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ORIGINAL RESEARCH

Fosfomycin: -A novel fighter for UTI causing escherichia coli???

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ABSTRACT

Introduction: In developing nations, urinary tract infections (UTIs) are the most common infectious disease that medical professionals encounter. There is an increasing need to identify new therapy choices. A broad-spectrum antibiotic like Fosfomycin which acts by preventing both gram-positive and gram-negative bacteria from synthesizing their cell walls is one such new option. The purpose of this work is to assess the in vitro susceptibility of urinary Escherichia coli (E coli) isolates to Fosfomycin.

Objectives:

1. Isolation and identification of E. coli from urine samples
2. To determine E. Coli isolate pattern of antimicrobial susceptibility in urine
3. To assess the E. coli isolates in-vitro susceptibility to Fosfomycin.

Materials and Methods: Every clean catch, midstream urine sample that was collected aseptically in sterile containers received at our lab was taken into consideration. For every urine sample that was received, wet mount was screened. From the urine samples E. Coli isolates were identified using accepted, conventional standard techniques. Petri plates with a colony count of more than 105 CFU per ml of urine were deemed significant in asymptomatic patients whereas count of >104CFU/ml was considered in symptomatic patients and 102 CFU/ml in patients with urethral syndrome. Antimicrobial susceptibility test was conducted using the Kirby Bauer disc diffusion method in accordance with CLSI (2023) recommendations. **Results**: 427 urine samples were included in the study; 341 of them had significant bacteriuria, and the remaining 86 had no growth or non-significant bacteriuria. 20% of the samples were male, while the remaining 80% were that of females.273 Gram negative isolates and 68 Gram positive isolates were found among the 341 urine bacterial isolates. Among 273 Gram negative isolates 83 were E coli. All E coli isolates were susceptible to Fosfomycin and next to Fosfomycin, there was a greater susceptibility to Nitrofurantoin (83%), followed by Meropenem (73.4%), and then Cotrimoxazole (68.6%). The highest percentage of resistance was for ciprofloxacin (85.5%). **Conclusion:** Fosfomycin has shown to be a promising treatment for multidrug resistant E coli including ESBL producers and carbapenem-resistant E. coli. The outcomes in our settings were encouraging and promising. It is crucial to follow careful stewardship procedures to stop this medication from becoming resistant.

Keywords: Fosfomycin, Escherichia coli, Urinary tract infection

INTRODUCTION

Urinary tract infections (UTI) are now the most prevalent bacterial illness in hospitals and the general population.[1]UTIs are divided into upper (pyelonephritis) and lower (urethritis, cystitis, and prostatitis) categories based on the site of infection.[2, 3] Based on the existence of specific risk factors, UTIs are further divided into complicated and uncomplicated infections.[2, 3]

UTIs are frequently caused by gram-negative bacteria, especially Enterobacterales.[4] Due to their rising incidence and constrained oral treatment choices, UTIs caused by antibiotic-resistant Gram-negative bacteria has become a big menace.[5]

Co-trimoxazole and fluoroquinolones are two frequently used medications for the treatment of UTIs. However, there has been a spike in the search for novel therapeutic alternatives or a re-evaluation of currently available medicines, such as Nitrofurantoin and Fosfomycin, for the treatment of UTIs due to the increased prevalence of drug resistance worldwide. More and more outpatients are now being prescribed

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Nitrofurantoin and Fosfomycin for the oral treatment of UTIs.[6] Strong in vitro action is shown by Fosfomycin against Escherichia coli and other prevalent uropathogens, such as isolates of Enterobacterales that produce AmpC, Resistant to carbapenem, and have extended-spectrum β-lactamase (ESBL). In E. coli, antimicrobial resistance to Fosfomycin is uncommon and is still rising. Fosfomycin was authorized in 2013 to treat acute, simple cystitis. Regardless of the patient's hepatic or renal function, a single oral dose of Fosfomycin (3 gms) is given for this reason [7]. In clinical settings, Fosfomycin has proven to be safe and effective in treating acute, simple cystitis. It is also well tolerated in older adults and pregnant women.[8]. This investigation was conducted to provide light on the current state of UTI-causing microbes, their patterns of antibiotic sensitivity, and the effectiveness of Fosfomycin against E. coli.

MATERIALS AND METHODS

After getting ethical approval from the institution's ethics committee, this cross-sectional study was carried out in the Department of Microbiology at KRIMS, Karwar, for a period of six months, from June to November 2023. Urine samples collected aseptically in sterile containers submitted to the clinical microbiology laboratory were considered. semi quantitative culture was done on Blood Agar and Mac Conkey Agar were inoculated with the obtained samples. After making an aerobic incubation at 37˚C, the plates exhibiting recommended significant count as per clinical presentation and type of urine specimen were processed further and the isolates were identified using conventional biochemical assays all the way up to the species level. (9, 10)

In accordance with CLSI recommendations, antibiotic sensitivity testing was conducted using the Kirby Bauer disc diffusion method.(10) The following antibiotic discs were utilized, with drug concentrations expressed in µg: Ampicillin(10μg), cefazolin(30μg), Cefotaxime (30μg), Amoxicillin/clavulanic acid (20/10 μg), Ampicillin sulbactam (10/10 μg), Piperacillin tazobactam(100/10 μg), Gentamicin *(10*μg), Nitrofurantoin (300 μg), Imipenem (10 μg), Fosfomycin (200 μg), Meropenem(10 μg), Tobramycin(10μg), Levofloxacin(5μg), Cefepime (30 μg),Cotrimoxazole (1.25/23.75 μg), Ciprofloxacin (5μg), Amikacin (30 μg), cefoxitin(30μg), Tetracycline(30μg).

RESULTS

427 urine samples were included in the study; 341 of them had significant bacteriuria and the remaining 86 had no growth or non-significant bacteriuria. Gram negative isolates made up 273 of the 341 urine bacterial isolates, whereas there were 68 Gram positive isolates.

All 83 E. Coli were susceptible to Fosfomycin. Next to Fosfomycin there was a greater susceptibility to Nitrofurantoin (83%) followed by Meropenem (73.4%) and then Cotrimoxazole (68.6%). The highest percentage of resistance was Ciprofloxacin (85.5%).

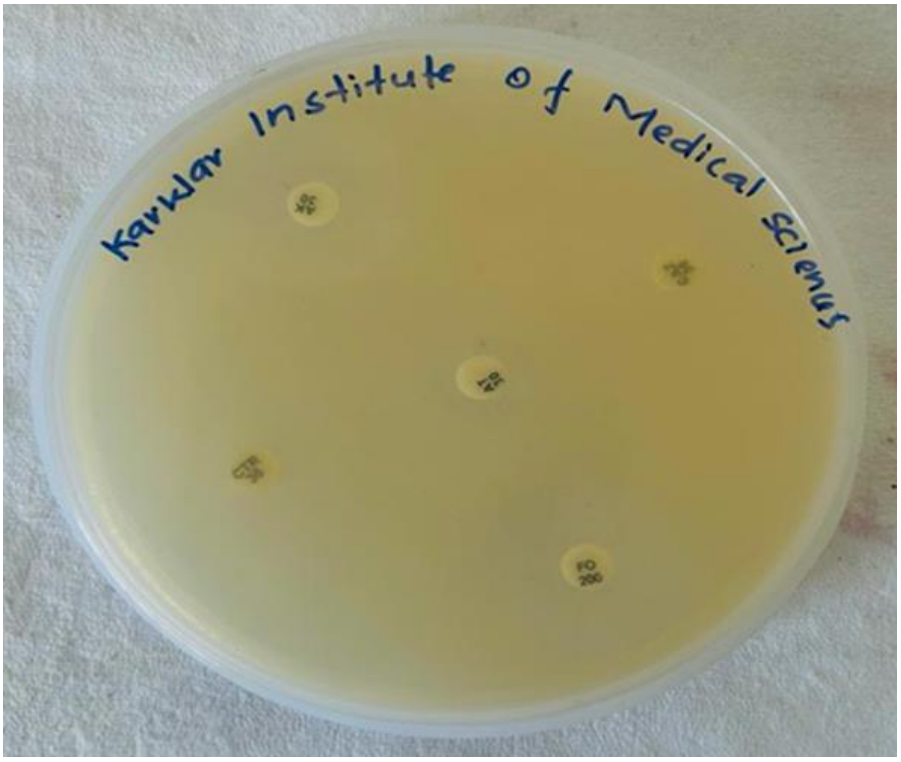

Figure 1: Kirby Bauer disk diffusion method using Fosfomycin

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Table-1 Various Gram-negative and Gram-positive organisms isolated.

Bacteria (n=427)	No. of strains
Gram negatives	**273**
Escherichia coli	83
Klebsiella	54
Proteus spp.	31
Pseudomonas	32
Acinetobacter baumannii	33
Morganellamorganii	40
Gram positives	**68**
CoNs	43
Enterococci	12
Staphylococcus aureus	13

Chart-1: Sex distribution of the E coli samples

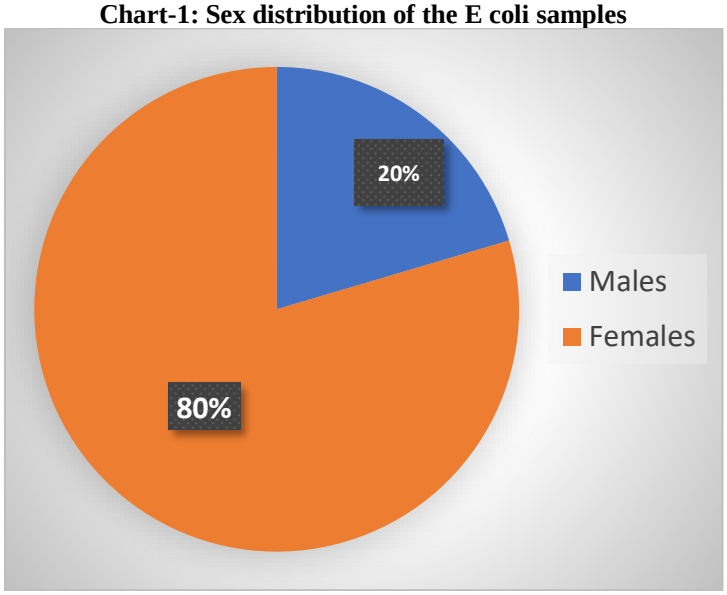

Chart-2: Department distribution of E coli samples

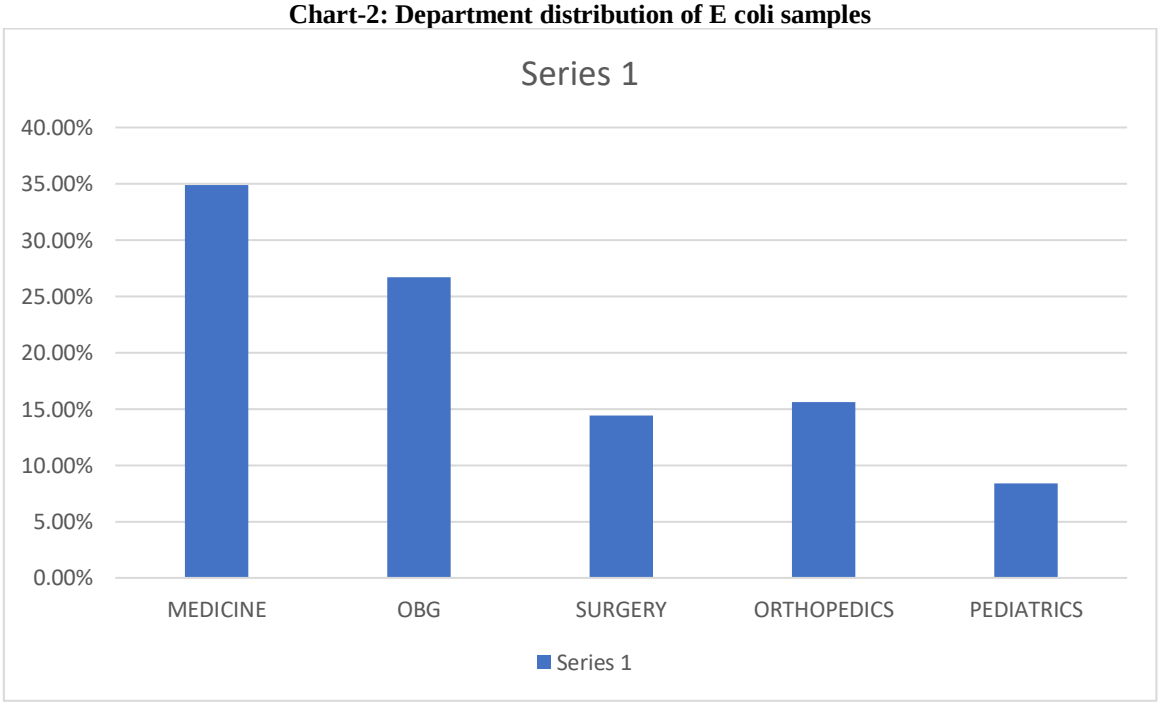

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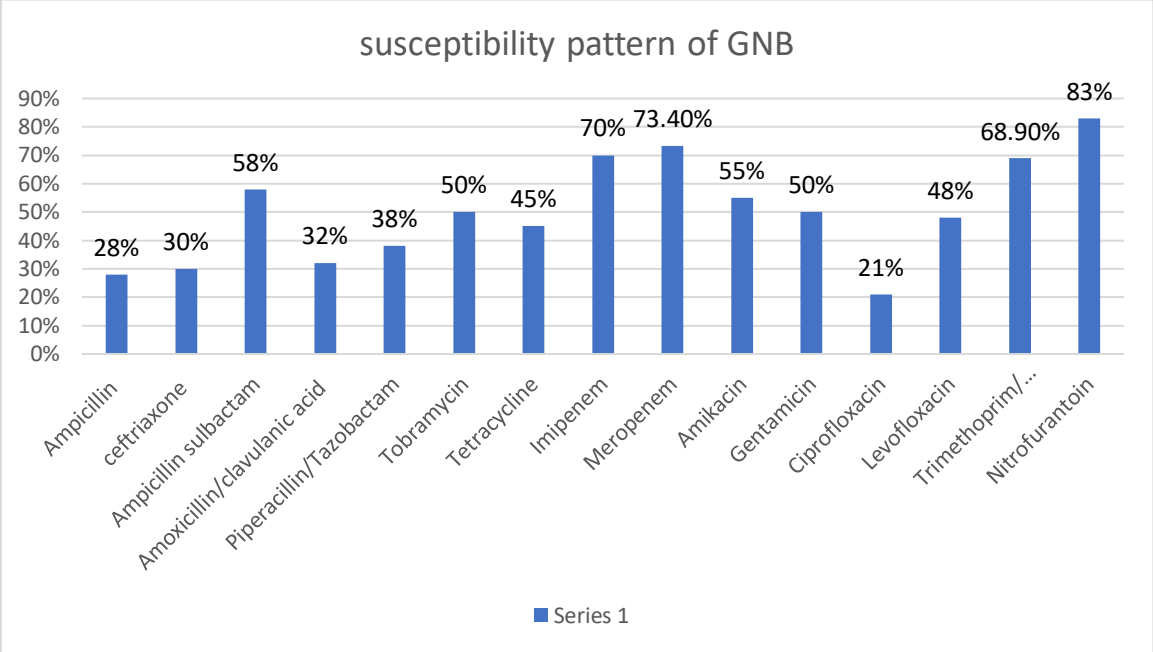
Chart 3: Antimicrobial susceptibility pattern of urinary E coli isolates



DISCUSSION

UTI is a very frequent form of bacterial infection that can afflict both healthy individuals and those who have co-occurring conditions. The patients often present with vague complaints and asymptomatic bacteriuria requiring the laboratory confirmation for successful treatment. At present, the emergence of resistance among common uropathogen like E coli to regularly used antibiotics has left limited therapeutic options for UTI. Hence, there is an increasing need to develop and introduce new antimicrobials for this purpose.

However, only a few newer antibiotics are in the pipeline of development. Fosfomycin a bactericidal agent against GPC's and GNB's including MDR enterobacterales is an alternative novel option for this purpose. Western countries have produced a growing body of research on the use of Fosfomycin in UTIs [11], but India has produced relatively little information on the drug's application.

In a study by de Cueto et al., the sensitivity of 428 strains of ESBL producing Escherichia coli and Klebsiella pneumoniae to Fosfomycin was tested in vitro, and all the isolate showed susceptibility to E. coli[13]. In their individual experiments conducted in Greece, Falagas et al. and Maraki et al. have similarly produced extremely positive susceptibility results. Fosfomycin was found to be effective in vitro against a significant proportion of urine isolates in a study by Maraki et al. These isolates showed high levels of resistance to antimicrobial drugs that are often used to treat urinary tract infections. [14,15]

The clinical efficacy rates of Fosfomycin tromethamine for acute uncomplicated cystitis, recurring lower urinary tract infection, and severe lower urinary tract infection were reported to be 94.71%, 77.22%, and 62.69%, respectively, in a study carried out at 12 medical centers in China. [16]

In our investigation, the susceptibility to Fosfomycin was 100% like other studies mentioned above.

CONCLUSION

Antibiotic therapy is crucial for treating UTIs. But in recent years, it has become more difficult since UTI pathogens are becoming increasingly resistant to the antibiotics that are commonly prescribed.

Our study reconfirms effective action of Fosfomycin on urinary E. coli isolates, as it can be used in all age groups including pregnant women. the drug can be considered as a drug of choice in uncomplicated UTIs. Fosfomycin represents a novel and effective option for the treatment of E. coli-related urinary tract infections. Its use could play a critical role in addressing the challenges posed by antibiotic-resistant pathogens, thereby enhancing patient outcome, and contributing to more effective UTI management strategies. Further studies and continuous monitoring are recommended to sustain its efficacy and optimize its clinical application.

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CONFLICT OF INTEREST

None declared.

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