



## TO EXAMINE THE PREVALENT REASONS FOR URINARY TRACT INFECTIONS IN FEMALE PATIENTS VISITING THE HOSPITAL, WITH PARTICULAR ATTENTION TO PREVENTING ANTIBIOTIC RESISTANCE.

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### Abstract

Urinary tract infections (UTIs) are commonly reported by women, both among the general population and in hospital environments. It is estimated that one in three women will face at least one episode of UTI in their lifetime. UTIs are among the most prevalent clinical bacterial infections in women, representing nearly 25% of all infections. Approximately 50–60% of women will experience UTIs at some point in their lives. There has been a rise in resistance among Gram-negative bacteria, particularly over the past six years. This increase is primarily attributed to the proliferation of strains that produce extended-spectrum  $\beta$ -lactamases (ESBLs), such as CTX-M enzymes or AmpC  $\beta$ -lactamases. Many of the isolates producing these enzymes also show resistance to trimethoprim, quinolones, and aminoglycosides, often due to the co-expression of other resistance mechanisms on plasmids. CTX-M-producing *Escherichia coli* is frequently found in the community, and since *E. coli* is one of the most common pathogens causing urinary tract infections (UTIs), the available options for treating these infections are becoming increasingly limited. This study aimed to identify the bacterial profile of urinary tract infections (UTI) in female patients. It was a hospital-based retrospective study conducted at Tertiary care hospital in south-central region of Rajasthan. Clean catch mid-stream urine samples from 500 suspected cases of urinary tract infections were processed following standard protocols. Out of the 500 patients, 88 were identified as culture positive.

**Keywords-** UTI, Antibiotic Resistance, Hospital Visiting Female, *E. coli*

### INTRODUCTION

Urinary tract infections (UTIs) are more prevalent in women compared to men, with a ratio of 8:1. Roughly 50–60% of women experience at least one UTI during their lifetime, and one in three will encounter at least one symptomatic UTI that requires antibiotic treatment by the age of 24. (1–3) A UTI indicates that there are actively multiplying organisms in the urinary tract (4,5), occurring in 3–5% of girls and 1% of boys during childhood, though it is more frequent in boys during their first year of life (6). Annually, around 250 million individuals globally suffer from UTIs. In India, UTIs

are the third leading cause of hospital admissions. It is estimated that approximately 6 million patients seek treatment for urinary tract infections (UTI) globally each year, with around 30,000 being admitted to the wards. UTI is one of the most prevalent serious bacterial infections in infants and children and is often overlooked, likely due to its vague symptoms. It causes distress for the child and worry for the parents. The clinical manifestations vary widely, ranging from the presence of bacteria in the urine without symptoms to severe kidney infections that can be life-threatening. While UTI primarily occurs due to bacteria ascending from the urethra, microorganisms can also reach the urinary tract through the bloodstream or lymphatic system. The ascending pathway is responsible for nearly 95% of UTI occurrences (11). Nonbacterial factors that commonly cause UTIs include hemorrhagic cystitis linked to adenovirus and *Candida* infections in those with weakened immune systems. Bacterial culprits typically involve gram-negative strains like *Escherichia coli*, *Klebsiella*, *Proteus*, *Enterobacter*, *Pseudomonas*, and *Serratia* species, as well as gram-positive organisms such as group B streptococci, *Enterococcus* species, and *Staphylococcus aureus* (12). *Escherichia coli* is the predominant bacterium responsible for UTIs in infants and children. Diagnosing a UTI can be challenging due to vague symptoms and the difficulty in acquiring an uncontaminated urine sample. The latest guidelines released by the American Academy of Pediatrics (1999) indicate that a UTI should be considered in infants and children showing symptoms, and they should undergo a urinalysis and urine culture (13). In recent years, the extensive use of antibiotics has led to a rising occurrence of antibiotic resistance among urinary tract pathogens globally. The rise of antibiotic resistance is becoming more prevalent among these urinary pathogens worldwide. The increase in microbial resistance to antimicrobial agents, particularly in hospitalized patients, necessitates the swift identification of the pathogens involved. Understanding the causes and the patterns of antibiotic sensitivity and resistance among organisms responsible for urinary tract infections is crucial. This study aimed to isolate and identify uropathogens that cause urinary tract infections and to gather information on the resistance patterns of these pathogens. Typically, the urinary tract is free of bacteria, but organisms may originate from the perianal area, potentially resulting in UTIs. Bacteria in the bladder may remain dormant or may cause symptoms such as increased urinary frequency and urgency, with about 8% of women experiencing asymptomatic bacteriuria. If bacteria enter the bloodstream, they can lead to serious complications, including septicemia, shock, and in rare cases, death. The term recurrent urinary tract infection (RUTI) refers to having three UTIs with three positive urine cultures within a 12-month period, or two infections in the preceding six months. UTIs are categorized into six different types. The first type is an uncomplicated infection, which occurs when the urinary tract is normal in terms of structure and function, and there are no underlying conditions that compromise the host's defense mechanisms. The second type is a complicated infection, which happens in an abnormal urinary tract, such as in cases of ureteric obstruction, kidney stones, or vesicoureteric reflux. The third type is an isolated infection, characterized by either being the first episode of UTI or episodes that occur six months apart. Isolated infections impact 25–40% of young females. The fourth type, an unresolved infection, occurs when treatment fails due to bacterial resistance or infection by two different bacteria with similarly limited susceptibilities. The fifth type, reinfection, happens when there is no bacterial growth after treating an infection, but then the same organism reappears two weeks post-therapy, or when a different microorganism is detected at any later time. This type represents 95% of RUTIs in women. Bacterial persistence occurs when treatment is hindered by bacteria accumulating in a site inaccessible to antibiotics, such as in infected stones, urethral diverticula, and infected paraurethral glands. The sixth type, relapse, occurs when the same microorganism causes a UTI within two weeks of treatment; however, distinguishing a reinfection from a relapse can be challenging.

## Materials and Methods

To recognize a UTI, watch for these signs:

- A burning sensation during urination

- A strong or continual urge to urinate, even if there is only a small amount that comes out
- Discomfort or pressure in your lower abdomen or back
- Urine that appears cloudy, dark, bloody, or has an unusual smelling
- Experiencing fatigue or trembling
- Having a fever or experiencing chills (indicating that the infection might have spread to your kidneys)

Urine samples from patients showing the aforementioned symptoms were dispatched to the Microbiology laboratory within 6 hours of collection. The samples were inoculated onto blood agar and MacConkey agar, then incubated at 37°C for 24 hours. All clinical isolates were visually assessed for colony characteristics on the agar media. Those that displayed mucoid colonies underwent further biochemical testing. The biochemical tests performed included urease production, citrate utilization, and sugar fermentation. Tests for sugar fermentation included sucrose, glucose, mannitol, lactose, adonitol, dulcitol, melibiose, and esculin. Additional tests for indole production and H<sub>2</sub>S generation on Triple Sugar Iron agar, as well as oxidase, catalase, and nitrate tests, were also conducted. Furthermore, motility and the organism's growth in potassium cyanide were evaluated. Standard procedures were followed for these biochemical tests [28]. Antibiotic susceptibility testing was performed on all isolates using Mueller-Hinton agar/Nutrient agar through a modified Kirby-Bauer disk diffusion method. Antibiotics tested included azithromycin (AZM), gentamicin (GM), augmentin (AUG), ceftriaxone (CTR), tobramycin (TOB), ceftazidime (OR), cefixime (CFM), piperacillin-tazobactam (PIT), imipenem (IMP), meropenem (MRO), chloramphenicol (C), ciprofloxacin (CIP), ofloxacin (OF), amikacin (AK), gentamicin (HLG), doxycycline (DO), cefoxitin (CX), norfloxacin (NX), nitrofurantoin (NIT), netilmicin (NIT), and cotrimoxazole (COT).

## Result and Conclusion

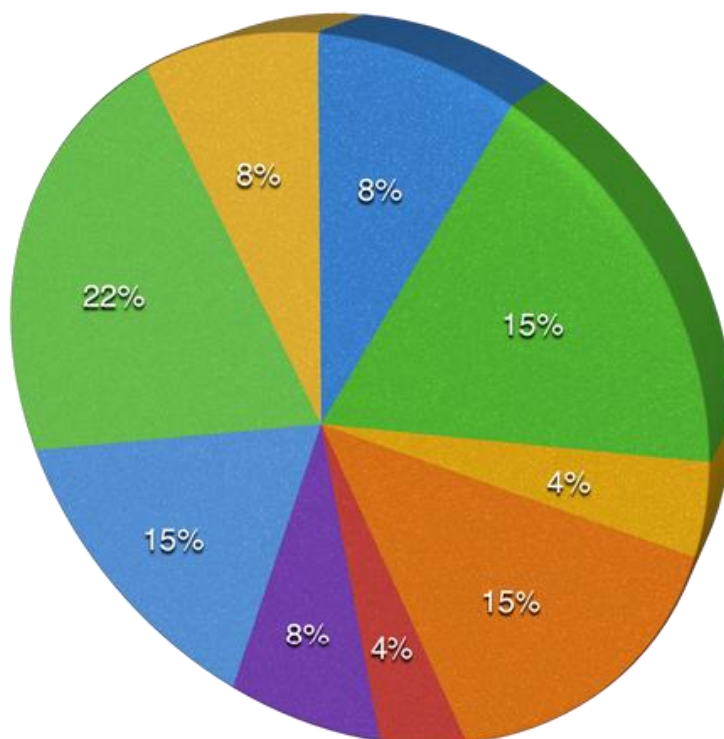
With the increasing understanding of antibiotic resistance and infections associated with healthcare, there is a need to revise guidelines to promote the use of narrow-spectrum agents when possible and to limit the empirical use of broad-spectrum antibiotics. The predominant bacteria causing urinary tract infections in this analysis were *Escherichia coli* and *Enterococcus* spp. Other identified organisms included *Klebsiella* spp., *Proteus* spp., *Pseudomonas* spp., coagulase-negative staphylococcus, *Citrobacter* spp., *Acinetobacter* spp., and *Staphylococcus aureus*. *E. coli* exhibited the highest sensitivity to Ceftriaxone-sulbactam, followed by nitrofurantoin and cotrimoxazole in that order. *Enterococcus* spp. showed the greatest sensitivity to cotrimoxazole and norfloxacin. Our research indicated that clinical isolates of *Klebsiella* spp. were highly responsive to Netilmicin, Tobramycin, Azithromycin, Amikacin, Gentamicin, Norfloxacin, Nitrofurantoin, and Ofloxacin when compared to other antibiotics. The findings also revealed that antibiotics such as Augmentin, Ceftazidime, and Cefixime displayed complete resistance, while Meropenem and Imipenem only demonstrated 11.5% susceptibility, attributed to the presence of *Klebsiella pneumoniae* carbapenemases (KPCs). *Klebsiella* isolates exhibited resistance to cefotaxime, ceftazidime, cefepime, cefoxitin, and ceftriaxone. About 10 isolates were completely resistant to all antibiotics tested, resembling superbugs, which serves as a significant warning for the medical community. Our findings indicate that aminoglycosides such as netilmicin, tobramycin, gentamicin, and amikacin have a considerable effectiveness, with susceptibility rates of 36.5%, 34.6%, 21.1%, and 30.7%, respectively, which remains unsatisfactory and suggests that *Klebsiella* is developing resistance to these drugs as well. According to our study results, *Pseudomonas* was most susceptible to aminoglycosides (Tobramycin-66%, Netilmicin-54%, Gentamicin-54%, Amikacin-45%), followed by fluoroquinolones (Norfloxacin-49%, Ciprofloxacin-18%) and carbapenems (Meropenem-24%, Imipenem-21%). Piperacillin-tazobactam showed nearly 24% susceptibility, whereas Doxycycline, Ceftriaxone, Nitrofurantoin, and Azithromycin had the lowest susceptibility rates. Monitoring patients for potential symptoms before starting antibiotic treatment has been recommended, though

it may not always be feasible in primary care environments. Minimizing the unnecessary prescription of antibiotics for asymptomatic bacteriuria is likely to help curb the development of antimicrobial resistance.

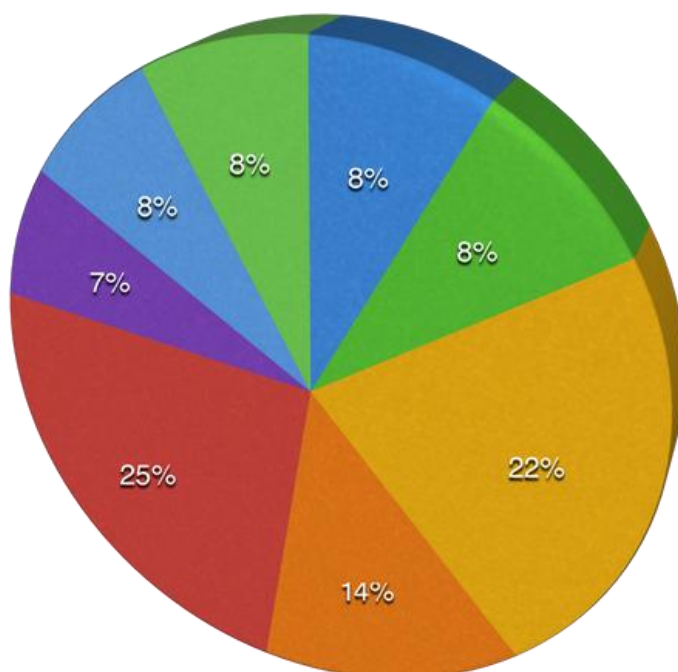
**Figure.1** Distribution of Organisms Isolated from Urine Sample

Antibiotic sensitivity of top three causative agents-

1.E.coli



2.Enterococcus



## Reference

1. Fihn SD. Clinical practice. Acute uncomplicated urinary tract infection in women. *N Engl J Med*. 2003 Jul 17;349(3):259-66. doi: 10.1056/NEJMcp030027. PMID: 12867610.
2. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. *Am J Med*. 2002 Jul 8;113 Suppl 1A:5S-13S. doi: 10.1016/s0002-9343(02)01054-9. PMID: 12113866.
3. Griebeling TL. Urologic diseases in America project: trends in resource use for urinary tract infections in women. *J Urol*. 2005 Apr;173(4):1281-7. doi: 10.1097/01.ju.0000155596.98780.82. PMID: 15758783.
4. Sharma A, Shrestha S, Upadhyay S, Rijal P. Clinical and bacteriological profile of urinary tract infection in children at Nepal Medical College Teaching Hospital. *Nepal Med Coll J*. 2011 Mar;13(1):24-6. PMID: 21991696.
5. Coulthard MG, Lambert HJ, Vernon SJ, Hunter EW, Keir MJ, Matthews JN. Does prompt treatment of urinary tract infection in preschool children prevent renal scarring: mixed retrospective and prospective audits. *Arch Dis Child*. 2014 Apr;99(4):342-7. doi: 10.1136/archdischild-2013-304428. Epub 2013 Dec 18. PMID: 24351607; PMCID: PMC3963540.
6. Muoneke V, Ibekwe M, Ibekwe R. Childhood urinary tract infection in abakaliki: etiological organisms and antibiotic sensitivity pattern. *Ann Med Health Sci Res*. 2012 Jan;2(1):29-32. doi: 10.4103/2141-9248.96933. PMID: 23209987; PMCID: PMC3507128.
7. Muzammil M, Adnan M, Sikandar SM, Waheed MU, Javed N, Ur Rehman MF. Study of Culture and Sensitivity Patterns of Urinary Tract Infections in Patients Presenting with Urinary Symptoms in a Tertiary Care Hospital. *Cureus*. 2020 Feb 16;12(2):e7013. doi: 10.7759/cureus.7013. PMID: 32211249; PMCID: PMC7081730. [SEP]
8. S, Akash & Eregowda, Adarsh. (2014). CLINICO - MICROBIOLOGICAL PROFILE OF UTI IN CHILDREN LESS THAN 10 YEARS IN DEPARTMENT OF PEDIATRICS IN TERTIARY CARE CENTRE. *Journal of Evolution of Medical and Dental Sciences*. 3. 3874-3882. 10.14260/jemds/2014/2370.
9. Cheng CH, Tsai MH, Huang YC, Su LH, Tsau YK, Lin CJ, Chiu CH, Lin TY. Antibiotic resistance patterns of community-acquired urinary tract infections in children with vesicoureteral reflux receiving prophylactic antibiotic therapy. *Pediatrics*. 2008 Dec;122(6):1212-7. doi: 10.1542/peds.2007-2926. PMID: 19047236. [SEP]
10. Rai GK, Upreti HC, Rai SK, Shah KP, Shrestha RM. Causative agents of urinary tract infections in children and their antibiotic sensitivity pattern: a hospital based study. *Nepal Med Coll J*. 2008 Jun;10(2):86-90. PMID: 18828428. [SEP]
11. Cascio S, Chertin B, Yoneda A, Rolle U, Kelleher J, Puri P. Acute renal damage in infants after first urinary tract infection. *Pediatr Nephrol*. 2002 Jul;17(7):503-5. doi: 10.1007/s00467-002-0923-1. Epub 2002 Jun 18. PMID: 12172762. [SEP]
12. Bagga A. Urinary tract infections: evaluation and treatment. *Indian J Pediatr*. 2001 Jul;68 Suppl 3:S40-5. PMID: 11980458.
13. Johnson JR, Russo TA. Molecular epidemiology of extraintestinal pathogenic (uropathogenic) *Escherichia coli*. *Int J Med Microbiol*. 2005 Oct;295(6-7):383-404. doi: 10.1016/j.ijmm.2005.07.005. PMID: 16238015.
14. Kahlmeter G, Poulsen HO. Antimicrobial susceptibility of *Escherichia coli* from community-acquired urinary tract infections in Europe: the ECO·SENS study revisited. *Int J Antimicrob Agents*. 2012 Jan;39(1):45-51. doi: 10.1016/j.ijantimicag.2011.09.013. Epub 2011 Nov 3. PMID: 22055529.
15. Runeheger, R., Kahlmeter, G. 2002. A 10- year study of the consumption of quinolones, trimethoprim and mecillinam 1 in relation to the development of antimicrobial resistance in a large number of species. *Clin. Microbiol. Infection*, 8 (Supplement 1): 64.

16. Pape L, Gunzer F, Ziesing S, Pape A, Offner G, Ehrich JH. Bakterielle Erreger, Resistenzentwicklung und Behandlungsoptionen beim ambulant erworbenen Harnwegsinfekt im Kindesalter [Bacterial pathogens, resistance patterns and treatment options in community acquired pediatric urinary tract infection]. *Klin Padiatr.* 2004 Mar-Apr;216(2):83-6. German. doi: 10.1055/s-2004-823143. PMID: 15106080.
17. Murray, B.E. 1989. Problems and mechanisms of antimicrobial resistance. *Infect. Dis. Clin. North America*, 3(3): 423–439.
18. Alon, U., Davidai, G., Berant, M., Merzbach, D. 1987. Five-year survey of changing patterns of susceptibility of bacterial uropathogens to trimethoprim- sulfamethoxazole and other antimicrobial agents. *Antimicrob. Agents and Chemother.*, 31(1): 126– 128.
19. Akash, S., Adarsh, E. 2014. Clinico- Microbiological Profile of UTI in Children less than 10 years in Department of Pediatrics in Tertiary Care Centre. *J. Evol. Med. Dent. Sci.*, Vol. 3, Issue 15, April 14; Page: 3874– 3882, DOI: 10.14260/jemds/2014/2370.
20. Kacmaz B, Cakir O, Aksoy A, Biri A. Evaluation of rapid urine screening tests to detect asymptomatic bacteriuria in pregnancy. *Jpn J Infect Dis.* 2006 Aug;59(4):261-3. PMID: 16936347.
21. Mohsin R, Siddiqui KM. Recurrent urinary tract infections in females. *J Pak Med Assoc.* 2010;60:55–9.[PubMed]
22. Williams GJ, Lee A, Craig JC. Long-term antibiotics for preventing recurrent urinary tract infection in children. *Cochrane Database Syst Rev.* 2001;(4):CD001534. doi: 10.1002/14651858.CD001534. Update in: *Cochrane Database Syst Rev.* 2006 Jul 19;(3):CD001534. doi: 10.1002/14651858.CD001534.pub2. PMID: 11687116.
23. Gopal M, Northington G, Arya L. Clinical symptoms predictive of recurrent urinary tract infections. *Am J Obstet Gynecol.* 2007;197:74.e1–4. [PubMed]
24. Foster RT., Sr Uncomplicated urinary tract infections in women. *Obstet Gynecol Clin North Am.* 2008;35:235–48. [PubMed] 25.American College of Obstetricians and Gynecologists ACOG Practice Bulletin No. 91: Treatment of urinary tract infections in nonpregnant women. *Obstet Gynecol.* 2008;111:785–94. [PubMed]
25. Al-Badr A, Al-Shaikh G. Recurrent Urinary Tract Infections Management in Women: A review. *Sultan Qaboos Univ Med J.* 2013 Aug;13(3):359-67. doi: 10.12816/0003256. Epub 2013 Jun 25. PMID: 23984019; PMCID: PMC3749018..
26. O'Reilly M. Recurrent urinary tract infection. In: Stanton SL, Dwyer PL, editors. *Urinary Tract Infection in the Female.* London: Martin Dunitz; 2000. pp. 227–40.
27. Cruickshank R. Medical Microbiology 1980, 12th eds. (revised reprint) Edinburg: Churchill Livingstone. 170 – 189.