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Brief communication

Four genotypes of carbapenem-resistant *Acinetobacter baumannii* strains lacking OXA-23 production in Korea

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Abstract

During nationwide Fantimicrobial surveillance (Korea Global Antimicrobial Resistance Surveillance System [Kor-GLASS]), the recent emergence of non-oxacillinase (OXA)-23 production by carbapenem-resistant *Acinetobacter baumannii* (CRAB) isolates was noted. In this study, we evaluated resistance mechanisms other than OXA-23 production to elucidate the shift in considerable CRAB clones. The presence of OXA carbapenemase genes, such as bla_{OXA-23}, bla_{OXA-24}, bla_{OXA-58}, and bla_{OXA-51}-IS*Aba1*, was determined by PCR. Other carbapenemase genes, such as bla_{IMP}, bla_{VIM}, bla_{NDM}, bla_{KPC}, bla_{GES}, and bla_{OXA-48}, were determined using sequencing. Strains lacking carbapenemase genes were subjected to whole genome sequencing, and resistance genes were analyzed using ResFinder. Four CRAB strains were collected through a Kor-GLASS study in 2022, in which OXA-23 production was not identified. The carbapenemase genotypes of the four CRAB strains lacking bla_{OXA-23} were bla_{OXA-51}-IS*Aba1*, $bla_{OXA-66/ACD25}$, $bla_{OXA-182}$, and bla_{NDM-1}. To the best of our knowledge, this is the first study to identify CRAB producing New Delhi metallo-β-lactamase (NDM)-1 in Korea. In conclusion, domestic CRAB resistance mechanisms may undergo subtle changes. Continuous observations are required to monitor the emergence of new clones.

Keywords: Carbapenem, Resistance, *Acinetobacter baumannii*, NDM-1, OXA-23

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Acinetobacter baumannii is an important pathogen that causes healthcare-associated infections, such as ventilator-associated pneumonia, line-associated bloodstream infections, and catheter-associated urinary tract infections [1]. Carbapenem is usually considered a treatment option for extended-spectrum ß-lactamase producers. The rapid increase in carbapenem-resistant *A. baumannii* (CRAB) isolation has been correlated with an increased nationwide prescription rate of carbapenems [2]. The carbapenem resistance rate is very

high in strains isolated in Korea, and multidrug resistance is common, hindering the selection of therapeutic options [3]. According to Kor-GLASS (Korea Global Antimicrobial Resistance Surveillance System) data, the imipenem-resistance rate of *A. baumannii* blood isolates was > 90% [3].

There are three classes of carbapenemase: Ambler class A (serine carbapenemases), class B (metallo-β-lactamase), and class D (oxacillinase carbapenemases) [4]. *Klebsiella pneumoniae* carbapenemase (class A), New Delhi metallo-β-lactamase (NDM, class B), and oxacillinase-48 (class D) are common in carbapenem-resistant Enterobacteriaceae [5]. Metallo-β-lactamases, such as Guiana extended-spectrum β-lactamase, imipenemase (IMP), Verona integron-encoded metallo-β-lactamase (VIM), and NDM, are frequently found in carbapenem-resistant *Pseudomonas aeruginosa* [6].

Carbapenemase types in carbapenem-resistant organisms other than *A. baumannii* vary. However, CRAB isolates uniformly carry $bla_{\text{OXA-23}}$ in Korea because of the notorious multidrug resistance clone, *A. baumannii* global clone 2 with sequencing type 191, which has become predominant in clinical settings worldwide, including Korea [7]. OXA-type β-lactamases are the primary resistance mechanism for CRAB, and a drastic increase in *A. baumannii* isolates with $bla_{\text{OXA-23}}$ has been observed since the mid-2000s [7]. IS*Aba1*-associated $bla_{\text{OXA-51}}$, another contributor to CRAB, has decreased since the mid-2000s [7].

The recent emergence of non-OXA-23 production of CRAB isolates was noted in a Kor-GLASS study. Therefore, in the present study, resistance mechanisms other than OXA-23 production were evaluated to elucidate the shift in significant CRAB clones.

In total, 366 *A. baumannii* isolates were collected according to the Kor-GLASS protocol in 2022 [8]. *A. baumannii* strains were identified using Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (Bruker Biotyper; Bruker Daltonics GmbH), and positive OXA-51 polymerase chain reaction (PCR) results confirmed the species identification. PCR methods determined the existence of OXA carbapenemase genes, such as $bla_{\text{OXA-23}}$, $bla_{\text{OXA-24}}$, $bla_{\text{OXA-58}}$, and $bla_{\text{OXA-51}}$-IS*Aba1* [8]. PCR sequencing methods also determined the presence of other carbapenemase genes, such as bla_{IMP}, bla_{VIM}, bla_{NDM}, bla_{KPC}, bla_{GES}, and $bla_{\text{OXA-48}}$ [8]. Strains without determination of carbapenemase genes using the aforementioned methods were subjected to whole genome sequencing, as previously described [9]. Using the NextSeq 550 instrument (Illumina), the entire genome was sequenced with 8 μg of input genomic DNA. Sequences were assembled using Spades (version 3.11.1) and annotated using Prokka (version 1.13.7). Resistance genes were determined using ResFinder 4.5 [10].

The resistance rate to imipenem was 85.2% in *A. baumannii* isolates in 2022, and 98.7% in OXA-24 producers. The carbapenemase genotypes of the four CRAB strains lacking $bla_{\text{OXA-23}}$ were $bla_{\text{OXA-66/ACD-25}}$, $bla_{\text{OXA-51}}$-IS*Aba1*, $bla_{\text{OXA-182,}}$ and $bla_{\text{NDM-1}}$ (Table 1).

Table 1. Distribution of imipenem resistance in 366 *A. baumannii* isolates (2022)

Imipenem susceptibility	Genotypes	No. (%)
Resistant		312 (85.2)
	OXA-23	308 (98.7)
	Non-OXA-23	4 (1.3)
	$bla_{\text{OXA-66/ACD-25}}$	1 (0.3)
	$bla_{\text{OXA-51}}$-IS*Aba1*	1 (0.3)
	$bla_{\text{OXA-182}}$	1 (0.3)
	$bla_{\text{NDM-1}}$	1 (0.3)
Susceptible		54 (14.8)
Total		366 (100)

IS*Aba1*-mediated intrinsic $bla_{\text{ADC-25}}$ and $bla_{\text{OXA-66}}$ overexpression has been reported in South Korea [11,12]. The carbapenem resistance mechanism of $bla_{\text{OXA-182}}$ has also been reported in Korea [13]. In this report, when 178 imipenem-non-susceptible *A. baumannii* isolates were collected from 12 Korean hospitals in 2007, 12 isolates from a Jeju Island hospital produced OXA-182 carbapenemase, which showed 93% identity with OXA-143 and 89% with OXA-40 [13].

To our knowledge, this is the first report of NDM-1 producing *A. baumannii* being detected. NDM-1 is one of the metallo-ß-lactamases (MBL), which originated in India and spread worldwide, especially in Enterobacteriaceae [5]. However, MBL production is sporadic in CRAB in Korea, and the few reports on MBL types include VIM-2, SIM-1, and IMP-1 [14,15]. Recently, the dissemination of NDM-1 in *A. baumannii* strains has been reported in China [16,17]; however, to the best of our knowledge, this is the first report of NDM-1-producing *A. baumannii*.

In conclusion, the mechanism of resistance via OXA-23 in CRAB may have subtly changed with the emergence of NDM-1-producing *A. baumannii* in Korea. Continuous observation is required to monitor the emergence of new clones.

Ethics statement

This study was approved by the Institutional Review Board of the National Health Insurance Ilsan Hospital (No. 2024-05-016), and the requirement for informed consent was waived.

Conflicts of interest

Jeong Hwan Shin is an associate editor and Young Uh and Nam Hee Ryoo are editorial board members of the *Annals of Clinical Microbiology*. However, they were not involved in the review process of this article. No other potential conflict of interest relevant to this article was reported.

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