

# Risk factors, therapy, & healthcare utilization in pediatric UTI due to third-generation cephalosporin-resistant Enterobacteriaceae (G3Cr-Eb)

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## BACKGROUND

- Beta-lactams are the most commonly prescribed antibiotic class for pediatric UTI in the US, despite reports of increasing drug resistance.
- Few recent data exist on risk factors, response to empiric therapy, and healthcare utilization in pediatric G3Cr-Eb UTI in the US.

## STUDY POPULATION

893 unique Eb isolates

860 susceptible

**N = 52 controls**

33 G3Cr-Eb

7 failed UA or cfu/mL criterion

**N = 26\* UTIs due to G3Cr-Eb**  
(13 girls, 0-5yo + 4 girls, ≥6yo;  
8 boys, 0-5yo + 1 boy, ≥6yo)

\*10 cases with incomplete documentation over 6-month post-index UTI period.

## METHODS

- Case-control study design
- Matched 1:2 by sex, age group (0-5 vs. ≥6yo)
- Study period Nov 2014 to Feb 2017
- Case ascertainment via micro surveillance reports
- UTI definition: pyuria/bacteriuria (if ≥2mo); AND ≥10<sup>4</sup> cfu/mL single pathogen (cath or clean-catch)
- G3Cr-Eb were defined according to CLSI's post-2010/4 MIC interpretive criteria
- Chart review up to 6-month post-index UTI

## G3Cr-Eb ISOLATES - CHARACTERISTICS

| Spp./Phenotype      | ESBL | AmpC | None |
|---------------------|------|------|------|
| <i>E. coli</i>      | 22   | 1    | -    |
| <i>P. mirabilis</i> | 1    | -    | 1    |
| <i>E. cloacae</i>   | -    | -    | 1    |

| Drug S/I/R           | S        | I       | R         |
|----------------------|----------|---------|-----------|
| Ampicillin/Sulbactam | 4 (15%)  | 1 (4%)  | 10 (38%)  |
| Cefazolin            | -        | N/A     | 26 (100%) |
| Nitrofurantoin       | 18 (69%) | 6 (23%) | 2 (8%)    |
| Ciprofloxacin        | 13 (50%) | 1 (4%)  | 12 (46%)  |
| Levofloxacin         | 14 (54%) | -       | 12 (46%)  |
| TMP/SMX              | 10 (38%) | N/A     | 16 (62%)  |
| Fosfomycin           | 21 (81%) | -       | 2 (8%)    |
| Ceftriaxone          | 0        | 1 (4%)  | 25 (96%)  |
| Ceftazidime          | 12 (46%) | 2 (8%)  | 12 (46%)  |
| Cefepime             | 0        | 1 (4%)  | 1 (4%)    |
| Gentamicin           | 15 (58%) | -       | 11 (42%)  |
| Piperacillin/tazo    | 17 (65%) | 4 (15%) | 1 (4%)    |
| Meropenem            | 22 (85%) | -       | -         |

## BIOSOCIAL RISK FACTORS

| n (%)  | G3Cr-Eb  | Controls |
|--|----------|----------|
| Race   |          |          |
| African American                             | 2 (8%)   | 7 (13%)  |
| Other  | 24 (92%) | 45 (87%) |
| Ethnicity                                    |          |          |
| Hispanic                                     | 19 (73%) | 36 (71%) |
| Not Hispanic                                 | 7 (27%)  | 12 (24%) |
| International travel                         |          |          |
| Yes  | 4 (19%)  | 3 (7%)   |
| No   | 17 (81%) | 38 (93%) |
| English-speaking                             |          |          |
| Yes  | 17 (65%) | 33 (65%) |
| No   | 9 (35%)  | 18 (35%) |
| Welfare recipient                            |          |          |
| WIC  | 6 (23%)  | 5 (10%)  |
| Medicaid                                     | 24 (92%) | 40 (78%) |
| Underlying medical conditions                |          |          |
| None   | 12 (46%) | 28 (54%) |
| Recurrent UTI                                | 3 (12%)  | 7 (14%)  |
| VUR  | 2 (8%)   | -        |
| Spinal dysraphism*                           | 3 (12%)  | -        |
| No. of sibs or other children*, median (IQR) | 1 (0, 2) | 1 (1, 3) |
| Prior hospitalization*                       |          |          |
| Yes  | 13 (50%) | 10 (20%) |
| No   | 13 (50%) | 39 (80%) |
| Prior antimicrobial therapy                  |          |          |
| Yes  | 13 (50%) | 16 (32%) |
| No   | 12 (46%) | 31 (62%) |

\*p-value < 0.05.

## TREATMENT OUTCOMES

|                                   | G3Cr-Eb | Controls |
|-----------------------------------|---------|----------|
| No therapy                        | 4       | 3        |
| Clinical improvement              | 2       | 1        |
| Clinical failure/progression      | -       | -        |
| Documentation unavailable         | 2       | 2        |
| Empiric therapy - appropriate     | 5       | 47       |
| Clinical improvement              | 4       | 24       |
| Clinical failure                  | 1       | -        |
| Documentation unavailable         | -       | 23       |
| Empiric therapy - not appropriate | 17      | 1        |
| Clinical improvement              | 8       | 1        |
| Clinical failure                  | 2       | -        |
| Documentation unavailable         | 7       | -        |

## HEALTHCARE UTILIZATION

|                                  | G3Cr-Eb             | Controls        |
|----------------------------------|---------------------|-----------------|
| Site of care*                    |                     |                 |
| Ambulatory                       | 15 (58%)            | 43 (84%)        |
| Ward                             | 8 (31%)             | 5 (10%)         |
| ICU/SDU                          | 3 (12%)             | 3 (6%)          |
| Length of stay, median (IQR)     | 4 days (3.75, 5.25) | 3 days (2.5, 4) |
| Treatment duration, median (IQR) | 9 days (5, 13)      | 10 days (7, 10) |
| ID consult*                      | 13 (50%)            | 1 (2%)          |
| Nephrology consult               | 1 (7%)              | -               |
| Urology consult*                 | 3 (20%)             | -               |
| Subsequent UCx's                 |                     |                 |
| Yes                              | 13 (81%)            | 17 (55%)        |
| No                               | 3 (19%)             | 14 (45%)        |
| GU-specific imaging studies      |                     |                 |
| Yes                              | 10 (63%)            | 12 (39%)        |
| No                               | 6 (38%)             | 19 (61%)        |
| Ionizing radiation*              | 4 (40%)             | -               |

\*p-value < 0.05.

## SUMMARY

- We present preliminary data from a public teaching hospital in LA County within a multi-center, case-control study on pediatric G3Cr-Eb UTI.
- 3.7% of Enterobacteriaceae isolates recovered in pediatric urine culture were G3Cr.
- 17 children with G3Cr-Eb UTI received inappropriate empiric therapy; clinical improvement occurred in 8 of them within a median of 3 days (IQR 2, 4).
- In this preliminary analysis: most risk factors were similar between groups; G3Cr-Eb UTI was managed on an ambulatory basis less often and incurred more ID & Urology consults, as well as more imaging with ionizing radiation; however, length of stay and treatment duration were similar. Multicenter data collection is ongoing, which we anticipate will provide more statistically robust and generalizable conclusions.