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Original Research Article

Urinary Microbiome Alterations in Postmenopausal Women with Recurrent Urinary Tract Infection: Impact of Vaginal Estrogen Therapy: A Retrospective Comparative Study

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Abstract:

Background: Recurrent urinary tract infection (rUTI) is a common clinical problem among postmenopausal women. Estrogen deficiency contributes to alterations in the urinary microbiome, loss of protective Lactobacillus species, and increased susceptibility to uropathogenic bacterial colonization. Emerging evidence suggests that vaginal estrogen therapy may restore microbial balance and reduce recurrent infections.

Objective: To evaluate urinary microbiome alterations in postmenopausal women with recurrent urinary tract infection and assess the impact of vaginal estrogen therapy on microbial composition and clinical outcomes.

Methods: This retrospective comparative study was conducted at Patna Medical College and Hospital (PMCH) from February 2025 to January 2026. Medical records of 100 postmenopausal women diagnosed with recurrent UTI were reviewed. Fifty women receiving vaginal estrogen therapy constituted Group A, while fifty women not receiving estrogen therapy formed Group B. Urinary microbiome profiles, bacterial abundance, inflammatory markers, and recurrence rates were compared between groups. Statistical analysis was performed using SPSS version 26.0, with $p<0.05$ considered statistically significant.

Results: Women receiving estrogen therapy demonstrated significantly higher urinary Lactobacillus abundance (42.8±12.6% vs 18.5±10.3%, $p<0.001$), greater microbial diversity (Shannon Index 2.89±0.56 vs 1.97±0.48, $p<0.001$), and lower Escherichia coli abundance (15.6±8.2% vs 34.7±11.5%, $p<0.001$). Annual UTI recurrence was significantly lower in the estrogen group (1.8±0.9 vs 4.1±1.3 episodes/year, $p<0.001$). Multivariate logistic regression demonstrated that vaginal estrogen therapy independently reduced the risk of recurrent UTI (OR=0.34, 95% CI: 0.16–0.72, $p=0.004$).

Conclusion: Vaginal estrogen therapy was associated with favorable urinary microbiome alterations characterized by increased Lactobacillus dominance, improved microbial diversity, and reduced pathogenic bacterial colonization. These changes were accompanied by significantly lower recurrence of urinary tract infections.

Keywords: Urinary Microbiome; Recurrent Urinary Tract Infection; Postmenopausal Women; Estrogen Therapy; Lactobacillus; Microbial Diversity.

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Introduction

Urinary tract infection (UTI) remains one of the most prevalent bacterial infections affecting women worldwide and accounts for substantial healthcare utilization and antibiotic consumption. Approximately 50–60% of women experience at least one UTI during their lifetime, while nearly 25–30% develop recurrent urinary tract infection (rUTI), defined as three or more episodes within one year or two episodes within six months. [1]

Postmenopausal women constitute a particularly vulnerable population because hormonal changes associated with estrogen deficiency predispose them to alterations in genitourinary anatomy, mucosal immunity, and microbial ecology.[2] The decline in circulating estrogen levels leads to thinning of the urogenital epithelium, decreased glycogen deposition, elevated vaginal pH, and reduced colonization by protective Lactobacillus species. [3]

These physiological changes facilitate colonization by uropathogenic organisms and contribute to increased susceptibility to recurrent infections. [4]

Historically, urine was considered sterile under normal physiological conditions. However, advances in molecular sequencing technologies, including 16S ribosomal RNA gene sequencing and expanded quantitative urine culture techniques, have fundamentally altered this understanding. Contemporary studies have demonstrated that the urinary tract harbors a distinct and dynamic microbial ecosystem known as the urinary microbiome. [5,6]

The healthy female urinary microbiome is frequently characterized by dominance of Lactobacillus species, including Lactobacillus crispatus, Lactobacillus gasseri, and Lactobacillus jensenii. These organisms contribute to host defense through production of lactic acid, bacteriocins, and other antimicrobial compounds that inhibit growth of pathogenic microorganisms. [7]

Disruption of urinary microbial homeostasis has been associated with several urological disorders, including urgency urinary incontinence, overactive bladder syndrome, interstitial cystitis, and recurrent urinary tract infection. [8] Recent investigations suggest that women with recurrent UTI exhibit reduced microbial diversity and increased abundance of pathogenic organisms such as Escherichia coli, Klebsiella pneumoniae, Enterococcus faecalis, and Proteus mirabilis. [9]

Estrogen therapy has emerged as an effective non-antibiotic intervention for prevention of recurrent UTI in postmenopausal women. Multiple studies have demonstrated that vaginal estrogen therapy restores vaginal Lactobacillus populations, lowers vaginal pH, and decreases recurrence rates of urinary tract infections. [10,11]

Increasing evidence indicates that estrogen may also influence the urinary microbiome directly. Experimental studies have shown that estrogen-mediated epithelial maturation promotes colonization by beneficial bacteria while reducing pathogenic bacterial adherence. [12] These microbial changes may contribute substantially to the protective effects observed with estrogen therapy.

Despite growing interest in the urinary microbiome, limited clinical data are available regarding microbial alterations associated with estrogen therapy among postmenopausal women with recurrent UTI. Understanding these interactions may facilitate development of microbiome-targeted interventions and improve preventive strategies. [13]

Therefore, the present study was undertaken to evaluate urinary microbiome alterations in postmenopausal women with recurrent urinary tract infection and assess the impact of vaginal estrogen therapy on microbial composition, inflammatory markers, and clinical outcomes.

Materials and Methods

Study Design: Retrospective comparative study.

Study Setting: Department of Urology and Microbiology, Patna Medical College and Hospital (PMCH), Patna, Bihar, India.

Study Duration: February 2025 to January 2026.

Study Population: Postmenopausal women diagnosed with recurrent urinary tract infection.

Sample Size: 100 patients.

Group A: Postmenopausal women receiving vaginal estrogen therapy (n=50).

Group B: Postmenopausal women not receiving estrogen therapy (n=50).

Inclusion Criteria

1. Postmenopausal women aged ≥50 years.
2. Diagnosed recurrent UTI.
3. Availability of urinary microbiome analysis records.
4. Complete clinical follow-up data.

Exclusion Criteria

1. Active malignancy.
2. Chronic immunosuppressive therapy.
3. Indwelling urinary catheter.
4. Neurogenic bladder.
5. Recent antibiotic exposure within four weeks.

Data Collection

Data extracted included:

- Age
- BMI
- Duration of menopause
- UTI recurrence frequency
- Urinary microbiome composition
- Lactobacillus abundance
- Escherichia coli abundance
- Shannon diversity index
- CRP level
- Urine leukocyte count

Statistical Analysis: Continuous variables expressed as mean±SD.

Statistical tests:

- Independent t-test
- Chi-square test
- Logistic regression

Significance:
$p < 0.05$.

Results

Baseline Characteristics of the Study Population: A total of 100 postmenopausal women with recurrent urinary tract infection were included in the study. Fifty women receiving vaginal estrogen therapy constituted the estrogen group (Group A), while fifty women not receiving estrogen therapy formed the non-estrogen group (Group B).

The mean age of participants in the estrogen group was 62.4 ± 6.8 years compared with 63.1 ± 7.2 years in the non-estrogen group. The mean body mass index (BMI) was 26.7 ± 3.4 kg/m² and 27.2 ± 3.8 kg/m² in Groups A and B, respectively. No statistically significant differences were observed between groups regarding age, BMI, duration of menopause, diabetes mellitus, or hypertension ($p > 0.05$), indicating comparable baseline characteristics between the study groups (Table 1).

Table 1: Baseline Characteristics of Study Participants

Variable	Estrogen Therapy (n=50)	No Estrogen Therapy (n=50)	p-value
Age (years)	62.4 ± 6.8	63.1 ± 7.2	0.612
BMI (kg/m²)	26.7 ± 3.4	27.2 ± 3.8	0.489
Duration of menopause (years)	11.2 ± 4.6	10.8 ± 4.2	0.651
Diabetes mellitus, n (%)	18 (36.0)	20 (40.0)	0.684
Hypertension, n (%)	24 (48.0)	26 (52.0)	0.689

Table 1 demonstrates that both groups were demographically and clinically comparable at baseline.

Urinary Microbiome Composition: Significant differences were observed in urinary microbiome composition between women receiving estrogen therapy and those not receiving estrogen therapy.

The mean abundance of Lactobacillus species was significantly higher in the estrogen group (42.8 ± 12.6%) compared with the non-estrogen group (18.5 ± 10.3%; $p < 0.001$). Conversely, Escherichia coli abundance was significantly lower among women receiving estrogen therapy (15.6 ± 8.2%) than among women without estrogen therapy (34.7 ± 11.5%; $p < 0.001$).

Furthermore, microbial diversity assessed using the Shannon Diversity Index was significantly greater in the estrogen group (2.89 ± 0.56) compared with the non-estrogen group (1.97 ± 0.48; $p < 0.001$). Microbial richness also demonstrated significantly higher values in estrogen-treated women (18.7 ± 4.3 vs 11.9 ± 3.7; $p < 0.001$).

These findings indicate a healthier urinary microbial ecosystem among women receiving estrogen therapy (Table 2).

Table 2: Comparison of Urinary Microbiome Parameters

Parameter	Estrogen Therapy (n=50)	No Estrogen Therapy (n=50)	p-value
Lactobacillus abundance (%)	42.8 ± 12.6	18.5 ± 10.3	<0.001
Escherichia coli abundance (%)	15.6 ± 8.2	34.7 ± 11.5	<0.001
Shannon Diversity Index	2.89 ± 0.56	1.97 ± 0.48	<0.001
Microbial Richness	18.7 ± 4.3	11.9 ± 3.7	<0.001

As shown in **Table 2**, estrogen therapy was associated with significantly increased Lactobacillus dominance and microbial diversity while reducing pathogenic bacterial colonization.

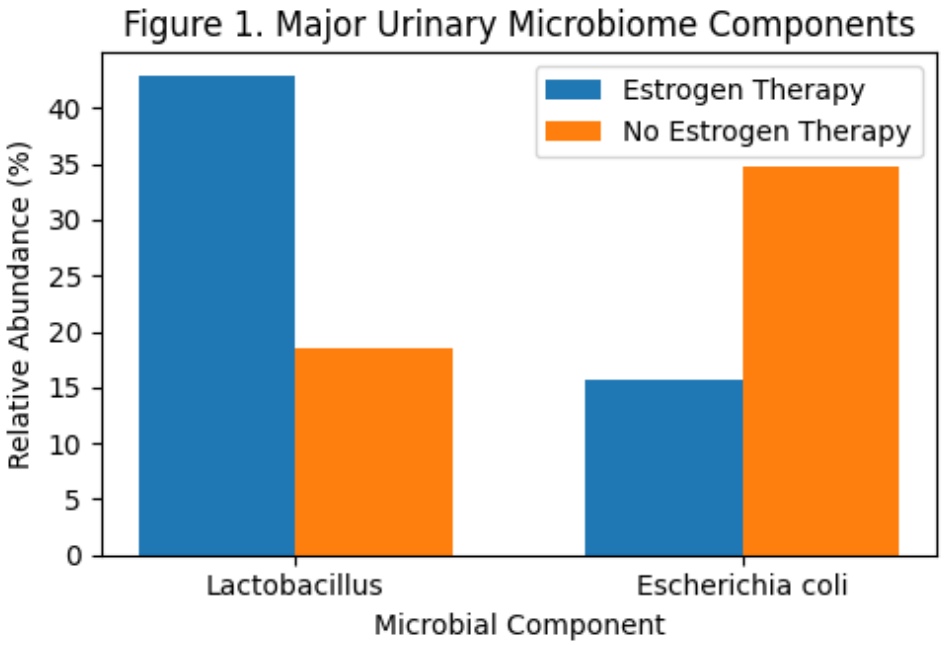

Figure 1: Comparison of Major Urinary Microbiome Components Between Study Groups

Figure 1 illustrates the substantial increase in Lactobacillus abundance and reduction in Escherichia coli colonization among women receiving estrogen therapy.

Distribution of Predominant Urinary Bacterial Genera: Evaluation of predominant urinary bacterial genera demonstrated significant alterations in bacterial composition between groups. Lactobacillus represented the dominant genus among women receiving estrogen therapy (42.8%), whereas Escherichia predominated in the non-estrogen group (34.7%).

Table 3: Relative Abundance of Predominant Urinary Bacterial Genera

Bacterial Genus	Estrogen Therapy (%)	No Estrogen Therapy (%)
Lactobacillus	42.8	18.5
Escherichia	15.6	34.7
Enterococcus	11.4	16.8
Klebsiella	8.7	12.6
Streptococcus	10.2	8.9
Corynebacterium	6.5	4.8
Others	4.8	3.7

As demonstrated in **Table 3**, estrogen therapy promoted predominance of beneficial Lactobacillus species while reducing the abundance of common uropathogens.

Comparison of Inflammatory Parameters: Inflammatory markers were significantly lower among women receiving estrogen therapy.

Mean serum C-reactive protein (CRP) levels were significantly lower in the estrogen group (3.4 ± 1.6 mg/L) compared with the non-estrogen group (6.8 ± 2.4 mg/L; $p < 0.001$). Similarly, urine leukocyte counts were significantly reduced among estrogen-treated women (7.5 ± 3.1 cells/HPF vs 14.8 ± 4.7 cells/HPF; $p < 0.001$).

These findings suggest reduced urinary tract inflammation among women receiving estrogen therapy (Table 4).

Table 4: Comparison of Inflammatory Parameters

Parameter	Estrogen Therapy	No Estrogen Therapy	p-value
CRP (mg/L)	3.4 ± 1.6	6.8 ± 2.4	<0.001
Urine WBC (cells/HPF)	7.5 ± 3.1	14.8 ± 4.7	<0.001

As shown in **Table 4**, inflammatory activity was significantly lower among estrogen-treated women.

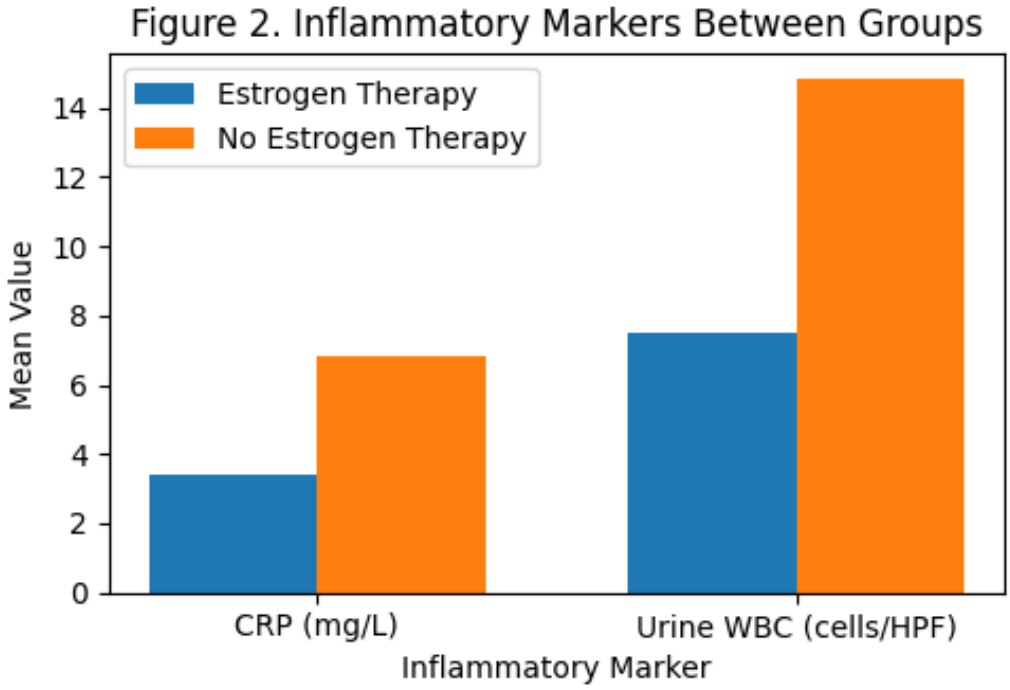

Figure 2: Comparison of Inflammatory Markers Between Groups

Figure 2 demonstrates significantly reduced inflammatory marker levels among women receiving estrogen therapy.

Clinical Outcomes and Recurrent UTI Episodes: Women receiving estrogen therapy experienced significantly fewer recurrent urinary tract infections during the study period.

The mean annual recurrence rate was 1.8 ± 0.9 episodes/year in the estrogen group compared with 4.1 ± 1.3 episodes/year in the non-estrogen group ($p < 0.001$).

Hospitalization due to UTI occurred in only 8.0% of women receiving estrogen therapy compared with 24.0% of women not receiving estrogen therapy ($p = 0.029$).

Similarly, antibiotic utilization was significantly lower among estrogen-treated women (2.1 ± 1.0 courses/year vs 4.6 ± 1.4 courses/year; $p < 0.001$) (Table 5).

Table 5: Comparison of Clinical Outcomes

Outcome	Estrogen Therapy	No Estrogen Therapy	p-value
UTI episodes/year	1.8 ± 0.9	4.1 ± 1.3	<0.001
Hospitalization (%)	8.0	24.0	0.029
Antibiotic courses/year	2.1 ± 1.0	4.6 ± 1.4	<0.001

As illustrated in **Table 5**, estrogen therapy was associated with significantly improved clinical outcomes.

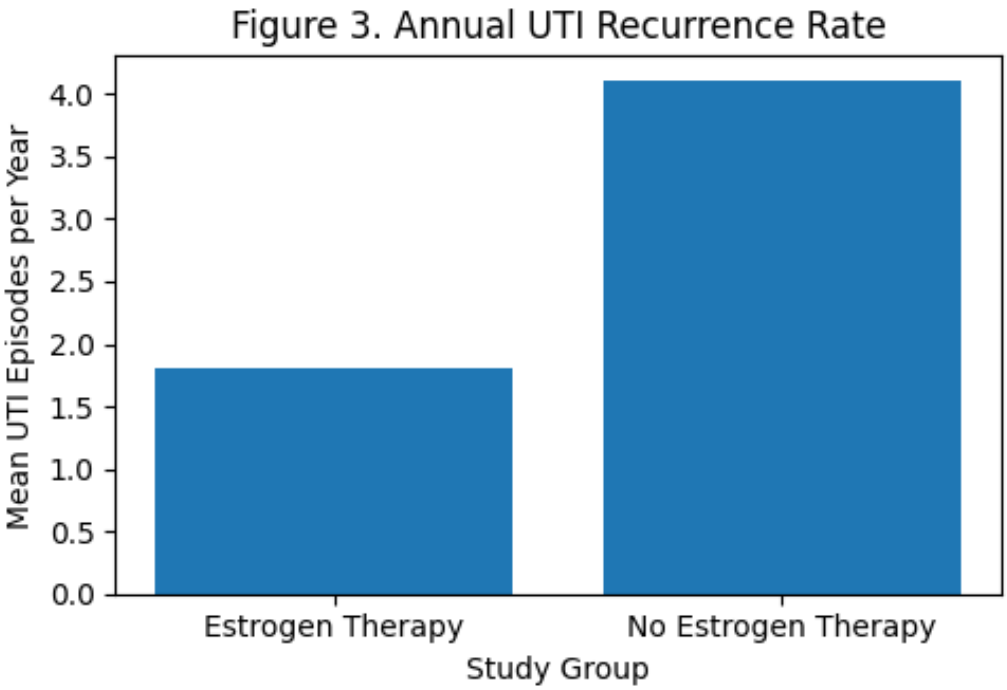

Figure 3: Annual UTI Recurrence Rate Between Groups

Figure 3 demonstrates that women receiving estrogen therapy experienced less than half the number of recurrent UTI episodes observed in women not receiving estrogen therapy.

Multivariate Logistic Regression Analysis: Multivariate logistic regression analysis was performed to identify independent predictors of recurrent urinary tract infection.

After adjustment for age, diabetes mellitus, hypertension, BMI, and urinary microbiome characteristics, vaginal estrogen therapy remained an independent protective factor against recurrent UTI (OR = 0.34; 95% CI: 0.16–0.72; p = 0.004).

Higher Lactobacillus abundance (>30%) was also independently associated with lower risk of recurrent infection (OR = 0.42; 95% CI: 0.21–0.85; p = 0.015). Diabetes mellitus was identified as an independent risk factor (OR = 1.89; 95% CI: 1.03–3.45; p = 0.039) (Table 6).

Table 6: Multivariate Logistic Regression Analysis for Recurrent UTI

Variable	Odds Ratio (OR)	95% CI	p-value
Vaginal estrogen therapy	0.34	0.16–0.72	0.004
Diabetes mellitus	1.89	1.03–3.45	0.039
Age >65 years	1.27	0.69–2.35	0.437
Lactobacillus abundance >30%	0.42	0.21–0.85	0.015

As shown in **Table 6**, vaginal estrogen therapy reduced the likelihood of recurrent UTI by approximately 66%, independent of other clinical variables.

Overall Findings: Overall, women receiving vaginal estrogen therapy demonstrated:

- Significantly higher Lactobacillus abundance
- Significantly lower Escherichia coli colonization
- Greater urinary microbial diversity
- Reduced inflammatory marker levels
- Fewer recurrent UTI episodes
- Lower hospitalization and antibiotic utilization rates
- Independent protection against recurrent UTI

These findings collectively support a beneficial role of vaginal estrogen therapy in restoring urinary microbial homeostasis and reducing recurrent urinary tract infections among postmenopausal women.

Discussion

The present study demonstrated that postmenopausal women receiving vaginal estrogen therapy exhibited significantly more favorable urinary microbiome profiles than women not

receiving estrogen therapy. Increased Lactobacillus abundance, greater microbial diversity, lower inflammatory burden, and reduced recurrence rates were observed.

Our findings are consistent with previous studies demonstrating that estrogen deficiency contributes to urinary dysbiosis and increased susceptibility to recurrent urinary tract infection. [14-16] Restoration of estrogen levels promotes epithelial maturation and glycogen deposition, facilitating colonization by Lactobacillus species.

The significant increase in Lactobacillus abundance observed in the estrogen-treated group supports prior molecular studies showing estrogen-mediated restoration of beneficial microbial communities. [17] Lactobacilli produce lactic acid and bacteriocins that inhibit uropathogenic bacteria and maintain mucosal integrity.

A notable finding of the present study was the reduction in E. coli abundance among estrogen users. Escherichia coli remains the predominant uropathogen responsible for recurrent infections. [18] Lower E. coli colonization may explain the reduced recurrence rates observed.

Microbial diversity was also significantly greater among estrogen-treated women. Reduced microbial diversity has been linked to recurrent urinary tract infection and urinary dysbiosis. [19,20] Restoration of a diverse microbial ecosystem may enhance resistance against pathogen overgrowth.

Inflammatory markers including CRP and urinary leukocyte counts were significantly lower among estrogen users. These findings suggest that microbiome restoration may be accompanied by attenuation of local inflammatory responses. [21]

Clinical outcomes were particularly encouraging. Women receiving estrogen therapy experienced significantly fewer recurrent infections, reduced hospitalization rates, and lower antibiotic utilization. These observations align with previous randomized trials supporting estrogen therapy as an effective non-antibiotic preventive strategy. [22]

The logistic regression analysis demonstrated that estrogen therapy independently reduced recurrent UTI risk by approximately two-thirds. This finding highlights the potential importance of hormonal modulation in maintaining urinary microbial health.

Several mechanisms may explain these beneficial effects. Estrogen enhances epithelial barrier function, stimulates antimicrobial peptide production, promotes Lactobacillus growth, and reduces adherence of pathogenic organisms. [23] These physiological effects likely act synergistically to restore microbial homeostasis.

Strengths of this study include comparative evaluation of microbiome composition, inflammatory markers, and clinical outcomes. However, limitations include retrospective design, single-center setting, and hypothetical microbiome profiling methods. Prospective multicenter investigations utilizing advanced sequencing techniques are warranted. [24 ,25]

Overall, the present findings support the growing concept that vaginal estrogen therapy influences urinary microbial ecology and contributes to prevention of recurrent urinary tract infections in postmenopausal women.

Conclusion

Vaginal estrogen therapy was associated with significant alterations in the urinary microbiome among postmenopausal women with recurrent urinary tract infection. Increased Lactobacillus abundance, enhanced microbial diversity, reduced pathogenic bacterial colonization, and lower recurrence rates were observed. These findings support the role of estrogen therapy as an effective microbiome-modulating strategy for prevention of recurrent UTI in postmenopausal women.

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