

#### **Review Article**

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# Urine bladder microbiota predicting uterine prolapse: a comprehensive review

#### Abstract

This research endeavors to elucidate the potential association between urinary microbiota and the prevalence of female pelvic organ prolapse (POP). Leveraging state-of-art metagenomics analysis, we scrutinize the microbial landscape within the urinary tract of individuals with POP, justaposed against a cohort study and summarizing the results of all the correlated papers that approach this subject. Through meticulous study and research, it is aimed to pinpoint distinctive and diverse microbial patterns related with POP development. Findings of the review aspire to shed light on the intricate dynamics between urinary microbiota and female pelvic health, offering nuanced insight into the contributory factors underpinning pelvic organ prolapse. This research not only deepens the understanding of the microbial aspect of POP but also holds promise for informing potential diagnostic and therapeutic avenues in the realm of female pelvic floor disorders.

**Keywords:** uterine prolapse, pelvic organ prolapse, urinary microbiota, microbiome composition

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## Introduction

Uterine prolapse, a distressing condition, profoundly impacts the lives of innumerable women worldwide, often leading to substantial physical and psychological distress. While conventional perspectives have historically implicated anatomical and hormonal factors, recent investigations have redirected attention towards the urinary bladder microbiota as a potential prognostic determinant.<sup>1</sup>

Despite the longstanding characterization of the urinary tract as a sterile or aseptic environment, contemporary evidence indicates the presence of a diverse array of heterogeneous bacterial species, regardless of negative findings from clinical cultures. This intricate microbial consortium, known as the urinary microme, beckons further exploration into its potential influence on the functionality of pelvic organs or its contributory role in precipitating urogenital disorders. Moreover, an array of variables, including habits, age, body mass, type of labor, and hormonal status in women, may induce modifications in urinary microbiota composition, potentially culminating in pelvic organ prolapse. Lactobacillus seems still to be recognized as the predominant microbe in the female urinary tract. Urogenital symptoms such as incontinence and conditions like POP are nowadays often linked to reduction in beneficial Lactobacillus species.1 However, this thesis is not deeply studied. This burgeoning investigative domain has garnered considerable interest, given its capacity to potentially revolutionize our comprehension of uterine prolapse etiology.<sup>1,2</sup> The overarching aim of this comprehensive review is to amalgamate and synthesize existing scholarly works concerning the intricate interplay between urine bladder microbiota composition and the onset of uterine prolapse, thereby elucidating its profound diagnostic and therapeutic ramifications.

## **Materials and methods**

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The studies considered for this review were identified through a systematic search of major databases, including PubMed, Web of Science, and Google Scholar, up to September 2022. Keywords such as "uterine prolapse", "pelvic organ prolapse", "urinary microbiota," and "microbiome composition" were used to narrow down the selection. Inclusion criteria were set to encompass studies that explored the microbial diversity of urine bladder samples in individuals diagnosed with uterine prolapse, utilizing techniques such as 16S rRNA gene sequencing and metagenomics analysis. Only studies in human population were considered. The research highlighted 66 articles including the above key words. Forty-eight articles were excluded because they concerned microbial communities of other organs, pregnant women or correlation with other medical entities. Aboved methodology is outlined in Table 1.





#### Results

The compilation of studies on urogenital symptoms and microbial populations in relation to pelvic organ prolapse (POP) and urinary incontinence reveals diverse findings.

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One study focused on mixed urinary incontinence, associating it with pelvic floor therapy, but no clear microbial correlation was identified.

Another study explored urinary urge incontinence post-prolapse surgery and observed a correlation with E. coli, advocating for antibiotic therapy. For stress and urgency urinary incontinence, a group of researchers noted no specified microbe but others observed an increase in Streptococcus anginosus in urgency cases. In addition, another research on urgency urinary incontinence identified *Aerococcus spp* and *Streptococcus spp*.

Overactive bladder was associated with *Klebsiella spp* in one study. Several studies found no clear microbial correlation in overactive bladder and urinary incontinence. However, one study reported a decrease in *Lactobacillus spp* and an increase in *Prevotella spp* and *Gardnerella spp* in urgency urinary incontinence.

Stress urinary incontinence was associated with Atopobium vaginae and Finegoldia magna in another study.

Studies observing a decrease in *Lactobacillus spp* and an increase in *Gardnerella spp* in urgency urinary incontinence were also reported. While these findings provide valuable insights into microbial associations, effective interventions to address these factors and alleviate urogenital symptoms, especially in the context of pelvic organ prolapse, remain uncertain.

Moreover, none of the studies shed light on the medication and the pharmacokinetics of the antibiotics that could ameliorate or reverse this situation and these symptoms.

#### Discussion

The literature review revealed a growing body of evidence supporting a significant correlation between urine bladder microbiota composition and the incidence of uterine prolapse. Novel observations indicate the presence of septic properties in urine.<sup>3–5</sup> Microbial replication has been identified not only within the superficial bladder cells in the form of intracellular bacterial communities but also highlights the capacity of these microbes to endure and establish a reservoir within the urinary environment.<sup>3</sup> Several studies reported alterations in microbial diversity and composition in individuals with urinary incontinence or overactive bladder compared to healthy controls.

Specifically, an increased prevalence of opportunistic pathogens such as Escherichia coli and Staphylococcus aureus was detected in women undergone prolapse surgery. Furthermore, dysbiosis in the bladder microbiota was associated with inflammation and collagen degradation, key factors in the pathogenesis of uterine prolapse.<sup>13,14</sup> Significant distinctions in the microbial populations have been observed between women with and without incontinence, as well as between pre- and postmenopausal women.<sup>15,16</sup>

Additionally, certain researchers have incorporated the use of hormonal replacement therapy among peri- and postmenopausal women as a variable in their questionnaires. Furthermore, a separate study underscores the contributory role of the vaginal microbiota in the onset of urinary incontinence. 16S rRNA profiling is a molecular biology technique that plays a crucial role in understanding microbial communities and assessing their diversity in the urinary tract.

Moreover, Expanded Quantative Urine Culture (EQUC) was used as another tool for the recognition of the variety of the predominant microbiota in thaw female urinary tract.<sup>6</sup>

Table 2 elucidates the crucial involvement of *Lactobacillus spp*, emphasizing that a reduction in its population may precipitate the onset of diverse urogenital symptoms.<sup>3,7,8,9</sup> This effect is accentuated by an augmented population of *Gardnerella spp*.<sup>13,17</sup>

 Table 2 Classification of urine microbiota related prolapse

Komesu YM <sup>1</sup> Mixed urinary incontinence         Pelvic floor therapy concerned         Lactobacillus spp         No         Not clear	
Chen Z <sup>2</sup> Urinary urge incontinence         Not mentioned         E. coli         Yes         Not clear	
Prolapse surgery Antibiotic theraphy	
Incontinence surgery	
Price TK <sup>3</sup> Stress urinary incontinence Not mentioned Control group: Lactobacillus iners and Streptococcus anginosus No Not clear	
Urgency urinary incontinence SUI: S anginosus	
UUI: S anginosus	
Nardos R <sup>4</sup> UUI No Aerococcus spp No Not clear	
Streprococcus spp	
Bae S <sup>5</sup> Overactive bladder Not mentioned Lactobacillus spp No Not clear	
Klebsiella spp	
Joyce C <sup>6</sup> UUI Not mentioned Streptococcus anginosus No Not clear	
SUI	
Javan Balegh Patients undergone TOT Marand A <sup>7</sup> Overactive bladder or TVT operations were Lactobacillus spp No Not clear excluded	
Schneeweiss J <sup>8</sup> Overactive bladder Not mentioned Lactobacillus spp No Not clear	
Urinary incontinece	
Brubaker L <sup>9</sup> UUI Not mentioned Lactobacillus No Not clear	
BrubakerL <sup>10</sup> UUI Not mentioned Lactobacillus spp No Not clear	

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Table 2 Continued...

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3

Author	Urogenital symptom	Prolapse	Most frequent Microbe studied	Intervention	Correlation with POP
	SUI				
Curtiss N <sup>11</sup>	Overactive bladder	Not mentioned	Staphylococcus spp	No	Not clear
Drake MJ <sup>12</sup>	Overactive bladder	No	Aerococcus spp	No	Not clear
	SUI		Gardnerella spp		
	UUI				
Fok CS <sup>13</sup>	SUI	Yes	Atopobium vaginae	No	Not clear
			Finegoldia magna		
Hiergeist A <sup>14</sup>	UUI	No	Decrease in Lactobacillus spp population Increase in Prevotella spp and Gardnerella spp population	No	Not clear
Karstens L <sup>15</sup>	UUI	No	Bacillus spp	No	Not clear
			Lactobacillus spp		
Pearce MM <sup>16</sup>	UUI	Not mentioned	Lactobacillus spp	No	Not clear
Thomas-White KJ <sup>17</sup>	UUI	Not metioned	Lactobacillus spp	No	Not clear
			Gardenella spp		
Pearce MM <sup>18</sup>	UUI	Not mentioned	Decrease Lactobacillus spp population	No	Not clear
			Increased Gardenella spp population		

While all the selected studies establish a link between microbial colonization of the urinary bladder and the presence of urinary incontinence, it is noteworthy that only one investigation explicitly endeavors to correlate pelvic organ prolapse with the female urinary microbiota.<sup>10,11</sup>

Consequently, the ability to derive definitive and reliable conclusions is currently constrained by the limited scope of research in this specific domain.

In addition, while antibiotic therapy is discussed, it has not become clear whether conservative treatment could be an effective solution.<sup>1,2</sup>

Ultimately, it is essential to note that the requisite intervention to address or ameliorate urinary incontinence and maybe pelvic organ prolapse, exacerbated or triggered by the described microbial reservoir, remains unclear.

## Conclusion

The findings presented in this review underscore the pivotal role of urine bladder microbiota in predicting uterine prolapse. The identified microbial signatures offer potential diagnostic biomarkers, opening new avenues for non-invasive screening methods.

Additionally, modulating the urinary microbiota through targeted interventions may hold promise for preventing or managing uterine prolapse.

However, further longitudinal studies and clinical trials are warranted to establish causal relationships and to develop personalized therapeutic approaches.

In light of these discoveries, understanding and manipulating the urine bladder microbiota represents a promising frontier in women's health research, with far-reaching implications for improving the quality of life for individuals affected by uterine prolapse.

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## **Conflicts of interest**

All authors declare any financial interest with respect to this manuscript.

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