



Active Surveillance for Carbapenem-resistant *Enterobacteriaceae* at a Single Center for Four Years

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Dear Editor,

The main resistance mechanism of carbapenem-resistant *Enterobacteriaceae* (CRE) is through acquired carbapenemases [1]. Carbapenemase-producing *Enterobacteriaceae* (CPE) harboring plasmid-encoded resistance genes easily spread the genes to different species [2]. A screening test for CPE should be performed for infection control and prevention [3]. The Korea Disease Control and Prevention Agency conducted a surveillance beginning in June 2017 [4]. A European study suggests that within-hospital transmission and inter-hospital spread of CPE is more frequent within countries rather than between countries [5]. Therefore, both hospital and national surveillance are important to help prevent the CPE spread.

We retrospectively analyzed active surveillance data for CRE at Hanyang University Seoul Hospital, Seoul, Korea, from July 2017 to December 2020. The candidates for CRE surveillance were patients who were transferred from long-term care facilities in the previous three months, those admitted to the intensive care unit, and those who had positive results for CRE isolates in the previous six months. Stool or rectal swab samples were inoculated onto chromID CARBA medium (bioMérieux, Marcy l'Etoile, France) and incubated at 35°C for 24 hours. Bacterial species were identified using matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) with a MALDI Biotyper (Bruker Daltonics, Bremen, Germany).

Antimicrobial susceptibility testing was performed using the MicroScan WalkAway system (Beckman Coulter, Brea, CA, USA). Screening for carbapenemase-producing organisms was carried out according to the Clinical Laboratory Standards Institute guidelines using the modified Hodge test (MHT) during 2017–2018 and the modified carbapenem inactivation method (mCIM) during 2019–2020 [6]. The carbapenemase inhibition test (CIT) using phenylboronic acid and EDTA was performed in conjunction with the MHT or mCIM [7]. Carbapenemase genes were detected using the Xpert Carba-R assay (Cepheid, Sunnyvale, CA, USA). The study was approved by the Hanyang University Hospital Institute Review Board, Seoul, Korea (IRB number 202105037).

During the four years of the study period, 10,174 surveillance tests were conducted. Among the patients tested, 229 (2.3%) were new cases that carried CRE and 182 (1.8%) were positive for CPE. The CRE trends were analyzed quarterly from 2017 to 2020. Trends in the number of CRE screening tests that identified CRE or CPE cases are shown in Fig. 1. The average number of CRE screening tests per three months was 727 (range: 580–893), including an average of 16 CRE (range: 9–30) and 10 CPE cases (range: 3–19). The CRE-positive rate was 2.3% (range: 1.1%–4.3%). Interestingly, the positive rates were highest in the third quarters of 2018 and 2020. Among the 229 total CRE isolates, *Klebsiella pneumoniae* (55.0%) was predominant,

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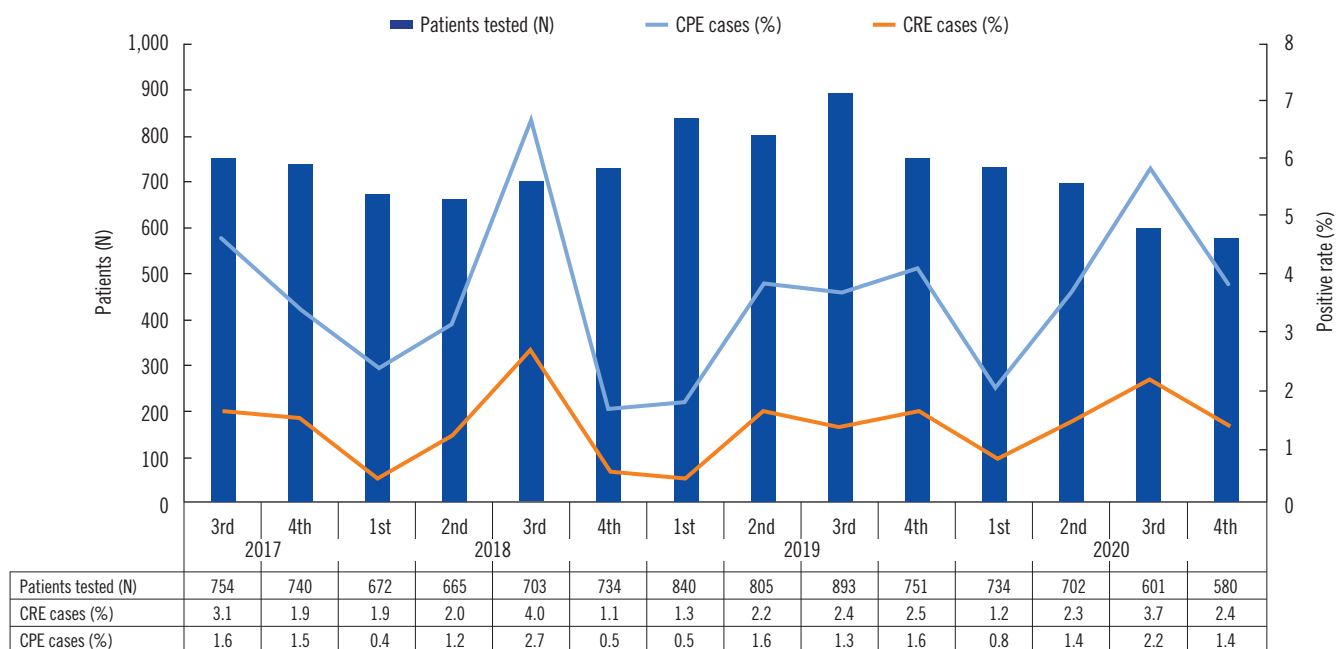


Fig. 1. Quarterly trends in the number of carbapenem-resistant *Enterobacteriaceae* (CRE) screening tests administered and the rates of positive CRE and carbapenemase-producing *Enterobacteriaceae* (CPE) cases from July 2017 to December 2020.

followed by *Escherichia coli* (28.4%), other *Klebsiella* spp. (8.3%), *Citrobacter* spp. (4.4%), and *Enterobacter* spp. (3.5%).

Carbapenemase screening using MHT or mCIM was performed on 229 CRE isolates (Table 1), of which, 147 isolates (64.2%) were positive and 82 (35.8%) were negative. The CIT results revealed that 151 isolates (65.9%) were positive. Carbapenemase-specific PCR was carried out for 178 CRE isolates, with carbapenemase genes being detected in 75.8% (135/178) of the isolates. Among the 135 isolates, 93 harbored *bla_{KPC}* (68.9%), which was the most prevalent gene, followed by 34 isolates with *bla_{NDM}* (25.2%) and two isolates with *bla_{OXA-48}* (1.5%). These data are very similar to the 2018–2019 Korean national data of 70.0% for *bla_{KPC}* and 24.0% for *bla_{NDM}* [4]. However, global surveillance has revealed that *bla_{KPC}* is the most common gene at 53.18%, followed by the *bla_{OXA-48}*-like gene at 20.09% and *bla_{NDM}* at 19.42% [8]. Among the 72 carbapenemase-producing *K. pneumoniae* isolates, 63 (87.5%) harbored *bla_{KPC}* while six (8.3%) carried *bla_{NDM}*. Meanwhile, among the 42 *E. coli* isolates, 20 (47.6%) carried *bla_{KPC}* and 18 (42.9%) carried *bla_{NDM}*.

This study investigated the trends for CRE and CPE cases at a single hospital for the past four years. Our results were similar to the 1.4% rate reported in another study conducted in 2017 [9]. CRE cases in this study may have exhibited seasonal and temperature variations, consistent with those shown in the study by Kim, *et al.* [10]. The current study has some limitations. First,

the medical records of the patients were analyzed retrospectively. Second, we used only a chromogenic agar and a commercially available kit for detection of CPE. Therefore, CPE genes other than *bla_{KPC}*, *bla_{NDM}*, *bla_{VIM}*, *bla_{IMP}*, and *bla_{OXA-48}* could not be detected.

In conclusion, the prevalence of CRE and CPE at the study hospital were 2.3% and 1.8%, respectively. The *bla_{KPC}* gene was detected in 68.9% of the CPE isolates. Continuous monitoring for CPE is necessary to prevent the spread of CPE.

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AUTHOR CONTRIBUTIONS

Lee Y designed the study; Choi I collected the data; and Lee Y and Choi I wrote, edited, and reviewed the manuscript. All authors revised and accepted the final version of the manuscript.

CONFLICTS OF INTEREST

No potential conflicts of interest relevant to this article were reported.

Table 1. Carbapenemase screening and PCR testing of carbapenemase genes for identified CRE isolates

	2017	2018	2019	2020	Total (%)
MHT or mCIM* (N=229)					
Positive	24	35	47	41	147 (64.2)
Negative	13	27	22	20	82 (35.8)
CIT (N=229)					
Positive	27	35	50	39	151 (65.9)
Negative	10	27	19	22	78 (34.1)
Carbapenemase gene (N=178)					
PCR Positive	23	34	41	37	135 (75.8)
<i>bla_{KPC}</i>	14	26	27	26	93 (68.9)
<i>bla_{NDM}</i>	8	5	12	9	34 (25.2)
<i>bla_{IMP-1}</i>	0	0	1	1	2 (1.5)
<i>bla_{VIM}</i>	0	1	0	0	1 (0.7)
<i>bla_{OXA-48}</i>	0	1	0	0	1 (0.7)
Other [†]	1	1	1	1	4 (3.0)
PCR Negative	11	14	10	8	43 (24.2)
CP-<i>K. pneumoniae</i> (N=72)					
<i>bla_{KPC}</i>	10	19	17	17	63 (87.5)
<i>bla_{NDM}</i>	3	0	2	1	6 (8.3)
<i>bla_{IMP-1}</i>	0	1	0	0	1 (1.4)
CP-<i>E. coli</i> (N=42)					
<i>bla_{KPC}</i>	1	5	7	7	20 (47.6)
<i>bla_{NDM}</i>	5	3	4	6	18 (42.9)
<i>bla_{OXA-48}</i>	0	0	1	1	2 (4.8)

*MHT and mCIM were used from 2017 to 2018 and from 2019 to 2020, respectively; [†]Harbored two genes, such as *bla_{KPC}* and *bla_{NDM}* in 2017, *bla_{NDM}* and *bla_{OXA-48}* in 2018, *bla_{KPC}* and *bla_{IMP-1}* in 2019, and *bla_{KPC}* and *bla_{OXA-48}* in 2020.

Abbreviations: CRE, carbapenem-resistant *Enterobacteriaceae*; MHT, modified Hodge test; mCIM, modified carbapenem inactivation method; CIT, carbapenemase inhibition test; CP, carbapenemase-producing; *K. pneumoniae*, *Klebsiella pneumoniae*; *E. coli*, *Escherichia coli*.

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REFERENCES

- Budhram DR, Mac S, Bielecki JM, Patel SN, Sander B. Health outcomes attributable to carbapenemase-producing *Enterobacteriaceae* infections: A systematic review and meta-analysis. *Infect Control Hosp Epidemiol* 2020;41:37-43.
- Bonomo RA, Burd EM, Conly J, Limbago BM, Poirel L, Segre JA, et al. Carbapenemase-producing organisms: A global scourge. *Clin Infect Dis* 2018;66:1290-7.
- Tucker A, George R, Welfare W, Cleary P, Cawthorne J, Dodgson A. Screening for carbapenemase-producing *Enterobacteriaceae* in previous carriers readmitted to hospital: evaluation of a change in screening policy. *J Hosp Infect* 2019;103:156-9.
- Seo AY, Jun BH, Lee Y. Epidemiology of carbapenem-resistant *Enterobacteriaceae* in Korea between 2018 and 2019. *Public Health Weekly Report* 2021;14:413-20.
- David S, Reuter S, Harris SR, Glasner C, Feltwell T, Argimon S, et al. Epidemic of carbapenem-resistant *Klebsiella pneumoniae* in Europe is driven by nosocomial spread. *Nat Microbiol* 2019;4:1919-29.
- CLSI. Performance standards for antimicrobial susceptibility testing. 31st ed. CLSI supplement M100S. Wayne, PA: Clinical and Laboratory Standards Institute. 2021.
- Song W, Hong SG, Yong D, Jeong SH, Kim HS, Kim HS, et al. Combined use of the modified Hodge test and carbapenemase inhibition test for detection of carbapenemase-producing *Enterobacteriaceae* and metallo- β -lactamase-producing *Pseudomonas* spp. *Ann Lab Med* 2015;35:212-9.
- Wu W, Feng Y, Tang G, Qiao F, McNally A, Zong Z. NDM metallo-beta-lactamases and their bacterial producers in health care settings. *Clin Microbiol Rev* 2019;32:e00115-8.
- Hwang JH, Park JS, Lee E, Bae JY, Song KH, Choe PG, et al. Active surveillance for carbapenem-resistant *Enterobacteriaceae*, vancomycin-resistant enterococci and toxigenic *Clostridium difficile* among patients transferred from long-term care facilities in Korea. *J Hosp Infect* 2018; 99:487-91.
- Kim YA, Kim JJ, Won DJ, Lee K. Seasonal and temperature-associated increase in community-onset *Acinetobacter baumannii* complex colonization or infection. *Ann Lab Med* 2018;38:266-70.