Enterobacteriaceae with acquired carbapenemases, 2016

Background

The acquired or transferable (as opposed to chromosomally encoded) carbapenemases found in Enterobacteriaceae belong to three of the four major classes of β-lactamases: classes A, B and D.[1] Class A acquired carbapenemases include the *Klebsiella pneumoniae* carbapenemases, the so-called KPCs. Class B metallo-β-lactamases (MBLs) include several types of acquired carbapenemases, the most common being the New Delhi metallo-β-lactamases (NDMs), and the IMP and VIM metallo-β-lactamases. Class D acquired carbapenemases in Enterobacteriaceae belong to the OXA-48 group of β-lactamases. DNA mutations resulting in changes in the amino acid sequence of the carbapenemase have produced an ever increasing range of subtypes or variants of each type of carbapenemase. For example, since the first NDM (NDM-1) was described in 2009, a further 17 subtypes (designated NDM-2 to NDM-18) have been described, with each subtype differing by at least one amino acid from any other subtype.

Methods

In New Zealand, diagnostic microbiology laboratories are requested to refer all isolates of possible carbapenemase-producing Enterobacteriaceae (CPE) to ESR for confirmation and further investigation. At ESR isolates are screened for carbapenemases using inhibitor-based tests, the modified Hodge test and the carbapenem inactivation method. PCRs are performed for the genes encoding KPCs (bla_{KPC}); NDM, IMP, VIM, GIM, SIM and SPM type MBLs (bla_{NDM}, bla_{IMP}, bla_{VIM}, bla_{GIM}, bla_{SIM} and bla_{SPM}); and the OXA-48-like carbapenemases ($bla_{OXA\text{-}48\text{-}like}$). When any of these carbapenemase genes are detected, the gene is sequenced to determine the subtype. Basic epidemiological data, including overseas travel and hospitalisation history, is collected for patients with confirmed CPE.

1. Queenan AM, Bush K. Carbapenemases: the versatile β-lactamases. Clin Microbiol Rev 2007; 20: 440-58.

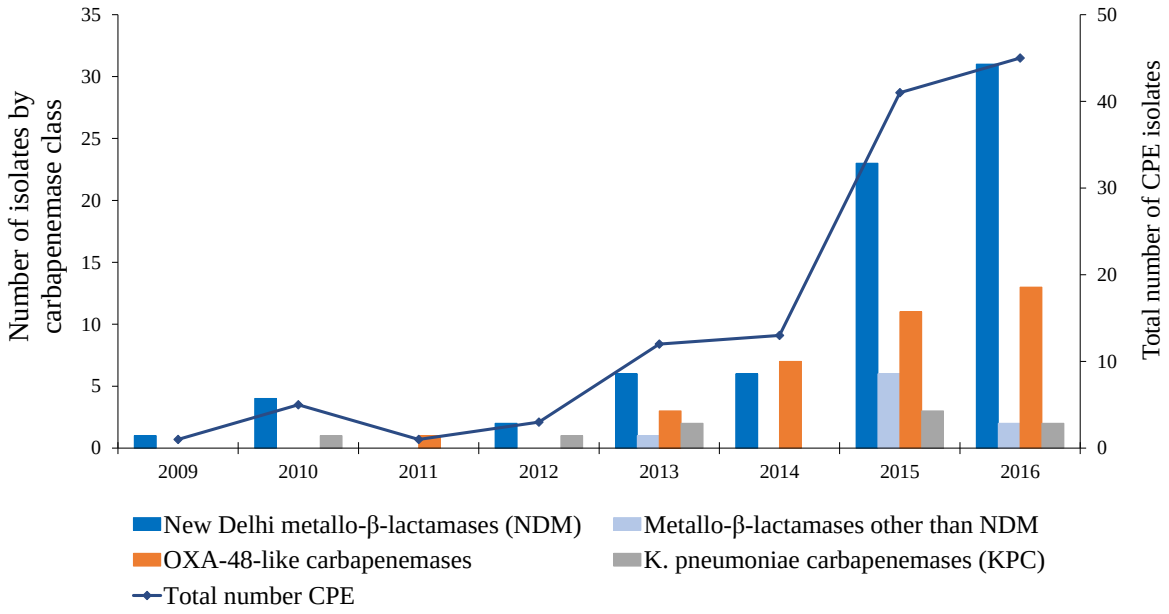
This report summarises information on CPE confirmed by ESR in 2016. Reports on CPE confirmed between 2009, when the first isolate was identified in New Zealand, and 2015 are available at https://surv.esr.cri.nz/antimicrobial/AccqEnterobacteriaceae.php.

Results

Forty-five distinct CPE were isolated from 38 patients in 2016. Six patients had ≥2 isolates with distinct carbapenemase types (See Table 1, footnote 3). The 45 CPE isolates confirmed in 2016 exceeded the total number (41) confirmed in 2015 (Figure 1).

75.6% (34/45) of the CPE confirmed in 2016 were isolated from specimens taken to screen for multidrug-resistant organisms. Among the 11 CPE from clinical specimens, 10 (90.9%) were from urinary sources.

Figure 1. Number of carbapenemase-producing Enterobacteriaceae (CPE) isolates identified in New Zealand, by carbapenemase class, each year from 2009 to 2016



Note: Multiple, distinct CPE isolates from the same patient are included, but duplicate isolates of the same species with the same type of carbapenemase from the same patient are excluded. In 2016, there were three CPE isolates that carried the genes encoding for an NDM and an OXA-48-like carbapenemase. These three isolates are counted in the number of isolates for both these carbapenemase classes.

Types of carbapenemases identified

The data in this section takes into account all carbapenemase genes of different classes found in CPE isolates. More than one class of carbapenemase was identified in three CPE isolates in 2016: two *Escherichia coli* isolates had NDM-1 and OXA-181 and one *K. pneumoniae* isolate had NDM-5 and OXA-232 (see Table 1, footnote 2).

As has been observed in earlier years, the most frequently identified carbapenemases among CPE identified in New Zealand in 2016 were various subtypes of NDM (Table 1). NDM carbapenemases accounted for 64.6% (31/48) of the carbapenemases identified in 2016, and have accounted for 57.9% (73/126) of carbapenemases identified in CPE in New Zealand to date. The only other MBL type identified in 2016 was IMP, which accounted for 4.2% (2/48) of the carbapenemases identified in 2016. IMP and VIM MBLs have accounted for 7.1% (9/126) of all carbapenemases identified in CPE in New Zealand.

The second most common carbapenemases identified were the OXA-48-like carbapenemases which accounted for 27.1 (13/48) of the carbapenemases identified in 2016 (Table 1), and have accounted for 27.8% (35/126) of all carbapenemases identified in CPE in New Zealand.

Only two (4.2%) of the 48 carbapenemases identified in 2016 were KPC types, and KPCs have accounted for 7.1% (9/126) of all carbapenemases identified in CPE in New Zealand. In New Zealand, KPCs have been identified exclusively in *K. pneumoniae*.

Table 1. Types of carbapenemases identified among carbapenemase-producing Enterobacteriaceae by species, 2016

Carbapenemase type and subtype	Number of isolates					
	Species					All species
	Escherichia coli	*Klebsiella pneumoniae*	*Klebsiella oxytoca*	*Enterobacter cloacae*	*Morganella morganii*	
KPC	**0**	**2**	**0**	**0**	**0**	**2**
KPC-2	0	2	0	0	0	2
NDM	**23**[1]	**3**	**2**	**2**	**1**	**31**
NDM-1	4	2	1	2	1	10
NDM-4	1[1]	0	0	0	0	1
NDM-5	18	1	1	0	0	20
NDM-7	1[1]	0	0	0	0	1
IMP	**1**	**0**	**1**	**0**	**0**	**2**
IMP-4	1	0	0	0	0	1
IMP-8	0	0	1	0	0	1
OXA-48-like	**7**	**6**	**0**	**0**	**0**	**13**
OXA-48	1	0	0	0	0	1
OXA-162	0	1	0	0	0	1
OXA-181	6	0	0	0	0	6
OXA-232	0	5	0	0	0	5
Total	**29**[2]	**10**[2]	**3**	**2**	**1**	**45**[2,3]

1 The 23 *E. coli* isolates with an NDM carbapenemase include one isolate that had two NDM subtypes: NDM-4 + NDM-7.

2 The 29 *E. coli* isolates include two isolates that had both NDM-1 + OXA-181. Therefore 31 carbapenemases of different classes were identified among the 29 *E. coli* isolates. The 10 *K. pneumoniae* isolates include one isolate that had both NDM-5 + OXA-232. Therefore 11 carbapenemases of different classes were identified among the 10 *K. pneumoniae* isolates. Correspondingly, a total of 48 carbapenemases of different classes were identified among the total 45 CPE isolates.

3 The 45 isolates include multiple, distinct CPE from six patients:

- *E. coli* with NDM-5 and *E. cloacae* with NDM-1;
- *E. coli* with NDM-4 + NDM-7 and *K. pneumoniae* with NDM-1;
- *E. coli* with NDM-1, *K. pneumoniae* with NDM-5 + OXA-232, and *E. cloacae* with NDM-1;
- *E. coli* with NDM-5 and *K. pneumoniae* with OXA-232;
- *E. coli* with NDM-5 and *E. coli* with OXA-181; and
- *E. coli* with NDM-5 and *E. coli* with NDM-1 + OXA-181.

Probable place of acquisition of carbapenemase–producing Enterobacteriaceae

Overseas travel and hospitalisation history was reported for the patients from whom 42 of the total 45 CPE were isolated in 2016 (see Table 2 footnote 3). 81.0% (34/42) of the CPE, from patients for whom travel history was reported, were from patients who had been overseas. India was by far the most common probable place of acquisition (Table 2).

67.6% (23/34) of the CPE apparently acquired overseas were from patients who were hospitalised overseas. Of the 11 CPE isolated from patients who had travelled but not been hospitalised overseas, all were probably acquired in India. All six patients who had ≥2 distinct carbapenemase-producing isolates had been hospitalised overseas (see Table 2, footnote 1), five in India and one in China. All four CPE isolates that had more than one type of carbapenemase were from patients who had been in India (see Table 2, footnote 7).

In 2016, CPE were isolated from eight patients who had no history of recent overseas travel. Two of these patients apparently acquired their CPE following cross-transmission events in New Zealand healthcare facilities (see next section). A further patient had a family member who had recently been in India (see Table 2, footnote 4). However, the likely source of the CPE for the other five patients who had not been overseas was not identified.

Transmission of carbapenemase–producing Enterobacteriaceae in New Zealand healthcare facilities

In 2016 there were two probable CPE cross-transmission events in New Zealand healthcare facilities. The same patient, originally identified in 2015 with *K. pneumoniae* with OXA-232 following hospitalisation in India, was the apparent index case in both cross-transmission events. The first event was in Middlemore Hospital where the index case was on the same ward as another patient who had not been overseas and from whom the same CPE strain was isolated. The second event occurred in an Auckland long-term care facility where the index case lived and the same CPE strain was isolated from another resident who had not been overseas (see Table 2, footnote 6).

Table 2. Probable place of acquisition of carbapenemase-producing Enterobacteriaceae, 2016

Carbapenemase type and subtype	Number of isolates[1]						
	Probable region of acquisition						
	India	Other parts of Asia[2]	Europe	Middle East	New Zealand	Unknown[3]	Total
KPC	**0**	**1**	**0**	**0**	**1**	**0**	**2**
KPC-2	0	1	0	0	1	0	2
NDM	**23**	**2**	**1**	**0**	**3**	**2**	**31**
NDM-1	8	1	0	0	1[4]	0	10
NDM-4	1	0	0	0	0	0	1
NDM-5	14	1	1	0	2	2[5]	20
NDM-7	1	0	0	0	0	0	1
IMP	**0**	**0**	**0**	**0**	**1**	**1**	**2**
IMP-4	0	0	0	0	0	1	1
IMP-8	0	0	0	0	1	0	1
OXA-48-like	**7**	**0**	**0**	**1**	**3**	**2**	**13**
OXA-48	0	0	0	0	0	1	1
OXA-162	0	0	0	1	0	0	1
OXA-181	4	0	0	0	1	1[5]	6
OXA-232	3	0	0	0	2[6]	0	5
Total	**27**[7]	**3**	**1**	**1**	**8**	**5**	**45**[7]

Footnotes on next page

Footnotes for Table 2:

1 Includes multiple isolates from six patients who had ≥2 distinct carbapenemase-producing isolates (see Table 1, footnote 3). Five of these six patients had been hospitalised in India and the sixth patient had both been in India and been hospitalised in China.

2 All Asia other than the Indian subcontinent.

3 Unknown includes both when the information was not reported for the patient (n=3 isolates) and when the patient had been in multiple countries (one patient with 2 isolates, see footnote 5 below).

4 The patient had a family contact that had recently been in India.

5 The patient with one of the isolates with NDM-5 carbapenemase and one of the isolates with OXA-181 carbapenemase had both been in India and been hospitalised in China.

6 One of these two isolates with OXA-232 was probably acquired in Middlemore Hospital, where the patient was in the same ward as another patient known to be colonised with the same CPE strain. The second isolate with OXA-232 was probably acquired in an Auckland long-term care facility, where the patient lived with another resident known to be colonised with the same CPE strain.

7 All four CPE isolates that had more than one type of carbapenemase gene (two *E. coli* with NDM-1 + OXA-181, one *K. pneumoniae* with NDM-5 + OXA-232, and one *E. coli* with NDM-4 + NDM-7) were from patients who had been in India. Therefore a total of 30 carbapenemases of different classes were identified among the total 27 CPE isolates from patients that had likely acquired their CPE in India, and a total of 48 carbapenemases of different classes were identified among the total 45 CPE isolates.