

THE FEMALE URINARY MICROBIOTA DIFFER BY PRIMARY LOWER URINARY TRACT DISORDER

Hypothesis / aims of study

To determine if Female Urinary Microbiota (FUM) differs between women with lower urinary tract disorders and non-symptomatic controls.

Study design, materials and methods

With IRB approval, transurethral catheterized urine samples were collected from 384 adult women, categorized into 4 groups: 75 with self-reported Urinary Tract Infection (UTI), 109 with Urgency Urinary Incontinence (UUI), 50 with Stress Urinary Incontinence (SUI), 150 without Lower Urinary Tract Symptoms (non-LUTS). Women with UUI and SUI were characterized by response to the Pelvic Floor Distress Inventory. Bacterial growth was assessed with Enhanced Quantitative Urine Culture (EQUC) protocol, which uses 100X more urine plated onto more types of media and cultured 2X longer under more environmental conditions relative to Standard Urine Culture (SUC). All bacteria detected by EQUC were identified using Matrix Assisted Laser Desorption/Ionization - Time of Flight Mass Spectrometry. Microbiota composition and diversity were compared in terms of relative proportion of genera amongst all cohorts and by dominant genera (>50% relative abundance) within each cohort.

Results

All cohorts were predominantly White/Caucasian. The Non-LUTS cohort was significantly younger ($p < 0.05$). The distribution of dominant genera differed amongst cohorts (**Fig. 1A**). Not surprisingly, genera containing typical pathogens (e.g., *Proteus*, *Pseudomonas*, *Klebsiella*, *Staphylococcus*, *Escherichia*) were enriched in the UTI cohort. Other genera were enriched in other cohorts (non-LUTS – *Micrococcus*, *Bacillus*; SUI - unclassified & *Alloscardovia*; UUI – *Actinobaculum*, *Bifidobacterium*). Some genera are common in all non-UTI cohorts (*Lactobacillus*, *Streptococcus*), while others were enriched in the incontinent (UUI, SUI) cohorts (*Gardnerella*) or in both UTI and UUI cohorts (*Aerococcus*). Most culture-negative samples appeared in non-LUTS, while most Mixed cultures (i.e. a single genus is not present at >50%) appeared in SUI and UUI. Amongst different patient cohorts, distinct microbial differences were detected (**Fig. 1B**). The non-LUTS cohort tended to be culture-negative or dominated by *Lactobacillus*, while *Escherichia* dominated the UTI cohort. The UUI and SUI cohorts appeared very similar and differed from the non-LUTS cohort primarily by the percentage of mixed cultures, suggesting lower diversity in the non-LUTS cohort; this is supported by Shannon Diversity Indices that are greater in UUI and SUI.

Interpretation of results

Compared to women without LUTS, the FUM differs in the presence of any of the studied LUTS. Moreover, the primary LUTS disorders appear related to FUM composition, with differences between women with UTI and common forms of UI. Although this analysis detected differences between women with SUI and UUI, they are relatively subtle. Enrichment of *Aerococcus* in the UTI and UUI cohorts supports the contention that this Gram-positive bacterium is an emerging uropathogen.

Concluding message

The Female Urinary Microbiota (FUM) differs in the presence of various Lower Urinary Tract Symptoms (LUTS).

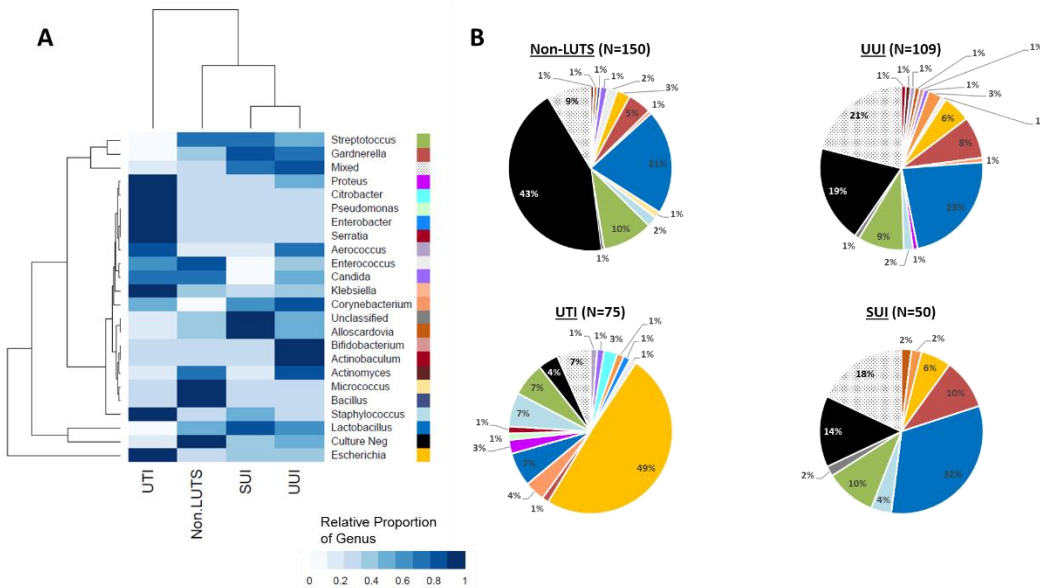


FIGURE 1. Microbial Composition of Patient Cohorts. (A) Depicts the relative proportion of each bacterial genus found within the cohorts. Each axes is clustered using the corresponding dendrogram based on Euclidean distance. “Culture Neg” indicates no bacterial growth present by EQUC. “Mixed” indicates that no single genus was present at >50% abundance in a sample. (B) Depicts the genus-level composition of each of the cohorts based on the percentage of samples dominated by the indicated genus.

Disclosures

Funding: R21 DK097435, R56 DK104718, R01 DK104718, Investigator Initiated Study VESI-12D01 from Astellas Scientific and Medical Affairs Inc. **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** Loyola University Chicago Institutional Review Board (IRB) **Helsinki:** Yes **Informed Consent:** Yes