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Original Article

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Carbapenem-resistant Enterobacteriaceae infection and associated factors in intensive care unit: a cross-sectional study

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Abstract

Introduction: Carbapenem-resistant Enterobacteriaceae (CRE) infection is an urgent threat to public health. The impact of CRE infection includes increased difficulty in treatment, and a high risk of death. intensive care unit (ICU) patients are particularly vulnerable to CRE infection due to severe illness and comorbidities,. This study aims to determine the prevalence of CRE infection and identify associated factors in the ICU setting.

Method: This cross-sectional study was conducted at a tertiary-level hospital, utilizing patient medical records to gather data. The study population included patients aged 18 and above who were treated in the ICU between July and December 2022. The data includes epidemiological and clinical characteristics, and CRE infection.

Results: During this period, 451 patients were included in the analysis. The key findings regarding the prevalence of CRE infection and associated factors are as follows.

Prevalence of CRE infection among the patients was 28.8%. Patients with surgical site infection had a 1.40 times higher prevalence of CRE infection (p<0.007, 95% CI 1.09–1.77). For every 1 unit increase in hospitalization time within the last 3 months, APACHE II score, and hospitalization time, the prevalence of CRE infection increased by 1%–3%. For every 1 unit increase in sequential organ failure assessment score, the prevalence of CRE infection decreased by 8% with p=0.042 (95% CI 0.85–0.99).

Conclusions: This high prevalence underscores the significant threat CRE poses in critical are settings and emphasized the urgent need for stringent infeciton control practices, including a prompt assessment of the patient's health condition before admission to the hospital.

Keywords: carbapenem-resistant Enterobacteriaceae; intensive care units; prevalence; infection control

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1. INTRODUCTION

Antimicrobial resistance (AMR) is one of the top ten public health threats worldwide [1]. Carbapenem antibiotics are a group of broad-spectrum ß-lactam antibiotics that are used as the last resort for the treatment of infections caused by AMR bacteria [2]. However, carbapenem resistance has emerged and become widespread globally, with the most common agent being the Enterobacteriaceae group [3,4]. In 2019, the Centers for Disease Control and Prevention (CDC) released a list of 18 alarming AMR bacteria, of which Carbapenem-resistant Enterobacteriaceae (CRE) belongs to the highest alert group, posing an urgent threat to public health with a mortality risk of up to 70% [5–7] In 2017, CRE was estimated to have caused 13,100 infections in hospitalized patients, resulting1,100 deaths, and $130 million in treatment costs in the USA [5]. In recent years, Vietnam has been identified as one of the countries with the highest AMR prevalence globally [8]. Several studies have demonstrated a significantly increase in CRE prevalence, rising from 0.3% in 2010 to 53.8% in 2020 among isolated Carbapenem-resistant Gram-negative bacteria strains [9,10].

Previous studies have evaluated various risk factors for CRE infection, including age, malignancies, heart disease, organ or stem cell transplantation, mechanical ventilation, antibiotic exposure, hospitalization duration, poor health status, length of intensive care unit (ICU) stay, and invasive procedures. These factors can contribute to CRE infection and potentially lead to death. Notably, evidence suggests that exposure to healthcare settings and antibiotics are the most critical factors for CRE infection [11]. Patients admitted to the ICU are at high risk for CRE infection due to severe illness, immunocompromised status, poor nutrition, comorbidities, and multidrug-resistant status. These patients are typically prescribed antibiotics base on the treating physician's clinical experience [12].

Currently, in Vietnam, the overall CRE infection and its associated factors remain unclear and insufficiently specific. Several studies have investigated the prevalence of CRE infection in the country, most have focused solely on laboratory specimens and have been limited in determining the prevalence and associated factors among patients. Controlling of AMR is crucial and urgent for healthcare facilities, especially in the ICU of tertiary-level hospitals.

Therefore, the study was conducted to determine the prevalence of CRE infection and associated factors in the ICU of the tertiary-level hospital in 2022. The analysis results will provide new insights into CRE infection, helping to improve the quality of patient care more comprehensively and prevent unwanted infections. This, in turn, will facilitate quicker patient recovery and mitigate the impact of AMR bacteria, particularly CRE in particular, within the hospital.

2. METHODS

2.1. Study design and participants

A cross-sectional study was conducted in the ICU of the tertiary-level hospital. The inclusion criteria comprised patients aged 18 and above who were admitted to the ICU from July 1, 2022, to December 31, 2022, and who underwent bacterial culture and identification testing. The patients are exclueded from the study if they lacked sufficient information about the tested results, such as the type of specimen infected with CRE, species CRE, and date of sample collection; the socio-demographics; or the treatment process in the ICU, as well as those non-compliant with treatment and arbitrarily ending the course of treatment without the consent of the doctor were excluded from the study.

2.2. Sample size and sampling

The sample size was determined using the formula for estimating a population proportion. The study used the expected prevalence p=0.541 based on an Egyptian ICU study conducted from 2011 to 2017 on CRE epidemiology, using national healthcare-associated infection (HAI) surveillance data [13] and the margin of error d=0.05. Together with the expected 10% sample loss, the minimum total sample size to collect was 425 patients. The total number of patients admitted to the ICU from July 1, 2022, to December 31, 2022, was 455, which was approximated by the initial expected sample size of 425. So, the study used the method of collecting all data that met the inclusion and exclusion criteria for patients in the ICU during this time period.

2.3. Data collection and tool

The study utilized patients' medical records to collect data, which involved completing an information collection form. This form included variables such as age, sex, source of patient, treatment department before admission to the ICU, hospitalization time within the last 3 months, comorbidities, CRE colonization, APACHE II score, sequential organ failure assessment (SOFA) score, Charlson comorbidity index (CCI) score, hospitalization time before CRE infection, surgery, HAI status, invasive procedure, exposure to antibiotics, treatment outcomes, hospitalization time, and CRE infection status.

Data were collected from July 2022 onward and included in the first ICU admission only. Each patient underwent daily monitoring from the ICU admission untill discharge or death at the hospital. Comprehensive patient information was collected from admission to the commencement of follow-up during this period.

As per CDC definition, CRE refers to an enteric bacteria that is resistant to at least one of the carbapenem antibiotics (minimum inhibitory concentration [MIC]≥4 μg/mL for Doripenem, Meropenem, or Imipenem, or ≥2 μg/mL for Ertapenem) or if they produce carbapenemase. *Proteus* spp., *Morganella* spp., and *Providencia* spp. may exhibited an elevated MIC for Imipenem. Therefore, to determine whether these microorganisms meet the criteria for CRE definition, the results of Ertapenem, Meropenem, and Doripenem should be considered [14].

Following the CDC's HAI monitoring guidelines, a patient is classified as having a CRE infection based on the results of bacterial culture and identification testing as follows: for blood samples, the patient has a positive result (R: resistant) with ≥1 CRE confirmed CRE infection; for urine, sputum, and other fluid specimens, patients with positive results (R: resistant) with ≥1 CRE and a bacteria count>10^5 CFU/mL are identified as having a CRE infection.

The type of specimen infected with CRE is a substance taken from the patient's body, such as sputum, blood, urine, and fluid, to perform tests and help diagnose diseases. The species CRE is a bacterium belonging to the group Enterobacteriaceae that resists Carbapenem recorded in the culture and identification of bacteria test results such as *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* spp., *Serratia* spp., and *Proteus mirabilis*. For each of thease variables, the study recorded only one occurrence of the specimen or bacteria. If a patient underwent culture at the same location more than once with consistent results, subsequent occurences were not recorded. This approahc ensured that results were not duplicated for the same patient.

This rate was calculated with the following formula:

$$\frac{\text{Total number of cases with blood/urine/sputum/other fluid specimens contaminated with CRE}}{\text{Total number of cases with CRE infected specimens}}$$

The source of the CRE infection was classified in accordance with the CDC's HAI monitoring criteria. This healthcare-associated CRE infection in the ICU was documented when a patient contracted a CRE infection during treatment at the ICU department and appeared 48 hours after the patient's admission to the department. Conversly, a non-healthcare-related CRE infection in the ICU was identified when a patient developed a CRE infection either prior to ICU admission or more than 48 hours after transfer to another department or discharge from the hospital. This classification was based on the date of sample collection recorded in the test results.

2.4. Bias control

Selection bias was mitigated through the compilation of a comprehensice list of patients aged 18 and above receiving treatment at the ICU from July to December 2022. Strict adherence to predefined research inclusion and exclusion criteria ensured clarity and simplicity. Information biase was controlled by clearly defining and specifying variables in the information collection form, which was desinged with precise objectives, clear language, ease of comprehension, and structured format. Investigators underwent thorough training and evaluation before official data collection commenced.

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following the data collection, 20% of the total collected forms were randomly selected for verification to completeness and accuracy by the researcher. These forms were also coded to facilitate management, data entry, data analysis, and report writing.

2.5. Statistical method

Data entry was performed using Epidata, and data analysis was carried out using STATA. Qualitative variables were decribed using frequency and percentage. Normally distributed quantitative variables were summarized using mean and SD, whereas non-normally distributed quantitative variables were descrived using median and interquartile range.

The Chi-square test and Poisson regression model were employed to assess the association between each factor and CRE infection. If more than 20% of the total cells had expected value less than 5, the Fisher test is used instead of the Chi-squared test. A significance level of $p<0.05$ was applied, and the prevalence ratio (PR) with a 95% confidence interval (CI) excluding 1 was considered statistically significant. Variables with $p<0.05$ in univariate analysis were selected for multivariable Poisson regression model to control for potential confounding factors and identify variables significantly associated with CRE infection.

2.6. Strengthening the reporting of observational studies in epidemiology (STROBE) checklist adherence

The research report is adheres to the guidelines and checklist of strengthening the reporting of observational studies in epidemiology (STROBE), established by the UK EQUATOR Center, and updated on March 6, 2023 [15]. The checklist includes 22 components organized into six main sections: title and abstract, introduction, methods, results, discussion, and other information required for a cross-sectional research report and enhances the reliability of the findings presented.

2.7. Ethical considerations

The questions posed in this study were desinged to safeguard the patient's automony and ensure their mental and physical well-being remained uncompromised. Personal information pertaining to the subjects were treated with confidentiality and was strictly utilzed for the purpose of the study alone. The analysis results derived from the study were employed solely for research-related objectives and were not utilized for any unrelated purposes.

The study protocol was approved in terms of research ethics by the Ethics Committee for Biomedical Research of the University of Medicine and Pharmacy at Ho Chi Minh City, No. 164/HĐĐĐ-ĐHYD, signed on February 14, 2023.

3. RESULTS

3.1. Participants

The study initially involved 455 patients admitted to the ICU from July to December 2022. However, four patients were excluded for not meeting the inclusion and exclusion criteria. This included one patient lacking information about their ICU treatment process and three patients who were still hospitalized at the time of sample collection. Consequently, the final anlaysis included 451 patients who met the criteria, meeting the minimum size requirement for the study. Therefore, the response rate for the initial expected sample size was 100% (Fig. 1).

3.2. Participant characteristics

This study populaiton had a median age 67 years, with majority being male (56.5%). A significant proportion of patients originated from home or the community, and they had received treatment in the inpatient and emergency departments

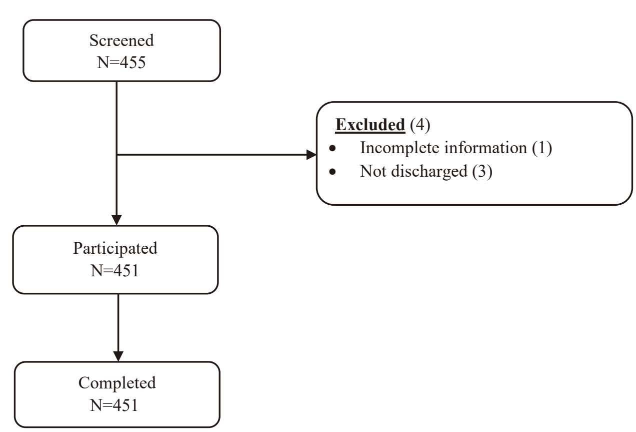

Fig. 1. Flow diagram.

before ICU admisison. The median hospitalization duration within the last 3 months was 3 days. Most of the patients presented with comorbidities, with a median of 7 comorbidities (per patients?). Besides the main disease, the patients had cardiovascular disease, diabetes, and chronic kidney disease. The CRE colonization screening results were mostly negative (74.3%). The medians of APACHE II, SOFA, and CCI scores were 19, 5, and 5, respectively (Table 1).

3.3. Clinical characteristics

The results showed that the median hospitalization duration prior to the CRE infection was 12 days. More than half of the patients had no surgery before determining the CRE infection. The prevalence of HAI was not high; however, patients with HAI mostly had bloodstream infections and ventilator-associated pneumonia. Most patients admitted to the ICU used invasive procedures such as endotracheal intubation, central venous catheters, arterial catheters, and urinary catheterization, which accounted for the largest proportion of invasive procedures. Most patients were exposed to antibiotics. The most commonly used group of antibiotics was ß-lactam, followed by Peptides, Quinolones, and at least Tetracyclines. The outcomes for patients were largely mitigated, with the median hospitalization time being 17 days (Table 2).

3.4. Carbapenem-resistant Enterobacteriaceae (CRE) infection

The results showed that the prevalence of CRE infection was 28.8%. The most common specimens and species of CRE were sputum and *K. pneumoniae*. More than half of patients with CRE infections were related to health care in the ICU (Table 3).

3.5. Factors associated with carbapenem-resistant Enterobacteriaceae (CRE) infection

In the univariate anlaysis, several factors showed association with the rate of CRE infection. To mitigate potential confounding effects, the study conducted multivariable analysis using a multivariable Poisson regression model. Variables with a p-value<0.05 in univariate analysis were incorporated into the multivariable model. These variables include age, hospitalization duration within the last 3 months, number and types of comorbidities, neuropathy, screening for CRE colo-

Table 1. Participant characteristics (n=451)

Characteristics	Frequency	Ratio (%)
Age[1)] (n=451)	67 (59–78)	
Sex (n=451)		
Male	255	56.5
Female	196	43.5
Department before admission to the ICU (n=451)		
Inpatient department	177	39.2
Emergency department	173	38.4
Anesthesiology-resuscitation department	79	17.5
ICUs	22	4.9
Source of patient (n=451)		
At home/community	285	63.2
Hospital/medical center/clinic in HCMC	82	18.2
Hospital/medical center/clinic outside HCMC	84	18.6
Hospitalization time within the last 3 months (days) [1)] (n=451)	3 (0–11)	
Comorbidities (n=451)		
Yes	449	99.6
No	2	0.4
Number of comorbidities[1)] (n=449)	7 (5–9)	
Types of comorbidities (n=449)		
Cardiovascular diseaes	296	65.9
Diabetes	187	41.7
Chronic kidney disease	123	27.4
Cancer	85	18.9
Neuropathy	63	14.0
Chronic liver disease	62	13.8
COPD	38	8.5
Peripheral vascular disease	35	7.8
Stomach ulcers	22	4.9
Connective tissue disease	16	3.6
Screening for CRE colonization (n=451)		
Negative	335	74.3
Positive	116	25.7
APACHE II score[1)] (n=451)	19 (14–26)	
SOFA score[1)] (n=451)	5 (3–8)	
CCI score[1)] (n=451)	5 (3–7)	

[1)] Median and interquartile range.
ICU, intensive care unit; CRE, carbapenem-resistant Enterobacteriaceae; SOFA, sequential organ failure assessment; HCMC, Ho Chi Minh City; COPD, chronic obstructive pulmonary disease; CCI, Charlson comorbidity index.

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Table 2. Clinical characteristics (n=451)

Characteristics	Frequency	Ratio (%)
Hospitalization time before CRE infection (days)[1] (n=130)	12 (5–22)	
Surgery before determining CRE infection (n=451)		
Yes	214	47.4
No	237	52.6
HAI (n=451)		
Yes	120	26.6
No	331	73.4
Types of HAI (n=120)		
Ventilator-associated pneumonia	64	53.3
Bloodstream infection	61	50.8
Urinary tract infection	20	16.7
Surgical site infection	15	12.5
Invasive procedures (n=451)		
Yes	438	97.1
No	13	2.9
Types of invasive procedures (n=438)		
Urinary catheterization	399	91.1
Central venous catheter	372	84.9
Intubation	329	75.1
Arterial catheter	255	58.2
Exposed to antibiotics (n=451)		
Yes	418	92.7
No	33	7.3
Types of antibiotics (n=418)		
ß-Lactam	410	92.7
Peptides	207	49.5
Quinolons	195	46.7
Oxazolidinones	103	24.6
5-Nitroimidazoles	56	13.4
Aminoglycoside	39	9.3
Lincosamide	27	6.5
Co-trimoxazole	16	3.8
Macrolide	5	1.2
Tetracyclines	3	0.7
Treatment outcome (n=451)		
Mitigation	276	61.2
Unchangeability	65	14.4
Aggravation	104	23.1
Death	6	1.3
Hospitalization time (days)[1] (n=451)	17 (10–28)	

[1] Median and interquartile range.
CRE, carbapenem-resistant Enterobacteriaceae; HAI, healthcare-associated infection.

Table 3. CRE infection (n=451)

Characteristics	Frequency	Ratio (%)
CRE infection (n=451)		
Yes	130	28.8
No	321	71.2
Types of specimen infected with CRE (n=130)		
Sputum	78	60.0
Blood	36	27.7
Urine	23	17.7
Other secretions	58	12.9
Species CRE (n=130)		
Klebsiella pneumoniae	114	87.7
Escherichia coli	19	14.6
Serratia spp.	12	9.2
Proteus mirabilis	11	8.5
Enterobacter spp.	6	4.6
Source of CRE infection (n=130)		
Relating to health care in the ICU	73	56.2
Not related to health care in the ICU	57	43.8

CRE, carbapenem-resistant Enterobacteriaceae; ICU, intensive care unit.

nization, APACHE II score, SOFA score, types of HAI, surgical site infection, types of invasive procedures, intubation, central venous catheter, arterial catheter, urinary catheterization, types of antibiotics: Aminoglycosides, Peptides, and Oxazolidinones; treatment outcomes; hospitalization time.

Results from the model showed that factors such as hospitalization time within the past 3 months, APACHE II score, SOFA score, surgical site infection, and hospitalization time were indeed associated with CRE infection.

Specifically, if the patient has 1 more day of hospital stay within the past 3 months, the prevalence of CRE infection will increase by 1% (p=0.026; PR=1.01; 95% CI 1.01–1.02). If patients' APACHE II score increases by 1 point, the prevalence of CRE infection will increase by 3% (p=0.022; PR=1.03; 95% CI 1.01–1.06). If patients' SOFA score increases by 1 point, the prevalence of CRE infection will decrease by 8% (p=0.042; PR=0.92; 95% CI 0.85–0.99). Patients with surgical site infection exhibited a 1.4 times higher prevalence of CRE infection compared to those without surgical site infection. The observed difference is statistically significant, with p-value=0.007 (PR=1.04, 95%

CI 1.09–1.77). For each additional day of hospital stay, the prevalence of CRE infection is expected to increase by 1% (p<0.001; PR=1.01; 95% CI 1.01–1.02) (Table 4).

4. DISCUSSION

The prevalence of CRE infection in the ICU was found to be 28.8%. The figure alignes with the CRE infection prevalence reported at Hue Central Hospital [16], but exceed rates observed in other studies in Asia [17–19] while being lower than those reported in the studies elsewhere globally [13,20]. Discrepancies in PR across different medical facilities may stem from various factors, including environmental disinfection conditions, tools, equipment, disease physiology, and especially the CRE infection surveillance system within each hospital. Furthermore, this study's focus solely on the ICU department contrasts with the broader scope of other investigations that emcompassed entire hospital settings. Nevertheless, the considerably high prevalence of CRE infection identified in this study warrants serious attention, especially in the context of rising AMR bacteria concerns, particularly within the Asian region.

Most of the CRE bacteria that the study recorded were *K. pneumoniae*, which accounted for more than 50% of sputum specimens, followed by *Escherichia coli* and blood specimens, which were 14.6% and 27.7%, respectively. This is consistent with the epidemiology of CRE bacteria, which is the fastest-spreading strain of the bacteria, according to most reports by the CDC and other countries around the world [21].

CRE infections related to health care in the ICU accounted for 56.2%. Patients receiving treatment in the ICU often undergo invasive procedures and antibiotic usage due to severe illness and serious infections. Additionally, the high frequency of patients-staff interactions in healthcare setting heightens the risk of AMR bacteria transmission through contaminated surfaces and the hands of healthcare professionel [12,22]. Therefore, the treatment and the care protocols implemented in ICU settings are recognized as significant contributors to CRE infection risk.

Regarding participant characteristics, hospitalization time within the past 3 months was found to be associated with the CRE infection. Patients with longer hospital stays prior to their current admission exhibited higher rates of CRE infection. This finding aligns with research conducted in Israel [17] and Columbia [23], where a correlation between previous hospitalization and CRE infection was observed. Repeated hospitalizations and exposure to healthcare services pose high-risk factors for various health issues, particularly CRE infections.

The study also identified an association between CRE infection and the APACHE II score and SOFA score. Specifically, patients with a higher APACHE II score exhibited a higher prevalence of CRE infection, consistent with the research conducted in Israel, Saudi Arabia, and Korea [17,22,24]. This shows the close relationship between initial health status CRE infection, highlighting that patients with compromised immune systems are at increased risk of CRE infection [25]. However, the study also found that higher the SOFA scores were associated with a lower prevalence of CRE infection. According to other studies around the world, the higher the SOFA score, the higher the risk of CRE infection. This difference may stem from in the timing of data collection for these variables. In this study, the SOFA score was assessed within the first 24 hous of the ICU admission to evaluate multiple organ failure and predict mortality for ICU patients. In addition, the more than 50% of CRE infections were identified as healthcare-related in the ICU, typilcally occuring after 48 hours of ICU admission. This temporal misalignment in data collection for SOFA score and CRE infection status could introducec errors, as the status of CRE infection may change within 24 hours of SOFA score assessment.

The study did not find an association between age, comorbidities, and the prevalence of CRE infection. Despite the majority of patients being adults over 65 years old and had comorbidities such as stroke, dementia, hemiplegia, chronic obstructive pulmonary disease, cardiovascular disease, and often hospitalization due to acute illnesses requiring specialized monitoring and care, no significant differences were observed in multivariable analysis.

According to the CDC, patients with CRE colonization are at risk of developing infection and spreading it to other patients. Therefore, screening patients for CRE colonization before admission to the hospital is a CDC-recommended mea-

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Table 4. **Factors associated with CRE infection according to the multivariable poisson regression model (n=451)**

Characteristics	Univariate analysis		Multivariate Analysis	
	p-value	PR (95% CI)	p-value	Adjusted PR (95% CI)
Age (n=451)	0.001	1.02 (1.01–1.03)	0.853	1.01 (0.99–1.01)
Hospitalization time within the last 3 months (days) (n=451)	0.001	1.01 (1.01–1.02)	0.025	1.01 (1.01–1.02)
Number of comorbidities (n=449)	0.001	1.07 (1.03–1.11)	0.238	0.98 (0.94–1.01)
Types of comorbidities (n=449)				
Neuropathy				
Yes	0.001	1.76 (1.28–2.41)	0.467	1.14 (0.85–1.54)
No		1		1
Screening for CRE colonization (n=451)				
Negative	0.001	1.69 (1.27–2.25)	0.287	1.16 (0.88–1.54)
Positive		1		1
APACHE II score (n=451)	<0.001	1.03 (1.02–1.05)	0.022	1.03 (1.01–1.06)
SOFA score (n=451)	0.008	1.06 (1.01–1.10)	0.042	0.92 (0.85–0.99)
Types of HAI (n=120)				
Surgical site infection				
Yes	0.010	1.56 (1.27–1.91)	0.007	1.40 (1.10–1.78)
No		1		1
Types of invasive procedures (n=438)				
Intubation				
Yes	<0.001	3.52 (1.98–6.29)	0.554	1.21 (0.64–2.27)
No		1		1
Central venous catheter				
Yes	0.001	2.66 (1.37–5.18)	0.251	0.68 (0.35–1.31)
No		1		1
Arterial catheter				
Yes	<0.001	2.34 (1.63–3.37)	0.326	1.28 (0.78–2.07)
No		1		1
Urinary catheterization				
Yes	<0.001	6.16 (1.58–23.93)	0.549	1.36 (0.50–3.67)
No		1		1
Types of antibiotics (n=418)				
Aminoglycoside				
Yes	0.027	1.59 (1.09–2.31)	0.575	0.89 (0.60–1.33)
No		1		1
Peptides				
Yes	0.041	1.35 (1.01–1.81)	0.793	0.96 (0.74–1.26)
No		1		1
Oxazolidinones				
Yes	0.037	1.39 (1.03–1.88)	0.961	1.01 (0.77–1.32)
No		1		1
Treatment outcome (n=451)				
Mitigation		1		1
Unchangeability	0.047	1.51 (1.01–2.26)	0.406	1.18 (0.80–1.76)
Aggravation	<0.001	1.86 (1.36–2.54)	0.083	1.33 (0.96–1.85)
Hospitalization time (days) (n=451)	<0.001	1.01 (1.01–1.02)	<0.001	1.01 (1.01–1.02)

CRE, carbapenem-resistant Enterobacteriaceae; PR, prevalence ratio; SOFA, sequential organ failure assessment; HAI, healthcare-associated infection.

sure to help prevent the spread of CRE [14]. However, this study did not find a significant association between CRE colonization screening and CRE infection in multivariable analysis. The study observed that the proportion of patients with CRE infection who had the result of screening CRE colonzation positive was lower than the proportion of patients with CRE infection who had the result of screening CRE colonzation negative. It is possible that, in addition to CRE colonization, there are other factors that can spread CRE infection in the ICU that the study has not mentioned nor controlled.

The study identified an association between surgical site infection and the prevalence of CRE infection, with patients having surgical site infections exhibiting a 1.40 times higher prevalence of CRE infection compared to those without such infections. This finding is concerning as concurrent occurrences of surgical site infection and the CRE infections can exacerbate treatment challenges, leading to prolonged hospitalization, increased treatment costs, as well as mortality risks [1]. Therefore, hospitals need to prioritize pre-surgical screening for CRE colonization in patients and implement stringent measures to prevent surgical site infection after surgery.

Whilte previous studies have found associations between CRE infection and factors such as invasive procedures and antibiotic exposure, our multivariable analysis did not corroborate these findings. This discrepancy may arise from the high frequency of using invasive procedures and antibiotics in the ICU, irrespective of CRE infection status. However, according to the CDC, these are two factors that have a high risk of causing CRE infection [14]. Therefore, this result should not be ignored, reducing the importance of preventing CRE infections for patients exposed to two factors: exposure to antibiotics and invasive procedures.

The total length of hospital stay was also found to be associated with CRE infection. Patients infected with CRE have a longer hospital stay compared to those without CRE infection, likely due to the challenges CRE infections, which prolong recovery times. This finding aligns with a study conducted in Korea (2023), with p=0.015 [22]. On the other hand, a prolonged hospital stay entail increased exposure to risk factors, leading to an increased risk of CRE infection and other nosocomial infections such as HAI. This not only burdens healthcare providers but also strains the healthcare system of the country.

The study did not find any association between treatment outcomes and the prevalence of CRE infection. This may be attributed to the fact that the study treated CRE infection as the dependent variable, while treatment outcomes were recorded subsequent to CRE infection. Consequently, treatment outcomes are unlikely to influence CRE infection as an independent variable to figure out any potential association between CRE infection and treatment outcomes.

This study encountred several limitations. The first limitation of the study is that there are very few studies analyzing the factors associated with CRE infection in Vietnam, so the references are limited. The second limitation is that the study was only conducted to the ICU of a single tertiary-level hospital, thus constraining its genearlizability to other healthcare facilities in Ho Chi Minh City and beyond.

5. CONCLUSION

In conclusion, this study revealed a relatively high prevalence of CRE infections within the ICU setting. Factors significantly associated with CRE infection included recent hospitalization (within the past 3 months), APACHE II score, SOFA score, surgical site infection, and hospitalization duration. Therefore, prioritizing infection control measures and thorough patient health assessment upon admission are essential. Further studies should be conducted on younger subjects, at other locations, and with a longitudinal study design to monitor and evaluate more accurately the influence of factors related to CRE infection.

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Conflict of interest

No potential conflict of interest relevant to this article was

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Authors' contributions
Conceptualization: NTT Pham.
Data curation: HGN Tran, LT Pham, YHV Nguyen, TT Trinh, TM Huynh.
Formal analysis: NTT Pham, QM Lam.
Methodology: QM Lam, HGN Tran, LT Pham.
Software: TC Dinh.
Validation: TM Huynh.
Investigation: NTT Pham, HGN Tran, LT Pham, YHV Nguyen, TT Trinh.
Writing - original draft: NTT Pham, QM Lam, TC Dinh.
Writing - review & editing: NTT Pham, QM Lam, HGN Tran, LT Pham, YHV Nguyen, TT Trinh, TC Dinh, TM Huynh.

Availability of data and material
Upon reasonable request, the datasets of this study can be available from the corresponding author.

Ethics Approval
The Council of Ethics in Biomedical Research at the University of Medicine and Pharmacy at Ho Chi Minh City approved this study on February 14th, 2023, No. 164/HĐĐĐ-ĐHYD.

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