those with simple infection (Table 4). The results revealed no statistically significant differences in gender ($\chi^2 = 1.045$, $p = 0.307$) or age ($\chi^2 = 0.535$, $p = 0.465$) between the two groups. Similarly, there was no significant difference in sample type between co-infected and monomicrobial-infected patients ($\chi^2 = 6.453$, $p = 0.168$).

However, when examining the affected systems, patients with co-infections exhibited a higher incidence of respiratory (11 cases), neurological (11 cases), and hematological (5 cases) infections. In contrast, patients with monomicrobial infections more frequently presented with urinary (16 cases) and gastrointestinal (7 cases) infections. This difference was statistically significant ($\chi^2 = 36.260$, $p < 0.01$).

Regarding departmental distribution, co-infections were significantly more frequent than simple infections in the ICU, with 21 and 5 cases, respectively. Conversely, patients with simple CRE infections were more commonly found in the urology department (12 cases), with a statistically significant difference between the two groups ($\chi^2 = 37.639$, $p < 0.01$). Notably, the rate of tracheal intubation was substantially higher in patients with co-infections (25 cases), compared to those with monomicrobial infections (4 cases); and this difference was also statistically significant ($\chi^2 = 17.188$, $p < 0.01$).

Trends in CREC co-infection with other carbapenem-resistant bacteria

Carbapenem-resistant genes are known to transfer easily between different species of pathogenic bacteria through horizontal gene transfer mechanisms [7,8]. The prevalence trends of CREC were statistically analyzed alongside other carbapenem-resistant pathogens (CRB co-infection) over the 3 years. Figure 2 presents bar

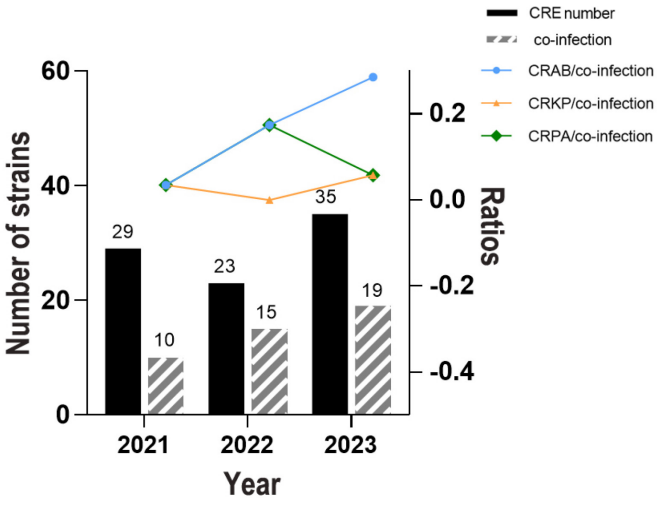
Table 4. Univariate analysis of combined other bacterial infections in patients with carbapenem-resistant *Escherichia coli* (CREC).

Variable	Co-infection	Single infection	χ^2	*p* value
Gender			1.045	0.307
Male	30	20		
Female	15	16		
Age (years)			0.535	0.465
< 60	14	14		
≥ 60	31	22		
Specimen type			6.453	0.168
Urine	13	19		
Sputum	20	9		
Secretions	4	3		
Blood	1	2		
Other	7	3		
Affected system			35.256	**< 0.01**
Urinary	6	16		
Respiratory	11	2		
Neurological	11	1		
Digestive	3	7		
Hematological	5	0		
Circulatory	4	0		
Reproductive	0	3		
Cardiovascular	0	3		
Other	5	4		
Department			37.639	**< 0.01**
Intensive care unit (ICU)	21	5		
Urology	2	12		
Neurology	10	1		
Hematology	6	1		
Burn and plastic surgery	3	1		
Gynecology	0	3		
Other	3	13		
Tracheal intubation			17.188	**< 0.01**
Yes	25	4		
No	20	32		

charts illustrating the total number of patients with CREC infections (black bars) and the number of patients with CRB co-infection (bars with diagonal stripes) for each year. Notably, the incidence of CREC infections decreased from 29 patients in 2021 to 23 in 2022, but increased significantly to 35 in 2023. Despite this decrease, the overall trend indicated a rise in CREC infections. Co-infections were also observed, with the number of CREC patients with CRB co-infection increasing from 10 in 2021 to 19 in 2023; highlighting the growing risk of CRB co-infection as CREC continues to spread.

Figure 2 presents line graphs displaying the proportion of patients with CRAB (blue line with dots), CRKP (orange line with triangles), and CRPA (green line with diamonds) among the total number of patients with co-infections. Of particular concern is the marked increase in co-infections with CRAB, rising from 1 patient in 2021 to 10 in 2023 (Supplementary Table 1). In contrast, co-infections with CRKP and CRPA remained stable or declined. Specifically, CRKP co-infections were recorded at 2 in 2021 and 1 in subsequent years, while CRPA co-infections remained consistently low (Supplementary Table 1).

Figure 2. Trends in other carbapenem-resistant bacteria in co-infections, 2021–2023.



The black bars indicate the number of CRE patients. The bars with diagonal stripes indicate the number of co-infected patients. The blue line with dots indicates the number of co-infected CRAB patients as a proportion of the number of co-infected patients. The orange line with triangles indicates the number of co-infected CRKP patients as a proportion of the number of co-infected patients. The green line with diamonds indicates the number of co-infected CRPA patients as a proportion of the number of co-infected patients. CRE: carbapenem-resistant *Enterobacteriaceae*; CRAB: carbapenem-resistant *Acinetobacter baumannii*; CRKP: carbapenem-resistant *Klebsiella pneumoniae*; CRPA: carbapenem-resistant *Pseudomonas aeruginosa*.

Discussion

The widespread clinical use of carbapenems has significantly contributed to the rise of drug-resistant pathogens, leading to an increase in the global detection rate of CRE in recent years [5]. Despite efforts to limit the use of antibiotics, resistance continues to escalate. Understanding the regional distribution of bacterial pathogens and their associated risk factors is critical for the prevention and control of drug-resistant infections [9]. In this study, the trends of major pathogenic bacteria isolated from clinical specimens at a tertiary hospital in southern Anhui Province between 2021 and 2023 were retrospectively analyzed, focusing specifically on the clinical characteristics of patients with CREC infections and identifying key risk factors for co-infection.

The findings revealed that *K. pneumoniae* and *E. coli* were the predominant pathogens during the study period, consistently ranking first and second in terms of composition ratio, aligning with other studies conducted in China, which highlight their central role in hospital-acquired infections [10,11]. Among the carbapenem-resistant pathogens, the proportion of CRKP and CREC exhibited a decreasing trend, which contrasts with previous reports [6,9,10]. This discrepancy may be attributed to the high isolation rate of *A. baumannii*, which skewed the overall statistics, as only the top four pathogens were considered. However, when analyzing CRE separately, CREC showed a clear upward trend, while CRKP fluctuated without a discernible pattern. Given the current research focus on CRKP in clinical practice, the increasing epidemiological importance of CREC has been somewhat overlooked [12]. The findings of this study underscore the need to prioritize CREC infections; enhance surveillance; and develop innovative treatment, prevention, and control strategies to curb the spread of hospital-acquired infections.

In this study, 87 CREC-positive specimens were isolated from 81 patients over the three-year period. The retrospective analysis revealed that 65.43% of the patients were over 60 years old. This finding is consistent with a study by Zhang *et al*. which reported that elderly patients comprised 59.6% of a cohort of 1,439 CREC cases [13], further reinforcing the conclusion that elderly individuals are at high risk for CREC infection. Elderly patients often face multiple underlying health conditions, weakened immune systems, and prolonged hospital stays; all of which elevate the risk of infection and complicate treatment [14].

Patients with co-infections tend to have more

complicated clinical courses and often require multiple treatments. The univariate analysis indicated that respiratory and neurological infections were significantly more common among co-infected patients compared to those with single bacterial infections. The risk of co-infection was notably higher in patients admitted to the ICU and those who underwent endotracheal intubation. These findings align with the observations of Tadese *et al.*, who noted that co-infected CREC patients were generally in more critical condition and had undergone invasive procedures [15]. It is likely that bacteria spread through tracheal secretions in ICU patients receiving mechanical ventilation.

An interesting observation in this study was that the majority of co-infected neurological CREC cases occurred in patients with intracranial injuries, whereas extracranial contusions accounted for only a small proportion of cases. Patients with intracranial contusions often undergo open surgery, have compromised respiratory function, and are more likely to require tracheal intubation [16–18]. In contrast, those with extracranial injuries may be at lower risk for infection due to more timely wound care. A study by Castellani *et al.* found that patients with severe acquired brain injuries are more susceptible to infections caused by multidrug-resistant organisms, and carriers of carbapenemase-producing Enterobacteriaceae (CPE) may face an elevated risk of healthcare-associated infections (HAIs) and poorer outcomes compared to non-carriers [19].

These findings underscore the importance of early intervention in preventing bacterial infections, particularly in patients with respiratory or neurological conditions. High-risk procedures, such as tracheal intubation, should be accompanied by stringent aseptic protocols and enhanced infection control measures to minimize the risk of hospital-acquired infections.

The overall trend in CREC infections showed a total of 29 patients with CREC infections in 2021, decreasing to 23 in 2022, and rising significantly to 35 in 2023. It did not show an increasing trend from year to year, and there was a decrease in 2022. This is presumed to be related to the fact that some CREC infected patients could not be diagnosed and treated in time due to the prevention and control of the New Crown outbreak.

CRAB is an opportunistic pathogen that can colonize surfaces and survive in diverse environments. The predominant carbapenem-resistant genes in CRAB, *OXA-23 and OXA-51*, can transfer between different bacterial hosts [20,21]. This gene transfer may explain the rise in CRAB co-infections in patients with CREC. Additionally, genes such as *NDM-1* and *KPC*, which are also major contributors to carbapenem resistance, can transfer between different strains of Enterobacteriaceae and other species [22]. The horizontal transfer of these resistance genes; including *OXA-23*, *OXA-51*, *NDM-1*, and *KPC*; may contribute to the increasing prevalence of carbapenem-resistant bacteria. However, this hypothesis requires further molecular research for validation. The growing prevalence of CRAB and other carbapenem-resistant pathogens raises concerns about the horizontal transfer of these genes to other bacterial species, increasing the risk of infections caused by additional carbapenem-resistant pathogens. This underscores the critical need for research into the mechanisms of resistance gene transmission and its implications for the spread of multidrug-resistant infections.

The findings of this study underscore the urgent need for enhanced surveillance and management of CREC infections; particularly in elderly patients, those in intensive care, and individuals undergoing invasive procedures. Strict infection control measures should be rigorously implemented in clinical settings, particularly in ICU and operating theatres, to mitigate the spread of resistant strains. The judicious use of carbapenem antibiotics is essential to curb resistance propagation, while increased vigilance is necessary in the care of elderly patients, including regular monitoring for infections. Prophylactic anti-infective strategies should be prioritized for high-risk individuals, especially those undergoing invasive procedures like tracheal intubation.

However, this study has several limitations. As a retrospective analysis, it is subject to inherent constraints in data collection and documentation, and certain confounding factors may not have been fully accounted for. The single-center design limits the generalizability of the results, as local antibiotic prescribing practices and infection control protocols may influence the findings. Additionally, the inclusion of community-acquired infections may confound hospital-associated trends. Furthermore, molecular-level validation was not possible due to the lack of access to bacterial strains, limiting the ability to confirm the findings at the genetic level.

Conclusions

This study reveals notable shifts in the composition of clinical isolates from a tertiary hospital in southern Anhui Province between 2021 and 2023. Elderly individuals and critically ill patients were identified as

high-risk groups for CREC infections, necessitating focused clinical attention. Patients with respiratory or neurological conditions, as well as those requiring endotracheal intubation, exhibited a heightened risk of co-infection. In light of evolving patterns of antibiotic resistance, hospitals must adapt their antimicrobial treatment strategies accordingly and reinforce infection prevention and control measures to mitigate the spread of drug-resistant bacteria.

Ethical approval

The collection and use of data in this study were approved by the Scientific Research and New Technology Institutional Review Board of Wannan Medical College, Yijishan Hospital.

Funding

This work was supported by the Wuhu City 'Hua Tuo Plan' Tiered Talent Training — Municipal Level Special Funds for Renowned Physicians.

Correspondending author

Xiaoning Li, MD, PhD.
Department of Laboratory Medicine, First Affiliated Hospital of Wannan Medical College,
Wuhu City, Anhui Province, China
Tel: +86 137 0553 1365
Fax: +86 553 573 8279
Email: lixiaoning19702006@126.com

Conflict of interests

No conflict of interests is declared.

References

1. Lei TY, Liao BB, Yang LR, Wang Y, Chen XB (2024) Hypervirulent and carbapenem-resistant *Klebsiella pneumoniae*: a global public health threat. Microbiol Res 288: 127839. doi: 10.1016/j.micres.2024.127839.
2. Lian S, Liu C, Cai M, Cao Y, Xu X (2024) Risk factors and molecular characterization of carbapenem resistant *Escherichia coli* recovered from a tertiary hospital in Fujian, China from 2021 to 2023. BMC Microbiol 24: 374. doi: 10.1186/s12866-024-03525-9.
3. Meng X, Liu S, Duan J, Huang X, Zhou P, Xiong X, Gong R, Zhang Y, Liu Y, Fu C, Li C, Wu A (2017) Risk factors and medical costs for healthcare-associated carbapenem-resistant *Escherichia coli* infection among hospitalized patients in a Chinese teaching hospital. BMC Infect Dis 17: 82. doi: 10.1186/s12879-016-2176-9.
4. Precit MR, Kauber K, Glover WA, Weissman S J, Robinson T, Tran M, D'Angeli M (2020) Statewide surveillance of carbapenemase-producing carbapenem-resistant *Escherichia coli* and *Klebsiella* species in Washington state, October 2012–December 2017. Infect Control Hosp Epidemiol 41: 716–722. doi: 10.1017/ice.2020.26.
5. Thomsen J, Abdulrazzaq NM, UAE AMR Surveillance Consortium, Everett DB, Menezes GA, Senok A (2023) Carbapenem resistant Enterobacterales in the United Arab Emirates: a retrospective analysis from 2010 to 2021. Front Public Health 11: 1244482. doi: 10.3389/fpubh.2023.1244482.
6. Oliveira M, Cunha E, Tavares L, Serrano I (2023) *P. aeruginosa* interactions with other microbes in biofilms during co-infection. AIMS Microbiol 9: 612–646. doi: 10.3934/microbiol.2023032.
7. Boutin S, Scherrer M, Späth I, Kocer, K, Heeg, K (2024) Cross-contamination of carbapenem-resistant Gram-negative bacteria between patients and the hospital environment in the first year of a newly built surgical ward. J Hosp Infect 144: 118–127. doi: 10.1016/j.jhin.2023.11.016.
8. Huang J, Lv C, Li M, Rahman T, Chang YF, Guo X, Song Z, Zhao Y, Li Q, Ni P, Zhu Y (2024) Carbapenem-resistant *Escherichia coli* exhibit diverse spatiotemporal epidemiological characteristics across the globe. Commun Biol 7: 51. doi: 10.1038/s42003-023-05745-7.
9. Obenhuber T, Scheier TC, Stutz T, Hug M, Fontein D, Kaiser A, Schoene S, Steiger P, Brugger SD, Zingg W, Schreiber PW (2024) An outbreak of multi-drug-resistant *Acinetobacter baumannii* on a burns ICU and its control with multi-faceted containment measures. J Hosp Infect 146: 102–108. doi: 10.1016/j.jhin.2024.01.002.
10. Antimicrobial Resistance Collaborators (2022) Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet 399: 629–655. doi: 10.1016/S0140-6736(21)02724-0.
11. Lyu ZY, Zhen JH, Meng QY, Zhou W, An JY, Dong F (2023) Bacterial etiology and antimicrobial resistance pattern of pediatric bloodstream infections in Beijing, 2015–2019. Infect Drug Resist 16: 6297–6308. doi: 10.2147/IDR.S426000.
12. Pu D, Zhao J, Chang K, Zhuo X, Cao B (2023) "Superbugs" with hypervirulence and carbapenem resistance in *Klebsiella pneumoniae*: the rise of such emerging nosocomial pathogens in China. Sci Bull (Beijing) 68: 2658–2670. doi: 10.1016/j.scib.2023.09.040.
13. Zhang W, Li Z, Wang N, Yang Z, Li J, Li C, Han X, Liu J, Li L, Wang S, Zhan M (2021) Clinical distribution characteristics of 1439 carbapenem-resistant *Escherichia coli* strains in China:

drug resistance, geographical distribution, antibiotic MIC50/90. Infect Drug Resist 14: 4717–4725. doi: 10.2147/IDR.S334283.
14. Li BR, Zhuo Y, Jiang YY, Zhang SY (2024) Random forest differentiation of *Escherichia coli* in elderly sepsis using biomarkers and infectious sites. Sci Rep 14: 12973. doi: 10.1038/s41598-024-63944-6.
15. Tadese BK, DeSantis SM, Mgbere O, Fujimoto K, Darkoh C (2022) Clinical outcomes associated with co-infection of carbapenem-resistant Enterobacterales and other multidrug-resistant organisms. Infect Prev Pract 4: 100255. doi: 10.1016/j.infpip.2022.100255.
16. Li Y, Liu C, Xiao W, Song T, Wang S (2020) Incidence, risk factors, and outcomes of ventilator-associated pneumonia in traumatic brain injury: a meta-analysis. Neurocrit Care 32: 272–285. doi: 10.1007/s12028-019-00773-w.
17. Robba C, Rebora P, Banzato E, Wiegers EJA, Stocchetti N, Menon DK, Citerio G (2020) Incidence, risk factors, and effects on outcome of ventilator-associated pneumonia in patients with traumatic brain injury: analysis of a large, multicenter, prospective, observational longitudinal study. Chest 158: 2292–2303. doi: 10.1016/j.chest.2020.06.064.
18. de Franca SA, Tavares WM, Salinet ASM, Paiva WS, Teixeira MJ (2020) Early tracheostomy in severe traumatic brain injury patients: a meta-analysis and comparison with late tracheostomy. Crit Care Med 48: e325–e331. doi: 10.1097/CCM.0000000000004239.
19. Castellani GB, Maietti E, Colombo V, Clemente S, Cassani I, Rucci P (2024) Impact of multidrug-resistant organisms on severe acquired brain injury rehabilitation: an observational study. Microorganisms 12: 830. doi: 10.3390/microorganisms12040830.
20. Dong N, Zeng Y, Wang Y, Liu C, Lu J, Cai C (2022) Distribution and spread of the mobilised RND efflux pump gene cluster *tmexCD-toprJ* in clinical Gram-negative bacteria: a molecular epidemiological study. Lancet Microbe 3: e901. doi: 10.1016/S2666-5247(22)00221-X.
21. Ibrahim ME (2019) Prevalence of *Acinetobacter baumannii* in Saudi Arabia: risk factors, antimicrobial resistance patterns and mechanisms of carbapenem resistance. Ann Clin Microbiol Antimicrob 18: 1. doi: 10.1186/s12941-018-0301-x.
22. Pesesky MW, Hussain T, Wallace M, Wang B, Andleeb S, Burnham CA (2015) *KPC* and *NDM-1* genes in related Enterobacteriaceae strains and plasmids from Pakistan and the United States. Emerg Infect Dis 21: 1034–1037. doi: 10.3201/eid2106.141504.

Annex – Supplementary Items

Supplementary Table 1. Co-infection cases with carbapenem-resistant bacteria, 2021–2023.

	2021	2022	2023
Co-infected patients	10	15	20
Co-infected with carbapenem-resistant bacteria	2	7	13
Co-infected with CRAB	1	4	10
Co-infected with CRPA	1	4	2
Co-infected with CRKP	1	0	2

CRAB: carbapenem-resistant *Acinetobacter baumannii*; CRKP: carbapenem-resistant *Klebsiella pneumoniae*; CRPA: carbapenem-resistant *Pseudomonas aeruginosa.*