Epidemiology of the Emergence of Carbapenemase-producing *Enterobacteriaceae* in South Central Ontario, Canada

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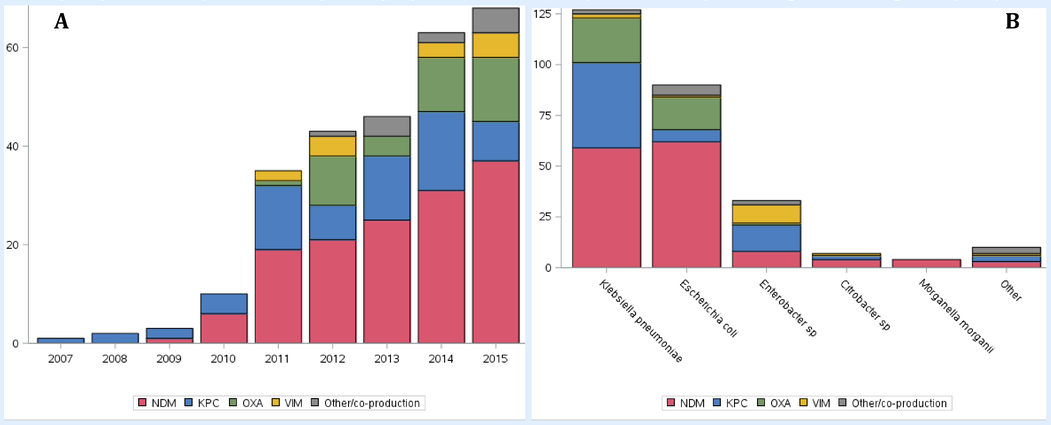
Background

- The emergence of carbapenemase-producing *Enterobacteriaceae* (CPE) threatens the ability of antibiotics to eradicate infection. Surveillance is an important measure to assess the burden of disease, characterize the bacterial strains involved, and to identify populations at risk. Here, we describe the results of CPE surveillance from south central Ontario, Canada,

Methods

- We analyzed population-based data from Toronto Invasive Bacterial Diseases Network (TIBDN) surveillance from first identified CPE in 2007 until December 2015.
- First patient isolates (screening and clinical samples) were used for description of the microbiological characteristics. All patient isolates taken within 2 days of the first isolate were defined as baseline samples, and used for assessment of CPE positive body sites. CPE patients with a clinical CPE sample at any time were included in incidence calculations. CPE incidence per 100 000 population was calculated using census data from Statistics Canada.
- Chart review was done for all hospital admissions in the TIBDN at time of and for 1 year prior to CPE detection, collecting information on patient risk factors and outcome. Four patient groups (i.e. isolation of any NDM, any KPC, OXA only, and of VIM and other carbapenemases) were compared.
- CPE infection was defined as any clinical sample in conjunction with a clinical diagnosis according to the treating physicians. Thirty-day mortality was calculated from date of first sample (for those without) or from date of the clinical sample (for those with infection).

Figure 1. A: First patient samples (n=271) by year and carbapenemase (including screening samples). B: First patient samples by species and carbapenemase (including screening samples).



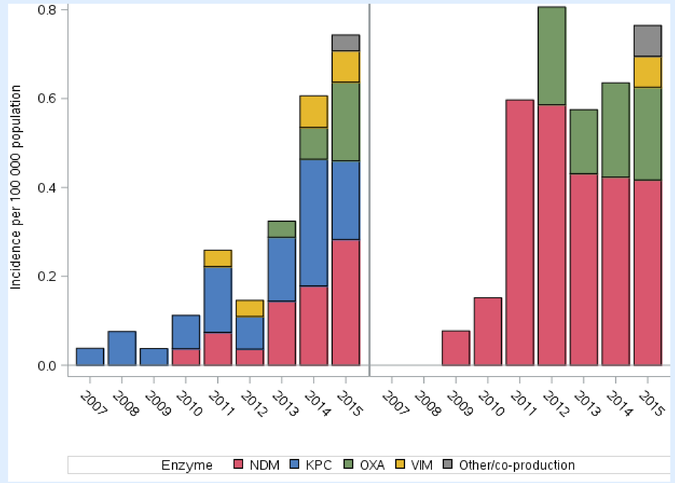
Results

- We identified 271 CPE colonized/infected patients. *Klebsiella pneumoniae* and *Escherichia coli* were the most common species, NDM and KPC the most common carbapenemases ***(Fig 1)***. Among baseline samples, CPE were most commonly cultured from the rectum (53%) and urine (35%). Of the 271 patients, 158 (58.3%) had ≥1 clinical sample, corresponding to an incidence of 0 in 2006 and 0.77/100 000 in 2015. Carbapenemase gene distribution varied significantly over time and in adjacent urban areas ***(Fig 2)***.
- A total of 418 chart reviews were performed for 259 patients. Median patient age was 70 years and most were male (65%). A total of 73 patients (28%) had a Charlson Score greater than 2. ***Table*** shows the main risk factors by type of carbapenemase. Of note, in a majority of patients (165/259, 64%) no healthcare visit outside of Canada was registered.
- CPE infection was diagnosed in 111/259 (43%) patients, thereof 74 urinary tract and 24 blood stream infections; 30-day mortality was 14% in those with and 8% in those without infection.

Table. Risk factors of CPE patients within 1 year of CPE detection by type of carbapenemase, n (%)

	Total n=259	NDM n=145	KPC n=64	OXA n=32	VIM/ Other n=18	p-value
Hospital admission > 24h	197 (76)	110 (76)	51 (80)	22 (69)	14 (78)	0.7
Healthcare visit abroad	94 (36)	64 (44)	18 (28)	10 (31)	2 (11)	**0.01**
Healthcare visit Indian subcontinent	71 (27)	63 (43)	1 (2)	7 (22)	0 (0)	**<.0001**
ICU admission	44 (17)	22 (15)	14 (22)	3 (9)	5 (28)	0.24
Surgery	89 (34)	27 (19)	41 (64)	13 (41)	8 (44)	**<.0001**
Central venous catheter	53 (21)	21 (15)	24 (38)	4 (13)	4 (22)	**0.001**
Antibiotic exposure	149 (58)	79 (55)	44 (69)	15 (47)	11 (61)	0.14

Figure 2. CPE incidence in Toronto and Peel region from 2007 to 2015 (only patients with at least 1 clinical sample)



Conclusions

- CPE are increasing in south central Ontario with NDM-producing *K. pneumoniae* and *E. coli* being the most frequent species.
- Differences in risk profiles between patients with different carbapenemases suggest differences in CPE sources: NDM- and OXA-producers - being more frequent in Peel region with high numbers of South-Asian immigrants - are strongly associated with healthcare exposure in the Indian subcontinent. However, a majority of patients appear to have acquired their CPE in a Canadian hospital. Future studies should aim to identify potential CPE sources and transmission routes within Canadian healthcare institutions.

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