Emerging Infections Program Network Report Healthcare-Associated Infections Community Interface Multi-site Gram-negative Surveillance Initiative Carbapenem-Resistant Enterobacteriaceae (CRE) Surveillance, 2012

EIP Areas
Georgia (8 county Atlanta area); Minnesota (2 county Minneapolis – St. Paul area); and Oregon (3 county Portland area).

Population
The surveillance areas represent 7,217,047 persons.
Source: National Center for Health Statistics bridged-race vintage 2012 postcensal file.

Case Definition
A CRE case was defined as isolation of *Escherichia coli*, *Enterobacter aerogenes* (now *Klebsiella aerogenes*), *Enterobacter cloacae* complex, *Klebsiella pneumoniae,* or *Klebsiella oxytoca* with the following criteria:

- Carbapenem-nonsusceptible (doripenem, imipenem, or meropenem) and resistant to all tested third generation cephalosporins (ceftriaxone, ceftazidime, or cefotaxime) using the 2012 Clinical and Laboratory Standards Institute (CLSI) clinical breakpoints (1);
- Isolated from either a normally sterile body site (e.g., blood, cerebrospinal fluid, pleural fluid, pericardial fluid, peritoneal fluid, joint/synovial fluid, bone, internal body sites, or muscle) or urine;
- Identified in residents of the surveillance area in 2012

Because the clinical breakpoint defining resistance to ertapenem in Enterobacteriaceae is lower than the clinical breakpoint for other carbapenems, ertapenem was excluded from this CRE definition to increase specificity for carbapenemase-producing CRE.

Methodology
Case finding was active, laboratory-based, and population-based. Clinical laboratories that serve residents of the surveillance area were routinely contacted for case identification through a query of minimum inhibitory concentration (MIC) values from automated testing instruments. When possible, the MIC values obtained directly from the automated testing instruments were used to determine if an isolate met the phenotypic case definition. An incident CRE case was defined as the first CRE isolate meeting the case definition from a patient during a 30-day period.

A standardized case report form was completed for each incident case through review of medical records. Inpatient and outpatient medical records were reviewed for information on patient demographics, clinical syndrome, outcome of illness, and relevant healthcare exposures.

A convenience sample of CRE isolates (N=52) was collected from EIP sites and submitted to CDC for additional testing including species confirmatory testing, antimicrobial susceptibility testing by reference broth microdilution, screening for carbapenemase production using the Modified Hodge Test (MHT), polymerase chain reaction (PCR) screening for KPC, NDM, and OXA-48-like carbapenemase genes, and PCR testing for other carbapenemase genes (i.e., VIM) if MHT positive and negative for KPC, NDM, and OXA-48-like genes.

Incidence rates for CRE cases were calculated using the 2012 US Census estimates of the surveillance area population as the denominator. Assessment of vital status in patients admitted to a hospital occurred at the time of discharge from the acute care hospital. For patients in a long-term care facility, long-term acute care facility, or in an outpatient dialysis center, vital status was assessed 30 days after culture collection. For all other patients, vital status was assessed using medical records from the healthcare facility encounter associated with the culture.

CRE surveillance data underwent regular data cleaning to ensure accuracy and completeness. Patients with complete case report form data as of 1/2/2020 were included in this analysis. Because data can be updated as needed, analyses of datasets generated on a different date may yield slightly different results.

Results

Table 1. Specimen Sources for Incident CRE Cases by Organism (N=212), 2012

CRE Organism	Total	Urine No.	Urine %	Blood[a] No.	Blood %	Other Sterile Sites No.	Other Sterile Sites %
Enterobacter (*Klebsiella*) *aerogenes*	25	21	84.0	2	8.0	2	8.0
Enterobacter cloacae complex	26	23	88.5	2	7.7	1	3.8
Escherichia coli	32	29	90.6	1	3.1	2	6.3
Klebsiella pneumoniae	127	111	87.4	15	11.8	1	0.8
Klebsiella oxytoca	2	2	100.0	0	0	0	0
Total	212	186	87.7	20	9.4	6	2.8

[a]Category includes 1 case with both a positive blood and urine specimen collected.

Table 2a. Molecular Characteristics of CRE Isolates Submitted to CDC Based on Testing Performed at CDC (N=52), 2012

Organism	Isolates Submitted to CDC	Carbapenemase-Producing No.[a, b]	%
Enterobacter (*Klebsiella*) *aerogenes*	13	1/13	7.7
Enterobacter cloacae complex	7	5/7	71.4
Escherichia coli	8	1/8	12.5
Klebsiella pneumoniae	24	20/24	83.3
Klebsiella oxytoca	0	0	0
Total	52	27/52	51.9

[a]Testing was performed by PCR.

[b]Carbapenemase-producing isolates were collected from urine (n=24/27; 88.9%), blood (n=2/27; 7.4%), and other sterile sites (n=1/27; 3.7%).

Table 2b. Molecular Characteristics of CRE Isolates Submitted to CDC Based on Testing Performed at CDC (N=52), 2012 by Carbapenemase Gene

Organism	KPC No.	KPC %	NDM No.	OXA-48-like No.
Enterobacter (*Klebsiella*) *aerogenes*	1	7.7	0	0
Enterobacter cloacae complex	5	71.4	0	0
Escherichia coli	1	12.5	0	0
Klebsiella pneumoniae	20	83.3	0	0
Klebsiella oxytoca	0	0	0	0
Total	27	51.9	0	0

Table 2c. Confirmatory Antimicrobial Susceptibility Results of CRE Isolates Submitted to CDC

Organism	Carbapenem-resistant No.[c]	Carbapenem-resistant %[c]	Difficult to Treat No.[d]	Difficult to Treat %
Enterobacter (*Klebsiella*) *aerogenes*	6	46.2	0	0
Enterobacter cloacae complex	7	100.0	5	71.4
Escherichia coli	5	62.5	2	25.0
Klebsiella pneumoniae	22	91.7	21	87.5
Klebsiella oxytoca	0	0	0	0
Total	40	76.9	28	53.9

[c]Carbapenem resistance is defined as resistance to doripenem, ertapenem, imipenem, or meropenem, which differs from the surveillance case definition.

[d]Difficult to treat is defined as non-susceptibility to all first-line agents tested (i.e., carbapenems, extended-spectrum cephalosporins, fluoroquinolones, piperacillin-tazobactam, and aztreonam) (2).

Table 3. Incidence Rates for CRE Cases by Sex, Race, and Age (N=212), 2012

Sex	No. of Cases	Crude Incidence Rate/ 100,000 Population	95% CI
Female	123	3.33	3.28, 3.38
Male	89	2.53	2.47, 2.58

Race	No. of Cases	Crude Incidence Rate/ 100,000 Population	95% CI
Black or African American	124	6.64	6.53, 6.75
White	80	1.69	1.65, 1.73
Other[a]	7	1.12	0.85, 1.48
Unknown	1	N/A	N/A

Age group, years	No. of Cases	Crude Incidence Rate/ 100,000 Population	95% CI
0–49	53	1.61	1.55, 1.67
50–64	73	5.45	5.31, 5.61
65–79	50	8.96	8.61, 9.32
≥80	36	18.20	17.23, 19.21
Invasive cases[b]	34	0.47	0.44, 0.50
All cases	212	2.94	2.91, 2.96

[a]Other race includes American Indian or Alaska Native and Asian.

[b]Invasive cases include cases with a sterile incident specimen source or an incident urine specimen with a subsequent non-incident sterile specimen collected on the date of incident specimen collection or in the 29 days after.

Table 4. Clinical Characteristics and Infection Types for Incident CRE Cases (N=212), 2012[a]

No. of Immunocompromised[b] Cases	%
15	7.1

Infection types	No. of Cases	%
Urinary tract infection[c]	148	69.8
Bacteremia[d]	32	15.1
Septic shock	6	2.8
Decubitus or pressure ulcer	4	1.9
Other infection types	12	5.7
None[e]	27	12.7
Unknown	8	3.8

[a]Patients could have more than one type of infection reported.

[b]Immunocompromised includes solid organ transplant recipients and patients with a documented diagnosis of AIDS or a hematologic malignancy.

[c]Among 148 cases with a documented urinary tract infection (UTI), 91 (61.5%) had signs and symptoms associated with a UTI documented in the medical record. Reported signs and symptoms included fever, dysuria, costovertebral angle pain or tenderness, frequency, suprapubic tenderness, urgency, and other symptoms.

[d]Bacteremia includes cases with a positive blood specimen (incident or non-incident) or a documented diagnosis of sepsis, septicemia, bacteremia, or blood stream infection.

[e]No infection types reported.

Table 5. Patient Location Before, During, and After Incident Specimen Collection Among Incident CRE Cases (N=212), 2012

Residence before incident specimen collection	No. of Cases	%
Private residence or homeless	99	46.7
Long-term care facility	60	28.3
Acute care hospital inpatient	35	16.5
Long-term acute care hospital	17	8.0
Unknown	1	0.5

Collection location	No. of Cases	%
Outpatient setting or emergency department	96	45.3
Acute care hospital	74	34.9
Long-term care facility	33	15.6
Long-term acute care hospital	9	4.2

Hospitalized on the day of or in the 29 days after the date of incident specimen collection	No. of Cases	%
Hospitalized	140	66.0
Not hospitalized	67	31.6
Unknown	5	2.4

Discharge location among hospitalized patients (N=140)	No. of Cases	%
Private residence	64	45.7
Long-term care facility	48	34.3
Long-term acute care hospital	12	8.6
Died during hospitalization	16	11.4

Table 6. Outcome of CRE Cases (N=212), 2012

Outcome	No. of Cases	%
ICU admission in the 6 days after the date of incident specimen collection	30	14.2
Died	18	8.5
Cases with a positive incident sterile site specimen (N=26)	7	26.9
Cases with a positive incident urine specimen (N=186)	11[a]	5.9

[a]Less than 5 cases had a subsequent non-incident blood specimen collected on the date of incident specimen collection or in the 29 days after.

Table 7. Selected Characteristics of Incident CRE Cases (N=212), 2012[a]

Exposure	No. of Cases	%
Healthcare facility stay in the year before the date of incident specimen collection	176	83.0
Acute care hospital	164	77.4
Long-term care facility	86	40.6
Long-term acute care hospital	21	9.9
Surgery in the year before the date of incident specimen collection	72	34.0
In ICU in the 7 days before the date of incident specimen collection	31	14.6
Specimen collected ≥3 days after hospital admission	44	20.8
Chronic dialysis	20	9.4
Selected medical device(s) in place in the 2 calendar days before the date of incident specimen collection	146	68.9
Urinary catheter	102	48.1
Central venous catheter	75	35.4
Other[b]	80	37.7
None of the above healthcare exposures[c]	15	7.1
International travel in the 2 weeks before the date of incident specimen collection	2	0.9

[a]Patients could have more than one prior healthcare risk factor reported.

[b]Other medical devices include: endotracheal or nasotracheal tube, tracheostomy, gastrostomy tube, nephrostomy tube, nasogastric tube.

[c]Defined as having no healthcare exposures in the year before specimen collection, no selected medical devices in place in the 2 days before specimen collection, and specimen collected before calendar day 3 after hospital admission if hospitalized.

Summary

The overall incidence rate of CRE was 2.94 cases per 100,000 persons. The incidence rate increased with age, was higher in women than men, and higher in persons of Black or African American race than persons of other races. Most CRE were isolated from a urine source than from normally sterile body sites. Prior healthcare exposures were reported for most cases, with hospitalization in the prior year being and the presences of indwelling medical devices, being the most common exposures. Most cases required hospitalization, and overall crude mortality rate was 8.5%, with higher mortality observed in cases with a sterile site specimen source compared to those with a urine specimen source.

References

1. Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Second Informational Supplement*. CLSI document M100-S22 (ISBN 1-56238-786-3). Wayne, PA 2012.
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Citation

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