Emerging Infections Program (EIP) Network Report
Healthcare-Associated Infections Community Interface Activity
Multi-site Gram-negative Surveillance Initiative
Extended-spectrum β-lactamase (ESBL)-producing Enterobacterales (ESBL-E) 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, 21.7% of cases did not have a complete medical record review compared to 3.4% in 2019. Therefore, the percentage of cases for which some information is unknown is higher than in previous years.

Case Definition:

An extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales (ESBL-E) case was defined as isolation of *Escherichia coli*, *Klebsiella pneumoniae,* or *Klebsiella oxytoca* with the following criteria:
- Extended-spectrum cephalosporin-resistant (ceftazidime, cefotaxime, or ceftriaxone) using the current Clinical and Laboratory Standards Institute clinical breakpoints (1); and
- Carbapenem non-resistant (i.e., susceptible or intermediate) (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 site, muscle) or urine;
- Identified in residents of the surveillance area in 2020.

Surveillance Catchment Areas:

Colorado (1 county Denver area); Georgia (2 county Atlanta area); Maryland (1 county Baltimore area); New Mexico (1 county Albuquerque area); New York (1 county Rochester area); Tennessee (4 county Columbia area).

Population:

The surveillance area represents 2,939,995 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 ESBL-E case was defined as the first ESBL-E 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 ESBL-E isolates (N=394) was collected from sites and submitted to CDC for additional testing including species confirmatory testing, reference antimicrobial susceptibility testing by using broth microdilution, phenotypic screening for ESBL production by using ceftazidime and cefotaxime alone and in combination with clavulanate, and molecular characterization.

Incidence rates for 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.

ESBL-E surveillance data underwent regular data cleaning to ensure accuracy and completeness. Patients with complete case report form data as of 7/26/2022 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:

Note: Due to the impact of the COVID-19 pandemic on case identification and case report form completion, the numbers of cases and denominators used for incidence rate calculations and case descriptions vary from table to table.

Tables 1, 2a, and 9 include all incident cases identified in 6 sites (4741). Incidence rates were calculated using the total population in the 6-site surveillance area.

Table 2b includes all incident cases identified in 5 sites (3564). Data on race were unavailable for most cases in the 6th site, which was excluded. Incidence rates were calculated using the total population in the 5-site surveillance area.

Tables 3–8 include incident cases with completed case report forms in 6 sites (2879). The number of cases with completed case report forms (2879) differs from the total number of incident cases (4741) for 2 reasons: 1) a case report form is completed for the first incident case per species per person during 2020 (except invasive cases, for which a case report form is always completed); and 2) case report forms were completed for only 3% of cases in 2020 in 1 of the 6 sites.

Table 1. Specimen Sources for ESBL-E Cases by Organism, 2020 (N=4741)

Organism	Total	Urine No.	Urine %	Blood[a] No.	Blood[a] %	Other Sterile Sites No.	Other Sterile Sites %
Escherichia coli	3807	3612	94.9	168	4.4	27	0.7
Klebsiella pneumoniae	788	714	90.6	68	8.6	6	0.8
Klebsiella oxytoca	146	133	91.1	10	6.8	3	2.1
Total	**4741**	**4459**	**94.1**	**246**	**5.2**	**36**	**0.8**

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

Table 2a: Incidence Rates of ESBL-E Cases by Sex and Age, 2020 (N=4741)

Sex	No. of Cases	%	Incidence Rate[a]
Female	3498	73.8	229.64
Male	1242	26.2	87.66
Unknown	1	0.0	-

Age groups, years	No. of Cases	%	Incidence Rate[a]
0–18	146	3.1	21.87
19–49	1156	24.4	92.91
50–64	1046	22.1	187.24
65–79	1485	31.3	407.81
≥80	908	19.2	860.79
Invasive cases[b]	326	6.9	11.09
All cases	4741	100.0	161.26

[a] Cases per 100,000 population for EIP areas (crude rates)
[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 2b: Incidence Rates of ESBL-E Cases by Race, 2020 (N=3564)

Race	No. of Cases	%	Incidence Rate[a]
White	2031	57.0	117.9
Black or African American	357	10.0	74.8
Other[b]	146	4.1	95.0
Unknown	1030	28.9	-

Note: Table includes data from five EIP sites
[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

Table 3. ESBL-E Cases by Race and Ethnicity, 2020 (N=2879)

Race/Ethnicity	No. of Cases	%
Hispanic, any race	580	20.1
Not known to be Hispanic[a] – White[b]	1586	55.1
Not known to be Hispanic[a] – Black or African American[c]	372	12.9
Not known to be Hispanic[a] – Asian[d]	98	3.4
Not known to be Hispanic – Other or multiple races[e]	41	1.4
Not known to be Hispanic[a,f]– Unknown race	202	7.0

Note: Table includes data from 6 sites; case report form data were available for only 3% of cases in one site
[a] Records either indicated ethnicity was non-Hispanic, or ethnicity was not known
[b] 177 ESBL-E cases with unknown ethnicity
[c] 10 ESBL-E cases with unknown ethnicity
[d] 9 ESBL-E cases with unknown ethnicity
[e] American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, or ≥2 races reported; 2 ESBL-E case with unknown ethnicity
[f] Of cases with unknown race, 163 ESBL-E cases had unknown ethnicity

Table 4. Selected Characteristics of ESBL-E Cases, 2020 (N=2879)

Location of patient on the 3rd calendar day before incident specimen collection	No. of Cases	%
Private residence	2363	82.1
Long-term care facility	320	11.1
Acute-care hospital (inpatient)	124	4.3
Homeless	13	0.5
Long-term care acute care hospital	6	0.2
Other	2	0.1
Unknown	51	1.8

Location of incident specimen collection	No. of Cases	%
Outpatient setting or emergency department	2391	83.0
Acute care hospital	279	9.7
Long-term care facility/long-term acute care hospital	181	6.3
Unknown	28	1.0

Infection types[a]	No. of Cases	%
Urinary tract infection	2262	78.6
Bacteremia[b]	270	9.4
Pyelonephritis	112	4.0
Other	133	4.6
None[c]	298	10.4
Unknown	103	3.6

Note: Table includes data from 6 sites; case report form data were available for only 3% of cases in one site
[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 ESBL-E Cases, 2020 (N=2879)

Charlson comorbidity index	No. of Cases	%
0	1019	35.4
1	602	20.9
≥2	1188	41.3
Unknown	70	2.4
Median (IQR)	1	0–3

Underlying conditions[a]	No. of Cases	%
Diabetes mellitus	828	28.8
Neurologic condition, any	813	28.2
Urinary tract problems/abnormalities	791	27.5
Cardiovascular disease[b]	739	25.7
Chronic pulmonary disease[c]	598	20.8
Chronic renal disease	516	17.9
Gastrointestinal disease[d]	365	12.7
Skin condition	349	12.1
Malignancy (hematologic or solid organ)	335	11.6
Transplant (hematopoietic stem cell or solid organ)	40	1.4
Unknown	70	2.4

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]	48/671	7.2

Note: Table includes data from 6 sites; case report form data were available for only 3% of cases in one site
[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 ESBL-E Cases, 2020[a] (N=2879)

Healthcare facility stay in the year before the date of incident specimen collection	No. of Cases	%
Any healthcare facility stay	1146	39.8
Acute care hospitalization	1038	36.1
Long-term care facility residence	473	16.4
Long-term acute care hospitalization	22	0.8
Surgery in the year before the date of incident specimen collection	483	16.8
Specimen collected ≥3 days after hospital admission	113	3.9
Chronic dialysis	70	2.4

Selected medical device(s) in place in the 2 calendar days before the date of incident specimen collection	No. of Cases	%
Urinary catheter	448	15.6
Central venous catheter	142	4.9
Other[b]	171	5.9
None of the above healthcare exposures[c]	1402	48.7
Healthcare exposures are unknown	55	1.9
International travel in the 2 months prior to date of incident specimen	100	3.5

Note: Table includes data from 6 sites; case report form data were available for only 3% of cases in one site
[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 ESBL-E Cases, 2020 (N=2879)

Outcomes	No. of Cases	%
Hospitalized on the day of or in the 29 days after the date of incident specimen collection	834	29.0
ICU admission in the 6 days after the date of incident specimen collection	114	4.0

Discharge location among hospitalized	No. of Cases	%
Private Residence	528/834	63.3
Long-term care facility	226/834	27.1
Died during hospitalization	63/834	7.6
Long-term acute care hospital	11/834	1.3
Other/unknown	6/834	0.7
Died within 30 days of incident specimen collection date	66	2.3
Cases with an incident sterile site specimen	28/167	16.8
Cases with an incident urine specimen[a]	38/2712	1.4

Note: Table includes data from 6 sites; case report form data were available for only 3% of cases in one site
[a] Data include 124 cases considered to be hospital-onset
[b] One incident ESBL-E case had a subsequent non-incident blood specimen collected on the date of incident specimen collection or in the 29 days after

Table 8. Prior Antimicrobial Use among ESBL-E Cases, 2020 [a] (N=2879)

Antimicrobial class	Antimicrobial agent[b, c]	No. of Cases	%
Any antimicrobial class	Any antimicrobial agent	855	29.7
Cephems	Cefazolin, cefdinir, cefepime, cefixime, cefotaxime,[d] cefoxitin, cefpodoxime, ceftaroline, ceftazidime, ceftizoxime, ceftriaxone, cefuroxime, cephalexin	405	14.1
Fluoroquinolones	Ciprofloxacin, delafloxacin, levofloxacin, moxifloxacin, nalidixic acid	193	6.7
Glycopeptides	Dalbavancin,[d] oritavancin, telavancin,[d] vancomycin (intravenous or oral)	112	4.0
Penicillins	Amoxicillin, ampicillin, penicillin, nafcillin, oxacillin	68	2.4
ß-lactam combination agents	Amoxicillin/clavulanic acid, ampicillin/sulbactam, ceftazidime/avibactam,[d] ceftolozane/tazobactam,[d] meropenem/vaborbactam	69	2.4
Tetracyclines	Doxycycline,[d] minocycline, tetracycline, tigecycline	63	2.2
Carbapenems	Doripenem,[d] ertapenem, meropenem, imipenem/cilastatin	33	1.2
Lincosamides	Clindamycin	23	0.8
Ansamycins	Rifaximin, rifampin	21	0.7
Aminoglycosides	Amikacin, gentamicin, tobramycin	19	0.7
Fosfomycins	Fosfomycin	13	0.5
Macrolides	Azithromycin, clarithromycin, erythromycin[d]	2	0.1
Folate pathway antagonists	Trimethoprim, trimethoprim/sulfamethoxazole	8	0.3
Lipopeptides	Daptomycin	7	0.2
Monobactams	Aztreonam	3	0.1

Note: Table includes data from 6 sites; case report form data were available for only 3% of cases in one site

[a] Antimicrobial use was reported in the 30 days before the date of incident specimen collection

[b] Patients could have more than one antimicrobial reported

[c] 16 (0.6%) were methenamine, unknown, unspecified (reported as other and not shown in table)

[d] No prior antimicrobial use reported

Laboratory Characterization:

Table 9. Antimicrobial Susceptibility and Molecular Characteristics of ESBL-E Isolates Based on Testing Performed at CDC, 2020 (N=394)

Organism	Isolates Submitted to CDC	Isolates meeting case definition, No.	Isolates meeting case definition, %	ESBL-producing organisms,[a] No.	ESBL-producing organisms,[a] %
Escherichia coli	307	290	94.5%	267	87.0%
Klebsiella pneumoniae [b]	82	79	96.3%	78	95.1%
Klebsiella oxytoca	5	5	100.0%	5	100.0%
Total	**394**	**374**	**94.9%**	**350**	**88.8%**

[a] Phenotypic screening for ESBL production was performed by using ceftazidime and cefotaxime alone and in combination with clavulanate according to CDC guidelines
[b] Includes *Klebsiella pneumoniae* and *Klebsiella variicola*

Summary:

Surveillance data from 2020 represent the second calendar year and first full year of population-based surveillance for ESBL-E through the Emerging Infections Program (surveillance was conducted for six months in 2019). The crude annual incidence rate of ESBL-E in 2020 was 161.26 cases per 100,000 persons. The incidence rate increased with age and was higher in women than in men and higher in persons of White race than in persons of other races. More ESBL-E were isolated from a urine source than from normally sterile body sites. Prior healthcare exposures were reported for over half of the cases, with an admission to a healthcare setting in the prior year and surgery in the prior year being the most common exposures. Approximately one-third of the ESBL-E cases were hospitalized, and overall crude 30-day mortality was 2.3%, 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 402 isolates submitted to CDC, 88.8% were ESBL-producing.

References:

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

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)