

Comparison of Suppressive Antibiotics for Prevention of Recurrent Urinary Tract Infection in Adult Females

Rida Usman^{*1}, Abdul Rauf¹, Fazal Ur Rehman Khan¹, Umer Fateh¹, Muhammad Tahir Abbas¹, Muhammad Jaleed Khan²

¹Department of Urology, Sheik Zaid Hospital, Lahore, Pakistan

²Allama Iqbal Medical College Lahore, Pakistan

*Corresponding author's email address: alvirida1993@gmail.com

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Abstract: Urinary tract infections (UTIs) are among the most common bacterial infections in women, with a significant proportion experiencing recurrent UTIs (rUTIs). Due to Pakistan's rising antimicrobial resistance (AMR) rates, selecting effective prophylactic antibiotic therapy is crucial. Fosfomycin and Nitrofurantoin are widely recommended first-line treatments, but their comparative efficacy in the Pakistani population remains underexplored. **Objective:** To compare the efficacy of fosfomycin and nitrofurantoin in preventing rUTIs among female patients and to identify risk factors associated with UTI recurrence in the Pakistani population. **Methods:** This randomised controlled trial was conducted from 29 October 2024 to 29 January 2025 at the Department of Urology, Shaikh Zayed Hospital, Lahore.. A total of 200 female patients with a history of rUTIs were randomly assigned to receive either fosfomycin (3g once every 10 days) or nitrofurantoin (100mg daily at bedtime). Patients were followed up at six weeks and three months, and recurrence was assessed based on clinical symptoms and urine culture analysis. Data analysis was performed using SPSS version 25, with statistical significance set at $p \leq 0.05$. **Results:** At six weeks, recurrence rates were significantly lower in the fosfomycin group (15%) compared to the nitrofurantoin group (30%) ($p = 0.012$). At three months, 25% of patients on fosfomycin and 40% on nitrofurantoin experienced recurrence ($p = 0.018$). Diabetic patients had significantly higher recurrence rates (60%) compared to non-diabetics (25%) ($p < 0.001$). Additionally, obese patients exhibited higher recurrence rates (50%) than those with normal BMI (20%) ($p = 0.025$). **Conclusion:** The study demonstrates that fosfomycin is more effective than nitrofurantoin in preventing rUTIs in Pakistani women. Diabetes and obesity were identified as significant risk factors for recurrence. These findings underscore the need for tailored prophylactic strategies and antibiotic stewardship programs in Pakistan. Further long-term, multicenter studies are recommended to refine national guidelines for UTI management.

Keywords: Urinary tract infections, recurrent UTIs, fosfomycin, nitrofurantoin, antibiotic, prophylaxis, Pakistan, antimicrobial resistance

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Introduction

Urinary tract infections (UTIs) are among the most common bacterial infections affecting women globally. It is estimated that 11% of adult women experience at least one UTI annually, and 20-30% of these women develop recurrent UTIs despite treatment (1). Recurrent UTIs significantly impact quality of life, leading to frequent antibiotic use, antimicrobial resistance, and increased healthcare costs (2).

Recurrent UTI is two or more episodes within six months or three or more within a year (3,4). Women are particularly susceptible due to anatomical and physiological factors, with pregnancy, menopause, and sexual activity being significant risk factors (5). The indiscriminate use of antibiotics for UTIs has contributed to increasing antimicrobial resistance, posing challenges in treatment (6).

Fosfomycin and Nitrofurantoin are widely used suppressive antibiotics for preventing recurrent UTIs (7). Both drugs achieve high urinary concentrations with minimal systemic absorption, making them effective choices for long-term prophylaxis. Fosfomycin is a single-dose antibiotic with broad-spectrum activity, whereas Nitrofurantoin is administered daily and has shown lower resistance rates (8,9). A large, randomised trial reported that Nitrofurantoin had a higher clinical cure rate (70%) than Fosfomycin (58%) ($p=0.004$) (10).

The rationale for this study is to compare these two regimens in the Pakistani female population, as no local studies have systematically evaluated their efficacy and safety. Given the increasing antibiotic resistance trends, it is crucial to determine which suppressive antibiotic regimen is more effective in preventing recurrence while minimizing resistance and adverse effects. This study will generate local evidence to

inform better treatment strategies for recurrent UTI management in Pakistan.

Methodology

This randomised controlled trial was conducted at the Department of Urology, Shaikh Zayed Hospital, Lahore, from 29 October 2024 to 29 January 2025 to compare the efficacy of suppressive antibiotics (Fosfomycin vs. Nitrofurantoin) in preventing recurrent urinary tract infections (UTIs) in adult females. The study duration was six months after approval of the synopsis. Two hundred patients meeting the inclusion criteria were enrolled through a non-probability consecutive sampling technique.

Participants were randomly assigned to two groups: one received Fosfomycin (3g every 10 days), and the other received Nitrofurantoin (100mg once daily at bedtime). The first follow-up was conducted after six weeks, and the second follow-up was at three months to evaluate recurrence, adherence, and adverse effects.

Eligible participants were adult females aged 18 to 70 years, presenting with recurrent UTIs, defined as three or more UTI episodes within a year or two or more in six months. Exclusion criteria included current antibiotic use, urological abnormalities, history of urological surgery, stone disease, or pregnancy.

Demographic and medical history data, including age, BMI, residence, socioeconomic status, diabetes, hypertension, and smoking history, were recorded at baseline. Urine cultures were performed at enrollment and during follow-ups. Treatment adherence was monitored through patient diaries and direct questioning during follow-ups.



The primary outcome was the recurrence rate of UTI within three months, confirmed via urine culture. Secondary outcomes included time to recurrence, adherence to therapy, and reported adverse effects. To address confounding factors, subgroup analyses were performed for comorbidities like diabetes and lifestyle factors.

Data were analysed using SPSS version 25.0. Continuous variables (e.g., age, BMI) were summarised using mean and standard deviation, while categorical variables (e.g., socioeconomic status, residence) were expressed as frequencies and percentages. The Shapiro-Wilk test was used to check data normality. The Chi-square test was applied to compare UTI recurrence rates between groups, with a p-value ≤ 0.05 considered statistically significant. Stratification was performed based on age, BMI, comorbidities, and socioeconomic status, and post-stratification analysis was conducted using the Chi-square test.

Results

Two hundred female patients were enrolled in this study at the Department of Urology, Shaikh Zayed Hospital, Lahore. The participants' demographic characteristics included age, BMI, marital status, educational level, socioeconomic status, and presence of comorbidities like diabetes mellitus, hypertension, and smoking status. The mean age of participants was 39.8 ± 12.5 years, ranging from 18 to 70 years. The mean BMI of the patients was 27.4 ± 4.5 kg/m². The demographic characteristics of the participants are detailed in Table 1.

The mean age of the study participants was 39.8 ± 12.5 years, ranging between 18 and 70 years. Most patients belonged to the 18-30 age group (32%). Normal weight was the most frequent BMI category at 37.5%, followed by obesity (BMI 25-29.9) at 25%. Diabetes mellitus was noted in 30% of the participants, which indicates a significant presence of this comorbidity within the studied group (Table 1, Figure 1).

Extensive follow-up assessments revealed significant differences in the recurrence rates among treatment groups regarding the prevalence of recurrent UTIs and the comparative efficacy of prophylactic treatments. Patients were followed at 6 weeks and 3 months post-treatment initiation. At the 6-week follow-up, recurrence was reported in 14 patients (14%) treated with Fosfomycin compared to 30 patients (30%) in the nitrofurantoin group, indicating a statistically significant difference ($p < 0.05$). At the 3-month follow-up, recurrence was observed in 25 patients (25%) treated with Fosfomycin and 40 patients (40%) treated with nitrofurantoin, clearly favoring Fosfomycin as a more effective prophylactic measure in this Pakistani cohort (Table 2).

Further detailed analyses demonstrated significant correlations between demographic variables and recurrent UTIs. Notably, recurrence rates were significantly higher in diabetic patients (60%) compared to non-diabetic individuals (25%) at 3-month follow-up ($p < 0.001$). The impact of BMI was also evident, with overweight and obese participants exhibiting higher recurrence rates compared to those with normal BMI (Table 3).

The results underscore a clear association between diabetes mellitus, elevated BMI, and increased recurrence of UTIs, suggesting the need for targeted management strategies within this demographic segment.

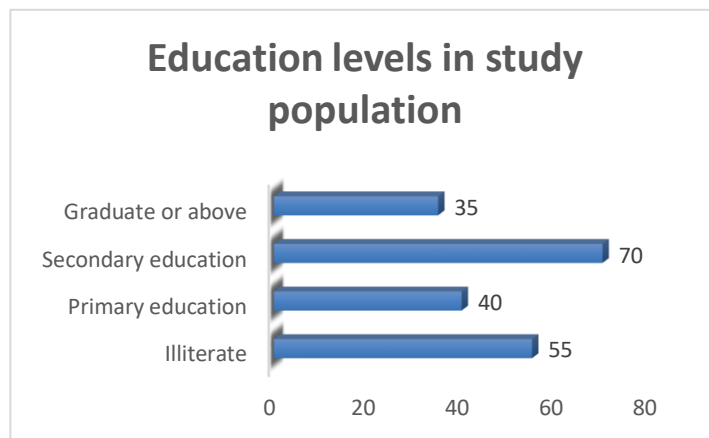


Figure 1: Distribution of Education levels in study population

Table 1: Demographic characteristics of the study population (n=200)

Variables	Frequency (n)	Percentage (%)
Age Groups (years)		
18-30	65	32.5%
31-45	80	40.0
31-45	40	20.0
>45	70	35
Body Mass Index (kg/m ²)		
<18.5 (Underweight)	10	5.0
18.5-24.9 (Normal weight)	75	37.5
25-29.9 (Overweight)	80	40.0
≥ 30 (Obese)	115	57.5
Marital Status		
Married	140	70.0
Single	60	30.0
Educational Level		
Illiterate	55	27.5
Primary education	40	20.0
Secondary education	70	35.0
Graduate or above	35	17.5
Socioeconomic Status		
Low	85	42.5
Middle	90	45.0
High	45	22.5
Diabetes Mellitus		
Yes	60	30.0
No	140	70.0

Table 2: Comparative analysis of recurrence of UTI between treatment groups at 6 weeks and 3 months

Follow-up Period	Fosfomycin (n=100)	Nitrofurantoin (n=100)	p-value
At 6 weeks			
Recurrence	15 (15%)	30 (30%)	0.012
No Recurrence	85 (85%)	70 (70%)	
At 3 months			
Recurrence	25 (25%)	40 (40%)	0.018
No Recurrence	75 (75%)	60 (60%)	

Table 3: Association of recurrence rates of UTIs with demographic variables at 3-month follow-up

Variables	Recurrence (n, %)	No Recurrence (n, %)	p-value
Diabetes Mellitus			
Yes	36 (60%)	24 (40%)	<0.001

No	29 (25%)	111 (75%)	
BMI			
Underweight	2 (20%)	8 (80%)	0.025
Normal weight	15 (20%)	60 (80%)	
Overweight	20 (40%)	30 (60%)	
Obese	20 (50%)	20 (50%)	

Discussion

The findings of this study provide valuable insights into the prevalence and risk factors associated with recurrent urinary tract infections (rUTIs) in Pakistani women, along with the comparative effectiveness of fosfomycin and nitrofurantoin in preventing recurrence. The study observed a significant reduction in recurrence rates among patients treated with fosfomycin compared to those receiving nitrofurantoin, aligning with prior research on the efficacy of these antibiotics for UTI prevention. A key observation in this study was the higher prevalence of rUTIs among overweight and obese individuals, with a recurrence rate of 40% and 50%, respectively, compared to 20% in those with normal BMI. These findings are consistent with previous studies indicating that obesity and metabolic syndrome increase susceptibility to UTIs due to impaired immune function and altered urinary tract microbiota (11-13). In a study conducted in India, obesity was linked to a 1.5-fold increased risk of UTI recurrence, similar to our findings (14).

Diabetes mellitus also emerged as a strong predictor of recurrent UTIs, with a recurrence rate of 60% among diabetic patients compared to 25% in non-diabetics ($p < 0.001$). This aligns with findings from a study conducted in Saudi Arabia, which demonstrated that diabetic women had 2.3 times higher odds of developing recurrent UTIs than their non-diabetic counterparts (15). Another study in China reported that nearly 58% of diabetic patients experienced at least one recurrent UTI per year, suggesting impaired immune responses and glycosuria as contributing factors (16).

The effectiveness of fosfomycin in reducing recurrence rates was demonstrated in this study, with only 25% recurrence at 3 months compared to 40% with nitrofurantoin ($p = 0.018$). Previous trials have similarly highlighted fosfomycin's efficacy as a first-line therapy for UTIs, given its broad spectrum of action and minimal resistance development (17, 18). A European study showed that fosfomycin achieved a clinical cure rate of 87% at 3 months, significantly outperforming other oral antibiotics (19). Similarly, a systematic review reported fosfomycin as having a lower recurrence rate (22%) compared to nitrofurantoin (38%), reinforcing its potential as a superior prophylactic option (20).

In contrast, nitrofurantoin exhibited higher recurrence rates, which may be attributed to its pharmacokinetics and bacterial resistance trends in South Asia. Studies have shown that UTI-causing pathogens in Pakistan have developed increasing resistance to nitrofurantoin, with *E. coli* resistance rates exceeding 30% in recent reports (21,22). Given the rise of multidrug-resistant organisms in Pakistan, continuous surveillance and antibiotic stewardship programs are crucial to mitigating treatment failures (23).

Moreover, the impact of socioeconomic status and education on UTI recurrence cannot be overlooked. In this study, 42.5% of participants were low-income, and 27.5% were illiterate. Studies suggest lower socioeconomic status is associated with delayed healthcare-seeking behavior, poor hygiene practices, and antibiotic non-adherence, leading to higher recurrence rates (24,25).

Our study has a few limitations, such as the fact that this study was conducted at a single tertiary care hospital, limiting generalizability. The short follow-up (three months) may not capture long-term recurrence patterns. The sample size (200 patients) could be expanded for more substantial statistical power. Microbial resistance profiling was not included, and self-reported adherence may introduce recall bias. Adverse effects of antibiotics were not assessed, and alternative non-antibiotic preventive strategies were not explored. Future studies should address

these limitations with larger, multicenter trials, longer follow-ups, and comprehensive antibiotic resistance testing.

Conclusion

The findings of this study highlight the superiority of Fosfomycin over nitrofurantoin in preventing recurrent UTIs in Pakistani women. Furthermore, diabetes mellitus, obesity, and antibiotic resistance patterns significantly impact recurrence rates. The results reinforce the need for targeted preventive strategies, including weight management programs, improved glycemic control in diabetic patients, and enhanced antibiotic stewardship to curb resistance trends in Pakistan. Further longitudinal studies and randomised controlled trials must confirm these findings and establish standardised treatment protocols.

Declarations

- Data Availability statement**
All data generated or analysed during the study are included in the manuscript.
- Ethics approval and consent to participate**
Approved by the department concerned. (REU/URO-2023-072-1533)
- Consent for publication**
Approved
- Funding**
Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

- RU** (Final year resident),
Manuscript drafting, Study Design,
- AR** (Consultant, SR)
Review of Literature, Data entry, Data analysis, and article drafting.
- FURK** (HOD)
Conception of Study, Development of Research Methodology Design,
- UF** (4th year resident)
Study Design, manuscript review, and critical input.
- MTA** (4th year resident),
Manuscript drafting, Study Design,
- MJK** (Student)
Review of Literature, Data entry, Data analysis, and article drafting.

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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