

Urinary Tract Infection among Inpatients: An Insight into Risk Factors and Antimicrobial Resistance

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ABSTRACT

Background: Gram negative organisms are the leading cause of Urinary tract infections with increasingly prevalent antimicrobial resistance. Thereby an observational cross sectional study was conducted to determine the rate of isolation, evaluation of the risk factors and antimicrobial resistance pattern of these organisms. **Methods:** In the prospective analysis, 72 urine samples with significant bacteriuria and culture positive for gram negative bacteria confirmed biochemically, among inpatients were taken into consideration. In addition presence of risk factors was evaluated. Antibiotic susceptibility test was performed using Kirby Bauer's disk diffusion method. **Results:** E. coli accounted for 56.9% followed by Klebsiella species (23.6%). Enterobacter, Pseudomonas and Acinetobacter species were 5-8% prevalent. The risk factors like diabetes mellitus and pregnancy were 20.8% and 13.8%. Other risk factors like recurrent UTI, renal stones, presence of indwelling catheter, smoking, use of OCP/IUCD and post menopausal oestrogen deficiency were 1-7%. The antimicrobial resistance for Enterobacteriaceae group of organisms were 70-90% for cefuroxime, ceftriaxone, cefepime and co-trimoxazole, 50-53% for ciprofloxacin and norfloxacin, 32.2% for ampicillin-sulbactam, 19.3% for nitrofurantoin, 8.1% for amikacin, 20.9% for piperacillin-tazobactam and 14.5% for imipenem. The antimicrobial resistance for Pseudomonas and Acinetobacter species was 50% for ceftazidime and ceftazidime and ceftazidime, 20% for amikacin, piperacillin-tazobactam and imipenem, and 0% for meropenem. **Conclusion:** The present study confers Escherichia coli as the predominant bacterial isolate and diabetes mellitus as the predominant risk factor causing UTI. Amikacin, piperacillin-tazobactam and imipenem are the most sensitive drugs.

Keywords: Antimicrobial resistance, Gram negative pathogens, Urinary tract infection, Risk factors.

INTRODUCTION

One of the most common bacterial diseases that have mired in quotidian medical practice, affecting people of all age groups is Urinary tract infections (UTIs). Gram negative bacteria are the significant cause of UTIs.^[1] Geographical location and a variety of risk factors like old age, sex (females), pregnancy, catheterization, patient undergoing long term treatment, diabetes mellitus, parity, gravidity, hormonal imbalance and immunosuppression play a predominant role in the causation of UTI.^[2] In comparison to the gram positive bacteria, gram negative organisms readily acquire the antimicrobial resistance and the development of newer antibiotics is a more substantial challenge.^[1] The resistance of bacteria causing UTI to commonly prescribed antibiotics is increasing both in developing as well as in developed countries. Over the past few years, the

etiology of UTI and the antibiotic resistance of uropathogens have been changing, both in community and nosocomial infections.^[3,4] Hence this study was conducted to assess the most common pathogens responsible for UTIs and the antimicrobial resistance pattern in a tertiary care hospital. In addition, the risk factors associated with significant bacteriuria have also been evaluated.

MATERIALS AND METHODS

The study was conducted in the Microbiology department of Indira Gandhi Medical College and Research Institute, Puducherry. A prospective analysis was carried out for a period of 2 months in mid 2016. Urine samples of seventy two inpatients, with significant bacteriuria ($>10^5$ cfu/ml) and culture positive for gram negative bacteria, who were willing to participate in the study, were taken into consideration after obtaining the ethical clearance from the Institute Ethics Committee. Gram negative pathogens were confirmed by standard biochemical reactions. [5] Escherichia coli ATCC 25922 and Pseudomonas aeruginosa ATCC 27853 were used as the control strains. Antibiotic susceptibility was performed using the Kirby Bauer disk diffusion

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method according to Clinical and Laboratory Standards Institute (CLSI) guidelines using commercially available disks (Hi-media, Mumbai): cefuroxime (30 µg), ceftriaxone (30 µg), ceftazidime (30 µg), norfloxacin (10 µg), nitrofurantoin (300 µg), ampicillin-sulbactam (10/10 µg), co-trimoxazole (1.25/23.75 µg), ceftazidime (30 µg), ciprofloxacin (5 µg), amikacin (30 µg), piperacillin-tazobactam (100/10 µg) imipenem (10 µg) and meropenem (10 µg).[6] Isolates with intermediate levels of resistance in disk diffusion were included in the percentage of resistant organisms for final analysis.

RESULTS

Among the 72 cases, majority of patients were females (58.3%) with a male to female ratio of 1:1.4. UTI occurred in all age groups. The highest isolation rate of 45.8% was found in the 19-50 years age group, with female preponderance [Table 1]. Out of the 72 gram negative urinary pathogens, *E. coli* were 41 (56.9%), *Klebsiella* species were 17 (23.6%), *Enterobacter* species were 4 (5.6%), *Pseudomonas* species were 4 (5.6%), and *Acinetobacter* species were 6 (8.3%) [Table 2].

Table 1: Age-wise and Sex-wise distribution of uropathogens.

| Age (years) | No. of Male (%) | No. of Female (%) | Total (%) |
|-------------|-----------------|-------------------|-----------|
| 0-18 | 13 | 14 | 27(37.5%) |
| 19-50 | 10 | 23 | 33(45.8%) |
| >50 | 7 | 5 | 12(16.7%) |
| Total | 30(41.7%) | 42 (58.3%) | 72(100%) |

Table 2: Bacterial isolates contributing to Urinary tract infection.

| Gram Negative Organisms | Rate of isolation in number (%) |
|---|---------------------------------|
| <i>E. coli</i> | 41(56.9%) |
| <i>Klebsiella</i> species | 17(23.6%) |
| <i>Enterobacter</i> species | 4(5.6%) |
| Enterobacteriaceae (<i>E. coli</i> + <i>Klebsiella</i> spp+ <i>Enterobacter</i> spp) | 62(86.1%) |
| <i>Pseudomonas</i> species | 4(5.6%) |
| <i>Acinetobacter</i> species | 6 (8.3%) |
| Non fermentors (<i>Pseudomonas</i> spp + <i>Acinetobacter</i> spp) | 10 (13.9%) |

Table 3: Resistance pattern of bacterial isolates

| Gram Negative Organisms | Cxm (%) | Ctr (%) | Caz (%) | Nx (%) | Nit (%) | As (%) | Cot (%) | Cpm (%) | Cip (%) | Ak (%) | Pit (%) | Ipm (%) | Mpm |
|---|---------|---------|---------|--------|---------|--------|---------|---------|---------|--------|---------|---------|-----|
| <i>E. coli</i> (n=41) | 87.8 | 75.6 | NA | 60.9 | 9.75 | 34.1 | 78 | 78 | 46.3 | 7.3 | 21.9 | 19.5 | NA |
| <i>Klebsiella</i> species (n=17) | 88.2 | 70.5 | NA | 41.1 | 41.1 | 35.2 | 64.7 | 64.7 | 35.2 | 11.7 | 17.6 | 5.8 | NA |
| <i>Enterobacter</i> species (n= 4) | 100 | 50 | NA | 75 | 75 | 0 | 100 | 50 | 25 | 0 | 25 | 0 | NA |
| Enterobacteriaceae (<i>E. coli</i> + <i>Klebsiella</i> spp+ <i>Enterobacter</i> spp)(n=62) | 88.7 | 72.5 | NA | 53.2 | 19.3 | 32.2 | 75.8 | 72.5 | 50 | 8.1 | 20.9 | 14.5 | NA |
| <i>Pseudomonas</i> species (n=4) | NA | NA | 25 | NA | NA | NA | NA | 25 | NA | 25 | 25 | 25 | 0 |
| <i>Acinetobacter</i> species (n=6) | NA | NA | 67 | NA | NA | NA | NA | 67 | NA | 17 | 17 | 17 | 0 |
| Non fermentors (<i>Pseudomonas</i> spp + <i>Acinetobacter</i> spp)(n=10) | NA | NA | 50 | NA | NA | NA | NA | 50 | NA | 20 | 20 | 20 | 0 |

Cxm: Cefuroxime, Ctr: Ceftriaxone, Caz: Ceftazidime, Nx: Norfloxacin, Nit: Nitrofurantoin, As: Ampicillin sulbactam, Cot: Co-trimoxazole, Cpm: Ceftazidime, Cip: Ciprofloxacin, Ak: Amikacin, Pit: Piperacillin-tazobactam Ipm: Imipenem and Mpm: Meropenem
NA – Not Applicable

The risk factors like diabetes mellitus were 15 (20.8%), recurrent UTI were 4 (5.5%), renal stones were 1(1.3%), presence of indwelling catheter were 3 (4.1%), smoking were 4 (5.5%), pregnancy were 10 (13.8%), use of OCP/IUCD were 3 (4.1%) and post menopausal oestrogen deficiency were 5 (6.9%) [Figure 1]. The antimicrobial resistance for Enterobacteriaceae group of organisms were 88.7% for cefuroxime, 72.5% for ceftriaxone, 53.2% for norfloxacin, 19.3% for nitrofurantoin, 32.2% for

ampicillin-sulbactam, 75.8% for co-trimoxazole, 72.5% for ceftazidime, 50% for ciprofloxacin, 8.1% for amikacin, 20.9% for piperacillin-tazobactam and 14.5% for imipenem. The antimicrobial resistance for *Pseudomonas* and *Acinetobacter* species was 50% for ceftazidime and ceftazidime, 20% for amikacin, piperacillin-tazobactam and imipenem, and 0% for meropenem [Table 3].

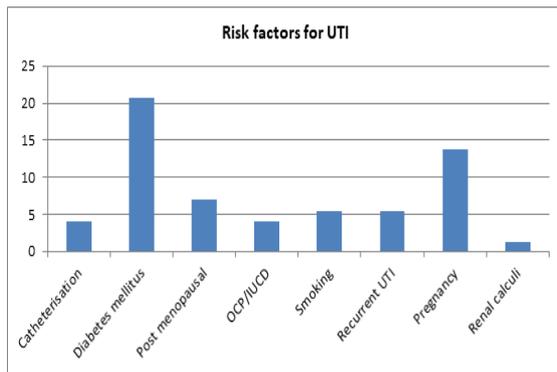


Figure 1: Distribution of risk factors for UTI in percentage

DISCUSSION

The cardinal issue with UTI is that it is a major public health problem in India.^[2] Being the most common infectious disease, urinary tract infections occurs both in the community as well as in the health care settings.^[7] Among the 72 cases, majority were females and most of them belonged to the age group of 19-50 years [Table 1]. This is in concordance with all other studies which attribute the reason to be the shorter length of the urethra, sexual intercourse and lack of post-coital voiding and use of spermicide which in turn promote colonization of the periurethral area with coliform bacteria in females.^[8,9]

Among the 72 gram negative uropathogens, *Escherichia coli* were the predominant isolate accounting for 56.9% of the cases followed by *Klebsiella* species (23.6%). All other gram negative pathogens were found only in small proportions (5-8%). The Enterobacteriaceae group of organisms were isolated in 86.1% of the cases while *Pseudomonas* and *Acinetobacter* species were isolated from 13.9% of the patients [Table 2]. This is partly in concordance with the study conducted by Haque *R et al*, in which *Escherichia coli* were the predominant isolate accounting for 59.30% followed by *Klebsiella* species (5.53%) and all others in small proportions (1-2%) including *Pseudomonas* species among the gram negative uropathogens.^[10] Similar results were obtained from other studies done in India and abroad.^[11,12]

In the study group of 72 inpatients, 37 (51.39%) patients did not present with any risk factors and are said to have uncomplicated UTI. The remaining 35 (48.61%) patients had either single or multiple risk factors [Figure 1]. Diabetes mellitus was the predominant risk factor (20.8%). The presence of glycosuria, neutrophil dysfunction and adherence of the bacteria to uroepithelial cells are the likely mechanisms that contribute to the increased frequency of UTIs in diabetic patients.^[13] Factors that were found to enhance the risk for UTI among the 15 diabetic patients, were age, sex (female) and

metabolic control. Four (26.6%) were post menopausal women, 3 (20%) were pregnant females who gave history of pregnancy induced diabetes mellitus and 1 (6.6%) female patient had recurrent UTI. However, the remaining 7 (46.6%) diabetic patients did not present with any other associated factors.

Following diabetes mellitus, pregnancy (13.8%) was the next risk factor. During pregnancy, risk of UTI has increased with multigravidity, number of intercourses (>3 times) per week and lack of personal hygiene like not voiding after coitus. This was in concordance with a study conducted by Thakre *S et al*.^[14] In a case control study conducted by Dienye *PO et al*, it was found that, there was about a three-fold increased risk of the development of urinary tract infection amongst patients who were on contraceptives compared to non-users. In our study, 3 (4.1%) were using OCP/IUCD.^[15] Estrogen stimulates the proliferation of lactobacillus in the vaginal epithelium, reduces pH, and avoids vaginal colonization of pathogenic bacteria.^[16] Lack of oestrogen, i.e post menopausal oestrogen deficiency has resulted in 5 (6.9%) of the UTI cases in our set up.

Recurrent UTIs are mainly caused by reinfection of the same pathogen and abnormalities of the renal tract.^[17] In the present study, recurrent UTI occurred in 4 patients (5.5%). Two were adults and two were from paediatric age group. Among the adult patients, one was diabetic and other was suffering from chronic kidney disease. Among the paediatric patients, one child presented with haematuria and renal stones while another child was diagnosed as nephrotic syndrome. Patients who are hospitalized for a long term with indwelling urinary catheters are prone to nosocomial infections.^[2] In our study, 3 patients (4.1%) had indwelling catheter. Smoking increases the risk of albuminuria and renal functional deterioration.^[18] In the present study, 4 (5.5%) were found to be smokers.

The alteration of the normal microbial flora of the reproductive tract and gastrointestinal tract occurs in patients who are commonly treated with antibiotics, especially those suffering from a symptomatic urinary tract infection and these treatments, in turn can lead to the development of multidrug-resistant microorganisms.^[19] The antimicrobial resistance for *Escherichia coli* were higher for Cephalosporins (75-88%), fluoroquinolones (46-61%), cotrimoxazole (78%) and ampicillin-sulbactam (34.1%) [Table 3]. This is in concordance with other studies conducted by Haque *R et al*, Ahmed *SM et al* and Rahaman *F et al*.^[10,11,20] The possible reason could be the wide spread use and over the counter availability of the above drugs. However, in a study by Yeshwondm *M.G*, cotrimoxazole showed only 22.6% of resistance in contrast to our study which showed 78% of resistance.^[12] This may be due to the geographical variation and the local prescribing

practice. The resistance was much lower for nitrofurantoin (9.75%), amikacin (7.3%), piperacillin-tazobactam (21.9%) and imipenem (19.5%). Similar trends were reported by other studies conducted by Ahmed SM *et al*, Rahaman F *et al* and Mandal J *et al*.^[11,20,21]

The resistance pattern of *Klebsiella* spp on comparison to *Escherichia coli* was lower in most of the antibiotics. It was slightly higher for cefuroxime and amikacin but notably higher for nitrofurantoin. *Escherichia coli* showed only 9.75% of resistance to nitrofurantoin while *Klebsiella* spp showed 41.1% of resistance [Table 3]. This was noted in other studies too, thereby rendering Nitrofurantoin as the drug of choice for UTI due to *Escherichia coli* but not for *Klebsiella* spp.^[10-12] *Enterobacter* spp (n=4) exhibited high level of resistance to all antibiotics (50-100%) except for ciprofloxacin and piperazillin tazobactam (25%).

The antimicrobial resistance for Enterobacteriaceae group of organisms were higher for cephalosporins (70-90%), fluoroquinolones (50-53%), cotrimoxazole (75.8%) and ampicillin-sulbactam (32.2%). But, the resistance was much lower for nitrofurantoin (19.3%), amikacin (8.1%), piperacillin-tazobactam (20.9%) and imipenem (19.5%), thus rendering them as drug of choice for UTI.

For the gram negative non fermentors namely *Pseudomonas* and *Acinetobacter* species, the antimicrobial resistance was 50% for ceftazidime and ceftazidime, 20% for amikacin, piperacillin-tazobactam and imipenem, and 0% for meropenem, [Table 3] which correlates well with the studies conducted by Rahaman F *et al* and Mandal J *et al*.^[20,21]

Both for Enterobacteriaceae group and non fermentor group of organisms amikacin, piperacillin-tazobactam and imipenem are still the promising drugs.

CONCLUSION

E. coli remains the predominant bacterial isolate causing UTI. Nitrofurantoin, an oral antibiotic is potent in case of *E. coli*. Antimicrobial resistance is on the increase for the commonly prescribed antibiotics. Justified use of the drugs, can control the spurt of resistance. Amikacin, piperacillin tazobactam and imipenem has showed low level of resistance and can be considered for complicated Urinary tract infections. Hygienic practices including sexual behaviour in females will definitely reduce the incidence of UTI in the vulnerable female population.

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