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Major Article

Carbapenem-resistant *Acinetobacter baumannii* complex in the United States—An epidemiological and molecular description of isolates collected through the Emerging Infections Program, 2019

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Background: Understanding the epidemiology of carbapenem-resistant *A. baumannii* complex (CRAB) and the patients impacted is an important step toward informing better infection prevention and control practices and improving public health response.

Methods: Active, population-based surveillance was conducted for CRAB in 9 U.S. sites from January 1 to December 31, 2019. Medical records were reviewed, isolates were collected and characterized including antimicrobial susceptibility testing and whole genome sequencing.

Results: Among 136 incident cases in 2019, 66 isolates were collected and characterized; 56.5% were from cases who were male, 54.5% were from persons of Black or African American race with non-Hispanic ethnicity, and the median age was 63.5 years. Most isolates, 77.2%, were isolated from urine, and 50.0% were collected in the outpatient setting; 72.7% of isolates harbored an acquired carbapenemase gene (aCP),

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predominantly bla_{OXA-23} or $bla_{OXA-24/40}$; however, an isolate with bla_{NDM} was identified. The antimicrobial agent with the most in vitro activity was cefiderocol (96.9% of isolates were susceptible).

Conclusions: Our surveillance found that CRAB isolates in the U.S. commonly harbor an aCP, have an antimicrobial susceptibility profile that is defined as difficult-to-treat resistance, and epidemiologically are similar regardless of the presence of an aCP.

BACKGROUND

Acinetobacter baumannii complex predominantly causes infections among patients with frequent health care exposure.[1–7] Common *A. baumannii* infections include bacteremia, urinary, wound, and respiratory tract infections.[4–6,8–10] Carbapenem-resistant *A. baumannii* (CRAB) is considered an urgent threat by the Centers for Disease Control and Prevention (CDC) because it causes difficult-to-treat infections with mortality rates ranging from 17.9% to 61.6%.[6,9,11–13]

Resistance to carbapenem antibiotics in *A. baumannii* can be conferred in several ways.[10,14,15] Of greatest concern is the acquisition of carbapenemase genes present on mobile genetic elements, such as bla_{OXA-23} or bla_{NDM}, which enable their spread via horizontal transmission.[7,9,10,14] Other contributing carbapenem resistance mechanisms include low outer membrane permeability and overexpression of $bla_{OXA-51-like}$ due to the presence of insertion sequence Aba_1.[10,14,16]

Understanding the epidemiology of CRAB and the patients impacted is an important step toward informing better infection prevention and control practices and improving public health response. We sought to describe the epidemiological and molecular characteristics of isolates collected from cases infected with CRAB identified through the Emerging Infections Program's (EIP's) Multisite Gram-negative Surveillance Initiative (MuGSI).[6] MuGSI is a laboratory- and population-based surveillance program that aims to describe the extent of select resistant gram-negative bacteria, to measure trends of these organisms over time, to identify those most at risk from illness with these pathogens, and to provide a platform to answer future questions about these pathogens.

METHODS

Population

Laboratory and population-based surveillance was conducted through the EIP's MuGSI program in selected counties in Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee from January 1 through December 31, 2019 (see Supplement).[17] The total population under surveillance in 2019 was 19,313,303.[18]

Due to small numbers, and to maintain confidentially of individual cases, sites were grouped as follows: "South" (TN, GA); "Northeast" (CT, NY, MD); and "West" (OR, CO, MN, NM).

Case definition

An incident case was the first isolation of carbapenem-resistant *A. baumannii-calcoaceticus* complex (*A. baumannii* complex) from a normally sterile site (including blood, cerebrospinal fluid, bone, joint/synovial fluid, internal body site, peritoneal fluid, pleural fluid, muscle, deep tissue, etc.) or urine resistant to meropenem, imipenem, or doripenem, in a 30-day period, from a surveillance area resident whose specimen was collected for a clinical purpose (see Supplement).[6,19] Each unique patient (case-patient) could contribute a new incident case to this surveillance every 30 days.

A patient's isolate was considered health care-associated if it met any of the following criteria: (1) the isolate was collected 3 or more days post hospital admission, (2) the patient had any of the following health care exposures in the prior year to case-defining culture—long-term care stay, prior hospitalization, prior outpatient or inpatient surgery, (3) the presence of an indwelling device at any time in the 2 days prior to case-defining culture (eg, foley catheter, central line, etc.), and/or (4) current chronic dialysis treatment. All other patients were considered community-associated (CA).

Case identification and data collection

Cases were identified by reviewing clinical laboratory-provided lists of *A. baumannii* complex isolated from a sterile site or urine. EIP site staff confirmed the organism met the defined phenotype and reviewed residential addresses to confirm that a case patient was a surveillance area resident. Associated medical records were reviewed as described in the supplement, and the Charlson Comorbidity Index was calculated.[6,20–22] Cases were matched with state vital records data to determine if death occurred within 30 days following the specimen collection date of the case-defining culture.

Analytic and statistical methods

A χ^2 test or Fisher's exact test (where applicable) were used to generate a *P*-value which was used to compare cases with and without a detected acquired carbapenemase gene (aCP), using SAS 9.4 (SAS Institute Inc.) using a ≤0.05 significance level. The crude incidence rate was calculated using denominator data from the 2019 U.S. Census Bridged-Race File.[18] Data reported to CDC as of August 26, 2022, were included in the analysis.

Isolate collection, submission, and evaluation at CDC laboratory

Isolate submission to CDC was initiated in 2019, and EIP site staff facilitated the collection by regularly communicating with local clinical laboratories.

All isolates submitted to the CDC underwent full evaluation (fully characterized), including identification, antimicrobial susceptibly testing, real-time polymerase chain reaction (PCR), and whole genome sequencing (see Supplementary Methods for more details). Identification was conducted using matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) on the BioTyper 3.1 matrix-assisted laser desorption ionization time-of-flight system (Bruker Daltonics). Real-time PCR assays for the detection of an aCP, defined as, bla_{KPC}, bla_{NDM}, bla_{VIM}, bla_{IMP}, $bla_{OXA-48-like}$, $bla_{OXA-23-like}$, $bla_{OXA-24/40-like}$, $bla_{OXA-58-like}$, and $bla_{OXA-235-like}$ were developed in-house and performed on all submitted isolates.[23–26]

Antimicrobial susceptibility testing was performed for 18 of the antibiotics represented in Table 3 at CDC (methods for cefiderocol are described separately) using frozen reference broth microdilution panels created in-house according to Clinical and Laboratory

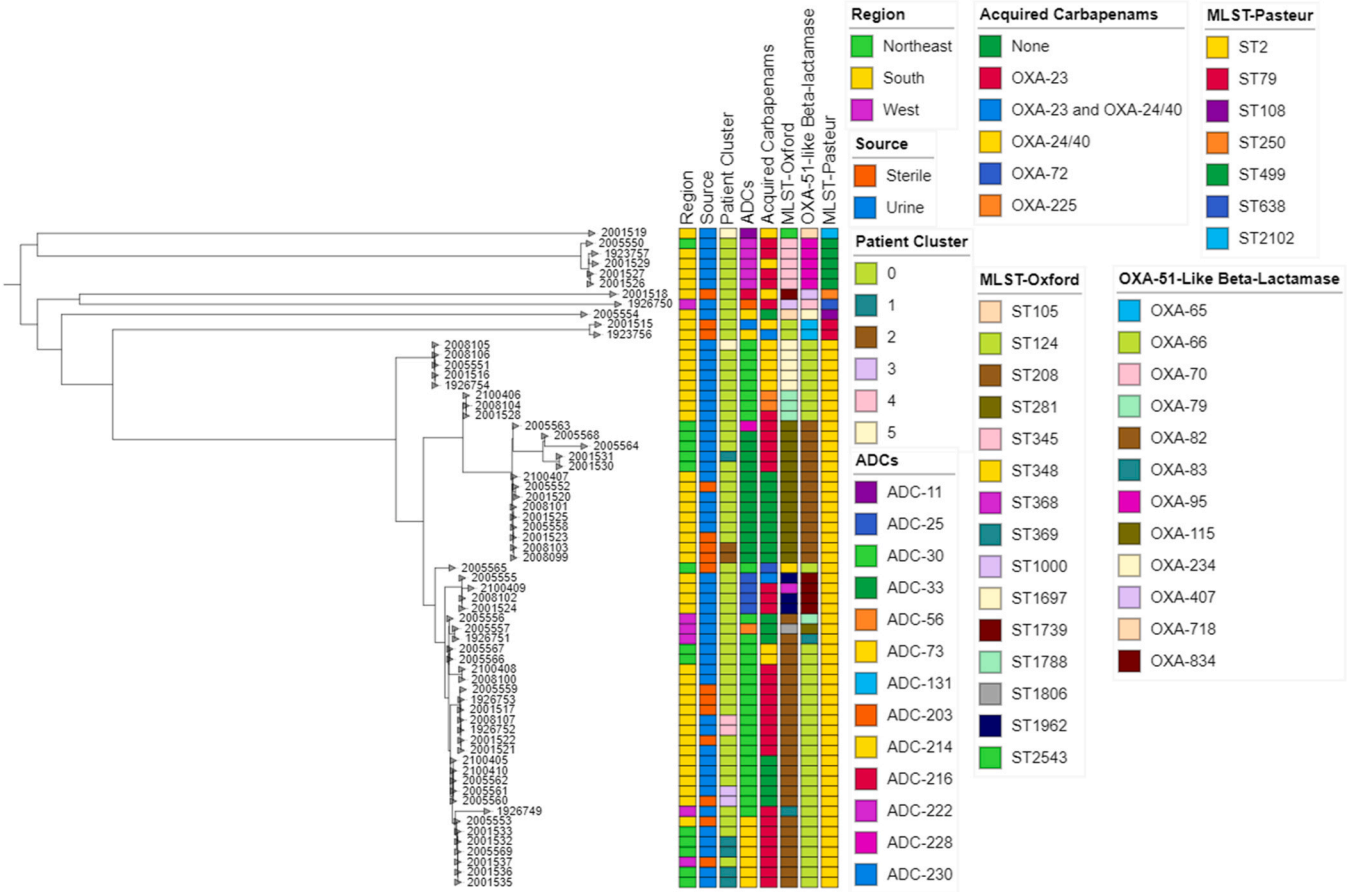

Fig. 1. Key molecular characteristics for 65 isolates of carbapenem-resistant *Acinetobacter baumannii* collected through the Emerging Infections Program, 2019. *Notes*: The sequencing information for these isolates can be found on NCBI (https://www.ncbi.nlm.nih.gov/bioproject/288601). Isolate characteristics are indicated in the key to the right of the figure. For the Patient Cluster column; 0 = a patient contributing one isolate, 1 = a unique patient contributing 5 isolates, 2 = a unique patient contributing 2 isolates, 3 = a unique patient contributing 2isolates, 4 = a unique patient contributing 2 isolates, 5 = a unique patient contributing 5 isolates). *Abbreviations*: MLST, Multilocus Sequencing Type; ADC, *Acinetobacter*-derived cephalosporinase genes; ST, sequence type; NCBI, National Center for Biotechnology Information.

Standards Institute (CLSI) guidelines with cation-adjusted Mueller–Hinton broth (BD Difco). Susceptibility was defined based on the 2022 CLSI breakpoints.[27,28] Details on this testing can be found in the Supplement. Isolates were classified as difficult-to-treat (DTR) based on the criteria set by Kadri et al (2018).[29]

Cefiderocol (Shionogi & Co. Ltd) susceptibility testing was performed, separately from the above testing, on all isolates received at CDC using a frozen reference broth microdilution panel created in-house with iron-depleted cation-adjusted Mueller–Hinton Broth (BD Difco) and Chelex (Bio-Rad Laboratories). Both the 2019 CLSI and Food and Drug Administration (FDA) breakpoints were used to define susceptibility (Table 4).[30,31] Isolates were tested in triplicate for cefiderocol susceptibility following the same methods as described in the Supplement, and the mode for the minimum inhibitory concentration (MIC) was reported for each isolate to account for trailing and skipped wells that can occur during testing. If a mode was not obtained after the third attempt of triplicate testing, the isolate was excluded from the analysis.

Whole genome sequencing (WGS) was completed on all isolates, and the methods are described in the Supplement. Figure 1 was created using Interactive Tree of Life (iTOL) v6 (https://itol.embl.de/).

Data availability

WGS raw reads for this collection were deposited in the Sequence Read Archive (SRR21065242 to SRR21065307) and are associated with National Center for Biotechnology Information Bio-Project PRJNA288601.

Ethical review

The EIP's MuGSI has been determined to be a nonresearch activity by the human subjects advisors at CDC's National Center of Emerging and Zoonotic Infectious Diseases, therefore CDC's institutional review board review was not required. This activity also underwent ethical review at each of the participating EIP sites and was either approved with a waiver of informed consent or was deemed a non-human research activity by the respective EIP site's institutional review boards.

RESULTS

From January 1 through December 31, 2019, 136 incident CRAB cases, representing 125 unique case-patients, were identified (Table 1). The crude incidence rate was 0.70 cases per 100,000 population. Sixty-six isolates (48.5%), representing 58 unique case-patients, were submitted to CDC from all participating sites except OR and NY. Five unique case-patients contributed more than one isolate to this sample, with a range of 2 to 5 isolates per case-patient. We compared characteristics of cases with an isolate received at CDC to cases without an isolate submitted and determined the data were comparable (see Table 1, Supplement). All patients' isolates were considered health care-associated based on characteristics collected

Table 1
Characteristics of incident cases with and without a carbapenem-resistant *Acinetobacter baumannii* isolate submitted to the Centers for Disease Control and Prevention for testing, 2019, n = 136

Characteristic	Overall	Isolate submitted to CDC	
		Yes	No
	N = 136 (%)	N = 66 (%)	N = 70 (%)
Patient demographic (case level)			
Sex			
Female	55 (40.4)	29 (43.9)	26 (37.1)
Male	81 (59.6)	37 (56.1)	44 (62.0)
Race*			
Black or African American, non-Hispanic	77 (56.6)	36 (54.6)	41 (58.6)
White, non-Hispanic	47 (34.6)	25 (37.9)	22 (31.4)
Asian, non-Hispanic	3 (2.2)	2 (3.0)	1 (1.4)
Hispanic, any race	3 (2.2)	1 (1.5)	2 (2.9)
Unknown race and ethnicity	5 (3.7)	2 (3.0)	3 (4.3)
Unknown race, non-Hispanic	1 (0.7)	0 (0.0)	1 (1.4)
Median age in years (IQR)	61.5 (49.0-77.0)	63.5 (51.0-78.0)	61.0 (46.0-76.0)
	N = 136 (%)	N = 66 (%)	N = 70 (%)
Culture source†			
Urine	98 (72.1)	51 (77.3)	47 (67.1)
Normally sterile site	38 (27.9)	15 (22.7)	23 (32.9)
	N = 136 (%)	N = 66 (%)	N = 70 (%)
Location of culture collection			
Outpatient location‡	69 (50.7)	33 (50.0)	36 (51.4)
Hospital inpatient§	48 (35.3)	21 (31.8)	27 (38.6)
Long-term care or long-term acute care	19 (14.0)	12 (18.2)	7 (10.0)
	N = 131 (%)	N = 64 (%)	N = 67 (%)
Common types of infections**			
Urinary tract infection or pyelonephritis	76 (58.0)	45 (40.3)	31 (46.3)
Bacteremia/sepsis	35 (26.7)	12 (18.8)	23 (34.3)
Septic shock	13 (9.9)	4 (6.3)	9 (13.4)
Skin infection††	6 (4.6)	4 (6.3)	2 (3.0)
Osteomyelitis	4 (2.9)	4 (6.3)	0 (0.0)
Pneumonia	2 (1.5)	1 (1.6)	1 (1.5)
	N = 133	N = 65	N = 68
	M, MD (IQR)	M, MD (IQR)	M, MD (IQR)
Comorbidities‡‡			
Charlson Comorbidity Index	3.0, 2.0 (2.0-4.0)	2.7, 2.0 (2.0-3.0)	3.0, 3.0 (2.0-4.0)
	N = 133 (%)	N = 65 (%)	N = 68 (%)
Chronic skin conditions§§	78 (58.6)	41 (63.1)	37 (54.4)
Urinary tract problems/abnormalities	61 (45.9)	32 (49.2)	29 (42.7)
Hemiplegia/paraplegia/quadriplegia	52 (39.1)	27 (41.5)	25 (36.8)
Diabetes	52 (39.1)	23 (35.4)	29 (42.7)
Cardiovascular disease	56 (42.1)	27 (41.5)	29 (42.7)
Chronic kidney disease	29 (21.8)	9 (13.9)	20 (29.4)
	N = 136 (%)	N = 66 (%)	N = 70 (%)
Health care facility exposures in the year prior to culture date***			
Admission to an ACH			
Stay in a LTCF	118 (86.8)	58 (87.9)	60 (85.7)
Prior outpatient or inpatient surgery	93 (68.4)	45 (68.2)	48 (68.6)
Admission to a LTACH	38 (27.9)	18 (27.3)	20 (28.6)
	6 (4.4)	4 (6.1)	2 (2.9)
	N = 136 (%)	N = 66 (%)	N = 70 (%)
Placement of an indwelling device in the 2 days prior to culture date†††			
Urinary catheter	83 (61.0)	43 (65.2)	40 (57.1)
Other indwelling device‡‡‡	38 (27.9)	9 (13.6)	29 (41.4)
Central vascular catheter	32 (23.5)	14 (21.2)	18 (25.7)
	N = 136 (%)	N = 66 (%)	N = 70 (%)
Other risk factors in the 7 days prior to the date of culture			
Admission to an ICU	25 (18.4)	14 (22.6)	11 (19.0)
Nebulizer treatment	13 (9.6)	1 (1.5)	12 (17.1)
Mechanical ventilation	12 (8.8)	3 (4.6)	9 (12.9)
Noninvasive positive pressure ventilation	5 (3.7)	1 (1.5)	4 (5.7)
	N = 136 (%)	N = (%)	N = (%)
Current chronic dialysis treatment	4 (2.9)	1 (1.5)	3 (4.3)

Table 1 (*continued*)

Characteristic	Overall	Isolate submitted to CDC	
		Yes	No
	N = 136 (%)	N = 66 (%)	N = 70 (%)
	N = 136 (%)	N = 66 (%)	N = 70 (%)
Hospitalized at the time of or within 30 days of culture collection§§§			
Yes	110 (80.9)	51 (77.3)	59 (84.3)
No	23 (16.9)	14 (21.1)	9 (12.9)
Unknown	3 (2.2)	1 (1.5)	2 (2.9)
	N = 136 (%)	N = 66 (%)	N = 70 (%)
Patient outcome at 30 days****			
Survived	107 (78.7)	55 (83.3)	52 (74.3)
Died	29 (21.3)	11 (16.7)	18 (25.7)

ACH, acute care hospital; CRAB, carbapenem-resistant *Acinetobacter baumannii* complex; ICU, intensive care unit; IQR, interquartile range; LTACH, long-term acute care hospital; LTCF, long-term care facility; MD, median.
NOTE. This table includes cases from all sites. OR did not identify CRAB cases in 2019 and NY identified only a single incident case.
*Persons whose race was reported to be American Indian or Alaska Native, or Native Hawaiian or Other Pacific Islander, were not identified in our population.
†To reduce reidentifiability of data when reporting, due to small numbers, culture sources were combined into 2 categories: normally sterile body sites (ie, blood, cerebral spinal fluid, pleural fluid, pericardial fluid, peritoneal fluid, joint/synovial fluid, bone, internal body site, muscle) and urine.
‡Outpatient collection locations include emergency room, outpatient clinic, outpatient surgical center, or another outpatient location.
§Hospital inpatient collection locations include ICU, operation room, or another inpatient location.
**The top 6 types of infection are reported here. A case can have more than one type of infection reported, 5 of the 136 cases had unknown types of infections recorded on the medical abstraction form and have been removed for this analysis, 15 of the 131 cases had no types of infections reported. A urinary tract infection was defined as a medical record abstractor seeing the term in the medical record.
††kin infections included skin abscess, chronic or decubitus ulcers.
‡‡The top 6 comorbid conditions are reported here. Case can have more than one type of comorbid condition reported, 3 cases had unknown comorbid conditions documented in the medical record and were excluded from this analysis.
§§Chronic skin conditions include decubitus/pressure ulcers, other chronic or surgical wounds, and burns.
***Cases could have more than one health care facility exposure in the year prior reported in the medical record.
†††Cases could have more than one type of indwelling device placed in the 2 days prior to culture collection.
‡‡‡Other indwelling devices include ET/NT tube, gastrostomy tube, NG tube, tracheostomy, nephrostomy tube, or other unspecified indwelling device.
§§§Patients' outcomes were assessed using the state death registry data. A patient was considered to have survived if there was no matching record in the state death registry data in the 30 days after the date of the case-defining culture.
****P-value determined to be significant at the .05 level.

from the medical record. Sites in the South contributed 68.2% of the isolates, sites in the Northeast contributed 22.7%, and sites in the West contributed 9.1% of isolates. All 66 isolates were determined to be part of the *A. baumannii* complex after sequencing, and 65 were confirmed to be *A. baumannii*; a single isolate was determined to be *Acinetobacter nosocomialis*.

Of the 66 isolates collected for this analysis, 37 (56.1%) were from males, 36 (54.6%) were from Black or African American, non-Hispanic, persons, and the median age of cases was 63.5 years (Table 2). Most isolates (n = 51, 77.2%) were from urine specimens, and half (n = 33, 50.0%) were collected in the outpatient setting (eg, emergency room, outpatient clinic, outpatient surgical center, or another outpatient location). Isolate characteristics, compared in Table 2, are not statistically different. Only 23% (n = 15) of the cases had the case-defining culture collected > 3 days after hospital admission (eg, were hospital-onset). Exposure to more than one health care risk factor (eg, exposure to more than one health care setting, or the presence of one or more indwelling device) did not result in a

Table 2
Characteristics of incident carbapenem-resistant *Acinetobacter baumannii* complex cases with and without an acquired carbapenemase gene as identified by whole genome sequencing, 2019, n = 66

Characteristic		Acquired Carbapenemase gene status for CRAB isolate	
	Overall	Yes	No
	N = 66 (%)	N = 48 (%)	N = 18 (%)
Patient demographics ()			
Sex			
Female	29 (43.9)	20 (41.7)	9 (50.0)
Male	37 (56.1)	28 (58.3)	9 (50.0)
Race*			
Black or African American, non-Hispanic	36 (54.5)	29 (60.4)	7 (38.9)
White, non-Hispanic	25 (37.9)	16 (33.3)	9 (50.0)
Asian, non-Hispanic	2 (3.0)	0 (0.0)	2 (11.1)
Hispanic, any race	1 (1.5)	1 (2.1)	0 (0.0)
Unknown race and ethnicity	2 (3.0)	2 (4.2)	0 (0.0)
	MD (IQR)	MD (IQR)	MD (IQR)
Age in years	63.5 (51.0-78.0)	59.5 (50.5-74.5)	71 (61.0-82.0)
	N = 66 (%)	N = 48 (%)	N = 18 (%)
Culture source†			
Urine	51 (77.3)	38 (79.2)	13 (72.2)
Normally sterile site	15 (22.7)	10 (20.8)	5 (27.8)
	N = 66 (%)	N = 48 (%)	N = 18 (%)
Location of culture collection			
Outpatient location‡	33 (50.0)	24 (50.0)	9 (50.0)
Hospital inpatient§	21 (31.8)	17 (35.4)	4 (22.2)
Long-term care facility or long-term acute care hospital	12 (18.2)	7 (14.6)	5 (27.8)
	N = 64 (%)	N = 46 (%)	N = 18 (%)
Common types of infections**			
Urinary tract infection or pyelonephritis	45 (70.3)	34 (73.9)	11 (61.1)
Bacteremia	10 (15.6)	6 (12.5)	4 (22.2)
Septic shock	4 (6.3)	3 (6.5)	1 (5.6)
Skin infection††	4 (6.3)	2 (4.4)	2 (11.1)
Osteomyelitis	4 (6.3)	4 (8.7)	0 (0.0)
Pneumonia	1 (1.6)	1 (2.2)	0 (0.0)
No infections reported	4 (6.3)	2 (4.4)	2 (11.1)
	N = 65	N = 47	N = 18
	MD (IQR)	MD (IQR)	MD (IQR)
Comorbidities‡‡			
Charlson comorbidity index	2 (2-3)	2 (2-4)	2 (2-3)
	N = 65 (%)	N = 47 (%)	N = 18 (%)
Chronic skin conditions§§	41 (63.1)	29 (61.7)	12 (66.7)
Urinary tract problems/ abnormalities	32 (49.2)	23 (48.9)	9 (50.0)
Hemiplegia/paraplegia/ quadriplegia	27 (41.5)	21 (44.68)	6 (33.3)
Diabetes	23 (35.4)	18 (38.3)	5 (27.8)
Cardiovascular disease	27 (41.5)	20 (42.6)	7 (38.9)
Chronic kidney disease	9 (13.8)	6 (12.8)	3 (16.7)
	N = 66 (%)	N = 48 (%)	N = 18 (%)
Health care facility exposures in the year prior to culture date***			
Admission to an ACH	58 (87.9)	41 (85.4)	17 (99.4)
Stay in a LTCF	45 (68.2)	34 (70.8)	11 (61.1)
Prior outpatient or inpatient surgery	18 (27.3)	15 (31.2)	3 (16.7)
Admission to a LTACH	4 (6.1)	2 (4.2)	2 (11.1)
	N = 66 (%)	N = 48 (%)	N = 18 (%)
Placement of an indwelling device in the 2 days prior to culture date			
Urinary catheter	43 (65.2)	33 (68.8)	10 (55.6)
Central vascular catheter	14 (21.2)	9 (18.8)	5 (27.8)
Other indwelling device†††	9 (13.6)	8 (16.7)	1 (5.6)
	N = 66 (%)	N = 48 (%)	N = 18 (%)
Other risk factors in the 7 days prior to the date of culture			
Nebulizer treatment	1 (1.5)	1 (2.1)	0 (0.0)
Mechanical ventilation	3 (4.5)	3 (6.3)	0 (0.0)
Non-invasive positive pressure ventilation	1 (1.5)	0 (0.0)	1 (5.6)
Admission to an ICU	14 (21.2)	13 (27.1)	1 (5.6)

Table 2 (*continued*)

Characteristic		Acquired Carbapenemase gene status for CRAB isolate	
	Overall	Yes	No
	N = 66 (%)	N = 48 (%)	N = 18 (%)
	N = 66 (%)	N = 48 (%)	N = 18 (%)
Current chronic dialysis treatment	1 (1.5)	1 (2.1)	0 (0.0)
	N = 66 (%)	N = 48 (%)	N = 18 (%)
Hospitalized at the time of or within 30 days of culture collection‡‡‡			
Yes	51 (77.3)	39 (81.3)	12 (66.7)
No	14 (21.2)	8 (16.7)	6 (33.3)
Unknown	1 (1.5)	1 (2.1)	0 (0.0)
	N = 66 (%)	N = 48 (%)	N = 18 (%)
Patient outcome at 30 days§§§			
Survived	55 (83.3)	41 (85.4)	14 (77.8)
Died	11 (16.7)	7 (14.6)	4 (22.2)
Among cases with sterile sites	5/11 (45.5)	3/7 (42.9)	2/4 (50.0)
Among cases with urine cultures	6/11 (54.5)	4/7 (57.1)	2/4 (50.0)

ACH, acute care hospital; CRAB, carbapenem-resistant *Acinetobacter baumannii* complex; ICU, intensive care unit; IQR, interquartile range; LTACH, long-term acute care hospital; LTCF, long-term care facility; MD, median.
NOTE. A test for significance was performed on each row in the table above; we found no significant difference between the 2 groups.
*Persons whose race was reported to be American Indian or Alaska Native, or Native Hawaiian or Other Pacific Islander, were not identified in our population.
†To reduce reidentifiability of data when reporting, due to small numbers, culture sources were combined into 2 categories: normally sterile body sites (ie, blood, cerebral spinal fluid, pleural fluid, pericardial fluid, peritoneal fluid, joint/synovial fluid, bone, internal body site, muscle) and urine.
‡Outpatient collection locations include emergency room, outpatient clinic, outpatient surgical center, or another outpatient location.
§Hospital inpatient collection locations include ICU, operation room, or another inpatient location.
**Cases could have more than one type of infection; 2 cases had unknown types of infections recorded on the medical abstraction form and have been removed for this analysis. A urinary tract infection was defined as a medical record abstractor seeing the term in the medical record.
††Skin infections included skin abscess, chronic or decubitus ulcers.
‡‡The most frequent comorbid conditions are presented here. Cases could have more than one comorbid condition documented. A single CRAB case had unknown comorbid conditions documented in the medical record and was excluded from this analysis.
§§Chronic skin conditions include decubitus/pressure ulcers, other chronic or surgical wounds, and burns.
***Cases could have more than one prior health care risk factor reported in the medical record.
†††Other indwelling devices include endotracheal/nasotracheal tube, gastrostomy tube, nasogastric tube, tracheostomy, nephrostomy tube, or other unspecified indwelling devices.
‡‡‡Patients' outcomes were assessed using the state death registry data. A patient was considered to have survived if there was no matching record in the state death registry data in the 30 days after the date of the case-defining culture.
§§§Cases could have more than one healthcare facility exposure in the year prior reported in the medical record.

case being more likely to have an isolate harboring an aCP (aCP isolate: n = 41, 85.4% vs non-aCP isolate: n = 15, 83.3% respectively, $P < .99$). Of the 66 isolates, 26 (39.4%) were documented as being polymicrobial (the organism other than CRAB is unknown) based on the medical record review; 19/48 (39.6%) of the isolates with an aCP and 7/18 (38.9%) of the isolates without an aCP; this finding was not statistically significantly different.

Among the 51 cases with isolates that were hospitalized at the time of, or in the 30 days after, the date of the case-defining culture, the median total length of hospital stay was 10 days interquartile range (IQR: 7-20 days). Cases with a CRAB isolate without an aCP had a similar length of stay (median: 8, IQR: 6-19.5 days) compared to

Table 3
Count of acquired carbapenemase gene by Multilocus Sequence Type (MLST) for isolates of carbapenem-resistant *Acinetobacter baumannii* complex collected though the Emerging Infections Program, 2019 (n = 66)

Acquired Carbapenemase gene	Multilocus sequence type scheme (count of isolates)	
	Oxford MLST scheme	Pasteur MLST scheme
NDM-1 (n = 1)	ST2544 (1)	ST279 (1)
OXA-225a (n = 2)	ST1788 (2)	ST2 (2)
OXA-23 (n = 31)	ST208 (16)	ST2 (26)
	ST281 (5)	ST499 (4)
	ST345 (4)	ST638 (1)
	ST1962 (2)	
	ST368 (1)	
	ST369 (1)	
	ST1000 (1)	
	ST1788 (1)	
OXA-23 and OXA-24/40 (n = 2)	ST124 (1)	ST2 (1)
	ST1962 (1)	ST79 (1)
OXA-24/40 (n = 11)	ST1697 (5)	ST2 (7)
	ST208 (2)	ST79 (1)
	ST124 (1)	ST250 (1)
	ST345 (1)	ST499 (1)
	ST1739 (1)	ST2102 (1)
	ST2543 (1)	
OXA-72b (n = 1)	ST348 (1)	ST2 (1)
No acquired carbapenemase identified (n = 18)	ST281 (9)	ST2 (17)
	ST208 (7)	ST108 (1)
	ST105 (1)	
	ST1806 (1)	

NOTE. ablaOXA-223 is a variant of blaOXA-23. bblaOXA-72 is a variant of blaOXA-24/40.

those with an aCP (median: 10, IQR: 7-20 days). Among cases that tested positive for CRAB after admission to an acute care hospital (n = 15), the median time between admission and case-defining culture date was 7 days (IQR: 5-10 days), and the median length of stay was 19 days (IQR: 10-24 days). The median time from admission to case-defining culture date for CRAB cases with an aCP (n = 13) was 7 days (IQR: 5-10 days). For the 2 cases without an aCP, times from admission to case-defining culture were 7 and 32 days.

Most isolates (n = 48, 72.7%) had an aCP identified through WGS (Fig 1). The real-time PCR results and WGS result for the detection of an aCP were 100% concordant. The frequency of the aCPs were as follows: 34 (51.5%) isolates had bla_{OXA-23}, 13 (19.7%) isolates had bla_{OXA-24}, 2 (3.0%) isolates had $bla_{OXA-225}$, 1 (1.5%) isolate had bla_{OXA-72}, and 1 (1.5%) isolate had bla_{NDM}. Two isolates harbored both a bla_{OXA-23} and a bla_{OXA-24} carbapenemase gene. The bla_{NDM} isolate was identified from the urine of a patient who was a nursing home resident with no prior travel history the year before culture, or indwelling device use (including the use of a tracheostomy); however, this patient was discharged from an acute care hospital about a month before the case-defining culture date. Forty-six isolates had both an acquired and intrinsic bla_{OXA} gene; the most common combination was bla_{OXA-23} and bla_{OXA-66} (n = 16). A depiction of key molecular characteristics overlayed by region where the isolate was collected, the culture source, and if the patient had multiple isolates, can be found in Figure 1. A crosswalk of the aCP and identified MLST types can be found in Table 3. *Acinetobacter*-derived cephalosporinas genes were present in all 66 isolates (Fig 1).

Sixteen unique sequence types (STs) were identified using the Oxford (OX) MLST scheme; the most common were $ST208_{OX}$ (n = 25, 37.9%), and $ST281_{OX}$ (n = 14, 21.1%). A total of 8 unique STs were identified using the Pasteur MLST scheme, $ST2_{IP}$ predominated (n = 54, 81.8%) (Fig 1). The count of isolates by MLST type and aCP is found in Table 3.

The number and percent susceptible of the isolates tested at CDC are presented in Table 4. All submitted isolates were confirmed to be carbapenem-resistant. None of the CRAB isolates with an aCP demonstrated susceptibility to ampicillin-sulbactam, although 50.0% of the isolates without an aCP were susceptible ($P < 0.0001$). Most CRAB isolates

Table 4
Antimicrobial susceptibility testing results, using the 2019 Clinical Laboratory Standards Institute (CLSI) breakpoints, for incident carbapenem-resistant *Acinetobacter baumannii* complex cases with and without an acquired carbapenemase gene, 2019, n = 66

Antimicrobial agent	Number and percent of isolates that tested susceptible		
		Acquired Carbapenemase gene status for CRAB isolate	
	Overall	Yes	No
	N = 66 (%)	N = 48 (%)	N = 18 (%)
Carbapenem			
Doripenem	0 (0)	0 (0)	0 (0)
Imipenem	4 (6.1)	0 (0)	4 (22.2)*
Meropenem	0 (0)	0 (0)	0 (0)
β-Lactam/β-Lactamase Combinations			
Ampicillin-sulbactam	9 (13.6)	0 (0)	9 (50.0)*
Piperacillin-tazobactam	0 (0)	0 (0)	0 (0)
Cephalosporin			
Ceftazidime	2 (3.0)	2 (4.2)	0 (0)
Cefepime	1 (1.5)	1 (2.1)	0 (0)
Cefotaxime	1 (1.5)	1 (2.1)	0 (0)
Ceftriaxone	1 (1.5)	1 (2.1)	0 (0)
Cefiderocol†	63 (96.9)	46 (97.9)	17 (94.4)
Lipopeptide			
Colistin‡	0 (0)	0 (0)	0 (0)
Aminoglycoside			
Gentamicin	17 (25.8)	11 (22.9)	6 (33.3)
Tobramycin	31 (47.0)	18 (37.5)	13 (72.2)
Amikacin	45 (68.2)	33 (68.8)	12 (66.8)
Tetracycline			
Minocycline	38 (57.6)	27 (56.3)	11 (61.1)
Tetracycline	4 (6.1)	4 (8.3)	0 (0)
Fluoroquinolone			
Ciprofloxacin	2 (3.0)	2 (4.2)	0 (0)
Levofloxacin	3 (4.5)	3 (6.3)	0 (0)
Folate Pathway Antagonist			
Trimethoprim-sulfamethoxazole	11 (16.7)	10 (20.8)	1 (5.6)

CRAB, carbapenem-resistant *Acinetobacter baumannii* complex.
NOTE. Isolates were tested against tigecycline, however, were not included in this table because of the lack of 2019 CLSI breakpoints.
*P-value determined to be significant.
†Interpretations displayed in the table were using CLSI breakpoints. Cefiderocol results were missing for 1 isolate; Using FDA breakpoints, 52 (80.0%) of all CRAB isolates tested susceptible, 39 (83.0%) of CRAB isolates with an acquired carbapenemase tested susceptible, and 13 (72.2%) of CRAB isolates without an acquired carbapenemase tested susceptible.
‡Colistin results were missing for 1 isolate; using 2019-CLSI breakpoints 56 (86.2%) of all CRAB isolates tested intermediate, 43 (91.5%) of CRAB isolates with an acquired carbapenemase tested intermediate, and 13 (72.2%) of CRAB isolates without an acquired carbapenemase tested intermediate.

displayed susceptibility to cefiderocol according to 2019 CLSI breakpoints (96.9%), but fewer displayed susceptibility according to FDA breakpoints (80.0%).[30,31] Cefiderocol testing resulted in a frequent occurrence of trailing and skipped wells, which often made the MIC difficult to determine. There are no CLSI or FDA breakpoints for *A. baumannii* complex and tigecycline, but the MIC_{50} and MIC_{90} were 1 and 2 μg/mL, respectively, and demonstrated an identical distribution for isolates that were aCP and non-aCP. Most isolates (n = 50, 75.8%) met the DTR definition.[29] Among the 11 case-patients that died, 9 had isolates that met the DTR definition. Four of the isolates were $ST208_{OX}$ (all 4 were DTR), 3 were $ST281_{OX}$ (1 was DTR), and 9 isolates were $ST2_{IP}$, 7 of which were DTR. For comparison, among the 41 case-patients that survived, 41 isolates met the DTR definition. The most frequent ST_{OX} type among this group, which was also DTR, was $ST208_{OX}$ (n = 17).

DISCUSSION

During 2019, we identified a low incidence rate of CRAB, with 0.70 cases per 100,000 population, across geographically diverse U.S.

metropolitan areas. Most CRAB cases occurred in older persons, and those of Black or African American (non-Hispanic) race. Seventy-three percent of isolates tested harbored an aCP, including a single isolate with bla_{NDM}. Cefiderocol, which was approved by the FDA in November 2019, had the most in vitro activity among the 19 antimicrobial agents tested.[32]

Our findings were similar to those from the Study Network of *Acinetobacter* as Carbapenem-Resistant Pathogen (SNAP), including similar characteristics of age, sex, and calculated Charlson Comorbidity Index. SNAP included 23 hospitals in 4 health systems in 2017 to 2018; they enrolled 120 patients with 1 to 5 isolates per patient identified through sentinel reporting.[33] Our population differed from SNAP in the percentage of persons of Black or African American, non-Hispanic, race (54.0% vs 28.0%), the percentage of cases who died by day 30 (16.7% vs 24.0%), and the difference in culture sources included (eg, SNAP included respiratory and wound samples).[33] These differences may be attributable to the difference in the underlying populations, the diversity of the health care facilities, and our methods of using population-based surveillance, which include only surveillance area residents, compared to SNAP's sentinel approach.

Our isolates were resistant to many first-line drugs used to treat CRAB infections, and 75.8% were found to have difficult-to-treat resistance.[11,29] In the Infectious Diseases Society of America (IDSA) guidance on treating CRAB, ampicillin-sulbactam, polymyxins, minocycline, tigecycline, and cefiderocol are suggested as possible treatments.[11] A smaller percentage of isolates with an aCP were susceptible to ampicillin-sulbactam, colistin, and minocycline. Only 13.6% of our isolates demonstrated susceptibility to ampicillin-sulbactam, IDSA's preferred treatment for CRAB, which is lower than in other studies of isolates from North America.[11,12,34] Using the pre-2019 CLSI breakpoints (MIC ≤2 μg/mL) 86.2% of isolates tested were susceptible to colistin, which is similar to other studies.[12] Susceptibility to minocycline was low. All but 2 isolates had a tigecycline MIC $\leq$ 2 μg/mL in our collection; however, this agent has been associated with increased mortality when used for treating severe infections, so monotherapy is not recommended for severe infections.[11,35]

Most of our CRAB isolates were susceptible to cefiderocol using either CLSI (96.9%) or FDA interpretive criteria (80.0%) suggesting that it remains a potentially useful therapeutic option as recommended in the current IDSA treatment guidance.[11,36–38] Our data affirm the results of other studies and provide evidence suggesting that cefiderocol could be a valuable treatment option for these infections as more data on clinical effectiveness becomes available.[11,36–38]

WGS demonstrated that $bla_{OXA\text{-}23}$ was the most common aCP in this study (51.5%), followed by $bla_{OXA\text{-}24}$ (19.7%), which is similar to other published studies.[33,39] One isolate was found to harbor bla_{NDM}, which is rare in CRAB in the U.S.[40–42] The CDC's Antimicrobial Resistance Laboratory Network reported 2.03% of all CRAB isolates tested in 2022 have this gene.[42] The patient with bla_{NDM} identified in this assessment had no prior travel history, was a resident of a nursing home, and had a prior acute care hospitalization which is similar to characteristics of patients reported in a multifacility outbreak of CRAB NDM in California.[41] Many of our isolates were $ST2_{IP}$ by Pasteur MLST scheme (81.8%) and $ST208_{OX}$ or $ST281_{OX}$ by the Oxford MLST scheme (59.0%), which is similar to other U.S. studies of CRAB isolates.[33,39] There were 54 isolates identified as $ST2_{IP}$, but these 54 isolates were classified as 16 different STs using the Oxford MLST scheme.[33,39] This suggests that the Oxford MLST scheme offers a higher resolution for distinguishing between isolates than the Pasteur MLST scheme.[39]

Limitations to this surveillance program include the following: small populations under surveillance, small number of geographic areas represented, restriction of the case definition to residents of the surveillance area and sterile site or urine culture sources, patient treatment data is not collected, and the lack of participation of some private specialty laboratories (eg, laboratories serving dialysis facilities).[6,22] Therefore, our results are not nationally representative. In 2021, this surveillance activity expanded the case definition to include wound and lower respiratory tract isolates, thus allowing this program to better characterize patients with CRAB moving forward. Combination drugs, such as sulbactam-durlobactam, were not available for testing. However, in 1 year of data, this assessment demonstrates a unique population-level perspective of CRAB in the U.S., including detailed clinical and microbiological data, allowing for a deeper understanding of the epidemiology of CRAB across the spectrum of health care. Additionally, all isolates sent for testing by CDC were confirmed to be CRAB, indicating that a phenotypic case definition based on local clinical laboratory antimicrobial susceptibility testing results is well-suited for surveillance.

CONCLUSIONS

In summary, most CRAB isolates across geographically diverse U.S. metropolitan areas harbored an aCP and demonstrated characteristics suggesting limited potential treatment options, supporting that this group of pathogens remains an urgent threat in the U.S. Certain strains of CRAB ($ST208_{OX}$ and $ST281_{OX}$) were prevalent, and the detection of an isolate harboring bla_{NDM} was identified. We found that cefiderocol had the most in vitro activity of the drugs tested, suggesting a potential treatment utility of this drug. This surveillance activity has demonstrated its value in helping to define the landscape of CRAB by providing a unique view of the molecular epidemiology of CRAB in the U.S., reinforcing the importance of tracking emerging and potentially transmissible resistance in *A. baumannii* complex to help inform and evaluate infection prevention and control strategies.

DISCLAIMER

The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

APPENDIX A. SUPPORTING INFORMATION

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ajic.2024.04.184.

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