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ORIGINAL ARTICLE

Microbiological Evaluation of Efficacy of Nitrofurantoin against Uropathogenic *E. coli*

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Abstract

Background: In Bangladesh, urinary tract infections (UTIs) are among the most prevalent bacterial infections. Antimicrobial resistance in uropathogenic Escherichia coli has become a growing concern due to the pervasive and indiscriminate use of antibiotics. The objective of this study was to conduct a microbiological assessment of the efficacy of nitrofurantoin against uropathogenic *E. coli.*

Methods: This prospective study was carried out in the Department of Microbiology, Dhaka National Medical College Hospital, Dhaka, over a one-year period from 1 July 2023 to 30 June 2024. A total of 4,375 urine specimens were aseptically collected in sterile containers from patients clinically suspected of urinary tract infection. Urine culture was performed, and antimicrobial susceptibility testing of the isolated *Escherichia coli* strains to nitrofurantoin was subsequently undertaken.

Result: Among 4375 urine samples, 1748 (63.68%) of significant growth were *E. coli* isolates. 177 (10.13%) of *E. coli* isolates were nitrofurantoin resistant.

Conclusion: UropathogenicE. coli were found to have excellent sensitivity against nitrofurantoin. So, the drug can be used as 1st line antibiotic to treat UTI, especially in uncomplicated cases.

Keywords: Efficacy, Nitrofurantoin, Uropathogenic *E. coli*.

Introduction

Urinary tract infection (UTI) stands out as one of the most common bacterial infections that necessitate medical intervention.[1] Each year, around 150 million people worldwide receive a diagnosis of a urinary tract infection.[2] While women of reproductive age are more frequently impacted,[2] it is important to recognize that men and children are also at risk. Nearly 50% of women are projected to encounter at least one episode of a urinary tract infection during their lifetime.[3] Various risk factors play a significant role in the onset of urinary tract infections. These include inadequate personal hygiene, older age, pregnancy, the use of urinary catheters, structural abnormalities within the urinary tract, and the presence of other health issues like diabetes.[4] The detection of significant bacteriuria can suggest either asymptomatic bacteriuria or an active infection, which may vary from uncomplicated to complicated urinary tract infections. Escherichia coli continues to be the leading cause of both uncomplicated and complicated cystitis and pyelonephritis. Among other significant uropathogens various members of the Enterobacteriaceae family, including Proteus mirabilis and *Klebsiella pneumoniae.* Additionally, *Pseudomonas aeruginosa, Acinetobacter baumannii,* and Gram-positive cocci such as *Staphylococcus saprophyticus* and Enterococcus spp. also play a crucial role in urinary tract infections.[5]

In addressing acute urinary tract infections (UTIs), it is customary to utilize antibiotics including trimethoprim-sulfamethoxazole, cefuroxime, ciprofloxacin, cefepime, and ampicillin.[6] Nonetheless, a number of these agents are not recommended for use during pregnancy and in pediatric populations.[7] Furthermore, the widespread and unregulated application of antimicrobials, especially common in underdeveloped and numerous developing nations, has played a significant role in the rise of resistance to these agents. This trend has resulted in an increasing scarcity of effective treatment options for urinary tract infections. Moreover, prolonged use of traditional antibiotics can disrupt the natural microbial balance in both the vagina and gastrointestinal tract, leading

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to additional complications.[6] This highlights the importance of recognizing safer and more effective alternatives. In an era where newer antimicrobials dominate the conversation, it is striking that some older antibiotics, which boast impressive efficacy, established safety records, and reliable drug interactions, continue to be underutilized. Moreover, these established medications are more affordable than many of the newer options, while still offering similar therapeutic effectiveness. Notably, several of these have shown enduring effectiveness with limited development of resistance as time progresses.[8]

Nitrofurantoin serves as a bactericidal agent, exerting minimal influence on the gastrointestinal flora.[9] First identified in 1953, this medication saw extensive use for treating lower urinary tract infections until the 1970s, when the introduction of newer β-lactam antibiotics and trimethoprim-sulfamethoxazole shifted the landscape of treatment options. The clinical significance was underscored when the Infectious Diseases Society of America (IDSA) guidelines endorsed it in 2010 for managing acute cystitis.[6] Upon oral administration, nitrofurantoin is swiftly absorbed and subsequently excreted into the urine, reaching elevated therapeutic concentrations. This antibiotic demonstrates a wide range of effectiveness, targeting the majority of prevalent Gram-negative and Gram-positive uropathogens.[10] As a result, clinicians often favor this treatment for managing lower UTIs in adults, children, and pregnant women.[9] It proves especially effective against uropathogens that show resistance to carbapenems, fluoroquinolones, aminopenicillins, and both vancomycin-sensitive and vancomycin-resistant Enterococcus strains.[10]

Nitrofurantoin is a synthetic antimicrobial that originates from furan, characterized by the addition of a nitro group and a side chain that includes hydantoin.[10] The exact mechanism of action remains to be fully clarified. Current evidence indicates that bacterial enzymes that can reduce nitrofurantoin play a crucial role in the activation of this drug. Strains that are sensitive to nitrofurantoin demonstrate the expression of flavoproteins responsible for facilitating this reduction.[11] In *Escherichia coli,* the pivotal enzymes are the type 1 oxygen-insensitive nitroreductases, which are encoded by the nfsA and nfsB genes.[6,11] The reduction process produces highly reactive electrophilic intermediates that bind nonspecifically to bacterial ribosomal proteins, resulting in the inhibition of protein synthesis.[6] Moreover, these intermediates disrupt the enzymes involved in the Krebs cycle, hindering carbohydrate metabolism,[10] and lead to damage of the bacterial cell wall and DNA, ultimately resulting in bacterial cell death.[11]

One important aspect of nitrofurantoin is that due to these multidirected mechanisms of action, the drug is less vulnerable to develop bacterial resistance.[6] Yet some studies report low level clinical resistance among uropathogenic *E. coli.*[12] Several mechanisms of nitrofurantoin resistance have been shown. The most important one for *E. coli* is mutation in nfsA & /or nfsB genes. Due to the mutation, reduction of nitrofurantoin does not occur & toxic intermediates are not produced.[6] Recent findings have revealed that plasmid-mediated efflux pump genes (oqxAB) play a role in the emergence of clinically significant nitrofurantoin resistance.[13] Furthermore, the deletion of the ribE gene, responsible for encoding lumazine synthase crucial for riboflavin biosynthesis, has been suggested as a potential alternative resistance mechanism.[14]

The antimicrobial susceptibility profile of uropathogens is in a state of continuous evolution, driven by the pervasive and growing application of antibiotics. Consequently, ongoing monitoring of resistance trends is crucial, not only for informing the choice of suitable agents but also for guaranteeing a logical approach to empirical therapy.[12] This study aims to assess the current susceptibility of uropathogenic Escherichia *coli* (UPEC) to nitrofurantoin, seeking to provide updated evidence that can guide clinical practice.

Methodology

This prospective study was carried out in the Department of Microbiology at Dhaka National Medical College Hospital from July 1, 2023 to June 30, 2024. Patients having a clinical diagnosis of urinary tract infection (UTI), regardless of age, gender, comorbidities, or previous medication use, were included. A total of 4,375 urine samples were evaluated. All patients have been informed about the study.

Sample Collection and Processing:

Fresh midstream urine samples (10-20 mL) were collected aseptically in wide-mouthed sterile plastic containers. Within an hour of collection, each specimen was inoculated on blood agar and MacConkey agar

with a calibrated 28G wire loop (internal diameter: 3.26 mm) capable of delivering 0.004 mL of urine. The inoculation plates were incubated aerobically at 37 degrees Celsius overnight. Colony counts $\geq 10^5$ CFU/mL of urine were deemed significant. Standard biochemical procedures were used to identify *Escherichia coli* isolates.[15]

Antimicrobial susceptibility testing:

All *E. coli* isolates were tested for antibiotic susceptibility using the Kirby-Bauer disc diffusion technique.[16] Bacterial suspensions were produced according to the McFarland method, and Mueller-Hinton agar plates were inoculated with sterile cotton swabs. Filter paper disks with 300 µg nitrofurantoin were applied. The results were interpreted using the Clinical and Laboratory Standards Institute (CLSI) 2022 guidelines,[17] and isolates were categorized as sensitive or resistant based on inhibition zone diameter. *Escherichia coli* ATCC 25922 served as a quality control strain.[12]

Statistical analysis:

All data were entered and analyzed with SPSS 23.0.

Result

In this study, total 4375 urine samples were studied. Significant growth was found from 2745(62.74%) urine samples.1748 (63.68%) of significant growth were *E. coli* isolates. Among significant growth of *E. coli*, 61.78% were from female patients. 177(10.13%) of *E. coli* isolates were nitrofurantoin resistant.

Table-I: Prevalence of significant bacteriuria

Significant bacteriuria	Number (%)
Yes	
E. coli	1748 (63.68)
OtherGram negative bacilli	741 (26.99)
Gram positive cocci	256 (9.33)
Total	**2745(100)**
No	1630
Grand Total of urine examined	**4375**

Table-II: Distribution of significant growth of *E. coli* according to sex

Sex	Number of Significant growth (%)
Male	668 (38.22)
Female	1080 (61.78)
Total	**1748(100%)**

Table-III: Distribution of significant growth of *E. coli* according to sex in different age groups

Age group(Yrs)	Male no.(%)	Female no.(%)
< 10	17(2.54)	00
10-19	13 (1.95)	101(9.35)
20-29	32 (4.8)	250(23.14)
30-39	44(6.59)	272(25.19)
40-49	106(15.87)	220(20.37)
50-59	246(36.82)	119(11.02)
60-69	121(18.11)	76(7.04)
≥70	89(13.32)	42(3.89)
Total	**668(100)**	**1080(100)**

Discussion

UTI has emerged as an important community acquired and nosocomial bacterial infection. The causative agents of UTI are mostly self intestinal microbiota.[12] In this study, significant bacteriuria was found in 62.74% urine samples. *E. coli* comprised 63.68% of significant bacteriuria of which 61.78 % were from female patients.This gender difference is in accordance with other studies.[12,18,19] But higher[18,19] & lower[12,20] rate of significant bacteriuria has been shown in different studies. Short urethra in females facilitates colonization of urinary tract by the microorganisms. Also females lack antibacterial prostatic fluid. All these factors explain the higher frequency of UTI in females than males. In the current study it was found that females of 30-39 years age group suffered more (25.19%) with UTI, followed by 20-29 years' group (23.14%). In case of male patients, 50-59 years' group suffered more (36.82%), followed by 60-69 years' group(18.11%).

Antibiotics that are prescribed frequently to treat UTI are fluoroquinolones (ciprofloxacin or levofloxacin), 1st and 2nd generations of cephalosporins, gentamicin & amoxicillin + clavulanate. Ciprofloxacin & Cephalosporins became more important drug to treat UTI due to their excellent activity against gram-negative bacteria.[21] It is seen that several of these drugs have become resistant to high level in many uropathogens. Being most commonly isolated organism in urine samples, increased antimicrobial resistance of *E. coli* has drawn attention. Several studies showed moderate to high level resistance of UPEC to some of commonly used antibiotics, like, gentamicin and ceftriaxone.[12, 22] In addition, their use is limited due to parenteral route and patient's noncompliance.[12] Several studies in Bangladesh have showed high rate

of ciprofloxacin resistance among *E. coli*.[12, 20, 22] Irrational and over-use of this broad spectrum molecule may be associated with loss of it's efficacy not only in UTI but in other infections too. It is till used as prophylactic antibiotic in UTI. But increasing drug resistance is a problem in treating infections including UTI. Also, ciprofloxacin use may be associated with some adverse incidence and their use should be reserved for infections other than acute cystitis.[21]Resistance of UPEC to 1st, 2nd and 3rd generation cephalosporins is also increasing.[12,19-23] In this situation, nitrofurantoin is a better & safer option to treat UPEC. This drug has been in choice to treat uncomplicated cystitis in many countries because of it's high efficiency & cost-effectiveness.[6] European Association of Urology recommends nitrofurantoin as 1st line empiric treatment of uncomplicated cystitis.[24]

In many countries, the resistance of uropathogenic *Escherichia coli* (UPEC) to nitrofurantoin remains low, supporting its recommendation as a first-line agent for the treatment of UTI.[22] In the present study, nitrofurantoin demonstrated high efficacy, with only 10.13% of UPEC isolates exhibiting resistance. Comparable findings have been reported in earlier studies.[3,12] This observation is particularly encouraging in the context of the declining susceptibility of UPEC to most other inexpensive oral antimicrobials commonly used for UTI management. In India, a study conducted in 2019 reported 13.3% resistance among UPEC isolated from hospitalized patients,[25] while similar resistance levels were documented in Mexico (12.7%),[26] Pakistan (6%),[27] and Iran (10.7%).[28] A study in Nepal found 9.7% of isolates resistant to nitrofurantoin, whereas resistance rates to ciprofloxacin and cephalosporins were considerably higher.[29] Collectively, these findings under score the continued utility of nitrofurantoin as an effective therapeutic and empirical option for lower UTIs. However, given its poor penetration into the renal parenchyma, nitrofurantoin should not be used for the treatment of pyelonephritis.[21] It is noteworthy that several studies conducted in Bangladesh and elsewhere have documented higher resistance rates than those observed in the current study.[19-21] For example, one Bangladeshi study demonstrated an alarming increase in nitrofurantoin resistance among UPEC from 9% in 2011 to 31.2% in 2021.[19] These variations highlight the importance of regional and temporal surveillance of antimicrobial susceptibility patterns, as UTIs caused by resistant pathogens are more likely to result in treatment failure, prolonged morbidity, and increased healthcare costs.

Conclusion

As it is seen that UPEC are mostly sensitive to nitrofurantoin, so, it can be considered as the main first-line, safe and cost-effective oral treatment rather an alternative drug in UTI especially in uncomplicated cases. At the same time, frequent studies have to be carried out so that any change in sensitivity pattern can be easily pointed out.

References

1. Dahiya A., Grover P., Arora B., Jain D., Chugh S. Efficacy of Nitrofurantoin and Fosfomycin against Extended Spectrum Beta Lactamase Producing Uropathogens in the Era of Antibiotic Resistance: A Cross-sectional Study. Asian Journal of Medicine and Health. 2024; 22(8)65-71
2. Kothari A, Sagar V. Antibiotic resistance in pathogens causing community-acquired urinary tract infections in India: A multicenter study. J Microbiol Res. 2008; 2(5):354-8.
3. Naseem S, Fatima A, Iqbal S, Fasih F, Naeem S.T., Bukhari U. Nitrofurantoin and Fosfomycin, effective oral empirical treatment options against multidrug resistant Escherichia coli. Journal of Rawalpindi Medical College. 2021;25 (4):507-11
4. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. The American Journal of Medicine. 2002;113(1):5-13.
5. Goddard J, Turner AN, Cumming AD, Stewart LH. Kidney and urinary tract disease. In: Boon NA, Colledge NR, Walker BR, Hunter JAA, editors. David son's principles and practice of Medicine. 20th ed. Edinburgh: Churchill Livinstone; 2006. p. 455–511.
6. Mahdizade A. M., Dashtbin S., Ghasemi F., Shahroodian S., kiani P., Bafandeh E., Darbandi T., Ghanavati R. and Darbandi A. Nitrofurantoin: properties and potential in treatment of urinary tract infection: a narrative review. Front. Cell. Infect. Microbiol. 13:1148603. doi: 10.3389/fcimb. 2023.1148603
7. Cassir N, Rolain J-M, Brouqui P. A new strategy to fight antimicrobial resistance: the revival of old antibiotics. Front. Microbiol. 5, 551 (2014)
8. Cunha, B. New uses for older antibiotics: nitrofurantoin, amikacin, colistin, polymyxin b, doxycycline, and minocycline revisited. Med. Clinics North America 2006; 90, 1089–1107
9. Gardiner BJ, Stewardson AJ, Abbott IJ, Peleg AY. Nitrofurantoin and fosfomycin for resistant urinary tract infections: old drugs for emerging problems. AustPrescr. 2019 Feb;42(1):14-19.

10. Munoz- Davila M. Role of Old Antibiotics in the Era of Antibiotic Resistance. Highlighted Nitrofurantoin for the Treatment of Lower Urinary Tract Infections. Antibiotics(Basel) 2014; 3:39-48
11. Paul R. race, Andrew L. Lovering , Richard M. Green, Abdelmijd O., et al. Structural and Mechanistic Studies of Escherichia coli Nitroreductase with the Antibiotic Nitrofurazone. Reversed binding orientations in different redox states of the enzyme. The J. of Biological Chemistry 2005; April 8, 14:13256-13264
12. Haque R., Akter M.L. and Salam M.A. Prevalence and susceptibility of uropathogens: a recent report from a teaching hospital in Bangladesh. BMC Res Notes, 2015; 8:416
13. Ho P., Ng K., Lo W. et al. Plasmid-mediated oqxAB is an important mechanism for nitrofurantoin resistance in Escherichia coli. Antimicrob. Agents Chemother. 2016; 60(1), 537–543
14. John Osei Sekyere. Genomic insights into nitrofurantoin resistance mechanisms and epidemiology in clinical Enterobacteriaceae. Future Sci. OA. 2018; 4(5)
15. McNulty CA, Bowen J, Clark G, Charlett A, Cartwright K, South West G, Microbiology Laboratory Use Group: How should general practitioners investigate suspected urinary tract infection? Variations in laboratory-confirmed bacteriuria in South West England. Commun Dis Public Health 2004, 7(3):220-6.
16. Bauer AW, Kirby WMM, Sherris JC, Turek M. Antibiotic susceptibility testing by a standardized single disc method. Am J ClinPathol. 1966;36: 493–6.
17. Performance Standards for Antimicrobial Susceptibility Testing. 33rd ed. CLSI supplement M100. Clinical and Laboratory Standards Institute; 2023.
18. Seifu W. D. and Gebissa A. D. Prevalence and antibiotic susceptibility of Uropathogens from cases of urinary tract infections (UTI) in Shashemene referral hospital, Ethiopia. BMC Infectious Diseases (2018) 18:30.
19. Majumder MMI, Mahadi AR, Ahmed T, Ahmed M, Uddin MN and Alam MZ. Antibiotic resistance pattern of microorganisms causing urinary tract infection: a 10-year comparative analysis in a tertiary care hospital of Bangladesh. Antimicrobial Resistance & Infection Control 2022; 11:156
20. Nahar A, Hasnat S, Akhter H, Begum N. Evaluation of antimicrobial resistance pattern of uropathogens in a tertiary care hospital in Dhaka city, Bangladesh. South East Asia Journal of Public Health 2017;7(2):12-18.
21. Gupta K., Hooton TM, Naber KG, Wullt B, Colgan R, et al. International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: A 2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clinical Infectious Diseases 2011;52(5): e103–e120
22. Akram M, Shahid M and Khan AU. Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in J N M C Hospital Aligarh, India. Annals of Clinical Microbiology and Antimicrobials 2007, 6:4 .
23. Chowdhury, S.S., Tahsin, P.; Xu, Y., Mosaddek, A.S.M., Muhamadali, H., Goodacre, R. Trends in Antimicrobial Resistance of Uropathogens Isolated from Urinary Tract Infections in a Tertiary Care Hospital in Dhaka, Bangladesh. Antibiotics 2024, 13, 925.
24. Reis ACC, Santos SRS, Souza SC, Saldanha MG, Pitanga TN, Oliveira RR. Ciprofloxacin resistance pattern among bacteria isolated from patients with community-acquired urinary tract infection. Rev Inst Med Trop Sao Paulo. 2016; 58:53.
25. Prasada S, Bhat A, Bhat S, ShenoyMulki S, Tulasidas S. Changing antibiotic susceptibility pattern in uropathogenic Escherichia coli over a period of 5 years in a tertiary care center. Infect Drug Resist. 2019 May; 12:1439–1443.
26. Ramírez-Castillo FY, Moreno-Flores AC, Avelar-González FJ, Márquez-Díaz F, Harel J, Guerrero-Barrera AL. An evaluation of multidrug-resistant Escherichia coli isolates in urinary tract infections from Aguascalientes, Mexico: cross-sectional study. Ann ClinMicrobiolAntimicrob. 2018 Dec;17(1):34.
27. Ali I, Rafaque Z, Ahmed S, Malik S, Dasti JI. Prevalence of multidrug resistant uropathogenic Escherichia coli in Potohar region of Pakistan. Asian Pac J Trop Biomed. 2016 Jan;6(1):60–66.
28. Vakilzadeh MM, Heidari A, Mehri A, Shirazinia M, Sheybani F. Antimicrobial Resistance among Community-Acquired Uropathogens in Mashhad, Iran. J of Environmental and public Health, October 2020.
29. Shakya S., Edwards J., Gupte H., Shrestha S., Shakya B., Parajuli K., Kattel H., Shrestha P., Ghimire R., Thekkur P. High multidrug resistance in urinary tract infections in a tertiary hospital, Kathmandu, Nepal. Public Health Action. 2021;11:24–31. doi: 10.5588/pha.21. 0035