Original Article

Prevalence of Urinary Tract Infections and Susceptibily Pattern of Uropathogens in Women of Reproductive age Group from North India

Arghya Das and Tuhina Banerjee

Department of Microbiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India

ABSTRACT

Urinary tract infections (UTI) are one of the most common infections causing morbidity in community and health care setup. Women in reproductive age group (15-49 yrs) are more prone to UTI. This study was undertaken to determine the prevalence of UTI, the microbial etiology and the antibiotic susceptibility profile of the isolates from women with symptomatic UTI in a tertiary care centre in north India. Clean catch midstream urine were processed by semi-quantitative culture and isolates identified by standard biochemical tests. Antibiotic sensitivity was performed by Kirby-Bauer disc diffusion test and data analyzed from January 2013 to September 2015. A total of 3141 cases were studied. Prevalence of UTI varied from 16.69% in 2013, 9.77% in 2014 to 8.45% in 2015. Majority of UTI occurred in the age group 21-30 yrs. E.coli was the commonest isolate causing UTI followed by *E.faecalis*. *E.coli* showed considerable resistance to ampicillin and fluoroquinolones but performed better against nitrofurantoin with greater than 90% susceptibility. Constant survey of uropathogens and their susceptibility profile is essential for deciding on the empirical treatment of UTI.

Keywords: Urinary tract infections, Microbial etiology, Antibiotic sensitivity, Fluoroquinolones, Uropathogens

It has been a well known fact that urinary tract infections (UTI) are one of the most common disease that affect all age groups ranging from neonates to the geriatric population. About 150 million people worldwide are diagnosed with UTI each year [1, 2], accounting for one-fifth of emergency visits in outpatient departments (OPD) [3]. Additionally, about 40-50% of women in the reproductive age group (15-49 yrs) have a history of at least a single episode of UTI in their lifetime [1].

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The microbiology of UTI has been almost consistent for years as evidenced by a number of studies. However, there have been subsequent changes in the characteristics of microorganisms, particularly due to the global problem of antimicrobial resistance [4]. As prevalence and etiology of UTI depend on various underlying factors, women in reproductive age group pose a vulnerable section due to several anatomical, physiological and metabolic factors [4]. In several

Address for correspondence

Tuhina Banerjee: Assistant Professor Department of Microbiology, Institute of Medical Science, Banaras Hindu Uni., Varanasi, India

E-mail: drtuhina@yahoo.com

circumstances, empirical treatment is often required for treating acute complicated UTI especially in women. For this, complete knowledge of current trend of microorganisms and their drug susceptibility pattern is necessary. With this background, the following study was undertaken to determine the status of UTI in women of the reproductive age group (15-49 yrs) over a period of nearly 3 years in a tertiary care hospital in north India.

Material and Methods

Study site and duration: The present study was conducted in the department of Microbiology and associated 1200 bedded university hospital in Varanasi in north India. The study was conducted from January 2013 to September 2015. Women in age group 15-49 yrs attending the Gynaecology OPD with signs and symptoms of UTI were considered for the study.

Collection and processing of samples: Mid-stream clean catch urine was collected from all patients suspected of UTI. Urine culture was done on cysteine lactose electrolyte deficient medium (CLED agar) (Hi-Media, India) by semiquantitative method [5]. Significant growth was considered in case of colony count amounting to greater than 10^5 cfu/ml as per standard [6]. For cases with lower colony count, a repeat urine culture with detail history and clinical presentation was performed. Symptomatic cases with a lower count were also considered for the study. Asymptomatic bacteriuria in pregnant cases was not included in this study.

Isolates were identified by Gram stain, motility testing and range of biochemical tests based on standard protocol [7, 8]. Yeast cells isolated from samples were further tested with India ink staining and germ tube formation [9].

Antimicrobial susceptibility testing: This was done by the modified Kirby Bauer disc diffusion method following the clinical laboratory standards institute (CLSI) guidelines [10]. All Enterobacteriaceae were tested against first line agents: ampicillin (10μg), cephalexin (30μg), gentamicin (10μg), nitrofurantoin (300μg), trimethoprim-sulphamethoxazole (co-trimoxazole) (1.25-23.75μg), norfloxacin (10μg) and ofloxacin (5μg); *Enterococcus* spp. against ampicillin (10μg), vancomycin (30μg), nitrofurantoin (300μg), ciprofloxacin (5μg), norfloxacin(10μg) and high level gentamicin (120μg); *Pseudomonas aeruginosa* against piperacillin (10μg), amikacin (30μg), gentamicin (10μg), ceftazidime (30μg) ofloxacin (5μg) and ciprofloxacin (5μg). *Acinetobacter* spp against gentamicin (10μg), ceftazidime (30μg), levofloxacin (5μg), ciprofloxacin (5μg), imipenem (10μg) and meropenem (10μg).

Second line antibiotics were tested only for organisms in those isolates resistant to all 1st line antimicrobials or on request by the physician. These included amikacin (30μg), imipenem (10μg), ertapenem (10μg), cefoperazone-sulbactam (75μg), cefepime (30μg) and piperacillin tazobactam (100/10μg) for all Enterobacteriaceae; imipenem (10μg), meropenem (10μg), cefepime (30μg) and piperacillin tazobactam (100/10μg) for *P.aeruginosa*.

E.coli ATCC 25922, *E.coli* ATCC 35218 and *P.aeruginosa* ATCC 27853 were used as controls.

Results and Discussion

A total of 3141 cases of symptomatic UTI in age group 15-49 years were studied in three years. Among these, no infectious etiology was found in 2762 (87.93%) cases by routine diagnostic methodology followed in this study and was reported 'sterile'. Prevalence of UTI varied from 16.69% in 2013, 9.77% in 2014 to 8.45 in 2015 as shown in Fig 1.

Yearwise distribution of the cases showed no seasonal variation in the study period. However, peak cases occurred in the hot humid summer months of April to September in all the three years (Fig 2).

Majority of UTI occurred in the age group 21-30 yrs in all the three years followed by 31-40 yrs (Fig 3).

E.coli was the commonest isolate causing UTI followed by *E.faecalis*. *Klebsiella* species along with other members of Enterobacteriaceae were also isolated. Among the non-fermenters, *Pseudomonas* and *Acinetobacter* species were isolated, though in less number. *Candida* spp also accounted for 3.94% and 8.16% UTI in 2013 and 2014 respectively in the studied population as shown in Table 1.

Antimicrobial profile of the major Gram negative isolate (*E.coli*) and Gram positive (*E.faecalis*) isolate was studied and has been mentioned in Table 2 and 3 respectively. As the number of isolates from other species was low in number, their susceptibility has not been discussed. *E.coli* showed considerable resistance to ampicillin and fluoroquinolones with susceptibilities ranging from 20-25% and 23-33% respectively. However, gentamicin susceptibility was seen to increase in the study period, thus providing a better option. It is worth mentioning that isolates of *E.coli* performed considerably better against nitrofurantoin with greater than 90% susceptibility.

In this study period, of the 228 total isolates of *E.coli* studied, 8 isolates were resistant to all the first line drugs shown in Table 2. These isolates were also resistant to ceftriaxone (8, 100%), cefepime (8, 100%), ertapenem (3/8, 37.5%) but were susceptible to piperacillin-tazobactum (100%), imipenem (100%) and amikacin (100%).

Similarly, isolates of *E.faecalis* were noted for their fluoroquinolone resistance, thus limiting use of this group of drug in treatment of UTI. However, high level gentamicin resistant was not very high. Ampicillin and gentamicin could be used to treat synergistically in enterococcal infections in our case.

UTI are a major health problem affecting both men and women, though clinical studies suggest their occurrence more in women [11]. The extensive and inappropriate use of antibiotics has invariably resulted in the worldwide dissemination of antibiotic resistance thus making it a global cause of concern [12]. To ensure proper empirical treatment, knowledge of the organisms that cause UTI and their antibiotic profile is mandatory along with their constant survey.

Global surveillance data has revealed the increase in fluoroquinolone resistance in both community and healthcare associated UTI, with major foci in some parts of the world including Asia [13]. Because fluoroquinolone resistance is often directly linked with fluoroquinolone use, the high fluoroquinolone resistance revealed in this study was expected in line with the status report of Global Antimicrobial Resistance Partnership (GARP) [14]. The mentioned report has shown that quinolone antibiotics are the highest sold ones in the country. As a result, even if Infectious Disease Society of America (IDSA) recommends ciprofloxacin for treatment of UTI owing to increasing resistance to co-trimoxazole [15], fluoroquinolones are not better option for any group of organism in our setup.

Nitrofurantoin has been in clinical use for decades with consistently low level of resistance against most of the organisms implicated in UTI [3]. Similar finding was also seen in our study. The advantage with nitrofurantoin is that it is both bactericidal and bacteriostatic without any cross resistance with other antibiotics. Consequently, development of resistance or resistant mutants is comparatively slower [16, 17]. However, nitrofurantoin has certain limitation, especially on our study population. Nitrofurantoin may cause major birth defects and should be cautiously used especially in women of reproductive age group [18].

Despite emergence of newer pathogens in relation to UTI, *E.coli* remains the predominant causative agent. *Enterococcus* spp on the other hand, has emerged as the secondmost or thirdmost common cause in most of the recent studies like ours [2,19]. In the mentioned studies, however, in contrast to ours, *Klebsiella* spp has been isolated in greater number than enterococcus. Studies elsewhere have also suggested an increase in enterococcal UTI along with emergence of *Candida* spp.[20]. The easy dissemination of drug resistance in enterococci via mobile genetic elements [21] could account for the increase in prevalence of enterococcal UTI and is a genuine cause of concern.

It might be emphasized that despite the etiology of UTI remaining almost constant, thorough knowledge of local antibiotic resistance profile is necessary for successful treatment. Besides cost effectiveness, selection of antibiotics must take into consideration geographical location and routine in vitro testing of urine samples as a basis for formulation of empirical treatment.

Table 1: Microorganisms causing UTI in women of reproductive age group (15-49 yrs)

Isolates	2013 n(%)	2014 n(%)	2015*n (%)
Escherichia coli	109 (53.69)	63(64.29)	56(71.79)
Enterococcus faecalis	45 (22.17)	18(18.37)	17(21.79)

Staphylococcus aureus	3 (1.48)	1(1.02)	2(2.56)
Klebsiella pneumoniae	9 (4.43)	5(5.01)	2(2.56)
Proteus species	4(1.97)	1(1.02)	0(0)
Citrobacter species	4(1.97)	0(0)	0(0)
Pseudomonas species	12(5.91)	1(1.02)	0(0)
Acinetobacter species	7(3.45)	1(1.02)	0(0)
Candida species	8(3.94)	8(8.16)	0(0)
Others	2(0.99)	0(0)	1(1.28)
Total	**203**	**98**	**78**

*Data included upto September 2015

Table 2: Susceptibility pattern of *E.coli* isolates

Antibiotics	2013 n(%)	2014 n(%)	2015*n(%)
Ampicillin	27 (24.77)	13 (20.63)	13 (23.21)
Cephalexin	41 (37.61)	20 (31.75)	23 (41.07)
Gentamicin	67 (61.47)	43 (68.25)	50 (89.29)
Ofloxacin	28 (25.69)	19 (30.16)	19 (33.93)
Norfloxacin	25 (22.94)	21 (33.33)	17 (30.36)
Cortrimoxazole	34 (31.19)	17 (26.98)	22 (39.29)
Nitrofurantoin	102 (93.58)	57 (90.48)	51 (91.07)

*Data included upto September 2015

Table 3: Susceptibility pattern of *E.faecalis* isolates

Antibiotics	2013 n(%)	2014 n(%)	2015*n(%)
Ampicillin	35 (79.55)	13 (72.22)	16 (94.12)
Norfloxacin	10 (22.73)	3 (16.67)	3 (17.65)
Ciprofloxacin	12 (27.27)	3 (16.67)	3 (17.65)
Nitrofurantoin	42 (95.45)	18 (100)	16 (94.12)
H.S. Gentamicin	28 (63.64)	11 (61.11)	11 (64.71)
Vancomycin	44 (100)	18 (100)	17 (100)
Linezolid	44 (100)	18 (100)	17 (100)

*Data included upto September 2015

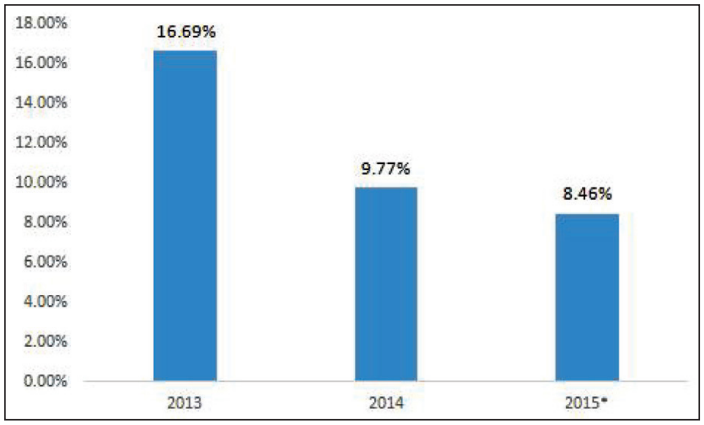

Fig 1: Prevalence of UTI in women of reproductive age group (15-49 yrs)

*Data included upto September 2015

Fig 2: Monthwise distribution of UTI cases during the study period

*Data included upto September 2015

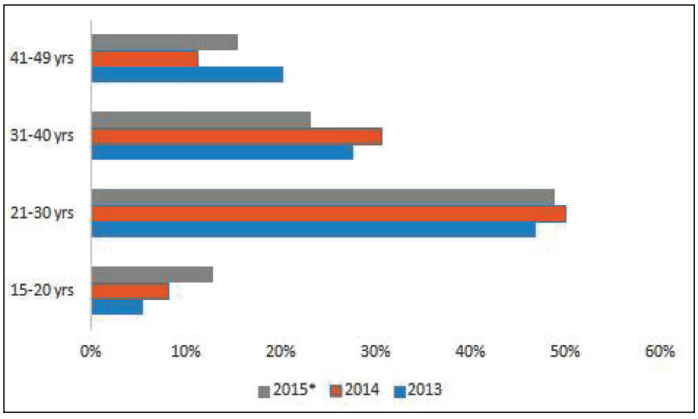

Fig 3: Prevalence of UTI in various age groups of women

*Data included upto September 2015

Conclusion

The study revealed the changing spectrum of UTI in women of reproductive age group (15-49 yrs) and the susceptibility profile of the uropathogens. Constant surveillance is essential to monitor emergence of antimicrobial resistance in these organisms. Thorough knowledge on their prevalence is essential for deciding on empirical treatment of UTI.

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