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STUDY OF NITROFURANTOIN SUSCEPTIBILITY IN URINARY PATHOGENS AT TERTIARY CARE HOSPITAL, GUJARAT.

Clinical Microbiology

Dr. Komal C. Vasavada Resident Docter Department Of Microbiology, M.P.Shah Government Medical College, Jamnagar

Dr. Krunal D. Mehta Associate Professor, Department Of Microbiology, M.P.Shah Government Medical College, Jamnagar

Dr. Hiral M. Gadhavi Assistant Professor Department Of Microbiology, M.P.Shah Government Medical College, Jamnagar

Dr. Hitesh K. Shingala Professor And Head Department Of Microbiology, M.P.Shah Government Medical College, Jamnagar

ABSTRACT

Introduction: Urinary Tract Infections (UTIs) are common infections, especially among women, typically caused by bacteria like E. coli and Klebsiella species. These infections can range from mild to severe and are a significant burden on healthcare systems. The rise of multidrug-resistant (MDR) organisms, particularly those producing extended-spectrum beta-lactamases (ESBLs), has made treatment more challenging, especially in countries like India. As newer antibiotics become less effective and development of new ones slows, attention is shifting back to older drugs like nitrofurantoin. **Aim:** This study aims to assess the susceptibility trends of urinary isolates to panel of antibiotics with particular reference to nitrofurantoin. **Materials And Methods:** This retrospective study was conducted in microbiology department, at a tertiary care hospital, Jamnagar from July 2024 to December 2024. Urine samples were cultured on blood agar and MacConkey agar and examined for bacterial growth by various microbiological methods on the next day. After identifying the bacterial pathogen, antimicrobial susceptibility testing for Nitrofurantoin was performed using the Kirby-Bauer disc diffusion method on Muller Hinton agar, following CLSI guidelines. A total of 761 culture-positive cases were evaluated for Nitrofurantoin susceptibility. **Results:** Out of the 2645 total urine samples received, 860 (32.51%) were culture positive and out of total culture positive 761 were evaluated for nitrofurantoin susceptibility. From 761 samples evaluated 710 were gram negative and 51 gram positive isolates. Nitrofurantoin susceptibility for E.coli was 89.57%, for K.pneumoniae 71.16%, for Enterococcus species was 67.44% and for S.aureus 87.50%. **Conclusion:** Nitrofurantoin continues to be an effective therapeutic agent in the treatment of urinary tract infections, particularly against common uropathogens like E.coli and S.aureus. Nitrofurantoin as a valuable options for empirical treatment of urinary tract infecton, especially in the face of rising antimicrobial resistance.

KEYWORDS

Urinary Tract Infection (UTI), Nitrofurantoin, Antimicrobial drug resistance, Extended spectrum beta-lactamase (ESBL)

INTRODUCTION

Urinary Tract Infection (UTI) is among the most frequently encountered infections globally, placing a substantial burden on clinical microbiology laboratories and healthcare providers [1].It is a common and painful condition that typically responds quickly to modern antibiotics, provided the appropriate medication is selected for the specific urinary pathogen involved[2]. UTIs can generally be categorized into two types—lower and upper—based on the parts of the urinary tract that are affected [1,3]. UTIs can present in several forms, including cystitis, pyelonephritis, asymptomatic bacteriuria, and both chronic and recurrent infections. Among these, cystitis—an infection of the urinary bladder—is the most common[4].

The condition is characterized by dysuria, increased urinary frequency and urgency, as well as suprapubic discomfort. It is more prevalent in females than in males, primarily due to anatomical and physiological factors such as sexual activity, hormonal fluctuations, a shorter urethra, and the close proximity of the urethral orifice to the anus[1,5]. It is one of the most common causes of healthcare associated infection[6]. UTIs are predominantly of bacterial origin, although fungal, viral, and parasitic pathogens may also be involved. [1]. The majority of uncomplicated UTIs are attributed to uropathogenicEscherichia coli (UPEC) and Klebsiella species, which together are responsible for approximately 75 to 95 percent of all cases[4].

The number of multidrug-resistant (MDR) organisms is increasing around the world, and this has become a serious problem in countries like India.UTIs caused by E. coli and Klebsiella pneumoniae that produce extended-spectrum beta-lactamases (ESBLs) are being reported more frequently in many countries, including India. These organisms are also often resistant to other types of antibiotics, such as oral cotrimoxazole and fluoroquinolones. In addition, the effectiveness of advanced antibiotics like third-generation cephalosporins and carbapenems is decreasing because of due to the rapid emergence and spread of ESBLs and carbapenemaseproducing organisms. Community- acquired urinary tract infections constitute a significant proportion of cases presenting to hospital outpatient departments (OPDs), with a considerable volume of oral antibiotics prescribed for their management. The presence of multidrug-resistant (MDR) organisms poses a major challenge for clinicians in selecting appropriate empirical therapy.Moreover, the development of new antibiotics has been slow, prompting the need to reassess the efficacy of traditional antimicrobials, such as nitrofurantoin, in combating multidrug-resistant uropathogens[1,4].

Nitrofurantoin is a synthetic chemotherapeutic agent belonging to the nitrofuran class, initially discovered in the 1940s and subsequently approved by the United States Food and Drug Administration (FDA) in 1953 for the treatment of lower UTI. It exhibits broad-spectrum antimicrobial activity against a wide range of Gram-positive and Gram-negative bacteria, including multiple strains of common uropathogens[7]. An important advantage of nitrofurantoin is its ability to reach high concentrations in urine, along with having few side effects and being low in cost[5]. Nitrofurantoin has been in clinical use for decades; however, the growing concern over antimicrobial resistance and the limited development of new antibiotics have renewed interest in its use for treating bacterial urinary tract infections. Notably, resistance to nitrofurantoin has remained relatively stable since its discovery.The present study was conducted to analyse the antimicrobial susceptibility trends of urinary isolates against a panel of antibiotics, with particular emphasis on the efficacy of nitrofurantoin.

MATERIALS AND METHODS

This retrospective study was conducted in microbiology department, at a tertiary care hospital, Jamnagar from July 2024 to December 2024. The urine samples were collected from both hospitalized and non-hospitalized patientsincluding both males and females, in sterile wide mouth container and sent to the microbiology department for analysis. Details such as the patient's age, sex, and clinical history was obtained from the standard requisition form.

- **Inclusion Criteria-** All samples of urine received in microbiology laboratory in sterile container with adequate volume for urine culture and sensitivity were included in the study.

- **Exclusion Criteria-** All samples which were not properly packed or labelled or with incomplete clinical data were excluded.

All samples were processed on the same day of receiving.A semi-quantitative technique was employed for the primary isolation of organisms, utilizing a calibrated 1 mm diameter loop which delivers 10 µL of sample. Samples were inoculated onto MacConkey agar and blood agar plates, then incubated aerobically at 37°C for 24 to 48 hours.Culture plates exhibiting colony as per standards guidelines were interpreted as positive for UTI. Cultures that showed no microbial growth within 24 to 48 hours were considered negative. From positive cultures, uropathogens were identified with the help of standard biochemical tests.

The antimicrobial susceptibility testing for positive cultures was performed by using the Kirby-Bauer disc diffusion method on Muller Hinton agar, following Clinical Laboratory Standards Institute (CLSI)guidelines [8].From total 2645 samples 761 were culture-positive and these were evaluated for Nitrofurantoin susceptibility.

Standard Operating Procedures (SOPs) were meticulously followed to ensure the reliability of results, including strict adherence to expiration dates and quality control standards for both culture media and antibiotic discs. Quality control testing was performed for each batch of media and antibiotic discs using reference strains: Escherichia coli (ATCC 35218), Staphylococcus aureus (ATCC 29213), Enterococcus faecalis (ATCC 29212), and Pseudomonas aeruginosa (ATCC 27853).

RESULTS

Out of the 2645 total urine samples received, 860 (32.51%) were culture positive with bacteriuria and out of them 761 were evaluated for nitrofurantoin susceptibility.A total of 511 (67.15%) were female patients and 250 (32.85%) were male.From total 761 samples evaluated 710 (93.29%) were gram negative isolates and 51 (6.70%) were gram positive isolates. A total of 726 were indoor cases and 35 were outdoor cases.

The urinary isolates majorly comprised 547 (71.89%) Escherichia coli, followed by 163 (21.41%) Klebsiella pneumoniae, 43 (5.65%) Enterococcusspecies and 8 (1.05%) Staphylococcus aureus. The organisms isolated from urine samples is shown in table-1.

Table-1 The Organisms Isolated From Urine Samples

Name of the organism	Number of isolates	Percentage
Escherichia coli	547	71.88%
Klebsiella pneumoniae	163	21.42%
Enterococcusspecies	43	5.65%
Staphylococcus aureus	8	1.05%
Total	761	100%

The sensitivity of different organism to Nitrofurantoin is shown in table-2.

Table-2 Nitrofurantoin Susceptibility Of Different Isolates

Name of the organism (isolates)	N (%)
Escherichia coli(547)	490(89.57%)
Klebsiella pneumoniae(163)	116(71.16%)
Enterococcusspecies (43)	29(67.44%)
Staphylococcus aureus(8)	7(87.50%)
Total (761)	**642 (84.36%)**

Note- "N" is number of isolates sensitive to nitrofurantoin

DISCUSSION

Urinary Tract Infection- Nitrofurantoin is advocated as first line therapy for uncomplicated UTIs in women. It is especially used to treat UTIs caused by Gram-negative bacteria, particularly Escherichia coli. Nitrofurantoin is being advised for adults and children in the therapy of acute symptomatic UTIs. Also, prescribed for the treatment of recurrent UTIs and for the prophylaxis of recurrent UTIs[7].

In the current study, carried out between July 2024 and December 2024, a total of 2, 645 urine samples were submitted to the microbiology laboratory. Among these, 860 samples (32.51%) yielded positive culture results.Similar culture positive rates were found in the study of Goyal Aet al (32.94%)[5] andVidya KRet al (33.96%) [8].

From 860 culture positive samples, 761 samples were evaluated for nitrofurantoin susceptibility. A total of 511 (67.15%) were female patients and 250 (32.85%) were male. Female predominance wasalso found in a study of Gupta Aet al[1], Goyal Aet al[5] and Bhargava Ket al [9].The high rate of urinary tract infections (UTIs) in females is mainly due to factors such as the close distance between the urethral opening and the anus, a shorter urethra, sexual activity, incontinence and inadequate toilet hygiene.

In this study gram negative pathogens outnumbered gram-positive organisms.Out of the 761 samples analysed, 710 (93.29%) were identified as Gram-negative isolates, while 51 (6.70%) were Gram-positive isolates.E. coli emerged as the dominant pathogen among Gram-negative bacteria. The results were concordant with the study of Goyal Aet al[5], Alam MSet al[6], Vidya KRet al[8] and Bashetti NRet al[10]. In the current situation, treating urinary tract infections has become more difficult due to the rise of drug-resistant Gram-negative uropathogens. This is a result of the frequent use of antibiotics, which contributes to the development of antibiotic resistance in uropathogens. This resistance results in unfavourable clinical outcomes, such as treatment failure, the development of bacteraemia, and the need for intravenous medication[4,10].

In the present study susceptibility of nitrofurantoin for E. coliwas 89.57%, for K. pneumoniae was71.16%, for Enterococcusspecies was 67.44% and for S. aureuswas87.50%. The susceptibility rate of nitrofurantoin of various studies are compared in the table-3.

Table-3 Comparison Of Nitrofurantoin Susceptibility Rates Of Different Studies

Organism	Nitrofurantoin susceptibility of isolates in present study (%)	Nitrofurantoin susceptibility of isolates in other studies (%)
E. coli	89.57%	Alam MSet al,2019 [6] (92.0%) Kanaujia Ret al,2020 [11] (91.74%) Gautam Get al,2021 [12] (85.6%) Vijayaet al,2021 [13] (90.3%)
K. pneumoniae	71.16%	Alam MSet al,2019 [6] (48.3%) Vijayaet al,2021 [13] (62.2%)
Enterococcusspecies	67.44%	Bhise Met al,2025 [14] (60%) Devi, Set al,2017 [15] (83.33%)
Staphylococcus aureus	87.50%	Devi, Set al,2017 [15] (83.33%) Naik TBet al,2018 [16] (93.33%)

The nitrofurantoin susceptibility of E. coli in present study is 89.57% which was similar to the study of Alam MSet al [6] (92.0%), Kanaujia Ret al [11] (91.74%), Gautam Get al[12] (85.6%) and Vijayaet al [13] (90.3%). For K. pneumonia nitrofurantoin sensitivity was 71.16%. The sensitivity rates were somewhat low in the studies of Vijayaet al, 2021 [13] (62.2%)and Alam MSet al [6](48.3%) compared to present study. This might be due to high rates of ESBL producing K. pneumoniae in their studies.For enterococcus species, susceptibility for nitrofurantoin in present study is 67.44% which was similar to the study of Bhise Met al, [14] (60%) and somewhat high in the study of Devi, Set al, [15] (83.33%), which may reflect local resistance patterns.Similary, our finding of 87.5% susceptibility in S.aureus is consistent with the 83.3% in Devi, Set al, [15]and93.33% in Naik TBet al, [16].These result reinforce the effectiveness of nitrofurantoin against staphylococcus aureus.

In the studies conducted by Gupta A et al[1] and Goyal Aet al [5]a high level of resistance was found among Gram-negative uropathogens to commonly prescribed antibiotics for UTIs, which includes ciprofloxacin(81.38% and 85%), ceftriaxone (91.32% and 81%) and cotrimoxazole(77.85% and 64%).In present study, a notable level of antimicrobial resistance was observed among E.coli and klebsiella pneumonia isolates.Resistance to ciprofloxacin was found to be 67% in E.coli and 51% in K. pneumoniae, similary resistance to ceftriaxone in E.coli was 70% and 64% in K. pneumoniae and for Cotrimoxazole resistance was observed in E.coli was 60% and in K. pneumoniae was 49%. These findings may reflect regional variations in prescribing patterns and local epidemiological trends. However, both studies reported that nitrofurantoin, a long-established oral medication, remained effective against these pathogens.The rapid development and spread of antimicrobial resistance among gram-negative bacteria have become a major public health concern. In this era of multidrug resistant organisms, Nitrofurantoin can be used as the better

therapeutic alternative as it is still showing good susceptibility towards E. coli, the most commonly isolated pathogen from UTI cases.

Nitrofurantoin resistance is believed to arise from stepwise mutations that disrupt intracellular nitroreductase activity, specifically affecting the DNA regions encoding the enzymes nsfA and nsfB, as well as deletions in the ribE gene, which encodes lumazine synthase involved in flavin mononucleotide synthesis. Additionally, in 2003, the plasmid-mediated efflux pump mutation OqxAB was identified as a key factor contributing to nitrofurantoin resistance. Given nitrofurantoin's critical role in treating acute uncomplicated UTIs and its effectiveness against multidrug-resistant (MDR) infections, careful prescribing practices are essential to prevent further resistance development among Enterobacteriaceae. It is also important to perform species identification and antibiotic susceptibility testing to avoid using nitrofurantoin for inherently resistant organisms. Stewardship efforts are crucial to maintain the long-term efficacy of nitrofurantoin for treating uncomplicated UTIs[12].

CONCLUSION

Nitrofurantoin continues to be an effective therapeutic agent in the treatment of urinary tract infections, particularly against common uropathogens like E.coli and Staphlococcus aureus.Despite the emergence of resistance, its high sensitivity profile supports its relevance in empirical therapy.These findings highlight Nitrofurantoin as a valuable options for empirical treatment of urinary tract infecton, especially in the face of rising antimicrobial resistance.Regular monitoring of local susceptibility patterns remains essential to guide appropriate antibiotics use and ensure optimal patient outcomes.

Ethical Approval

The Institutional Ethics Committee of Shri M.P. Shah Government Medical College and Guru Gobind Singh Hospital in Jamnagar approved this study with reference number 24/01/2025 on March 23, 2025.

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