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, 2021

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 specimen (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 2021.

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 2,947,518 persons.
Source: Starting with the 2021 surveillance year, population estimates were obtained from the U.S. Census Bureau, Population Division, Vintage 2021 Special Tabulation. This file includes population estimates for the five single-race categories and a multiple-race category specified in the 1997 Office of Management and Budget (OMB) standards for racial categories. The population estimates for previous reports were obtained from the National Center for Health Statistics, which bridged the multiple-race group population counts to the four single-race categories specified in the 1977 OMB standards.

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=350) was collected from EIP 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 2021 U.S. 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 7/7/2023 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: The numbers of cases and denominators used for incidence rate calculations and case descriptions vary from table to table.

Tables 1 and 2a include all incident cases identified in 6 EIP sites (4849). Incidence rates were calculated using the total population in the 6-site surveillance area.

Table 2b includes all incident cases identified in 5 EIP sites (n=3776). Data on race were unavailable for most cases in the 6th EIP site, which was excluded. Incidence rates were calculated using the total population in the 5-site surveillance area.

Tables 3–8 include 3023 incident cases with completed case report forms (n=2,931) or with unavailable charts (n=92) in 6 EIP sites (3023). This number differs from the total number of incident cases (n=4849) for 2 reasons: 1) a case report form is completed for the first incident case per species per person during 2021 (except invasive cases, for which a case report form is always completed); and 2) case report forms were completed for <1% of cases in 2021 in 1 of the 6 EIP sites.

Table 1. Specimen Sources for ESBL-E Cases by Organism, 2021 (N=4849)

Organism	Total	Urine No.	Urine %	Blood[a] No.	Blood[a] %	Other sterile specimens No.	Other sterile specimens %
Escherichia coli	3896	3706	95.1	161	4.1	29	0.7
Klebsiella pneumoniae	817	737	90.2	74	9.1	6	0.7
Klebsiella oxytoca	136	123	90.4	8	5.9	5	3.7
Total	**4849**	**4566**	**94.2**	**243**	**5.0**	**40**	**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, 2021 (N=4849)

Sex	No. of Cases	%	Incidence Rate[a]
Female	3532	72.8	232.4
Male	1301	26.8	91.1
Unknown	16	0.3	-

Age groups, years	No. of Cases	%	Incidence Rate[a]
0–18	148	3.1	22.1
19–49	1120	23.1	90.1
50–64	1060	21.9	188.7
65–79	1652	34.1	442.4
≥80	869	17.9	881.3
Invasive cases[b]	339	7.0	11.5
All cases	4849	100.0	164.5

[a] Cases per 100,000 population for EIP sites (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, 2021 (N=3776)

Race	No. of Cases	%	Incidence Rate[a]
White	2144	56.8	126.2
Black or African American	366	9.7	79.5
Other[b]	182	4.8	86.1
Unknown	1084	28.7	-

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, 2021 (N=3023)

Race/Ethnicity	No. of Cases	%
Hispanic, any race	638	21.1
Not known to be Hispanic[a] – White[b]	1667	55.1
Not known to be Hispanic[a] – Black or African American[c]	347	11.5
Not known to be Hispanic[a] – Asian[d]	122	4.0
Not known to be Hispanic – Other or multiple races[e]	65	2.2
Not known to be Hispanic[a,f]– Unknown race	184	6.1

Note: Table includes data from six EIP sites; case report form data were available for <1% of cases in one EIP site

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

[b] 110 ESBL-E cases with unknown ethnicity

[c] 23 ESBL-E cases with unknown ethnicity

[d] 6 ESBL-E cases with unknown ethnicity

[e] American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, or ≥2 races reported; 3 ESBL-E case with unknown ethnicity

[f] Of cases with unknown race, 146 ESBL-E cases had unknown ethnicity

Table 4. Selected Characteristics of ESBL-E Cases, 2021 (N=3023)

Location of patient on the 3rd calendar day before incident specimen collection	No. of Cases	%
Private residence	2473	81.8
Long-term care facility	265	8.8
Acute-care hospital (inpatient)	181	6.0
Homeless	14	0.5
Long-term care acute care hospital	7	0.2
Unknown	83	2.7

Location of incident specimen collection	No. of Cases	%
Outpatient setting or emergency department	2417	80.0
Acute care hospital	384	12.7
Long-term care facility	148	4.9
Long-term acute care hospital	8	0.3
Autopsy/unknown	66	2.2

Infection types[a]	No. of Cases	%
Urinary tract infection	2285	75.6
Bacteremia[b]	286	9.5
Pyelonephritis	101	3.3
Other	144	4.8
None[c]	329	10.9
Unknown	160	5.3

Note: Table includes data from six EIP sites; case report form data were available for <1% of cases in one EIP 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, 2021 (N=3023)

Charlson comorbidity index	No. of Cases	%
0	1043	34.5
1	641	21.2
≥2	1248	41.3
Unknown	91	3.0
Median (IQR)	1	0–3

Underlying conditions[a]	No. of Cases	%
Diabetes mellitus	883	29.2
Neurologic condition, any	837	27.7
Urinary tract problems/abnormalities	782	25.9
Cardiovascular disease[b]	742	24.5
Chronic pulmonary disease[c]	620	20.5
Chronic renal disease	573	19.0
Gastrointestinal disease[d]	392	13.0
Malignancy (hematologic or solid organ)	349	11.5
Skin condition	325	10.8
Transplant (hematopoietic stem cell or solid organ)	38	1.3
Unknown	91	3.0

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]	151/710	21.3

Note: Table includes data from six EIP sites; case report form data were available for only <1% of cases in one EIP 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, 2021[a] (N=3023)

Exposure	No. of Cases	%
Healthcare facility stay in the year before the date of incident specimen collection – any healthcare facility stay	1124	37.2
Healthcare facility stay in the year before the date of incident specimen collection – acute care hospitalization	1016	33.6
Healthcare facility stay in the year before the date of incident specimen collection – long-term care facility residence	430	14.2
Healthcare facility stay in the year before the date of incident specimen collection – long-term acute care hospitalization	19	0.6
Surgery in the year before the date of incident specimen collection	474	15.7
Specimen collected ≥3 days after hospital admission	159	5.3
Chronic dialysis	67	2.2
Selected medical device(s) in place in the 2 calendar days before the date of incident specimen collection – urinary catheter	454	15.0
Selected medical device(s) in place in the 2 calendar days before the date of incident specimen collection – central venous catheter	147	4.9
Selected medical device(s) in place in the 2 calendar days before the date of incident specimen collection – other [b]	208	6.9
None of the above healthcare exposures [c]	1503	49.7
Healthcare exposures are unknown	82	2.7
International travel in the 12 months prior to date of incident specimen	61	2.0

Note: Table includes data from six EIP sites; case report form data were available for only <1% of cases in one EIP site

[a] Patients could have more than one prior healthcare exposure or 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, 2021 (N=3023)

Outcomes	No. of cases	%
Outcomes – hospitalized on the day of or in the 29 days after the date of incident specimen collection[a,b]	902	29.8
Outcomes – ICU admission in the 6 days after the date of incident specimen collection[a]	86	2.8
Discharge location among hospitalized patients – private residence	579/902	64.2
Discharge location among hospitalized patients – long-term care facility	230/902	25.5
Discharge location among hospitalized patients – died during hospitalization	71/902	7.9
Discharge location among hospitalized patients – long-term acute care hospital	11/902	1.2
Discharge location among hospitalized patients – unknown/other	10/902	1.1
Died within 30 days of incident specimen collection date	67	2.2
Cases with an incident sterile site specimen	24/177	13.6
Cases with an incident urine specimen[c]	43/2803	1.5

Note: Table includes data from six EIP sites; case report form data were available for <1% of cases in one EIP site

[a] Patients could have more than one outcome

[b] Data include 181 cases considered to be hospital-onset

[c] 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, 2021[a] (N=3023)

Antimicrobial class	Antimicrobial agent [b, c]	No. of Cases	%
Any antimicrobial class	Any antimicrobial agent	806	26.7
Cephems	Cefazolin, cefdinir, cefepime, cefixime, cefotaxime, cefoxitin, cefpodoxime, ceftaroline, ceftazidime, ceftizoxime, ceftriaxone, cefuroxime, cephalexin	411	13.6
Fluoroquinolones	Ciprofloxacin, delafloxacin, levofloxacin, moxifloxacin, nalidixic acid	153	5.1
Glycopeptides	Dalbavancin,[d] oritavancin, telavancin,[d] vancomycin (intravenous or oral)	127	4.2
Penicillins	Amoxicillin, ampicillin, penicillin, nafcillin, oxacillin	66	2.2
ß-lactam combination agents	Amoxicillin/clavulanic acid, ampicillin/sulbactam, ceftazidime/avibactam, ceftolozane/tazobactam,[d] meropenem/vaborbactam	72	2.4
Tetracyclines	Doxycycline, minocycline, tetracycline, tigecycline	66	2.2
Carbapenems	Doripenem,[d] ertapenem, meropenem, imipenem/cilastatin	33	1.1
Lincosamides	Clindamycin	18	0.6
Ansamycins	Rifaximin, rifampin	14	0.5
Aminoglycosides	Amikacin, gentamicin, tobramycin	21	0.7
Fosfomycins	Fosfomycin	16	0.5
Macrolides	Azithromycin, clarithromycin, erythromycin	5	0.2
Folate pathway antagonists	Trimethoprim, trimethoprim/sulfamethoxazole	2	0.1
Lipopeptides	Daptomycin, polymyxin B,[d] polymyxin E[d]	8	0.3
Monobactams	Aztreonam	2	0.1

Note: Table includes data from six EIP sites; case report form data were available for <1% of cases in one EIP 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] 19 (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, 2021 (N=350)

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	260	244	93.8	226	86.9
Klebsiella pneumoniae [b]	88	83	94.3	81	92.0
Klebsiella oxytoca	2	2	100	2	100
Total	**350**	**329**	**94.0**	**309**	**88.3**

[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 2021 represent the third calendar year and second 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 2021 was 164.5 cases per 100,000 persons. The incidence rate increased with increasing age, 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 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 2.2%, with a higher 30-day mortality observed in cases with a sterile site specimen source compared to those with a urine specimen source. More than one-fifth of patients in the hospital on the date of incident specimen collection (21.3%) had a positive viral test for SARS-CoV-2 during their hospitalization and on or before date of incident ESBL-E specimen collection. Among the 350 isolates submitted to CDC, 88.3% were ESBL-producing.

References:

1. CLSI. *Performance Standards for Antimicrobial Susceptibility Testing.* 31st ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2021.

Citation:

Centers for Disease Control and Prevention. 2023. Emerging Infections Program, Healthcare-Associated Infections – Community Interface Surveillance Report, Multi-site Gram-negative Surveillance Initiative (MuGSI), Extended-spectrum β-lactamase -producing Enterobacterales Surveillance, 2021. Available at: https://www.cdc.gov/hai/eip/pdf/mugsi/2021-ESBL-Report-508.pdf

For more information, visit our web sites:

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