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ORIGINAL RESEARCH

Analysis of Carbapenem-Resistant Enterobacterales Resistance in a Hospital in Kunming Over the Past Two Years

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Objective: To examine the species distribution, clinical prevalence, antimicrobial profiles, and carbapenemase phenotypes of carbapenem-resistant Enterobacterales (CRE) isolated from a tertiary hospital over the past two years, thereby providing a reference for clinical anti-infection strategies and hospital infection control measures.

Methods: A retrospective analysis was performed to examine the distribution of CRE strains isolated from inpatients at a tertiary hospital between 2023 and 2024, their resistance profiles to commonly used antibiotics and carbapenemase phenotypes.

Results: A total of 239 distinct CRE strains were identified between 2023 and 2024, predominantly in sputum, urine, and blood samples. The primary species of CRE include *Klebsiella pneumoniae, Escherichia coli*, and *Proteus mirabilis*. These CRE strains were mainly isolated from departments such as geriatrics, intensive care units (ICU), and respiratory medicine. Among the 239 CRE isolates, there was a notably high resistance rate to cephalosporins, enzyme inhibitor combinations, aminoglycosides, and quinolones, exceeding 85%, with carbapenems exhibiting a resistance rate of over 90%. Conversely, the resistance rates to tigecycline, ceftazidime/avibactam, and polymyxin B were 1.26%, 24.24%, and 5.43%, respectively. The majority of strains (74.06%) produced class A serine carbapenemases, specifically the KPC type.

Conclusion: The CRE isolation and resistance rates in this hospital are similar to international trends, both showing an upward trend, and comparison with domestic data reveals significant regional differences. CRE infections are difficult to treat and have a high mortality rate. Therefore, to meet the needs of Infection Prevention and Control, it is necessary to strengthen the monitoring of CRE resistance in this institution, contributing to the prevention, control, and clinical management capabilities for infections.

Keywords: Enterobacterales, carbapenemase-resistant, drug resistance, enzyme types

Introduction

Enterobacteriales constitute a substantial group of Gram-negative bacilli, encompassing species such as *Klebsiella pneumoniae, Escherichia coli*, and *Proteus mirabilis*, among other prevalent pathogenic bacteria. These microorganisms are ubiquitously found in the natural environment and in the intestines of animals.[1,2] Under conditions where the host site is altered or immune function is compromised, these bacteria can become pathogenic, resulting in infections across multiple body sites.[3] They are frequently implicated in extraintestinal infectious diseases, including pulmonary and bloodstream infections,[4] thereby prolonging hospitalization and increasing the familial burden on patients.[4–6]

Carbapenems are essential agents for the management of multidrug-resistant gram-negative bacterial infections because of their potent antibacterial efficacy and resistance to β-lactamase degradation.[7] They are frequently regarded as one of the last lines of defense against antibiotic therapy.[8] In 2017, the World Health Organization (WHO) classified carbapenem-resistant Enterobacterales (CRE) as a critical antibiotic-resistant pathogen.[9] According to the Centers for Disease Control and Prevention (CDC), CRE is defined as Enterobacterales that demonstrate in vitro resistance to carbapenem antibiotics.[5] Owing to their pronounced drug resistance and high mortality rates, these bacteria pose

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a significant latent threat to global public health[10–12]and present a formidable challenge for clinical management.[13,14] The occurrence of CER varies in different regions around the world,[15] and its resistance patterns also differ.[16] The occurrence and resistance patterns in different hospitals across various regions of our country also vary.[17–19] Reports from a tertiary children's hospital in Kunming, Yunnan[20] found resistance patterns that differ significantly from the conclusions of a 2016 study conducted in Yunnan Province.[21]

Based on this difference, the objective of this study was to analyze the clinical distribution characteristics and drug resistance of CRE within this hospital, thereby providing a scientific basis for the rational use of antibiotics and the development of infection control measures. Additionally, the findings of this study may serve as a reference for other medical institutions to promote the prevention and control of CRE infections.

Materials and Methods

Experimental Strains

From January 2023 to December 2024, specimens of patients were collected from a tertiary hospital, Bacterial isolation and culture were conducted in strict accordance with the National Clinical Inspection Operation Procedures (4th edition). Samples were inoculated on Columbia blood agar plates (AutoBio, China) and MacConkey agar plates (AutoBio, China) using the partition method (sputum, secretions, lavage fluid and blood) and the coating method (urine). After 24–48h of culture at 35°C and 5% carbon dioxide, a single colony was isolated. Blood samples were cultured using BACTEC 9240 (Becton, Dickinson and Company, America) and BacT/Alert 3D 240 (BioMérieux, France) blood culture instruments and supporting blood culture bottles. After the positive alarm of blood culture, a single colony was isolated according to the above plate marking method. Duplicate isolates from the same anatomical site in the same patient were excluded from this study. At the same time, for the same patient, if the same type of strain is isolated from different anatomical sites during the same hospitalization period, only the first isolate is included according to the CLSI M39 standard.

Bacterial Identification and Drug Sensitivity

The VITEK-2 Compact (bioMérieux, France) automatic identification and drug sensitivity analyzer was employed for isolation, identification, and antimicrobial susceptibility test, while the disk diffusion method (K-B method, disk: Oxoid, UK) was utilized for supplementary antimicrobial susceptibility test. The minimum inhibitory concentration and area diameter were explained according to the Clinical and Laboratory Standards Institute (CLSI) standard M100-S34 issued in 2024. According to the United States Centers for Disease Control and Prevention (CDC), CRE is characterized by *Morganella morganii, Proteus*, or *Providencia* species that exhibit resistance to carbapenems, with the exception of imipenem, or Enterobacterales that are resistant to ertapenem, meropenem, imipenem, or are carbapenemase-producing Enterobacterales, excluding the aforementioned strains. This definition encompasses instances where the minimum inhibitory concentration (MIC) for imipenem, meropenem, or doripenem is ≥4 mg/L; for ertapenem, the MIC is ≥2mg/L; or where carbapenemase-producing Enterobacterales are confirmed.

Detection of Drug-Resistant Enzyme Types of Strains

The NG test CARBA 5 (NG Biotech, Guipry, France) was used to determine the carbapenemase detection of carbapenem-resistant Enterobacterales isolates. Multiple articles indicate that this reagent kit has good performance.[22–24] In accordance with the reagent instructions, prior to the experiment, both the kit and the plate containing the strain to be tested were equilibrated to a temperature range of 15°C to 30°C. Initially, five drops of sample treatment solution were introduced into a sterile EP tube, followed by the transfer of a monoclonal colony using an inoculation loop into the EP tube. The tubes were sealed and thoroughly mixed using a vortex oscillator. Subsequently, 50 µL of the treatment solution was dispensed into the sample wells of the detection card. The results were obtained within 10–30 min. A quality control line (line C) was used for internal quality assurance. If the quality control line did not exhibit coloration, the results were considered to be invalid. Freeze-dried powders of quality control products require reconstitution prior to use. The cap of the quality control product bottle was carefully removed, and 1mL of sample processing liquid was added, mixed thoroughly until completely dissolved, and immediately analyzed. The results indicated red bands on both the detection (T) and control (C) lines, indicating positive test outcomes. A red band solely on the C-line denotes a negative result; the absence of a red band on the C-line renders the detection invalid, necessitating re-evaluation.

Quality Control

Quality control strains, including *Escherichia coli* ATCC 25922, *Escherichia coli* ATCC 35218, *Klebsiella pneumoniae* ATCC 700603, ATCC BAA1705 and ATCC BAA1706, along with the experimental strains, were inoculated, cultured, and assessed for drug sensitivity to ensure the reliability of the experiment. The quality control strains were obtained from the China National Health Commission Clinical Laboratory Center (NCCL). The strains were preserved in −80°C refrigerator.

Data Analysis

Data processing and statistical analysis of bacterial identification and drug sensitivity test results were conducted using WHONET 5.6 and SPSS 27.0. The Chi-square test or Fisher's exact test (small sample size) was employed to compare annual trends. The 95% confidence interval (*95% CI*) was used to explain the drug resistance rate. Statistical significance was set at $P<0.05$.

Results

CRE Strain Specimen Source

Between 2023 and 2024, 239 CRE strains were identified in a tertiary hospital. Most of these strains, specifically 211, were isolated from sputum, urine, and blood samples, representing 88.28% of the total. Sputum specimens accounted for 137 cases (57.32%), whereas urine specimens accounted for 64 cases (26.78%). Blood samples were collected from 10 patients (4.18%). Additionally, drainage fluid specimens accounted for 9 cases (3.77%), secretion specimens for 8 cases (3.35%), alveolar lavage fluid specimens for 7 cases (2.93%), ascites specimens for 1 case (0.42%), vaginal secretion specimens for 2 cases (0.84%), and pleural effusion specimens for 1 case (0.42%). The detection rate of CRE in sputum samples in 2024 was lower compared to 2023, while the detection rate in urine samples was higher in 2024 than in 2023. However, these variations were not statistically significant (sputum: $\chi^2=0.084$, $P>0.05$; urine: $\chi^2=3.621$, $P>0.05$). Conversely, the detection rate in blood samples exhibited a significant increase in 2024, with a statistically significant difference ($\chi^2=16.892$, $P<0.001$), as demonstrated in Table 1 and Figure 1.

Table 1 The Source, Departments, Strains Species, Carbapenemase Phenotype, of Distribution of 239 CRE Specimens

Specimen Type	2023 (n=89)		2024 (n=150)		Sum-Up (n=239)		χ2	P
	Number	Constituent Ratio	Number	Constituent ratio	Number	Constituent Ratio		
Department source of strains								
Geriatrics	13	14.61%	54	36.00%	67	28.03%	12.67	<0.001+
ICU	19	21.35%	24	16.00%	43	17.99%	1.08	0.298
Department of respiration	17	19.10%	17	11.33%	34	14.23%	2.76	0.097
Chinese traditional medicine	0	0.00%	32	21.33%	32	13.39%	21.86	<0.001+
Oncology department	15	16.85%	0	0.00%	15	6.28%	26.93	<0.001+
Urinary surgery	6	6.74%	4	2.67%	10	4.18%	2.07	0.15
Neurosurgery	4	4.49%	3	2.00%	7	2.93%	0.3	0.584*
Department of cardiology	4	4.49%	1	0.67%	5	2.09%	4.15	0.042*
Clinic	4	4.49%	0	0.00%	4	1.67%	5.38	0.020*
Department of general surgery	2	2.25%	2	1.33%	4	1.67%	0.22	0.639
Infection department	0	0.00%	4	2.67%	4	1.67%	3.35	0.067*
Renal medicine	2	2.25%	1	0.67%	3	1.26%	1.17	0.28
Breast department	0	0.00%	2	1.33%	2	0.84%	1.33	0.249*

(*Continued*)

Table 1 (Continued).

Specimen Type	2023 (n=89)		2024 (n=150)		Sum-Up (n=239)		χ2	P
	Number	Constituent Ratio	Number	Constituent ratio	Number	Constituent Ratio		
Digestive department	1	1.12%	1	0.67%	2	0.84%	0.15	0.689*
Orthopaedics department	0	0.00%	2	1.33%	2	0.84%	1.33	0.249*
Hepatology department	1	1.12%	1	0.67%	2	0.84%	0.15	0.689*
Neurological department	0	0.00%	1	0.67%	1	0.42%	0.3	0.584*
Obstetrics	1	1.12%	0	0.00%	1	0.42%	1.33	0.249*
Cardiothoracic surgery	0	0.00%	1	0.67%	1	0.42%	0.3	0.584*
Specimen source of strains								
Sputamentum	52	58.43%	85	56.67%	137	57.32%	0.084	0.772
Urine	18	20.22%	46	30.66%	64	26.78%	3.621	0.057
Blood	9	10.11%	1	0.67%	10	4.18%	16.892	<0.001+
Drainage fluid	4	4.49%	5	3.33%	9	3.77%	0.216	0.642
Secretion specimens	3	3.37%	5	3.33%	8	3.35%	0	1
Bronchoalveolar lavage fluid	2	2.25%	5	3.33%	7	2.93%	0.312	0.577
Vaginal discharge	1	1.13%	1	0.67%	2	0.84%	0.184	0.668
Ascites	0	0	1	0.67%	1	0.42%	-	0.456*
Chest water	0	0	1	0.67%	1	0.42%	-	0.456*
Distribution of CRE strains								
Klebsiella pneumoniae	65	73.00%	124	82.60%	189	79.08%	3.621	0.057
Escherichia coli	13	14.60%	15	10.00%	28	11.72%	1.119	0.29
Citrobacter freundii	5	5.60%	2	1.30%	7	2.93%	-	0.118*
Proteus mirabilis	1	1.10%	2	1.30%	3	1.26%	-	1.000*
Klebsiella oxytoca	2	2.20%	1	0.60%	3	1.26%	-	0.561*
Providencia spp	0	0.00%	3	2.00%	3	1.26%	-	0.068*
Klebsiella aerogenes	1	1.10%	1	0.60%	2	0.84%	-	1.000*
Morganella morganii	1	1.10%	0	0.00%	1	0.42%	-	0.417*
Proteus vulgaris	1	1.10%	0	0.00%	1	0.42%	-	0.417*
Citrobacter brucei	0	0.00%	1	0.60%	1	0.42%	-	0.417*
Ornithine klebsiella bacteria	0	0.00%	1	0.60%	1	0.42%	-	0.417*
Enzyme type distribution of strains								
Producing class A serine enzyme	61	68.54%	116	77.33%	177	74.06%	1.931	0.165
Producing class B metalloenzymes	18	20.22%	27	18.00%	45	18.83%	0.193	0.66
Producing class D OXA enzyme (OXA-48)	3	3.37%	1	0.67%	4	1.67%	-	0.302*
Producing type A enzyme + type B enzyme	3	3.37%	2	1.33%	5	2.09%	-	1.000*
No enzyme production	4	4.49%	4	2.67%	8	3.35%	0.564	0.453

Notes: The P value marked with "*" is the Fisher 's exact test result, and the rest is the chi-square test result. '+" is *P*<0.001, which is highly statistically significant. Number, Number of strains.

Distribution of Clinical Departments of CRE Strains

The CRE strains were mainly isolated from the departments of geriatrics, ICU, respiratory medicine, and traditional Chinese medicine. The proportions were as follows: geriatrics (67 cases, 28.03%), ICU (43 cases, 17.99%), respiratory medicine (34 cases, 14.23%), traditional Chinese medicine (32 cases, 13.39%), oncology (15 cases, 6.28%), urology (10 cases, 4.18%), neurosurgery (7 cases, 2.93%), cardiology (5 cases, 2.09%), outpatient care (4 cases, 1.67%), general surgery (4 cases, 1.67%), and infection (4 cases, 1.67%). As shown in Figure 2A and B, CRE detection in 2023 and 2024 shows significant differences in the distribution of departments. The specific performances were as follows: the proportion of CRE detected in the geriatric department increased significantly (χ^2=12.67, P<0.05), the traditional Chinese medicine department increased significantly (χ^2=21.86, P<0.001), and the oncology department decreased significantly (χ^2=26.93, P<0.001). Further details are provided in Table 1 and Figure 2C.

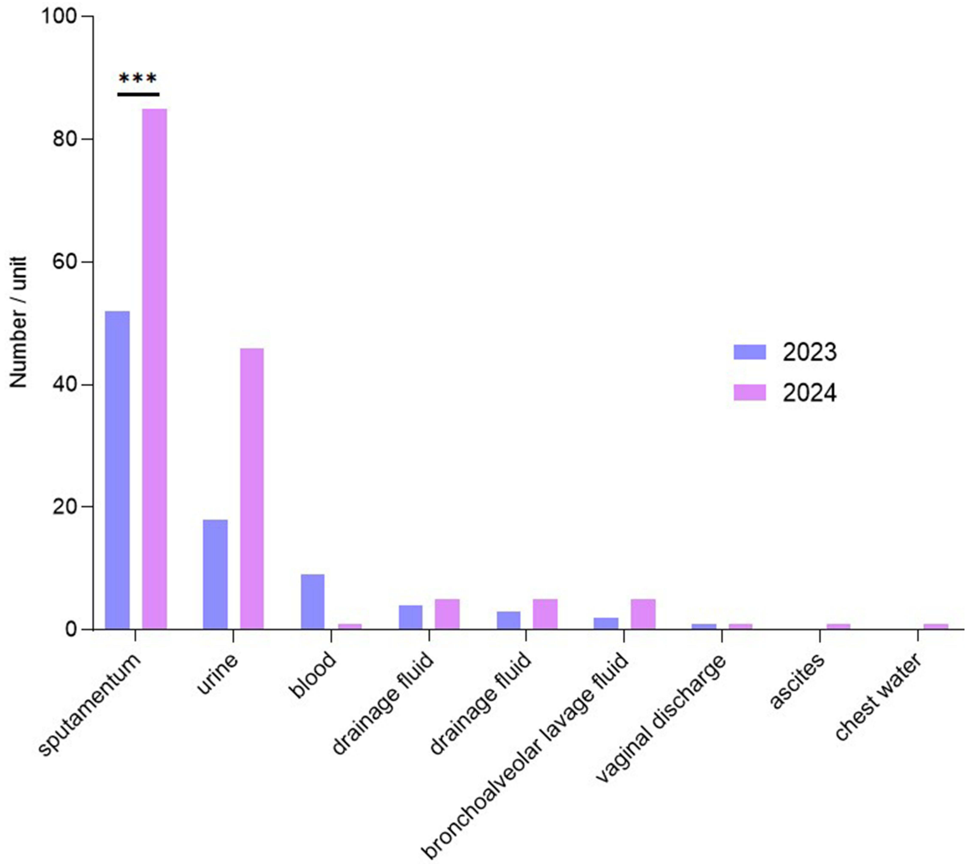

Figure 1 Specimen type of isolates.
Notes: ^{ns}P>0.05; *P<0.05; **P<0.01; ***P<0.001.

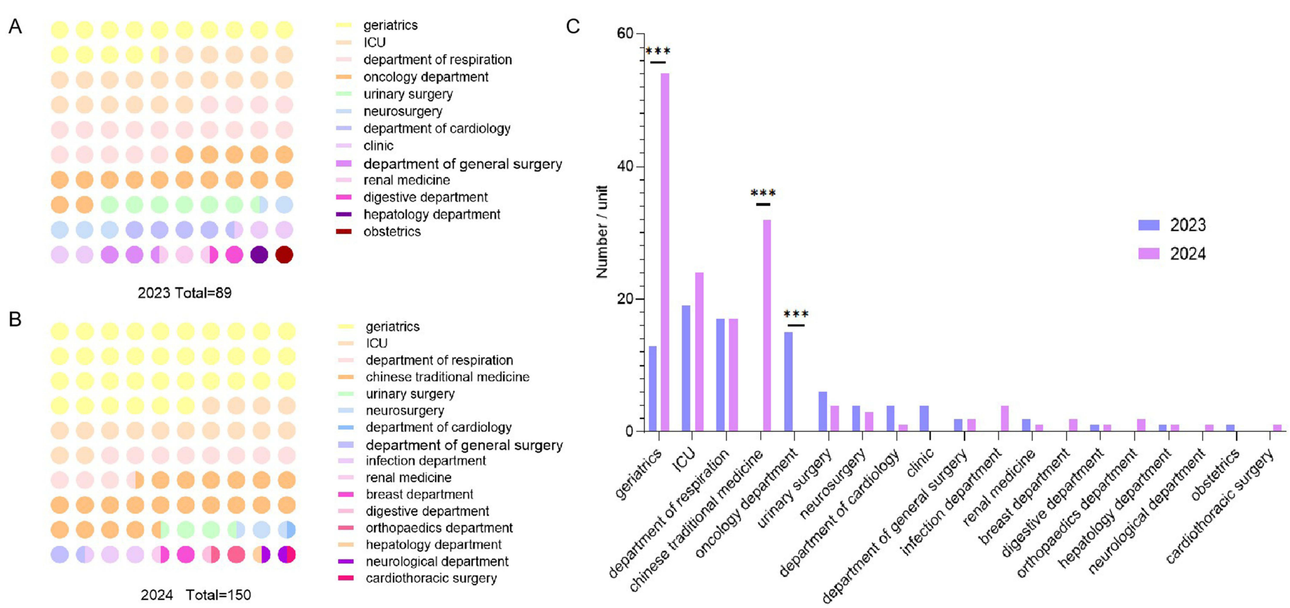

Figure 2 The distribution of the source departments of the strains. (**A**) The distribution trend of strains source departments in 2023. (**B**) The distribution trend of strains source departments in 2024. (**C**) Comparison of the distribution of strains from departments in 2023 and 2024.
Notes: ^{ns}P>0.05; *P<0.05; **P<0.01; ***P<0.001.

Species Distribution of CRE Strains

The distribution of the 239 detected CRE strains was as follows: *Klebsiella pneumoniae* constituted 189 strains (79.08%), *Escherichia coli* comprised 28 strains (11.72%), *Citrobacter freundii* accounted for 7 strains (2.93%), *Proteus mirabilis* included 3 strains (1.26%), *Klebsiella oxytoca* also included 3 strains (1.26%), *Providencia* species were represented by 3 strains (1.26%), *Klebsiella aerogenes* by 2 strains (0.84%), and *Morganella morganii, Proteus vulgaris, Citrobacter buchneri*, and *Klebsiella ornitholyticus* each by 1 strain (0.42%). Refer to Table 1 for detailed distribution. Figure 3A and B illustrates the strain distribution of CRE in 2023 and 2024, highlighting a significant increase in detections from 89 cases in 2023 to 150 cases in 2024. In both years, *Klebsiella pneumoniae* was the predominant bacterium, comprising 73.03% of cases in 2023 and 82.67% in 2024. As depicted in Figure 3C, there was no statistically significant difference in the composition of the CRE strains detected between the two years ($P>0.05$).

Drug Resistance of CRE Strains

The composition ratio of the bacterial resistance of the 239 CRE strains is shown in Figure 4D. 239 strains of CRE were highly resistant to many common antibiotics and were generally resistant to cephalosporins, enzyme-inhibitor compound drugs, aminoglycosides, quinolones, and other antibiotics. The resistance rates to ampicillin, cefazolin, and cefuroxime were 100%, and the resistance rate to ceftriaxone was 99.58%. The resistance rates to ceftazidime, cefotaxime, amoxicillin/clavulanic acid, cefoxitin, cefoperazone/sulbactam, cefepime, ciprofloxacin, levofloxacin, and aztreonam were all greater than 90%, and the resistance rates to carbapenem antibiotics were all greater than 90%. Resistance rates to ertapenem, imipenem, and meropenem were 97.07%, 94.56%, and 93.72%, respectively. The resistance rates to gentamicin, amikacin, ampicillin/sulbactam, and nitrofurantoin were 83.68%, 76.15%, 79.08%, and 71.43%, respectively. It had a high sensitivity rate to tigecycline, polymyxin B, and ceftazidime/avibactam, and its drug resistance rates were 1.26%, 5.43%, and 24.24%, respectively, as shown in Table 2.

Among the 239 CRE strains examined, 177 were identified as producers of class A serine enzymes. Figure 4E illustrates the composition ratio of the drug susceptibility test for 177 class A enzyme-producing strains. Statistical analysis of drug susceptibility revealed that all 177 strains exhibited a 100% resistance rate to ampicillin, cefazolin, cefuroxime, ceftriaxone, and aztreonam. The rates of resistance to meropenem and imipenem were 96.05% . Both ciprofloxacin and levofloxacin showed resistance rates of 98.31%. The resistance rates to gentamicin and amikacin were 89.83% and 90.96%, respectively.

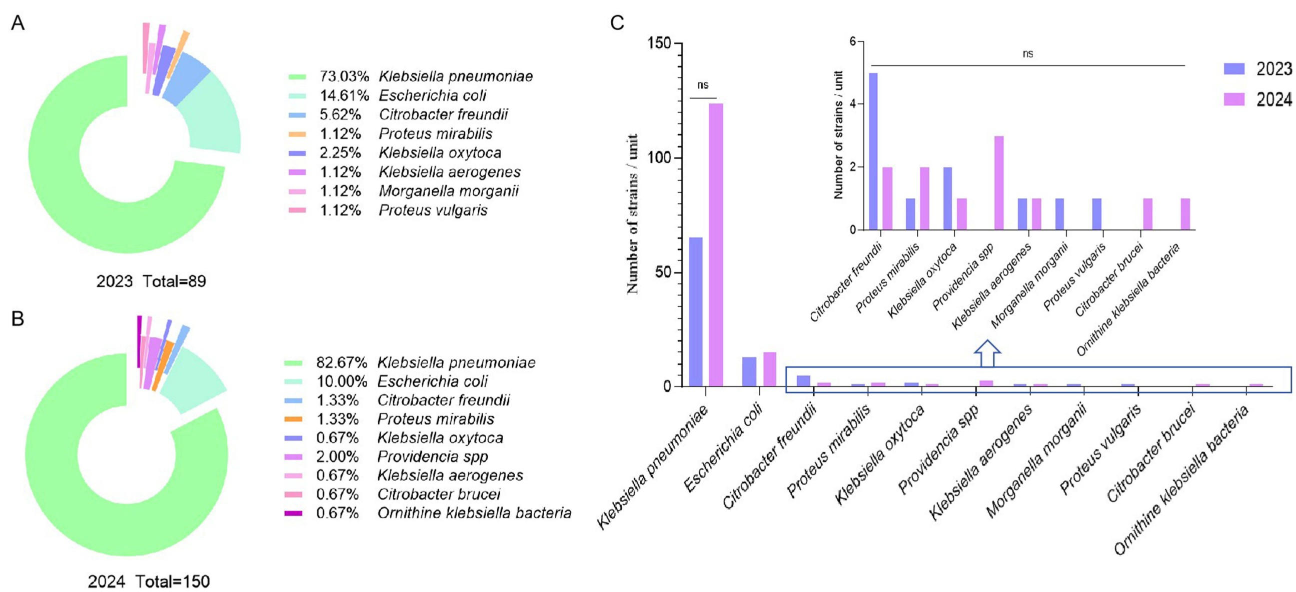

Figure 3 The species distribution of strains. (**A**) The species distribution trend of strains in 2023. (**B**) The species distribution trend of strains in 2024. (**C**) Comparison of species distribution of strains in 2023 and 2024.
Notes: $^{ns}P>0.05$; $^{*}P<0.05$; $^{**}P<0.01$; $^{***}P<0.001$.

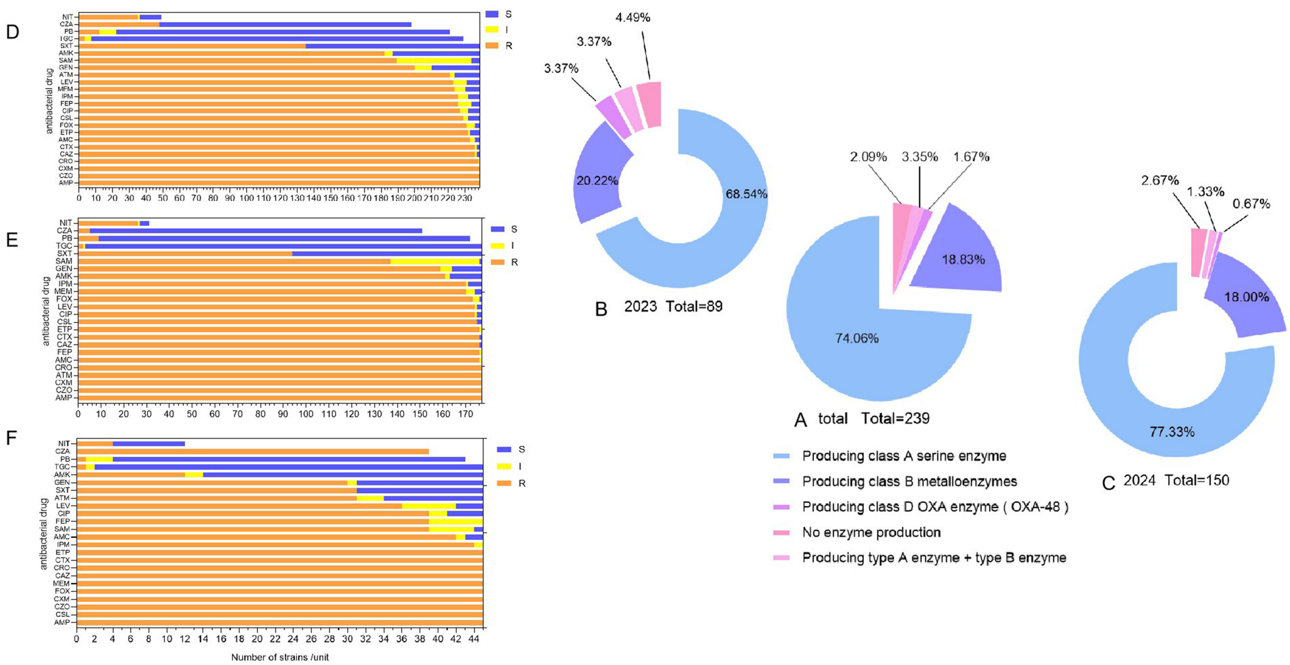

Figure 4 Analysis of enzyme production type and drug resistance rate of isolated strains. (**A**) The overall distribution trend of enzyme production of 239 CRE strains in two years. (**B**) The distribution trend of enzyme production of 89 CRE isolates in 2023. (**C**) The distribution trend of enzyme production of 150 CRE strains in 2024. (**D**): The overall drug resistance trend of 239 CRE isolates. (**E**)The drug resistance trend of 177 CRE isolates producing class A serine enzyme was analyzed. (**F**)The drug resistance trend of 45 CRE isolates producing class B metallo-β-lactamases was analyzed.

Abbreviations: AMP, ampicillin; CZO, cefazolin; CXM, cefuroxime; CRO, ceftriaxone; CAZ, ceftazidime; CTX, cefotaxime; AMC, amoxicillin/clavulanic acid; FOX, cefoxitin; CSL, cefoperazone/sulbactam; FEP, cefepime; ETP, ertapenem; IPM, imipenem; MEM, meropenem; CIP, ciprofloxacin; LEV, levofloxacin; ATM, aztreonam; SAM, ampicillin/sulbactum; SXT, trimethoprim/sulfamethoxazole; GEN, gentamicin; AMK, amikacin; TGC, tigecycline; PB, polymyxin B; CZA, ceftazidime/avibactam.

Additionally, the resistance rates for trimethoprim-sulfamethoxazole, tigecycline, polymyxin B, and ceftazidime/avibactam were 53.11%, 1.13%, 5.23%, and 3.31%, respectively, as detailed in Table 2.

A total of 45 strains producing class B metalloenzymes were identified. Figure 4F illustrates the composition ratio derived from the drug sensitivity tests conducted on these strains. Statistical analysis of the drug sensitivity results

Table 2 Antimicrobial Susceptibility Test Results of CRE Isolates, Enzyme-Producing Type A and Enzyme-Producing Type B

Anti-Biotic	Number of Strains	Resistance(R)			Intermediate(I)		Sensitivity(S)	
		Number of Strains	%	*95% CI*	Number of Strains	%	Number of Strains	%
Antibiotic susceptibility test results of 239 CRE strains								
AMP	239	239	100.00%	None	0	0.00%	0	0.00%
CZO	239	239	100.00%	None	0	0.00%	0	0.00%
CXM	239	239	100.00%	None	0	0.00%	0	0.00%
CRO	239	238	99.58%	99.16%-100.00%	1	0.42%	0	0.00%
CAZ	239	236	98.74%	98.02%-99.46%	1	0.42%	2	0.84%
CTX	239	236	98.74%	98.02%-99.46%	1	0.42%	2	0.84%
AMC	239	233	97.49%	96.48–98.50%	3	1.26%	3	1.26%
ETP	239	232	97.07%	95.98–98.16%	1	0.42%	6	2.51%
FOX	239	231	96.65%	95.49–97.81%	5	2.09%	3	1.26%
CSL	239	229	95.82%	94.53–97.11%	3	1.26%	7	2.93%
CIP	239	227	94.98%	93.57–96.39%	5	2.09%	7	2.93%
FEP	239	226	94.56%	93.09–96.03%	8	3.35%	5	2.09%
IPM	239	226	94.56%	93.09–96.03%	6	2.51%	7	2.93%

(*Continued*)

Table 2 (Continued).

Anti-Biotic	Number of Strains	Resistance(R)			Intermediate(I)		Sensitivity(S)	
		Number of Strains	%	*95% CI*	Number of Strains	%	Number of Strains	%
MEM	239	224	93.72%	92.15%+95.29%	6	2.51%	9	3.77%
LEV	239	223	93.31%	91.69–94.93%	8	3.35%	8	3.35%
ATM	239	221	92.47%	90.76–94.18%	3	1.26%	15	6.28%
GEN	239	200	83.68%	81.29–86.07%	10	4.18%	29	12.13%
SAM	239	189	79.08%	76.45–81.71%	45	18.83%	5	2.09%
AMK	239	182	76.15%	73.39–78.91%	5	2.09%	52	21.76%
SXT	239	135	56.49%	53.28–59.70%	0	0.00%	104	43.51%
TGC	239	3	1.26%	0.54–1.98%	4	1.67%	222	92.89%
PB	221	12	5.43%	3.96–6.90%	10	4.52%	199	90.05%
CZA	198	48	24.24%	21.47–27.01%	0	0.00%	150	75.76%
NIT	49	35	71.43%	68.51–74.35%	1	2.04%	13	26.53%
Antibiotic susceptibility test results of 177 CRE strains producing class A serine enzyme								
AMP	177	177	100.00%	None	0	0.00%	0	0.00%
CZO	177	177	100.00%	None	0	0.00%	0	0.00%
CXM	177	177	100.00%	None	0	0.00%	0	0.00%
ATM	177	177	100.00%	None	0	0.00%	0	0.00%
CRO	177	177	100.00%	None	0	0.00%	0	0.00%
AMC	177	176	99.44%	98.88–100.00%	1	0.56%	0	0.00%
FEP	177	176	99.44%	98.88–100.00%	1	0.56%	0	0.00%
CAZ	177	176	99.44%	98.88–100.00%	0	0.00%	1	0.56%
CTX	177	176	99.44%	98.88–100.00%	0	0.00%	1	0.56%
ETP	177	176	99.44%	98.88–100.00%	1	0.56%	0	0.00%
CSL	177	175	98.87%	98.08–99.66%	0	0.00%	2	1.13%
CIP	177	174	98.31%	97.34–99.28%	1	0.56%	2	1.13%
LEV	177	174	98.31%	97.34–99.28%	1	0.56%	2	1.13%
FOX	177	173	97.74%	96.62–98.86%	3	1.69%	1	0.56%
MEM	177	170	96.05%	94.59–97.51%	4	2.26%	3	1.69%
IPM	177	170	96.05%	94.59–97.51%	1	0.56%	6	3.39%
AMK	177	161	90.96%	88.80–93.12%	2	1.13%	14	7.91%
GEN	177	159	89.83%	87.56–92.10%	5	2.82%	13	7.34%
SAM	177	137	77.40%	74.26–80.54%	39	22.03%	1	0.56%
SXT	177	94	53.11%	49.36–56.86%	0	0.00%	83	46.89%
TGC	177	2	1.13%	0.34–1.96%	1	0.56%	174	98.31%
PB	172	9	5.23%	3.56–6.90%	0	0.00%	163	94.77%
CZA	151	5	3.31%	1.97–4.65%	0	0.00%	146	96.69%
NIT	31	26	83.87%	81.11–86.63%	1	3.23%	4	12.90%
Antibiotic susceptibility test results of 45 CRE strains producing class B metalloenzymes								
AMP	45	45	100.00%	None	0	0.00%	0	0.00%
CSL	45	45	100.00%	None	0	0.00%	0	0.00%
CZO	45	45	100.00%	None	0	0.00%	0	0.00%
CXM	45	45	100.00%	None	0	0.00%	0	0.00%
FOX	45	45	100.00%	None	0	0.00%	0	0.00%
MEM	45	45	100.00%	None	0	0.00%	0	0.00%
CAZ	45	45	100.00%	None	0	0.00%	0	0.00%
CRO	45	45	100.00%	None	0	0.00%	0	0.00%
CTX	45	45	100.00%	None	0	0.00%	0	0.00%
ETP	45	45	100.00%	None	0	0.00%	0	0.00%
IPM	45	44	97.78%	95.58–99.98%	1	2.22%	0	0.00%
AMC	45	42	93.33%	89.61–97.05%	1	2.22%	2	4.44%
SAM	45	39	86.67%	81.60–91.74%	5	11.11%	1	2.22%
FEP	45	39	86.67%	81.60–91.74%	6	13.33%	0	0.00%

(*Continued*)

Table 2 (Continued).

Anti-Biotic	Number of Strains	Resistance(R)			Intermediate(I)		Sensitivity(S)	
		Number of Strains	%	*95% CI*	Number of Strains	%	Number of Strains	%
CIP	45	39	86.67%	81.60–91.74%	2	4.44%	4	8.89%
LEV	45	36	80.00%	74.04–85.96%	6	13.33%	3	6.67%
ATM	45	31	68.89%	61.99–75.79%	3	6.67%	11	24.44%
SXT	45	31	68.89%	61.99–75.79%	0	0.00%	14	31.11%
GEN	45	30	66.67%	59.64–73.70%	1	2.22%	14	31.11%
AMK	45	12	26.67%	20.08–33.26%	2	4.44%	31	68.89%
TGC	45	1	2.22%	0.02–4.42%	1	2.22%	43	95.56%
PB	40	1	2.50%	0.17–4.83%	3	7.50%	39	97.50%
CZA	39	39	100.00%	None	0	0.00%	0	0.00%
NIT	12	4	33.33%	26.30–40.36%	0	0.00%	8	66.67%

Abbreviations: AMP, ampicillin; CZO, cefazolin; CXM, cefuroxime; CRO, ceftriaxone; CAZ, ceftazidime; CTX, cefotaxime; AMC, amoxicillin/clavulanic acid; FOX, cefoxitin; CSL, cefoperazone/sulbactam; FEP, cefepime; ETP, ertapenem; IPM, imipenem; MEM, meropenem; CIP, ciprofloxacin; LEV, levofloxacin; ATM, aztreonam; SAM, ampicillin/sulbactum; SXT, trimethoprim/sulfamethoxazole; GEN, gentamicin; AMK, amikacin; TGC, tigecycline; PB, polymyxin B; CZA, ceftazidime/avibactam; NIT, furadantin. *95% CI*, 95% confidence interval; "%", constituent ratio.

revealed that the resistance rates of the 45 class B metalloenzyme strains to ampicillin, cefoperazone/sulbactam, cefazolin, cefuroxime, cefoxitin, ceftazidime, ceftriaxone, and cefotaxime were 100%. Similarly, the resistance rates to meropenem and ertapenem were 100%. In contrast, the resistance rate to imipenem was slightly lower (97.78%) and the resistance rate to aztreonam was 68.89%. The resistance rates to ciprofloxacin and levofloxacin were 86.67% and 80%, respectively. Additionally, the resistance rates to cotrimoxazole and gentamicin were 68.89% and 66.67%, respectively. In comparison, the resistance rates to amikacin, ceftazidime/avibactam, tigecycline, and polymyxin B were 26.67%, 100%, 2.22%, and 2.50%, respectively, as detailed in Table 2.

The Drug-Resistant Enzyme Types of CRE Strains

Among the 239 CRE strains analyzed, 177 strains (74.09%) were found to produce class A serine enzymes, with the KPC type being the predominant enzyme. A total of 45 strains (18.83%) produced class B metalloenzymes, with the NDM type as the primary enzyme. Four strains (1.67%) produced class D OXA enzymes, specifically the OXA-48 type. Additionally, five strains (2.09%) simultaneously produced class A serine enzymes KPC and class B metalloenzyme VIM. The remaining eight strains (3.35%) did not produce any enzymes. The detailed composition is shown in Figure 4A. The enzyme types for the years 2023 and 2024 are depicted in Figures 4B and C, respectively. Statistical analysis revealed no significant difference in bacterial enzyme production between 2023 and 2024 ($P>0.05$), as presented in Table 1.

The 239 CRE strains detected contained 11 bacteria, mainly *Klebsiella pneumoniae* and *Escherichia coli*, as shown in Table 3 and Figure 5A. Most of the 189 carbapenem-resistant *Klebsiella pneumoniae* strains produced class A serine enzymes, including 172 strains producing class A serine enzymes, 10 strains producing class B metalloenzymes, four strains producing class D OXA

Table 3 239 CRE Strains to Detect Enzyme Type Composition Ratio

CRE Type	Number of Detections	Constituent Ratio	Type of Enzyme				Non-Producing
			A Type	B Type	D Type (OXA-48)	A+B	
Klebsiella pneumoniae	189	79.08%	172	10	4	3	-
Escherichia coli	28	11.72%	4	22	-	1	1
Citrobacter freundii	7	2.93%	1	6	-	-	-
Proteus mirabilis	3	1.26%	-	-	-	-	3
Providencia spp	3	1.26%	-	3	-	-	-
Klebsiella oxytoca	3	1.26%	-	3	-	-	-
Klebsiella aerogenes	2	0.84%	-	-	-	-	2

(*Continued*)

Table 3 (Continued).

CRE Type	Number of Detections	Constituent Ratio	Type of Enzyme				Non-Producing
			A Type	B Type	D Type (OXA-48)	A+B	
Morganella morganii	1	0.42%	-	-	-	-	1
Proteus vulgaris	1	0.42%	-	-	-	-	1
Citrobacter brucei	1	0.42%	-	-	-	1	-
Ornithine klebsiella bacteria	1	0.42%	-	1	-	-	-
Total number	239	100%	177	45	4	5	8

Notes: A type, the number of strains producing enzyme type A; B type, the number of strains producing enzyme type B; D type, the number of strains producing enzyme type D; A+B, Number of strains producing enzyme type A and enzyme type B together.

enzymes, and three strains producing both class A and class B metalloenzymes, as shown in Figure 5B. Among the 28 strains of carbapenem-resistant *Escherichia coli*, 22 strains produced class B metalloenzymes, four strains produced class A serine enzymes, one strain produced both class A and class B metalloenzymes, and one strain did not produce enzymes (Figure 5C). Seven strains of carbapenem-resistant *Citrobacter freundii* produced class B metallo-β-lactamases (six strains). Carbapenem-resistant *Klebsiella oxytoca, Providencia* spp, *Klebsiella ornithinolytica* all produced class B Metallo-β-lactamases. Carbapenem-resistant *Proteus mirabilis, Morganella morganii, Proteus vulgaris*, and *Klebsiella aerogenes* were non-enzyme-producing strains (Table 3 and Figure 5D).

Comparison of Antimicrobial Resistance Rates of CRE Bacteria in Different Specimen Types

The drug sensitivity results of 137 sputum and 64 urine specimens were statistically analyzed, and the drug resistance rates of several antibiotics with different drug resistance rates were compared. For aztreonam, the drug resistance rate of sputum specimens (98.5%) was significantly higher than that of urine specimens (76.56%), and the difference was statistically significant (P<0.05), as shown in Table 4. These results suggest that for sputum-derived CRE infections, the

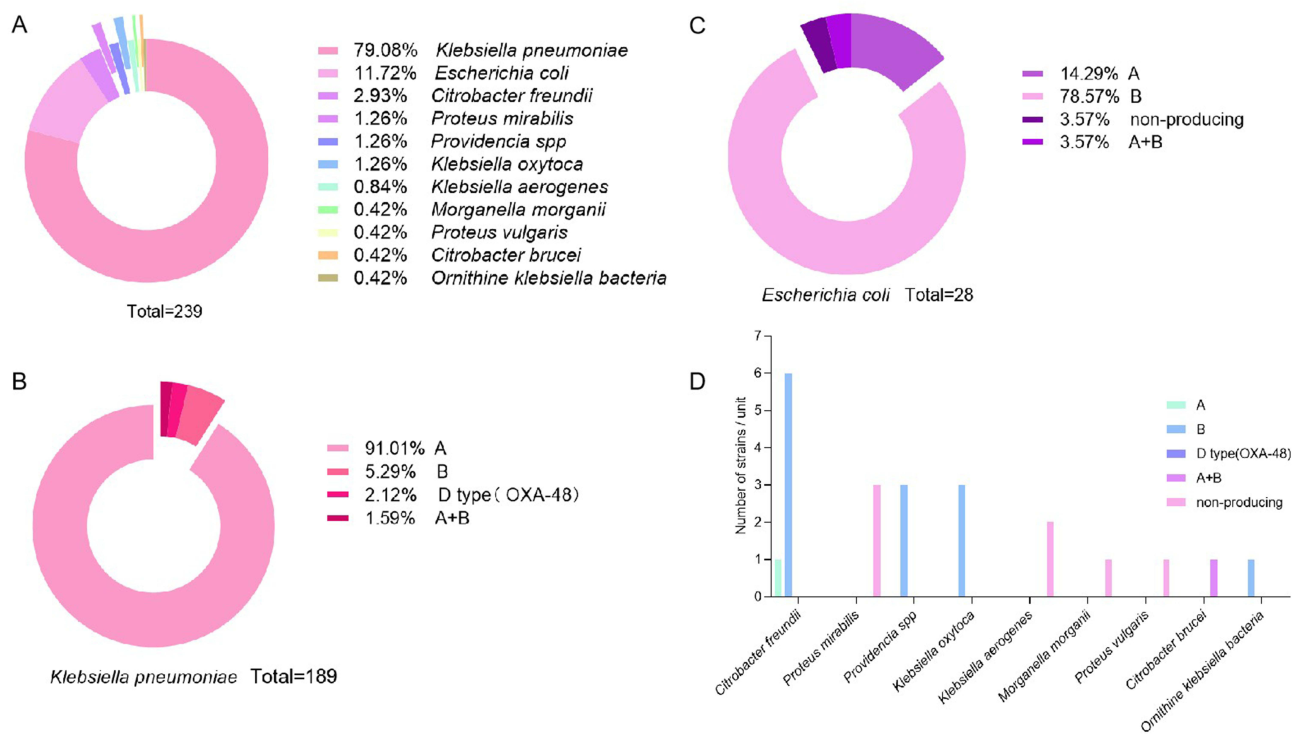

Figure 5 The species distribution and enzyme production distribution trend of 239 CRE strains. (**A**) The classification trend of 239 CRE strains in two years. (**B**) The distribution trend of enzyme production types in 189 strains of Klebsiella pneumoniae isolates. (**C**) The distribution trend of enzyme production types of 28 Escherichia coli isolates. (**D**) The distribution trend of enzyme production types of 22 other isolates.

Notes: A, producing class A serine enzyme; B, producing class B metal-β-lactamases; A+B, At the same time, it produces class A serine enzyme and class B metal-β-lactamases.

Table 4 Comparison of Antimicrobial Resistance Rates of CRE Bacteria in Different Specimens and Enzyme Types

Anti-Biotic	N	n	Resistance Rate (%)	*95% CI*	N	n	Resistance Rate (%)	*95% CI*	*χ2*	*P*
	Sputum samples				**Urine specimens**					
AMC	137	137	100.00%	None	64	60	93.75%	90.72–96.78%	-	-
AMP	137	137	100.00%	None	64	64	100.00%	None	-	-
CXM	137	137	100.00%	None	64	64	100.00%	None	-	-
CRO	137	137	100.00%	None	64	63	98.43%	96.88–99.98%	-	-
CTX	137	137	100.00%	None	64	62	96.88%	94.71–99.05%	-	-
CZO	137	137	100.00%	None	64	63	98.43%	96.88–99.98%	-	-
CAZ	137	136	99.27%	98.54–100.00%	64	63	98.43%	96.88–99.98%	-	-
ETP	137	135	98.54%	97.52–99.56%	64	61	95.31%	92.67–97.95%	-	-
FOX	137	135	98.54%	97.52–9.56%	64	61	95.31%	92.67–97.95%	-	-
ATM	137	135	98.50%	97.46–99.54%	64	49	76.56%	71.26–81.86%	27.22	<0.001
CSL	137	134	97.81%	96.56–99.06%	64	60	93.75%	90.72%-96.78%	-	-
MEM	137	133	97.08%	95.64–98.52%	64	55	85.94%	81.59–90.29%	-	-
CIP	137	131	95.62%	93.87–97.37%	64	62	96.88%	94.71–99.05%	-	-
ETP	137	131	95.62%	93.87–97.37%	64	59	92.19%	88.84–95.54%	-	-
FEP	137	130	94.89%	93.01–95.55%	64	58	90.63%	86.99–94.27%	-	-
LEV	137	128	93.43%	91.31–95.55%	64	62	96.88%	94.71–99.05%	-	-
GEN	137	115	83.94%	80.80–87.08%	64	54	84.38%	79.84–88.29%	-	-
AMK	137	110	80.29%	76.89–83.69%	64	48	75.00%	69.59–80.41%	-	-
SAM	137	108	78.83%	75.34–82.32%	64	48	75.00%	69.59–80.41%	-	-
SXT	137	68	49.64%	45.37–53.91%	64	45	70.31%	64.60–76.02%	7.42	0.006
CZA	112	19	16.96%	13.41–20.51%	51	14	27.45%	21.20–33.70%	2.38	0.12
PB	129	2	1.55%	0.46–2.64%	56	6	10.71%	6.58–14.84%	-	0.002
TGC	137	1	0.73%	0.00–1.46%	64	2	3.13%	0.95–5.31%	-	-
NIT	137	0	0.00%	None	49	36	73.47%	67.16–79.78%	-	-
	Class A enzymes				**Class B enzymes**					
ATM	177	177	100.00%	None	45	31	68.89%	61.99–75.79%	-	<0.001
AMP	177	177	100.00%	None	45	45	100.00%	None	-	-
CZO	177	177	100.00%	None	45	45	100.00%	None	-	-
CXM	177	177	100.00%	None	45	45	100.00%	None	-	-
CRO	177	177	100.00%	None	45	45	100.00%	None	-	-
CAZ	177	176	99.44%	98.88–100.00%	45	45	100.00%	None	-	-
CTX	177	176	99.44%	98.88–100.00%	45	45	100.00%	None	-	-
AMC	177	176	99.44%	98.88–100.00%	45	42	93.33%	89.61–97.05%	-	-
FEP	177	176	99.44%	98.88–100.00%	45	39	86.67%	81.60–91.74%	-	-
CSL	177	175	98.87%	98.08–99.66%	45	45	100.00%	None	-	-
CIP	177	174	98.31%	97.34–99.28%	45	39	86.67%	81.60–91.74%	-	-
ETP	177	174	98.31%	97.34–99.28%	45	45	100.00%	None	-	-
LEV	177	174	98.31%	97.34–99.28%	45	36	80.00%	74.04–85.96%	-	-
FOX	177	173	97.74%	96.62–98.86%	45	45	100.00%	None	-	-
ETP	177	170	96.05%	94.59–97.51%	45	44	97.78%	95.58–99.98%	-	-
MEM	177	170	96.05%	94.59–97.51%	45	45	100.00%	None	-	-
AMK	177	161	90.96%	88.80–93.12%	45	12	26.67%	20.08–33.26%	-	<0.001
GEN	177	159	89.83%	87.56–92.10%	45	30	66.67%	59.64–73.70%	-	-
NIT	31	26	83.87%	77.26–90.48%	12	4	33.33%	19.72–46.94%	-	-
SAM	177	137	77.40%	74.26–80.54%	45	39	86.67%	81.60–91.74%	-	-

(*Continued*)

Table 4 (Continued).

Anti-Biotic	N	n	Resistance Rate (%)	*95% CI*	N	n	Resistance Rate (%)	*95% CI*	*χ2*	*P*
SXT	177	94	53.11%	49.36–56.86%	45	36	80.00%	74.04–85.96%	-	0.001
PB	172	9	5.23%	3.53–6.93%	40	1	2.50%	0.03–4.97%	-	0.664
CZA	151	5	3.31%	1.85–4.77%	39	39	100.00%	None	-	<0.001
TGC	177	2	1.13%	0.34–1.92%	45	1	2.22%	0.02%-4.425	-	0.365

Notes: "-" means that the Fisher 's exact probability test (expected frequency<5) is used, and there is no chi-square statistic output.
Abbreviations: AMP, ampicillin; CZO, cefazolin; CXM, cefuroxime; CRO, ceftriaxone; CAZ, ceftazidime; CTX, cefotaxime; AMC, amoxicillin/clavulanic acid; FOX, cefoxitin; CSL, cefoperazone/sulbactam; FEP, cefepime; ETP, ertapenem; IPM, imipenem; MEM, meropenem; CIP, ciprofloxacin; LEV, levofloxacin; ATM, aztreonam; SAM, ampicillin/sulbactum; SXT, trimethoprim/sulfamethoxazole; GEN, gentamicin; AMK, amikacin; TGC, tigecycline; PB, polymyxin B; CZA, ceftazidime/avibactam; NIT, furadantin. *95% CI*, 95% confidence interval. N, Total number of strains; n, Number of drug-resistant strains.

risk of resistance to aztreonam is higher, and for urinary infections, the risk of resistance to cotrimoxazole and polymyxin B is higher. The resistance rates to ceftazidime/avibactam and tigecycline were not significantly different between the two specimens and could be used as alternative drugs for empirical treatment.

Comparison of Antimicrobial Resistance Rates of CRE Bacteria with Different Enzyme Types

The drug sensitivity results for 177 strains of CRE bacteria producing class A serine enzymes and 45 strains of CRE bacteria producing class B metal enzymes were statistically analyzed. The drug resistance rates of several antibiotics were compared. The resistance rates of CRE strains with different enzyme types to aztreonam, amikacin, and ceftazidime/avibactam were significantly different (*P*<0.05), as shown in Table 4 and Figure 4E and F.

These results suggest that the difference in resistance rates between class A and class B enzymes CRE is mainly reflected in three drugs: aztreonam, amikacin, and ceftazidime/avibactam, whereas tigecycline and polymyxin B are effective against both types of strains. Clinical treatment should be combined with enzyme test results, and sensitive drugs should be preferred (such as ceftazidime/avibactam for class A infections and tigecycline for class B infections).

Discussion

The spread of CRE poses a severe threat to human health and imposes significant burdens on healthcare systems. This study analyzes the distribution of CRE populations, clinical prevalence, antimicrobial susceptibility profiles, and carbapenemase phenotypes to inform clinical diagnostic strategies and hospital infection control measures. Over the past two years, CRE strains isolated from hospitals have predominantly originated from sputum, urine, and blood samples, with the majority associated with geriatric medicine departments, ICU, and respiratory medicine departments. All antibiotics except tigecycline, ceftazidime/avibactam, and polymyxin B demonstrated high resistance to these strains, with KPC-type carbapenems being the predominant detected resistance enzyme.

The 239 CRE strains analyzed in this study were primarily collected from 137 sputum samples (57.32%), 64 urine samples (26.78%), and 10 blood samples (4.18%). This distribution pattern likely stems from the clinical environment's preference for easy collection, non-invasive procedures, and frequent sampling of sputum and urine. Similar to Some literatures report,[25,26] most CRE cases originated from urine, sputum, secretions, and blood. However, Rajni E et al's research indicates that urine and blood remain predominant sources.[27] Regional variations in CRE origins were observed, with departmental distribution showing higher rates in geriatrics (67 cases, 28.03%), ICU (43 cases, 17.99%), and respiratory medicine (34 cases, 14.23%). These findings align with multiple studies.[26,28,29] According to Aleidan et al's,[30] risk factors for CRE infection include advanced age, immunocompromised status, prolonged antibiotic use (particularly recent carbapenem exposure), invasive procedures, ICU treatment, and extended hospital stays—all of which may influence CRE distribution across departments. The notable increase in CRE cases in geriatric departments likely results from combined factors including patient demographics, medical interventions, antimicrobial stewardship pressures, and enhanced infection control measures.

From 2023 to 2024, CRE strains were mainly *Klebsiella pneumoniae*, followed by *Escherichia coli, Citrobacter freundii* and *Proteus mirabilis*. The results were consistent with the results of CRE in Zhejiang, Henan and Shandong, which were mainly *Klebsiella pneumoniae* and *Escherichia coli*.[31–33] Several foreign research articles also support this conclusion.[1,25,34,35] *Citrobacter freundii* ranked third in this isolation study, consistent with research indicating higher prevalence in Yunnan Province.[36] It is worth noting that carbapenem-resistant *Enterobacter cloacae* (CREC) were not detected in this study. It is speculated that there are two reasons. One may be that the hospital strictly implements infection control measures such as hand hygiene, environmental cleaning and disinfection, and isolation of infected patients, which effectively reduces the spread and colonization of CREC, thereby reducing the detection rate. Second, the rational use of antibiotics to avoid excessive use of carbapenems, reducing the screening and reproduction of drug-resistant strains. Of course, the above reasons are only speculation, and the real reasons need further research in the future. There was no significant difference in the composition of strains between 2023 and 2024. It is unclear whether CRE infections are on the rise. This may be due to the relatively few years of data included in this study, and the data being sourced from a single center, which may not reflect the trend of CRE. However, CRE is a growing threat to global human health,[37] showing an upward trend in the world,[38,39] showing high mortality.[4] Compliance with the antibiotic management plan (ASP) and the development of anti-infection strategies include compliance with standards and contact prevention measures, environmental disinfection, isolation of infected persons, and comprehensive education and training of medical staff to prevent and control the risk of CRE transmission.[40–42] Global action is imperative, with tailored strategies for low-and high-income countries.[43]

Most carbapenem resistance is caused by three enzyme groups: serine protease (enzyme type A), metal-β-lactamase (enzyme type B), and oxacillinase-48 (enzyme type D).[16,44] Among the 239 CRE strains in this study, 177 produced A-type serine proteases (74.06%), mainly KPC enzymes. 45 strains produced B-type metal β-lactamases (18.83%), predominantly NDM-type, consistent with global and China's epidemiological research findings.[45,46] However, this study found a higher incidence of enzyme type A in the hospital, reflecting regional differences in CRE. The prevalence trends of CRE enzyme types identified in 2023 and 2024 showed no significant difference, indicating stable CRE control in the hospital. Among them, 189 carbapenem-resistant *Klebsiella pneumoniae* (CRKP) strains were identified, primarily producing A-type serine proteases (91.01%), consistent with China's local epidemiological trends and aligning with Li J J et al[47] finding that the predominant genotype of CRKP is KPC-2, while enzyme type B is mainly prevalent in Pakistan.[48] Although enzyme type B (5.29%) was not frequently isolated in this region, it still warrants attention to prevent its spread.[49] A total of 28 CREC strains were isolated, predominantly enzyme type B. This aligns with the prevalence pattern of the domestic CREC genotype (NDM-5).[50]

The 239 CRE strains included in this study showed significant resistance to β-lactams, cephalosporins, enzyme inhibitors, aminoglycosides, quinolones and other antibiotics. The resistance rates to ampicillin, cefazolin, cefuroxime and ceftriaxone were 100%. Among the carbapenems, the resistance rates of ertapenem (97.07%), imipenem (94.56%) and meropenem (93.72%) were high. It is worth noting that ceftazidime/avibactam (sensitivity rate of 75.76%), tigecycline (sensitivity rate of 92.89%) and polymyxin B (sensitivity rate of 90.05%) still maintain high antibacterial activity, which is consistent with the results of many domestic studies.[51–54] The widespread resistance in CRE strains primarily results from the synergistic effects of multiple resistance mechanisms.[55] Recent studies indicate that these bacteria develop resistance through various pathways, including carbapenemase production; overexpression of AmpC enzymes, or generation of broad-spectrum β-lactamases (ESBLs) accompanied by loss of outer membrane porin expression and enhanced efflux pump activity.[56,57] Among them, the production of carbapenemases is particularly critical. The genes encoding these enzymes are usually located on mobile genetic elements such as plasmids or transposons. This horizontal gene transfer feature allows drug resistance genes to be widely spread among different strains.[58] For CRE resistant to conventional antibiotics, novel agents such as ceftazidime-avibactam, meropenem-vaborbactam, imipenem-robustin, cefdinir, and newer aminoglycosides or tetracyclines may be considered.[37]

The clinical use and intensity of carbapenem antibiotics have been increasing annually, while the resistance rate of Enterobacteriaceae to these drugs has also risen significantly.[59] CRE is characterized by high drug resistance,[60] strong transmissibility,[61] and high pathogenicity.[62] However, effective treatment options for CRE infections remain limited in clinical practice.[63] Therefore, monitoring and analysis of CRE are crucial for developing clinical strategies and improving hospital infection control.

Limitations of Research

This study has limitations, as the data sources are confined to hospital internal records. Future research could expand data diversity and establish a multi-regional, comprehensive research framework. Additionally, the NG test CARBA 5 kit (produced by NG Biotech, GIPRI, France) was used to detect carbapenemase activity in CRE strains, without performing individual genotype comparisons, which introduces potential bias.

Conclusion

In recent years, CRE isolation and drug resistance rates have generally shown an upward trend around the world, and the isolates and drug resistance rates of different medical institutions in different provinces of China vary greatly. Our hospital mainly isolated CRE from sputum and urine samples from geriatrics, ICU and respiratory medicine. These strains showed high resistance to most antibiotics. This result is roughly the same as the international trend. The drug resistance phenotypes are mainly KPC and NDM, and different enzyme types have different sensitivity to antibiotics, emphasizing the importance of individualized treatment strategies for CRE. However, due to regional and population differences, the prevalence of CRE in our hospital (Kunming area) is significantly different from that in other parts of the country, and it is also different from that in different hospitals in the same region. Therefore, it is recommended to carry out rapid enzyme detection in the initial treatment stage and dynamically adjust the treatment plan according to the results of drug sensitivity test, so as to improve clinical efficacy and curb the spread of drug-resistant bacteria. CRE infection shows difficulty in treatment and high mortality. To meet the needs of Infection Prevention and Control (IPC), strengthen the resistance monitoring of CRE in our institution, and contribute to the capacity building of infection prevention, control and diagnosis and treatment.

Ethics Approval

This study has been approved by the ethics committee at Kunming First Hospital [Approval Number: Research ethics review (single)-2025-057-01]. As this study primarily employed retrospective analysis of patients' medical records, although it utilized identifiable human specimens or data, the subject could not be located. Moreover, the research project did not involve personal privacy or commercial interests. Therefore, we obtained exemption from informed consent forms through the ethics committee and received their approval. The study strictly adhered to the principles outlined in the Helsinki Declaration.

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Disclosure

The authors assert that the study was conducted without any business or financial affiliations that could be construed as a potential conflict of interests.

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