Int.J.Curr.Microbiol.App.Sci (2018) *7*(3): 506-512

International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Volume 7 Number 03 (2018)**
Journal homepage: http://www.ijcmas.com

Original Research Article https://doi.org/10.20546/ijcmas.2018.703.060

Profile of Urinary Tract Infections and Resistance Patterns in a Tertiary Care Hospital in India

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Keywords

Antimicrobial resistance, Resistance patterns

Article Info

Accepted:
07 February 2018
Available Online:
10 March 2018

A B S T R A C T

Antimicrobial resistance to urinary tract pathogens has been on steady rise worldwide. Community-acquired urinary tract infections (CA-UTI) are treated empirically based on their antimicrobial resistance patterns in a population of specific geographical location. Given the increased resistance of community bacteria to antimicrobials, local knowledge of susceptibility rates of uropathogens is essential for therapeutic decision making regarding patients with urinary tract infections.

Introduction

Urinary tract infection (UTI) is one of the common infections worldwide which are more common in women than in men (Mihankhah Abbas *et al.*, 2017). It remains a major public health problem in terms of morbidity with an estimated 150 million cases annually worldwide, costing global economy in excess of 6 billion US dollars (Gonzalez and Schaeffer, 1999). UTI is defined as presence of bacteria in urine along with urinary symptoms like dysuria, frequency, urgency and occasionally suprapubic tenderness (Dash Muktikesh *et al.*, 2013). It may involve the lower or upper urinary tract. UTI occurring in premenopausal and non-pregnant women and in people with no known urological abnormalities are classified as uncomplicated, while others are considered complicated UTI (Hsueh *et al.*, 2011).

UTIs to a great extent are caused by Gram-negative bacteria, like *Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Enterobacter* spp. UTI'S are also caused by gram positive organisms like Group B *Streptococcus* and *Staphylococcus saprophyticus and Enterococcus* spp (Saadeh and Mattoo, 2011).

Differences in microbial spectrum and susceptibility patterns may occur in different regions, and the knowledge of antimicrobial use serves as an important predictor of resistance (Kiffer *et al.*, 2011).

Some Enterobacteriaceae are resistant to nearly all antibiotics, including carbapenems, which are often considered the antibiotics of last resort (Centers for Disease Control and Prevention, 2013). More than 9,000 healthcare-associated infections are caused by CRE each year. Each year, approximately 600 deaths result from infections caused by the two most common types of CRE, carbapenem-resistant *Klebsiella* spp. and carbapenem-resistant *E. coli* (Centers for Disease Control and Prevention, 2013). CA-UTIs are treated empirically, in most of the situations. Hence the choice of appropriate antimicrobial agents should be determined by the most likely pathogen isolated and their resistance pattern in a geographic area. Therefore there is need for periodic monitoring of etiologic agents of UTI, and their resistance pattern in the community.

Materials and Methods

The present retrospective study was carried out in the central clinical microbiology laboratory of a tertiary care hospital in Tamilnadu, India and catering patients mostly from rural areas. The duration of the study was 10 months from Feb 2017 to December 2017.

Study population

A total of 644 adult patients with signs to symptoms of UTI who attended the outpatient departments (OPDs) and inpatients of our hospital were recruited for this study. Verbal informed consent was obtained from all patients prior to specimen collection. The study was conducted after due approval from institutional ethical committee.

Sample collection and processing

Freshly voided, clean-catch midstream urine sample were collected from patients in sterile screw-capped universal container. The specimen was labeled and transported to the microbiology laboratory for processing within 2 h. Semi quantitative urine culture was done using a calibrated loop. A loopful (0.001 mL) of well mixed un-centrifuged urine was inoculated in cysteine lactose electrolyte deficient medium and Blood agar. The culture plates were incubated aerobically at 37°C for 18-24 h and count were expressed as colony forming units (cfu) per milliliter (ml). For this study, significant bacteriuria was defined as culture of a single bacterial species from the urine sample at a concentration of 10^5 cfu/ml associated with microscopy findings of >10 white blood cells (WBCs) per high power field. (Kass, 1957) Only patients with significant bacteriuria ($\geq 10^5$ cfu/ml) were included for microbiological analysis. The culture isolates were identified by standard microbiological methods (Collee *et al.*, 2006). All culture media were procured from HiMedia Laboratories, Mumbai, India.

Isolates were tested for antimicrobial susceptibility testing by the standard Kirby-Bauer disc diffusion method according to Bauer *et al.*, (1966). Mueller-Hinton agar plates were incubated for 24 h after inoculation with organisms and placement of discs. After 24 h the inhibition zones were measured. The following standard antibiotic discs for the isolates were used; ampicillin (10 mcg), augmentin i.e. amoxicillin + clavulinic acid (20/10 mcg), co-trimoxazole (23.75/1.25 mcg), nitrofurantoin (300 mcg), ciprofloxacin (5 mcg), ofloxacin (5 mcg), cefaclor (30 mcg), cefpodoxime cefpodoxime proxetil (10 mcg), gentamicin (10 mcg) and amikacin (30 mcg). Antibiotic discs were obtained from HiMedia Laboratories, Mumbai, India. The results were interpreted according to Clinical and Laboratory Standards Institute guidelines. (Clinical and Laboratory Standards Institute, 2016) The quality control strains used were *E. coli* American type culture collection (ATCC)

25922, *Pseudomonas aeruginosa* ATCC 27853, *Enterococcus fecalis* ATCC 29212 and *Staphylococcus aureus* ATCC 25923 for antimicrobial discs.

Results and Discussion

From a total of 644 urine samples collected from CA-UTI patients 409 (63.51%) yielded significant pathogens. A significantly low value of 39.7% was obtained by Oladeinde *et al.,* in a community in Nigeria (Oladeinde *et al.,* 2011). The culture positive rate for CA-UTI was higher in our study in comparison with other studies conducted in India (17.19%) and Aligarh, India (10.86%). (Oladeinde *et al.,* 2011; Akram *et al.,* 2007) Geographical location may be the reason for this wide difference.

The finding showed that females (63.51%) had higher prevalence of UTI in comparison with males (30.32%) which is in agreement with other previous studies (Oladeinde *et al.,* 2011; Akram *et al.,* 2007; Kashef *et al.,* 2010). Presence of a short urethra, situation of the female urethral meatus in close proximity to anus and increased frequency of sexual intercourse in middle age group women have been reported as factors contributing to higher prevalence in women (Omoregie *et al.,* 2008).

The age group analysis showed that young female patients in the range of 20-35 years had highest prevalence rate (31.05%) of CA-UTI which is in agreement with previous studies (Akram *et al.,* 2007; Hooton *et al.,* 1996). The incidence of UTI is quite high among sexually active young women which is strongly related to recent use of diaphragm with spermicide and history of recurrent UTIs (Khameneh and Afshar, 2009). Studies have shown that the incidence of UTI increases among males due to prostate enlargement and neurogenic bladder. This study showed a higher incidence of UTI (14.43%) in elderly males (≥60 years) in comparison to the elderly females (5.13%) In a study conducted by Sood *et al.,* similar results were seen (Hooton *et al.,* 1996). In this study Gram-negative bacteria (73.75%) were isolated predominantly among which *E. coli* was the commonest uropathogen accounting for 33.49% of all culture-positive isolates. About 19.8% of isolates were *Klebsiella spp*. in this study. The percentage of bacterial species isolated in other studies also showed similar results (Hooton *et al.,* 1996; García-Morúa *et al.,* 2009). In a study conducted by Garcia-Morŭa *et al.,* showed that *E. coli* was the commonest organism in UTI (24.7%), followed by *Candida albicans* (23.7%) among Mexican population group (Das *et al.,* 2006). Members of Enterobacteriaceae colonize the urogenital mucosa with adhesins, pili, fimbriae, and P-1 blood group phenotype receptor (Gupta *et al.,* 2011).

The infectious disease society of America guidelines considers co-trimoxazole, fluoroquinolones, nitrofurantoin, and β-lactams as current standard empirical therapy for uncomplicated UTI in women (Kothari and Sagar, 2008). However in developing countries like India antimicrobial susceptibility patterns and antibiotic policies must be considered before choosing an antibiotic for treatment. Uncomplicated UTIs are frequently treated empirically with oral antibiotics. Urine culture and antibiotic susceptibility testing are conducted only during treatment failure, recurrence or relapsing infection.

In our study among Gram-negative bacteria, *E. coli* showed high level of resistance to frequently used antibiotics like β-lactams (ampicillin, augmentin, cefaclor, and cefpodoxime), fluoroquinolones (ciprofloxacin and ofloxacin) and co-trimoxazole (Hooton *et al.,* 1996; Larsson *et al.,* 2000) (Table 1 and 2).

Table.1 Effect of gender on prevalence of urinary tract infection

Gender	No. tested	Total No. of urine specimen	
		No. infected	No. not infected
Male	209	124	85
Female	435	285	150
Total	644	409	235

Table.2 Profile of uropathogens isolated in mono microbial cultures (N=409)

S. No	Organism isolated	Total Numbers	Percentage
1.	*Escherichia coli*	137	33.49
2.	*Klebsiella spp*	81	19.8
3.	*Pseudomonas spp*	43	10.51
4.	*Proteus spp*	40	9.77
5.	*Enterococcus spp*	31	7.57
6.	*Staphylococcus aureus*	35	8.56
7.	*Candida spp*	22	5.38
8.	*Streptococcus spp*	20	4.89

Chart.1 Age wise distribution on prevalence of urinary tract infection

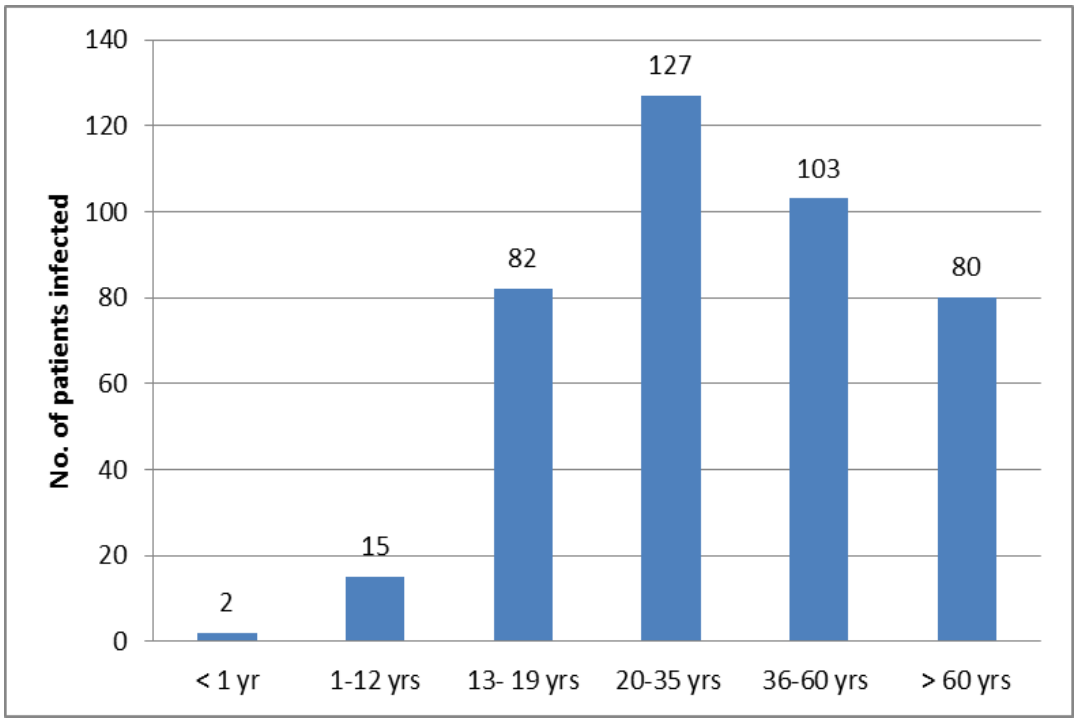
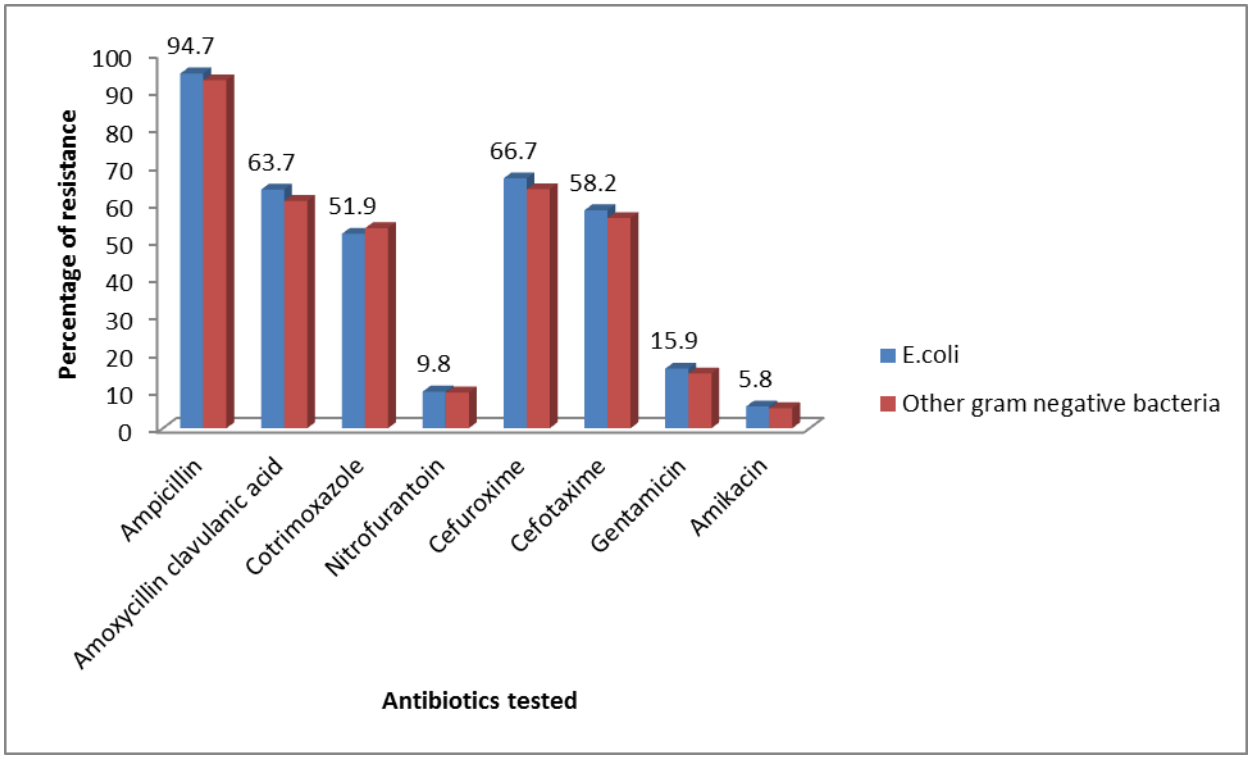


Chart.2 Resistance patterns of *Escherichia coli* and other Gram-negative isolates



The high resistant rates among the uropathogens could be due to indiscriminate use of antimicrobials by private practitioners, pharmacists and nurses, inappropriate dosing and short course of therapy with antibiotics. Availability of over the counter drugs all over the country has played an important role for this widespread resistance in antibiotics. The widespread use of antimicrobials in Farming animals may be another factor for the emergence of resistant strains as reported in enterococcus.

Gentamicin and Amikacin showed resistant rates of 15.9% and 5.8%, respectively for *E. coli* among the aminoglycosides.

In this study, less than 10% resistance has been shown by nitrofurantoin with superior activity to most uropathogens and hence can be considered as a choice for treating uncomplicated UTI. Nitrofurantoin being an oral antibiotic can be used in community and rural settings. Low rates of resistance have also been reported from studies conducted in various regions throughout India (Hooton *et al.*, 1996; Shaifali *et al.*, 2012). Therapy with Nitrofurantoin has limited usage in treating complicated UTI and in elderly patients (Vasquez and Hand, 2004).

Urinary tract infections are common in females when compared with males and the commonest uropathogen isolated was *Escherichia coli.* Gram negative isolates were isolated predominantly showing resistance to most of the antibiotics. International guidelines of treatment of guidelines cannot be applied in developing country like India.

Hence proper antibiotic policies must be formulated and followed to curb the antibiotic resistance. Treatment must be started based on culture reports and resistance patterns reported in specific location.

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How to cite this article:

Maheswary, D. and Chitralekha Saikumar. 2018. Profile of Urinary Tract Infections and Resistance Patterns in a Tertiary Care Hospital in India. *Int.J.Curr.Microbiol.App.Sci.* 7(03): 506-512. doi: https://doi.org/10.20546/ijcmas.2018.703.060