ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 04 | April - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

# EVALUATION OF NITROFURANTOIN SUSCEPTIBILITY AGAINST UROPATHOGENS IN THE CURRENT SCENARIO OF ANTIMICROBIAL RESISTANCE: A STUDY FROM A TERTIARY CARE HOSPITAL.

Medical Microbiology

**Navneet Garg** Research Assistant VRDL, Department Of Microbiology GGSMCH Faridkot
**Dr. Shilpa Arora** Professor, Department Of Microbiology GGSMCH Faridkot
**Dr. Vishal Sharma** Professor & Head, Department Of Microbiology GGSMCH Faridkot

## ABSTRACT

**Background-** Urinary tract infection (UTI) is one of the most common bacterial infections encountered in clinical practice both in community and hospital setting. Antimicrobial resistance among uropathogens is cause of concern in many countries. This has made nitrofurantoin a suitable candidate for the treatmemt of urinary tract infections caused by multidrug resistant pathogens. The present study was conducted to study the susceptibility of nitrofurantoin among the uropathogens especially multidrug resistant organisms. **Methedology-** A total of 100 consecutive urine specimens obtained from clinically suspected patients of urinary tract infection were subjected to semiquantitative culture and antimicrobial susceptibility testing. **Result-** Out of 65 isolates the most common isolated organisms from urine samples were gram negative bacilli (97%), with only 3% being gram positive cocci. Out of 65 isolates, the most common was E.coli (71%). The overall prevalence of MDR was 75.3%. Nitrofurantoin susceptibility among MDR isolates was 57.1% with highest being in MDR E. coli (69.4%) **Conclusion-** 57.1% susceptibility in MDR isolates suggests that nitrofurantoin can be used among MDR organisms but its use should be judicious.

## KEYWORDS

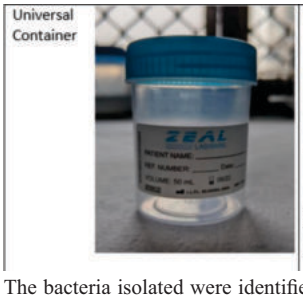
Nitrofurantoin , Uropathogens, Multidrug resistance.

## INTRODUCTION

Urinary tract infection is one of the most common bacterial infections, encountered in clinical practice, mainly caused by Gram Negative Bacilli.(1) Resistance to many of commonly prescribed antibiotics has emerged over past several years. Nitrofurantoin has a broad- spectrum activity against the main uropathogens and has also been shown to be active against extended spectrum beta-lactamase (ESBL) producing Enterobacteriaceae and Vancomycin – resistant Enterococci (VRE).(2) The present study was undertaken to evaluate the susceptibility of Nitrofurantoin among the Uropathogens, especially the multi-drug resistant (MDR) organisms.

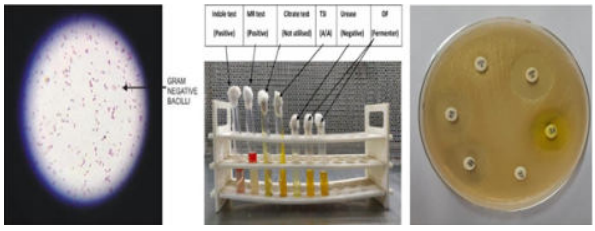
## MATERIAL AND METHODS

A total of 100 consecutive Indoor/ Outdoor patients who presented to tertiary care hospital during 6 month of duration were enrolled in this study. After recording the demographic profile, mid-stream urine samples were collected in a sterile leak-proof universal containers. In catheterized patient urine sample was collected using aseptic precaution, catheter tubing was clamped off above the port and semi-quantitative culture was done on cysteine lactose electrolyte deficient (CLED) agar.




Cysteine lactose electrolyte deficient (CLED) agar showing growth of lactose fermenting colony.

The bacteria isolated were identified using standard microbiological methods and tested against a wide-spectrum of antimicrobial agents using the Kirby Bauers disc diffusion method, following the Clinical and Laboratory Standards Institute (CLSI) guidelines (3).




**Biochemical reactions of Escherichia coli**

**Antibiotic susceptibility testing (Kirby Bauer Disc Diffusion Method)**

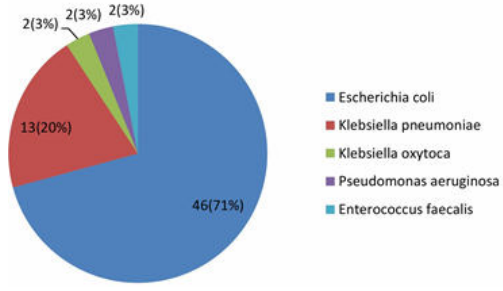
## OBSERVATIONS AND RESULTS

- Out of total 100 samples, 65 isolates were found.
- Most common age group of culture positive cases was 1-15 years (23%), followed by 16-30 years (20%) (as shown in Table-1)
- Out of 65 isolates, 58% were isolated from males, and 42% from females, with male to female ratio 1.4:1.

**Table-1 : Age Distribution Of Culture Positive Cases (n=65)**

| S.no | Age group (year) | No. Of patients | Percentage (%) |
|---|---|---|---|
| 1 | 1 to 15 | 15 | 23 |
| 2 | 16 to 30 | 13 | 20 |
| 3 | 31 to 45 | 12 | 19 |
| 4 | 46 to 60 | 9 | 14 |
| 5 | 61 to 75 | 12 | 18 |
| 6 | 76 to 90 | 4 | 6 |

- The most common isolate was E.coli (71%), followed by K.pneumoniae (20%).(figure-1)




- Most of the E.coli isolates were sensitive to Nitrofurantoin (76%), followed by Piperacillin-tazobactum (54.3%) and Amikacin (52.1%) and minimum susceptibility was observed against Norfloxacin (6.5%), Nitrofurantoin was found to be significantly higher (p.value< 0.00001) than Norfloxacin.(Table-2)

**Table-2: Prevalence Of Antimicrobial Susceptibility Among Various Isolates (n=65)**

| ANTIBIOTICS | EC(n=46) | KP(n=13) | KO(n=2) | PA(n=2) | TOTAL GNB(n=63) | EF(n=2) |
|---|---|---|---|---|---|---|
| AMPICILLIN | NT | NT | NT | NT | - | 1(50%) |
| CEFOTAXIME | NT | 3(23%) | NT | NT | 3(4.76%) | NT |
| NORFLOXACIN | 3(6.5) | 2(15%) | 0 | 1(50%) | 6(9.5%)b | NT |
| NITROFURANTOIN | 35(76%) | 4(30.7%) | 0 | 0 | 39(61.9%)a | 1(50%) |
| IMIPENEM | 17(36.9%) | 4(30.7%) | 1(50%) | 1(50%) | 23(36.5%) | 0 |

| | | | | | | |
|---|---|---|---|---|---|---|
| PIPRACILLIN+ TAZOBACTAM | 25(54.3%) | 4(30.7%) | 1(50%) | 1(50%) | 31(48.2%) | 0 |
| AMIKACIN | 24(52.1%) | 5(38.4%) | 1(50%) | 1(50%) | 31(48.2%)c | 0 |
| VANCOMYCIN | NT | NT | NT | NT | - | 1(50%) |
| LINEZOLID | NT | NT | NT | NT | - | 2(100%) |

EC (Escherichia Coli), KP (Klebsiella Pneumoniae), KO (Klebsiella Oxytoca), PA (Pseudomonas Aeruginosa) EF (Enterococcus Faecalis), NT (Not Tested)Overall prevalence of MDR was 75.3%.: Nitrofurantoin susceptibility among MDR isolates was 57.1% (**Table-3)**

**Table-3 : Nitrofurantoin Susceptibility Among MDR Isolates.**

| No. of MDR isolates | No. of Nitrofurantoin sensitive isolates | Percentage (%) |
|---|---|---|
| Escherichia coli (n=36)a | 25 | 69.4 |
| Klebsiella spp. (n=11)b | 3 | 27.2 |
| Pseudomonas aeruginosa (n=1) | 0 | 0 |
| Enterococcus faecalis (n=1) | 0 | 0 |
| TOTAL (n=49) | 28 | 57.1 |

p value <0.0068 (Pearson's Chi Square Test), $X^2$ (<0.05 significant), df=1 (between a & b)

## DISCUSSION

The present study showed that most of the patients from whom positive urine culture was obtained were from the age group 1 to 15 years (23%) followed by 16 to 30 years (20%).

Both age groups comprised 43% of total study population. The least common was 76-90 years age group (6%) (Table1). Similar results were observed in a study conducted byBakshi et al in 2015. which reported that out of 2290 UTI positive patients, 62.6% were below 30 years and only 2.5% in more than 60 years of age group (4). In another study, Madhuri et al also observed that the highest rate of UTI was within 18-40 years of age group (41.3%) and only 15.3% were in more than 81 years age group (5).

Of the 65 isolates, maximum (58%) isolates were from males as compared to females with male to female ratio 1.4:1. Preethishree et al and Bakshi et al have reported majority cases of UTI in females accounting for 51.65% and 66% respectively (6,4).The prevalence and incidence of UTI is higher in women than in men due to several clinical factors including anatomic differences, hormonal effects, and behavioral pattern. A greater number of affected males in our study could be because of the small sample size.

Among the gram negative bacilli, the maximum were E. coli 46 (71%) followed by K. pneumoniae 13 (20%) (figure-1). Our study corresponds with the findings of Parkash et al. that showed the presence of E. coli in 66% specimens and K. pneumoniae in 29% (7). A study conducted by Dimitrov et al isolated 48% E. coli and 12.2% Klebsiellaspp.Similar results were also seen in the study ofAkram et al (8). However, the results of present study differ from the studies conducted by Ehinmidu et al, and Aboderil et al. In their studies, P. aeruginosa and Klebsiellaspp. were reported as predominant bacteria in UTI (9,10). Regarding gram positive cocci, the prevalence of E. faecalis in our study was 3% which is less than that reported by Behera et al (11).Most susceptible antibiotic for E.coli was found to be nitrofurantoin (76%) followed by piperacillin-tazobactum (54.3%), amikacin (52.1%) and imipenem (36.9%)(Table-2). None of the strain was sensitive to cefotaxime. K. pneumoniae was 38.4% sensitive to amikacin followed by nitrofurantoin,imipenem andpiperacilin-tazobactum (30.7% each) and sensitivity to cefotaxime being 23%. Our study is in concordance with the study done by Jain S et al in 2017 in which they reported nitrofurantoin to be the most susceptible antibiotic for E.coli.

K.pneumoniae was found to be 50% sensitive to carbapenems, 43.48% to amikacin, 41.3% to piperacillintazobactum and only 30.43% to nitrofurantoin (12). Bhattar S et al also reported 80.6% nitrofurantoin susceptibility in case of E. coli which was just after imipenem (83.7%)

(13). In case of K. pneumoniae, they reported 56.09% nitrofurantoin susceptibility which was lesser than imipenem (87.8%), gentamicin (60.97%) and piperacillin-tazobactum (58.5%). Considering total gram negative isolates sensitivity to nitrofurantoin was found to be significantly higher (p.value< 0.00001) than norfloxacin. Although susceptibility was also higher than amikacin but the difference was not statistically significant (p.value>0.151494). Similar findings were also shown by Pai et al and Bhatt et al (14,15). High floroquinolone resistance rate was also reported by Francesco and Tankhiwale et al (16,17). This highlights the importance of nitrofurantoin for the treatment of uncomplicated UTIs in the current era of increasing floroquinolone resistance among uropathogens. Its use as first line therapy will definitely contribute to the overall reduction in floroquinolone use and thus resistance against quinolones. Of the 2 Enterococcus faecalis isolates, the susceptibility to nitrofurantoin was 50% which was equivalent to the vancomycin and no strain was found to be resistant to linezolid.

In the present study, the overall nitrofurantoin susceptibility among MDR isolates was found to be 57.1% with maximum being in MDR E.Coli(69.4%) followed by Klebsiella spp.(27.2%), while there was no nitrofurantoin susceptibility among MDR P. aeruginosa and E. faecalis.

The difference of nitrofurantoin susceptibility among MDR E. coli &Klebsiellaspp. was found to be statistically significant (pvalue=< 0.0068)(Table-3) The present study corresponds with the study done by Rajkumar et al in 2015 in which it was reported that the susceptibility rate of E.coli among the ESBL isolates for nitrofurantoin was 65% while that of K. pneumonia was 5% (18). Lieu et al have also reported higher susceptibility of nitrofurantoin in ESBL associated E.coli (79%) than K. pneumoniae (13%). Among gram positive bacteria only 1 vancomycin resistant E.faecalis was isolated which was found to be resistant to nitrofurantoin (19). However, Rajkumar et al have reported nitrofurantoin susceptibility in VRE isolates to be 66% (18).

In order to use any antibiotic as an agent for empiric therapy for treatment of UTIs, it should fulfil certain criteria such as: low resistance rates against potential pathogens, ability to achieve significant urinary concentration and must be cost effective with minimal adverseeffects. And Nitrofurantoin fulfils all these, it is a cost-effective oral antibiotic with minimal adverse drug effects thus having good patient compliance rates.

## CONCLUSION

- The higher susceptibility of nitrofurantoin shows that it is a promising drug to be used a first line therapy in UTI, thus preventing development of resistance against other antibiotics.
- 57.1% susceptibility in MDR isolates suggests that nitrofurantoin can be used among MDR organisms but its use should be judicious.

Antimicrobial resistance is on the rise due to injudicious use of antibiotics. Hence, it becomes very essential to analyse the causative agents for UTI, study their antimicrobial susceptibility, establish antibiotic policies, and take stringent measures to ensure effectiveness of the same.

**Funding;** No funding sources
**Conflict of interest;** None declared
**Ethical approval;** The approval from the ethical Committee of the Guru Gobind Singh Medical College& Hospital. Faridkot, Punjab was taken before conducting the present study

## REFERENCES

1. Kalra OP, Raizada A. Management issues in urinary tract infection. J Gen Med. 2006;18:16-22.
2. Cunha BA. Nitrofurantoin: an update. ObstetGynecolSurv. 1989;44:399-406.
3. CLSI supplement M100.Wayne, PA: Clinical and Laboratory Standards institute;2020
4. Bakshi R, Walia G, Gupta A. Microbiological profile of UTI along with their antibiotic sensitivity pattern with special reference to Nitrofurantoin. Inter J Med Health Sci. 2015;1;9(9):712-5
5. Lawhale MA, Naikwade R. Recent pattern of drug sensitivity of most commonly isolateduropathogens from Central India. Inter J Res Med Sci. 2017;5(8):3631-6.
6. Preethishree P, Rai R, Kumar KV, Pai KA, Bhat UP. Uropathogens and their antibiotic susceptibility pattern at a tertiary care teaching hospital in Coastal Karnataka, India. Int J CurrMicrobiol App Sci. 2016;5(1):23 31.
7. Prakash D, Saxena RS. Distribution and antimicrobial susceptibility pattern of bacterial pathogens causing urinary tract infection in urban community of meerut city, India. Inter Scholarly Res Notices. 2013;29:1-13.
8. Akram M, Shahid M, Khan AU. Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in JNMC Hospital Aligarh, India. Ann ClinMicrobiol Antimicrobial. 2007;6:4.
9. Ehinmidu JO, Bolaji RO, Adegboye EE. Isolation and antibiotic susceptibility profile of Neisseria gonorrhoeae isolated from urine samples in Zara, Northern Nigeria. J Phytomedicine Therap. 2004;9:20-24.
10. Aboderin OA, Abdu AR, Odetoyin BW, Lamikanra A. Antimicrobial resistance in Escherichia coli strains from urinary tract infections. J National Med Assoc. 2009;101:

1268-73.
11. Behera PK, Tripathy KP, Mishra SN, Panigrahi R. Microbiological profile and antibiotic sensitivity pattern in community acquired Urinary tract infection: study from a tertiary care hospital. J Den Med Sci. 2016;15:17-22.
12. Jain S, Agarwal SG, Jain S, Rukadikar A, Sarwaria M. Study of Nitrofurantoin susceptibility in bacterial isolates from patient of urinary tract infection attending tertiary care centre. Int J CurrMicrobiol App Sci. 2017;6(6):2611-5.
13. Bhattar S, Qureshi S, Aggarwal R, Shingare P, TiggaRA. Nitrofurantoin revisited for uropathogens: easing out therapeutic dilemma for clinicians in 2020;9:M001-3. an upcoming super speciality hospital.NJLM.
14. Pai AK, Rai R, Sanjeev H, Karnaker VK, Krishnaprasad MS. Nitrofurantoin: An alternative therapy for uncomplicated cystitis in the era of antimicrobial resistance. J ClinDiagn. 2011;5:964-6.
15. BHAT PV, Sarkar A. Emergence and control of multidrug resistant organisms in small cities in India: a wake up call. Indian J of Med Sci. 2011;65(8):337-43.
16. De-Francesco MA, Ravizzola G, Peroni L, Negrini R, Manca N. Urinary tract infections in Brescia, Italy: etiology of uropathogens and antimicrobial resistance of common uropathogens. Medisci monitor. 2007;13(6):BR136-44.
17. Tankhiwale SS, Jalgaonkar SV, Ahamad S, Hassani U. Evaluation of extended spectrum beta lactamase in urinary isolates. Indian J Med Res. 2004;120(6):553-6.
18. Singh RM, Devi MU, Singh KL, Singh HL, Keisham C, Singh KH. Evaluation of nitrofurantoin activity against the urinary isolates in the current scenario of antimicrobial resistance. Ann of Trop Med Public Health. 2015.1;8(6):280.
19. Liu HY, Lin HC, Lin YC, Yu SH, Wu WH, Lee YJ. Antimicrobial susceptibilities of urinary extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiellapneumoniae to fosfomycin and nitrofurantoin in a teaching hospital in Taiwan. J of Microbiol, Immun and Infect. 2011;44(5):364-8.