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Colonization with extended-spectrum cephalosporin-resistant Enterobacterales (ESCrE) in hospitalized patients in Botswana

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Background: The epidemiology of extended-spectrum cephalosporin-resistant Enterobacterales (ESCrE) in hospitalized patients in low- and middle-income countries (LMICs) is poorly described. Although risk factors for ESCrE clinical infection have been studied, little is known of the epidemiology of ESCrE colonization. Identifying risk factors for ESCrE colonization, which can predispose to infection, is therefore critical to inform antibiotic resistance reduction strategies. **Methods:** This study was conducted in 3 hospitals located in 3 districts in Botswana. In each hospital, we conducted ongoing surveillance in sequential units hospitalwide. All participants had rectal swabs collected which were inoculated onto chromogenic media followed by confirmatory testing using MALDI-TOF MS and VITEK-2. Data were collected via interview and review of the inpatient medical record on demographics, comorbidities, antibiotic use, healthcare exposures, invasive procedures, travel, animal contact, and food consumption. Participants with ESCrE colonization (cases) were compared to non-colonized participants (controls) using bivariable and multivariable analyses to identify risk factors for ESCrE colonization. **Results:** Enrollment occurred from January 15, 2020, to September 4, 2020, and 469 participants were enrolled. The median age was 42 years (IQR, 31–58) and 320 (68.2%) were female. The median time from hospital admission to date of sampling was 5 days (IQR, 3–12). There were 179 cases and 290 controls (ie, 38.2% of participants were ESCrE colonized). Independent risk factors for ESCrE colonization were a greater number of days on antibiotic, recent healthcare exposure, and tending swine prior to hospitalization. (Table). **Conclusions:** ESCrE colonization among hospitalized patients was common and was associated with several exposures. Our results suggest prior healthcare exposure may be important in driving ESCrE. The strong link to recent antibiotic use highlights the potential role of antibiotic stewardship interventions for prevention. The association with tending swine suggests that animal husbandry practices may play a role in community exposures, resulting in colonization detected at the time of hospital admission. These findings will help to inform future studies assessing strategies to curb further emergence of hospital ESCrE in LMICs.
Disclosures: None

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Carbapenem-resistant Enterobacterales susceptibility patterns to new antimicrobials: A single-center analysis

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Background: Multidrug-resistant bacteria are of high concern, and empiric antimicrobial choice for infections caused by these pathogens, while awaiting susceptibilities, is increasingly encountered. We describe the susceptibility patterns of ceftazidime-avibactam (CZA), imipenem-rel-ebactam (I-R), meropenem-vaborbactam (MVB), cefiderocol (FDC), ceftolozone-tazobactam (C/T), minocycline (MIN), and tigecycline (TGC) for carbapenem-resistant Enterobacterales at an academic medical center. **Methods:** We performed a single-center analysis of Enterobacterales isolates from 110 hospitalized adult patients who had CZA, I-R, MVB, FDC, MIN, or TGC susceptibility testing performed between October 2020 and September 2022. The study included 1 isolate per patient per infection site per year. Isolates were divided into carbapenem susceptible and non susceptible categories. For carbapenem nonsusceptible isolates, phenotypic confirmatory testing of carbapenem nonsusceptibility was performed using disk diffusion, gradient diffusion, and/or broth microdilution. Interpretive categories were applied using CLSI- or FDA-approved break-points where applicable. Carbapenemase testing was also performed using the modified carbapenem inactivation method (mCIM) and, where applicable, this testing was confirmed at the Massachusetts State Public Health Laboratory using genotypic methods. **Results:** In total, 125 unique isolates were reviewed: 34 meropenem-susceptible and 91 meropenem-intermediate or resistant isolates. CZA, I-R, MVB, and FDC were active against all tested meropenem-susceptible isolates; however, 50% of tested isolates were susceptible to C/T. MIN and TGC, when tested, were active against 2 of 11 isolates (18%) and 14 of 16 isolates (86%), respectively. Of 91 meropenem-nonsusceptible isolates, most tested isolates were susceptible to MVB (59 of 72, 82%), followed by CZA (63 of 82, 77%), I-R (8 of 11, 73%), FDC (9 of 16, 56%), and C/T (1 of 12, 8%). TGC retained activity against 78 of 81 (96%) tested isolates. In contrast, MIN retained activity against 8 of 45 isolates (18%). Additionally, all (28 of 28, 100%) isolates that were nonsusceptible to at least 1 novel agent (CZA, I-R, MVB, FDC, or C/T) remained susceptible to TGC. State laboratory confirmatory testing was available for 75 isolates. Of 43 mCIM-positive isolates, all 28 KPC-producing isolates were susceptible to CZA, I-R, MVB, FDC and TGC. **Conclusions:** Among Enterobacterales, CZA, MVB, and I-R retained activity against most non-NDM CRE isolates in this local analysis, with comparable susceptibilities. TGC demonstrated excellent susceptibility for CRE and meropenem-susceptible isolates, offering an alternative for nonbloodstream infections. Choice of empiric agent with a newβ-lactam, β-lactam–β-lactamase inhibitors, or TGC appear to be reasonable empiric therapeutic options at our institution. CT and MIN warrant confirmatory testing prior to use due to low susceptibility rates among meropenem nonsusceptible isolates.
Disclosures: None

Table. Multivariable Risk Factors for ESCrE

Covariate	Adjusted Odds Ratio (95%CI)	P value
Age (per year)	1.00 (0.99, 1.01)	0.590
Days from Hospital Admission to Study Enrollment	1.01 (0.99, 1.03)	0.092
Inpatient Antibiotic Days Prior to Study Enrollment	1.07 (1.02, 1.11)	0.002
Visited Hospital for Care in Past 3 Months	1.71 (1.01, 2.89)	0.045
Foreign Travel in Past 6 Months	2.81 (0.88, 9.02)	0.082
Tended Swine at Home in Week Prior to Hospitalization	2.90 (1.25, 6.74)	0.013

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Real-world clinical outcomes of cefiderocol therapy in the Veterans Health Administration, 2019–2022

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Background: Cefiderocol is a novel siderophore cephalosporin with broad-spectrum activity. In the CREDIBLE-CR phase 3 clinical trial examining treatment of carbapenem-resistant gram-negative infections, cefider-

Table 1. Clinical characteristics and outcomes of 48 patients who received cefiderocol for gram-negative infections

Age, median (IQR)	70.5 (61-75)
Male sex, n (%)	45 (95.7%)
Charlson Comorbidity Index, age unadjusted, median (IQR)	6 (2-9)
Renal replacement therapy when cefiderocol initiated, n (%)	10 (20.8%)
Creatinine clearance >120 mL/min [1], n (%)	10 (20.8%)
Infectious syndrome(s)[2]:	
Lower respiratory tract infection, n (%)	23 (47.9%)
Urinary tract infection, n (%)	14 (29.2%)
Endovascular infection, n (%)	9 (18.8%)
Bone/joint infection, n (%)	4 (8.3%)
Other, n (%)	8 (16.7%)
Infectious organism(s)[2]:	
Pseudomonas aeruginosa, n (%)	30 (62.5%)
Enterobacterales, n (%)	17 (35.4%)
Acinetobacter baumannii, n (%)	10 (20.8%)
Stenotrophomonas maltophilia, n (%)	3 (6.3%)
Other, n (%)	2 (4.2%)
Negative cultures, n (%)	3 (6.3%)
Clinical failure, n (%)	17 (35.4%)
30-day all-cause mortality, n (%)	13 (27.1%)
90-day all-cause mortality, n (%)	22 (45.8%)
30-day microbiologic failure, n (%)	16 (33.3%)
90-day microbiologic failure, n (%)	22 (45.8%)

[1]: FDA package insert recommends increased dosing frequency (2g every 6 hours) compared with standard dosing (2g every 8 hours).

[2]: A patient may have one or more infectious syndromes and/or one or more organisms.

ocol had similar clinical and microbiological efficacy compared to the best available therapy, but the mortality rate was unexpectedly higher in the cefiderocol group. We investigated the postapproval, real-world clinical outcomes of cefiderocol therapy. **Methods:** We conducted a prospective, observational study of patients who received cefiderocol for at least 2 days within the Veterans' Health Administration (VHA) between the date of approval by the US Food and Drug Administration (FDA), November 14, 2019, and August 31, 2022. Types of infections were defined by NHSN criteria. Clinical failure was a composite outcome based on type of infection including survival (30- and 90-day mortality) and resolution of signs and symptoms of infection. Microbiologic failure was defined as culturing the same organism, as defined by the CDC NHSN, at least 7 days after the start of cefiderocol. Structured data were sourced from the VHA Corporate Data Warehouse, and each eligible episode underwent manual chart review. **Results:** During the study period, 8,763,652 patients across 132 VA medical centers received 1,142,940,842 prescriptions (not limited to antibiotics). Overall, 48 unique individuals had received cefiderocol, with 48 cefiderocol courses prescribed. Patients had a median age of 70.5 years (range, 61–75), and a median Charlson comorbidity score of 6 (range, 2–9). The most common infectious syndromes were lower respiratory tract infection in 23 (47.9%) of these 48 patients and urinary tract infection in 14 (29.2%) of these patients. The most common pathogens cultured were *P. aeruginosa* in 30 patients (62.5%), Enterobacterales in 17 patients (35.4%), and *A. baumannii* in 10 patients (20.8%). The clinical failure rate was 35.4% (17 of 48), and 15 (88.2%) of these 17 patients died within 3 days of clinical failure. The 30-day and 90-day microbiologic failure rates were 33.3% (16 of 48) and 45.8% (22 of 48), respectively. The 30-day and 90-day all-cause mortality rates were 27.1% (13 of 48) and 45.8% (22 of 48), respectively (Table 1). **Conclusions:** Our study cohort included older individuals with multiple comorbidities who were treated with cefiderocol mainly for lower respiratory tract and urinary tract infections, with *Pseudomonas aeruginosa* as the main causative pathogen. Clinical and microbiologic failure were seen in >30% of patients, and >40% of these patients died within 90 days. These data contribute to the growing body of literature on the real-world use of cefiderocol and provide outcome data on clinical failure, microbiologic failure, and mortality.

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Identifying patients at high risk for carbapenem-resistant Enterobacterales carriage upon admission to acute-care hospitals

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Background: Prompt identification of patients colonized or infected with carbapenem-resistant Enterobacterales (CRE) upon admission can help ensure rapid initiation of infection prevention measures and may reduce intrafacility transmission of CRE. The Chicago CDC Prevention Epicenters Program previously created a CRE prediction model using state-wide public health data (doi: 10.1093/ofid/ofz483). We evaluated how well a similar model performed using data from a single academic healthcare system in Atlanta, Georgia, and we sought to determine whether including additional variables improved performance. **Methods:** We performed a case–control study using electronic medical record data. We defined cases as adult encounters to acute-care hospitals in a 4-hospital academic healthcare system from January 1, 2014, to December 31, 2021, with CRE identified from a clinical culture within the first 3 hospital days. Only the first qualifying encounter per patient was included. We frequency matched cases to control admissions (no CRE identified) from the same hospital and year. Using multivariable logistic regression, we compared 2 models. The "public health model" included 4 variables from the Chicago Epicenters model (age, number of hospitalizations in the prior 365 days, mean length of stay in hospitalizations in the prior 365 days, and hospital admission with an infection diagnosis in the prior 365 days). The "healthcare

Table 1: Key Characteristics of Cases and Controls and Results from Univariable Analyses

	Cases (n=105)	Controls (n=441,460)	Unadjusted odds ratio	95% CI
Age (years), median (IQR)	66 (57–74)	60 (44–72)	1.02	1.01–1.03
Male sex, n (%)	57 (54)	196,174 (44)	1.49	1.01–2.18
Race and ethnicity, n (%)				
Non-Hispanic Black	39 (37)	187,429 (43)	1.19	0.77–1.84
Non-Hispanic White	41 (39)	165,868 (38)	1.36	0.83–2.25
Other[a]	25 (24)	88,163 (20)	ref	
Hospitalizations in the prior 365 days, median (IQR)	1 (0–3)	0 (0–1)	1.15	1.09–1.21
Mean (SD) LOS (days) in hospitalizations from prior 365 days	14.2 (12.3)	6.9 (7.7)	1.01	1.01–1.02
Prior infection diagnosis[b], n (%)	48 (46)	44,331 (10)	7.54	5.14–11.08
Prior admission to an ICU[b], n (%)	24 (23)	17,198 (4)	7.31	4.63–11.53
Prior malignancy diagnosis[b], n (%)	15 (14)	22,257 (5)	3.14	1.82–5.43
Elixhauser score, median (IQR)	6 (5–9)	4 (2–6)	1.29	1.22–1.37
Inpatient antibiotic DOT in the prior 365 days, median (IQR)	27 (14–47)	12 (4–30)	1.57	1.31–1.89

Abbreviations: CI, confidence interval; IQR, interquartile range; SD, standard deviation; LOS, length of stay; ICU, intensive care unit; DOT, days of therapy

a. Includes Hispanic, Asian, Native Hawaiian or Other Pacific Islander, American Indian or Alaskan Native, Multiple Races, and Unknowns

b. Within the prior 365 days from current admission

Table 2. Comparison of the Two Logistic Regression Models Predicting CRE Carriage on Admission

	Public Health Model		Healthcare System Model	
	aOR	95% CI	aOR	95% CI
Prior infection diagnosis[a]	5.56	3.32–9.34	3.21	1.79–5.77
Hospitalizations in the prior 365 days	1.14	1.04–1.24	0.99	0.85–1.16
Age	1.01	1.00–1.03	1.01	1.00–1.03
Mean LOS (days) in hospitalizations from prior 365 days	1.01	1.01–1.02	1.01	1.00–1.02
Prior admission to an ICU[a]			2.48	1.43–4.31
Prior malignancy diagnosis[a]			1.70	0.92–3.13
Elixhauser score			1.10	1.01–1.21
Inpatient antibiotic DOT in prior 365 days[b]			1.49	1.14–1.93
AUC		**0.76**		**0.79**

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; LOS, length of stay; ICU, intensive care unit; DOT, days of therapy

a. Within the prior 365 days from current admission

b. This variable was log transformed