

Address correspondence to Duo-shuang Xie, MD, PhD, Department of Infection Control, Taihe Hospital, Hubei University of Medicine, No 32 Renmin Road, Shiyan, Hubei 430030, P.R. China (xieds8@163.com)
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The Carbapenemase Menace: Do Dual Mechanisms Code for More Resistance?

To the Editor—Carbapenems (imipenem, meropenem, and doripenem) are used as the drugs of last resort to treat patients with resistant bacterial infections. These drugs possess a broad range of activity against numerous β-lactamases. The increasing

TABLE 1. Relation of Minimum Inhibitory Concentrations to Carbapenemase Mechanisms in the Predominant Enterobacteriaceae

Mechanism (N = 74)	Organism	Imipenem (µg/mL)			Meropenem (µg/mL)			Doripenem (µg/mL)					
		<2	2–4	6–12	16–≥32	<2	2–4	6–12	16–≥32	<2	2–4	6–12	16–≥32
OXA-48/181 (29)	<i>Escherichia coli</i> (4)	-	4	-	-	1	1	2	1	1	-	-	2
	<i>Enterobacter</i> spp. (11)	-	4	2	5	-	2	-	-	1	-	-	9
	<i>Klebsiella</i> spp. (14)	1	5	5	3	1	-	1	12	1	1	1	11
NDM-1 (28)	<i>Escherichia coli</i> (9)	1	1	1	6	-	1	2	6	1	2	-	6
	<i>Enterobacter</i> spp. (6)	-	2	2	2	-	3	1	2	-	3	1	2
	<i>Klebsiella</i> spp. (13)	2	3	1	7	-	2	3	8	1	3	1	8
OXA 48/181 plus NDM-1 (12)	<i>Escherichia coli</i> (3)	-	-	2	1	-	-	3	-	-	-	-	3
	<i>Enterobacter</i> spp. (6)	-	-	-	6	-	-	6	-	-	-	-	6
	<i>Klebsiella</i> spp. (3)	-	-	-	3	-	-	3	-	-	-	-	3
NDM-1 plus VIM (5)	<i>Escherichia coli</i> (1)	-	-	-	1	-	-	1	-	-	-	-	1
	<i>Enterobacter</i> spp. (2)	-	-	-	2	-	-	2	-	-	-	-	2
	<i>Klebsiella</i> spp. (2)	1	-	-	1	-	-	1	-	-	-	-	1

NOTE. NDM-1, New Delhi Metallo-beta-lactamase-1; OXA 48/181, Oxacillinase 48/181; VIM, Verona integron-encoded metallo-β-lactamase.

plight of carbapenem-resistant Enterobacteriaceae has become a serious healthcare concern.¹ The current antimicrobial susceptibility testing is based on breakpoints and does not emphasize the resistant mechanism involved. From March 1 through September 30, 2013, we performed an E-test for all 3 carbapenems (imipenem, meropenem, and doripenem) for a total of 74 nonduplicate clinical isolates. These isolates consisted of urine (28), blood (13), stool (9), sputum (8), tissue (6), synovial fluids (4), bile (2), wound swab specimens (2), bronchoalveolar lavage specimens (1), and other (1). For bacterial identification, susceptibility testing was performed as per Clinical and Laboratory Standards Institute guidelines² of 2013 and the E-test was performed as per manufacturer's instructions. An in-house multiplex polymerase chain reaction test was designed to identify the predominant carbapenemases *bla*_{NDM}, *bla*_{OXA}, *bla*_{KPC}, *bla*_{VIM}, and *bla*_{IMP}.³ Of the 74 clinical isolates, 32 (43%) consisted of *Klebsiella* spp., 25 (34%) of *Enterobacter* spp., and 17 (23%) of *Escherichia coli*. Table 1 demonstrates the relation between minimum inhibitory concentrations and carbapenemase mechanisms in the predominant Enterobacteriaceae.

The present study highlights 2 issues: First, the absence of *Klebsiella pneumoniae* carbapenemase in our region demonstrates epidemiologic differences in geographic areas. Second, most isolates with dual carbapenemase producers (New Delhi Metallo-beta-lactamase-1 together with Oxacillinase 48/181 and New Delhi Metallo-beta-lactamase-1 together with Verona integron-encoded metallo-β-lactamase) had minimum inhibitory concentration values greater than 32 µg/mL. Though New Delhi Metallo-beta-lactamase-1 producers also showed higher minimum inhibitory concentrations, they did demonstrate a wider range. However, Oxacillinase-48/181 carbapenemases alone tended to have lower minimum inhibitory concentrations. In countries where colistin is used with carbapenems, this has clinical implications in the choice of the carbapenem.

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**Mubin Kazi, PhD fellow;¹
Anjali Shetty, MRCP, FRCPath;¹
Camilla Rodrigues, MD¹**

Affiliations: 1. P. D. Hinduja National Hospital and Medical Research Centre, Department of Microbiology, Veer-Savarkar Marg, Mahim, Mumbai, India;

Address correspondence to Camilla Rodrigues, MD, P. D. Hinduja National Hospital and Medical Research Centre, Department of Microbiology, Veer-Savarkar Marg, Mahim (West), Mumbai 400016, India (dr_crodrigues@hindujahospital.com).

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