Urinary microbiomic profiling in female lower urinary tract symptoms

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HYPOTHESIS/AIMS OF STUDY

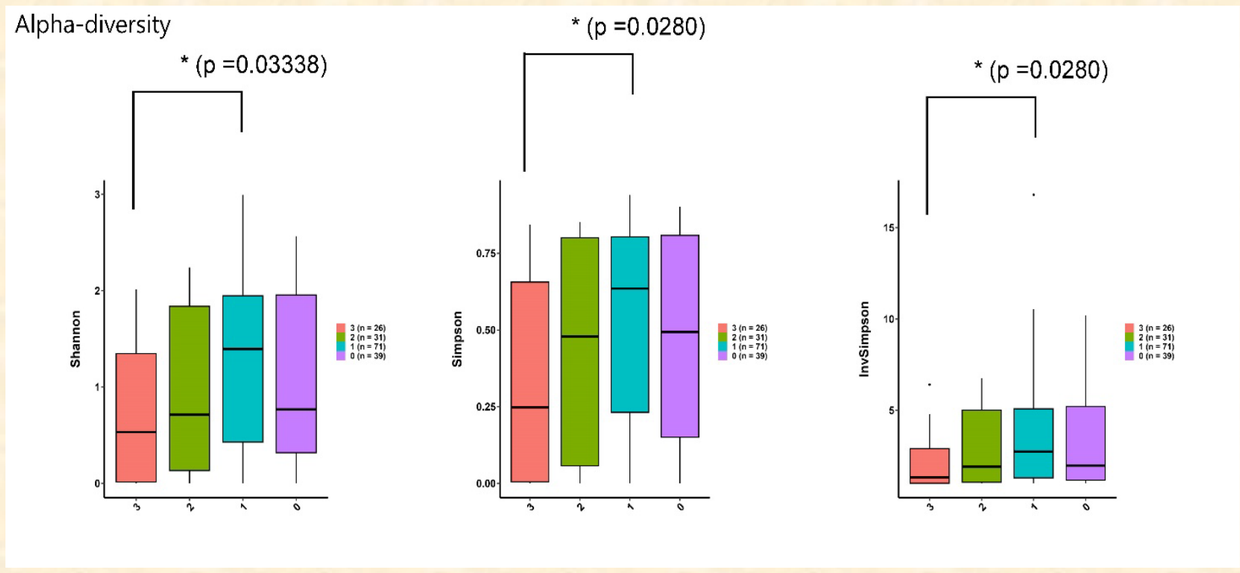
Overactive bladder (OAB) and interstitial cystitis/bladder pain syndrome (IC/BPS) accompany wide range of lower urinary tract symptoms (LUTS) that differential diagnosis is often challenging. As both disease entities require exclusion of on-going urinary tract infection, accurate and timely diagnosis is more confusing in cases of patients with chronic or recurrent cystitis (RC). For those who present urgency with ambiguous pain, repeated counselling and urinalysis including culture are common and further optional work-ups such as cystoscopy or urodynamic study are needed. The etiological role of urinary microbiota in various lower urinary tract dysfunctions (LUTDs) is controversial. In present study, we investigated urinary microbiome profiles in OAB, IC/BPS, and RC.

METHODS

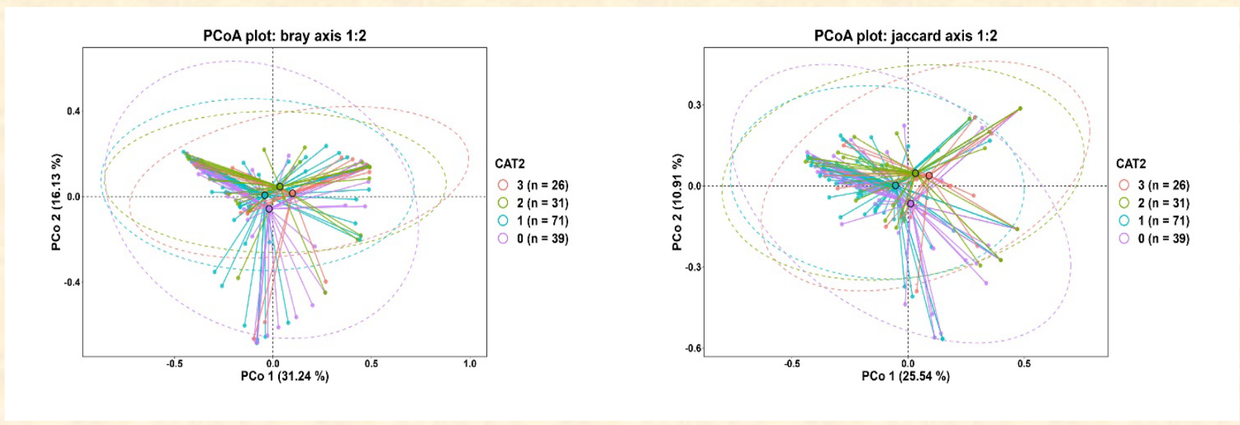
Female patients who underwent 16s rDNA sequencing between September and December 2022 at initial visit to the urology clinic were reviewed retrospectively. Midstream urine samples were and sequencing named 16s rDNA amplification was used for urine microbiota analysis. Patients whose final diagnosis were bladder malignancy or radiation cystitis were excluded from the study. In cases of troubleshooting cases, further work-ups including cystoscopy, urodynamic study, and imaging study were applied unhesitatingly. The final diagnosis was categorized into four groups; OAB (CAT 1), IC/BPS (CAT 2), RC (CAT 3), and others (microscopic hematuria without any LUTS or other LUTS except for OAB and pain; CAT 0). Based on the diagnostic category, microbiome diversity and patterns were compared.

RESULTS

A total of 235 patients underwent 16s rDNA sequencing during the study period. After excluding 4 patients (bladder cancer (n=2), radiation cystitis (n=2)), 231 patients with mean age of patients were 56.7 ± 14.2 years were included. Forty patients had too low bacterial loads (insufficient for microbiome analysis) and 24 patients had bacteriuria, but there were no significant differences in proportions among subgroups (p=0.537 and p=0.835, respectively). Microbiome diversity and pattern analysis was performed in 167 patients consisting of OAB (CAT 1; n=71), IC/BPS (CAT 2; n=31), RC (CAT 3; n=26), and others (CAT 0; n=39). Lactobacillus, prevotella, anaerococcus, peptoniphilus, and finegoldia were most frequently observed in all patients. The presence of uropathogens did not differ among groups. Overall, there were no significant differences in alpha diversity. However, on one to one comparison (ex; CAT 1: CAT 2), OAB group presented more microbiomic diversities than RC group ($p < 0.05$, Figure 1).



On beta diversity analysis, there was no differences among and between groups $p > 0.05$, Figure 2).



INTERPRETATION OF RESULTS

OAB patients presented more diverse urinary microbiome than RC groups, but there was no difference in composition of microbial communities among groups. Although present study could not demonstrate the diagnostic potential of urinary microbiome analysis as initial work-up, diversity of microbiota in OAB might reflect underlying heterogeneous and complexity of the disease. This intriguing result should be interpreted with caution as this is the retrospective study to figure out the diagnostic potential of 16s rDNA for various LUTDs. The study population was small, included patients with short follow-ups (maximum of five months) and patients' routine life style and dietaries could not be taken into account fully. Moreover, considering the chronic wax and wane nature of LUTDs, there could be a modification in current diagnosis depending on patients' perception on treatment response. Prospective studies set selection criteria to improve the diagnostic accuracy and representativeness of the study group. However, both OAB and IC/BPS are symptomatic diagnosis based on excluding possible pathologies and overlapping clinical cases are common. Future studies with long term follow-ups including various clinical courses for better disease categorization is needed.

CONCLUSIONS

Current urinary microbiome research is limited to profiling the urinary microbiota in patients with various LUTDs that significance of each microbiome is uncertain. Further studies to better understand the microbial composition of human urine and its variations are mandatory.

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