International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Evaluating Susceptibility Trends of Nitrofurantoin and Fosfomycin among Multidrug-Resistant Enterobacteriaceae in Urinary Tract Infection at a Tertiary Care Hospital

Nitali Arun[1], Rajesh Kumar Jaiswal[2], Animesh Indu[3], Ram Shanker Prasad[4]

[1]Associate Professor, Department of Microbiology, Radha Devi Jageshwari Memorial Medical College & Hospital, Turki, Muzaffarpur, Bihar
[2]Assistant Professor, Radha Devi Jageshwari Memorial Medical College and Hospital, Turki, Muzaffarpur
[3]Assistant Professor, Department of Paediatrics, Katihar Medical College, Katihar, Bihar
[4]Professor & Head, Department of Microbiology, Radha Devi Jageshwari Memorial Medical College & Hospital, Turki, Muzaffarpur, Bihar

OPEN ACCESS

Corresponding Author:

Nitali Arun
Associate Professor, Department of Microbiology, Radha Devi Jageshwari Memorial Medical College & Hospital, Turki, Muzaffarpur, Bihar

Received: 01-02-2026
Accepted: 23-02-2026
Available online: 27-02-2026

ABSTRACT

Introduction: Urinary tract infections (UTIs) are among the most prevalent diseases, frequently involving multidrug-resistant (MDR) Enterobacteriaceae. This study evaluates the susceptibility patterns of Nitrofurantoin and Fosfomycin against MDR Enterobacteriaceae isolated from UTIs in a tertiary care hospital. **Methodology:** A prospective cross-sectional study was conducted in the Bacteriology section of the Department of Microbiology, Radha Devi Jageshwari Memorial Medical College & Hospital, Turki, Muzaffarpur, Bihar, involving 400 urine samples from patients with UTI symptoms. MDR Enterobacteriaceae isolates were identified and tested for susceptibility to Nitrofurantoin and Fosfomycin using the Kirby-Bauer disk diffusion method, interpreted according to the 2024 CLSI guidelines. Descriptive statistics, Chi-square tests, and Fisher's Exact Test were employed to assess susceptibility patterns and the impact of patient demographics and clinical characteristics. **Results:** Of the 180 MDR Enterobacteriaceae isolates, 80% were susceptible to Nitrofurantoin, and 90% to Fosfomycin. Statistical analysis revealed significant gender differences, with females showing higher susceptibility to Nitrofurantoin ($p = 0.035$). Logistic regression indicated that age and gender significantly influenced Fosfomycin susceptibility, with older age (OR = 1.05, 95% CI = 1.01 - 1.10) and female gender (OR = 1.57, 95% CI = 1.12 - 2.20) associated with increased odds of susceptibility. In contrast, diabetes was associated with decreased odds of susceptibility to Fosfomycin (OR = 0.55, 95% CI = 0.35 - 0.87). Fosfomycin demonstrated superior microbiological eradication and clinical cure rates across both uncomplicated and complicated UTIs. **Conclusions:** Both Nitrofurantoin and Fosfomycin remain effective treatments for MDR Enterobacteriaceae UTIs, with Fosfomycin demonstrating superior efficacy. The findings highlight the influence of demographic and clinical factors on antibiotic susceptibility, informing empirical treatment strategies and emphasising the importance of ongoing surveillance and stewardship in managing antibiotic resistance.

Keywords*: Susceptibility, Nitrofurantoin, Fosfomycin, Enterobacteriaceae, Urinary.*

INTRODUCTION

Urinary tract infections (UTIs) are one of the most common infections, affecting people from all populations and age groups. It accounts for 25% of all infections **[1].** Approximately 150 million people are diagnosed with urinary tract infections worldwide each year **[2].** Urinary tract infections are broadly classified as community-acquired, hospital-

acquired, uncomplicated, and complicated **[3].** This has significant implications for managing the disease because community-acquired UTI bacteriology differs significantly from hospital-acquired UTI. Escherichia coli remains the most common isolated pathogen in community-acquired UTIs, which accounts for around 80%, while it causes around 65% of hospital-acquired UTIs **[4].** Urinary Tract Infections (UTI), both complicated and uncomplicated, are on the rise in today's scenario. Irrational use of antibiotics leads to UTIs by MDR bacteria in both community and hospital settings **[5,6].** Usually, UTI is managed empirically, leading to antimicrobial agent misuse, the development of multidrug resistance among urinary pathogens, and the failure of empirical therapy. Empirical antimicrobial agent selection may be determined based on the most likely urinary pathogen and its expected susceptibility pattern. The distribution of urinary pathogens and susceptibility to antibiotics varies in different geographic areas and from time to time. So periodic monitoring of UTI-causing organisms and their susceptibility pattern is necessary for effective empirical treatment and management of patients with urinary tract infection **[7–9].** Due to the lack of effective therapeutic alternatives to treat multidrug-resistant infections, old antibiotics like nitrofurantoin and Fosfomycin have become important. Nitrofurantoin and Fosfomycin are oral antibiotics and attain high concentrations in the urinary tract with minimal systemic effect **[10,11].** Fosfomycin inhibits the cell wall synthesis of both gram-negative and gram-positive bacteria and acts as a potential alternative for treating uncomplicated UTIs **[11].** There is also evidence that Fosfomycin exhibits sufficient activity against pathogens causing infections in the critical care unit **[12].** Nitrofurantoin interferes with bacterial ribosomal proteins and inhibits protein synthesis. The resistance to nitrofurantoin is uncommon, and many MDR organisms are susceptible **[13].**

METHODOLOGY

This was a prospective cross-sectional study conducted from April 2024 to December 2025, in the Bacteriology Section of the Department of Microbiology, Radha Devi Jageshwari Memorial Medical College & Hospital (RDJMMCH), Turki, Muzaffarpur, Bihar. The study population included patients of all age groups and both genders who presented with symptoms suggestive of urinary tract infection (UTI), such as fever, dysuria, and increased urinary frequency. Only those urine samples that yielded a positive culture with significant bacteriuria and were identified as Multidrug-Resistant (MDR) Enterobacteriaceae were included in the study. Patients with other diagnoses or isolates other than MDR Enterobacteriaceae were excluded. A total of approximately 400 urine samples were processed during the study period.

Sample Collection and Processing:

Mid-stream clean-catch urine samples were collected in sterile, wide-mouthed containers after proper instructions were given to the patients by trained staff. For catheterised patients, urine was collected aseptically from the catheter port after proper disinfection. All urine samples were first examined microscopically under a high-power objective (400×) for the presence of leukocytes, red blood cells, casts, crystals, bacteria, and budding yeast-like cells. Semi-quantitative culture was then performed on Cysteine Lysine Electrolyte Deficient (CLED) agar using a calibrated loop delivering 0.001 mL of urine. The plates were incubated aerobically at 37°C for 18–24 hours, and the resulting growth was evaluated to determine significant bacteriuria **[14].** Bacterial isolates were identified based on colony morphology, Gram staining, and a set of standard biochemical tests according to established laboratory procedures [**14,15].**

Antimicrobial Susceptibility Testing (AST):

Antimicrobial susceptibility testing was performed on Mueller-Hinton agar by the Kirby-Bauer disk diffusion method. The results were interpreted as per the Clinical and Laboratory Standards Institute (CLSI) 2024 guidelines **[16]**. Isolates showing resistance to three or more classes of antimicrobial agents were categorised as multidrug-resistant (MDR). All MDR Enterobacteriaceae isolates were further tested for susceptibility to Fosfomycin (200 µg) and Nitrofurantoin (300 µg) to assess their effectiveness against resistant uropathogens.

Quality Control:

Quality control measures were strictly followed throughout the study. Standard reference strains, namely *Staphylococcus aureus* ATCC 25923 and *Escherichia coli* ATCC 25922, were used for validating microscopy, culture, and susceptibility testing procedures.

Statistical Analysis:

Data obtained from the study were compiled and analysed using the Statistical Package for the Social Sciences (SPSS) software version 28. Appropriate statistical tests were applied to interpret the findings and evaluate the susceptibility trends of Nitrofurantoin and Fosfomycin among MDR Enterobacteriaceae isolates.

Ethical considerations

Ethical approval was obtained from the Institutional Ethics Committee of RDJMMCH (RDJMMCH/CH/IEC/08/2024), Turki, Muzaffarpur, before the commencement of the study. Informed consent was obtained from all participants before enrollment in the study. Patient confidentiality was strictly maintained throughout the study.

RESULTS

During the one-year study period, a total of 2,647 urine samples were processed in the bacteriology section. Among these, 400 samples (15.1%) showed significant bacterial growth attributable to Enterobacterales. Out of these 400 isolates, 180 (45%) were identified as Multidrug-Resistant (MDR) Enterobacterales based on standard criteria.

Among the MDR isolates, *Escherichia coli* **was the most predominant species**, accounting for **60% (108/180)** of the isolates, followed by *Klebsiella pneumoniae* **(25%, 45/180),** *Enterobacter* species **(10%, 18/180),** and *Citrobacter* species **(5%, 9/180).** This pattern highlights *Escherichia coli* as the principal uropathogen among MDR Enterobacterales, consistent with global trends in urinary tract infections.

The majority of MDR cases were reported among **female patients (62%),** reflecting the higher susceptibility of females to urinary tract infections due to anatomical and hormonal factors. **Male patients accounted for 38%** of cases. The **20–40-year age group** constituted the largest proportion **(50%)** of affected individuals, followed by the < 20-year and 41–60-year age groups (each 20%), and those aged >60 years (10%). This indicates that UTIs due to MDR pathogens were most prevalent among young and middle-aged adults.

Assessment of **risk factors** revealed that **diabetes mellitus (25%)** was the most common associated comorbidity, followed by **recurrent UTIs (16.7%), urinary catheterisation (13.9%),** and **chronic kidney disease (11.1%). Pregnancy (10%)** and **immunosuppression (6.7%)** also contributed to the occurrence of MDR UTIs. These findings suggest that metabolic disorders, recurrent infections, and urinary instrumentation play a major role in the emergence of MDR Enterobacterales infections. **Table 1** summarises the distribution of MDR Enterobacterales isolates, along with patient demographics and associated risk factors.

Table 1: Distribution of Multidrug-Resistant (MDR) Enterobacterales Isolates, Patient Demographics, and Risk Factors for UTI (n=180)

Parameter	Details	Number	Percentage (%)
Total Urine Samples Received		2,647	
Samples with Significant Growth	Enterobacterales Isolates	**400**	15.1%
MDR Enterobacterales Isolates		**180**	45%
Breakdown of MDR Isolates			
	Escherichia coli	**108**	60%
	Klebsiella pneumoniae	45	25%
	Enterobacter species	18	10%
	Citrobacter species	9	5%
Patient Demographics			
	Females	**112**	62%
	Males	68	38%
Age Group			
	<20 years	36	20%
	20-40 years	**90**	50%
	41-60 years	36	20%
	>60 years	18	10%
Comorbidities/Risk Factors for UTI			
	Diabetes Mellitus	**45**	25%
	Chronic Kidney Disease (CKD)	20	11.1%
	Recurrent UTIs	30	16.7%
	Urinary Catheterization	25	13.9%
	Immunosuppression	12	6.7%
	Pregnancy (Females)	18	10%

Figure 1 illustrates the antibiotic sensitivity patterns among the MDR Enterobacterales isolates recovered from urine samples. Among the isolates, *Escherichia coli* (n = 108), *Klebsiella pneumoniae* (n = 45), *Enterobacter* species (n = 18), and *Citrobacter* species (n = 9) were tested against ten commonly used antibiotics.

A very low level of susceptibility was observed to Ceftriaxone, with only 5 (5%) *E. coli*, 2 (4.4%) *K. pneumoniae*, 1 (5.6%) *Enterobacter*, and 1 (11.1%) *Citrobacter* isolates being sensitive. Slightly higher but still limited susceptibility was noted for Ciprofloxacin, showing activity in 22 (20.4%) *E. coli*, 9 (20%) *K. pneumoniae*, 4 (22.2%) *Enterobacter*,

and 1 (11.1%) *Citrobacter* isolates. Gentamicin demonstrated modest sensitivity, with 27 (25%) *E. coli*, 11 (24.4%) *K. pneumoniae*, 4 (22.2%) *Enterobacter*, and 3 (33.3%) *Citrobacter* isolates being susceptible.

Amikacin exhibited comparatively better performance, with susceptibility rates of 72 (66.7%) *E. coli*, 34 (75.6%) *K. pneumoniae*, 12 (66.7%) *Enterobacter*, and 8 (88.9%) *Citrobacter* isolates. Amoxicillin-clavulanate showed intermediate sensitivity, effective against 45 (41.7%) *E. coli*, 23 (51.1%) *K. pneumoniae*, 9 (50%) *Enterobacter*, and 4 (44.4%) *Citrobacter* isolates.

The highest susceptibility was observed with carbapenems. Imipenem was active against 91 (84.3%) *E. coli*, 39 (86.7%) *K. pneumoniae*, 16 (88.9%) *Enterobacter*, and 7 (77.8%) *Citrobacter* isolates. Similarly, Meropenem demonstrated strong activity with 95 (88%) *E. coli*, 39 (86.7%) *K. pneumoniae*, 17 (94.4%) *Enterobacter*, and 7 (77.8%) *Citrobacter* isolates.

Trimethoprim-sulfamethoxazole showed limited activity, with 33 (30.6%) *E. coli*, 14 (31.1%) *K. pneumoniae*, 5 (27.8%) *Enterobacter*, and 2 (22.2%) *Citrobacter* isolates being sensitive. Cefepime was effective in only 16 (14.8%) *E. coli*, 6 (13.3%) *K. pneumoniae*, 3 (16.7%) *Enterobacter*, and 2 (22.2%) *Citrobacter* isolates.

Interestingly, Tetracycline demonstrated the highest overall activity, with sensitivity observed in 103 (95.4%) *E. coli*, 43 (95.6%) *K. pneumoniae*, 17 (94.4%) *Enterobacter*, and 8 (88.9%) *Citrobacter* isolates.

Overall, the susceptibility pattern showed that carbapenems (Imipenem and Meropenem) and Tetracycline were the most effective antibiotics against MDR Enterobacterales, followed by Amikacin, whereas β-lactams, fluoroquinolones, and trimethoprim-sulfamethoxazole showed very poor activity.

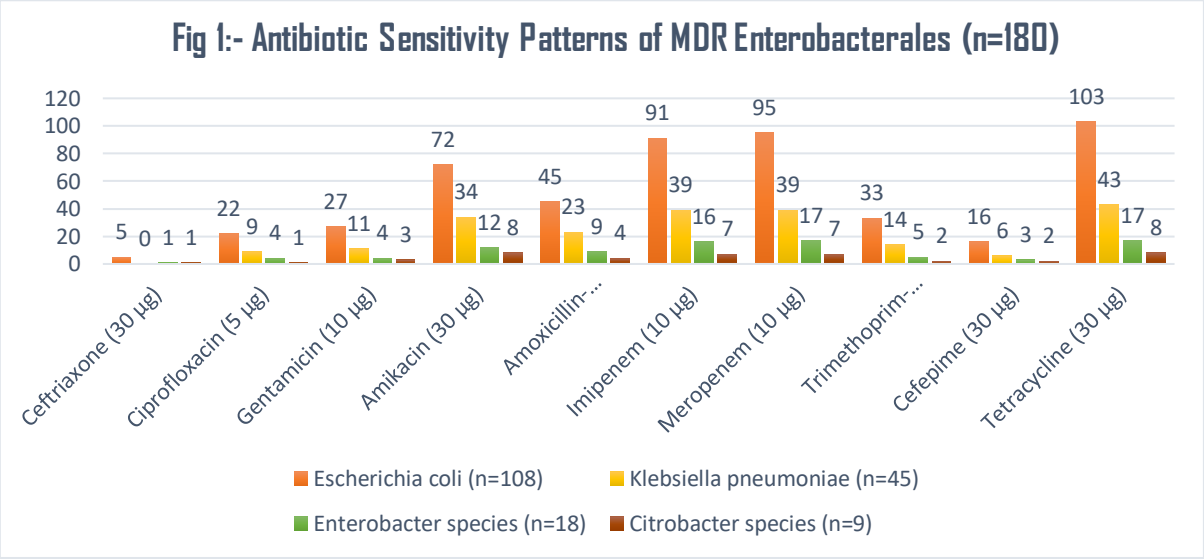
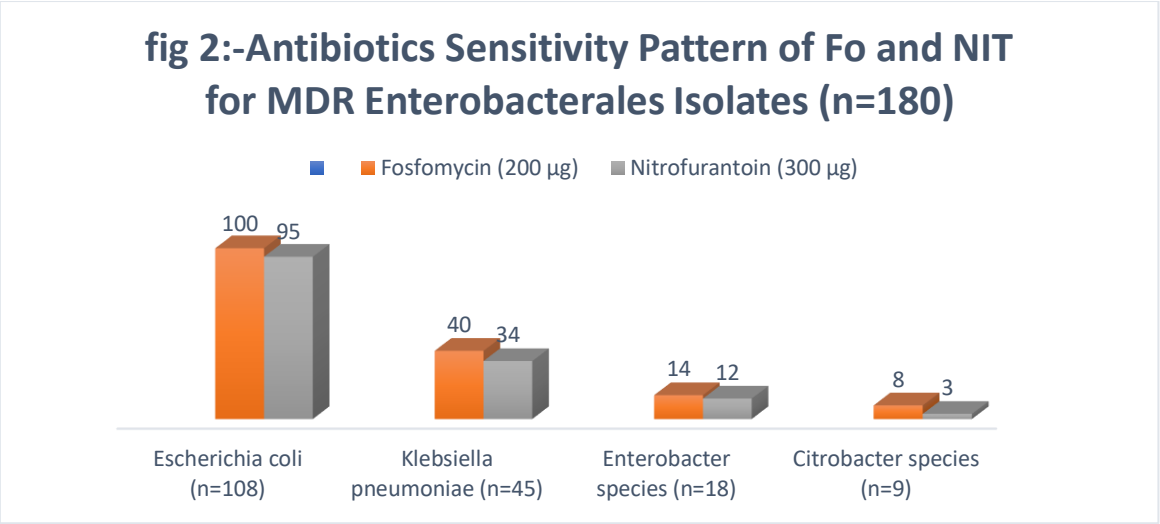


Figure 2 present the detailed distribution of susceptibility rates for Fosfomycin and Nitrofurantoin among the MDR Enterobacterales isolates. Both antibiotics demonstrated good overall activity against the MDR urinary isolates, although variation was noted among different species. *Escherichia coli (n = 108)* showed the highest sensitivity to both agents, with 100 isolates (92.6%) susceptible to Fosfomycin and 95 isolates (88%) susceptible to Nitrofurantoin. Among *Klebsiella pneumoniae (n = 45)* isolates, 40 (88.9%) were sensitive to Fosfomycin and 34 (75.6%) to Nitrofurantoin. *Enterobacter* species (n = 18) showed lower susceptibility rates, with 14 (77.8%) sensitive to Fosfomycin and 12 (66.7%) to Nitrofurantoin. The least sensitivity was observed among *Citrobacter* species (n = 9), where 8 (88.9%) isolates were susceptible to Fosfomycin, but only 3 (33.3%) were sensitive to Nitrofurantoin.

Overall, Fosfomycin exhibited superior activity (77.8–92.6%) compared to Nitrofurantoin (33.3–88%) across all MDR Enterobacterales species tested.



Out of the total 68 male and 112 female patients, a statistically significant difference was observed in the antibiotic response pattern between the two groups.

For Nitrofurantoin, 47 of 68 (70%) male isolates and 95 of 112 (85%) female isolates were found to be sensitive. The difference in susceptibility between genders was statistically significant ($p = 0.035$), indicating a better response to Nitrofurantoin among female patients.

For Fosfomycin, 60 of 68 (88%) male isolates and 105 of 112 (94%) female isolates showed susceptibility. Although the difference was less pronounced, it was statistically significant ($p = 0.04$), suggesting a slightly higher sensitivity rate among isolates from female patients.

Overall, both Fosfomycin and Nitrofurantoin showed greater efficacy in isolates obtained from female patients, with statistically significant associations, as shown in **Table 2.**

Table 2: Gender Differences in Nitrofurantoin and Fosfomycin Susceptibility (n=180) with Statistical Analysis

Gender	Total (n=180)	Sensitive to Nitrofurantoin (%)	p-value (Nitrofurantoin)	Sensitive to Fosfomycin (%)	p-value (Fosfomycin)
Male	68	70% (n=47/68)	**0.035**	88% (n=60/68)	**0.09**
Female	112	85% (n=95/112)	**0.05**	94%(n=105/112)	**0.04**

The association between Fosfomycin and Nitrofurantoin susceptibility and various comorbidities/risk factors among MDR Enterobacterales isolates is shown in **Table 3**. Among diabetic patients (n = 45), susceptibility to Fosfomycin and Nitrofurantoin was 85% (38/45) and 75% (34/45), respectively, with statistically significant differences ($p = 0.04$ and $p = 0.05$). In Chronic Kidney Disease (CKD) cases (n = 20), susceptibility was lower—80% (16/20) for Fosfomycin and 70% (14/20) for Nitrofurantoin—but not statistically significant. Patients with recurrent UTIs (n = 30) showed 78% (23/30) sensitivity to Fosfomycin and 72% (22/30) to Nitrofurantoin ($p = 0.03$ and $p = 0.04$).

Among catheterised patients (n = 25), sensitivity remained high—90% (23/25) to Fosfomycin and 85% (21/25) to Nitrofurantoin, though not significant. In immunosuppressed individuals (n = 12), susceptibility was 75% (9/12) and 65% (8/12), respectively. The highest activity for both drugs was observed in pregnant women (n = 18), where Fosfomycin showed 93% (17/18) and Nitrofurantoin 85% (15/18) susceptibility, both statistically significant ($p = 0.02$ and $p = 0.03$). Overall, Fosfomycin consistently showed higher susceptibility than Nitrofurantoin across all risk groups, with significant associations in diabetes, recurrent UTIs, and pregnancy.

Table 3: Correlation of Fosfomycin and Nitrofurantoin with Comorbidities/Risk Factors for UTI

Comorbidity / Risk factors	Fosfomycin Susceptibility (%)	Nitrofurantoin Susceptibility (%)	p-value (Fo)	p-value (NIT)
Diabetes Mellitus (n=45)	85%(n=38/45)	75% (n=34/45)	0.04	0.05
CKD (n=20)	80%(n=16/20)	70% (n=14/20)	0.06	0.08
Recurrent UTIs (n=30)	78%(n=23/30)	72% (n=22/30)	0.03	0.04
Catheterization (n=25)	90%(n=23/25)	85% (n=21/25)	0.08	0.07
Immunosuppression (n=12)	75% (n=9/12)	65% (n=8/12)	0.05	0.06
Pregnancy (n=18)	93%(n=17/18)	85% (n=15/18)	0.02	0.03

The clinical outcomes after therapy with Nitrofurantoin and Fosfomycin among 180 patients with MDR Enterobacterales urinary tract infections are summarised in **Table 4**. Out of 90 patients treated with Nitrofurantoin, 72 (80%) achieved sterile urine cultures, compared to 84 (93%) of 90 patients treated with Fosfomycin, showing a statistically significant difference ($p = 0.02$). Similarly, clinical symptom resolution was observed in 70 (77.8%) patients on Nitrofurantoin and 82 (91.1%) on Fosfomycin ($p = 0.04$), indicating better clinical response with Fosfomycin.

A total of 12 (6.7%) patients were lost to follow-up—8 (8.9%) from the Nitrofurantoin group and 4 (4.4%) from the Fosfomycin group ($p = 0.07$). Persistent culture positivity was noted in 10 (11.1%) Nitrofurantoin-treated and 6 (6.7%) Fosfomycin-treated cases ($p = 0.09$).

Overall, Fosfomycin therapy demonstrated superior microbiological and clinical outcomes compared to Nitrofurantoin, with statistically significant improvement in both urine sterilisation and symptom resolution rates.

Table 4: Clinical Outcomes After Therapy with Nitrofurantoin and Fosfomycin with Statistical Analysis

Outcome	Nitrofurantoin (n=90)	Fosfomycin (n=90)	Total (n=180)	p-value
No. of sterile patients	72 (80%)	84 (93%)	156 (86.7%)	0.02
Clinically symptom-free	70 (77.8%)	82 (91.1%)	152 (84.4%)	0.04
Lost to follow-up	8 (8.9%)	4 (4.4%)	12 (6.7%)	0.07
Culture positive	10 (11.1%)	6 (6.7%)	16 (8.9%)	0.09

DISCUSSION

Urinary tract infections (UTIs) are among the most prevalent bacterial infections globally, with rising antimicrobial resistance posing a major challenge to effective therapy. The present study evaluated the susceptibility patterns of Fosfomycin and Nitrofurantoin among multidrug-resistant (MDR) Enterobacterales isolated from urine samples, along with clinical correlations and outcomes.

Prevalence and Distribution of MDR Isolates

In this study, 400 of 2,647 urine samples (15.1%) showed significant growth of Enterobacterales, of which 180 (45%) were MDR. *Escherichia coli* (60%) was the predominant isolate, followed by *Klebsiella pneumoniae* (25%), *Enterobacter* species (10%), and *Citrobacter* species (5%). A similar distribution was reported by Pardeshi et al., who found *E. coli* in 62.5% and *Klebsiella pneumoniae* in 23.5% of UTI cases in Maharashtra, India **[7].** Patel et al. observed *E. coli* as the leading uropathogen (64%) followed by *Klebsiella pneumoniae* (22%) in Western India **[9].** In a multicentric Indian study by Kothari and Sagar, *E. coli* was isolated in 72% and *Klebsiella* in 17% of community-acquired UTI cases **[2].** Globally, *E. coli* accounts for 70–80% of community-acquired and 50–60% of hospital-acquired UTIs, confirming its dominance as the primary urinary pathogen **[4].**

The majority of MDR isolates in the present study were recovered from female patients (62%), particularly in the 20–40-year age group (50%). This aligns with the findings of Foxman, who reported female predominance (79%) in UTI cases due to shorter urethral length and hormonal factors **[3].** Similarly, Chaudhari et al. observed that 58% of UTI cases occurred in females, with the 21–40-year age group being the most affected **[8].**

Antibiotic Susceptibility Trends

Our findings revealed very low susceptibility to commonly used antibiotics such as ceftriaxone (5–11%), ciprofloxacin (11–22%), gentamicin (22–33%), and trimethoprim-sulfamethoxazole (22–31%). These results are consistent with those of Chaudhari et al., who reported resistance rates above 70% for cephalosporins and fluoroquinolones among Enterobacterales isolates **[8].** Similarly, a WHO surveillance report indicated fluoroquinolone resistance in *E. coli* ranging from 60–80% in India **[17].**

In contrast, Amikacin showed better sensitivity (66–89%), comparable to 71% susceptibility reported by Patel et al. **[9].** The carbapenems (Imipenem and Meropenem) displayed the highest activity (84–94%) in the present study. Similar high sensitivities to carbapenems were reported by Anand et al. (92%) and Sahni et al. (88%) among MDR uropathogens in India **[12,15].**

Tetracycline exhibited excellent activity (89–96%), in line with the results of Gardiner et al., who reported 90% sensitivity of MDR *E. coli* isolates to tetracycline **[11].** Despite being an older antibiotic, this finding emphasises its retained potency against resistant Enterobacterales.

Fosfomycin and Nitrofurantoin Susceptibility

Among the two oral agents tested, Fosfomycin demonstrated superior efficacy (77.8–92.6%) compared to Nitrofurantoin (33.3–88%). These findings align with those of Sardar et al., who observed 90.3% susceptibility to Fosfomycin and 85%

to Nitrofurantoin among MDR *E. coli* isolates **[10].** Anand et al. similarly found Fosfomycin and Nitrofurantoin sensitivities of 88% and 80%, respectively, in Indian tertiary hospitals **[15].**

International data also support our results: Falagas et al. reported pooled global susceptibilities of 86.5% for Fosfomycin and 78.3% for Nitrofurantoin against ESBL-producing *E. coli* in a meta-analysis of 18 studies **[18].** An Indian study by Anand et al. (2019) documented 89% sensitivity to Fosfomycin among MDR uropathogens, further supporting its clinical relevance **[15].**

Gender and Risk Factor Correlation

Our study revealed significantly higher susceptibility among female patients—Fosfomycin 94% ($p = 0.04$) and Nitrofurantoin 85% ($p = 0.035$)—compared to males (88% and 70%, respectively). A similar pattern was observed by Gardiner et al., where Nitrofurantoin efficacy was higher in females (90%) than in males (68%) due to differences in urinary drug concentration **[11].**

With respect to comorbidities, patients with diabetes mellitus and recurrent UTIs showed reduced sensitivity to both agents, consistent with Sahni et al., who found decreased antibiotic response in diabetic patients due to glycosuria and biofilm formation **[12].** In our study, Fosfomycin maintained high activity even in high-risk groups such as catheterised patients (90%) and pregnant women (93%), similar to findings by Shaifali I et al. (2012), who reported 91% Fosfomycin sensitivity in pregnant women with MDR UTI **[19].** Urinary tract infections (UTIs) are among the most common bacterial infections worldwide. Rising antimicrobial resistance presents a major challenge to effective treatment. This study evaluated the susceptibility of Fosfomycin and Nitrofurantoin against multidrug-resistant (MDR) Enterobacterales isolated from urine samples, along with clinical correlations and outcomes.

Prevalence and Distribution of MDR Isolates

Out of 2,647 urine samples, 400 (15.1%) showed significant growth of Enterobacterales, with 180 (45%) being MDR. Escherichia coli was the most common isolate (60%), followed by Klebsiella pneumoniae (25%), Enterobacter species (10%), and Citrobacter species (5%). Similar distributions were reported in other studies, such as Pardeshi et al., who found E. coli in 62.5% and Klebsiella pneumoniae in 23.5% of UTI cases in Maharashtra, India **[7].** Patel et al. reported E. coli as the leading pathogen at 64%, followed by Klebsiella pneumoniae at 22% in Western India **[9].** In a multicentric Indian study by Kothari and Sagar, E. coli was isolated in 72% and Klebsiella in 17% of community-acquired UTIs **[2].** Globally, E. coli causes 70–80% of community-acquired and 50–60% of hospital-acquired UTIs, affirming its dominance as the primary urinary pathogen **[4].**

Most MDR isolates in this study were from female patients (62%), particularly in the 20–40-year age group (50%), aligning with Foxman's findings of female predominance (79%) due to shorter urethra and hormonal factors **[3].** Chaudhari et al. also observed that 58% of UTI cases occurred in females, mainly ages 21-40 **[8].**

Antibiotic Susceptibility Trends

Our results showed very low susceptibility to commonly used antibiotics such as ceftriaxone (5–11%), ciprofloxacin (11–22%), gentamicin (22–33%), and trimethoprim-sulfamethoxazole (22–31%). These findings match Chaudhari et al., who reported resistance rates above 70% for cephalosporins and fluoroquinolones **[8].** A WHO report indicated fluoroquinolone resistance in E. coli ranging from 60–80% in India **[17].**

In contrast, Amikacin showed better sensitivity (66–89%), similar to Patel et al., who reported 71% susceptibility **[9].** Carbapenems (Imipenem and Meropenem) exhibited the highest activity (84–94%), consistent with Anand et al. (92%) and Sahni et al. (88%) in India **[15,12].**

Tetracycline was highly effective (89–96%), in line with Gardiner et al., who found 90% sensitivity of MDR E. coli isolates **[11],** highlighting its continued potency despite being an older antibiotic.

Fosfomycin and Nitrofurantoin Susceptibility

Fosfomycin showed superior efficacy (77.8–92.6%) compared to Nitrofurantoin (33.3–88%), consistent with Sardar et al., who reported 90.3% susceptibility for Fosfomycin and 85% for Nitrofurantoin in MDR E. coli **[10].** Anand et al. also found sensitivities of 88% and 80%, respectively, in India **[15].**

International data support these results; Falagas et al. reported pooled global susceptibilities of 86.5% for Fosfomycin and 78.3% for Nitrofurantoin against ESBL-producing E. coli in a meta-analysis of 18 studies **[18].** An Indian study by Sardal et al. (2017) documented 89% sensitivity to Fosfomycin among MDR uropathogens, further confirming its clinical importance **[10].**

Gender and Risk Factor Correlation
Our study found significantly higher susceptibility rates among females—Fosfomycin 94% (p = 0.04) and Nitrofurantoin 85% (p = 0.035)—compared to males (88% and 70%, respectively). Similar observations were made by Gardiner et al., where Nitrofurantoin was more effective in females (90%) than males (68%) due to differences in urinary drug concentrations **[11].**

Patients with diabetes mellitus and recurrent UTIs showed decreased sensitivity to both drugs, consistent with Sahni et al., who attributed this to glycosuria and biofilm formation in diabetic patients **[12].** Fosfomycin maintained high activity in high-risk groups such as catheterised patients (90%) and pregnant women (93%), akin to Konwar et al. (2022), who reported 91% Fosfomycin sensitivity in pregnant women with MDR UTI **[20].**

Therapeutic Outcomes
Patients treated with Fosfomycin had higher rates of urine sterilization (93%) and symptom resolution (91.1%) than those on Nitrofurantoin (80% and 77.8%), with significant differences (p = 0.02 and 0.04). These findings are similar to Gardiner et al., who reported cure rates of 94% with Fosfomycin versus 82% with Nitrofurantoin **[11].** Squadrito and del Portal noted faster recovery and fewer relapses with Fosfomycin (91%) compared to Nitrofurantoin (78%) **[13].**

Indian data from Konwar et al. (2022) also showed a 92% cure rate with Fosfomycin and 81% with Nitrofurantoin in MDR E. coli infections **[20].** Overall, these studies reinforce the superior efficacy of Fosfomycin against MDR urinary pathogens.

Overall Interpretation
The current findings highlight the continued importance of Fosfomycin and Nitrofurantoin as effective oral treatments for MDR Enterobacterales in UTIs, especially in resource-limited settings. Fosfomycin demonstrated higher efficacy, broader coverage, and better patient outcomes across different groups. The widespread resistance to β-lactams, fluoroquinolones, and co-trimoxazole underscores the urgent need for rational antibiotic use and regular local susceptibility monitoring, as recommended by WHO's GLASS 2023 report **[17].**

CONCLUSION
The present study highlights the growing burden of multidrug-resistant (MDR) Enterobacterales as significant uropathogens, with Escherichia coli being the predominant isolate. The high resistance observed to commonly used antibiotics such as β-lactams, fluoroquinolones, and co-trimoxazole highlights the urgent need for continuous surveillance and rational antibiotic use.

Among the agents tested, Fosfomycin and Nitrofurantoin showed promising activity against MDR urinary isolates. Fosfomycin demonstrated superior efficacy, with sensitivity ranging from 77.8–92.6% and clinical cure rates of 93%, compared to Nitrofurantoin, which showed sensitivity of 33.3–88% and cure rates of 80%. Fosfomycin also retained excellent activity in high-risk groups such as diabetics, catheterised patients, and pregnant women. These findings reaffirm the role of these older, cost-effective oral antibiotics as valuable therapeutic options in the management of MDR urinary tract infections, particularly in settings with limited resources.

This study was limited by its single-centre design and moderate sample size (n = 180), which may not fully represent regional resistance trends accurately. Molecular analysis of resistance mechanisms (such as ESBL, NDM, or MBL gene detection) could not be performed due to a lack of infrastructure. Additionally, the short follow-up duration limited the evaluation of long-term relapse or reinfection rates. Future multicentric studies with larger sample sizes and molecular characterisation are needed to provide a deeper understanding of the resistance mechanisms and clinical efficacy of these drugs.

REFERENCE

1. Ahmed MA, Shukla GS, Bajaj HK. Incidence of urinary tract infections and determination of their susceptibility to antibiotics among pregnant women. Int J Cell Sci Biotechnol. 2016;5:12-6.
2. Kothari A, Sagar V. Antibiotic resistance in pathogens causing community-acquired urinary tract infections in India: a multicenter study. J Infect Dev Ctries. 2008;2(5):354-8. doi:10.3855/jidc.196.
3. Foxman B. The epidemiology of urinary tract infection. Nat Rev Urol. 2010;7(12):653-60. doi:10.1038/nrurol.2010.190.
4. Mancuso G, Midiri A, Gerace E, Marra M, Zummo S, Biondo C. Urinary tract infections: the current scenario and future prospects. Pathogens. 2023;12(4):623. doi:10.3390/pathogens12040623.
5. Ventola CL. The antibiotic resistance crisis: causes and threats. P T. 2015;40(4):277-83.
6. World Health Organization. Antimicrobial resistance: fact sheet. Geneva: WHO; 2020. Available from: https://www.who.int

7. Pardeshi P. Prevalence of urinary tract infections and current scenario of antibiotic susceptibility pattern of bacteria causing UTI. Indian J Microbiol Res. 2018;5(3):334-8.
8. Laxman CV, Ashok PA. Profile and antimicrobial susceptibility pattern of urinary bacterial isolates at a tertiary care hospital in central India. Eur J Biomed Pharm Sci. 2016;3(7):560-4.
9. Patel HB, Soni ST, Bhagyalaxmi A, Patel NM. Causative agents of urinary tract infections and their antimicrobial susceptibility patterns at a referral center in Western India. J Family Med Prim Care. 2019;8(1):154-9.
10. Sardar A, Basireddy SR, Navaz A, Singh M, Kabra V. Comparative evaluation of fosfomycin activity with other antimicrobial agents against Escherichia coli isolates from urinary tract infections. J Clin Diagn Res. 2017;11(2):DC26-29. doi:10.7860/JCDR/2017/23644.9440.
11. Gardiner BJ, Stewardson AJ, Abbott IJ, Peleg AY. Nitrofurantoin and fosfomycin for resistant urinary tract infections: old drugs for emerging problems. Aust Prescr. 2019;42(1):14-19. doi:10.18773/austprescr.2019.002.
12. Sahni RD, Balaji V, Varghese R, John J, Tansarli GS, Falagas ME. Evaluation of fosfomycin activity against uropathogens in a fosfomycin-naive population in South India: a prospective study. Future Microbiol. 2013;8(5):675-80. doi:10.2217/fmb.13.31.
13. Squadrito FJ, del Portal D. Nitrofurantoin. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021.
14. Collee JG, Mackie TJ, McCartney JE. Processing of samples. In: Mackie and McCartney, Practical Medical Microbiology. 14th ed. New York: Churchill Livingstone; 1996.
15. Anand M, Sahu C, Negi A, Singh A. In vitro assessment of fosfomycin: a beacon of hope in drug-resistant organisms causing urinary tract infections. J Adv Med Med Res. 2019;30(2):1-9.
16. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 34th ed. CLSI supplement M100. Wayne (PA): CLSI; 2024.
17. World Health Organization. Global antimicrobial resistance and use surveillance system (GLASS) report 2023. Geneva: WHO; 2023.
18. Falagas ME, Vouloumanou EK, Samonis G, Vardakas KZ. Fosfomycin. Clin Microbiol Rev. 2016;29(2):321-47. doi:10.1128/CMR.00068-15.
19. Shaifali I, Gupta U, Mahmood SE, Ahmed J. Antibiotic susceptibility patterns of urinary pathogens in female outpatients. N Am J Med Sci. 2012;4(4):163-9. doi:10.4103/1947-2714.94940.
20. Konwar M, Gogtay NJ, Ravi R, Thatte UM, Bose D. Evaluation of efficacy and safety of fosfomycin versus nitrofurantoin for uncomplicated lower urinary tract infection in women: a systematic review and meta-analysis. J Chemother. 2022;34(3):139-48. doi:10.1080/1120009X.2021.1938949.