IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 25, Issue 3 Ser. 2 (March. 2026), PP 61-66
www.iosrjournals.org

Time To Change Antibiotic Preference: Evaluation of Sensitivity Profile of Fosfomycin in MDR Gram Negative Organisms: A Study Done on In-Patients in a Tertiary Care Hospital

Iram Rafique[1]*, Sanchita Tuteja[2]*, Monica Chaudhary , Sonal Saxena [3]

1 Hamdard Institute of Medical Sciences and Research (HIMSR) And Associated HAH Centenary Hospital
2 LAL Diagnostic Centre, South Delhi
3 Department of Microbiology, Maulana Azad Medical College, Delhi, India
4 Department of Emergency Microbiology Lab, Lok Nayak Hospital, New Delhi, India
*Corresponding author: Dr. Iram Rafique, Assistant Professor, Department of Microbiology, Hamdard Institute of Medical Sciences and Research (HIMSR) And Associated HAH Centenary Hospital Delhi, India., and
Dr Sanchita Tuteja, Consultant Microbiologist at Lal Diagnostic Centre.

Abstract
Uncomplicated cystitis is a common presentation of urinary tract infections prompting healthcare consultation, with Escherichia coli as the predominant etiological agent followed by Klebsiella spp. and Pseudomonas spp. According to the World Health Organization (WHO) AWaRe classification, oral Fosfomycin is categorized in the "Watch" group and the intravenous formulation in the "Reserve" group for UTIs; although Fosfomycin was previously a highly effective antimicrobial agent, its clinical use declined with the widespread introduction of β-lactams, cephalosporins, and fluoroquinolones.
This prospective study analyzed bacterial isolates from 2,680 urine samples processed in the Department of Emergency Microbiology, Lok Nayak Hospital, Maulana Azad Medical College, New Delhi, between November 2023 and April 2024.Isolates were sub-cultured and streaked for single colonies on cysteine-lactose-electrolyte-deficient (CLED) agar. Vitek-2 was used to identify the organisms with GN ID card. Antimicrobial susceptibility testing of 509 isolates showing significant growth was performed using the Kirby-Bauer disk diffusion method, and results were interpreted according to CLSI guidelines (M100-S23) .
Of the 506 positive samples isolated, the most common uro-pathogen was Escherichia coli, followed by K pneumoniae. Fosfomycin showed a good in vitro sensitivity of approximately 94% in all Gram Negative isolates.
Available evidence supports Fosfomycin as effective oral empirical therapies for uncomplicated E. coli UTIs, including those caused by multidrug-resistant strains

Keywords: *E. coli, Fluoroquinolones, Fosfomycin, Multidrug Resistant (MDR), UTI treatment*

Date of Submission: 05-03-2026 Date of Acceptance: 15-03-2026

I. Introduction

Uncomplicated cystitis is one of the most common clinical presentations of urinary tract infections (UTIs), for which patients seek healthcare attention for both diagnostic and therapeutic purposes. *Escherichia coli* is the most common etiological agent, followed by *Klebsiella* spp. and *Pseudomonas* spp.

In recent years, the emergence of multidrug-resistant (MDR) uropathogens—including extended-spectrum β-lactamase (ESBL)–producing organisms, carbapenem-resistant *Klebsiella pneumoniae*, and multidrug-resistant *Pseudomonas aeruginosa*—has posed a significant therapeutic challenge. MDR organisms are defined as those non-susceptible to at least one agent in three or more antimicrobial categories[1],[2]. In this context, reassessing the susceptibility of older and neglected antibiotics such as fosfomycin represents a promising strategy to address the growing burden of antimicrobial resistance.

Fosfomycin was previously used as a highly effective antimicrobial agent for the treatment of UTIs; however, with the widespread introduction of β-lactams, cephalosporins, and fluoroquinolones, its clinical use declined[3]. According to the World Health Organization (WHO) **AWaRe** classification, oral fosfomycin is

categorized under the "Watch" group, while the intravenous formulation is listed as a "Reserve" antibiotic for UTIs.

Fosfomycin (phosphomycin), first introduced in 1969, is a broad-spectrum, bactericidal antibiotic that inhibits bacterial cell wall synthesis by blocking phosphoenolpyruvate transferase, the first enzyme involved in peptidoglycan synthesis .

We conducted a one-year study to determine the fosfomycin susceptibility pattern of uropathogenic isolates obtained from hospitalized patients with UTIs.

II. Materials And Methods

Study design and isolates

This was a prospective study done in the Department of Emergency Microbiology, Lok Nayak Hospital, Maulana Aazad Medical College, New Delhi, on bacteria isolated from 2680 urine samples collected between November 2023 and April 2024 in the microbiology laboratory. To avoid selection bias, the study protocol required collection of urine samples from all consecutively sampled hospitalised patients who according to clinical referral were believed to have a lower UTI. No clinical data were collected and since the 'study subjects' were the uro-pathogens, not the patients, only limited institutional review was required and obtained.

Sample processing and analysis

Isolates were subcultured and streaked for single colonies on cysteine–lactose–electrolyte-deficient (CLED) agar. Vitek was used to identify the organisms with GN ID card. A total of 509 patients showed significant growth and their antibiotic sensitivity testing was done by Kirby-Bauer disc diffusion testing and interpretation was done according to the CLSI guidelines (M100-S23) [5]. Diffusion susceptibility tests were performed for each isolate using disks containing amoxyclav (20/10 µg), amikacin (30 µg), nitrofurantoin (300 µg), co-trimoxazole (25 µg), ceftriaxone (30 µg), piperacillin/tazobactum (100/10 µg), imipenem (10 µg), fosfomycin (200 µg). American Type Culture Collection (ATCC) E. coli 25922 was used as control strain. Statistical analysis was done by using chi-square test.

III. Result And Observation

During the study period of 6 months, a total of 2680 urine samples were received in the microbiology laboratory from inpatients after fulfilling the inclusion criteria, which were processed following standard guidelines and aseptic microbiological techniques. Of these total samples received, 18.992% (509) samples showed significant growth on culture, 286 (56.118%) were females and 223 (43.81%) were males, whereas 81.007% (2171) samples showed no growth, insignificant growth, mixed growth or candida isolates **(Table 1).**

All the culture-positive urine samples from different inpatient department's, maximum were from Medicine (40.66%), Obstetrics and Gynaecology (28.29%), and Surgery ward (19.64%) followed by Intensive Care Units (ICU's) (6.87%), Paediatrics (2.94%) and Casualty (1.57%) **(Table 2).**

Of the 506 positive samples isolated, the most common uro-pathogen was Escherichia coli, 50.88% (259), followed by K pneumoniae, 32.61% (166), Pseudomonas species 6.67% (34), Proteus mirabilis 3.53% (18), Citrobacter species 3.14% (16), Enterecoccus species 1.96% (10) and Staphylococcus aureus 1.17% (6) (Table 3 and Fig 1).

TABLE 1: DISTRIBUTION OF TOTAL AND CULTURE POSITIVE URINE SAMPLES

DISTRUBUTION OF URINE SAMPLES RECEIVED (N)			
TOTAL URINE SAMPLES	CULTURE POSITIVE		
2680 (100%)	509 (18.99%)	MALES	223
		FEMALES	286

TABLE 2: DEPARTMENTWISE DISTRIBUTION OF UROPATHOGEN ISOLATED

LOCATION	NUMBER OF UROPATHOGENS (N)	PERCENTAGE OF ISOLATES %
MEDICINE	207	40.66%
OBSTETRICS & GYNAECOLOGY	144	28.29%
SURGERY	100	19.64%
ICU	35	6.87%
PAEDIATRICS	15	2.94%
CASUALTY	8	1.57%

TABLE 3: Distribution of Isolated Uropathogens (n = 509)

ISOLATES	NUMBER OF ISOLATES	PERCENTAGE
E. coli	259	50.88%
K. pneumoniae	166	32.61%
P. aeruginosa	34	6.67%
P. mirabilis	18	3.53%,
Citrobacter species	16	3.14%
Enterococcus species	10	1.96%
Staphylococcus aureus	06	1.18%

Fig 1: Distribution of different uro-pathogen

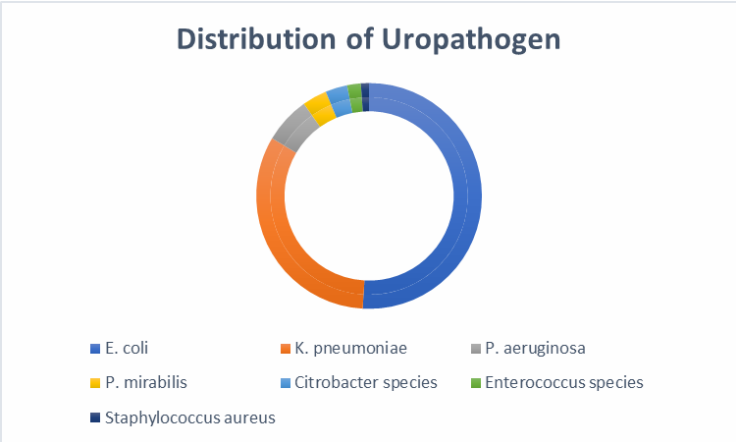
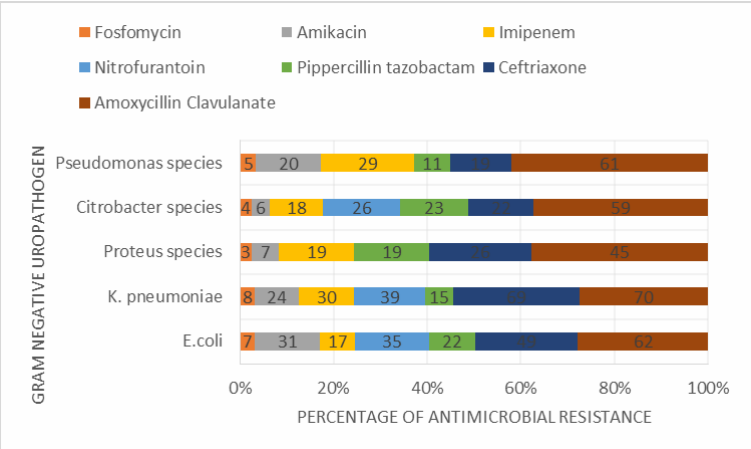


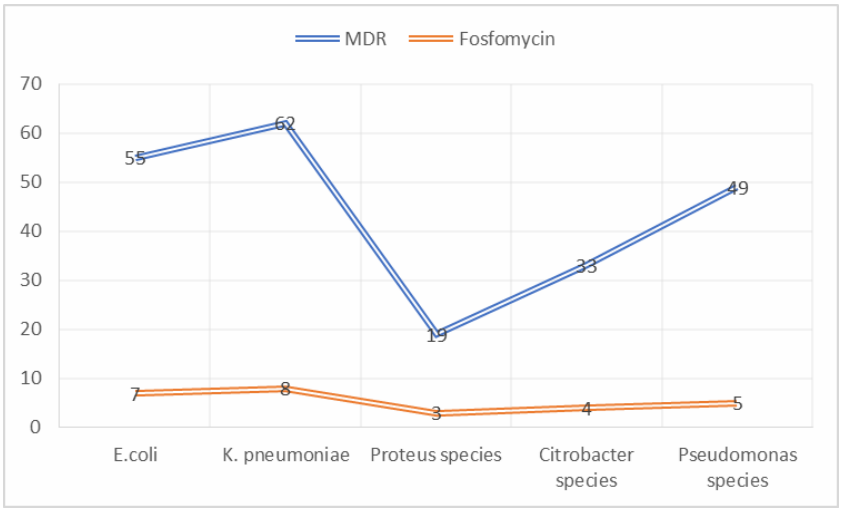
Fig 2: Percentage of Antimicrobial resistance in isolated Gram Negative uropathogens



Among the gram negative isolates, lower rates of resistance were observed for Amikacin in Citrobacter (6%) and Proteus spp (7%) followed by Imipenem in E.coli (17%). Piperacillin tazobactam showed resistance of 18% while Ceftriaxone showed resistance of 37% in all isolates out of which K. pneumoniae, E.coli and Proteus spp showed maximum resistance. Most of the isolates were resistant to Amoxy-clavulanate (59.4%). Fosfomycin showed a good in vitro sensitivity of approximately 94% in all Gram Negative isolates. Nitrofurantoin showed 74% sensitivity in Citrobacter followed by E. coli (65%) and K. pneumoniae (61%) **(Fig 2).**

Among all the isolated uropathogens, 43.6% were multidrug-resistant out of which 94.6% depicted Fosfomycin susceptibility **(Fig 3).**

Fig 3: Comparison of Antimicrobial Resistance to Fosfomycin to Isolated MDR



IV. Discussion

UTI is a common bacterial infection occurring in a large number of patients and women are particularly at greater risk of developing a UTI than men. UTIs continue to be a major public health concern, thus highlighting the urgent need to understand the dynamics of causative uropathogens, their antibiotic resistance profiles, and treatment outcomes to determine informed clinical decision-making. We conducted a prospective study over a period of 6 months to determine the prevalence and antimicrobial resistance patterns of different uropathogens among inpatient admissions in a tertiary care hospital in North India.

A total of 2680 urine samples were received in the microbiology laboratory from inpatients after fulfilling the inclusion criteria, out of which 18.9% (509) samples showed significant growth on culture. Similar findings of 16.9% and 16.69% culture positivity were found in studies conducted in tertiary hospital in North India by Chooramani et al[6] and Das et al[7]**.** Of these total 509 positive samples, 286 (56.118%) were females and 223 (43.81%) were males, indicating a predominance of female population which is in accordance with studies by Marepalli et al[8] and Mohapatra et al[9].

All the culture-positive urine samples were obtained from different inpatient departments. Amongst these, maximum samples were isolated from Medicine (40.66%) followed by Obstetrics and Gynaecology (28.29%), Surgery ward (19.64%), Intensive Care Units (ICU's) (6.87%), Paediatrics (2.94%) and lastly Casualty (1.57%). Hence, the study comprises majorly of adult population with a small proportion of paediatric inpatients.

A total of 509 samples were positive for uropathogens (18.9%) out of 2680 urine specimens processed in the microbiology lab. Gram negative bacilli constituted 96.86% and gram positive cocci constituted 3.14% of the total isolates. Around 90% of the uropathogens belonged to Enterobacterales predominantly constituting E. coli and K. pneumoniae. Similar observations were recorded in previous studies by Mohapatra et al[9] and Tutone et al[10].

Among the enterobacterales, the most prevalent uropathogen was E. coli (259; 50.88%), followed by Klebsiella spp. (166; 32.61%), Proteus spp. (18; 3.53%) and lastly Citrobacter spp. 3.14%). Escherichia coli was the most frequently isolated urinary pathogen in our study which is in concordance to study conducted by Mares et al[11] which also reported a similar finding of 55.34% isolation of E.coli. Chooramani et al[5] also reported 41.9% isolates of E.coli among the studied inpatient department. In contrast to this, a higher rate of E.coli isolates were detected in studies by Tutone et al[10] (72.5%) and Marepalli et al[8] (75%). The lesser percentage of isolates in our study could be attributed to the fact that this study focussed only on inpatient urine isolates while E.coli is also a major cause of Community acquired UTI (CA- UTI) as highlighted in a multicentric-cross-sectional study at the community level targeting patients attending the out-patient department (OPD) patients by Mohapatra et al[9]**.**

K. pneumonia (166; 32.61%) was the second most common uropathogen after E. coli isolated in the present study. In concordance to this, 33.3% Klebsiella spp. were isolated in the study conducted by Diriba et

al[12]. Studies conducted by Mares et al[11] and Marepalli et al[8] reported around 15% isolation of Klebsiella species in the studied patients' samples which is lower than the findings in the present study.

The prevalence of P. aeruginosa, which is considered mostly a pathogen in nosocomial settings was 6.67% and this was in accordance with the findings in the study conducted by Dutta et al[13] (7%).

Gram positive cocci including *Staphylococcus aureus* and Enterococcus spp accounted for 3.14% of the total uropathogens isolated in this study which is similar to the findings in the studies conducted by Marepalli et al[8] (5%) and Dutta et al[13] (5%). Conversely, higher percentages were detected in studies by Mares et al[11] (20.4%) and Chooramani et al[6] (30%).

Antibiotic Resistance

After a massive use of cephalosporins and fluoroquinolones, multidrug-resistant (MDR) isolates have spread dramatically worldwide. As a consequence, the consumption of last-resort i.v drugs, such as carbapenems and Piperacillin tazobactam have increased over the last decade, which in turn is facilitating the dramatic spread of resistance to these drugs as well. These outcomes suggest that finding alternatives for the treatment of MDR uropathogens is an urgent medical need.

In the current study, antibiotic sensitivity patterns of most commonly isolated gram negative bacteria were studied and compared. Figure 2 depicts highest susceptibility to Fosfomycin amongst all the isolated uropathogens followed by Amikacin, Piperacillin tazobactam and Imipenem. Amikacin showed sensitivity of 69% and 76% in E.coli and Klebsiella species respectively which is similar to the findings of a multicentric study across various regions of India by Rizvi et al[9] reflecting 80% susceptibility. Another study by Bhargava et al[10] reported 77% susceptibility for amikacin for E. coli in North India. In contrast to this, Mohapatra et al[8] reported a lower resistance rate of 7.2% for Amikacin.

Piperacillin/tazobactam susceptibility was recorded as 82% overall, whereas amoxicillin/clavulanic acid was active only against 40.6% of the isolates. Similar findings of 81% susceptibility to piperacillin/tazobactam and 47% for amoxicillin/clavulanic acid were also reported by Rizvi et al[9]. Another muticenteric study across India by Mohapatra et al[9] reported similar (75.1%) susceptibility data for piperacillin/tazobactam but much higher susceptibility (74.7%) for amoxicillin/clavulanic acid among Gram-negative uropathogens.

For complicated UTI (high fever, sepsis, vomiting) or severe pyelonephritis, third generation cephalosporins applied intravenously serve as alternative empiric therapy[11]. In the present study, Ceftriaxone showed overall resistance of 37% in all isolates out of which K. pneumoniae (69%), E.coli (49%) and Proteus species (26%) showed maximum resistance. Rizvi et al[9] reported the national susceptibility rate to third-generation cephalosporins as 46.3% which is consistent with the findings of this study. In contrast to this, a significantly higher rate of resistance (83%) was reported by Srivastava et al[17].

Carbapenems are recommended for the treatment of acute uncomplicated pyelonephritis, complicated UTI and urosepsis[16]**.** Our study reported around 22% overall resistance to Imipenem which was in concordance with the findings of study by Srivastava et al[17] (28%). In the multicentre study by Rizvi et al[14], a higher resistance was reported in North India (20-40%) as compared to other regions of the country (5-10%). Bhargava et al[15], likewise, reported low susceptibility (57.4%) for imipenem from Allahabad, North India, testing E. coli from in- and out-patients.

According to the European Association of Urology guidelines (Bonkat et al[18]**.** 2017), nitrofurantoin is recommended for the treatment of uncomplicated cystitis as first-line empiric therapy. The present study reported 33% resistance to nitrofurantoin with maximum resistance seen in Klebsiella spp. Surprisingly, higher rates of resistance were detected as compared to many recent studies conducted across India which reported much lower resistance rates such as Rizvi et al[14] (85%), Marepalli et al[8] (E.coli- 5% and Klebsiella species-22%) and Srivastava et al[17] (E.coli- 8%). This could be attributed to the fact that our facility is a higher tertiary center that received more referrals and the study focussed only on inpatients. These findings were corroborated in the study by Chooramani et al[6] who similarly reported 75.9% sensitivity to Nitrofurantoin in E.coli isolates and 40% sensitivity for Klebsiella spp in inpatients as opposed to 89.2% for E.coli and 52% for Klebsiella spp.

Fosfomycin is an old antibiotic used for the treatment of various bacterial infections. Fosfomycin shows activity against several Enterobacteriaceae species, including those expressing extended-spectrum β-lactamases (ESBL) and metallo-β-lactamases (MBL)[11]. It is recommended as a first-line treatment for uncomplicated UTIs in the European Association of Urology (EAU) and IDSA guidelines on urological infections[10].

In our study, Fosfomycin, with 94.6% overall susceptibility, emerged as the most reliably active antimicrobial against uropathogens. These findings are in accordance with other studies in India, including data by Behera et al[19], where susceptibility rates of 99% and 91.3% were recorded for E. coli and K. pneumoniae, respectively and Rizvi et al[14]**,** who reported 94% national susceptibility to Fosfomycin. Recent international studies by Mares et al[6] and Tutone et al[5] also reported similar susceptibility rates of 96.5% and 96.4% for E.coli isolates.

Among all the isolated uropathogens, 43.6% were multidrug-resistant out of which 94.6% depicted Fosfomycin susceptibility. A review study conducted by Falagas et al[20] included 17 antimicrobial-susceptibility studies accounting for 5057 clinical isolates of Enterobacteriaceae with advanced resistance to antimicrobial drugs; 11 of the 17 studies reported that at least 90% of the isolates were susceptible to fosfomycin. According to the latest IDSA (The Infectious Diseases Society of America) 2024 guidelines[21], oral fosfomycin 3 grams as a single oral dose is an alternative treatment option exclusively for uncomplicated antibiotic resistant E.coli causing cystitis in adults. However, fosfomycin is not suggested for the treatment of pyelonephritis or complicated UTI due to its limited renal parenchymal concentrations. Hence, more studies are needed to evaluate the role of oral fosfomycin for patients with pyelonephritis or complicated UTI, particularly when administered as a multidose regimen and after several days of preferred therapy.

V. Conclusion:

Escherichia coli remains the most common causative uropathogen isolated worldwide. Our study indicates that the use of cephalosporins and amoxicillin/clavulanic acid needs to be restricted for empirical treatment of UTIs due to high resistance rates. Carbapenems can be preserved for highly suspected MDR strains. However, there have been various reports of increasing rates of carbapenem resistance in the last few years. β- lactam/β-lactamase inhibitor combinations, mainly Piperacillin tazobactam and aminoglycosides likely remain the best carbapenem-sparing agents, where ascending infection demands intravenous therapy. The currently available evidence supports the clinical recommendation of fosfomycin and nitrofurantoin as excellent oral empirical choices for uncomplicated UTIs due to E. coli, including MDR cases.

References

[1]. Cassir N, Rolain JM, Brouqui P: A New Strategy To Fight Antimicrobial Resistance: The Revival Of Old Antibiotics. Frontiers In Microbiology. 201420, 5:551.

[2]. Kaase M, Szabados F, Anders A, Gatermann SG: Fosfomycin Susceptibility In Carbapenem-Resistant Enterobacteriaceae From Germany. Journal Of Clinical Microbiology. 2014, 52:1893-7.

[3]. Mayer WA: Commentary In Response To BMC Urology Publication Entitled “Infection-Related Hospitalization Following Ureteroscopic Stone Treatment: Results From A Surgical Collaborative”. BMC Urology. 2021, 6:150.

[4]. Cockerill F, Patel J, Alder J, Bradford P, Dudley M, Eliopoulos G: Performance Standards For Antimicrobial Susceptibility Testing: Twenty-Third Informational Supplement. 100-23.

[5]. Raz R: Fosfomycin: An Old—New Antibiotic. Clinical Microbiology And Infection. 20121, 18:4-7.

[6]. Chooramani G, Jain B, Chauhan PS: Prevalence And Antimicrobial Sensitivity Pattern Of Bacteria Causing Urinary Tract Infection; Study Of A Tertiary Care Hospital In North India. Clinical Epidemiology And Global Health. 2020, 8:890-3.

[7]. Das A, Banerjee T: Prevalence Of Urinary Tract Infections And Susceptibily Pattern Of Uropathogens In Women Of Reproductive Age Group From North India. Journal Of Advances In Medicine. 2015, 4:5-9.

[8]. Marepalli NR, Nadipelli AR, Jain RJ, Parnam LS, Vashyani A, Reddy Marepalli N, Sai Parnam L: Patterns Of Antibiotic Resistance In Urinary Tract Infections: A Retrospective Observational Study. Cureus. 202420, 16:

[9]. Mohapatra S, Panigrahy R, Tak V, JV S, KC S, Chaudhuri S, Pundir S, Kocher D, Gautam H, Sood S, Das BK: Prevalence And Resistance Pattern Of Uropathogens From Community Settings Of Different Regions: An Experience From India. Access Microbiology. 2022, 9:000321.

[10]. Tutone M, Johansen TE, Cai T, Mushtaq S, Livermore DM: Susceptibility And Resistance To Fosfomycin And Other Antimicrobial Agents Among Pathogens Causing Lower Urinary Tract Infections: Findings Of The SURF Study. International Journal Of Antimicrobial Agents. 20221, 59:106574.

[11]. Mareş C, Petca RC, Popescu RI, Petca A, Mulțescu R, Bulai CA, Ene CV, Geavlete PA, Geavlete BF, Jinga V: Update On Urinary Tract Infection Antibiotic Resistance—A Retrospective Study In Females In Conjunction With Clinical Data. Life. 2024, 9:106.

[12]. Diriba, A., Gizaw, S., Alemu, F., Tesfaye, K., Tesfaye, E., Chali, M., & Jobir, G. (2025: Prevalence, Antimicrobial Sensitivity Patterns And Associated Factors Of Urinary Tract Infection Among Patients Attending Nekemte Comprehensive Specialized Hospital, Western Ethiopia, 2024: A Cross-Sectional Study. BMC Infectious Diseases. 25:1-12.

[13]. Dutta, B., Dutta, T., Rima, U. S., Islam, J., Roy, A., Mim, S. I., & Ferdaus, F. (2024: Burden Of Antibiotic- Resistant Urinary Tract Infections In Rural Females: Insights From A Cross-Sectional Study In Bangladesh. Asia Pacific Journal Of Surgical Advances. 1:72-79.

[14]. Rizvi, M., Malhotra, S., Agarwal, J., Siddiqui, A. H., Devi, S., Poojary, A., ... & Livermore, D. M. (2024: Regional Variations In Antimicrobial Susceptibility Of Community-Acquired Uropathogenic Escherichia Coli In India: Findings Of A Multicentric Study Highlighting The Importance Of Local Antibiograms. IJID Regions. 11:100370.

[15]. Bhargava K, Nath G, Bhargava A, Kumari R, Aseri GK, Jain N: Bacterial Profile And Antibiotic Susceptibility Pattern Of Uropathogens Causing Urinary Tract Infection In The Eastern Part Of Northern India. Front Microbiol. 2022, 13:965053. 10.3389/Fmicb.2022.965053

[16]. Kot, B. (2019: Antibiotic Resistance Among Uropathogenic Escherichia Coli. Polish Journal Of Microbiology.68:403.

[17]. Srivastava, N., Verma, S., Singh, M., & Kumar, A. (2024: A Short-Term Study On Statistical Numeration Of Multidrug Resistant Escherichia Coli Isolates Among The Patients With Urinary Tract Infection: Multiple Antimicrobial Resistance Among The E. 119:125.

[18]. Bonkat, G., Pickard, R., & Bartoletti, R: EAU Guidelines On Urological Infections [İnternet]. Arnhem, The Netherlands. European Association Of Urology [Erişim 26. 2020,

[19]. Behera B, Mohanty S, Sahu S, Praharaj AK: In Vitro Activity Of Fosfomycin Against Multidrug-Resistant Urinary And Nonurinary Gram-Negative Isolates. Indian J Crit Care Med. 2018, 22:533-6. 10.4103/Ijccm.IJCCM_67_18

[20]. Falagas, M. E., Kastoris, A. C., Kapaskelis, A. M., & Karageorgopoulos, D. E. (2010: Fosfomycin For The Treatment Of Multidrug-Resistant, Including Extended-Spectrum B-Lactamase Producing, Enterobacteriaceae Infections: A Systematic Review. The. Lancet. 10:43-50.

[21]. Pranita D Tamma, Emily L Heil, Julie Ann Justo: Amy J Mathers, Michael J Satlin, Robert A Bonomo, Infectious Diseases Society Of America 2024 Guidance On The Treatment Of Antimicrobial-Resistant Gram- Negative Infections, Clinical Infectious Diseases. 2024403.