Epidemiological characteristics of carbapenem-resistant Enterobacteriaceae and carbapenem-resistant Acinetobacter baumannii in a tertiary referral hospital in Korea

Sollan Kang¹, Ihn Sook Jeong²

¹Infection Control Team, Inje University Busan Paik Hospital, Busan, Korea
²College of Nursing, Pusan National University, Yangsan, Korea

ABSTRACT

Objectives: This study aimed to identify the epidemiological characteristics of patients with carbapenem-resistant Enterobacteriaceae and Acinetobacter baumannii (CRE/CRAB) isolates in a tertiary referral hospital in Korea.

Methods: We collected and analyzed data from 528 adults admitted to a tertiary referral hospital from August 1, 2018 to February 29, 2020. The CRE/CRAB isolates were confirmed as being present at the time of patients' admission or acquired during hospitalization based on their medical records. The t-test, chi-square test, or Fisher exact test and stepwise multiple logistic regression were performed.

Results: While the proportion of community-acquired CRE/CRAB was low (6%), 20% of CRE/CRAB isolates were identified in patients at the time of hospitalization. The risk of CRAB isolation was positively associated with mechanical ventilator use (odds ratio [OR], 3.52; 95% confidence interval [CI], 1.96–6.33) and total parenteral nutrition use (OR, 3.64; 95% CI, 1.87–7.08).

Conclusion: Over 20% of CRE/CRAB isolates in a tertiary referral hospital in Korea were found at the time of patients’ admission. Furthermore, patients with mechanical ventilation and/or total parenteral nutrition tended to acquire CRAB more frequently. Thus, active surveillance for CRE/CRAB at the time of hospitalization is strongly required, particularly for patients who are expected to require mechanical ventilation or total parenteral nutrition.

Keywords: Acinetobacter baumannii; Carbapenem-resistant Enterobacteriaceae; Drug resistance, multiple
Introduction

The World Health Organization declared antibiotic resistance to be 1 of 10 international health threats to human life, and pointed out problems such as the prolongation of hospital stays, the economic burden due to the use of expensive antibiotics, death, and disability [1]. For some carbapenem-resistant organisms (CROs), genes encoding carbapenemases are located in mobile genetic elements, such as plasmids or transposons; these can cause rapid transmission of resistant bacteria between patients [2,3], making them highly likely to spread from healthcare settings to the local community [4]. In Korea, carbapenem-resistant Enterobacteriaceae (CRE) and multidrug-resistant Acinetobacter baumannii are designated as infectious diseases that must be reported to health authorities by law [5]. According to the United States Centers for Disease Control and Prevention (CDC), CRE and carbapenem-resistant Acinetobacter baumannii (CRAB) are classified as the most urgent threats among antibiotic-resistant microorganisms, for which reason the CDC has strengthened antibiotic resistance management [6].

Several studies have investigated the epidemiological characteristics and risk factors of acquiring CROs in patients admitted to intensive care units (ICUs) and organ transplantation wards in the United States [7], those admitted to a general hospital for CRE [8]; those admitted to the Taiwan General Hospital for CRAB [9], those admitted to an acute care health hospital for carbapenem-resistant Gram-negative bacteremia in Taiwan [10]; and CRE-infected patients in acute care health hospitals in China [11]. Those studies also sought to describe the prevalence, incidence, and epidemiological characteristics of multidrug-resistant Gram-negative bacteria and CROs, including colonization and infection in ICUs, using data entered into a German infection monitoring system [12]. However, relatively few studies have been conducted in Korea; examples include a study aiming to identify risk factors for CRE colonization in patients admitted to the ICUs of general hospitals [13,14] and a study on the acquisition of carbapenem-resistant Escherichia coli in hospitalized patients [15]. These studies mainly targeted patients admitted to the ICU and focused on CRE. Therefore, limited information is available on the epidemiological characteristics of CROs in other hospital settings, including general wards, and other types of CROs, such as CRAB. In addition, a case of CRE acquisition in a patient who had not visited a hospital within 3 months was reported [16], and approximately 30% of cases confirmed at hospitals are found within 48 hours of hospitalization [17]. Therefore, it is necessary to understand the characteristics of CRE/CRAB isolates, including both healthcare-acquired (HA) and community-acquired (CA) CRE/CRAB, but few studies on CA CRE/CRAB have been reported in Korea. The purpose of this study was to identify the epidemiological characteristics of patients from whom CRE/CRAB was isolated among those admitted to a tertiary referral hospital, and to conduct a comparison between CRE and CRAB isolates, and between CA and HA CRE/CRAB.

Materials and Methods

Study Design and Participants

This was a retrospective cohort study that used patients’ medical records. It was conducted at Inje University Busan Baik Hospital, an 800-bed tertiary referral hospital in Busan, Republic of Korea. The participants were CRE/CRAB cases who met all the following criteria: (1) adult patients aged 19 years or older, (2) admitted to any ward, including the emergency room and ICU, from August 1, 2018 to February 29, 2020, and (3) confirmed to have CRE/CRAB either by a CRE active surveillance culture using a rectal swab or on a culture using blood or another clinical specimen. Both colonization and infection were included. In this hospital, active CRE surveillance culture is conducted only for patients admitted to the ICU, and all departments collect clinical samples when necessary for culture and antibiotic resistance tests. During the study period, only the initial hospitalization and isolate were included in cases of rehospitalization and duplicate isolations of CRE or CRAB, and only the initial isolate was included if both CRE and CRAB were isolated. In total, 65,337 patients were hospitalized during the study period, and CRE/CRAB isolation was confirmed in 528 patients (isolation rate, 0.81%).

Definition and Variables

Cases were defined following the recommendations of the Korea Disease Control and Prevention Agency based on the recommendations of the Clinical and Laboratory Standards Institute (M100-S27) [18,19]. Antimicrobial susceptibility to carbapenems was assessed using the disk diffusion method. CRE was defined based on resistance to imipenem (≤19 mm), meropenem (≤19 mm), or ertapenem (≤18 mm), and CRAB was defined based on resistance to imipenem (≤18 mm) or meropenem (≤14 mm). The CA group was defined as having confirmed CRE/CRAB at the time of hospitalization or within 48 hours of hospitalization, and the HA group was defined as patients transferred from a long-term care facility, regardless of the period, or in whom isolates were obtained after 48 hours of hospitalization in an acute care hospital. The variables examined in this study were general
characteristics, multidrug-resistant organism (MDRO)-related characteristics, treatment-related characteristics, and clinical outcomes, referring to the questions used in previous studies [7,11,13] on the characteristics of CRE or CRO isolation. General characteristics included sex, age, hospitalization route, history of hospitalization within 6 months, comorbidities, and the Charlson comorbidity index score (CCIS). MDRO-related characteristics included whether the MDRO was isolated before CRE/CRAB acquisition, the CRE/CRAB acquisition time, specimen source, and strain. Treatment-related characteristics included invasive procedures performed during hospitalization and invasive devices and drugs used for more than 48 hours. Status at discharge was analyzed as a clinical outcome.

Data Collection
With the help of the infection control office of the study hospital, one researcher obtained a list of patients with confirmed CRE/CRAB isolates and selected those who met the inclusion criteria. Data were collected using structured data sheets from electronic medical records, including nursing care, hospitalization-related information, prescriptions, operations, procedures, and diagnostic test results. The CCIS was calculated directly by the researcher, referring to each patient’s medical record. When a history of admission to medical institutions other than the study hospital or MDRO isolation was not confirmed, we classified these variables as “unknown.” Treatment-related characteristics prior to admission to the study hospital could not be collected due to a lack of information in the medical record. For every CA or HA case transferred from a long-term care facility, data collection was based on the time of hospitalization. For HA cases with CRE/CRAB confirmed after hospitalization, the data collection period was from the time of hospitalization to the date of CRE/CRAB isolation.

Data Analysis
The collected data were analyzed using IBM SPSS ver. 26.0 (IBM Corp., Armonk, NY, USA). The 2-tailed test was performed at a significance level (α) of 0.05. Frequency and percentage, mean and standard deviation, and median and interquartile ranges were calculated for the characteristics of the study participants. The t-test, chi-square test, or Fisher exact test was performed to compare characteristics between the CRE and CRAB groups and the CA and HA groups. With significant variables from the bivariate analysis as explanatory variables, we calculated the odds ratio and its 95% confidence interval using stepwise multiple logistic regression analysis after confirming the absence of deviation from the assumption of multicollinearity using a coefficient of determination of less than 0.80 [20].

IRB/IACUC Approval
Prior to data analysis, this study was approved by the Institutional Review Board of Inje University Busan Baik Hospital (20-0114), and the requirement for written consent was waived.

Results
Characteristics of Study Participants
Among the 528 study participants, CRAB was isolated in 67.6%, and 94.1% of cases were HA. At the time of hospitalization, 20.8% of the participants had either CRE or CRAB (Table 1). Tables 2–4 show the characteristics of the study participants. Overall, 63.4% were males, their mean age was 67.7 years, 72.2% had a history of hospitalization within the last 6 months, 49.2% had been transferred from other healthcare facilities, and 50.0% had a history of diagnosed hypertension. Regarding MDRO history, 22.0% had vancomycin-resistant Enterococcus, followed by extended-spectrum β-lactamase–producing organisms (16.7%). The majority of CRE/CRAB isolates occurred in respiratory specimens (60.0%), and the major strains were Acinetobacter baumannii (67.6%) and Klebsiella spp. (23.9%). Almost one-third (32.6%) of participants died before discharge. During hospitalization, 51.4% underwent surgery, 90.9% used a

### Table 1. Distribution of CRE and CRAB isolates (n = 528)

| Type  | CRE (n = 171) | CRAB (n = 357) | Total          |
|-------|--------------|----------------|----------------|
|       | At the time of hospitalization | After hospitalization | At the time of hospitalization | After hospitalization |                      |
| HA    | 36 (6.8)     | 116 (22.0)     | 43 (8.1)       | 302 (57.2)      | 497 (94.1)          |
| CA    | 19 (3.6)     | 0 (0)          | 12 (2.3)       | 0 (0)           | 31 (5.9)            |
| Total | 55 (10.4)    | 116 (22.0)     | 55 (10.4)      | 302 (57.2)      | 528 (100.0)         |

Data are presented as n (%). CRE, carbapenem-resistant Enterobacteriaceae; CRAB, carbapenem-resistant Acinetobacter baumannii; HA, healthcare-acquired; CA, community-acquired.
Comparison of Characteristics between the CRE and CRAB Group, and the CA and HA Group

There were significant differences in the characteristics of the CRE and CRAB groups with regard to the history of hospitalization within 6 months, hypertension, treatment in the ICU, MDRO history, the source of the specimen from which CRE/CRAB was isolated, and the use of arterial catheters, mechanical ventilation, and total parenteral nutrition (TPN) (Tables 2 and 3). Compared to the CRE group, the CRAB group showed lower frequencies of hospitalization within 6 months ($p=0.006$), hypertension, treatment in the ICU ($p=0.001$), and mechanical ventilation ($p<0.001$), with higher frequencies of the specimen source of RESpiratory ($p<0.001$) and Rectal swab ($p=0.001$).
Table 3. Comparison of treatment-related characteristics between patients with CRE and those with CRAB

| Variable                        | Category                  | Total (n = 418) | CRE (n = 116) | CRAB (n = 302) | p     |
|---------------------------------|---------------------------|-----------------|---------------|---------------|-------|
| Invasive procedures             | Surgery                   | 215 (51.4)      | 63 (54.3)     | 152 (50.3)    | 0.466 |
|                                 | Bronchoscopy              | 94 (22.5)       | 22 (19.0)     | 72 (23.8)     | 0.285 |
|                                 | G-endoscopy               | 63 (15.1)       | 22 (19.0)     | 41 (13.6)     | 0.168 |
| Invasive device                 | Urinary catheter          | 380 (90.9)      | 103 (88.8)    | 277 (91.7)    | 0.351 |
|                                 | Central catheter          | 352 (84.2)      | 93 (80.2)     | 259 (85.8)    | 0.161 |
|                                 | Gastrointestinal tube     | 336 (80.4)      | 88 (75.9)     | 248 (82.1)    | 0.149 |
|                                 | Arterial catheter         | 322 (77.0)      | 77 (66.4)     | 245 (81.1)    | 0.001 |
|                                 | Mechanical ventilator     | 275 (65.8)      | 58 (50.0)     | 217 (71.9)    | < 0.001 |
|                                 | Drainage tube             | 138 (33.0)      | 42 (36.2)     | 96 (31.8)     | 0.390 |
| Antibiotics                     | Penicillin                | 274 (65.6)      | 68 (58.6)     | 206 (68.2)    | 0.065 |
|                                 | Quinolone                 | 237 (56.7)      | 59 (50.9)     | 178 (58.9)    | 0.136 |
|                                 | Carbapenem                | 228 (54.5)      | 58 (50.0)     | 170 (56.3)    | 0.247 |
|                                 | Cephalosporin             | 225 (53.8)      | 62 (53.4)     | 163 (54.0)    | 0.923 |
|                                 | Vancomycin                | 165 (39.5)      | 43 (37.1)     | 122 (40.4)    | 0.533 |
| Medication                      | Antiacids                 | 375 (89.7)      | 103 (88.8)    | 272 (90.1)    | 0.701 |
|                                 | Steroids                  | 187 (44.7)      | 46 (39.7)     | 141 (46.7)    | 0.195 |
|                                 | TPN                        | 369 (88.3)      | 90 (77.6)     | 279 (92.4)    | < 0.001 |

Data are presented as n (%).
CRE, carbapenem-resistant Enterobacteriaceae; CRAB, carbapenem-resistant Acinetobacter baumannii; TPN, total parenteral nutrition.

Table 4. Factors associated with CRAB isolation (n = 418)

| Variable                        | OR (95% CI)   | p   |
|---------------------------------|---------------|-----|
| Hypertension                    | 0.56 (0.35−0.89) | 0.014 |
| Treatment in ICU               | 0.34 (0.16−0.72) | 0.005 |
| History of vancomycin-resistant Enterococcus<sup>a</sup> | 0.49 (0.29−0.83) | 0.008 |
| History of extended-spectrum Lactamase<sup>a</sup> | 0.48 (0.26−0.87) | 0.017 |
| Use of mechanical ventilator<sup>b</sup> | 3.52 (1.96−6.33) | < 0.001 |
| Use of total parenteral nutrition<sup>b</sup> | 3.64 (1.87−7.08) | < 0.001 |

CRAB, carbapenem-resistant Acinetobacter baumannii; OR, odds ratio; CI, confidence interval; ICU, intensive care unit.
<sup>a</sup>Reference group = No (carbapenem-resistant Enterobacteriaceae/CRAB-isolated patients without the corresponding condition).

The CA and HA groups showed significant differences in hospitalization route, hypertension, cerebrovascular disease, treatment in the ICU, MDRO history, and the source of the specimen from which CRE/CRAB was isolated (Table 5). The HA group showed higher frequencies of transfer from other healthcare facilities (p < 0.001), cerebrovascular disease (p = 0.011), and treatment in the ICU (p < 0.001), and lower frequencies of hypertension (p = 0.016), MDRO history (p < 0.001), and extended-spectrum β-lactamase-producing organism history (p = 0.004) compared to the CA group (Table 5). Multiple logistic regression analysis showed that the risk of HA-CRE/CRAB isolation was 6.30 times higher in patients diagnosed with cardiovascular disease than in those without cardiovascular disease (Table 6).

### Discussion

In this study, we identified the epidemiological characteristics of patients with confirmed CRE or CRAB isolation among inpatients in wards and the ICU, and compared the characteristics between the CRE and CRAB groups and between the HA and CA groups.

CRAB isolation was common in this tertiary hospital in Korea, suggesting that A. baumannii constitutes a large proportion of carbapenem-resistant bacteria in domestic medical institutions. According to the results of the global antimicrobial resistance surveillance system in Korea (KOR-GLASS) from 2016 to 2019, the imipenem resistance rates were 0.1% in blood and 0.1% in urine for E. coli, 10.0% in blood...
and 1.2% in urine for *Klebsiella pneumoniae*, and 90.3% in blood for *A. baumannii*, which was a very alarming finding [21]. The reported types of CROs differ across studies. CROs isolated from carbapenem-resistant bloodstream infections in Taiwan were higher in *Acinetobacter* spp. and *Pseudomonas* spp. than in CREs, including *E. coli*, *Klebsiella* spp., and *Enterobacter* spp. [10]. In contrast, a study on carbapenem-resistant Gram-negative bacteremia at a

### Table 5. Comparison of general characteristics between patients with healthcare-acquired and community-acquired infections

| Variables | Category | Total (n = 528) | HA (n = 497) | CA (n = 31) | p |
|-----------|----------|----------------|-------------|-------------|---|
| Sex       | Male     | 335 (63.4)     | 315 (63.4)  | 20 (64.5)   | 0.899 |
|           | Female   | 193 (36.6)     | 182 (36.6)  | 11 (35.5)   |     |
| Age (y)   |          | 67.7 ± 14.0    | 67.5 ± 14.0 | 71.2 ± 14.0 | 0.146 |
| History of hospitalization within 6 months | No | 147 (27.8) | 136 (27.4) | 11 (35.5) | 0.310 |
|           | ACH      | 301 (57.0)     | 283 (56.9)  | 18 (58.1)   |     |
|           | LTCF     | 80 (15.2)      | 78 (15.7)   | 2 (6.5)     |     |
| Source of hospitalization | ACH, transfer | 184 (34.8) | 184 (37.0) | 0 (0) | <0.001 |
|           | LTCF, transfer | 76 (14.4) | 76 (15.3) | 0 (0) |     |
|           | Community | 268 (50.8) | 237 (47.7) | 31 (100.0) |     |
| Comorbidities | Hypertension | 264 (50.0) | 242 (48.7) | 22 (71.0) | 0.016 |
|           | Diabetes mellitus | 186 (35.2) | 171 (34.4) | 15 (48.4) | 0.114 |
|           | CVD      | 158 (29.9)     | 155 (31.2)  | 3 (9.7)     | 0.011 |
|           | Cancer   | 140 (26.5)     | 132 (26.6)  | 8 (25.8)    | 0.927 |
|           | CKD      | 64 (12.1)      | 61 (12.3)   | 3 (9.7)     | 1.000 |
|           | Liver disease | 52 (9.8) | 49 (9.9) | 3 (9.7) | 1.000 |
|           | CRD      | 49 (9.3)       | 45 (9.1)    | 4 (12.9)    | 0.517 |
| Charlson comorbidity index score |          | 4.6 ± 2.3 | 4.6 ± 2.3 | 4.3 ± 2.4 | 0.541 |
| Treatment in ICU | No | 190 (36.0) | 159 (32.0) | 31 (100.0) | <0.001 |
|           | Yes      | 338 (64.0)     | 338 (68.0)  | 0 (0)       |     |
| MDRO history | VRE | 116 (22.0) | 113 (22.7) | 3 (9.7) | 0.088 |
|           | MRSA     | 55 (10.4)      | 53 (10.7)   | 2 (6.5)     | 0.760 |
|           | ESBL     | 88 (16.7)      | 77 (15.5)   | 11 (35.5)   | 0.004 |
|           | MRPA     | 11 (2.1)       | 9 (1.8)     | 2 (6.5)     | 0.132 |
| Specimen source of CRE/CRAB | Respiratory | 317 (60.0) | 307 (61.8) | 10 (32.3) | 0.001 |
|           | Rectal swab | 126 (23.9) | 117 (23.5) | 9 (29.0) |     |
|           | Urine    | 33 (6.3)       | 27 (5.4)    | 6 (19.4)    |     |
|           | Blood    | 18 (3.4)       | 15 (3.0)    | 3 (9.7)     |     |
|           | Others   | 34 (6.4)       | 31 (6.2)    | 3 (9.7)     |     |
| Strain of CRE/CRAB | Acinetobacter baumannii | 357 (67.6) | 345 (69.4) | 12 (38.7) | <0.001 |
|           | Klebsiella spp. | 126 (23.9) | 113 (22.7) | 13 (41.9) | 0.015 |
|           | Escherichia coli | 36 (6.8) | 31 (6.2) | 5 (16.1) | 0.051 |
|           | Enterobacter spp. | 11 (2.1) | 10 (2.0) | 1 (3.2) | 0.489 |
|           | Others   | 3 (0.6)        | 2 (0.4)     | 1 (3.2)     | 0.166 |
| Status at discharge | Alive | 356 (67.4) | 335 (67.4) | 21 (67.7) | 0.969 |
|           | Dead     | 172 (32.6)     | 162 (32.6)  | 10 (32.3)   |     |

Data are presented as n (%) or mean ± standard deviation.

HA, healthcare-acquired; CA, community-acquired; ACH, acute care hospital; LTCF, long-term care facilities; CVD, cardiovascular disease; CKD, chronic kidney disease; CRD, chronic respiratory disease; ICU, intensive care unit; MDRO, multidrug-resistant organism; VRE, vancomycin-resistant *Enterococcus*; MRSA, methicillin-resistant *Staphylococcus aureus*; ESBL, extended-spectrum β-lactamase; MRPA, multidrug-resistant *Pseudomonas aeruginosa*; CRE, carbapenem-resistant *Enterobacteriaceae*; CRAB, carbapenem-resistant *Acinetobacter baumannii*.

a) Multiple responses, b) Fisher exact test.

### Table 6. Factors associated with healthcare-acquired CRE and CRAB isolation (n = 528)

| Variable | OR 95% CI | p |
|----------|-----------|---|
| Hypertension | 0.35 0.15−0.83 | 0.016 |
| Cardiovascular disease | 6.30 1.82−21.85 | 0.004 |

CRE, carbapenem-resistant *Enterobacteriaceae*; CRAB, carbapenem-resistant *Acinetobacter baumannii*; OR, odds ratio; CI, confidence interval.

Reference group = No (CRE/CRAB-isolated patients without the corresponding conditions).
university hospital in the United States [22] and a study in the ICU and transplant ward of a university hospital in the United States [7] showed the order of *Pseudomonas aeruginosa* and *K. pneumoniae*, indicating that the isolation rate of *Acinetobacter* spp. was lower than that of other strains.

*A. baumannii* is commonly found in hospital environments and is known to cause various healthcare-associated infections, such as sepsis, pneumonia, urinary tract infections, wound infections, and postoperative infections [23]. Most strains are resistant to various antibiotics, including carbapenem [24,25]. In the Kor-GLASS analysis, the majority of *Enterobacteriaceae* cases were community-associated, whereas 86.9% of *Acinetobacter* spp. Cases were healthcare-associated [21]. Although *A. baumannii* is a Gram-negative bacterium, it tolerates a dry environment well [26]. Many CRAB epidemics have been reported in healthcare settings, including ICUs, and the vulnerability to these outbreaks has been increasing due to the growing number of patients with underlying diseases, invasive catheters, and mechanical ventilation, as well as the use of broad-spectrum antibiotics [27–29]. In this study, 64% of participants received ICU treatment, and many participants underwent invasive procedures and received antibiotic treatment, which may explain the higher rate of CRAB isolation.

The risk of CRAB isolation increased with mechanical ventilator use and TPN use. TPN use was also confirmed as a risk factor for CRAB bloodstream infection in a of patients at the Taiwan Veterans Hospital [9]. In this study, TPN was used by approximately 88% of the participants. Therefore, we can expect that MDRO prevention and control measures, including thorough hand hygiene, will lead to significant reductions in MDROs, including CRAB, among TPN-using patients [18,30].

Approximately 6% of the participants in this study were found to have CA infections. The percentage of CA infections relative to HA infections varied from 6% [31] to 10% [8] in the United States and from 12% [32] to 30% [17] in Taiwan. According to the results of this study, it would be difficult to say that CRE/CRAB is prevalent in communities in Korea; however, continuous monitoring is required considering the possibility of its spread to the community. CRE and CRAB are designated as legally notifiable infectious diseases and are under mandatory and sentinel surveillance systems, respectively [5,33]. Therefore, it is possible to determine whether spread has occurred to the local community by reporting HA and CA separately to health authorities. Although there were relatively few CA infections in this study, 1 out of 5 CRE/CRAB was isolated at the time of hospitalization among CRE/CRAB isolated patients, suggesting that CRE/CRAB management at the time of hospitalization is important.

Similar to previous studies [7], the primary hospitalization route of patients was from the community, followed by transfer from acute care hospitals and transfer from long-term care facilities. Approximately half of the participants were transferred from acute care hospitals and long-term care facilities. Approximately 70% of the study participants had a history of hospitalization within 6 months, and about 65% to 90% of patients had a history of hospitalization within 1 year in a previous study in the United States [8]. Thus, for patients with a history of hospitalization within 6 months to 1 year, a system for active surveillance cultures is required at the time of hospitalization. However, for hospitals to which a large number of patients are transferred, such as the hospital in this study, the application of active surveillance culture for all inpatients and outpatients would be burdensome in terms of time and cost. As an alternative, selectively performing active monitoring cultures for high-risk groups by applying a previously developed risk model can be considered [8,13,14].

Most patients had invasive devices within 3 months of the survey, with urinary catheters being the most prevalent, followed by central venous catheters, gastrointestinal tubes, arterial catheters, and mechanical ventilators. According to previous studies, although the duration of keeping invasive devices varied from 30 days to 3 months from the point of the survey, the most common type of invasive device was the urinary catheter [7,9,10,13]. Among drugs other than antibiotics, gastric acid inhibitors (including proton pump inhibitors or histamine H₂ receptor antagonists) were frequently used among the patients in this study, consistent with a previous study [7].

The mortality rate at discharge in this study was 32.6%, which was higher than the 17.0% reported in a previous domestic study [13] on the isolation of CRE from patients admitted to the ICU, with a 30-day mortality rate of 14.2% to 24.8% [22], in patients whose culture was positive for carbapenem-resistant Gram-negative bacteremia during hospitalization between 2000 and 2017 at a hospital in the United States. Patients with CRAB have been reported to have a lower survival rate than those with other carbapenem-resistant Gram-negative bacteremia [22]. Considering the previous study [22], the relatively high mortality rate in this study may be related to the higher proportion of CRAB compared to CRE.

**Strengths and Limitations**

This study is significant in that it identified and analyzed the characteristics of all hospitalized patients in whom CRE or CRAB was isolated, including those in the emergency
department and the ICU. However, this study has the following limitations that need to be considered when interpreting its results. First, the number of CRE/CRAB cases may have been underestimated because active surveillance cultures were only performed for patients admitted to the ICU, and only the first case was included in the analysis when both CRE and CRAB were isolated. Second, this study was limited to CRE and CRAB among carbapenem-resistant Gram-negative bacteremia, according to the MDRO management policy of the research institution. Third, for cases of HA infections in patients who were transferred from long-term care facilities or acute care hospitals, the length of stay and treatment-related characteristics at the previous institutions could not be considered due to data limitations. Fourth, the data on patients’ general characteristics were based on the “history taking” results in patients’ electronic medical records, as collected at the time of hospitalization. Therefore, the responses for certain items, such as history of hospitalization within 6 months and comorbidities, may have been biased. Finally, this study cannot be generalized to other types of medical institutions because the data were collected from a tertiary referral hospital.

Conclusion

Over 20% of CRE/CRAB isolates in a tertiary referral hospital in Korea were found at the time of admission. Furthermore, CRAB isolation occurred more frequently in patients with mechanical ventilation and/or TPN than in those without. Thus, active surveillance of CRE/CRAB at the time of hospitalization is strongly required, particularly for patients who are expected to require mechanical ventilation or TPN.

Notes

Ethics Approval

This study was approved by the Institutional Review Board of Inje University Busan Baik Hospital (20-0114), and performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was waived.

Conflicts of Interest

The authors have no conflicts of interest to declare.

Funding

None.

Availability of Data

The datasets are not publicly available but are available from the corresponding author upon reasonable request.

References

1. World Health Organization (WHO). Antimicrobial resistance [Internet]. Geneva: WHO; 2021 [cited 2021 Dec 30]. Available from: https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance.
2. Tamma PD, Huang Y, Opene BN, et al. Determining the optimal carbapenem MIC that distinguishes carbapenemase-producing and non-carbapenemase-producing carbapenem-resistant Enterobacteriaceae. Antimicrob Agents Chemother 2016;60:6425–9.
3. Tangden T, Giske CG. Global dissemination of extensively drug-resistant carbapenemase-producing Enterobacteriaceae: clinical perspectives on detection, treatment and infection control. J Intern Med 2015;277:501–12.
4. Kelly AM, Mathema B, Larson EL. Carbapenem-resistant Enterobacteriaceae in the community: a scoping review. Int J Antimicrob Agents 2017;50:127–34.
5. Ministry of Government Legislation. Infectious disease control and prevention act [Internet]. Sejong: Korean Law Information Center; 2021 [cited 2021 Dec 30]. Available from: https://www.law.go.kr/lsSc.do?section=8menul=18subMenul=15tabMenul=81eventGubun=060101query=%22%28%22EC%98%88%EC%97%BC%EB%83%91+%EC%98%88%EB%B0%A9%EB%B2%95%22%22%EB%9D%8C%EB%B2%88%ED%8C%8C%ED%8A%B8%EB%B3%BD%EF%BC%8C%EB%8C%95%22%22%20%27%3D%22%22
6. Centers for Diseases Control and Prevention (CDC). Antibiotic resistance threats in the United States 2019 [Internet]. Atlanta: U.S. Department of Health and Human Services, CDC, 2019 [cited 2021 Dec 30]. Available from: https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf.
7. Goodman KE, Simner PJ, Klein EY, et al. Predicting probability of perirectal colonization with carbapenem-resistant Enterobacteriaceae (CRE) and other carbapenem-resistant organisms (CROs) at hospital unit admission. Infect Control Hosp Epidemiol 2019;40:541–50.
8. Miller BM, Johnson SW. Demographic and infection characteristics of patients with carbapenem-resistant Enterobacteriaceae in a community hospital: development of a bedside clinical score for risk assessment. Am J Infect Control 2016;44:134–7.
9. Huang ST, Chiang MC, Kuo SC, et al. Risk factors and clinical outcomes of patients with carbapenem-resistant Acinetobacter baumannii bacteremia. J Microbiol Immunol Infect 2012;45:356–62.
10. Ting SW, Lee CH, Liu JW. Risk factors and outcomes for the acquisition of carbapenem-resistant Gram-negative bacillus bacteremia: a retrospective propensity-matched case control study. J Microbiol Immunol Infect 2018;51:621–8.
11. Zhang Y, Wang Q, Yin Y, et al. Epidemiology of carbapenem-resistant enterobacteriaceae infections: report from the China CRE network. Antimicrob Agents Chemother 2018;62:e01882–17.
12. Maechler F, Pena Diaz LA, Schroder C, et al. Prevalence of carbapenem-resistant organisms and other Gram-negative MDRO in German ICUs: first results from the national nosocomial infection surveillance system (KISS). Infection 2015;43:163–8.

https://doi.org/10.24171/j.phrp.2022.0097
13. Song JY, Jeong IS. Development of a risk prediction model of carbapenem-resistant Enterobacteriaceae colonization among patients in intensive care units. Am J Infect Control 2018;46:1240–4.
14. Seo SM, Jeong IS, Song JY, et al. Development of a nomogram for carbapenem-resistant Enterobacteriaceae acquisition risk prediction among patients in the intensive care unit of a secondary referral hospital. Asian Nurs Res (Korean Soc Nurs Sci) 2021;15:174–80.
15. Ahn JY, Song JE, Kim MH, et al. Risk factors for the acquisition of carbapenem-resistant Escherichia coli at a tertiary care center in South Korea: a matched case-control study. Am J Infect Control 2014;42:621–5.
16. European Centre for Disease Prevention and Control (ECDC). Carbapenem-resistant Enterobacteriaceae, second update [Internet]. Stockholm: ECDC; 2019 [cited 2021 Dec 30]. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/carbapenem-resistant-enterobacteriaceae-risk-assessment-rev-2.pdf.
17. Tang HJ, Hsieh CF, Chang PC, et al. Clinical Significance of community- and healthcare-acquired carbapenem-resistant Enterobacteriaceae isolates. PLoS One 2016;11:e0151897.
18. Korea Centers for Disease Control and Prevention (KCDC). Guidelines for healthcare associated infection (VRSA/CRE) prevention and control [Internet]. Cheongju: KCDC; 2019 [cited 2021 Dec 30]. Available from: http://www.cdc.go.kr/upload_comm/syview/doc.html?fn=157311529530900.pdf&rs=/upload_comm/docu/0019/.
Korean.
19. Clinical Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 27th ed. Wayne, PA: Clinical Laboratory Standards Institute; 2017.
20. Kim JH. Multicollinearity and misleading statistical results. Korean J Anesthesiol 2019;72:558–69.
21. Kim JW, Bae SM, Lee SY, et al. Trends of antimicrobial resistance rates of major clinical pathogens isolated from general hospitals in Korea in 2016-2019: results from Kor-GLASS. Public Health Wldy Rep 2021;14:2007–24. Korean.
22. Babiker A, Clarke LG, Saul M, et al. Changing epidemiology and decreased mortality associated with carbapenem-resistant gram-negative bacteria, 2000-2017. Clin Infect Dis 2021;73:e4521–30.
23. Agodi A, Voulgaris E, Barchitta M, et al. Spread of a carbapenem- and colistin-resistant Acinetobacter baumannii ST2 clonal strain causing outbreaks in two Sicilian hospitals. J Hosp Infect 2014;86:260–6.
24. Towner KJ. Acinetobacter: an old friend, but a new enemy. J Hosp Infect 2009;73:355–63.
25. Magiorakos AP, Srinivasan A, Carey RB, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect 2012;18:268–81.
26. Kramer A, Schwebke I, Kampf G. How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. BMC Infect Dis 2006;6:130.
27. Bianco A, Quirino A, Giordano M, et al. Control of carbapenem-resistant Acinetobacter baumannii outbreak in an intensive care unit of a teaching hospital in Southern Italy. BMC Infect Dis 2016;16:747.
28. Alon D, Mudrik H, Chowers M, et al. Control of a hospital-wide outbreak of carbapenem-resistant Acinetobacter baumannii (CRAB) using the Israeli national carbapenem-resistant Enterobacteriaceae (CRE) guidelines as a model. Infect Control Hosp Epidemiol 2020; 41:926–30.
29. Playford EG, Craig JC, Iredell JR. Carbapenem-resistant Acinetobacter baumannii in intensive care unit patients: risk factors for acquisition, infection and their consequences. J Hosp Infect 2007;65:204–11.
30. Centers for Disease Control and Prevention (CDC). Facility guidance for control of carbapenem-resistant Enterobacteriaceae (CRE): November 2015 update-CRE toolkit [Internet]. Atlanta: CDC; 2015 [cited 2021 Dec 21]. Available from: https://www.cdc.gov/hai/pdfs/cre/CRE-guidance-508.pdf.
31. Thaden JT, Lewis SS, Hazen KC, et al. Rising rates of carbapenem-resistant enterobacteriaceae in community hospitals: a mixed-methods review of epidemiology and microbiology practices in a network of community hospitals in the southeastern United States. Infect Control Hosp Epidemiol 2014;35:978–83.
32. Lai CC, Wu UI, Wang JT, et al. Prevalence of carbapenemase-producing Enterobacteriaceae and its impact on clinical outcomes at a teaching hospital in Taiwan. J Formos Med Assoc 2012;111:268–75.
33. Korea Disease Control and Prevention Agency (KDCA). Infectious disease portal [Internet]. Cheongju: KDCA; 2021 [cited 2021 Dec 27]. Available from: https://www.kdca.go.kr/npt/biz/npp/portal/nplwcrclcMain.do. Korean.