Prevalence and antibiotic susceptibility pattern of multi-drug resistant *Escherichia coli* isolates from urinary tract infection (UTI) patients in Kancheepuram dist

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Abstract

Background- *E.coli* is found to be the commonest cause of UTI. However *E. coli* antibiotic resistance has escalated over the past many years. **Objective-** To provide an update of prevalence of multidrug resistant *E.coli* isolates and their antibiotic susceptibility pattern with special reference to northern region of Tamilnadu. **Methods-** This retrospective study was conducted in the Department of Microbiology, Hindu Mission Hospital, Tambaram west, Chennai, Tamilnadu from January 2016 to March 2016 using urine samples from outdoor patients of UTI. A total of 307 urine samples were processed for bacterial culture using standard methods. For these urinary isolates, susceptibility to various antibiotics was checked as per standard CLSI guidelines version 2016. Final resistance to various antibiotics from the urinary isolates was analysed. **Results-** A total of 75 urine samples (41%) showed growth of *E. coli*. Out of these 43 isolates (57%) were multi drug resistant. High level of resistance was seen to ciprofloxacin, amoxicillin, cotrimaxozole, norfloxacin ranging from 70-95% whereas combination drugs (piperacillin +tazobactam),(ceftazidime + clavulinic) along with amikacin, imipenem showed low level of resistance. However Nitrofuratoin was found to be highly sensitive to all urinary isolates of *E.coli* including multidrug resistant strains. **Conclusion-** *E.coli* was found to be the commonest cause of UTI in our study population. Multi drug resistance was high among the prevalent strains which emphasizes the judicious use of antibiotics.

Keywords: UTI, Multi Drug Resistance, Antibiotics, Sensitive, Resistance

Introduction

UTI is a spectrum of disease caused by microbial invasion of the genitourinary tract that extends from the renal cortex of the kidney to the urethral meatus. It is mainly found in females; 20-30% of women have recurrent UTI. Human acquire UTI mostly by ascending route because of the shorter ureathra, close proximity to vaginal and anal orifice. The predisposing factor in female is the higher risk in women is mostly due to the shortness of the female urethra, during pregnancy, menopause, and catheterization. In males it is caused by prostate hypertrophy and other immunocompromised conditions.

UTI is majorly caused by *E.coli* about 50-90% and it is the major cause of both community acquired and hospital acquired UTI as 80% and 40% respectively. E.coli is a Gram negative red measuring1.3x0.4-0.7 micrometer in size. It is motile with peritrichate flagella.

Bacterial resistance often in treatment failure, which can have serious consequences. Prolonged therapy with antimicrobial agents may also lead to the development of low-level resistance that compromises therapy but that may not be detected by routine susceptibility testing methods used in hospital laboratories. A clinically important bacterium such as MRSA and ESBL plays a major role in the mechanism of drug resistance. Beta-lactamase is the most important class of antibiotics. This is because they inhibit peptidoglycon synthesis, a reaction that does not exist in the eukaryotic world.

Broad spectrum beta-lactamase producing organisms are a growing worldwide problem (Livermore 2001). It was first observed in 1983 in isolates of *Klebsiella pneumoniae* (Knothe et al 1983). The extended spectrum beta-lactamase (ESBL) producing strains have variable susceptibility rates for fluoroquinolones, aminoglycosides and fourth generation cephalosporins (Lautenbach 2001 and Kariuki et al 2007).

Urinary tract infection is one of the most common bacterial infections and Gram- negative bacteria are among the most prevalent bacteria detected from UTI patients (Selvarangan et al,2004). The organism is of clinical importance due to its cosmopolitan nature and ability to initiate, establish and cause various kinds of infections. It is one of the most frequently isolated organism from different clinical cases of diarrhea (Olive et al;2003, Tobih et al;2006). More than 50% of UTI infections in patients is accounted for E.coli. (Blomgran et al;2004,Jha and Bapat;200 5). Resistance to antibiotics is highly prevalent in bacterial isolates

worldwide, particularly in developing countries The aim of the present study was to investigate urine cultures and to evaluate antibiotic resistance pattern of the most frequent bacterium detected from urine culture in urinary tract infection from the northern part of Chandigarh (India).

Methods

The study was carried from January 2016 to March 2016 at the Department of Microbiology, Hindu Mission Hospital, Tambaram west, Chennai, Tamilnadu. 307 urine sample from outdoor patients of UTI. Urinalysis done and cultured on blood agar and MacConkey agar incubated at 37^0 C overnight. The positive samples were processed using biochemical tests and identification of microorganism according to standard procedure. The standard disk diffusion microbial sensitivity test based on Kirby –Bauer method on Mueller Hinton agar was utilized for all the isolates to assess the antibiotic resistance using antibiotic discs. Multidrug resistant isolates- Isolates resistant to more than two different classes of antibiotics were considered as multi-drug resistant.

Results

Out of the 307 urine samples processed for bacterial culture, 184 (60%) were positive for growth. The frequencies for the pathogens in the positive cases were as follows, most frequent gram-negative bacterium was *E. coli* with75 cases (41%),other gram- negative bacilli including *Klebsiella, Pseudomonas* and *Proteus* were 19 cases (10%).

Table – 1 Distribution of bacteria in UTI	
Bacteria	**N=184 (60%)**
E.coli	75 (41%)
Other GNB (*Klebsiella, Pseudomonas, Proteus*)	19 (10%)
GPC (*Staphylococcus* spp, *Enterococcus*)	16 (8%)

Fig.1. DISTRIBUTION OF BACTERIA IN UTI (n=184)

14% GPC (Staphylococcus spp, Enterococcus)
17% Other GNB (Klebsiella, Pseudomonas, Proteus)
69% E.coli
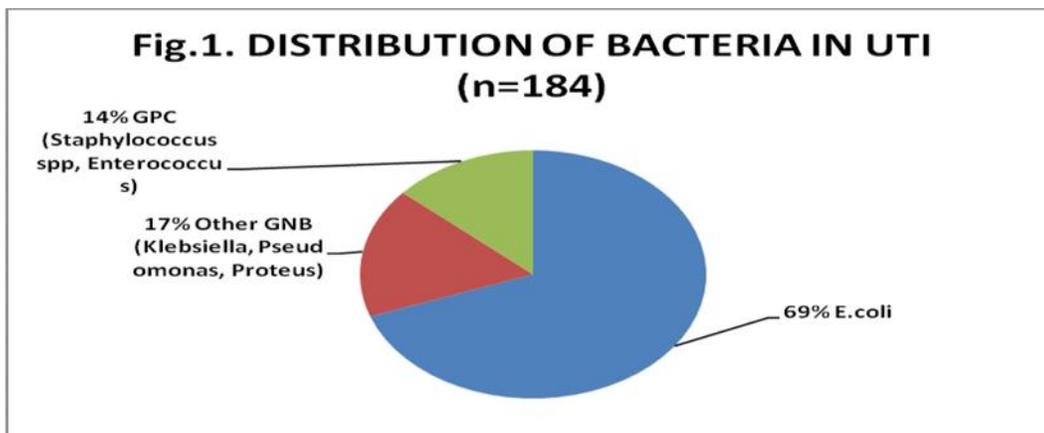
Table – 2 Resistance pattern of *E.coli* isolates		
Antibiotic	**Isolates resistance (n)**	**%**
Augmentin	40	53%
Amoxycillin	33	44%
Norfloxacin	37	49%
Nalidixic Acid	35	46%
Nitrofurantoin	3	4%
Ciprofloxacin	31	41%
Amikacin	2	3%
Gentamycin	22	30%
Ceftazidime/Clavulinic acid	10	13%
Piperacillin/Tazobactum	7	9%
Cefepime	12	16%

Table – 3 % Resistance in *E.coli* isolates according to age					
Age (yrs)	**1-20 yrs**	**21-40 yrs**	**41-60 yrs**	**61-80 yrs**	**>80 yrs**
Augmentin	20	53	53	55	67
Norfloxacin	25	53	53	58	67
Nitrofurantoin	0	0	0	9	0
Ciprofloxacin	0	29	31	54	67
Cefta/Clav	0	5	5	19	33
Pipera/Tazobac	0	0	0	16	33

The gram-positive cocci isolated were *Staphylococcus, Enterococcus* 16 cases (8%) [Table-1]. The resistance rate of E.*coli* detected from culture was found to be 53% for augmentin, 44% to amoxicillin, 49% to Norfloxacin,46% to Nalidixic acid and 41% to Ciprofloxacin [Table -2]. Urinary E.coli isolates were studied and separated according to different age groups [Table-3]. The percentage resistance in each age group was seen [Table 4]. 43 *E.coli* isolates (57%) were multidrug resistant.

Discussion

The study shows most frequent gram negative bacteria isolated as *E.coli* (41%). This is in similarity with the results of other studies (Jha and Bapat;2005, Astal ZE;2005,Kresken and Hefner;2006,Olewe et al;2008, Mohammadi etal;2010). *E.coli* has widely been implicated in various clinical infections as hospital acquired and community infections as hospital acquired and community infections as reported (Shah et al,2002). The study was most frequent gram negative bacteria isolated as *E.coli* . This is in similarly with the results of other studies (Jha and Bapat: 2005, Astal ZE: 2005, Kresken and Hefner : 2006, Olewe et al 2008 and Mohammed et al 2010). *E.coli* has widely been implicated in various clinical infections as hospital acquired and community infections as hospital acquired and community infections as reported (Shah

et al 2002). Pathogenic isolates of *E.coli* have relatively high potential of developing resistance. (Karlowsky et al 2004). High resistance of *E.coli* to antimicrobial agents tested was observed in this study. High level of resistance was seen to Cotrimaxozole among uropathogens. In our study we have found a very high i.e. 92% resistance to Ampicillin followed by Cotrimaxozole. In females UTI was maximally seen in 18-25 years age group and while male of >61 years were most commonly affected amongst all the age groups. A higher level of resistance was seen in elderly males as compared to females which can be due to prostatic enlargement predisposing to recurrent UTI and Chronic use of antibiotics. The reason for the high antibiotic resistance could be previous antibiotic treatment, nosocomial vs community acquired infections, urinary catheterization and urinary tract abnormalities but further studies are required to look at these variables acting as independent risk factors. Pathogenic isolates of *E.coli* have relatively high potentials of developing resistance (Karlowsky et al,2004). High resistance of *E.coli* to antimicrobial agents tested was observed in this study. High level of resistance was seen to Ciprofloxacin, amoxicillin, Cotrimaxozole, Norfloxacin ranging from 70-95% whereas combination drugs (piperacillin+ tazobactam) (Ceftazidime + Clavulinic acid) along with amikacin, imipenem showed low level of resistance. Although fluoroquinolones are among

the most effective drugs in treating UTI (Kurutepe et al, 2005) diverse studies have revealed increasing resistance to fluoroquinolones. Our study also shows a high level of resistance to Ciprofloxacin. The results of other studies have also revealed that the resistance of *E.coli* to Ciprofloxacin, the most effective drug to UTI is increasing. Astals study , 2005 in China shows increase in resistance from 46.6 to 59.4% during the years 1998-2000. Kurutepe et al ,2005 found increase in resistance from 2.9% in 2000 to 11.3% in 2002. Our study shows Nitrofuratoin to be highly sensitive to all urinary isolates of *E.coli* including multidrug resistant strains. The consistent and high level susceptibility of *E.coli* to nitrofuratoin may be influenced by nitrofuratoins narrow spectrum of activity, limited indication (treatment of acute cystitis),narrow tissue distribution and limited contact with bacteria outside the urinary tract (James et al,2002). There is a reluctance to prescribe Nitrofuratoin due to its side effect profile but it stands as a important first – line drug against UTI before culture and sensitivity.

Studies in other developing countries have shown that the trend in enteric pathogens is toward increasing antibiotic resistance (Hoge et al, 2002). When divided for age groups, most *E.coli* resistance was seen in older population (age more than 61 years). Nitrofuratoin showed low level resistance at all ages. In a study reported from Spain (Ena et al, 1995) age more than 64 was found to be a high risk factor for antibiotic resistance against *E.coli.* The reason for the high antibiotic resistance coluld be previous antibiotic treatment, nosocomial *vs* community acquired infections, urinary catheterization and urinary tract abnormalities but further studies are required to look at these variables acting as independent risk factors.

Conclusion

Antimicrobial resistant patterns are constantly evolving, it is a present global public health problem and there is the necessity for constant antimicrobial sensitivity surveillance. This will help clinicians provide safe and effective empiric therapies. Continuous analysis of antibiotic resistance patterns act as a guide to initiate the empirical treatment but for institution of appropriate therapy urine culture and sensitivity is the gold standard even in community. One can truly affirm that the choice of drugs in the treatment of UTI is quite narrow today due to the wide scale resistance that the common UTI pathogens show to drugs which have been used

previously. Antimicrobial resistant patterns are constantly evolving, it is a present global public health problem, there is the necessity for constant antimicrobial sensitivity surveillance. This will help clinicians provide safe and effective empiric therapies.

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