Gardnerella vaginalis is Associated with UTI Symptoms in Both Pediatric and Older Adult Females

Emery Haley[1] , Xiaofei Chen[1], Natalie Luke[1], Jim Havrilla[1], Margo Lee[1], William Lai[1]; Temitayo Famoroti[1], and Melanie Schlittenhardt[2*]

[1]Pathnostics, Irvine, CA; [2]Pelican Health Clinic, Bismark, ND

*Board Certified Urology Nurse Practitioner and Doctor of Nursing Practice

1. Purpose

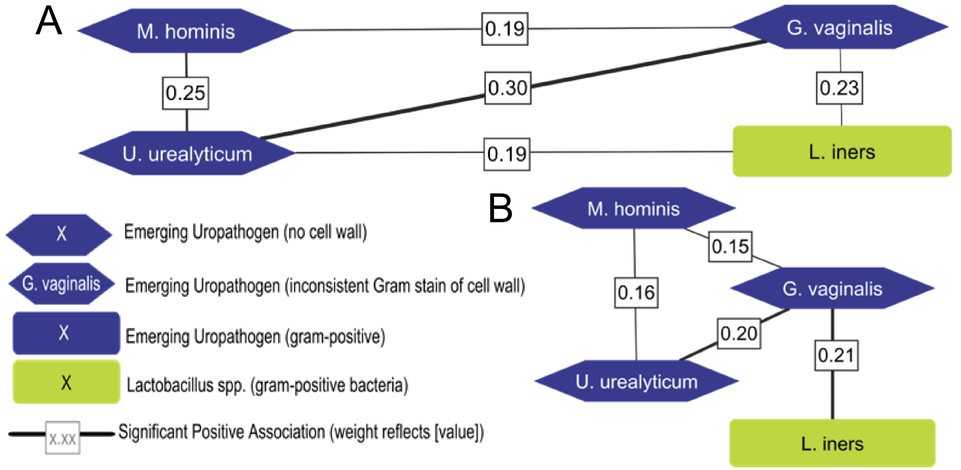
To determine the prevalence of *Gardnerella vaginalis* and map its microbial associations in Urinary Tract Infections (UTIs) in females.

2. Background

G. vaginalis, considered a part of the vaginal microbiome, has been dismissed as a contaminant in midstream voided urine specimens.[1,2] However, *G. vaginalis* has recently been associated with recurrent UTIs and dysbiosis.[3–5]

Figure 1. *G. vaginalis* and Associated Organisms

Associations with adjusted p-values < 0.05 and (A) Phi coefficient or (B) Pearson's Correlation ≥ 0.1 were plotted in Cytoscape using weighted, undirected pairwise networks



3. Methods

Multiplex polymerase chain reaction (M-PCR) was used for microbial identification and quantification in midstream urine specimens from females with UTI symptoms between 2/25/2022 and 11/22/2023.

The study analyzed samples from 8,638 women ≥60 (mean 69.5 years) from 594 outpatient urology/urogynecology specialty clinics in 42 states, exempted by the Western Institutional Review Board WIRB-Copernicus Group under 45 CFR § 46.104. Additionally, 44 specimens from patients aged 3-21 (mean 12.3 years) were collected at Hackensack University Medical Center's Pediatric Emergency Department in New Jersey, approved reference Pro2021-0783.

Associations between microorganism pairs were assessed using Pearson's correlation (PCC) and Phi (φ) coefficients. Statistical significance was assessed using Fisher's exact test with Benjamini Hochberg FDR controlling procedure for multiple testing adjustments.

4. Results

G. vaginalis was present in 12% of adult and 31% of pediatric specimens. In women ≥ 60, *G. vaginalis* associated *with U. urealyticum* (φ=0.20, PCC=0.30), *M. hominis* (φ=0.15, PCC=0.18), and *L. iners* (φ=0.21, PCC=0.19), which unlike other *Lactobacillus* species,[6–8] is associated with dysbiosis.[9–17] In girls aged 9-21, monomicrobial *G. vaginalis* was associated with pyuria (presence of white blood cells and + Leukocyte Esterase) on urinalysis and with abdominal pain or altered urinary frequency.

5. Implications

G. vaginalis should be considered a potential uropathogen in females with UTI symptoms.

1. Jespers V, Hardy L, Buyze J, Loos J, Buvé A, Crucitti T. Association of Sexual Debut in Adolescents With Microbiota and Inflammatory Markers. Obstet Gynecol. 2016;128(1):22-31. doi:10.1097/aog.0000000000001468
2. Hickey RJ, Zhou X, Settles ML, Erb J, Malone K, Hansmann MA, et al. Vaginal Microbiota of Adolescent Girls Prior to the Onset of Menarche Resemble Those of Reproductive-Age Women. mBio. 2015;6(2):e00097-15. doi:10.1128/mbio.00097-15
3. Yoo JJ, Song JS, Kim WB, Yun J, Shin HB, Jang MA, et al. Gardnerella vaginalis in Recurrent Urinary Tract Infection Is Associated with Dysbiosis of the Bladder Microbiome. J Clin Med. 2022;11(9):2295. doi:10.3390/jcm11092295
4. Leadbetter G, Slavin S. Pediatric urinary tract infectionSignificance of vaginal bacteria. Urology. 1974;3(5):581-588. doi:10.1016/s0090-4295(74)80252-9
5. Curley T, Forster CS. Recurrent UTIs in Girls: What Is the Role of the Microbiome? Urology. 2021;151:94-97. doi:10.1016/j.urology.2020.04.091
6. Price T, Hilt E, Thomas-White K, Mueller E, Wolfe A, Brubaker L. The urobiome of continent adult women: a cross-sectional study. Bjog Int J Obstetrics Gynaecol. 2020;127(2):193-201. doi:10.1111/1471-0528.15920
7. Jacobs KM, Price TK, Thomas-White K, Halverson T, Davies A, Myers DL, et al. Cultivable Bacteria in Urine of Women With Interstitial Cystitis: (Not) What We Expected. Female Pelvic Med Reconstr Surg. 2021;27(5):322-327. doi:10.1097/spv.0000000000000854
8. Ammitzbøll N, Bau BPJ, Bundgaard-Nielsen C, Villadsen AB, Jensen AM, Leutscher PDC, et al. Pre- and postmenopausal women have different core urinary microbiota. Sci Rep. 2021;11(1):2212. doi:10.1038/s41598-021-81790-8
9. Jung CE, Estaki M, Chopyk J, Taylor BC, Gonzalez A, McDonald D, et al. Impact of Vaginal Estrogen on the Urobiome in Postmenopausal Women With Recurrent Urinary Tract Infection. Female Pelvic Med Reconstr Surg. 2022;28(1):20-26. doi:10.1097/spv.0000000000001051
10. Atassi F, Brassart D, Grob P, Graf F, Servin AL. Lactobacillus strains isolated from the vaginal microbiota of healthy women inhibit Prevotella bivia and Gardnerella vaginalis in coculture and cell culture. FEMS Immunology & Medical Microbiology. 2006;48(3):424-432. doi:10.1111/j.1574-695x.2006.00162.x
11. Atassi F, Ahn DLPV, Moal VLL. Diverse Expression of Antimicrobial Activities Against Bacterial Vaginosis and Urinary Tract Infection Pathogens by Cervicovaginal Microbiota Strains of Lactobacillus gasseri and Lactobacillus crispatus. Front Microbiol. 2019;10:2900. doi:10.3389/fmicb.2019.02900
12. Song CH, Kim YH, Naskar M, Hayes BW, Abraham MA, Noh JH, et al. Lactobacillus crispatus Limits Bladder Uropathogenic E. coli Infection by Triggering a Host Type I Interferon Response. Proc Natl Acad Sci. 2022;119(33):e2117904119. doi:10.1073/pnas.2117904119
13. He Y, Niu X, Wang B, Na R, Xiao B, Yang H. Evaluation of the Inhibitory Effects of Lactobacillus gasseri and Lactobacillus crispatus on the Adhesion of Seven Common Lower Genital Tract Infection-Causing Pathogens to Vaginal Epithelial Cells. Front Med. 2020;7:284. doi:10.3389/fmed.2020.00284
14. Watanabe T, Sadahira T, Hirakawa H, Huang P, Zhou T, Iwata T, et al. Exploration of the protein-dependent mechanism of Lactobacillus crispatus GAI98322 to prevent recurrent cystitis. J Infect Chemother. 2023;29(10):1001-1004. doi:10.1016/j.jiac.2023.06.013
15. Nadifah F, Artama WT, Daryono BS, Retnaningrum E. Overabundance of Lactobacillus iners in the Urogenital Microbiome of a Female Patient with Urinary Tract Infection. :52-58.
16. A. C Christopher, E. S Ann, Yuliya YY, E. S Walter. Phase I Trial of a Lactobacillus crispatus Vaginal Suppository for Prevention of Recurrent Urinary Tract Infection in Women. Infect Dis Obstet Gynecol. 2007;2007:35387. doi:10.1155/2007/35387
17. Abdul-Rahim O, Wu Q, Price TK, Pistone G, Diebel K, Bugni TS, et al. Phenyl-Lactic Acid Is an Active Ingredient in Bactericidal Supernatants of Lactobacillus crispatus. J Bacteriol. 2021;203(19):e00360-21. doi:10.1128/jb.00360-21