American Journal of Biochemistry and Biotechnology

Review Article

Carbapenem-Resistant *Enterobacteriaceae* in Korean Elderly Nursing Hospitals in 2023: Prevalence, Mortality, and Resistance Patterns

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Article history
Received: March 03, 2025
Revised: May 19, 2025
Accepted: July 08, 2025

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Abstract: Infections caused by Carbapenem-Resistant *Enterobacteriaceae* (CRE) represent a critical threat in healthcare settings owing to limited therapeutic options and high associated mortality. However, the epidemiological patterns and dynamics of CRE transmission in geriatric care hospitals remain poorly characterized. We elucidated the monthly incidence, bacterial species distribution, resistance genotypes, and patient demographics of CRE infections among inpatients at a senior care hospital in Gyeonggi-do, South Korea, between January and December 2023. In this retrospective cohort study, we analyzed 41,374 culture tests performed weekly throughout 2023 on 2,500 patients hospitalized at a specialized infectious disease geriatric care hospital in Korea. The distribution and prevalence of CRE infections were categorized according to months, sample type, sex, and age. In total, 4,636 CRE cases (1,913 men and 2,723 women) were detected, a majority of which (3,962) were diagnosed from rectal swab samples, with *Klebsiella pneumoniae* accounting for the highest number of cases (3,606). The most affected age group was < 70 years (3,336 cases). The peak months for CRE detection were August and November, whereas the highest number of deaths was recorded in December, indicating an increase throughout the year. A pre-emptive microbiological culture test was conducted on 2,500 inpatients in 2023, with a detection rate of 11.2% from 41,374 tests. These findings indicate that continuous monitoring and robust prevention strategies are essential for controlling the spread of CRE and protecting vulnerable inpatient populations. Our findings highlight the efficacy of pre-emptive microbiological culture tests, and show that enhanced monitoring and stringent isolation practices can prevent CRE infections in medical settings.

Keywords: Carbapenem-Resistant *Enterobacteriaceae* (CRE), *Klebsiella pneumonia*, Antimicrobial Resistance, Long-Term Care Hospitals, Elderly Patients, Mortality, Resistance Patterns, Sustainable Development Goals (SDG 3: Good Health and Well-Being, SDG 10: Reduced Inequalities)

Introduction

Carbapenem-Resistant *Enterobacteriaceae* (CRE) infections are classified as a second-class infectious disease under Article 2, Paragraph 1 of the Infectious Disease Prevention Act, designated by the Government of the Republic of Korea. Given the high risk of transmission, infections involving resistance to carbapenem-based antibiotics must be reported within 24 h of detecting an occurrence. Following the revision of the Infectious Disease Prevention Act in 2023, the regulations, including a name change for CRE infection, were updated on June 13, 2023, and took effect on December 14, 2023. Notably, carbapenem resistance is a major concern in hospitals for elderly care.

CRE carriers may harbor carbapenemase-producing *Enterobacteriaceae*. The genes encoding carbapenemases are located on plasmids that can readily transmit resistance genes to other bacteria, thereby contributing to a potentially substantial spread of CRE. Notably, the incidence of infections caused by these carbapenemase-producing organisms has been increasing in recent years

(Lee and Kim, 2023; Korea Centers for Disease Control and Prevention, 2024), thereby presenting major challenges that demand global cooperative efforts to develop new antimicrobial therapies. *Klebsiella* is a bacterial species of great significance in both medical and environmental health contexts (Carramaschi *et al*., 2021). Patients with *K. pneumoniae* Carbapenemase (KPC)-positive CRE are at an elevated risk of subsequent CRE infections during hospitalization (Lin *et al*., 2021).

Carbapenems, antibiotics considered the last line of defense, are critically prescribed for several major hospital-acquired pathogens (Adegoke *et al*., 2022). Consequently, selecting appropriate antibiotics for the treatment of patients with CRE colonization, who subsequently develop CRE infections, is essential for reducing the associated morbidities and mortalities (Wangchinda *et al*., 2022). The persistence of CRE infections poses a substantial public health threat (Villegas *et al*., 2022). In most Enterobacterales species, resistance to carbapenems is primarily associated with the production of the enzyme carbapenemase (Sader *et al*., 2023). Resistance strains harboring multiple resistance genes require treatments with enhanced potency compared with those required for carbapenem-sensitive strains (Tompkins and van Duin, 2021). Antimicrobial resistance is considered the greatest threat to global public health and development (World Health Organization, 2023), and currently available antimicrobial alternatives are limited (He *et al*., 2023). The global spread of CRE, particularly KPC-CRE (Tompkins and van Duin, 2021), has led both the American Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing to lower the thresholds in their diagnostic criteria for CRE and CPE (Venkatesan, 2021). Consequently, clinicians are increasingly employing combination antimicrobial therapies to treat infections caused by CRE or CPE (Yoo *et al*., 2023). As of 2023, the prevalence of CRE infections in South Korea is higher than that in other countries. CRE infections frequently occur in medical facilities such as elderly nursing hospitals in Korea, highlighting the urgent need for specialized management of high-risk groups. CRE infection remains a significant global issue, and concerns about the spread of resistant pathogens are growing in Europe and the United States. Furthermore, high-quality studies focusing on the underlying epidemiology and resistance mechanisms are necessary to guide effective personalized and targeted therapy for CRE bacteremia.

In this study, we aimed to elucidate the monthly incidence, bacterial species distribution, resistance genotypes, and patient demographics of CRE infections among inpatients at a senior care hospital in Gyeonggi-do, South Korea.

Materials and Methods

Participants

A single 220-bed long-term care hospital specializing in infectious diseases, located in Gyeonggi Province, South Korea, was selected for this study. A retrospective survival analysis was conducted based on weekly pre-emptive microbial culture data collected from 2,500 patients hospitalized between January 1 and December 31, 2023. Focusing on CRE detection, the data were categorized by specimen type, month, and bacterial species. This study was approved by Dankook University (DKU 2024-06-022-002 IRB). As this study was retrospectively designed, no informed consent was required.

Data Collection

In 2023, pre-emptive microbial culture tests were performed on all 2,500 inpatients, and the Seagen Medical Foundation (Seongdong-gu, Seoul) analyzed the data collected. The study participants' personal data were handled with strict confidentiality to ensure that patient identities could not be determined. The study was conducted using only the microbial culture test results, thereby ensuring full anonymity. A limitation of the study is that the analysis of mortality did not consider comorbidities or other risk factors. Data analysis was conducted using a retrospective study with survival analysis to examine mortality based on the time of occurrence in 2023.

Criteria for Determining the Susceptibility of Enterobacteriaceae to Carbapenem Antibiotics

The criteria for determining carbapenem resistance in *Enterobacteriaceae* were based on the Clinical Laboratory Standards Institute guidelines (Table 1).

Microbiological Tests

In 2023, all 2,500 inpatients in long-term care hospitals underwent microbiological tests. Sputum, urine, abscess, rectal swab, and blood culture tests were performed at weekly intervals, with the Seagene Medical Foundation managing sample processing. Upon the identification of bacteria based on antibiotic susceptibility testing, the data were collated and analyzed accordingly.

Table 1: Susceptibility testing for carbapenem

	Disk concentration	Zone diffusion (mm)			Minimum inhibitory concentration (μg/mL)		
		Sensitivity	Moderate	Resistance	Sensitivity	Moderate	Resistance
Doripenem	10 μg	≥ 23	20–22	≤ 19	≤ 1	2	≥ 4
Imipenem	10 μg	≥ 23	20–22	≤ 19	≤ 1	2	≥ 4
Meropenem	10 μg	≥ 23	20–22	≤ 19	≤ 1	2	≥ 4
Ertapenem	10 μg	≥ 22	19–21	≤ 18	≤ 0.5	1	≥ 2

Data Analysis

The incidence and mortality rates were analyzed based on the microbial test results by reviewing the detected cases and CRE data. Monthly detection rates were classified based on species, and CRE detection and resistance rates were analyzed according to sample type and species, respectively. In addition, the characteristics of the isolated strains and mortality of CRE carriers were examined to investigate the trends and changes of CRE in 2023.

Results

CRE Cases Detected Per Month

Between January and December 2023, 41,374 tests were conducted on 2,500 hospitalized patients, among whom 4,636 cases of CRE were detected, representing a detection percentage of 11.2%. The monthly breakdown of CRE cases revealed that the highest number of detections occurred in August, indicating a peak during the summer months (Fig. 1).

Outbreak Status and Number of Deaths

In 2023, 308 patients died due to CRE infections. The number of CRE-related deaths by month was as follows: 26 in January, 26 in February, 20 in March, 19 in April, 19 in May, 18 in June, 15 in July, 20 in August, 20 in September, 36 in October, and 36 in November. December recorded the highest number of CRE-related deaths in 2023, with 52 cases. In December alone, the mortality rate accounted for 16.1% of the annual CRE mortality rate.

Number of CRE Detections Based on the Bacterial Species

The most frequently detected CRE species was K. pneumoniae, accounting for 3,606 cases (77.8%), followed by E coli with 839 cases (18.1%). Among other species, there were 54, 52, 26, 19, 4, 12, and 8 cases of infection with Citrobacter koseri (Citrobacter diversus), Citrobacter freundii, K. oxytoca, Citrobacter amalonaticus, Enterobacter aerogenes, Enterobacter cloacae, and Serratia marcescens, respectively, along with four cases of K. pneumoniae ssp. pneumoniae and single cases of Kluyvera ascorbata and Raoultella ornithinolytica (Fig. 2).

Sex-Based Distribution of Patients with CRE Infections

Among the cases in which CRE were isolated, 41.3 and 58.7% were reported in males and females, respectively, indicating a significantly higher female CRE detection rate (Fig. 3).

Age-Based Classification of Patients with CRE Infections

Among the cases of CRE detected, 1,973 occurred in patients aged 81 years or older, accounting for 42.6% of the total. The number of CRE-infected patients by age group is shown in Fig. 4.

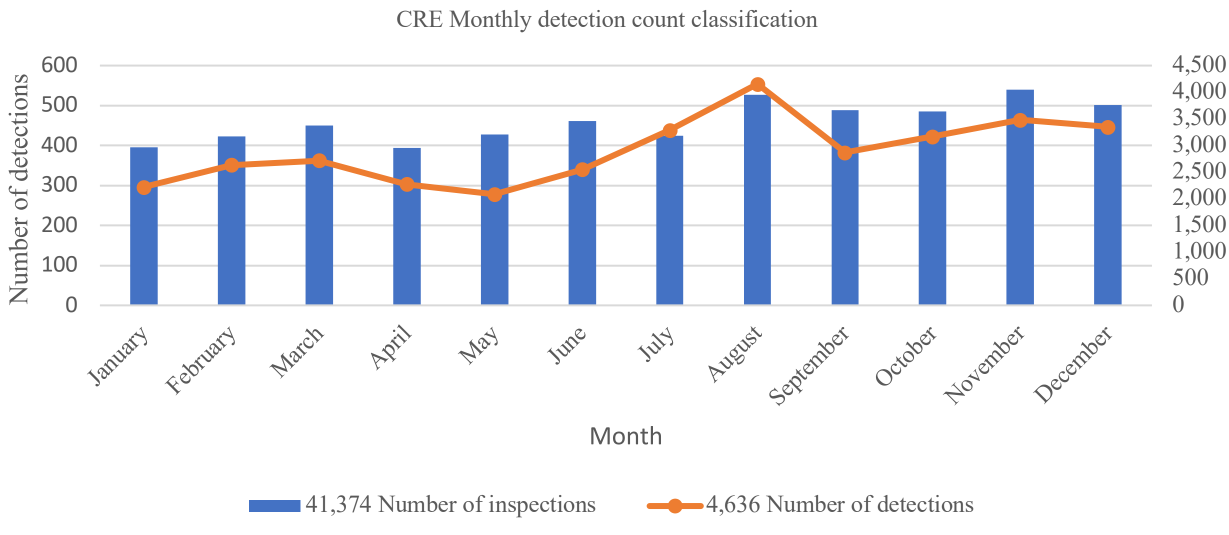

Fig. 1: Annual prevalence of Carbapenem-Resistant Enterobacteriaceae (CRE) in elderly nursing hospitals in Korea, 2023.The bar chart displays the overall prevalence of CRE among all Enterobacteriaceae isolates. CRE accounted for X% of total isolates, with Klebsiella pneumoniae representing the predominant species

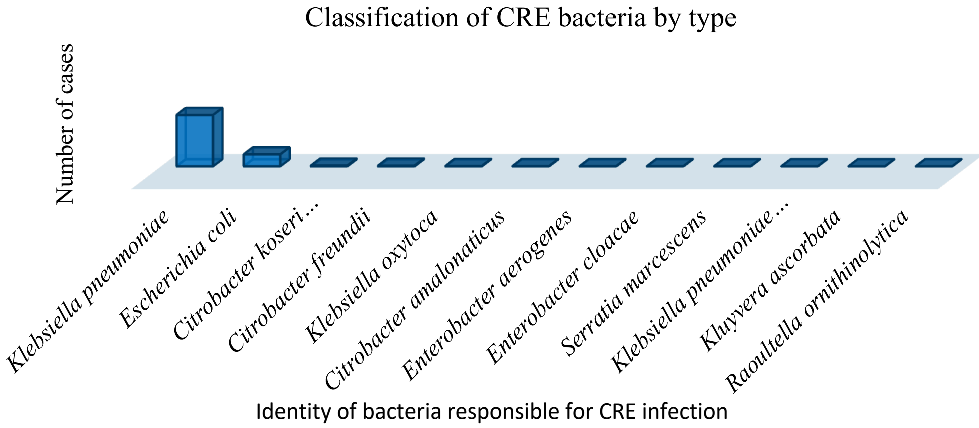

Fig. 2: Number of cases of CRE is based on bacterial species (n = 4,636). Species distribution of carbapenem-resistant Enterobacteriaceae isolates.Pie chart showing the proportion of major CRE species identified. K. pneumoniae was the most common, followed by Escherichia coli and Enterobacter cloacae

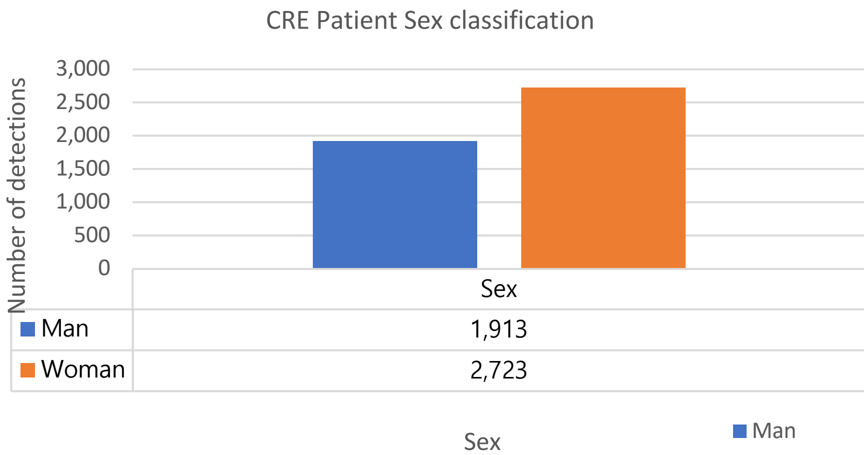

Fig. 3: CRE prevalence by sex and age group.Comparison of CRE positivity between male and female patients across elderly inpatients. Women demonstrated a slightly higher prevalence, reflecting the demographic predominance of female patients in long-term care hospitals

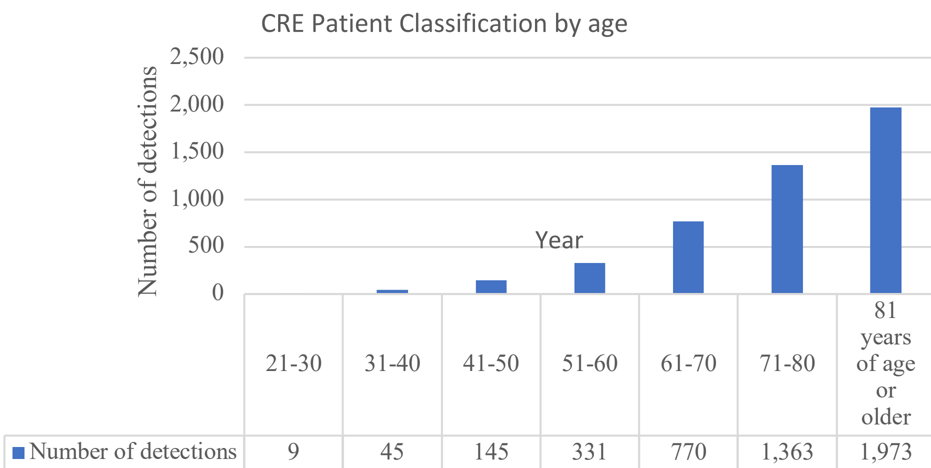

Fig. 4: CRE classification by patient age (n = 4,636). Antibiotic resistance patterns of CRE isolates

Analysis of the CPE Positivity Rate

Testing for the presence of CPE is a proactive measure designed to manage contact with patients and prevent further transmission based on epidemiological investigations during infectious disease outbreaks.

Regarding newly identified CRE strains, CPE testing revealed that among the 374 new cases, 301 (80.5%) tested positive for CPE, indicating a high positivity rate.

Bar graph summarizing resistance rates of CRE strains to commonly tested antimicrobial agents, including aminoglycosides, fluoroquinolones, and cephalosporins. High resistance was observed across multiple drug classes, reflecting multidrug-resistant phenotypes.

Classification of CRE Genotypes Detected in Patients

In order of prevalence, we detected carbapenemase-2 (KPC-2), New Delhi metallo-β-lactamase-1 (NDM-1), and oxacillinase-181 (OXA-181) among patients. The main types of CPE are classified based on how an enzyme functions, the target antibiotics it degrades, and the bacteria in which it is found. The main CPE types are as follows.

Serine Proteases (CPEs) of class A are associated with infections in medical institutions. Among these, KPC, which confers resistance to carbapenem antibiotics, is particularly found in *K. pneumoniae.* Global extended-spectrum enzymes are resistant to a wide spectrum of β-lactams and are found in a range of bacteria, whereas *Serratia marcescens* enzymes are primarily resistant to penicillin and cephalosporin. These enzymes are closely linked to hospital-linked infections and present difficulties in the treatment of these infections.

Class B (metallo-beta-lactamase) CPEs include imipenemase, which is found in a range of Gram-negative bacteria, indicating their resistance to carbapenem. NDM, an enzyme first discovered in New Delhi, India, is characterized by notably high resistance, whereas Verona integron-encoded metallo-β-lactamase is found in the prevalence of Gram-negative bacteria and shows resistance to a wide range of β-lactams. These enzymes present considerable challenges in treatment and are closely associated with Multidrug-Resistant (MDR) bacteria. Class C (serine proteases) are represented by oxacillinase (OXA), which is found in *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, in which it confers resistance to a range of β-lactams. Hospital infections are typically associated with OXA enzymes, thereby limiting treatment options.

In 2023, CRE genotyping was performed for 301 newly detected CRE cases, the results of which revealed KPC to be the most prevalent type, detected in 238 patients (79.1%), followed by NDM in 58 patients (19.3%) and OXA-181 in five patients (1.6%).

Annual CRE Report Status

The number of new CRE cases reported to the Korea Disease Control and Prevention Agency (Epidemic Control System) by year is shown in Fig. 5

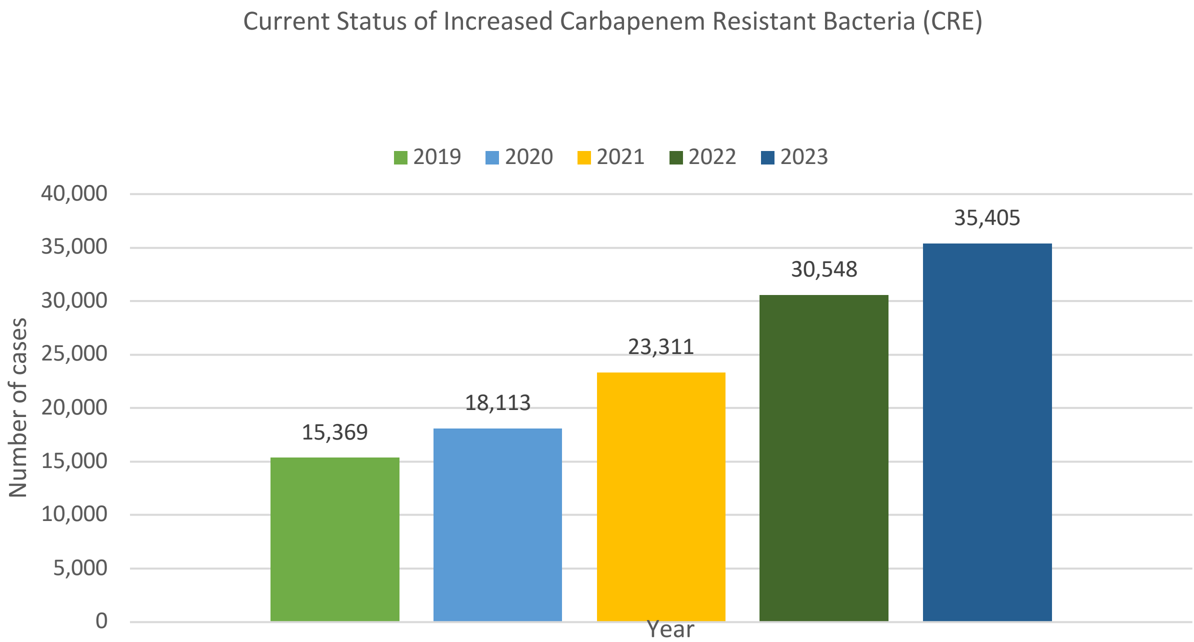

Fig. 5: CRE Report Status from 2019 to 2023. Source: Quality Management Agency. Mortality associated with CRE infection

Kaplan–Meier survival curve showing mortality outcomes of patients with confirmed CRE infections. The 30-day mortality was 10%, and mortality risk was highest among patients aged ≥80 years.

Antibiotic Resistance Cases Based on Bacterial Strain

K. pneumoniae was the most frequently detected species, with 4,961 cases, of which 3,603 were resistant, showing a high resistance rate of 72.6%.

K. pneumoniae was most frequently detected in August, with 568 cases, whereas 519 cases were detected in November, of which 409 were resistant, with the highest resistance rate of 78.8%.

Citrobacter freundii 9%; 117 cases). Although more frequently detected with 2,157 cases, *E. coli* showed a lower rate of resistance (38.9%). Among other detected species, *K. oxytoca and E. aerogenes* showed resistance rates of 20.9 and 16.3%, respectively, with resistance rates of 12.8, 10.6, and 4.8% reported for *K. pneumoniae* ssp. *pneumoniae* (6 of 47 cases), *C. koseri*, and *E. cloacae*, respectively. Although *K. ascorbata* showed a considerably higher resistance rate (50%), this value was based on only two cases of CRE bacteria. *R. ornithinolytica* and *S. marcescens* showed comparatively low levels of resistance at 2.8% (1 of 64 cases) and 1.1% (8 of 606 cases), respectively (Table 2).

Table 2: Monthly cases of antibiotic resistance based on bacterial species

By bacterial species	Month / R/S (%)	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
Klebsiella pneumoniae	Cases (n = 4,961)	293	357	394	305	302	390	369	568	519	495	519	450
	R (%)	224 (76.5)	275 (77.0)	272 (69.0)	207 (67.9)	193 (63.9)	259 (66.4)	262 (71.0)	395 (69.5)	370 (71.3)	366 (73.9)	409 (78.8)	342 (76.0)
	S (%)	69 (23.5)	82 (23.0)	120 (31.0)	98 (32.1)	109 (36.1)	131 (33.6)	107 (29.0)	173 (30.5)	149 (28.7)	129 (26.1)	110 (21.2)	108 (24.0)
Escherichia coli	Cases (n = 2,157)	172	194	184	166	176	183	157	188	207	157	179	194
	R (%)	64 (37.2)	86 (44.3)	69 (37.5)	69 (41.6)	80 (45.5)	82 (44.8)	70 (44.6)	95 (50.5)	64 (30.9)	42 (26.8)	51 (28.5)	66 (34.0)
	S (%)	108 (62.8)	108 (55.7)	115 (62.5)	97 (58.4)	96 (54.5)	101 (55.2)	87 (55.4)	93 (49.5)	143 (69.1)	115 (73.2)	128 (71.5)	128 (66.0)
Citrobacter koseri (*Citrobacter diversus*)	Cases (n = 541)	51	62	41	43	60	60	35	40	38	23	42	46
	R (%)	3 (5.9)	0	0	2 (4.7)	0	0	0	3 (7.5)	13 (34.2)	2 (8.7)	15 (35.7)	14 (30.4)
	S (%)	48 (94.1)	62	41	41 (95.3)	6	6	35	37 (92.5)	25 (65.8)	21 (91.3)	27 (64.3)	32 (69.6)
Citrobacter freundii	Cases (n = 117)	9	12	4	15	7	6	8	6	9	13	17	11
	R (%)	1 (11.1)	4 (33.3)	3 (75.0)	12 (80.0)	6 (85.7)	5 (83.3)	3 (37.5)	3 (50.0)	5 (55.6)	2 (15.4)	3 (17.6)	2 (18.2)
	S (%)	8 (88.9)	8 (66.7)	1 (25.0)	3 (20.0)	1 (14.3)	1 (16.7)	5 (62.5)	3 (50.0)	4 (44.4)	11 (84.6)	14 (82.4)	9 (81.8)
Klebsiella oxytoca	Cases (n = 112)	4	3	10	12	9	11	9	9	10	17	12	6
	R (%)	3 (75.0)	0	4 (40.0)	5 (41.7)	4 (44.4)	2 (18.2)	0	0	0	4 (23.5)	1 (8.3)	0
	S (%)	1 (25.0)	3	6 (60.0)	7 (58.3)	5 (55.6)	9 (81.8)	9	9	10	13 (76.5)	11 (91.7)	6
Citrobacter amalonaticus	Case (n = 10)	0	0	0	0	0	3	0	4	0	2	0	1
	R (%)	0	0	0	0	0	3	0	4	0	2	0	1
	S (%)	0	0	0	0	0	0	0	0	0	0	0	0
Enterobacter aerogenes	Cases (n = 77)	0	2	2	8	7	4	10	10	2	6	6	20
	R (%)	0	0	0	0	1 (14.3)	2 (50.0)	0	0	0	4 (66.7)	3 (50.0)	3 (15.0)
	S (%)	0	2	2	8	6 (85.7)	2 (50.0)	10	10	2	2 (33.3)	3 (50.0)	17 (85.0)
Enterobacter cloacae	Cases (n = 151)	1	9	7	3	15	18	18	18	11	13	22	16
	R (%)	1	0	0	0	1 (6.7)	2 (11.1)	0	0	0	1 (7.7)	3 (13.6)	3 (18.8)
	S (%)	0	9	7	3	14 (93.3)	16 (88.9)	18	18	11	12 (92.3)	19 (86.4)	13 (81.2)
Serratia marcescens	Cases (n = 606)	24	27	40	45	64	39	33	33	69	60	96	76

	R (%)	0	0	0	0	0	2 (5.1)	0	0	0	1 (1.7)	1 (1.0)	4 (5.3)
	S (%)	24	24	40	45	64	37 (94.9)	33	33	69	59 (98.3)	95 (99.0)	72 (94.7)
Klebsiella pneumoniae ssp. *pneumoniae*	Cases (n = 47)	0	1	2	0	0	0	0	0	1	1	2	0
	R (%)	0	1	1 (50.0)	0	0	0	0	0	1	1	2	0
	S (%)	0	0	1 (50.0)	0	0	0	0	0	0	0	0	0
Kluyvera ascorbata	Cases (n = 2)	0	0	0	0	1	0	0	0	0	1	0	0
	R (%)	0	0	0	0	0	0	0	0	0	1	0	0
	S (%)	0	0	0	0	1	0	0	0	0	0	0	0
Raoultella ornithinolytica	Cases (n = 64)	5	2	2	3	4	7	8	8	5	9	8	3
	R (%)	0	0	0	0	0	0	0	0	0	0	0	1 (33.3)
	S (%)	0	2	2	3	4	7	8	8	5	9	8	2 (66.7)

R: Resistant, S: Sensitivity.

Comparison of the Number of Cases Based on the Sample Type

In 2023, 4,636 cases of CRE bacteria were detected among 41,374 microbiological culture tests conducted on 2,500 patients, representing a detection rate of 11.2%. Among the detected CRE cases, rectal swabs, sputum samples, and urine samples accounted for 3,962 (85.5), 479 (10.3), and 161 (3.5%) of the detected CRE cases, respectively. Additionally, 22 cases were identified based on blood culture tests, accounting for 0.5% of cases, and seven cases were detected in wound or abscess samples, representing 0.2% of cases.

Comparisons of the proportion of detected CRE cases with respect to month and sample type revealed that rectal swabs produced the highest detection rate in August, with 554 of 1,650 tests (33.6%), followed by July, with 386 of 1,260 tests (30.6%). Detection in sputum peaked in August, with 57 of 479 cases (11.9%), and among the 161 CRE cases detected based on urine sample analysis, the highest rates were obtained in October, with 37 cases (23.0%). Comparatively, blood culture tests and pus samples had low detection rates, making it difficult to identify any seasonal trends for these specimen types (Table 3).

Discussion

CRE represents a collective term encompassing a range of antibiotic-resistant pathogenic bacteria, primarily within the Enterobacteriaceae family. Infections with these bacteria, which are particularly resistant to carbapenem-based antibiotics, are difficult to treat. Given that CRE are resistant to one of the most recently developed groups of antibiotics used in modern medicine, this can markedly limit the available treatment options. The impact of these carbapenem-resistant bacteria on society is substantial. CRE infection occurs and spreads primarily within hospital settings, and it can cause high levels of multiple infections within medical institutions. The risk is particularly high in immunocompromised and critically ill patients, the elderly, and patients undergoing surgery, thereby highlighting the potential risks associated with the spread of infection in hospitals. With respect to the spread of antibiotic resistance, the fact that CRE infection has a high likelihood of transmitting resistance to other bacteria emphasizes the threat of a more general increase in the resistance to antibiotics, and thus increasingly fewer treatable infections. Although CRE infection primarily occurs in hospitals, these bacteria can spread beyond hospital settings, thereby posing a heightened risk of infection throughout society. In particular, the spread of CRE outside the hospital environment can cause social anxiety and fear, as well as the burden of socializing owing to the increase in infectious diseases. In addition, CRE infection primarily affects people with weakened immunity and thus can have a proportionally greater impact on the economically and socially vulnerable. This can exacerbate the social burden and health inequality of infectious diseases, highlighting the necessity to develop new antibiotics capable of treating MDR bacteria such as CRE. However, pharmaceutical companies typically do not actively participate in this development because antibiotic development necessitates prolonged research and development and is comparatively commercially unprofitable. This eventually leads to difficulties in the global response to the problem of antibiotic resistance at a time when the need to develop new antibiotics is becoming increasingly important. CRE infectious diseases require specialized management, and infection control should thus be strengthened. Accordingly, in-hospital infection control is particularly important for preventing the spread of CRE. Stringent hygiene management, patient isolation, and disinfection of medical equipment are required, and hospitals should invest additional manpower and resources to ensure the maintenance of sufficiently high safety standards. Preparing measures to strengthen public health response is also necessary. Policies and strategies must be prepared to prevent the spread of CRE at both the national and community levels. This emphasizes the importance of cooperation among health authorities in individual countries and the need for international cooperation.

CRE family members are among the MDR bacteria that are becoming increasingly difficult to treat owing to the loss of efficacy of existing antibiotics. Treatment methods are typically limited if a patient is infected, and in some cases, life can be threatened.

CRE comprises *Enterobacteriaceae* species resistant to one or more carbapenem-family antibiotics, including imipenem, meropenem, doripenem, and ertapenem. The emergence and spread of MDR and XDR pathogens highlight the growing global importance of antibiotic resistance. The World Health Organization (WHO) has identified this as the primary threat to global public health. The intestinal tract is the main reservoir of CRE, and stool samples are commonly used for CRE testing. The spread of MDR and extensively drug-resistant pathogens is becoming increasingly important worldwide (Tselepis *et al*., 2020). CRE are antibiotic-resistant bacteria that pose a serious and ongoing threat to global public health (Irekeola *et al*., 2024). Analysis of CRE occurrence reports in Korea from 2019 to 2023 reveals a consistent annual increase in these infections (Fig. 5). The rising number of infections and limited antibiotic treatment options highlight *K. pneumoniae* as an urgent public health threat (Hu *et al*., 2020). Several factors render patients more susceptible to microbial infections, typically with fatal consequences (Li *et al*., 2020). Mortality associated with MDR organisms has escalated annually, resulting in the prescription of appropriate empirical antibiotics for infections caused by polydrug-resistant organisms (Urzedo *et al*., 2020). Bacteria in the genera *Morganella*, *Proteus*, and *Providencia* are characterized by an intrinsic resistance to imipenems and thus do not meet the typical resistance criteria (Wang *et al*., 2021). Among CRE species, we found that *K. pneumoniae* prevails in terms of antibiotic resistance rates, followed by *E. coli*, which is consistent with previous findings (Kim *et al*., 2023). Among the 4,636 CRE cases detected in hospitals in Gyeonggi-do, South Korea, in 2023, 3,606 involved *K. pneumoniae*, representing 77.8% of all detected cases, with a further 839 cases (18.1%) involving *E. coli* (Table 3). The high prevalence of extended-spectrum b-lactamase and carbapenemase genes (Paveenkittiporn *et al*., 2021) highlights the need for accurate identification of carbapenem-resistant enterobacteria that express these carbapenem-degrading enzymes, which is essential for managing CRE infections (Wyres *et al*., 2020). Similarly, rapid and cost-effective detection of high-risk *K. pneumoniae* clones is vital (Lin *et al*., 2021). *K. pneumoniae* is the species most associated with *Klebsiella* (Peirano *et al*., 2020). Carbapenemase enzymes significantly contribute to carbapenem resistance (Korea Disease Control and Prevention Agency, 2022). According to the CLSI guidelines (M100-30 edition, 2020), CRE infections show resistance to doripenems, imipenems, and meropenems at minimum inhibition concentrations (MICs) of ≥ 4, and to ertapenems at an MIC of ≥ 2 (El-Defrawy *et al*., 2022).

Table 3. Number of CRE cases detected based on the sample type

Total number of cases	Month	Jan	Feb	Mar	April	May	June	July	Aug	Sep	Oct	Nov	Dec
Test count (n = 41,374)		2,968	3,171	3,373	2,958	3,210	3,455	3,186	3,954	3,661	3,635	4,048	3,755
Case count (n = 4,636)		296	351	362	303	278	340	438	554	382	422	464	446
Rectal swab	Test count	1,092	1,223	1,396	1,156	1,194	1,427	1,260	1,650	1,435	1,403	1,699	1,498
	Case count	245	275	310	257	256	291	386	475	364	346	397	360
Sputum	Test count	573	701	623	582	664	655	627	823	715	702	889	726
	Case count	41	66	29	22	16	40	36	57	11	39	66	56
Urine	Test count	610	662	763	610	621	1,351	652	648	814	656	710	795
	Case count	8	5	15	19	0	9	16	22	0	37	0	30
Blood	Test count	665	559	1,096	582	703	573	639	825	684	864	731	730
	Case count	2	2	8	0	3	0	0	0	7	0	0	0
Pus	Test count	28	21	41	28	25	22	8	8	3	10	19	6
	Case count	0	3	0	3	0	0	0	0	0	0	1	0

Early detection of CRE facilitates prompt establishment of contact precautions, thereby contributing to the prevention of transmission to other patients (Yoo *et al*., 2023). MDR bacteria can pose a threat to the patient's health and may cause hospital-acquired infections (Al-Jabri *et al*., 2022). Moreover, there is a substantial risk of infection in severely ill patients, highlighting the importance of pre-emptive testing for carbapenem-degrading enterobacteria in epidemiological investigations of cluster outbreaks.

CPE testing plays an essential role in segregating positive and negative patients, thereby preventing further cross-infection. Pre-emptive testing and monitoring of MDR bacteria require stringent cohort management, infection control measures, and the use of protective equipment to control transmission. Elderly care hospitals, which serve to accommodate older patients and those with chronic diseases that have persisted for extended periods, represent high-risk environments for CRE infections. The weakened immune systems of older patients, coupled with chronic diseases, long-term use of medical devices such as catheters and ventilators, and proximity living conditions, are particularly conducive to the spread of CRE. Moreover, the frequent and improper administration of antibiotics is also a risk factor. Although Enterobacteriaceae, Gram-negative bacteria found in the intestine and other environments, do not typically cause infections, they can lead to severe infections in immunocompromised individuals. CRE infections are challenging to treat, pose serious threats, and are potentially fatal, leading to high mortality rates. Current treatment options are limited, and carbapenem resistance prompts the use of less effective alternative antibiotics. Moreover, contagious CRE can be readily transmitted among patients, and increased transmissibility is a source of concern, particularly in healthcare settings.

We analyzed the monthly incidence, predominant bacterial species, resistance genotypes, and patient characteristics of CRE infections among inpatients in Gyeonggi Province's elderly care hospitals in 2023. *K. pneumoniae* was identified as the most common pathogen, with KPC and NDM being the predominant carbapenem resistance genes. The monthly incidence showed an increasing trend in the latter half of the year. The findings of this study align with previous domestic and international research, indicating a high prevalence of *K. pneumoniae* CRE infections among elderly patients, with prolonged hospitalization and underlying medical conditions identified as major risk factors. However, the results may reflect region-specific characteristics because this study was based on data from a single region.

This study has certain limitations. First, our research was based on data from a single hospital specializing in elderly care. Although all inpatients underwent microbial culture tests, comprehensive comparative analyses using data obtained from multiple elderly care hospitals should be included in future studies. Second, nursing home healthcare workers were excluded, thereby eliminating the consideration of CRE transmission via contact infection among this group. Finally, we did not investigate deaths caused by underlying diseases or other complications. More in-depth research is needed to classify deceased patients based on underlying conditions and surgical history.

Despite these limitations, we applied in-depth clinical management strategies by conducting pre-emptive microbial culture tests on all 2,500 patients admitted to elderly care hospitals, subsequently categorizing them into CPE-positive and CPE-negative groups based on the outcomes of CPE screening tests. Future research should be conducted to assess the associations between the underlying diseases of patients with CRE bacterial infections and expand pre-emptive testing to other medical facilities or groups. We believe that pre-emptive testing for MDR bacteria and engaging in research for the professional management and screening of patients, based on detailed identification of risk factors and varied patterns, are essential.

Carbapenem-resistant bacteria are an important class of microorganisms that have a pronounced influence on public health, the economy, and social stability. Consequently, systematic efforts are required to prevent and manage this threat. Different measures, such as reducing antibiotic abuse and promoting the development of new antibiotics, are needed. There are no short-term solutions to the problem of resistant bacteria such as CRE, and the threat posed by these microorganisms must be addressed from a long-term perspective at the global level.

To date, there has been a lack of professional and systematic evaluation regarding the prevalence of CRE in elderly care hospitals. Most existing studies have focused on acute care hospitals, leaving a critical gap in understanding CRE dynamics within long-term care facilities, where the elderly, a particularly vulnerable population, reside. This study addresses this gap by examining the prevalence and mortality associated with CRE in a long-term care hospital specializing in infectious diseases.

Our findings demonstrate that CRE infections are prevalent in geriatric care settings, with a measurable impact on patient outcomes, including mortality. Given the unique characteristics of elderly inpatients—such as weakened immune systems, chronic comorbidities, frequent use of invasive devices, and long hospital stays—this population is particularly susceptible to colonization and infection by MDR organisms. The relatively high mortality observed in this study highlights the urgent need for strengthened infection control measures and routine surveillance protocols tailored specifically to long-term care environments.

Furthermore, the results reinforce the importance of early detection strategies, such as pre-emptive microbial culture testing, as a critical tool for infection prevention and control. This approach enables early identification of CRE carriers and timely implementation of isolation procedures to prevent cross-transmission.

This study highlights the significant risk of CRE spread within long-term care hospitals, emphasizing the importance of infection control in such settings. Previous research has primarily reported high CRE prevalence in intensive care units and acute hospitals, associated with invasive procedures and extensive antibiotic use (Lee *et al*., 2020). However, our findings suggest that CRE can also be disseminated in resource-limited environments, such as long-term care hospitals. CRE is mainly transmitted through contact and environmental contamination, and its ability to survive in the environment necessitates robust environmental management and surveillance systems. Although earlier studies have not identified clear seasonal or sex differences in the prevalence of CRE (Choi *et al*., 2019), we observed an increase in the prevalence of CRE in summer months and higher positivity rates in female patients, indicating that patient characteristics in long-term care facilities may influence the risk of infection. Therefore, existing CRE-focused infection control guidelines have limitations, and tailored strategies adapted to the long-term care hospital environment are urgently needed.

Conducting studies focused on proactive screening for MDR organisms is necessary to more thoroughly identify risk factors and various patterns, thereby enabling more specialized patient management and screening strategies. In the future, comparative studies using multicenter data, analysis of transmission routes including healthcare workers, and detailed examinations of deceased patients considering underlying diseases and surgical history are needed to better understand the pathophysiology and transmission mechanisms of CRE infections.

Conclusion

This study provides important epidemiological insights into the prevalence of CRE, antimicrobial resistance patterns, and associated mortality among patients in a geriatric long-term care hospital in South Korea. This study highlights the significant burden of CRE infections in elderly care settings by analyzing monthly detection frequencies, resistance rates, and mortality trends further stratified by age, sex, and bacterial species. The annual increase in CRE incidence, both domestically and globally, highlights the urgent need for sustained surveillance and robust infection control interventions.

Our findings emphasize the critical role of pre-emptive microbial culture testing for CPE as a frontline strategy in the early identification and containment of CRE carriers, particularly in high-risk environments such as geriatric hospitals. Elderly inpatients represent a particularly susceptible population due to immunosenescence, comorbidities, and prolonged hospitalization, all of which facilitate propagation of MDR organisms. Therefore, strengthening institutional infection prevention and control protocols is of paramount importance. Ultimately, a coordinated, evidence-based strategy incorporating early detection, systematic surveillance, and policy-level support is necessary to limit the spread of CRE and reduce the associated morbidity and mortality among vulnerable populations.

In conclusion, our study demonstrates how CRE infections can spread in environments with a high concentration of patients with chronic illnesses, such as elderly care hospitals, and highlights the importance of regular surveillance and pre-emptive screening. This study shows that conducting universal culture tests enables early detection of infections and helps prevent further transmission.

Acknowledgement

We would like to express our gratitude to Yonsei Soo Nursing Hospital and Seegene Medical Foundation for their valuable support during this study.

Funding Information

This work was supported by the Department of Biomedical Laboratory Science and the Research-Focused Department Pro-motion & Interdisciplinary Convergence Research Project as a part of the Support Program for University Development for Dankook University in 2024.

Author's Contributions

Lee Hye Seong: Conceptualization, Software development, Validation, Formal analysis, Investigation, Visualization, and Writing original draft preparation.
Jang Sung Hun: Writing review and editing.
Kim Jae Kyung: Supervision and Project administration.

This study was approved by the Institutional Review Board of Dankook University (IRB No. DKU 2024-06-022-002). As this was a retrospective study based on anonymized clinical data, the requirement for informed consent was waived.

References

Adegoke, A. A., Ikott, W. E., & Okoh, A. I. (2022). Carbapenem resistance associated with coliuria among outpatient and hospitalised urology patients. *New Microbes and New Infections*, *48*, 101019. https://doi.org/10.1016/j.nmni.2022.101019

Al-Jabri, R. M., Al-Hejin, A. M., Gashgari, R., Abu-Zeid, M., Bataweel, N. M., & M. Ahmed, M. M. (2022). Diversity and Resistance of Bacteria Isolated from a Neonatal Intensive Care Unit (NICU) Surfaces and the Hands of Nurses in Jeddah-Saudi Arabia. *OnLine Journal of Biological Sciences*, *22*(3), 299–308. https://doi.org/10.3844/ojbsci.2022.299.308

Carramaschi, I. N., dos S. B. Ferreira, V., Chagas, T. P. G., Corrêa, L. L., Picão, R. C., de C. Queiroz, M. M., Rangel, K., Jardim, R., da Mota, F. F., & Zahner, V. (2021). Multidrug-resistant Klebsiella quasipneumoniae subsp. similipneumoniae carrying blaNDM-blaCTX-M15 isolated from flies in Rio de Janeiro, Brazil. *Journal of Global Antimicrobial Resistance*, *24*, 1–5. https://doi.org/10.1016/j.jgar.2020.11.021

Choi, M., Lee, J.-H., Kim, S.-Y., & Park, Y. (2019). Risk factors for carbapenem-resistant Enterobacteriaceae colonization and infection in long-term care facilities. *Infection Control & Hospital Epidemiology*, *40*(5), 547–553.

El-Defrawy, I., Gamal, D., El-Gharbawy, R., El-Seidi, E., El-Dabaa, E., & Eissa, S. (2022). Detection of intestinal colonization by carbapenem-resistant Enterobacteriaceae (CRE) among patients admitted to a tertiary care hospital in Egypt. *Egyptian Journal of Medical Human Genetics*, *23*(1). https://doi.org/10.1186/s43042-022-00295-9

He, W., Gao, M., Lv, L., Wang, J., Cai, Z., Bai, Y., Gao, X., Gao, G., Pu, W., Jiao, Y., Wan, M., Song, Q., Chen, S., & Liu, J.-H. (2023). Persistence and molecular epidemiology of blaNDM-positive Gram-negative bacteria in three broiler farms: A longitudinal study (2015–2021). *Journal of Hazardous Materials*, *446*, 130725. https://doi.org/10.1016/j.jhazmat.2023.130725

Hu, H., Mao, J., Chen, Y., Wang, J., Zhang, P., Jiang, Y., Yang, Q., Yu, Y., & Qu, T. (2020). Clinical and Microbiological Characteristics of Community-Onset Carbapenem-Resistant Enterobacteriaceae Isolates *Infection and Drug Resistance*, *Volume 13*, 3131–3143. https://doi.org/10.2147/idr.s260804

Irekeola, A. A., Shueb, R. H., Engku Abd Rahman, E. N. S., Afolabi, H. A., Wada, Y., Elmi, A. H., Hakami, M. A., Alghzwani, S. M., Elnoubi, O. AE., & Alshehri, A. A. (2024). High prevalence of carbapenem-resistant Enterobacterales (CRE) in human samples from Nigeria: A systematic review and meta-analysis. *Heliyon*, *10*(15), e34926. https://doi.org/10.1016/j.heliyon.2024.e34926

Kim, M.K., S.J. Joo, E.K. Shin, J.Y. Kim and J.I. Yoo. (2023). Characteristics and resistance trends of Carbapenem-resistant Enterobacteriaceae. *Public Health Weekly Report*, *16*(18), 541–559. https://doi.org/10.56786/phwr.2023.16.18.1

Korea Centers for Disease Control & Prevention (KCDC). (2024). Infectious Disease Portal. *Kcdc*. Https://www.kdca.go.kr/filepath/boardsyview.es?bid=0019&list_no=725322&seq=1

Korea Disease Control and Prevention Agency. (2022). Korea disease control and prevention agency's partnership with the global outbreak alert and response network. *Western Pacific Surveillance and Response Journal*, *15*(5), 51–53. https://doi.org/10.5365/wpsar.2024.15.5.1093

Lee, M., & Kim, H. (2023). Risk factors for the colonization of carbapenem-resistant Enterobacteriaceae in patients transferred to a small/medium-size hospital in Korea: a retrospective study. *Journal of Korean Biological Nursing Science*, *25*(4), 285–294. https://doi.org/10.7586/jkbns.23.0021

Lee, Y., Kim, J., Park, S., & Choi, H. (2020). Epidemiology and risk factors of carbapenem-resistant enterobacteriaceae infections in intensive care units: a multicenter study. *Journal of Hospital Infection*, *104*(2), 190–196.

Li, J., Bi, W., Dong, G., Zhang, Y., Wu, Q., Dong, T., Cao, J., & Zhou, T. (2020). The new perspective of old antibiotic: In vitro antibacterial activity of TMP-SMZ against Klebsiella pneumoniae. *Journal of Microbiology, Immunology and Infection*, *53*(5), 757–765. https://doi.org/10.1016/j.jmii.2018.12.013

Lin, Q., Wu, M., Yu, H., Jia, X., Zou, H., Ma, D., Niu, S., & Huang, S. (2021). Clinical and Microbiological Characterization of Carbapenem-Resistant Enterobacteriales: A Prospective Cohort Study. *Frontiers in Pharmacology*, *12*. https://doi.org/10.3389/fphar.2021.716324

Lin, Q., Wang, Y., Yu, J., Li, S., Zhang, Y., Wang, H., Lai, X., Liu, D., Mao, L., Luo, Y., Tang, G., Chen, Z., & Sun, Z. (2021). Bacterial characteristics of carbapenem-resistant Enterobacteriaceae (CRE) colonized strains and their correlation with subsequent infection. *BMC Infectious Diseases*, *21*(1). https://doi.org/10.1186/s12879-021-06315-0

Paveenkittiporn, W., Lyman, M., Biedron, C., Chea, N., Bunthi, C., Kolwaite, A., & Janejai, N. (2021). Molecular epidemiology of carbapenem-resistant Enterobacterales in Thailand, 2016–2018. *Antimicrobial Resistance & Infection Control*, *10*(1). https://doi.org/10.1186/s13756-021-00950-7

Peirano, G., Chen, L., Kreiswirth, B. N., & Pitout, J. D. D. (2020). Emerging Antimicrobial-Resistant High-Risk Klebsiella pneumoniae Clones ST307 and ST147. *Antimicrobial Agents and Chemotherapy*, *64*(10). https://doi.org/10.1128/aac.01148-20

Ryu, K., Choi, J.-Y., Kim, M.-J., & Lee, Y.-J. (2023). Surveillance and molecular epidemiology of carbapenem-resistant enterobacteriaceae in ulsan from 2018 to 2021. *Journal of Bacteriology and Virology*, *53*(1), 19–27.

Sader, H. S., Castanheira, M., Kimbrough, J. H., Kantro, V., & Mendes, R. E. (2023). Aztreonam/avibactam activity against a large collection of carbapenem-resistant Enterobacterales (CRE) collected in hospitals from Europe, Asia and Latin America (2019–21). *JAC-Antimicrobial Resistance*, *5*(2). https://doi.org/10.1093/jacamr/dlad032

Tompkins, K., & van Duin, D. (2021). Treatment for carbapenem-resistant Enterobacterales infections: recent advances and future directions. *European Journal of Clinical Microbiology & Infectious Diseases*, *40*(10), 2053–2068. https://doi.org/10.1007/s10096-021-04296-1

Tselepis, L., Langley, G. W., Aboklaish, A. F., Widlake, E., Jackson, D. E., Walsh, T. R., Schofield, C. J., Brem, J., & Tyrrell, J. M. (2020). In vitro efficacy of imipenem-relebactam and cefepime-AAI101 against a global collection of ESBL-positive and carbapenemase-producing Enterobacteriaceae. *International Journal of Antimicrobial Agents*, *56*(1), 105925. https://doi.org/10.1016/j.ijantimicag.2020.105925

Urzedo, J. E., de Paula Menezes, R., Porto, J. P., Ferreira, M. L., Gonçalves, I. R., de Brito, C. S., Gontijo-Filho, P. P., & Ribas, R. M. (2020). High mortality by nosocomial infections caused by carbapenem-resistant P. aeruginosa in a referral hospital in Brazil: facing the perfect storm. *Journal of Medical Microbiology*, *69*(12), 1388–1397. https://doi.org/10.1099/jmm.0.001273

Venkatesan, P. (2021). WHO 2020 report on the antibacterial production and development pipeline. *The Lancet Microbe*, *2*(6), e239. https://doi.org/10.1016/s2666-5247(21)00124-5

Villegas, R., Hitchingham, E., Wilson, C., Gambrell, A., Mounsey, J., & Muleta, D. (2022). Trends in the Incidence of Carbapenem-Resistant Enterobacterales (CRE) and Carbapenemase Producing CRE (CP-CRE) in Davidson and Surrounding Counties, Tennessee, 2016-2021. *Open Forum Infectious Diseases*, *9*(Supplement_2). https://doi.org/10.1093/ofid/ofac492.1677

Wang, C.-H., Ma, L., Huang, L.-Y., Yeh, K.-M., Lin, J.-C., Siu, L. K., & Chang, F.-Y. (2021). Molecular epidemiology and resistance patterns of blaOXA-48 Klebsiella pneumoniae and Escherichia coli: A nationwide multicenter study in Taiwan. *Journal of Microbiology, Immunology and Infection*, *54*(4), 665–672. https://doi.org/10.1016/j.jmii.2020.04.006

Wangchinda, W., Thamlikitkul, V., Watcharasuwanseree, S., & Tangkoskul, T. (2022). Active Surveillance for Carbapenem-Resistant Enterobacterales (CRE) Colonization and Clinical Course of CRE Colonization among Hospitalized Patients at a University Hospital in Thailand. *Antibiotics*, *11*(10), 1401. https://doi.org/10.3390/antibiotics11101401

World Health Organization (WHO). (2023). *Antibiotic Resistance*. https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance

Wyres, K. L., Nguyen, T. N. T., Lam, M. M. C., Judd, L. M., van Vinh Chau, N., Dance, D. A. B., Ip, M., Karkey, A., Ling, C. L., Miliya, T., Newton, P. N., Lan, N. P. H., Sengduangphachanh, A., Turner, P., Veeraraghavan, B., Vinh, P. V., Vongsouvath, M., Thomson, N. R., Baker, S., & Holt, K. E. (2020). Genomic surveillance for hypervirulence and multi-drug resistance in invasive Klebsiella pneumoniae from South and Southeast Asia. *Genome Medicine*, *12*(1). https://doi.org/10.1186/s13073-019-0706-y

Yoo, E. H., Hong, H.-L., & Kim, E. J. (2023). Epidemiology and Mortality Analysis Related to Carbapenem-Resistant Enterobacterales in Patients After Admission to Intensive Care Units: An Observational Study. *Infection and Drug Resistance*, *Volume 16*, 189–200. https://doi.org/10.2147/idr.s391409