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*Original Research Article*

# Trends in Bacterial Spectrum of Community Acquired Urinary Tract Infections (UTIs): A Comparison of Data for Years 2011 & 2014 at a Tertiary Care Teaching Hospital

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## ABSTRACT

**Introduction:** Urinary tract infections are a significant problem both in community and health care settings. Antimicrobial resistance is on the rise even in uropathogens and a cause of major concern.
**Materials and methods:** Records for urine cultures for the years 2011 & 2014 were retrospectively analysed for trends in percentage culture positivity, bacterial spectrum and resistance to commonly used antibiotics. The results were compared between genders, outdoor (OPD) and indoor (IPD) settings, and major disciplines for each year. Any difference was statistically analysed for significance.
**Results and Conclusions:** 7217 and 10067 samples were processed in 2011 and 2014 respectively. Significant increase in culture positivity was detected in 2014 (21%vs 29.6%, $p<0.0001$). There was no significant difference in the frequency of isolation of different bacteria between the years and between outdoor and indoor patients.
E.coli was the commonest pathogen in all comparison groups. Enterococcus was the most common Gram positive coccus in both years. Isolation of Klebsiella spp, was significantly higher in women ($p=0.001$), and other Enterobacteriaeceae in men ($p\leq0.0001$). The isolation of E.coli was significantly higher in outdoor as compared to indoor patients in both years ($p=0.0338$ and $p=0.0002$), while the isolation of Acinetobacter spp. and Candida spp. was significantly higher in indoor patients ($p<0.01$). For E.coli, there was a significant increase in resistance to nitrofurantoin (15.7% vs 22.2%, $p=0.0035$). Resistance to co-amoxiclav and amikacin had increased and resistance to norfloxacin and gentamicin had decreased but not significantly. More resistant uropathogens were recovered from indoor patients ($p<0.01$). Overall resistance was highest in the discipline of medicine, followed by urology and finally obstetrics and gynaecology. Resistance to commonly used urinary antibiotics, mandates the testing of culture and sensitivity of urine for both outpatients and inpatients attending tertiary care settings to decide apt therapy and avoidance of drug resistance.

***Key words:*** Urinary tract infection, Uropathogens, Antimicrobial resistance.

## INTRODUCTION

Urinary tract infections (UTIs) are defined as diseases which are caused by the invasion of the genitourinary tract by microorganisms. Despite the advances in and the wide spread availability of antimicrobials, UTIs continue to be the most common causes of infections in hospitalized patients, accounting for approximately 40% of hospital acquired infections. [1] UTI is described as a bacteriuria with urinary symptoms. [2] UTI can affect lower and sometimes both lower and upper urinary tracts. [3]

It has been estimated that worldwide about 150 million people suffer from asymptomatic and symptomatic UTIs each year. [2] In most developing parts of the world, UTI is amongst the most common health problem occurring both in the community and hospitalized patients. Since the last two to three decades, like other community and hospital acquired bacterial infections, UTIs due to multidrug resistant uropathogens have caused a growing concern worldwide. [4]

Although UTIs occur in both men and women, clinical studies suggest that the overall prevalence of UTI is higher in women. Uncomplicated UTIs in healthy women have an incidence of 50/1000/year. [5] An estimated 50% of women experience at least one episode of UTI at some point in their lifetime and between 20% and 40% of women have recurrent episodes. [6] Approximately 20% of all UTIs occur in men. [7]

In community and hospital settings the etiology of UTIs and the antimicrobial susceptibility of uropathogens have been changing over the years. Factors such as the changing patient population, extensive use and misuse of Antimicrobial agents could all contribute to changes in the bacterial profile of UTI. [8] Organisms tend to develop unpredictable resistance pattern thereby indicating the necessity for constant surveillance of antibiograms to observe trends among uropathogenic isolates. [9]

Hence this retrospective study was undertaken to assess the changing prevalence, gender distribution, pattern of isolation of uropathogens in outdoor patient (OPD) and indoor patients (IPD), disciple wise distribution, and resistance pattern of commonly used antibiotics in UTI treatment. These important changes are essential to identify as they impact empirical treatment and antibiotic stewardship.

## MATERIALS AND METHODS

This retrospective study was carried out in the department of microbiology of a tertiary care teaching hospital in Mumbai. All urine samples received during years 2010 and 2014 were analyzed for trends in percentage culture positivity, bacterial spectrum and resistance to norfloxacin, nitrofurantoin, amoxiclav, amikacin, gentamicin and co-trimoxazole. The results were compared between genders, outdoor (OPD) and indoor (IPD) settings, and major disciplines for each year. Any difference was statistically analyzed for significance. All the samples from pediatric age group (New born- 12 years) were excluded from the study.

**Sample collection and processing**

Urine samples were voided clean-catch midstream specimen, or catheterized samples. Isolation of uropathogens was done using 0.01ml calibrated inoculating wire loop by surface streak method on blood agar and MacConkey's agar. After 18-24 hours of incubation at $37^{o}$C aerobically, colony count of $10^5$ colony forming unit (CFU)/ml was considered as significant and further bacterial identification was done by using standard biochemical tests. [10] Colony count of $10^3$ to $10^4$ CFU /ml was considered as significant in symptomatic patients. Colony count of $10^3$ to $10^4$ CFU /ml was considered insignificant bacteriuria in asymptomatic patients. Isolation of more than two bacterial species was considered as polymicrobial growth.

**Susceptibility testing**

For antibiotic susceptibility testing Kirby Bauer disc diffusion method was used. Performance and interpretation was done as per clinical laboratory standard institute (CLSI) standards. [11,12] The antibiotics tested were nitrofurantoin (FD) (300µg), norfloxacin (NF) (10µg), amikacin (AK) (30µg), gentamicin (GM) (10g), amoxiclav (AMC) (20/10µg) and co-trimoxazole (CO) (1.25/23.75µg) while for the gram positive bacteria, penicillin G (PG) (10µg), vancomycin (VA) (5µg), and high level gentamicin (HLG) (120µg) were added.

**Quality control**

Each lot of media prepared was tested for their ability to support growth of standard strains and sterility. For antibiotic susceptibility testing ATCC *S. aureus* 25923, ATCC *E. coli* 25922 and ATCC *P. aeruginosa* 27853 were used.

***Statistical analysis***

For any difference in parameters analyzed, chi square test was used to determine the significance and p value less the 0.05 was considered statistically significant.

## RESULTS

7217 and 10067 urine samples were processed in 2011 and 2014 respectively. Polymicrobial growth was observed in 4.8% and 8.8%, and insignificant bacteriuria was observed in 4.4% and 4.1% for the year 2011 and 2014 respectively.

Of theses, 2337 and 2754 were men and 4880 and 7313 were women in the two years.

In 2011 and 2014, cultural positivity was 21% and 29.6% respectively. The difference was statistically significant (p<0.0001). Culture positivity was 24.6% and 35% in men and 19.3% and 27.5% in women.

**Table 1: Distribution of uropathogens in OPD and IPD settings**

| Year | 2011 (n=7217) | | 2014 (n =10067) | |
|---|---|---|---|---|
| Samples | Total | % growth | Total | % growth |
| OPD | 1095 | 191(17.4%) | 2533 | 632 (25%) |
| IPD | 6122 | 1324(21.6%) | 7534 | 2345(31.1%) |

Culture positivity in OPD setting (Table 1) was 17.4% and 25% and in IPD setting 21.6% and 31.1% for 2011 and 2014 respectively. The difference in culture positivity in OPD and IPD setting was statistically significant. (p=0.001 in 2011, p=0.002 in 2014).

For both years Gram negative bacilli (GNB) were the predominant pathogens (81.7% in 2011 and 82.3% in 2014). Candida species accounted for five percent of total isolates.

*E.coli* was the commonest pathogen in all comparison groups (gender, OPD/IPD settings, and discipline). *Enterococcus* was the most common Gram positive organism in both years (Table2a, 2b). Isolation of *Klebsiella pneumoniae*, was significantly higher in women (p=0.001) in year 2014, and other Enterobacteriaceae in men (p≤0.0001).

**Table 2(a): Distribution frequency of isolated uropathogens in men and women**

| Year 2011 | | | |
|---|---|---|---|
| Organism | Total (n=1515) | Men (M) | Women (W) |
| E.coli | 627 (41.4%) | 214 | 413 |
| Klebsiella sp | 262 (17.3%) | 101 | 161 |
| Other enterobacteriaceae | 52 (3.4%) | 26 | 26 |
| Acinetobacter | 151 (10%) | 93 | 58 |
| Pseudomonas | 141 (9.3%) | 38 | 103 |
| Other non fermenters | 4 (0.3%) | 2 | 2 |
| S. aureus | 30 (2.0%) | 12 | 18 |
| Enterococcus | 117 (7.7%) | 47 | 70 |
| Other Gram positive | 55 (3.6%) | 11 | 44 |
| Candida | 76 (5%) | 31 | 45 |

**Table 2(b): Distribution frequency of isolated uropathogens in men and women**

| Year 2014 | | | |
|---|---|---|---|
| Organism | Total (n=2977) | Men | Women |
| E.coli | 1250 (42%) | 387 | 863 |
| Klebsiella sp | 590 (19.8%) | 157 | 433 |
| Other enterobacteriaceae | 86 (2.9%) | 45 | 41 |
| Acinetobacter | 270 (9.1%) | 63 | 82 |
| Pseudomonas | 193 (6.5%) | 111 | 207 |
| Other non fermenters | 60 (2%) | 32 | 28 |
| S. aureus | 39 (1.3%) | 8 | 31 |
| Enterococcus | 293 (9.8%) | 85 | 208 |
| Other Gram positive | 35 (1.2%) | 6 | 29 |
| Candida | 161 (5.4%) | 69 | 92 |

**Table 3 (a): Distribution of uropathogens OPD and IPD settings**

| YEAR 2011 | | | | | |
|---|---|---|---|---|---|
| | OPD (n=191) | % | IPD (n=1325) | % | P value |
| E.coli | 93 | 48.7 | 534 | 40.3 | p=0.0338 |
| Klebsiella sp | 32 | 16.8 | 230 | 17.4 | Non significant (NS) |
| Other enterobacteriaceae | 5 | 2.6 | 47 | 3.5 | NS |
| Acinetobacter | 5 | 2.6 | 136 | 10.3 | p=0.0011 |
| Pseudomonas | 15 | 7.9 | 136 | 10.3 | Ns |
| Other non fermenters | 0 | 0.0 | 4 | 0.3 | NS |
| S. aureus | 10 | 5.2 | 21 | 1.6 | NS |
| Enterococcus | 14 | 7.3 | 103 | 7.8 | NS |
| Other Gram positive | 15 | 7.9 | 40 | 3.0 | NS |
| Candida | 2 | 1.0 | 74 | 5.6 | p=0.0039 |

**Table 3 (b): Distribution of uropathogens OPD and IPD settings**

| YEAR 2014 | | | | | |
|---|---|---|---|---|---|
| | OPD (n=632) | % | IPD (n=2345) | % | P value |
| E.coli | 307 | 48.6 | 943 | 40.2 | p=0.0002 |
| Klebsiella sp | 137 | 21.7 | 453 | 19.3 | NS |
| Other enterobacteriaceae | 14 | 2.2 | 72 | 3.1 | NS |
| Acinetobacter | 24 | 3.8 | 246 | 10.5 | p<0.0001 |
| Pseudomonas | 18 | 2.8 | 175 | 7.5 | p<0.0001 |
| Other non fermenters | 6 | 0.9 | 54 | 2.3 | p=0.0366 |
| S. aureus | 19 | 3.0 | 20 | 0.9 | NS |
| Enterococcus | 85 | 13.4 | 208 | 8.9 | p=0.0009 |
| Other Gram positive | 16 | 2.5 | 19 | 0.8 | NS |
| Candida | 6 | 0.9 | 155 | 6.6 | p<0.0001 |

The isolation of *E.coli* was significantly higher in outdoor as compared to indoor patients in both years (p=0.0338 and p=0.0002), while the isolation of *Acinetobacter spp.* and *Candida spp.* was significantly higher in indoor patients (p<0.01) (Table3a, 3b).

Maximum culture positivity was in samples referred from medicine (Table4a, 4b).

Resistance was highest in the discipline of medicine, followed by urology and obstetrics and gynaecology (Table 5a, 5b).

**Table 4(a): Discipline wise distribution of uropathogens**

| 2011 | Obs & Gynaec | Medicine | Urology | Surgical | Allied medicine |
|---|---|---|---|---|---|
| Total samples | 3130 | 1258 | 927 | 605 | 1144 |
| % Growth | 15.8 | 32.8 | 23.5 | 28.3 | 16.2 |
| E. coli | 189 | 169 | 101 | 78 | 80 |
| Klebsiella | 90 | 62 | 39 | 46 | 46 |
| Other GNB | 134 | 89 | 52 | 27 | 25 |
| Enterococcus | 31 | 40 | 13 | 12 | 15 |
| Other GPC | 43 | 17 | 11 | 6 | 11 |
| Candida | 07 | 36 | 2 | 2 | 1 |

**Table 4(b): Discipline wise distribution of uropathogens**

| 2014 | Obs & Gynaec | Medicine | Urology | Surgical | Allied medicine |
|---|---|---|---|---|---|
| Total samples | 5535 | 1141 | 1296 | 510 | 1313 |
| % Growth | 25.4 | 41.2 | 40.7 | 38.8 | 26.8 |
| E. coli | 567 | 213 | 252 | 92 | 138 |
| Klebsiella | 342 | 62 | 100 | 48 | 89 |
| Other GNB | 287 | 77 | 113 | 30 | 32 |
| Enterococcus | 127 | 45 | 43 | 15 | 22 |
| Other GPC | 51 | 06 | 11 | 8 | 13 |
| Candida | 32 | 67 | 9 | 5 | 3 |

**Table 5(a): Discipline wise percentage of resistance (%R)**

| 2011 | Obs & Gynaec | Medicine | Urology | Surgical | Allied medicine |
|---|---|---|---|---|---|
| NF | 62.8 | 86.3 | 76.0 | 58 | 56.3 |
| FD | 12.2 | 21.8 | 17.8 | 11.3 | 10.2 |
| AMC | 87.5 | 96.3 | 83.3 | 84.7 | 81.1 |
| AK | 4.3 | 25.0 | 7.7 | 4.1 | 3.8 |
| GM | 25 | 68.3 | 60.7 | 32.6 | 36.4 |
| CO | 60.2 | 59.8 | 67.4 | 65.6 | 68.0 |

**Table 5(b): Discipline wise percentage of resistance**

| 2014 | Obs & Gynaec | Medicine | Urology | Surgical | Allied medicine |
|---|---|---|---|---|---|
| NF | 62.3 | 96.4 | 82.4 | 62.1 | 60.2 |
| FD | 17.3 | 29.1 | 26.1 | 15.6 | 14.3 |
| AMC | 88.9 | 91.5 | 93.0 | 84.7 | 83.4 |
| AK | 10.2 | 27.0 | 21.7 | 9.3 | 7.8 |
| GM | 36.7 | 69.8 | 51.1 | 35.3 | 33.0 |
| CO | 57.2 | 64.8 | 71.4 | 54.7 | 56.3 |

For *E.coli*, (Table 6) there was a significant increase in resistance to nitrofurantoin over the years (15.7% vs 22.2%, p=0.0035). Resistance to amoxiclav and amikacin had increased while resistance to norfloxacin, gentamicin and co-trimoxazole had decreased but not significantly. More resistant uropathogens were recovered from indoor patients ($p<0.01$) (Table 7).

**Table 6: Percentage resistance in E. coli**

| | YEAR 2011 Total %R | YEAR 2014 Total %R |
|---|---|---|
| NF | 75.9 | 74.9 |
| FD | 15.7 | 22.2 |
| AMC | 92.2 | 92.4 |
| AK | 14.7 | 16.7 |
| GM | 50.9 | 48.8 |
| CO | 62.1 | 59.8 |

**Table 7: Overall percentage of resistance in Gram negative uropathogens**

| | 2011 (Total GNB=1237) | | | 2014 (Total GNB=2449) | | |
|---|---|---|---|---|---|---|
| | Total %R | OPD %R | IPD %R | Total %R | OPD %R | IPD %R |
| NF | 72.3 | 24.5 | 47.8 | 69.6 | 23.1 | 46.5 |
| FD | 42.1 | 16.6 | 25.5 | 48.0 | 15.7 | 32.3 |
| AMC | 92.7 | 48.2 | 44.5 | 93.3 | 38.3 | 55.0 |
| AK | 30.0 | 8.7 | 21.3 | 32.5 | 10.1 | 22.4 |
| GM | 55.2 | 14.8 | 40.4 | 54.1 | 22.5 | 31.6 |
| CO | 67 | 37.5 | 29.5 | 65.5 | 36.6 | 28.9 |

**Table 8: Percentage resistance in Enterococcus**

| | YEAR 2011 Total %R | YEAR 2014 Total %R |
|---|---|---|
| NF | 48.8 | 51.3 |
| PG | 68.5 | 74.3 |
| VA | 3.4 | 2.7 |
| HLG | 76.3 | 72.6 |
| AMC | 79.2 | 80.3 |

## DISCUSSION

The culture positive rate of UTI in this study was found to be 21% in 2011 and 29.6% in 2014. This is higher than that reported by Sood S *et a*l (17.19%), [13] Akram M *et al* (10.86%) [14] and Kashef N *et al* (6.3%), [15] while studies by Prakash D *et a*l (53.82%), [16] Mehta M *et al* (36.68%) [17] and Orrett FA *et al* (49%) [18] have reported higher rate of culture positivity. This disparity of rates may be attributed to the differences in study samples.

Though a greater number of samples were received from women, culture positivity was higher in men (24.6% M: 19.3% W in year 2011; 35% M: 27.5% W in year 2014). This is in contrast with studies by Prakash D *et al* (35.14% M: 73.57% W), [16] Manjunath GN *et al* (41.5 % M: 58.5% W) [19] and Sood S *et al* (37.67% M: 62.42 % W) [13] which showed higher culture positivity in women.

Murugan et al [20] have reported an insignificant difference in gender and age wise distribution of uropathogens. Shafiyabi S *et al* [21] have mentioned the male preponderance where out of 52.2% culture positive samples, E. coli was isolated in 120 (39.6%) samples, of which 78 (65%) were males and 42 (35%) were females.

Das R et al [22] have reported that elderly (61 years or more) males had a higher incidence of UTI (49.23%) compared to the elderly females (21.75%). This is probably because with advancing age, the incidence of UTI increases is men due to prostate enlargement and neurogenic bladder. In the present study an age wise analysis was not carried out. However from clinical notes, it was observed that a majority of women whose urine samples were screened were as a part of routine ante natal care (ANC) check-ups and they were asymptomatic, while men had symptomatic UTI. In a study Pallavi K *et al* [23] reported the gender difference was negligible in the indoor patients. UTI may be more common in females in outdoor set up but hospitalised males may be having some co morbid conditions such as renal stones, obstruction of urinary outflow, surgical procedures, instrumentation, strictures, and immunosuppressive drugs etc which act as risk factors for development of UTI in admitted males.

In this study there was no significant difference in isolation of different bacteria between different comparison groups. *E. coli* was the commonest pathogen in both years followed by *Klebsiella* and other enterobacteriaceae. *Acinetobacter spp*. was the most common amongst non fermenters.

*Enterococcus* was the commonest amongst the Gram positive pathogens.

Moges Tiruneh et al [24] have reported similar findings on urinary isolates for year 2002 and 2012 with *E. coli* as the commonest isolate in both years followed by *Klebsiella* and other Enterobacteriaceae. Amongst Gram negative non fermenters' only *Pseudomonas* was isolated and *S. aureus* was the commonest amongst the Gram positive pathogens. Sood S et al [13] also observed no change in the prevalence of *E. coli* over a two and half year period. Sundvall PD et al [25] compared 2003 to 2012, and reported *E. coli* as the commonest isolate in both years followed by *Klebsiella*. Amongst Gram negative non fermenters' only *Pseudomonas* was isolated, and *Enterococcus* was the commonest amongst the Gram positive pathogens.

The isolation of *E.coli* was significantly higher in outdoor as compared to indoor patients in both years (48.7% OPD vs 40.3% IPD p=0.0338 in year 2011 and 48.6% OPD vs 40.2% IPD p=0.0002 in year 2014). Similar findings have been reported by Mokta K *et al* [26] for isolation of *E. coli* which was 64.6% OPD vs 58.48% IPD, p=0.01. The isolation of *Acinetobacter spp.* and *Candida spp*. was significantly higher in indoor patients (p<0.01). In this context, a hospitalised patient is more likely to be catheterized and therefore more exposed to infections caused by multi-resistant bacteria. Antimicrobial resistance among intensive care unit pathogens is generally increasing, probably due to individual antimicrobial use patterns. [27]

In this study the Gram negative bacteria including *E. coli* showed highest resistance to amoxiclav, followed by norfloxacin, co-trimoxazole, nitrofurantoin, gentamicin and amikacin. A similar pattern has also been reported in various studies from India by Gupta S *et a*l, [28] Kahdri H *et al,* [29] Akram M *et al.* [14]

For *E. coli* there was a significant increase in resistance only to nitrofurantoin over the years (p=0.0035). The study by Grunde N *et al* [30] has also reported higher degree of resistance to nitrofurantoin. This may be due to the fact that nitrofurantoin is an exclusively urinary antibiotic, usually administered orally and is highly concentrated in urine; and therefore is the most common agent for empirical treatment of uncomplicated UTI. The overuse or misuse of this antibiotic may have lead to development of higher resistance

***Limitations:*** No paediatric age group was involved in the study, and age wise analysis was not done.

## CONCLUSION

E.coli continues to be the most common uropathogen. Organisms other than E.coli are more common in indoor settings. Resistance to commonly used urinary antibiotics is high and is ever increasing in outpatient and inpatient settings. The high resistance rates mandate testing of culture and sensitivity of urine for both outpatients and inpatients attending tertiary care settings to decide apt therapy and avoidance of drug resistance.

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