Emerging Infections Program (EIP) Network Report
Healthcare-Associated Infections Community Interface Activity
Multi-site Gram-negative Surveillance Initiative
Carbapenem-Resistant Enterobacterales (CRE) Surveillance, 2020

Note: The COVID-19 pandemic caused significant delays in 2020 case identification, data collection, data entry, data cleaning, and isolate collection and submission in all EIP sites. Medical record review for some cases could not be completed. In 2020, 6.6% of cases did not have a complete medical record review compared to 5.2% in 2019. Therefore, the percentage of cases for which some information is unknown is higher than in previous years.

Case Definition:

A carbapenem-resistant Enterobacterales (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-resistant (doripenem, imipenem, meropenem, or ertapenem) using the current Clinical and Laboratory Standards Institute clinical breakpoints (1);
- Isolated from 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 2020.

Surveillance Catchment Areas:

California (3 county San Francisco area), Colorado (5 county Denver area); Connecticut (statewide); Georgia (8 county Atlanta area); Maryland (4 county Baltimore area); Minnesota (2 county Minneapolis – St. Paul area); New Mexico (1 county Albuquerque area); New York (1 county Rochester area); Oregon (3 county Portland area); and Tennessee (8 county Nashville area).

Population:

The surveillance area represents 23,064,316 persons.
Source: National Center for Health Statistics bridged-race vintage 2020 file.

Methods:

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.
Standardized case report forms were completed for incident cases 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=785) was collected from sites and submitted to CDC for additional testing including species confirmatory testing, antimicrobial susceptibility testing by reference broth

microdilution with a metallo-β-lactamase (MBL) screen, screening for carbapenemase production using the Modified Carbapenem Inactivation Method (mCIM), real-time polymerase chain reaction (PCR) screening for carbapenemase-encoding genes, including *bla*$_{KPC}$, *bla*$_{NDM}$, and *bla*$_{OXA-48-like}$ genes, and PCR testing for other carbapenemase genes (i.e., *bla*$_{VIM}$) if MBL screen positive and negative for *bla*$_{KPC}$, *bla*$_{NDM}$, and *bla*$_{OXA-48-like}$ genes.

Incidence rates for CRE cases were calculated using the 2020 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 8/26/2022 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 CRE Cases by Organism, 2020 (N=1244)

Organism	Total	Urine No.	Urine %	Blood[a] No.	Blood[a] (%)	Other Sterile Sites No.	Other Sterile Sites %
Enterobacter cloacae complex	474	410	86.5	44	9.3	20	4.2
Klebsiella pneumoniae	347	306	88.2	33	9.5	8	2.3
Escherichia coli	323	285	88.2	31	9.6	7	2.2
Klebsiella aerogenes	75	60	80.0	11	14.7	4	5.3
Klebsiella oxytoca	25	21	84.0	4	16.0	0	0.0
Total	**1244**	**1082**	**87.0**	**123**	**9.9**	**39**	**3.1**

[a] Category may include cases with both a positive blood and urine specimen collected

Table 2. Incidence Rates of CRE Cases by Sex, Race and Age, 2020 (N=1244)

Sex	No. of Cases	%	Incidence Rate[a]
Female	742	59.6	6.30
Male	502	40.4	4.45

Race	No. of Cases	%	Incidence Rate[a]
White	692	55.6	4.37
Black or African American	286	23.0	6.42
Other[b]	62	5.0	2.23
Unknown	204	16.4	-

Age groups, years	No. of Cases	%	Incidence Rate[a]
0–18	34	2.7	0.65
19–49	203	16.3	2.03
50–64	274	22.0	6.26
65–79	431	34.6	16.02
≥80	302	24.3	37.33
Invasive cases[c]	172	13.8	0.75
All cases	1244	100.0	5.39

[a] Cases per 100,000 population for EIP areas (crude rates)

[b] Other race includes Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, or ≥2 races reported

[c] 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 3. CRE Cases by Race and Ethnicity, 2020 (N=1244)

Race/Ethnicity	No. of Cases	%
Hispanic, any race	113	9.1
Not known to be Hispanic[a] – White[b]	642	51.6
Not known to be Hispanic[a] – Black or African American[c]	282	22.7
Not known to be Hispanic[a] – Asian[d]	53	4.3
Not known to be Hispanic – Other or multiple races[e]	8	0.6
Not known to be Hispanic[a,f]– Unknown race	146	11.7

[a] Records either indicated ethnicity was non-Hispanic, or ethnicity was not known

[b] 45 CRE cases with unknown ethnicity

[c] 15 CRE cases with unknown ethnicity

[d] 6 CRE cases with unknown ethnicity

[e] American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, or ≥2 races reported; 1 CRE case with unknown ethnicity

[f] Of cases with unknown race, 128 CRE cases had unknown ethnicity

Table 4. Selected Characteristics of CRE Cases, 2020 (N=1244)

Location of patient on the 3rd calendar day before incident specimen collection	No. of Cases	%
Private residence or other location	725	58.3
Acute-care hospital (inpatient)	208	16.7
Long-term care facility	192	15.4
Long-term care acute care hospital	29	2.3
Homeless/incarcerated/other location	7	0.6
Unknown	83	6.7

Location of incident specimen collection	No. of Cases	%
Outpatient setting or emergency department	738	59.3
Acute care hospital	315	25.3
Long-term care facility	103	8.3
Long-term acute care hospital	32	2.6
Unknown	56	4.5

Infection types[a]	No. of Cases	%
Urinary tract infection	822	66.1
Bacteremia[b]	173	13.9
Septic shock	49	3.9
Other	261	21.0
None[c]	141	11.3
Unknown	82	6.6

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

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

[c] No infection types reported

Table 5. Selected Clinical Characteristics of CRE Cases, 2020[a] (N=1244)

Charlson comorbidity index	No. of Cases	%
0	237	19.1
1	219	17.6
≥2	728	58.5
Unknown	60	4.8
Median (IQR)	2	1–4

Underlying conditions	No. of Cases	%
Cardiovascular disease[b]	452	36.3
Diabetes mellitus	440	35.4
Neurologic condition, any	406	32.6
Urinary tract problems/abnormalities	389	31.3
Chronic renal disease	313	25.2
Chronic pulmonary disease[c]	266	21.4
Malignancy (hematologic or solid organ)	245	19.7
Skin condition	244	19.6
Gastrointestinal disease[d]	188	15.1
Transplant (hematopoietic stem cell or solid organ)	45	3.6
Unknown	60	4.8

SARS-CoV-2 testing	No. of Cases	%
Positive test for SARS-CoV-2 during hospitalization and on or before date of incident specimen collection[e]	47/530	8.9

[a] Patients could have more than one underlying condition reported

[b] Defined as myocardial infarction, congestive heart failure, congenital heart disease, stroke, transient ischemic attack, or peripheral vascular disease

[c] Defined as cystic fibrosis or any chronic respiratory condition resulting in symptomatic dyspnea

[d] Defined as diverticular disease, inflammatory bowel disease, peptic ulcer disease, short gut syndrome, or liver disease

[e] Among patients in the hospital on the date of incident specimen collection. Excludes patients who were admitted to the hospital after the date of incident specimen collection. A positive SARS-CoV-2 test was defined as any positive viral test for SARS-CoV-2, including antigen and nucleic acid amplification tests. Serologic tests were excluded

Table 6. Selected Healthcare Exposures or Risk Factors of CRE Cases, 2020a (N=1244)

Healthcare facility stay in the year before the date of incident specimen collection	**No. of Cases**	**%**
Any healthcare facility stay	773	62.1
Acute care hospitalization	715	57.5
Long-term care facility residence	311	25.0
Long-term acute care hospitalization	52	4.2

Exposure	**No. of Cases**	**%**
Surgery in the year before the date of incident specimen collection	373	30.0
Specimen collected ≥3 days after hospital admission	188	15.1
Chronic dialysis	46	3.7

Selected medical device(s) in place in the 2 calendar days before the date of incident specimen collection	**No. of Cases**	**%**
Urinary catheter	385	31.0
Central venous catheter	188	15.1
Other[b]	238	19.1
None of the above healthcare exposures[c]	282	22.7
Healthcare exposures are unknown	50	4.0
International travel in the 2 months prior to date of incident specimen	30	2.4

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

[b] Other medical devices: 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

Table 7. Outcomes of Incident CRE Cases, 2020 (N=1244)

Outcomes	**No. of Cases**	**%**
Hospitalized on the day of or in the 29 days after the date of incident specimen collection[a]	628	50.5
ICU admission in the 6 days after the date of incident specimen collection	86	6.9

Discharge location among hospitalized	**No. of Cases**	**%**
Private residence or other location	353/628	56.2
Long-term care facility	185/628	29.5
Died during hospitalization	69/628	11.0
Long-term acute care hospital	17/628	2.7
Unknown	4/628	0.6
Died within 30 days of incident specimen collection date	57	4.6
Cases with an incident sterile site specimen	26/162	16.0
Cases with an incident urine specimen[b]	31/1082	2.9

[a] Data include 208 cases considered to be hospital-onset

[b] One incident CRE case had a subsequent non-incident blood specimen collected on the date of incident specimen collection or in the 29 days after

Laboratory Characterization:

Table 8a. Antimicrobial Susceptibility and Molecular Characteristics of CRE Isolates Based on Testing Performed at CDC, 2020 (N=785)

Organism	Isolates Submitted to CDC	Carbapenemase-producing, [a,b,c] - N	%
Enterobacter cloacae complex	327	24	7.3
Klebsiella pneumoniae[g]	202	85	42.1
Escherichia coli	195	28	14.4
Klebsiella aerogenes	47	0	0.0
Klebsiella oxytoca	14	5	35.7
Total	**785**	**142**	**18.1**

Table 8b. Molecular Characteristics of CRE Isolates Based on Testing Performed at CDC by Carbapenemase Gene, 2020 (N=785)

Organism	*bla*$_{KPC}$ - N	*bla*$_{KPC}$ - %	*bla*$_{NDM}$ - N	*bla*$_{NDM}$ - %	*bla*$_{OXA-48-like}$ - *N*	*bla*$_{OXA-48-like}$ - *%*	*bla*$_{vim}$[e] - *N*	*bla*$_{vim}$[e] - *%*	*bla*$_{imp}$[e] - N	*bla*$_{imp}$[e] - %
Enterobacter cloacae complex	17	5.2	3	0.9	0	0.0	1	0.3	4	1.2
Klebsiella pneumoniae[g]	76	37.6	5	2.5	4	2.0	0	0.0	0	0.0
Escherichia coli	13	6.7	13	6.7	2	1.0	0	0.0	0	0.0
Klebsiella aerogenes	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Klebsiella oxytoca	5	35.7	0	0.0	0	0.0	0	0.0	0	0.0
Total	**111**	**14.1**	**21**	**2.7**	**6**	**0.8**	**1**	**0.1**	**4**	**0.5**

Table 8c. Confirmatory Antimicrobial Susceptibility Results of CRE Isolates Submitted to CDC

Organism	Carbapenem-resistant - N	Carbapenem-resistant - %	Difficult to treat[f] - N	Difficult to treat[f] - %
Enterobacter cloacae complex	169	51.7	12	3.7
Klebsiella pneumoniae[g]	123	60.9	49	24.3
Escherichia coli	94	48.2	17	8.7
Klebsiella aerogenes	30	63.8	0	0.0
Klebsiella oxytoca	8	57.1	2	14.3
Total	**424**	**54.0**	**80**	**10.2**

[a] Testing was performed by PCR

[b] Carbapenemase-producing isolates were collected from urine (n=108/142; 76.1%), blood (n=32/142; 22.5%), and other normally sterile site (n=2/142; 1.4%)
[c] All isolates that were mCIM positive were also PCR positive, except for two isolates that were mCIM positive and PCR negative
[d] One isolate had *bla*$_{kpc}$ and *bla*$_{imp}$ gene
[e] Testing was not done prior to 2019
[f] Difficult to treat (2) is defined as non-susceptibility to all first-line agents tested (i.e., carbapenems, extended-spectrum cephalosporins, fluoroquinolones, piperacillin-tazobactam, and aztreonam)
[g] Includes *Klebsiella pneumoniae* and *Klebsiella variicola*

Summary:

Surveillance data from 2020 represent the ninth full year of population-based surveillance for CRE through the Emerging Infections Program. The overall crude incidence rate of CRE in 2020 was 5.39 cases per 100,000 persons. The incidence rate increased with age and was higher in women than in men and higher in persons of Black or African American race than in persons of other races. More CRE were isolated from a urine source than from normally sterile body sites. Underlying conditions were commonly reported, with more than half of CRE cases having a Charlson comorbidity index of ≥2. Prior healthcare exposures were reported for most cases, with an admission to a healthcare setting in the prior year, presence of indwelling medical devices, and surgery in the prior year being the most common exposures. Approximately half of the CRE cases were hospitalized, and overall crude 30-day mortality was 4.6%, with a higher 30-day mortality observed in cases with a sterile-site specimen source compared to those with a urine specimen source.

Among the 785 CRE isolates submitted to CDC, 18.1% were carbapenemase-producing. KPC was detected in 14.1% of the isolates, NDM in 2.7% of the isolates, OXA-48-like in 0.8% of the isolates, IMP in 0.5% of the isolates, and VIM in 0.1% of the isolates.

References:

1. CLSI. *Performance Standards for Antimicrobial Susceptibility Testing.* 30th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2020.

2. Kadri SS, Adjemian J, Lai YL, Spaulding AB, Ricotta E, Prevots DR, et al. Difficult-to-Treat Resistance in Gram-negative Bacteremia at 173 US Hospitals: Retrospective Cohort Analysis of Prevalence, Predictors, and Outcome of Resistance to All First-line Agents. Clin Infect Dis. 2019 Nov 28;67(12):1803-14.

Citation:

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For more information, visit our web sites:

- Multi-site Gram-negative Surveillance Initiative (MuGSI) (https://www.cdc.gov/hai/eip/mugsi.html)
- Healthcare-Associated Infections - Community Interface Data Visualization (HAICViz) (https://www.cdc.gov/hai/eip/haicviz.html)