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Letters to the Editor

High Prevalence of KPC-2-Type Carbapenemase Coupled with CTX-M-Type Extended-Spectrum β-Lactamases in Carbapenem-Resistant *Klebsiella pneumoniae* in a Teaching Hospital in China▽

Carbapenems such as imipenem and meropenem are the first-line agents for the treatment of serious nosocomial infections caused by multidrug-resistant *Enterobacteriaceae* clinical isolates (2). However, the phenomenon of carbapenem resistance is emerging among a wide variety of these species (11). Carbapenemases have been widespread in recent years and predominantly contribute to carbapenem resistance among *Enterobacteriaceae*, especially *Klebsiella pneumoniae* and *Citrobacter freundi* (8). For screening of the carbapenem-resistant *Enterobacteriaceae* clinical isolates, we conducted a surveillance study of carbapenem-resistant *Enterobacteriaceae* isolates in order to investigate the frequency and prevalence of *K. pneumoniae* carbapenemase (KPC)-type genes in Huashan Hospital (Fudan University, Shanghai, China), a 1,300-bed tertiary care hospital. We hereby report a high prevalence of carbapenem-resistant *K. pneumoniae* isolates carrying the KPC-2-type carbapenemase gene or KPC-2-type carbapenemase gene coupled with the CTX-M-type extended-spectrum β-lactamase (ESBL) gene.

From January 2005 to March 2010, 109 nonduplicate *Klebsiella pneumoniae* isolates with resistance to ertapenem were collected. Antimicrobial susceptibility testing was performed by the agar dilution method, and MICs were interpreted following CLSI (4) or British Society for Antimicrobial Chemotherapy (BSAC) criteria (1). The presence of genes encoding β-lactamases, including metallo-β-lactamases (MBLs), KPC-type and OXA-type carbapenemases, ESBLs, and plasmid-mediated AmpC enzymes were screened by PCR using primers described by Rasheed et al. (10). All amplified products were then subjected to direct nucleotide sequencing. The results were analyzed with the software available on the National Center for Biotechnology Information website (http://www.ncbi.nlm.nih.gov).

TABLE 1. Microbiological activities of various antimicrobial agents against 109 carbapenem-resistant *K. pneumoniae* isolates

Drug	MIC (μg/ml)[a]			% susceptible
	Range	50%	90%	
Imipenem	0.25–256	32	128	4.6
Meropenem	0.5–>256	64	128	2.8
Ertapenem	1–>256	128	>256	0.0
Panipenem	1–>512	64	256	
Colistin	0.5–128	1	2	96.3
Tigecycline	0.25–8	1	4	66.1
Minocycline	0.06–128	2	32	74.3
Doxycycline	0.06–64	4	64	64.2
Fosfomycin	0.5–256	128	256	45.0
Cefepime	2–256	256	256	1.8
Ceftazidime	1–>256	256	>256	1.8
Cefotaxime	4–>256	>256	>256	0.0
Cefoxitin	0.06–>256	128	>256	1.8
Cefoperazone-sulbactam	2–256	256	256	4.6
Piperacillin-tazobactam	0.25–256	256	256	1.8
Aztreonam	16–>256	>256	>256	0.0
Amikacin	1–512	>256	>256	14.7
Ciprofloxacin	<0.06–256	256	256	8.3

[a] 50% and 90%, MIC_{50} and MIC_{90}, respectively. According to the British Society for Antimicrobial Chemotherapy (BSAC) criteria (1), a colistin MIC of ≤2 mg/liter indicates susceptible and >2 mg/liter indicates resistant and a tigecycline MIC of ≤1 mg/liter indicates susceptible, 2 mg/liter indicates intermediate, and >2 mg/liter indicates resistant.

The susceptibility rates of 109 *K. pneumoniae* isolates to imipenem, meropenem, and ertapenem were 4.6%, 2.8%, and 0.0%, respectively (Table 1). Carbapenem-resistant *Enterobacteriaceae* isolates exhibited high resistance rates against the carbapenem agents tested, with MIC_{90} values of 128 μg/ml or higher. Totals of 96.3%, 74.3%, 66.1%, and 64.2% of isolates were susceptible to colistin, minocycline, tigecycline, and doxycycline, respectively (Table 1). KPC-2-type carbapenemase was the most predominant carbapenemase, present in 70.6% (77/109) of isolates. KPC-2-type carbapenemase coupled with CTX-M-14- or CTX-M-15-type ESBL accounted for 59.6% (65/109) of isolates. A total of 10.1% (11/109) of KPC-positive isolates were simultaneously producing both CTX-M-14-type ESBL and DHA-1-type plasmid-mediated AmpC enzymes. GIM-1-type or VIM-1-type MBL, OXA-type carbapenemases were detected in 9.2% (10/109) and 10.1% (11/109) of isolates, respectively.

In this study, we have reported for the first time the frequency of KPC-2-type carbapenemases with or without CTX-M-type ESBLs among carbapenem-resistant *K. pneumoniae* isolates in China. In our hospital, the incidence of carbapenem-resistant *K. pneumoniae* isolates showed a significant increase from 0.9% in 2005 to 12.9% in 2009. These results suggested that the rapidly increased prevalence of carbapenem resistance among *K. pneumoniae* isolates in our hospital could be the consequence of the failure to control the spread of these strains. Therefore, prompt detection of carbapenemase-producing *Enterobacteriaceae* isolates, active antibiotic resistance surveillance, and strict implementation of infection control measures are critical to avoid the rapid spread or outbreaks by these multidrug-resistant or pan-drug-resistant isolates in health care-associated facilities (3, 5–7, 9).

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Shudan Chen
Fupin Hu*
Xiaogang Xu
Yang Liu
Weihong Wu
Demei Zhu
Institute of Antibiotics
Huashan Hospital
Fudan University
Shanghai 200040, China

Honghai Wang
State Key Laboratory of Genetic Engineering
Institute of Genetics
School of Life Sciences
Fudan University
12 Wulumuqi Zhong Road
Shanghai 200433, China

*Phone: 86 21 52888186
Fax: 86 21 62484347
E-mail: hufupin@163.com

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