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# Bacterial Uropathogens and Empirical Treatment in Urinary Tract Infection in a Tertiary Care Institute

**Surinder Kumar\*, Diksha Budhani and Pallavi Sayal**

Department of Microbiology, BPS GMC (W)Khanpur Kalan, Sonepat, India
*\*Corresponding author*

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The aim of study was to determine the bacterial uropathogens and empirical treatment in urinary tract infection in a tertiary institute. The present study was conducted in Department of Microbiology of a tertiary care hospital in North India from July to September 2015.A total of 2200 samples from the outpatient department (OPD) and inpatient department (IPD) were recruited for this study. Urine culture was done by semi-quantitative method. Antibiotic sensitivity was done as per Clinical and Laboratory Standards Institute (CLSI) guidelines. Out of 2200 samples 390 were culture positive (17.7%). The prevalence of UTI was more in females (66.66%). *Escherichia coli* was the predominant causative bacteria (48.41%). Gram negative bacilli isolated showed maximum sensitivity to imipenem, amikacin and nitrofurantoin and Gram positive cocci to vancomycin and linezolid. Imipenem, Amikacin and Nitrofurantoin can be used as empirical treatment in patients with symptoms of UTI.

## Introduction

Urinary tract infection (UTI) is a significant and a serious health affecting problem encountered both in the community and hospital settings each year worldwide (Bano *et al.,* 2012). It is one of the most important cause of morbidity in the world affecting all age groups and involving both genders and usually requires medical treatment (Omoregie *et al.,* 2008).Urinary tract infection is defined as bacteriuria along with urinary symptoms. It may involve only the lower urinary tract or may involve both the upper and lower tract.

The symptoms of UTI includes dysuria, frequency, urgency, and suprapubic tenderness (Zelikovic *et al.,* 1992). Most of the UTI are caused by Gram negative bacteria like *Escherichia coli, Proteus* spp., *Klebsiella* spp., *Pseudomonas aeruginosa, Acinetobacter, Serratia* and *Morganella morgani*. *Enterococcus, Staphylococcus* especially coagulase negative staphylococci and *Streptococcus agalactiae*are the important Gram positive bacteria responsible for UTI (Mohamed Shaaban *et al.,* 2012). Among both outpatients and inpatients, *Escherichia coli*is the most

common urinary tract pathogen, accounting for 75% to 90% of both community acquired and hospital acquired UTI. UTI is much more common in females than males due to anatomical and physiological reasons. The anatomical position of urogenital tract in females is responsible for bacterial infections caused by both internal and external flora (Shanthi, 2012).

The extensive use of antimicrobial agents have invariably led to the development of antibiotic resistance, which, in recent years, has become a significant problem worldwide (Kumar MS *et al.,* 2006). In almost all cases of UTI, empirical antimicrobial treatment initiates before the laboratory results of urine culture are not available. This frequent use of antibiotics often leads to increase in antibiotic resistance in uropathogens. The magnitude of problem of drug resistance in patients with UTI is increasing and varies according to geographical and regional location (Mohamed Shaaban *et al.,* 2012).

This study determines the prevalent uropathogens and their antibiogram according to age and sex at a medicalcollege hospital among outpatient department (OPD) and inpatient department (IPD). In the present scenario, where the antibiotic resistance pattern ischanging, our study aims at outlining the recommendations for empirical treatment of UTI. Moreover, the data would also help authorities to formulate antibiotic prescription policies.

## Materials and Methods

**Sample collection**: The present retrospective study was conducted in the Department of Microbiology at a tertiary level teaching health care facility from July 2015 to Sep 2015. A total of 2200 urine samples were received from both indoor and outdoor patients irrespective of age and gender. Freshly voided, clean-catch midstream urine was collected from each patient into sterile screw-cappeduniversal container. The specimen was labelled and transported to the microbiology laboratory for processing within 2 hours of collection.

## Isolation and Identification

Routine microscopic examination of urine samples was done to look for pus cells, red blood cells and epithelial cells. Semi quantitative urine culture was done using a calibrated loop. A loopful (0.001 ml) of well mixed uncentrifuged urine was inoculated onto the surface of blood agar and MacConkey agar. All plates were then incubated at 37°C aerobically for 24 hrs. The plates were then examined macroscopically for bacterial growth. A significant growth is considered if the number of colony is $>10^5$ colony forming unit (cfu)/ml. The colonies were further processed for identification by Gram staining, oxidase test, catalase test and other standard biochemical tests.

## Antimicrobial Susceptibility Testing

The isolates were subjected to antibiotic susceptibility testing by Kirby-Bauer disc diffusion method using CLSI criteria on Mueller-Hinton agar (MHA) (CLSI document, 2006). Antibiotic discs used in the study were procured from Hi-media® Laboratories, Mumbai, India and from BD diagnostics ® USA. American Type Culture Collection (ATCC) strain viz. *E. coli*. ATCC 25922 was employed as a control strain (Koneman's color Atlas and Textbook of Diagnostic Microbiology, 6th edn). Discs of the following antimicrobial agents, with their disc concentration, in brackets, were used: Amikacin (30μg), Gentamycin(10μg), Ciprofloxacin(5μg), Ceftriaxone (30μg), Ampicillin/sulbactam(10/10mcg), Imipenem

(10µg), Cefoxitin (30g), Cefazolin (30mcg), Nitrofurantoin (300mcg), Cefepime (30µg), Ofloxacin (5mcg), Linezolid (15µg) and Vancomycin (30µg) and Azithromycin (15mcg). The results were read after overnight incubation and compared with standard chart

## Results and Discussion

Out of 2200 samples, 390 urine samples yielded significant growth(17.7%).Out of these 390 isolates, 252(64.61%) isolates were from OPD and 138(35.38%) from IPD.(Table I) Among these 390 isolates, 345(88.46%) were gram negative bacilli and 45(11.54%) were gram positive cocci. *Escherichia coli* was the most commonly isolated urinary pathogen (46.41%) followed by *Enterobacter* spp (15.64%), *Klebsiella* spp (12.82%) and *Staphylococcus aureus* (5.12%). (Table I) Male and female culture positivity was 47.61 % (120/252) and 52.38%(132/252) in OPD and 7.24%(10/138) and 92.75%(128/138) respectively in IPD samples.(Table II) Forty three per cent of all *E.coli* isolates were found to be resistant to ciprofloxacin. Resistance to the aminoglycosides amikacin and gentamicin was low, 6.72 and 13.55 percent respectively. The percentage of isolates of *E. coli* resistant to ampicillin/sulbactam was found to be as much as 57.52 per cent. The rates of resistance among Gram-negative uropathogens to third generation cephalosporins like ceftriaxone were high. Ceftriaxone resistance were seen in 56.48 and 46.6 per cent of all isolates of *E. coli* and *K. pneumoniae.* Resistance to imipenem and nitrofurantoin was comparatively less among isolates of *E.coli* (Table III and IV). Amongst the Gram-positive isolates, *Staphylococcus aureus* was the most commonly isolated organism with 6.6 per

cent resistance to vancomycin. Resistance to ofloxacin, nitrofurantoin and gentamicin was 33.33%, 20% and 13.3% respectively (Table V and VI).

Effective management of patients suffering from bacterial UTIs depends majorly on the type of organisms and selection of an effective antibiotic agent to the organism. Diagnosis of UTIs and its treatment requires a good cooperation between the clinician and the microbiologist. In our study prevalence rate of infection of urinary pathogen was 17.72% which is similar to study by Kattel *et al.,* 2008 in which 26% of urine specimens showed significant bacterial growth. The prevalence of UTI is more in females (66.66%) when comparing males (33.33%). This correlates with other study reported by Adedeji *et al.,* in 2009.Women are more prone to UTIs than men because of short urethra and close proximity to the anus. Among patients with UTI, females were most commonly in the age group between 21-40 years and males were between 41-60 years.

The results were similar to a study by Nerukar in 2012, who reported that 52.16% females were in the age group 21-40 years. He concluded that most uncomplicated urinary tract infections occurs in women who are sexually active, as compared to older women, those who are pregnant, and in men. In older men, the incidence of UTI may increase due to prostatic obstruction or subsequent instrumentation. This was in consistent with the study by Banerjee et al. 2009. *E.coli* was the predominant bacteria (48.41%) found in our study. This result is consistent with reports from other studies Abubakar, 2009, Daza *et al.,* 2001. In our study gram negative bacilli isolated from UTI were sensitive to imipenem, amikacin, nitrofurantoin.

## Table.1 Distribution of Organisms Causing UTI

| Organism | Isolates causing UTI in OPD patients | | Isolates causing UTI in IPD patients | | |
|---|---|---|---|---|---|
| | No. of isolates | Percentage (%) | No. of isolates | Percentage (%) | P-Value |
| *Escherichia coli* | 122 | 48.41 | 59 | 42.75 | 0.284 |
| *Enterobacter spp.* | 35 | 13.88 | 26 | 18.84 | 0.198 |
| *Klebsiella spp.* | 30 | 11.90 | 20 | 14.49 | 0.465 |
| *Staphylococcus.aureus* | 15 | 5.95 | 5 | 3.62 | 0.319 |
| *CONS* | 14 | 5.55 | 11 | 7.97 | 0.473 |
| *Citrobacter spp.* | 12 | 4.76 | 8 | 5.79 | 0.658 |
| *Acinetobacter spp.* | 11 | 4.36 | 1 | 0.72 | 0.047 |
| *Pseudomonas aeruginosa* | 7 | 2.77 | 6 | 4.34 | 0.409 |
| *Proteus spp.* | 5 | 1.98 | 2 | 1.44 | 0.704 |
| *Edwardsiella spp.* | 1 | 0.39 | 0 | 0 | NA |
| **Total** | 252 | | 138 | | |

Legend: P> 0.005 (not significant) and P<0.005 (highly significant), NA= Not Applied, UTI= Urinary Tract Infection, OPD= Outpatient Department, IPD=In Patient Department

## Table.2 Age and Sex Distribution of Culture Positive Patients

| Age in year | OPD | | | | | IPD | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male in no. | (%) | Female in no. | (%) | Mean±SD | Male in no. | (%) | Female in no. | (%) | Mean±SD | P Value |
| 0-10 | 8 | 6.66 | 0 | 0 | 5.625±3.50 | 1 | 10 | 3 | 2.34 | 5.50±1.73 | 0.018 |
| 11-20 | 3 | 2.5 | 15 | 11.36 | 17.88±2.72 | 0 | 0 | 15 | 11.71 | 18.73± 2.76 | 0.233 |
| 21-30 | 10 | 8.33 | 49 | 37.12 | 24.57±2.95 | 5 | 50 | 85 | 66.40 | 24.40± 2.14 | 0.024 |
| 31-40 | 9 | 7.5 | 32 | 24.24 | 36.09±3.33 | 0 | 0 | 7 | 5.46 | 34.85± 3.18 | 0.047 |
| 41-50 | 8 | 6.66 | 24 | 18.18 | 46.59±3.2 | 1 | 10 | 8 | 6.25 | 58.20± 3.32 | 0.654 |
| 51-60 | 21 | 17.5 | 7 | 5.30 | 58.57±2.18 | 2 | 20 | 8 | 6.25 | 58.20±3.01 | 0.006 |
| 61-70 | 29 | 24.16 | 3 | 2.27 | 67.17±3.05 | 0 | 0 | 2 | 1.56 | 65.50± 6.36 | 0.018 |
| 71-80 | 22 | 18.33 | 1 | 0.75 | 75.34±2.75 | 1 | 10 | 0 | 0 | NA | NA |
| >81 | 32 | 26.66 | 2 | 1.51 | 86.63±5.44 | 0 | 0 | 0 | 0 | NA | NA |
| Total | 120 | | 132 | | | 10 | | 128 | | | |

Legend: SD= Standard Deviation, OPD= Outpatient Department, IPD=In Patient Department, NA= Not Applied

**Table.3 In-Vitro Antibiotic Sensitivity in Isolated Gram Negative Uropathogens from OPD**

| Drugs | E.coli (%) | | | Enterobacter spp. (%) | | | Klebsiella spp. (%) | | | Citrobacter spp. (%) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | S | IS | R | S | IS | R | S | IS | R | S | IS | R |
| Gentamicin | 102(86.44) | 0 | 16 (13.55) | 27 (79.41) | 0 | 7 (20.58) | 25(83.33) | 0 | 5(16.66) | 11(91.66) | 0 | 1(8.33) |
| Amikacin | 111(93.27) | 0 | 8(6.72) | 27(87.09) | 0 | 4(12.90) | 26(89.65) | 0 | 3(10.34) | 9(81.81) | 2(18.18) | 0 |
| Ciprofloxacin | 53(46.90) | 11 (9.73) | 49 (43.36) | 18(64.28) | 3(10.71) | 7(25) | 19(63.33) | 2(6.66) | 9(30) | 8(66.66) | 0 | 4(33.33) |
| Imipenem | 114(97.43) | 0 | 3(2.56) | 28(96.55) | 0 | 1(3.44) | 30(100) | 0 | 0 | 8(72.72) | 0 | 3(27.27) |
| Ampicillin/sulbactam | 44(38.93) | 4(3.53) | 65 (57.52) | 15(48.38) | 1(3.22) | 15(48.38) | 12(41.37) | 1(3.44) | 16(55.17) | 9(75) | 0 | 3(25) |
| Ceftriaxone | 47(43.51) | 0 | 61(56.48) | 12(40) | 2(6.66) | 16(53.33) | 16(53.33) | 0 | 14(46.66) | 8(66.66) | 0 | 4(33.33) |
| Cefazolin | 45(41.28) | 0 | 64(58.71) | 9(33.33) | 0 | 18(66.66) | 14(50) | 0 | 14(58) | 6(50) | 0 | 6(50) |
| Nitrofurantoin | 99(94.28) | 2(1.90) | 4(3.80) | 26(76.47) | 3(8.82) | 5(14.70) | 18(69.23) | 1(3.84) | 7(26.92) | 8(66.66) | 0 | 2(16.66) |

Legend: R-Resistant, IS-Intermediate Resistant, S-Sensitive

**Table.4 In-Vitro Antibiotic Sensitivity in Isolated Gram Negative Uropathogens from IPD**

| Drugs | E.coli (%) | | | Enterobacter spp. (%) | | | Klebsiella spp. (%) | | | Citrobacter spp. (%) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | S | IS | R | S | IS | R | S | IS | R | S | IS | R |
| Gentamicin | 35(59.32) | 0 | 24(40.67) | 16964) | 0 | 9(36) | 14(70) | 0 | 6(30) | 2(25) | 0 | 6(75) |
| Amikacin | 32(54.23) | 3(5.08) | 24(40.67) | 14(66.66) | 0 | 7(33.33) | 15(75) | 0 | 5(25) | 3(37.5) | 0 | 5(62.5 |
| Ciprofloxacin | 24(43.63) | 4(7.27) | 27(49.09) | 11(52.38) | 0 | 10(47.61) | 12(60) | 1(5) | 7(35) | 4(57.14) | 0 | 3(42.85) |
| Imipenem | 49(85.96) | 4(7.01) | 4(7.01) | 16(76.19) | 0 | 5(23.80) | 19(95) | 1(5) | 0 | 5(62.5) | 0 | 3(37.5) |
| Ampicillin/sulbactam | 8(13.55) | 1(1.69) | 50(84.74) | 8(38.09) | 0 | 13(61.90) | 9(45) | 2(40) | 9(45) | 2(25) | 0 | 6(75) |
| Ceftriaxone | 11(20.75) | 0 | 42(79.24) | 7(35) | 0 | 13(65) | 6(37.5) | 0 | 10(62.5) | 1(14.28) | 0 | 6(85.71) |
| Cefazolin | 10(17.24) | 0 | 48(82.75) | 5(23.80) | 0 | 16(76.19) | 5(25) | 0 | 15(75) | 2(25) | 0 | 6(75) |
| Nitrofurantoin | 45(84.90) | 1(1.88) | 7(13.20) | 19(73.07) | 0 | 7(26.92) | 14(70) | 2(40) | 4(20) | 4(57.14) | 0 | 3(42.85) |

Legend: R-Resistant, IS-Intermediate Resistant, S-Sensitive

**Table.5 In-Vitro Antibiotic Sensitivity in Isolated Gram Positive Uropathogens from OPD**

| Drugs | *Staphylococcus aureus* | | | CONS | | |
|---|---|---|---|---|---|---|
| | S | IS | R | S | IS | R |
| **Azithromycin** | 9(60) | 0 | 6(40) | 6(46.15) | 0 | 7(53.84) |
| **Vancomycin** | 14(93.33) | 0 | 1(6.66) | 12(92.30) | 0 | 1(7.69) |
| **Linezolid** | 13(86.66) | 2(13.33) | 0 | 11(91.66) | 0 | 1(8.33) |
| **Gentamicin** | 13(86.66) | 0 | 2(13.33) | 13(92.85) | 0 | 1(7.14) |
| **Ofloxacin** | 9(60) | 0 | 5(33.33) | 9(81.81) | 0 | 2(18.18) |
| **Cefoxitin** | 10(66.66) | 0 | 4(26.66) | 7(58.33) | 0 | 5(41.66) |
| **Nitrofurantoin** | 8(53.33) | 0 | 3(20) | 4(66.66) | 0 | 2(33.33) |

Legend: R-Resistant, IS-Intermediate Resistant, S-Sensitive

**Table.6 In-Vitro Antibiotic Sensitivity in Isolated Gram Positive Uropathogens from IPD**

| Drugs | *Staphylococcus aureus* (%) | | | CONS (%) | | |
|---|---|---|---|---|---|---|
| | S | IS | R | S | IS | R |
| **Azithromycin** | 4 (80) | 0 | 1(20) | 2(18.18) | 0 | 9(81.81) |
| **Vancomycin** | 3(60) | 0 | 2(40) | 9(81.81) | 0 | 2(18.18) |
| **Linezolid** | 5(100) | 0 | 0 | 10(90.90) | 0 | 1(9.09%) |
| **Gentamicin** | 5(100) | 0 | 0 | 4(36.36) | 0 | 7(63.63) |
| **Ofloxacin** | 3(60) | 0 | 2(40) | 4(50) | 0 | 4(50) |
| **Cefoxitin** | 1(20) | 0 | 4(80) | 1(11.11) | 0 | 8(88.88) |
| **Nitrofurantoin** | 3(100) | 0 | 0(0) | 6(75) | 0 | 2(25) |

Legend: R-Resistant, IS-Intermediate Resistant, S-Sensitive

The findings are consistent with the previous study conducted by Amit A. Rangari *et al.,* 2015 who also showed that *E. coli* showed high sensitivity to imipenem 98.88% (178), nitrofurantoin 97.22% (175) and amikacin 92.77% (167) but in contrast to our study, Saghir ahmad et al 2014 stated resistance rates for nitrofurantoin (52.5%), gentamicin (70%), amikacin (55%), imipenem (32.5%) among uropathogens.

In present study, a high level of bacterial resistance was seen to Ampicillin/sulbactam and ceftriaxone. The resistance was more in IPD patients when compared with OPD patients. This may be due to more use of these higher antibiotics in hospitals. This result is supported by study by Keith S. Kaye et al 2000.Gram positive cocci were sensitive to Vancomycin and linezolid, similar findings were seen in study by Zahra

Tayebi *et al.,* 2014 who also concluded that Vancomycin seem to be the most effective drugs for treatment of gram positive cocci causing UTI.

The most effective antimicrobial agents in our study in IPD patients were imipenem, nitrofurantoin and gentamicin for Gram negative bacilli and in OPD patients the most effective antibiotics were imipenem, nitrofurantoin and amikacin. However, isolated Gram positive cocci in both IPD and OPD patients were fully sensitive to vancomycin and linezolid.

In conclusion, Urinary tract infections pose a great threat to health and impose an economic and social burden due to the stigma associated with these infections. Gram negative organisms are most commonly isolated organisms in UTI among

which *E.coli* is the biggest culprit. Females are more prone to UTIs. Isolates showed lower resistance rates to Imipenem, Amikacin and Nitrofurantoin. Therefore these can be used as empirical treatment in patients with symptoms of UTI. Routine surveillance and monitoring studies should be conducted to help physician to initiate most effective empirical treatment.

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