Detection of Carbapenemases in Clinical Enterobacteriaceae Isolates Using the VITEK AST-N202 Card

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Background: The rapid and accurate detection of carbapenemase-producing Enterobacteriaceae (CPE) in clinical microbiology laboratories is essential for the treatment and control of infections caused by these microorganisms. This study was performed to evaluate the ability of the VITEK AST-N202 card to detect CPE isolates.

Materials and Methods: A total of 43 (Klebsiella pneumoniae, n = 37; Escherichia coli, n = 3; and Enterobacter cloacae, n = 3) CPE isolates and 79 carbapenemase-non-producing Enterobacteriaceae (CNE) isolates were included in this study. The CPE isolates harbored KPC-2 (n = 11), KPC-3 (n = 20), GES-5 (n = 5), VIM-2 (n = 2), IMP-1 (n = 1), NDM-1 (n = 2), or OXA-232 (n = 2). Of the 79 CNE isolates, eight K. pneumoniae isolates were resistant to ertapenem, imipenem, and meropenem, while the remaining 71 isolates were susceptible to the carbapenems. Antimicrobial susceptibilities were tested using the VITEK AST-N202 card, and the results were interpreted as positive when the isolates showed resistant or intermediate results. Modified-Hodge tests (MHTs) were performed using ertapenem or meropenem disks for the screening of carbapenemase production. Polymerase chain reaction (PCR) and direct sequencing were used to identify β-lactamase genes.

Results: Sensitivity of MHT with ertapenem and meropenem disks for the detection of carbapenemase was 81.4% (35/43) and 81.4% (35/43), respectively, and a combination with both antibiotic disks increased the sensitivity to 88.4% (38/43). Specificity of the MHT was 100% (79/79) for the CNE isolates. Sensitivity of ertapenem, imipenem, and meropenem as assessed by the VITEK AST-N202 card was 100% (43/43), 93% (40/43), and 95.3% (41/43), respectively. Specificity (89.8%, 71/71) of the test with each carbapenem was improved to 100% (71/71) when eight carbapenem-resistant CNE isolates were excluded from the testing.

Conclusion: The VITEK AST-N202 card showed high sensitivity for the detection of carbapenemases in Enterobacteriaceae strains. PCR and sequencing experiments for the detection of carbapenemases are recommended when clinical Enterobacteriaceae isolates show non-susceptibility to carbapenems.

Key Words: Carbapenemase-producing Enterobacteriaceae; VITEK AST-N202 card; KPC; GES; NDM
Introduction

Carbapenems have been used as the drug of choice for the treatment of infections caused by multi-drug resistant Gram-negative rods because these drugs easily permeate the porins of outer cellular membranes, exhibit high affinity with penicillin-binding proteins, and are stable against various β-lactamases produced by Gram-negative rods [1-4]. However, carbapenem-resistant Enterobacteriaceae (CRE) has appeared as a consequence of the frequent use of these drugs for the treatment of widespread extended-spectrum β-lactamase- and/or AmpC β-lactamase-producing Enterobacteriaceae [5]. Dissemination of CRE is considered a serious clinical threat because available antimicrobials for the treatment of infections caused by CRE are very limited.

Although Enterobacteriaceae can acquire carbapenem resistance via various mechanisms, the most important one is the production of plasmid-mediated carbapenemases [5]. Diverse types of carbapenemases have appeared in Enterobacteriaceae, including 1) KPC- and GES-type enzymes belonging to class A, 2) IMP-1, VIM-1, and NDM-type metallo-β-lactamases (MBLs) belonging to class B, and 3) OXA-48 and its variants belonging to class D. Enterobacteriaceae strains producing these various carbapenemases have already appeared in Korea [6].

The rapid and accurate detection of carbapenemase-producing Enterobacteriaceae (CPE) in clinical laboratories is essential for the treatment of infections and infection control. However, the identification of CPE strains can be difficult because some CPE clinical isolates exhibit low-level resistance or susceptibility to carbapenems [7]. This study was performed to evaluate the ability of VITEK AST-N202 cards (bioMérieux, Marcy l’Etoile, France) to reliably detect CPE strains isolated from a clinical setting.

Materials and Methods

1. Bacterial strains and susceptibility testing

A total of 122 Enterobacteriaceae clinical isolates, 43 CPE and 79 carbapenemase-non-producing Enterobacteriaceae (CNE), were included in this study (Table 1). The CPE clinical isolates were identified as follows: 37 Klebsiella pneumoniae, three Escherichia coli, and three Enterobacter cloacae. The CPE clinical isolates produced KPC-2 (n = 11), KPC-3 (n = 20), GES-5 (n = 5), VIM-2 (n = 2), IMP-1 (n = 1), NDM-1 (n = 2), and OXA-232 (n = 2) carbapenemases. Of the 79 CNE clinical isolates, eight K. pneumoniae isolates were resistant to ertapenem, imipenem, and meropenem, while the remaining 71 isolates were susceptible to these carbapenems; E. coli (n = 35), K. pneumoniae (n = 17), Klebsiella oxytoca (n = 1), E. cloacae (n = 1), Enterobacter aerogenes (n = 6), Enterobacter asburiae (n = 2), Serratia marcescens (n = 4), Citrobacter freundii (n = 1), Citrobacter koseri (n = 1), Morganella morganii (n = 2), and Proteus mirabilis (n = 1). Bacterial species were identified using matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) (Bruker Daltonics, Bremen, Germany) and by analysis of partial 16S rDNA sequences. Antimicrobial susceptibilities of the clinical isolates were determined using VITEK AST-N202 cards (bioMérieux, Table 2). Genes encoding β-lactamases, including TEM-, SHV-, CTX-M-, GES-, and KPC-types of class A; IMP-, VIM-, and NDM-types...
Table 1. Continued

| Strain                  | β-Lactamase         | Modified-Hodge test | Antimicrobial susceptibility<sup>a</sup> |
|-------------------------|---------------------|---------------------|----------------------------------------|
|                         | Carbapenemase       | Others              | Ertapenem | Meropenem | Ertapenem | Imipenem | Meropenem |
| **Klebsiella pneumoniae** |                     |                     |           |           |           |           |           |
| *Klebsiella pneumoniae* | KPC-3               | SHV-12, TEM-1, CMY-2| +         | +         | R         | R         | R         |
|                         | KPC-3               | SHV-12, SHV-1, TEM-1| +         | +         | R         | R         | R         |
|                         | KPC-3               | SHV-12, SHV-1, TEM-1| +         | +         | R         | R         | R         |
|                         | KPC-3               | SHV-12, SHV-1, TEM-1| +         | -         | R         | R         | R         |
|                         | KPC-3               | SHV-12, SHV-1, TEM-1| +         | +         | R         | R         | R         |
|                         | KPC-3               | SHV-12, SHV-1, TEM-1| +         | +         | R         | R         | R         |
|                         | KPC-3               | SHV-12, SHV-1, TEM-1| +         | +         | R         | R         | R         |
|                         | KPC-3               | SHV-12, SHV-1, TEM-1| +         | +         | R         | R         | R         |
|                         | KPC-3               | SHV-12, SHV-1, TEM-1| +         | +         | R         | R         | R         |
|                         | KPC-3               | SHV-12, SHV-1, TEM-1| +         | +         | R         | R         | R         |
|                         | KPC-3               | SHV-12, SHV-1, TEM-1| +         | +         | R         | R         | R         |
|                         | KPC-3               | SHV-12, SHV-1, TEM-1| +         | +         | R         | R         | R         |
|                         | GES-5               | SHV-12              | +         | +         | R         | R         | R         |
|                         | GES-5               | SHV-12              | +         | +         | R         | R         | R         |
|                         | GES-5               | SHV-12              | +         | +         | R         | R         | R         |
|                         | GES-5               | SHV-12, CMY-2       | -         | -         | R         | I         | R         |
|                         | NDM-1               | SHV-12              | -         | +         | R         | R         | R         |
|                         | NDM-1               | SHV-12              | -         | +         | R         | R         | R         |
| **Escherichia coli**    |                     |                     |           |           |           |           |           |
| *Escherichia coli*      | GES-5               | SHV-12              | -         | -         | R         | S         | S         |
|                         | OXA-232             | SHV-12              | -         | +         | R         | S         | R         |
|                         | OXA-232             | SHV-12              | -         | -         | R         | S         | S         |
| **Enterobacter cloacae**|                     |                     |           |           |           |           |           |
| *Enterobacter cloacae*  | VIM-2               | SHV-12              | -         | -         | R         | R         | R         |
|                         | VIM-2               | SHV-12              | -         | -         | R         | R         | R         |
|                         | IMP-1               | SHV-12              | -         | -         | R         | R         | R         |
| **Klebsiella pneumoniae** | CTX-M-6, SHV-12, DHA-1, TEM-1 | -         | -         | R         | R         | R         |
|                         | CTX-M-14, SHV-2a, DHA-1 | -         | -         | R         | R         | R         |
|                         | CTX-M-14, SHV-12, DHA-1 | -         | -         | R         | R         | R         |
|                         | CTX-M-15, DHA-1     | -         | -         | R         | R         | R         |
|                         | SHV-12, DHA-1       | -         | -         | R         | R         | R         |
|                         | DHA-1               | -         | -         | R         | R         | R         |
|                         | DHA-1               | -         | -         | R         | R         | R         |
|                         | SHV-1, CMY-1        | -         | -         | R         | R         | R         |

<sup>a</sup>Antimicrobial susceptibility was tested using the VITEK AST-N202 card.
Table 2. Carbapenem disk contents of the VITEK AST-N202 card

| Carbapenem disk | Indication MIC (μg/mL) | MIC interpretive criteria (μg/mL) | FDA indication for use |
|-----------------|------------------------|----------------------------------|------------------------|
| Ertapenem       | 0.5, 1, 6              | 0.5                              | 8                      |
|                 |                        | Susceptible                      | Resistance             |
| Imipenem        | 1, 2, 6, 12            | 0.25                             | 16                     |
| Meropenem       | 0.5, 2, 6, 12          | 0.25                             | 16                     |

* Klebsiella oxytoca (excluding ESBL-producing strains)

MIC, minimal inhibitory concentration; FDA, Food and Drug Administration; ESBL, extended-spectrum β-lactamase.

Table 3. Nucleotide sequences of primers used in this study

| Primer name | Target gene | Nucleotide sequence (5' to 3') | Product size (bp) | Reference |
|-------------|-------------|--------------------------------|-------------------|-----------|
| KPC-F       | KPC-type    | GTCACGTGATTCGCCTAGTTC           | 909               | This study|
| KPC-R       |             | TGGTGGGCAATAGATGATT             |                   |           |
| GES-F       | GES-type    | CGTCATCCTACGCAGATT             | 855               | [8]       |
| GES-R       |             | GTCGTGATGGCCAATGATT             |                   |           |
| IMP-1F      | IMP-1 variants | AAGCGGTTATGTCATCTCTCG          | 605               | This study|
| IMP-1R      |             | TTTAACCCGCTGCTTAAGTAA          |                   |           |
| VIM-2F      | VIM-2 variants | ATCAAGCCGCTGCTGATCC           | 749               | [9]       |
| VIM-2R      |             | ACGACTGAGCGATTGTTG            |                   |           |
| NDM-F       | NDM-type    | GCCCAATATATGACACCG            | 738               | This study|
| NDM-R       |             | CTCAAGCCGCTGCTGACC          |                   |           |
| OXA-48F     | OXA-48 variants | GATTATCGGAATGCTGCCG         | 845               | [10]      |
| OXA-48R     |             | CTCAAGCCGCTGCTGACC          |                   |           |
| TEM-F       | TEM-type    | CTGAGAGCAAGGACGCTGGG          | 997               | [11]      |
| TEM-R       |             | TGACTCCCCGCTGCTGAGTA          |                   |           |
| SHV-F       | SHV-type    | CGCGGCTTATCACGTTG            | 936               | This study|
| SHV-R       |             | CGCGGCTTATCACGTTG            |                   |           |
| CTXM-1F     | CTXM-1 variants | CCGTCAGCCCTGTTTAGG         | 782               | [8]       |
| CTXM-1R     |             | ACGGGCTTCTGCTGTTTAGG         |                   |           |
| CTXM-9F     | CTXM-9 variants | CAAAGAGAGTGCAAACGGATG       | 862               | [8]       |
| CTXM-9R     |             | CCTCCGGGAGGGTTTCC           |                   |           |
| CMY-1F      | CMY-1 variants | CAACGACAATCCATCTCTG          | 1,007             | This study|
| CMY-1R      |             | GAGCCGGTCTTGTGAGAGA          |                   |           |
| CMY-2F      | CMY-2 variants | AGTAAAGCTTAAACGGGCTGT        | 749               |           |
| CMY-2R      |             | TTATGCAACCAGGTGTTTT         |                   |           |
| DHA-F       | DHA type    | ACAATCGCCACCTGTTTTC         | 976               | This study|
| DHA-R       |             | TGGTGGACAGCACATTAA          |                   |           |
of class B; CMY-1-, CMY-2-, and DHA-types of class C; and OXA-48-types of class D, were identified by PCR and sequencing (Table 3) [8-11].

2. Detection of carbapenemases

Carbapenemases were screened using VITEK AST-N202 cards and modified Hodge tests (MHTs). If an isolate exhibited intermediate or resistance designations to more than one of the carbapenems, ertapenem, imipenem, or meropenem, based on the VITEK AST-N202 card, then the isolate was considered CPE. MHTs were performed with ertapenem and meropenem disks, separately, as described previously [12]. Briefly, a suspension of *E. coli* ATCC 25922 at a 0.5 McFarland turbidity unit concentration was spread on the entire surface of a MacConkey agar (Becton and Dickinson Company, Sparks, MD, USA) plate. Disks containing ertapenem or meropenem (10 μL, Becton and Dickinson Company) were placed on the center of the agar using a cotton swab, and then the clinical isolates were thickly inoculated from the edge of the disk to the periphery of the agar using a platinum loop. After overnight incubation, if a thickening of the inoculation line of a clinical isolate was observed on the edge of an inhibition zone, then the isolate was considered a CPE strain.

### Results

1. Ability of MHTs to identify CPE strains

Of the 43 CPE isolates, 35 (81.4%) exhibited positive results in the MHTs with ertapenem or meropenem disks. In the ertapenem MHTs, eight CPE isolates showed false-negative results, including KPC-2-producing *K. pneumoniae* (n = 2), KPC-3-producing *K. pneumoniae* (n = 1), GES-5-producing *K. pneumoniae* (n = 1), GES-5-producing *E. coli* (n = 1), OXA-232-producing *E. coli* (n = 1), and VIM-2-producing *E. cloacae* (n = 2). Five CPE isolates showed false-negative results in both ertapenem and meropenem MHTs, including GES-5-producing *K. pneumoniae* (n = 1), GES-5-producing *K. pneumoniae* (n = 1), NDM-1-producing *K. pneumoniae* (n = 1), GES-5-producing *E. coli* (n = 1), OXA-232-producing *E. coli* (n = 1), and VIM-2-producing *E. cloacae* (n = 2). All 79 CNE isolates showed negative results regardless of carbapenem susceptibility. Sensitivities of the ertapenem and meropenem MHTs for CPE were both 81.4% (35/43), and that was increased to 88.4% (38/43) when the MHTs were performed with both antibiotics. Specificity of the MHTs was 100% (79/79) (Table 4).

2. Ability of the VITEK AST-N202 card to identify CPE strains

In antimicrobial susceptibility testing using VITEK AST-N202 cards, all 43 CPE isolates exhibited resistance to ertapenem, while only 38 and 41 of the CPE isolates showed resistance to imipenem and meropenem, respectively. Two and three CPE isolates exhibited intermediate and susceptibility patterns to imipenem, respectively, and two isolates were susceptible to meropenem. Three isolates exhibiting susceptibility patterns to imipenem included one GES-5-producing *E. coli* isolate and two OXA-232-producing *E. coli* isolates. Two isolates exhibited susceptibility to meropenem, including one GES-5-producing *E. coli* isolate and one OXA-232-producing *E. coli* isolate. Of the 79 CNE isolates, eight exhibited resistance to ertapenem, imipenem, and meropenem, while the remaining 71 isolates were susceptible to these carbapenems. Sensitivities to ertapenem, imipenem, and meropenem of the CPE strains when assessed using the VITEK AST-N202 cards were 100% (43/43), 88.4% (38/43), and 95.3% (41/43), respectively. Sensitivity of the VITEK 2 AST-N202 cards for the CPE

| Methods                  | Antimicrobial agent(s) | Sensitivity | Specificity |
|--------------------------|------------------------|-------------|-------------|
| Modified-Hodge test      | Ertapenem              | 81.4% (35/43) | 100% (79/79) |
|                          | Meropenem              | 81.4% (35/43) |
|                          | Ertapenem + meropenem  | 88.4% (38/43) |
| VITEK AST-N202 card      | Ertapenem              | 100.0% (43/43) | 89.9% (71/79)* |
|                          | Meropenem              | 95.3% (41/43)  |
|                          | Imipenem               | 93.0% (40/43)  |

CPE, carbapenemase-producing enterobacteriaceae.

*The results of eight carbapenem-resistant clinical CRE isolates are excluded.*
strains when using all three carbapenems was 100%. Specificities of the three carbapenems for CPE strains using the VITEK AST-N202 cards were all 89.8% (71/79); however, that reached 100% (71/71) when the eight carbapenem-resistant clinical CNE isolates were excluded (Table 4).

**Discussion**

Although the prevalence of CPE strains is still low (<1%) in Korea, various types of carbapenemases have been identified (Table 4). Since the first isolation of *S. marcescens*-producing class B VIM-2 MBL in Korea in 2002, VIM-2-producing *E. cloacae* have repeatedly been reported (Table 5) [13-25]. An outbreak of NDM-1-producing *K. pneumoniae* sequence type 340 (ST340) was reported in 2012, and the NDM-1-producing *E. coli* ST101 strain appeared in Korea in 2013 [26]. In a nationwide survey of antimicrobial resistance performed in 2003, a class A GES-5 carbapenemase was first identified in two clinical *K. pneumoniae* isolates from a hospital in Gyeonggi province, and an outbreak caused by the strain occurred in that same hospital in the next year [19]. Furthermore, a GES-5-producing *E. coli* ST31 strain was detected in 2011 [18]. An infection caused by the KPC-2-producing *K. pneumoniae* ST11 strain was first reported in 2010; thereafter, outbreaks caused by the KPC-2-producing *K. pneumoniae* ST258 strain have been repeatedly reported in several hospitals in Korea [13, 14]. In 2014, an outbreak caused by *K. pneumoniae* ST14-producing OXA-232, a variant of class D OXA-48, occurred in a hospital in Seoul, Korea, and *E. coli* isolates producing this carbapenemase were also detected from rectal swab specimens [25]. Therefore, the development of rapid and accurate methods for the detection of CPE is needed for adequate treatment of infections caused by these microorganisms and for prevention of further dissemination.

Recently, the Clinical and Laboratory Standard Institute (CLSI) recommended MHTs with ertapenem disks as the standard detection method for CPE strains [12]. This study was performed to compare the ability of ertapenem and meropenem MHTs with VITEK AST-N202 cards. Both ertapenem and meropenem MHTs detected 35/43 (81.4%) CPE isolates, and sensitivity was increased to 88.4% (38/43) when the MHTs were performed with both carbapenem disks. The results indicate that the detection of CPE strains is dependent on whether MHTs fail in some cases, especially in cases of CPE strains harboring carbapenemases (GES-5, OXA-232, and MBLs) other than KPC. Ertapenem susceptibility testing using the VITEK AST-N202 card detected all 43 CPE isolates as resistant, while three and two CPE isolates respectively exhibited susceptibility patterns to imipenem and meropenem using this commercial card. CPE isolates harboring GES-5 or OXA-232 exhibited susceptibility to these carbapenems. The results suggest that CPE detection must be conducted based on ertapenem susceptibility when using VITEK AST-N202 cards.

**Table 5. Carbapenemase-producing Enterobacteriaceae in Korea**

| Carbapenemase | Species | Strain | MIC (μg/mL) | Reference |
|---------------|---------|--------|-------------|-----------|
|               |         |        | Imipenem    | Meropenem |          |
| KPC-2         | *K. pneumoniae* | KPN-DK2 | 16          | 16        | [13]     |
| KPC-2         | *K. pneumoniae* | KPN1010 | >256        | >256      | [14]     |
| KPC-2         | *K. pneumoniae* | 6 isolates | 32-128   | 64-256    | [15]     |
| KPC-2         | *K. pneumoniae* | 3 isolates | 2-4       | 2-16      | [16]     |
| KPC-2         | *K. pneumoniae* | MP14    | ND          | ≥16       | [17]     |
| GES-5         | *K. pneumoniae* | 2 isolates | ND        | ND        | [18]     |
| GES-5         | *K. pneumoniae* | 6 isolates | 0.5-1     | ND        | [19]     |
| GES-5         | *E. coli* | BD07372 | 0.5         | 0.25      | [20]     |
| VIM-2         | *S. marcescens* | YMC00/4/1391 | 64       | 64        | [21]     |
| VIM-2         | *E. cloacae* | KU680 | 4           | 4         | [22]     |
| VIM-2         | *E. cloacae* | YMC08/12/3793 | 4        | 0.75      | [23]     |
| VIM-2         | *E. cloacae* | YMC03/4/397 | 4         | 4         | [23]     |
| NDM-1         | *K. pneumoniae* | 4 isolates | 1- >128  | 2- >128   | [24]     |
| OXA-232       | *E. coli* | 2 isolates | 1          | 0.5-1     | [25]     |
|               | *K. pneumoniae* | 16 isolates | 4-16     | 8-16      |           |
In conclusion, the VITEK AST-N202 card showed excellent performance for the detection of CPE strains. It is recommended that ertapenem-resistant Enterobacteriaceae clinical isolates should be directly subjected to molecular diagnostic methods for the identification of carbapenemase genes, because MHTs did now show sufficient sensitivity for the detection of CPEs.

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References
1. Bergogne-Bérézin E, Towner KJ. Acinetobacter spp. as nosocomial pathogens: microbiological, clinical, and epidemiological features. Clin Microbiol Rev 1996;9:148-65.
2. Gehrlein M, Leying H, Cullman W, Wendt S, Opferkuch W. Imipenem resistance in Acinetobacter baumannii is due to altered penicillin binding proteins. Chemotherapy 1991;37:405-12.
3. Urban C, Go E, Mariano N, Rahal JJ. Interactions of sulbac-tam, clavulanic acid and tazobactam with penicillin binding proteins of imipenem-resistant and susceptible Acinetobacter baumannii. FEMS Microbiol Lett 1995;125:193-7.
4. Clark RB. Imipenem resistance among Acinetobacter baumannii association with reduced expression of a 33-36 kDa outer membrane protein. J Antimicrob Chemother 1996;38:245-51.
5. Walsh TR. Emerging carbapenemase: a global perspective. Int J Antimicrob Agents 2010;36 (Suppl 3):S8-14.
6. Nordmann P, Naas T, Poirel L. Global spread of carbapenemase-producing Enterobacteriaceae. Emerg Infect Dis 2011;17:1791-8.
7. Carrér A, Frotineau N, Nordmann P. Use of ChromID extended-spectrum β-lactamase medium for detecting carbapenemase-producing Enterobacteriaceae. J Clin Microbiol 2010;48:1913-4.
8. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing: twenty-three informational supplement (M100-S23). Wayne, PA, USA: CLSI; 2013.
9. Bae IK, Jang SJ, Kim J, Jeong SH, Cho B, Lee K. Interspecies dissemination of the bla gene encoding PER-1 extended-spectrum β-lactamase. Antimicrob Agents Chemother 2011;55:1305-7.
10. Tam VH, Chang KT, Abdelraouf K, Brioso CG, Ameka M, McCaskey LA, Western JS, Caeiro JP, Garey KW. Prevalence, resistance mechanisms, and susceptibility of multidrug-resistant bloodstream isolates of Pseudomonas aeruginosa. Antimicrob Agents Chemother 2010;54:1160-4.
11. Park KO, Son HC, Bae IK, Jeong SH. Molecular epidemiology of infection caused by OXA-23 or IMP-1 β-lactamase-producing Acinetobacter baumannii. Korean J Clin Microbiol 2005;8:121-9.
12. Bae IK, Lee YN, Jeong SH, Lee K, Yong D, Lee J, Hong SG, Park YJ, Choi TY, Uh Y, Shin JH, Lee WG, Ahn JY, Lee SH, Woo GJ, Kwak HS. Emergence of CTX-M-12, PER-1 and OXA-30 β-lactamase-producing Klebsiella pneumoniae. Korean J Clin Microbiol 2006;9:102-9.
13. Rhee JY, Park YK, Shin JY, Choi JY, Lee MY, Peck KR, Song JH, Ko KS. KPC-producing extreme drug-resistant Klebsiella pneumoniae isolate from a patient with diabetes mellitus and chronic renal failure on hemodialysis in South Korea. Antimicrob Agents Chemother 2010;54:2278-9.
14. Roh KH, Lee CK, Sohn JW, Song W, Yong D, Lee K. Isolation of a Klebsiella pneumoniae isolate of sequence type 258 producing KPC-2 carbapenemase in Korea. Korean J Lab Med 2011;31:298-301.
15. Yoo JS, Kim HM, Yoo JI, Yang JW, Kim HS, Chung GT, Lee YS. Detection of clonal KPC-2-producing Klebsiella pneumoniae ST258 in Korea during nationwide surveillance in 2011. J Med Microbiol 2013;62:1338-42.
16. Hong SK, Yong D, Kim K, Hong SS, Hong SG, Khosbayan T, Song W, Roh KH, Jeong SH, Lee K, Chong Y. First outbreak of KPC-2-producing Klebsiella pneumoniae sequence type 258 in a hospital in South Korea. J Clin Microbiol 2013;51:3877-9.
17. Lee Y, Kim BS, Chun J, Yong JH, Lee YS, Yoo JS, Yong D, Hong SG, D’Souza R, Thomson KS, Lee K, Chong Y. Clonality and resistome analysis of KPC-producing Klebsiella
pneumoniae strain isolated in Korea using whole genome sequencing. Biomed Res Int 2014;2014:352862.

18. Ryoo NH, Kim EC, Hong SG, Park YJ, Lee K, Bae IK, Song EH, Jeong SH. Dissemination of SHV-12 and CTX-M-type extended-spectrum β-lactamases among clinical isolates of Escherichia coli and Klebsiella pneumoniae and emergence of GES-3 in Korea. J Antimicrob Chemother 2005;56:698-702.

19. Jeong SH, Bae IK, Kim D, Hong SG, Song JS, Lee JH, Lee SH. First outbreak of Klebsiella pneumoniae clinical isolates producing GES-5 and SHV-12 extended-spectrum β-lactamas in Korea. Antimicrob Agents Chemother 2005;49:4809-10.

20. Kim J, Hong SG, Bae IK, Kang JR, Jeong SH, Lee W, Lee K. Emergence of Escherichia coli sequence type ST131 carrying both the blaGES-5 and blaCTX-M-15 genes. Antimicrob Agents Chemother 2011;55:2974-5.

21. Yum JH, Yong D, Lee K, Kim HS, Chong Y. A new integron carrying VIM-2 metallo-β-lactamase gene cassette in a Serratia marcescens isolate. Diagn Microbiol Infect Dis 2002;42:217-9.

22. Jeong SH, Lee K, Chong Y, Yum JH, Lee SH, Choi HJ, Kim JM, Park KH, Han BH, Lee SW, Jeong TS. Characterization of a new integron containing VIM-2, a metallo-β-lactamase gene cassette, in a clinical isolate of Enterobacter cloacae. J Antimicrob Chemother 2003;51:397-400.

23. Lee Y, Choi H, Yum JH, Kang G, Bae IK, Jeong SH, Lee K. Molecular mechanisms of carbapenem resistance in Enterobacter cloacae clinical isolates from Korea and clinical outcome. Ann Clin Lab Sci 2012;42:281-6.

24. Kim MN, Yong D, An D, Chung HS, Woo JH, Lee K, Chong Y. Nosocomial clustering of NDM-1-producing Klebsiella pneumoniae sequence type 340 strains in four patients at a South Korean tertiary care hospital. J Clin Microbiol 2012;50:1433-6.

25. Jeong SH, Lee KM, Lee J, Bae IK, Kim JS, Kim HS, Song W. Clonal and horizontal spread of the blaOXA-232 gene among Enterobacteriaceae in a Korean hospital. Diagn Microbiol Infect Dis 2015;82:70-2.

26. Yoo JS, Kim HM, Koo HS, Yand JW, Yoo JI, Kim HS, Park HK, Lee YS. Nosocomial transmission of NDM-1-producing Escherichia coli ST101 in a Korean Hospital. J Antimicrob Chemother 2013;68:2170-2.