J. Microbiol. Biotechnol. (2014), 24(6), 765–770
http://dx.doi.org/10.4014/jmb.1306.06036

jmb

Characterization of CTX-M-14- and CTX-M-15-Producing *Escherichia coli* and *Klebsiella pneumoniae* Isolates from Urine Specimens in a Tertiary-Care Hospital

Semi Kim[1], Ji Youn Sung[2], Hye Hyun Cho[3], Kye Chul Kwon[1], and Sun Hoe Koo[1]*

[1]*Department of Laboratory Medicine, College of Medicine, Chungnam National University, Daejeon 301-721, Republic of Korea*
[2]*Department of Biomedical Laboratory Science, Far East University, Eumseong 369-700, Republic of Korea*
[3]*Department of Biomedical Laboratory Science, Jeonju Kijeon College, Jeonju 560-701, Republic of Korea*

Received: June 13, 2013
Revised: December 26, 2013
Accepted: March 13, 2014

First published online
March 13, 2014

**Corresponding author*
Phone: +82-42-280-7798;
Fax: +82-42-257-5365;
E-mail: shkoo@cnu.ac.kr

pISSN 1017-7825, eISSN 1738-8872

This study aimed to characterize CTX-M producers of urinary *E. coli* and *K. pneumoniae* isolates and to determine the prevalence of plasmid-mediated antimicrobial resistance genes among them. Minimum inhibitory concentrations (MICs) were determined, and PCR and sequencing were performed. Among the 42 (82.3%) *E. coli* and 24 (77.4%) *K. pneumoniae* isolates containing $bla_{\text{CTX-M}}$, $bla_{\text{CTX-M-14}}$ and $bla_{\text{CTX-M-15}}$ were detected in 23 and 19 *E. coli* isolates, respectively, and in 7 and 17 *K. pneumoniae* isolates, respectively. CTX-M producers of urinary *E. coli* and *K. pneumoniae* were resistant to multiple antibiotics and contained other antimicrobial resistance genes. CTX-M-15 producers contained more antimicrobial resistance genes than did CTX-M-14 producers.

Keywords: CTX-M-14, CTX-M-15, extended-spectrum β-lactamase (ESBL), *E. coli*, *K. pneumoniae*

Urinary tract infections (UTIs) are the most prevalent bacterial infections in humans, and *Escherichia coli* and *Klebsiella pneumoniae* are the most important causes of nosocomial UTIs. Narrow- and extended-spectrum cephalosporins have been used to treat infections by these species [19, 20]. However, management of UTIs has become increasingly problematic owing to the increasing production of extended-spectrum β-lactamases (ESBLs) [17, 25]. According to several studies in Korea, 10–17% of *E. coli* isolates and 22–31% of *K. pneumoniae* isolates produce ESBLs [9, 10, 13].

Until the late 1990s, TEM-52, SHV-12, and SHV-2a were the most common ESBLs in *E. coli* and *K. pneumoniae* found in Korea, but CTX-M have spread rapidly in the past few decades [4, 9, 28]. Recently, CTX-M-14 and CTX-M-15 have been frequently shown to be the most prevalent genotype of ESBLs in *E. coli* and *K. pneumoniae* strains isolated in the world, including Korea [9, 13, 21, 27].

With ESBLs, co-production of plasmid-mediated AmpC β-lactamases (PABLs) and/or plamid-mediated quinolone resistance genes, especially *qnr* and *aac(6')-Ib-cr*, and/or *arm*A, has been frequently reported in many countries, including Korea [6, 7, 10, 13, 14, 16, 17, 22, 24].

Plasmid-mediated antimicrobial resistance genes, including those of ESBLs, spread widely, and ESBL producers are generally resistant to quinolones and aminoglycosides. Although the literature contains many studies on ESBL producers, reports comparing the prevalence of antimicrobial resistance genes between CTX-M-14- and CTX-M-15-producing *E. coli* and *K. pneumoniae* isolates are rare. Therefore, in this study, we aimed to describe the characteristics of CTX-M-producing urinary *E. coli* and *K. pneumoniae* isolates, and to determine the prevalence of PABL, *qnr*, *aac(6')-Ib-cr*, and *arm*A genes in CTX-M producers.

Non-duplicate ceftazidime- and/or cefotaxime-resistant isolates of *E. coli* and *K. pneumoniae* were obtained from urine specimens collected at the Chungnam National University Hospital from November 2011 to July 2012. All isolates were identified with the Vitek GNI card system (bioMèrieux Vitek Inc., Hazelwood, MO, USA).

MICs were determined using the agar dilution method according to Clinical and Laboratory Standards Institute (CLSI) guidelines [2]. The following antibiotics were tested:

cefotaxime, ceftazidime, amikacin, gentamicin, levofloxacin, and ciprofloxacin (Sigma-Aldrich, St. Louis, MO, USA). *E. coli* ATCC 25923 and *Pseudomonas aeruginosa* ATCC 27853 were used as control strains.

PCR and sequencing were performed as previously described [26]. For detection of the genes of ESBL, bla_{CTX-M}, bla_{TEM}, and bla_{SHV} were included. Then, for strains harboring bla_{CTX-M}, PABL, *qnr*, *aac(6′)-Ib-cr*, and *arm*A genes were detected. All primers used for ESBLs [12], PABLs [18], *qnr* [1], *aac(6′)-Ib-cr* [25], and *arm*A [25] were previously published.

To determine clonality, epidemiological typing was performed by rep-PCR for *E. coli* [26] and ERIC-PCR for *K. pneumoniae* [3].

During the study period, 298 *E. coli* and 98 *K. pneumoniae* isolates were obtained, and 51 *E. coli* and 31 *K. pneumoniae* isolates were resistant to ceftazidime and/or cefotaxime.

42 (82.3%) *E. coli* and 24 (77.4%) *K. pneumoniae* isolates were positive by PCR for bla_{CTX-M}. Among the isolates, $bla_{CTX-M-14}$ and $bla_{CTX-M-15}$ were detected in 23 and 19 *E. coli* isolates, respectively, and in 7 and 17 *K. pneumoniae* isolates, respectively.

Among the *E. coli* isolates, the gene encoding DHA-1 AmpC β-lactamase was detected in 1 CTX-M-14 producer. The *qnr*B6 gene was detected in 1 CTX-M-15 producer, and the *aac(6′)-Ib-cr* gene was detected in 12 CTX-M-15 producers and in 8 CTX-M-14 producers (Table 1).

Among the *K. pneumoniae* isolates, the gene encoding DHA-1 AmpC β-lactamase was detected in 2 CTX-M-15 producers. The *qnr*B1 and *qnr*B4 genes were both detected in 2 CTX-M-15 producers each. The *qnr*S1 gene was detected in three CTX-M-14 producers and in 1 CTX-M-15 producer. The *aac(6′)-Ib-cr* gene was detected in 4 CTX-M-14 producers and in 17 CTX-M-15 producers. The *arm*A gene was detected in 2 CTX-M-15 producers (Table 2).

Strains of *E. coli* and *K. pneumoniae* showed diverse band patterns according to rep-PCR and ERIC-PCR, respectively. However, 17 *E. coli* strains displayed an identical rep-PCR type: type a (Fig. 1).

Similar to previous reports, a total of 17.1% (51) of *E. coli* and 31.6% (31) of *K. pneumoniae* isolates were found to produce ESBL. Among them, 42 (82%) *E. coli* and 24 (77%) *K. pneumoniae* isolates contained bla_{CTX-M}. CTX-M-15 producers were predominantly observed among *K. pneumoniae* isolates (70.8%), whereas a similar occurrence of CTX-M-14 (54.7%) and CTX-M-15 (45.2%) was observed among *E. coli* isolates. Unlike previous reports, other CTX-M types including CTX-M-3 and CTX-M-9, and other ESBLs such as TEM-52, SHV-2a, and SHV-12 were not detected, although other studies report their genes at low rates in Korea [4, 6, 11]. Although this study was limited to a single area, however, these results show ESBL types are completely changed to CTX-M, and that CTX-M-15 is distributed in *K. pneumoniae* isolates rather than in *E. coli* isolates.

Generally, most CTX-M β-lactamases are known to hydrolyze cefotaxime more efficiently than ceftazidime, but CTX-M-15 also hydrolyzes ceftazidime efficiently [1, 21]. In this study, CTX-M producers efficiently hydrolyzed cefotaxime (MIC50 > 128 μg/ml); however, when comparing the MIC50s for ceftazidime, the values were 8 to 128 times higher in CTX-M-15 producers than in CTX-M-14 producers. Therefore, CTX-M-15 appears to be superior to CTX-M-14 at hydrolysis of ceftazidime. Additional studies are needed to investigate the correlation between CTX-M and hydrolysis of ceftazidime.

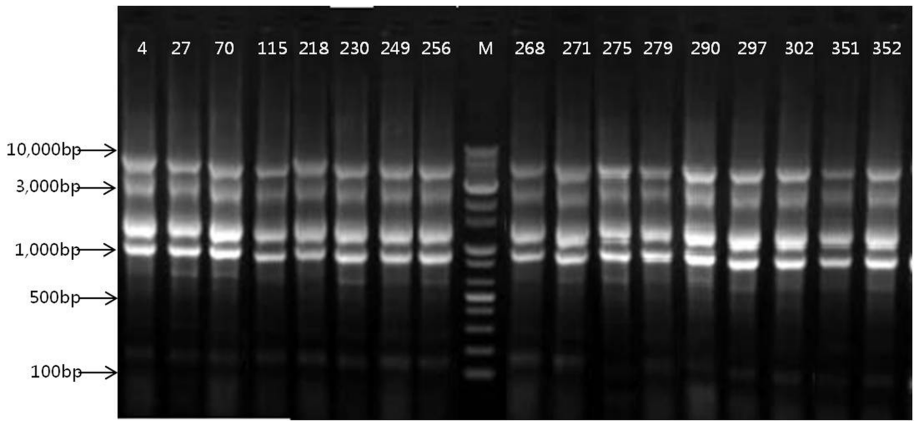

Fig. 1. Repetitive extragenic palindromic element sequence-based (REP)-PCR patterns of genomic DNA from 14 CTX-M-producing *E. coli* isolates.

Lane M, 1 kb DNA size marker. lanes 3 to 352, identical rep-PCR patterns of 17 *E. coli* clinical isolates, respectively.

Table 1. Characteristics of CTX-M-14- and/or CTX-M-15-producing *E. coli* isolates in urine specimens.

Isolates	MIC of agents (μg/ml)						Antimicrobial resistance genes		
	CTX	CAZ	AMK	GEN	LEV	CIP	PABL	*qnr*, *aac(6′)-Ib-cr*	REP-PCR pattern
CTX-M-14 producers									
EC3	128	<2	<2	128	<2	<1			
EC22	16	<2	<2	32	<2	<1			
EC69	64	<2	>256	256	>32	>32			
EC70	64	8	<2	<2	>32	>32			a
EC74	128	4	<2	32	>32	>32		*aac(6′)-Ib-cr*	
EC75	>256	32	4	<2	>32	>32	bla_{DHA-1}	*aac(6′)-Ib-cr*	
EC85	128	<2	<2	<2	<2	<1			
EC95	256	<2	<2	<2	>32	<1			
EC115	128	<2	4	<2	<2	16		*aac(6′)-Ib-cr*	a
EC117	128	<2	<2	<2	<2	<1			
EC230	128	<2	4	128	>32	16			a
EC244	>256	256	32	128	>32	<1			
EC268	32	4	4	<2	16	32			a
EC273	64	<2	<2	<2	<2	<1			
EC293	64	<2	<2	<2	<2	4			
EC295	>256	16	8	64	>32	>32		*aac(6′)-Ib-cr*	
EC296	128	<2	<2	64	4	4		*aac(6′)-Ib-cr*	
EC297	16	<2	<2	64	32	32		*aac(6′)-Ib-cr*	a
EC303	64	<2	<2	<2	>32	>32		*aac(6′)-Ib-cr*	
EC351	>256	4	<2	<2	32	32			a
EC352	32	<2	4	<2	32	32			a
EC357	64	4	<2	<2	8	8			
EC358	>256	32	8	256	>32	>32		*aac(6′)-Ib-cr*	
CTX-M-15 producers									
EC4	256	16	4	<2	32	32			a
EC27	>256	128	16	64	>32	>32		*aac(6′)-Ib-cr*	a
EC169	256	16	<2	32	<2	<1		*aac(6′)-Ib-cr*	
EC218	256	32	8	64	>32	>32		*aac(6′)-Ib-cr*	a
EC249	>256	64	16	256	>32	>32		*aac(6′)-Ib-cr*	a
EC252	128	16	4	64	<2	4		*aac(6′)-Ib-cr*	
EC254	128	16	4	<2	4	4			
EC256	128	16	<2	<2	>32	>32		*aac(6′)-Ib-cr*	a
EC266	256	16	<2	64	8	8			
EC267	256	32	<2	<2	>32	32			
EC270	128	8	4	<2	<2	<1			
EC271	256	16	4	64	>32	>32		*aac(6′)-Ib-cr*	a
EC275	256	64	8	256	>32	>32		*aac(6′)-Ib-cr*	a
EC278	256	256	<2	<2	<2	8			
EC279	256	32	8	128	>32	>32		*aac(6′)-Ib-cr*	a
EC287	128	8	4	<2	<2	32		*aac(6′)-Ib-cr*	
EC290	256	64	16	4	>32	>32		*qnrB6*, *aac(6′)-Ib-cr*	a
EC302	>256	256	4	64	16	>32		*aac(6′)-Ib-cr*	a
EC356	256	<2	<2	<2	<2	<1			

Abbreviations : MIC, minimum inhibitory concentration; CTX, cefotaxime; CAZ, ceftazidime; AMK, amikacin; GEN, gentamicin; LEV, levofloxacin; CIP, ciprofloxacin; PABL, plamid-mediated AmpC β-lactamase.

Table 2. Characteristics of CTX-M-14- and/or CTX-M-15-producing *K. pneumoniae* isolates in urine specimens.

Isolates	MIC of agents (μg/ml)						Antimicrobial resistance genes		
	CTX	CAZ	AMK	GEN	LEV	CIP	PABL	*qnr*, *aac(6')-Ib-cr*	*arm*A
CTX-M-14 producers									
KP33	>256	4	<2	>256	<2	<1		*aac(6')-Ib-cr*	-
KP111	128	>256	32	<2	>32	>32		*aac(6')-Ib-cr*	-
KP202	64	<2	<2	128	<2	<1			-
KP241	64	<2	<2	64	<2	<1		*qnrS1*	-
KP351	256	4	<2	<2	<2	<1			-
KP352	64	<2	<2	64	<2	<1		*qnrS1*, *aac(6')-Ib-cr*	-
KP355	32	<2	<2	<2	<2	<1		*qnrS1*, *aac(6')-Ib-cr*	-
CTX-M-15 producers									
KP3	>256	>256	8	128	<2	<1		*aac(6')-Ib-cr*	-
KP20	>256	256	4	<2	<2	<1		*aac(6')-Ib-cr*	-
KP61	>256	>256	4	128	<2	2		*aac(6')-Ib-cr*	-
KP112	256	64	8	<2	>32	>32		*qnrS1*, *aac(6')-Ib-cr*	-
KP118	>256	>256	8	128	<2	2		*aac(6')-Ib-cr*	-
KP133	>256	256	4	64	4	8		*aac(6')-Ib-cr*	-
KP135	256	64	64	32	4	32		*aac(6')-Ib-cr*	-
KP141	>256	8	8	128	<2	2		*qnrB1*,*aac(6')-Ib-cr*	-
KP157	>256	256	32	<2	8	>32		*aac(6')-Ib-cr*	-
KP167	>256	128	>256	>256	4	32	bla_{DHA-1}	*qnrB4*, *aac(6')-Ib-cr*	+
KP169	>256	>256	16	128	<2	<1		*aac(6')-Ib-cr*	-
KP176	>256	>256	4	128	<2	2		*aac(6')-Ib-cr*	-
KP201	>256	64	4	128	<2	2		*qnrB1*, *aac(6')-Ib-cr*	-
KP211	>256	128	>256	>256	<2	8	bla_{DHA-1}	*qnrB4*, *aac(6')-Ib-cr*	+
KP212	>256	64	4	64	<2	4		*aac(6')-Ib-cr*	-
KP218	>256	>256	4	128	<2	4		*aac(6')-Ib-cr*	-
KP219	>256	256	8	128	<2	2		*aac(6')-Ib-cr*	-

Abbreviations: MIC, minimum inhibitory concentration; CTX, cefotaxime; CAZ, ceftazidime; AMK, amikacin; GEN, gentamicin; LEV, levofloxacin; CIP, ciprofloxacin; PABL, plamid-mediated AmpC β-lactamase.

In this study, DHA-1 AmpC β-lactamase was detected in 1 and 2 CTX-M-producing *E. coli* and *K. pneumoniae* isolates, respectively. These results are similar to previous reports, where DHA AmpC β-lactamase was the most prevalent PABL gene in *E. coli* and *K. pneumoniae* isolates [5, 14], indicating that ESBLs play a greater role in resistance to β-lactams than PABLs.

ESBL-producing *Enterobacteriaceae* are frequently resistant to quinolones and aminoglycosides [28], where higher rates of quinolone resistance are found in ESBL producers of *E. coli* and *K. pneumoniae* in many countries [17, 22]. In this study, similar to previous reports in Korea, *qnr* and *aac(6')-Ib-cr* genes were found in 2.3% (1) and 47.6% (20) CTX-M-producing *E. coli* isolates, respectively, and in 33.3% (8) and 87.5% (21) CTX-M-producing *K. pneumoniae* isolates, respectively [9, 12]. Interestingly, many *E. coli* isolates without *qnr* genes were resistant to levofloxacin, whereas *K. pneumoniae* isolates with *qnr* genes were not. Moreover, the *aac(6')-Ib-cr* gene was widely distributed among both *E. coli* and *K. pneumoniae* isolates, and partial isolates with *aac(6')-Ib-cr* were resistant to ciprofloxacin. These results show that *qnr* and *aac(6')-Ib-cr* genes are distributed among CTX-M-producing *E. coli* and *K. pneumoniae*, but are not major determining factors in quinolone resistance.

Although *E. coli* isolates did not contain an *arm*A gene, *arm*A-containing *K. pneumoniae* isolates were detected, and these were intensively resistant to amikacin and gentamicin. In Korea, 4 *E. coli* isolates from urine collected in 2009 and 2

K. pneumoniae isolates in 2007 contained both *armA* and bla_{CTX-M} genes and were reported to be resistant to the aminoglycosides amikacin and gentamicin [10, 25].

In this study, 17 *E. coli* strains displayed an identical rep-PCR type (type a), and were present in both CTX-M-14 and CTX-M-15 producers alike. These strains were presumed to be the same clone.

In conclusion, CTX-M-types were the most common type of ESBLs in urinary *E. coli* and *K. pneumoniae* isolates. CTX-M-14 and CTX-M-15 producers were usually resistant to aminoglycoside and/or quinolone antibiotics, including cefotaxime and/or ceftazidime, and contained multiple antimicrobial resistance genes, such as bla_{DHA-1}, *qnr*, *aac(6′)-Ib-cr*, and *arm*A. CTX-M-15 producers contained more antimicrobial resistance genes than did CTX-M-14 producers.

References

1. Cattoir V, Poirel L, Rotimi V, Soussy CJ, Nordmann P. 2007. Multiplex PCR for detection of plasmid-mediated quinolone resistance *qnr* genes in ESBL-producing enterobacterial isolates. *J. Antimicrob. Chemother*. **60:** 394-397.
2. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; sixteenth informational supplement. M100-S16. Wayne, Pensylvania: CLSI, 2006.
3. Duan H, Chai T, Liu J, Zhang X, Qi C, Gao J, *et al*. 2009. Source identification of airborne *Escherichia coli* of swine house surroundings using ERIC-PCR and REP-PCR. *Environ. Res*. **109:** 511-517.
4. Dhanji H, Doumith M, Rooney PJ, O'Leary MC, Loughrey AC, Hope R, *et al*. 2011. Molecular epidemiology of fluoroquinolone-resistant ST131 *Escherichia coli* producing CTX-M extended-spectrum beta-lactamases in nursing homes in Belfast, UK. *J. Antimicrob. Chemother*. **66:** 297-303.
5. Jeong HS, Bae IK, Shin JH, Jung HJ, Kim SH, Lee JY, *et al*. 2011. Prevalence of plasmid-mediated quinolone resistance and its association with extended-spectrum beta-lactamase and AmpC beta-lactamase in Enterobacteriaceae. *Korean J. Lab. Med*. **31:** 257-264.
6. Kang HY, Kim J, Seol SY, Lee YC, Lee JC, Cho DT. 2009. Characterization of conjugative plasmids carrying antibiotic resistance genes encoding 16S rRNA methylase, extended-spectrum beta-lactamase, and/or plasmid-mediated AmpC beta-lactamase. *J. Microbiol*. **47:** 68-75.
7. Kim HB, Park CH, Kim CJ, Kim EC, Jacoby GA, Hooper DC. 2009. Prevalence of plasmid-mediated quinolone resistance determinants over a 9-year period. *Antimicrob. Agents Chemother*. **53:** 639-645.
8. Kim J, Bae IK, Jeong SH, Chang CL, Lee CH, Lee K. 2011. Characterization of IncF plasmids carrying the $bla_{CTX-M-14}$ gene in clinical isolates of *Escherichia coli* from Korea. *J. Antimicrob. Chemother*. **66:** 1263-1268.
9. Kim MH, Lee HJ, Park KS, Suh JT. 2010. Molecular characteristics of extended spectrum beta-lactamases in *Escherichia coli* and *Klebsiella pneumoniae* and the prevalence of *qnr* in extended spectrum beta-lactamase isolates in a tertiary care hospital in Korea. *Yonsei Med. J*. **51:** 768-774.
10. Kim MH, Sung JY, Park JW, Kwon GC, Koo SH. 2007. Coproduction of *qnr*B and *armA* from extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae*. *Korean J. Lab. Med*. **27:** 428-436.
11. Ko KS, Lee MY, Song JH, Lee H, Jung DS, Jung SI, *et al*. 2008. Prevalence and characterization of extended-spectrum beta-lactamase-producing Enterobacteriaceae isolated in Korean hospitals. *Diagn. Microbiol. Infect. Dis*. **61:** 453-459.
12. Lewis JS 2nd, Herrera M, Wickes B, Patterson JE, Jorgensen JH. 2007. First report of the emergence of CTX-M-type extended-spectrum beta-lactamases (ESBLs) as the predominant ESBL isolated in a US health care system. *Antimicrob. Agents Chemother*. **51:** 4015-4021.
13. Li XM, Jang SJ, Bae IK, Park G, Kim YS, Shin JH, *et al*. 2010. Frequency of extended-spectrum β-lactamase (ESBL) and AmpC β-lactamase genes in *Escherichia coli* and *Klebsiella pneumoniae* over a three-year period in a University Hospital in Korea. *Korean J. Lab. Med*. **30:** 616-623.
14. Park SD, Uh Y, Lee G, Lim K, Kim JB, Jeong SH. 2010. Prevalence and resistance patterns of extended-spectrum and AmpC β-lactamase in *Escherichia coli, Klebsiella pneumoniae*, *Proteus mirabilis*, and *Salmonella serovar* Stanley in a Korean tertiary hospital. *APMIS* **118:** 801-808.
15. Park SH, Byun JH, Choi SM, Lee DG, Kim SH, Kwon JC, *et al*. 2012. Molecular epidemiology of extended-spectrum β-lactamase-producing *Escherichia coli* in the community and hospital in Korea: emergence of ST131 producing CTX-M-15. *BMC Infect. Dis*. **12:** 149.
16. Park Y, Kang HK, Bae IK, Kim J, Kim JS, Uh Y, *et al*. 2009. Prevalence of the extended-spectrum beta-lactamase and *qnr* genes in clinical isolates of *Escherichia coli*. *Korean J. Lab. Med*. **29:** 218-223.
17. Paterson DL. 2006. Resistance in gram-negative bacteria: Enterobacteriaceae. *Am. J. Med*. **119:** S20-S28; discussion S62-S70.
18. Pérez-Pérez FJ, Hanson ND. 2002. Detection of plasmid-mediated AmpC beta-lactamase genes in clinical isolates by using multiplex PCR. *J. Clin. Microbiol*. **40:** 2153-2162.
19. Piatti G, Mannini A, Balistreri M, Schito AM. 2008. Virulence factors in urinary *Escherichia coli* strains: phylogenetic background and quinolone and fluoroquinolone resistance. *J. Clin. Microbiol*. **46:** 480-487.
20. Podschun R, Ullmann U. 1998. *Klebsiella* spp. as nosocomial pathogens: epidemiology, taxonomy, typing methods, and pathogenicity factors. *Clin. Microbiol. Rev*. **11:** 589-603.

21. Rossolini GM, D'Andrea MM, Mugnaioli C. 2008. The spread of CTX-M-type extended-spectrum beta-lactamases. *Clin. Microbiol. Infect*. **14(Suppl 1):** 33-41.
22. Ruiz E, Sáenz Y, Zarazaga M, Rocha-Gracia R, Martínez-Martínez L, Arlet G, Torres C. 2012. *qnr*, *aac(6')-Ib-cr* and *qepA* genes in *Escherichia coli* and *Klebsiella* spp.: genetic environments and plasmid and chromosomal location. *J. Antimicrob. Chemother*. **67:** 886-897.
23. Shin J, Kim DH, Ko KS. 2011. Comparison of CTX-M-14- and CTX-M-15-producing *Escherichia coli* and *Klebsiella pneumoniae* isolates from patients with bacteremia. *J. Infect*. **63:** 39-47.
24. Seo MR, Park YS, Pai H. 2010. Characteristics of plasmid-mediated quinolone resistance genes in extended-spectrum cephalosporin-resistant isolates of *Klebsiella pneumoniae* and *Escherichia coli* in Korea. *Chemotherapy* **56:** 46-53.
25. Song S, Lee EY, Koh EM, Ha HS, Jeong HJ, Bae IK, Jeong SH. 2009. Antibiotic resistance mechanisms of *Escherichia coli* isolates from urinary specimens. *Korean J. Lab. Med*. **29:** 17-24.
26. Sung JY, Koo SH, Kwon KC, Park JW, Ko CS, Shin SY, Song JH. 2009. Characterization of class 1 integrons in metallo-β-lactamase-producing *Pseudomonas aeruginosa*. *Korean J. Clin. Microbiol.* **12:** 17-23.
27. Yoo JS, Byeon J, Yang J, Yoo JI, Chung GT, Lee YS. 2010. High prevalence of extended-spectrum beta-lactamases and plasmid-mediated AmpC beta-lactamases in Enterobacteriaceae isolated from long-term care facilities in Korea. *Diagn. Microbiol. Infect. Dis*. **67:** 261-265.
28. Yum JH, Kim S, Lee H, Yong D, Lee K, Cho SN, Chong Y. 2005. Emergence and wide dissemination of CTX-M-type ESBLs, and CMY-2- and DHA-1-type AmpC beta-lactamases in Korean respiratory isolates of *Klebsiella pneumoniae*. *J. Korean Med. Sci*. **20:** 961-965.