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Original Article

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

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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

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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

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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 *A. 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 *Enterobacteriacae*; CRAB, carbapenem-resistant *Acinetobacter baumannii*; HA, healthcare-acquired; CA, community-acquired.

Table 2. Comparison of general characteristics, MDRO-related characteristics, and clinical outcome between patients with CRE and those with CRAB

Variable	Category	Total (*n* = 528)	CRE (*n* = 171)	CRAB (*n* = 357)	*p*
Sex	Male	335 (63.4)	107 (62.6)	228 (63.9)	0.773
	Female	193 (36.6)	64 (37.4)	129 (36.1)	
Age (y)		67.7 ± 14.0	68.7 ± 13.7	67.2 ± 14.1	0.251
History of hospitalization within 6 months	No	147 (27.8)	33 (19.3)	114 (30.9)	0.006
	ACH	301 (57.0)	113 (66.1)	188 (52.7)	
	LTCF	80 (15.2)	25 (14.6)	55 (15.4)	
Route of hospitalization	ACH, transfer	184 (34.8)	64 (37.4)	12 0(33.6)	0.680
	LTCF, transfer	76 (14.4)	23 (13.5)	53 (14.8)	
	Community	268 (50.8)	84 (49.1)	184 (51.5)	
Comorbidities[a)]	Hypertension	264 (50.0)	100 (58.5)	164 (45.9)	0.007
	Diabetes mellitus	186 (35.2)	70 (40.9)	116 (32.5)	0.057
	CVD	158 (29.9)	48 (28.1)	110 (30.8)	0.520
	Cancer	140 (26.5)	49 (28.7)	91 (25.5)	0.441
	CKD	64 (12.1)	24 (14.0)	40 (11.2)	0.351
	Liver disease	52 (9.8)	23 (13.5)	29 (8.1)	0.055
	CRD	49 (9.3)	15 (8.8)	34 (9.5)	0.781
Charlson comorbidity index score		4.6 ± 2.3	4.4 ± 2.1	4.7 ± 2.4	0.281
Treatment in ICU	No	190 (36.0)	79 (46.2)	111 (31.1)	0.001
	Yes	338 (64.0)	92 (53.8)	246 (68.9)	
MDRO history[a)]	VRE	116 (22.0)	48 (28.1)	67 (19.0)	0.019
	MRSA	55 (10.4)	20 (11.7)	35 (9.8)	0.505
	ESBL	88 (16.7)	46 (26.9)	42 (11.8)	< 0.001
	MRPA	11 (2.1)	3 (1.8)	8 (2.2)	1.000[b)]
Specimen source of CRE/CRAB	Respiratory	317 (60.0)	15 (8.8)	302 (84.6)	< 0.001
	Rectal swab	126 (23.9)	125 (73.1)	1 (0.3)	
	Urine	33 (6.3)	15 (8.8)	18 (5.0)	
	Blood	18 (3.4)	2 (1.2)	16 (4.5)	
	Others	34 (6.4)	14 (8.2)	20 (5.6)	
Strain of CRE/CRAB[a)]	*Acinetobacter baumannii*	357 (67.6)	0 (0)	357 (100.0)	< 0.001
	Klebsiella spp.	126 (23.9)	126 (100.0)	0 (0)	< 0.001
	Escherichia coli	36 (6.8)	36 (21.1)	0 (0)	< 0.001
	Enterobacter spp.	11 (2.1)	11 (6.4)	0 (0)	< 0.001[b)]
	Others	3 (0.6)	3 (1.8)	0 (0)	< 0.001[b)]
Status at discharge	Alive	356 (67.4)	119 (69.6)	237 (66.4)	0.462
	Dead	172 (32.6)	52 (30.4)	120 (33.6)	

Data are presented as *n* (%) or mean ± standard deviation.
MDRO, multidrug-resistant organism; CRE, carbapenem-resistant *Enterobacteriaceae*; CRAB, carbapenem-resistant *Acinetobacter baumannii*; ACH, acute care hospital; LTCF, long-term care facilities; CVD, cardiovascular disease; CKD, chronic kidney disease; CRD, chronic respiratory disease; ICU, intensive care unit; VRE, vancomycin-resistant *Enterococcus*; MRSA, methicillin-resistant *Staphylococcus aureus*; ESBL, extended-spectrum β-lactamase; MRPA, multidrug-resistant *Pseudomonas aeruginosa*.
[a)]Multiple responses, [b)]Fisher exact test.

urinary catheter, 84.2% used a central venous catheter, and 54.5% used carbapenem as an antimicrobial agent.

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

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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[a)]	0.56 (0.35–0.89)	0.014
Treatment in ICU[a)]	0.34 (0.16–0.72)	0.005
History of vancomycin-resistant *Enterococcus*[a)]	0.49 (0.29–0.83)	0.008
History of extended-spectrum β-lactamase[a)]	0.48 (0.26–0.87)	0.017
Use of mechanical ventilator[a)]	3.52 (1.96–6.33)	< 0.001
Use of total parenteral nutrition[a)]	3.64 (1.87–7.08)	< 0.001

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

(*p* = 0.007), VRE history (*p* = 0.019), and broad-spectrum β-lactamase–producing organism history (*p* < 0.001), but higher frequencies of ICU stay (*p* = 0.001), arterial catheter use (*p* = 0.001), mechanical ventilator use (*p* < 0.001), and TPN use (*p* < 0.001). CRE was more prevalent in rectal swab specimens at the time of hospitalization, whereas CRAB was more prevalent in respiratory specimens after hospitalization (both *p* < 0.001) (Tables 2 and 3). Multiple logistic regression analysis showed that CRAB isolation was positively associated with mechanical ventilator use and TPN use. The risk of CRAB isolation was 3.52 times higher in those who used a mechanical ventilator and 3.64 times higher in those who used TPN compared to their counterparts (Table 4).

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*, 1.0% in blood

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[a]	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[b]
	Liver disease	52 (9.8)	49 (9.9)	3 (9.7)	1.000[b]
	CRD	49 (9.3)	45 (9.1)	4 (12.9)	0.517[b]
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[a]	VRE	116 (22.0)	113 (22.7)	3 (9.7)	0.088
	MRSA	55 (10.4)	53 (10.7)	2 (6.5)	0.760[b]
	ESBL	88 (16.7)	77 (15.5)	11 (35.5)	0.004
	MRPA	11 (2.1)	9 (1.8)	2 (6.5)	0.132[b]
Specimen source of CRE/CRAB	Respiratory	317 (60.0)	307 (61.8)	10 (32.3)	0.001[b]
	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[a]	*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[b]
	Enterobacter spp.	11 (2.1)	10 (2.0)	1 (3.2)	0.489[b]
	Others	3 (0.6)	2 (0.4)	1 (3.2)	0.166[b]
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[a]	0.35	0.15–0.83	0.016
Cardiovascular disease[a]	6.30	1.82–21.85	0.004

CRE, carbapenem-resistant *Enterobacteriaceae*; CRAB, carbapenem-resistant *Acinetobacter baumannii*; OR, odds ratio; CI, confidence interval.
[a]Reference group = No (CRE/CRAB-isolated patients without the corresponding conditions).

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

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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 *Actinetobacter* 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 *Actinetobacter* 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 H_2 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.

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None.

Availability of Data

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

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