Characteristics of Carbapenem-Resistant Enterobacteriaceae (CRE)-Positive Patients in Oregon

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ABSTRACT

Background:
Carbapenem-resistant Enterobacteriaceae (CRE) are an emerging public health problem. This review was performed to better understand statewide CRE epidemiology and characteristics of CRE-positive patients.

Methods:
Mandatory reporting of CRE in Oregon began in December 2011. We reviewed medical records of all patients with CRE-positive cultures reported to the Oregon Health Authority through March 2013. Patient demographics and risk factors for CRE were analyzed. Carbapenemase production was assessed via Modified Hodge Test (MHT) and PCR for *Klebsiella pneumoniae* carbapenemase (KPC) and New Delhi metallo-beta-lactamase (NDM).

Results:
CRE were reported in 48 patients; median age was 66 (IQR 48, 76) and the majority were female (n=31; 63%). Most patients (n=31; 65%) were hospitalized at the time cultures were obtained; other healthcare settings from which CRE were isolated included outpatient clinics (n=11; 23%), emergency departments or urgent care (n=4; 8%), and long-term care facilities (n=2; 4%). Culture site and results of carbapenemase testing arranged by species are summarized in the Results section. PCR testing for NDM was negative in all tested isolates. The three patients harboring KPCs were not epidemiologically linked, and each had received recent healthcare outside Oregon.

Background

CRE: Enterobacteriaceae that meet any of the following criteria:

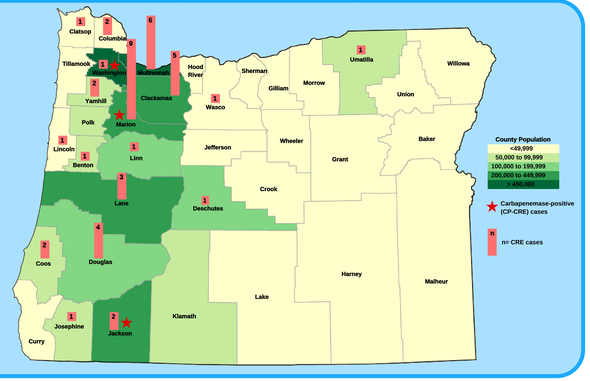
- Are non-susceptible (intermediate or resistant) to ANY carbapenem (doripenem, ertapenem, imipenem, meropenem)
  AND
  resistant to ANY of the following 3rd generation cephalosporins tested (cefotaxime, ceftriaxone, or ceftazidime)
- Possess/contain a gene sequence specific for carbapenemase (PCR)
- Are positive for carbapenemase production by a phenotypic test (e.g., Modified Hodge Test)

CP-CRE: Carbapenemase-producing CRE

DROP-CRE Network: Drug-Resistant Organism Prevention and Coordinated Regional Epidemiology Network: A multi-disciplinary advisory committee consisting of representatives from academic institutions and public health, convened to assist with planning and implementation of CRE epidemiology and control efforts

Methods: All isolates reviewed were from clinically obtained samples. No active surveillance was undertaken except for in the case of KPC isolate #1 where patients in the same ward were screened. Susceptibility interpretation was obtained from reporting laboratories using the CLSI breakpoints in place at each lab at the time of reporting.

RESULTS



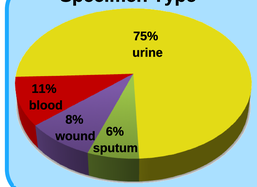
Patient Characteristics

Median Age (IQR)	66 (50,78)
Female	63%

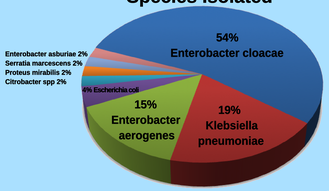
Location at time of culture

Hospitalized	65%
Median Hosp Days (IQR)	9.5 (5,24)
Clinic	23%
ED/Urgent Care	8%
LTAC	4%

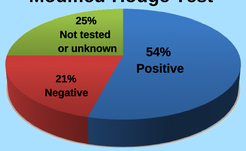
Specimen Type



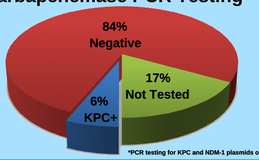
Species Isolated



Modified-Hodge Test



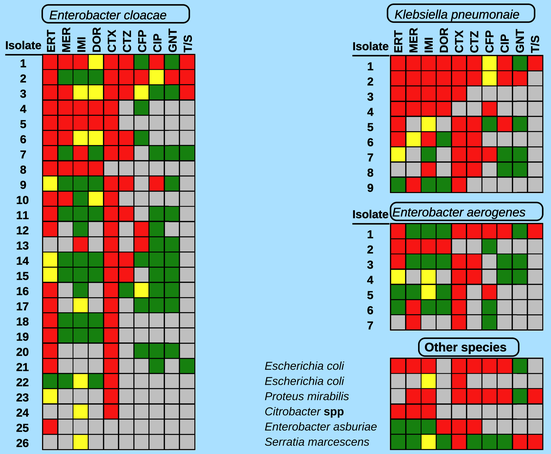
Carbapenemase PCR Testing*



*PCR testing for KPC and NDM-1 plasmids only

RESULTS

Antimicrobial Susceptibility



resistant
intermediate
sensitive
Not tested/unknown

ERT: ertapenem
MER: meropenem
IMI: imipenem/cilastatin
DOR: doripenem
CTX: ceftriaxone
CTZ: ceftazidime
CFP: cefepime
CIP: ciprofloxacin
GNT: gentamicin
T/S: trimethoprim/sulfmethoxazole

Sensitivities were interpreted by the reporting laboratory using the CLSI break-points in use at the reporting laboratory at time of testing

★ Carbapenemase-positive Patients (n=3)

- Three isolates had positive PCR carbapenemase tests
- All three isolates were *Klebsiella pneumoniae* harboring KPCs
- NDM-1 was not isolated in any samples
- no epidemiological link was found between these three patients

Isolate	Source	Species	ERT	MER	IMI	DOR	CTX	CTZ	CFP	CIP	GNT	T/S	Recent Healthcare
1	sputum	*Klebsiella pneumoniae*	R	R	R	R	R	R	I	R	R	R	VA
2	urine	*Klebsiella pneumoniae*	R	R	R	R	R	R	S	S	S	S	OH and PA
3	blood + wound	*Klebsiella pneumoniae*	R	R	R	R	R	R	S	S	S	S	CA and AZ

CONCLUSIONS

- CRE cases are infrequently reported in Oregon
- Only 3 CP-CRE cases have been reported to date
- Most isolates from reported cases were *Enterobacter* spp obtained from urinary tract samples
- All CP-CRE were KPC-producing *Klebsiella pneumoniae* in patients recently receiving care outside of Oregon
- No epidemiological link between the CP-CRE cases was identified

The paucity of reported carbapenemase-producing CRE indicates that the transmission of CP-CRE in Oregon is not yet widespread. This presents a unique opportunity for a coordinated regional approach to rapidly detect and prevent the spread of CRE in Oregon.

FUTURE WORK

- Continue statewide surveillance and analyze epidemiological and microbiological data to identify a more specific case definition targeting CP-CRE and risk factors for non-CP-CRE
- develop criteria for colonization versus infection and associated mortality data
- complete a local point-prevalence study to more accurately measure prevalence of CRE

Acknowledgements and References

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References:

Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-resistant Enterobacteriaceae: epidemiology and prevention. Clin Infect Dis. 2011;53(1):60-67.
Nordmann P, Naas T, Poirel L. Global spread of Carbapenemase-producing Enterobacteriaceae. Emerg Infect Dis. 2011;17(10):1791-1798
Centers for Disease Control andPrevention. Vital signs: carbapenem-resistant Enterobacteriaceae. MMWR Morb Mortal Wkly Rep. 2013;62(9):165-170
Won SY, Munoz-Price LS, Lolans K, et al. Emergence and rapid regional spread of Klebsiella pneumoniae carbapenemase-producing Enterobacteriaceae. Clin Infect Dis. 2011;53(6):532-540.
Oregon Health Authority. Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE): 2013 Oregon Toolkit. http://public.health.oregon.gov/DiseasesConditions/DiseasesAZ/CRE. Accessed Sept 12, 2013.