Carbapenem-Resistant *Enterobacterales* in Children:
A Multicenter Prospective Cohort Study

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Background

- Carbapenem-resistant *Enterobacterales* (CRE) have been designated by the CDC as an urgent public health threat with significant morbidity and mortality
- Although the prevalence of CRE in children has been increasing in the US over the past two decades, more understanding of the epidemiology in the pediatric population is needed

Objective

- Describe the clinical and molecular epidemiology of CRE in a multicenter pediatric cohort

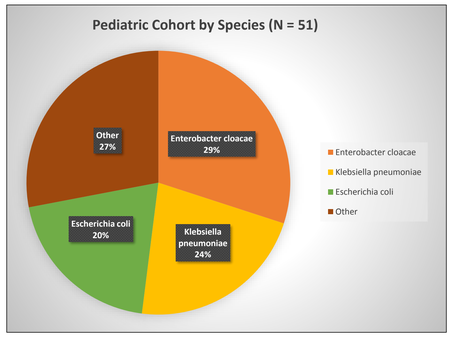
Methods

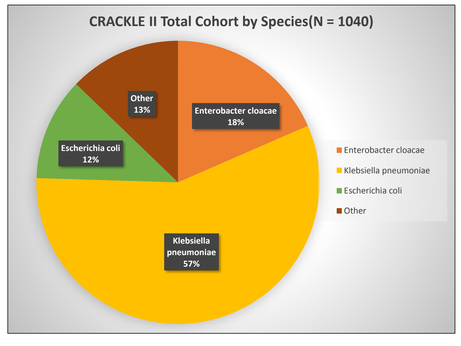
- Patients under 18 years of age with CRE positive cultures between April 30 2016 and August 31 2017 were identified from among 49 hospitals participating in the Consortium on Resistance Against Carbapenems in Klebsiella and Other Enterobacteriaceae
- Bacterial identification and antimicrobial susceptibility testing were performed at each contributing hospital and confirmed at a central microbiology laboratory
- Carbapenem resistance was defined per CDC criteria as those isolates displaying imipenem, doripenem, or meropenem MIC ≥4 µg/mL or ertapenem MIC ≥2 µg/mL.
- Carbapenemase genes were detected with PCR
- Clinical and epidemiological data were obtained from the electronic health record.

Results

- Fifty-one pediatric patients with CRE were identified at 17 hospitals (Table 1)
- All regions of the US were represented with highest prevalence in the southern states (46%)
- The median age at time of positive culture was 8 months. 66% of patients were under age 2 years

Table 1. Demographics and Clinical Characteristics		N = 51
Gender	Male	53%
	Female	47%
Age at pos. culture (mos.) Median (Q1 , Q3)		8 (2.6 , 85)
Age subgroups	0 - 2 months	14 (27%)
	3 months – 2 years	20 (39%)
	>2 years	17 (33%)
Race/Ethnicity	White	20 (39%)
	Black	20 (39%)
	Asian	1 (2%)
	Other	2 (4%)
	Unknown	8 (16%)
	Hispanic or Latino	9 (18%)
Region	Northeast	12 (24%)
	South	23 (46%)
	Midwest	10 (20%)
	West	5 (10%)
Pre-admission origin	Community	34 (67%)
	Outside hospital transfer	11 (22%)
	Long term care facility	3 (6%)
	Unknown	3 (6%)
Admitted on day of life 0		10 (20%)
Intensive Care Unit		37 (73%)
Mechanical ventilation prior to culture		21 (41%)
Days from admission to culture Median (Q1 , Q3)		11 (1 , 26)
Pitt bacteremia score Median (Q1 , Q3)		3 (1, 6)
Charlson co-morbidity index Median (Q1, Q3)		0 (0 , 2)
Source of culture	Urine	16 (31%)
	Respiratory	13 (25%)
	Blood	9 (18%)
	Wound	5 (10%)
	Abdomen	4 (8%)
	Other	4 (8%)
Colonization		23 (45%)
Infection		28 (55%)
Antibiotics received 14 days prior to culture	Ampicillin/Sulbactam	2 (4%)
	Carbapenem	2 (4%)
	Cefepime	3 (6%)
	Ceftriaxone	6 (12%)
	Piperacillin-Tazobactam	4 (8%)
	Fluoroquinolone	1 (2%)





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- Median time from admission to positive culture was 11 days. 72% of children were in an ICU and 41% required mechanical ventilation prior to culture
- A majority of children had no underlying co-morbidities. The most commonly cited co-morbidity was malignancy (14%)
- Most common species were *Enterobacter cloacae* (29%), *Klebsiella pneumoniae* (24%), and *E. coli* (20%)
- Carbapenemase genes were detected in 23% of 35 isolates tested
- Resistance was observed to multiple classes of antibiotics (Table 2).
- Overall 90 day mortality was 9 out of 51 (18%)

Table 2. Antibiotic Susceptibility (N = Tested)	Percent susceptible
Amikacin (23)	61
Aztreonam (23)	13
Cefepime (34)	41
Ceftazidime/Avibactam (4)	25
Ceftriaxone (30)	3
Ciprofloxacin (26)	65
Colistin (5)	20
Ertapenem (31)	0
Gentamicin (35)	63
Imipenem (17)	59
Meropenem (33)	39
Piperacillin-Tazobactam (35)	26
PolymixinB (4)	75
Tobramycin (28)	50
Trimethoprim/Sulfamethoxazole (33)	58

Conclusions

- CRE infection or colonization in children in the U.S. was geographically widespread, likely hospital-acquired, and associated with high mortality. A significant portion of patients were infants
- Antibiotic resistance was extensive across multiple classes. Few children received effective empiric antibiotic therapy on the day the culture was obtained