Disclosures. All Authors: No reported Disclosures.

2847. Comparative Genomics and Clonal Tracking of Multi-drug-Resistant Uropathogens Implicates the Fecal Microbiome as a Potential Reservoir for Recurrent Urinary Tract Infections
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Background. Multi-drug-resistant organisms (MDRO) have complicated the treatment of urinary tract infections (UTIs), especially in patients with recurrent UTIs (rUTI). The objective of this pilot prospective cohort study is to determine the role of the fecal microbiome in rUTIs.

Methods. Stool and urine specimens were prospectively collected from patients with MDRO UTIs at 6 time points during and after the UTI, and with any rUTI. Specimens underwent semi-quantitative culture on differential and selective media for MDROs, and isolates underwent phenotypic susceptibility testing and whole-genome sequencing. Comparative genomics and clonal tracking were used to detect clonal uropathogen strains in the urinary and gastrointestinal tracts. Resistance genes, resistance-plasmids, and virulence genes of MDROs were characterized in silico.

Results. A total of 110 isolates (95 Escherichia coli, 2 Klebsiella pneumoniae, 13 Proteus mirabilis) were cultured from the urine and stool of 15 patients (7 non-rUTI, 8 rUTI). Clonal uropathogens were isolated between the urinary tract and their intestinal reservoir (Figure 1). Integration of clonality information with semiquantitative culturing implied three potential routes for recurrence of UTIs: (i) bladder colonization following an intestinal bloom of uropathogens, (ii) reinfection from an external source, and (iii) bacterial persistence within the urinary tract (Figures 2 and 3). Antibiotic susceptibility testing and genomic profiling indicated that antibiotic-resistant uropathogen populations colonizing the urinary tract and intestinal reservoir at symptomatic and asymptomatic timepoints have similar resistance profiles that are largely determined via a pool of shared resistance plasmids (Figure 3).

Conclusion. This study provides the first time-resolved analysis of uropathogen persistence following UTIs, showing that clonal antibiotic-resistant uropathogens can be detected in both the urine and stool at varying time points post-initial infection. The study implicates 3 potential routes of rUTI, including uropathogen persistence within the gut microbiota, reinfection from an external source, and persistent bacteriuria. Study findings could be utilized to inform future diagnostics and therapies for treatment of rUTIs.
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2848. Spatial Distribution of Community-Acquired Extended-Spectrum β-Lactamase-Producing Enterobacteriaceae Infections and its Association with Sewer Overflows in Middle Georgia
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Background. Extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL-PE) were described first in relation to hospital-acquired infections. However, infections by these organisms acquired in the community have become a public health problem. There are no well-known risk factors for acquisition of these bacteria in the community. Surface waters and sanitation conditions may serve as reservoir and transmission.

Methods. We conducted a retrospective study over 12 months of patients who had positive cultures with ESBL-PE in our laboratory. We excluded patients with hospitalization in the previous 3 months, those in skilled nursing facilities, and those whose culture was taken 3 or more days after hospitalization. Geographic Information System analysis was performed based on patient’s residence, population, and sewer overflow public data.

Results. Among 485 patients with cultures positive for ESBL-PE in 2018, 64 were included in the study. Mean age was 54, and 68.7% were females. Organisms isolated included in the study. Mean age was 54, and 68.7% were females. Organisms isolated were E. coli (78.2%) and K. pneumoniae ESBL (21.8%). These were isolated from urine 47 (73.4%), blood 5 (7.8%), abscess 6 (9.3%), ulcers 5 (7.8%), and sputum 1 (1.5%). Antibiotic exposure in the preceding 3 months was noted in 12 patients (18.7%). Spatial distribution of patients in the community was not random based on nearest neighbor analysis (Z score = -2.6). Kernel density estimation showed clustering of cases. Infection rates were calculated per census tracts. There was poor correlation between infection rate and mean family income (R2 = 0.18, P = 0.017). Analysis of Kernel density estimations showed that sewer overflow distribution explained over 50% of the variance of distribution of cases with ESBL-PE (R2 = 0.51, P < 0.001).

Conclusion. Patients presenting with infections due to ESBL-PE acquired in the community did not have a random spatial distribution. Other factors besides prior antibiotic use and financial status should be investigated. Proximity to sanitary sewer overflows may be a contributing factor. Location of residence within a community may aid in identifying patients at risk for acquisition of ESBL-PE.

2849. Gut Microbiota Differences at the Time of Medical Intensive Care Unit (MICU) Admission Are Associated with Acquisition of Multi-drug-Resistant Organisms (MDROs) Among Patients Not Already Colonized with an MDRO

Methods. Rectal swab samples were collected from patients admitted to an 11-bed MICU at a large urban academic medical center from October 1, 2017 to December 31, 2018. Patients were screened for MDRO colonization by selective culture (see Figure 1 for MDRO types); those with ≥2 swabs and MICU stays ≥3 days were studied. Bacterial 16S rRNA gene amplicon sequences were used for microbiota analysis. Medical records were reviewed.

Results. In preliminary analysis, 2,480 samples were collected from 627 patients who acquired 170 MDROs (Figure 1). Deblurring, co-morbidities, and certain medical devices were associated with MDRO acquisition, though admission MDRO status was not (Table). While no interactions were detected between admission MDRO status and clinical predictors of MDRO acquisition, there were significant differences in gut microbiota composition at the time of MICU admission between patients colonized with an MDRO on admission and those not colonized (P < 0.001, analysis of variance (AMOVA) on distances). Therefore, we stratified our analysis by admission MDRO colonization status. For patients MDRO-colonized at admission, there were no significant differences in microbiota of patients who later did or did not acquire an MDRO (AMOVA: P > 0.05). For patients not MDRO-colonized on admission, there was a significant difference in microbiota of patients who later acquired an MDRO and those who did not (AMOVA: P < 0.05). Differentially abundant operational taxonomic units (OTUs, based on 3% sequence difference) included OTUs classified as Anaerococcus and as other Clostridiales (higher in patients who remained uncolonized) and as Enterococcus (higher in patients who acquired an MDRO) (Figure 2). Diversity was also higher in patients who remained uncolonized than those who acquired an MDRO (Figure 2). Diversity was also higher in patients who remained uncolonized (Wilcoxon test P-value: 0.035) (Figure 3).

Conclusion. Among patients not already colonized with an MDRO on admission, we identified gut microbiota differences associated with MDRO acquisition that could help explain patient-level variation in MDRO colonization resistance.

Disclosures. All Authors: No reported Disclosures.

Table 1. Univariate associations of clinical factors with MDRO acquisition (N = 627 patients)

| Clinical Factor                              | MICU Admission (627) | MDRO (51) | p-value     |
|---------------------------------------------|----------------------|-----------|-------------|
| Age (years), mean ± SD                      | 64 ± 19              | 64 ± 18   | 1.00 (0.00, 1.00) | 0.62 |
| Gender, % (M/F)                             | 397 (99%/51%)        | 51 (98%/2%) | 5.12 (97.9%, 99.9%) | 0.05 |
| Race, % (White/Other)                       | 279 (45%)            | 9 (18%)   | 1.17 (0.94, 1.49) | 0.37 |
| Admission infection, % (Yes/No)             | 250 (40%)            | 41 (80%)  | -0.96 |
| Functional status before admission, % (Yes/No) | 130 (21%)            | 39 (78%)  | 1.36 (0.75, 2.48) | -0.06 |
| Comorbidities dependent with MDROs           | 31 (5%)              | 15 (30%)  | -0.58 |
| Immunosuppressive medications                 | 137 (22%)            | 21 (42%)  | -0.02 |
| Antibiotic exposure for > 14 days             | 25 (4%)              | 4 (8%)    | -0.01 |
| Medical Sepsis on admission, % (Yes/No)      | 107 (17%)            | 20 (40%)  | -0.02 |
| Cancer diagnosis                             | 107 (17%)            | 20 (40%)  | -0.02 |
| Diabetes                                     | 107 (17%)            | 20 (40%)  | -0.02 |
| Metabolic acidosis                           | 107 (17%)            | 20 (40%)  | -0.02 |
| History of hospitalization of < 30 days      | 107 (17%)            | 20 (40%)  | -0.02 |
| History of hospitalization of ≥ 30 days      | 107 (17%)            | 20 (40%)  | -0.02 |
| History of antibiotic admission              | 107 (17%)            | 20 (40%)  | -0.02 |

Figure 1. a) Heatmap of community-acquired ESBL-PE infections by patient’s residence. b) Heatmap of sewer overflow events in Macon-Bibb county, Georgia