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Genetic Characterization of Carbapenem-Resistant Enterobacteriaceae (CRE) Identified During Population-based Surveillance in Alameda County, 2017-2020

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BACKGROUND

- Alameda County Public Health Department (ACPHD) mandates submission of all carbapenem-resistant isolates of *Escherichia coli*, *Klebsiella* spp., and *Enterobacter* spp.
- There are few published reports on genomic surveillance of CRE in the US that presents data on carbapenemase alleles, such as New Delhi metallo-β-lactamase (NDM)-1, and sequence type.
- We used whole genome sequencing (WGS) to assess genetic profiles of CRE isolates for multilocus sequence types (MLST) and antimicrobial resistance genes, including carbapenemases, extended-spectrum β-lactamases (ESBL), and other β-lactamases.

Alameda County

- Population 1.67 Million
- 13 Acute Care Hospitals
- 1 Long Term Acute Care Hospital
- 76 Skilled Nursing Facilities

- **Table 2** shows genetic and clinical characteristics of isolates with detectable NDM. Repeat sequence types are highlighted in grey.
- 64% had detectable ESBL (n=16).
- 16% had a documented recent (i.e. within 90 days) health care exposure outside the US (n=4)
- 12% were collected as a rectal swab for surveillance purposes (n=6)

RESULTS

Table 1: Carbapenemases, ESBL, and Other β-lactamases by Organism, June 2017-April 2020

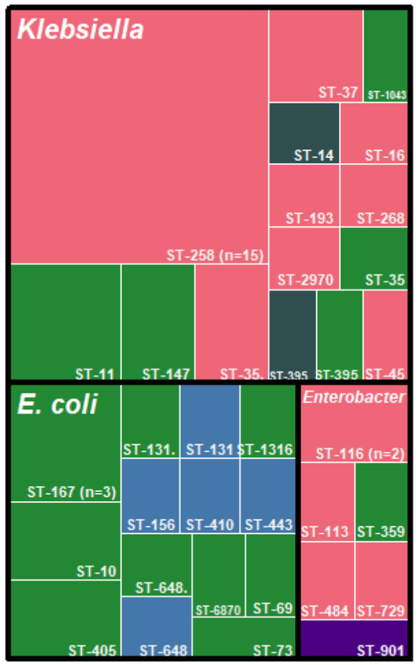
		KPC (n=30, 12%)		NDM (n=25, 10%)			OXA-48-like (n=8, 3 %)			IMI (n=2, 1%)		ESBL (n=104 , 43%)		Other β-lactamase (n=171, 70%)	
Organism	Isolates (%)	KPC-2	KPC-3	NDM-1	NDM-5	NDM-7	OXA-48	OXA-181	OXA-232	IMI-1	IMI-3	SHV-group	CTX-M-group	TEM-1	AmpC-type
Enterobacter spp.	78 (32)	5	0	0	1	0	0	0	0	1	1	3	1	9	60
E. coli	66 (27)	0	0	1	11	1	2	4	0	0	0	1	35	28	27
Klebsiella spp.	99 (41)	11	14	5	5	1	0	1	1	0	0	61	22	42	22
TOTAL	243	16	14	6	17	2	2	5	1	1	1	65	58	79	109

- **Table 1** shows that, among 243 isolates tested, 63 (26%) had detectable carbapenemase genes, including 25 (10%) isolates with NDM.

Table 2: Genetic and Clinical Characteristics of Isolates with Detectable NDM (n=25)

Genus & Species	Sequence Type	Carbapenemase	Other β-lactamase
E. cloacae	ST-359	NDM-5	ACT-4
E. coli	ST-10	NDM-5	CTX-M-14, TEM-1
E. coli	ST-10	NDM-5	CTX-M-14, TEM-1
E. coli	ST-131	NDM-1	None
E. coli	ST-1316	NDM-7	None
E. coli	ST-167	NDM-5	TEM-1, CMY
E. coli	ST-167	NDM-5	CTX-M-15, OXA-1
E. coli	ST-167	NDM-5	CTX-M-14, TEM-1
E. coli	ST-648	NDM-5	TEM-1
E. coli	ST-405	NDM-5	CTX-M-15, TEM-1
E. coli	ST-405	NDM-5	CTX-M-15, TEM-1, OXA-1
E. coli	ST-6870	NDM-5	CMY-2
E. coli	ST-69	NDM-5	TEM-1
E. coli	ST-73	NDM-5	TEM-1
K. pneumoniae	Unknown	NDM-1	None
K. pneumoniae	ST-1043	NDM-1	SHV-172
K. pneumoniae	ST-11	NDM-1	SHV-182, OXA-1
K. pneumoniae	ST-11	NDM-1	SHV-182
K. pneumoniae	ST-11	NDM-7	SHV-12, CTX-M-15, TEM-1
K. pneumoniae	ST-14	NDM-5/OXA-181	SHV, TEM-1, OXA-9
K. pneumoniae	ST-147	NDM-5	SHV-5, CTX-M-15, TEM-1
K. pneumoniae	ST-147	NDM-5	SHV-12, CTX-M-15, TEM-1
K. pneumoniae	ST-35	NDM-5	SHV-5, TEM-1
K. pneumoniae	ST-395	NDM-1	SHV-182, CTX-M-15
K. pneumoniae	ST-395	NDM-5/OXA-232	SHV-12, CTX-M-15, TEM-1

Figure 1: Multilocus Sequence Type (MLST) Among CRE with Detectable Carbapenmeases (n=59*)



*4 CP-CRE had an unknown MLST

KPC **OXA-48-like** **IMI**
NDM **NDM/OXA-48-like**

- 19 of 31 (61%) sequence types occurred only once during the study.
- The predominant ST was *K. pneumoniae* ST-258 (15 KPC), comprising 6% of all CRE isolates (**Figure 1**).
- For all isolates with a known MLST (n=206) the Simpson's index of diversity was high (0.975).

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METHODS

- Isolates are submitted to the Alameda County Public Health Laboratory (ACPHL), where antimicrobial resistance genetic markers are identified by whole genome sequencing (WGS) using single-end, 150-cycle reactions in a MiSeq (Illumina).
- Resistance genes were identified using pipelines built in Geneious and confirmed with Resfinder.
- All epidemiological analyses were conducted using R (Version 4.0).

CONCLUSIONS

- Compared to US data, Alameda County CRE produced proportionally fewer KPC and more NDM and OXA-48-like carbapenemases.[1]
- WGS data showed a high degree of diversity among carbapenemase alleles and sequence types, suggesting multiple introductions of different strains of CP-CRE over time rather than transmission between patients.
- Sequencing all CRE isolates in a region enables public health departments to track trends in CP-CRE incidence over time, monitor genetic diversity among CRE species, and identify the emergence of unusual antimicrobial resistance genes that may be associated with elevated resistance to β-lactams (e.g., bla_{NDM-5}, bla_{NDM-7}). [2, 3]

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