

Original Research Article

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Antimicrobial Resistance Pattern in *Escherichia coli* Causing Urinary Tract Infection among Inpatients - A Retrospective Study

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ABSTRACT

Urinary tract infections (UTIs) are second most common medical problem of humans after respiratory tract infection. They are often recurrent, difficult to treat, and can cause parenchymal damage to the kidney, leading to renal insufficiency and further complications. The aim is to study increasing rates of antimicrobial resistant *Escherichia coli* (*E. coli*) among patients admitted with urinary tract infections. The details of *E. coli* isolates from urine samples and their antibiotic sensitivity pattern were collected from the laboratory registers and the patient details were collected from the case records. The urine samples were processed using standard methods as per CLSI guidelines and antibiotic susceptibility was done by Kirby-Bauer disk diffusion test. Of the total 117 *E. coli* isolates, 27 (23.8%) were isolated from in-patients, which were considered for the study. Of these 27 *E. coli* isolates, 15 (55.55%) were multi drug resistant (MDR). The isolates showed high levels of resistance to ampicillin (81.48%), amoxyclav (70.3%), cefuroxime (74.07%), cefazolin (70.37%), cefotaxime (62.96%), ceftazidime (59.26%), Ciprofloxacin (74.07%), norfloxacin (66.67%). The isolates were highly sensitive to piperacillin-tazobactam (96.30%), Meropenam (100%), tobramycin (96.30%), aztreonam (74.07%), amikacin (74.07%), nitrofurantoin (74.07%) and, ceftazidime-clavulanic acid (74.07%), co-trimoxazole (74.07%) and tetracycline (55.56%). Of the 15 cases of UTI are due to MDR *E. coli*, 14 improved on treatment and 1 was referred to higher centres.

Keywords

Antimicrobial resistance, *Escherichia coli*, MDR, therapy, UTI

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Introduction

Urinary tract infections (UTIs) are an important medical problem, being the second most common bacterial infection of humans after respiratory tract infection. They are often recurrent, difficult to treat, and can cause parenchymal damage to the kidney, leading to renal insufficiency and further complications (Draghijeva *et al.*, 1999; Leroy *et al.*, 2009

and Prakash Kalra *et al.*, 2010). UTIs impose a substantial burden on society and the health care system in relation to diagnosis, management, lost productivity, morbidity, and sometimes death (Foxman *et al.*, 2000, Griebing *et al.*, 2005). Furthermore, increasing resistance to therapeutically important antimicrobial agents and the recent emergence of the virulent and multidrug-resistant *Escherichia coli* Sequence Type 131

clonal group have made UTI management progressively more costly and challenging (Ikram *et al.*, 2015; Johnson *et al.*, 2012).

Escherichia coli are the leading cause of urinary tract infections in humans. Increasing rates of antimicrobial resistance among *E. coli* is a growing concern world-wide. However, to curb the problem, there is need of clinical data on the prevalence of resistance

Up to 60% of women have symptomatic UTIs during their lifespan, and 10% of men have UTIs annually. UTI in men is uncommon but often associated with structural abnormality (Nicolle *et al.*, 2008). Since the resistance patterns of *E. coli* strains causing UTI varies considerably between regions and countries, a specific treatment recommendation may not be universally suitable for all regions or countries (Gupta *et al.*, 2011). Active surveillance studies of in vitro susceptibility of uropathogens in women with uncomplicated cystitis are helpful in making decisions about empirical therapy (Gupta *et al.*, 2011). Evidence proves that antibiotic-resistance genes were already present in the era before antibiotic therapy was available, and they probably originated from antibiotic-producing bacteria (Medeiros *et al.*, 1997; Gardner *et al.*, 1969). Indiscriminate use of antibiotics, inappropriate dosing, and incomplete treatment in both humans and also some animals are some of the factors leading to development of resistance in common bacteria (Sarkar *et al.*, 2015).

Multidrug resistant (MDR) bacterial infections are now becoming quite common, not only in hospital settings but also in the community. Thus, this is not just a clinical problem now but a public health concern, especially in developing countries where the need for higher antibiotics puts a strain on the already restricted health budget. *Escherichia coli* (*E. coli*), a common human pathogen of the

urinary tract, is well known for being MDR, including resistance to the fluoroquinolones. (Levy SB *et al.*, 2004) This is especially common in South-East Asia. A very recent study from India showed high level (upto 80%) of expression of drug efflux pumps in *E. coli* specimens, which is indicative of antimicrobial resistance (Sarkar *et al.*, 2015). Similarly, another recent study from South India also depicted high levels of resistance to β -lactam and fluoroquinolones antibiotics in *E. coli* specimens isolated from urinary samples (Somashékara *et al.*, 2014).

Since *E. coli* is the most common uropathogen in India, its drug resistance patterns will have the greatest impact on clinical management and the healthcare costs. (Hasan AS *et al.*, 2007)

Materials and Methods

We carried out this study in a tertiary care hospital, Mahavir Institute of Medical sciences, Vikarabad, in south India. This was done in patients admitted from January to December 2018. Patients coming with symptoms of urinary tract infection (UTI with dysuria, hematuria, sudden incontinence, or increased frequency of urination were provisionally included. Out of 4167 urine samples 9.64 % were obtained from inpatients over a period of one year (January to December 2018). Midstream urine (MSU) sample was collected in sterile, wide mouth, leak proof container and transported immediately to Microbiology laboratory. Catheterized urine samples were collected as per standard guidelines. Semi-quantitative culture of urine was done on Cysteine Lactose Electrolyte Deficient (CLED) media, blood agar, and MacConkey agar by standard loop method. The culture plates were incubated at 37°C for 18-24 h under aerobic conditions. Identification of bacterial growth was confirmed by standard microbiological

techniques (Forbes *et al.*, 2007; Collee *et al.*, 2008). Bacterial colony count more than 10^5 colony-forming units (CFU)/ml was taken as significant bacteriuria.

Antibiotic sensitivity testing was done by Kirby–Bauer disc diffusion method on Mueller-Hinton agar, as per Clinical and Laboratory Standards Institute guidelines (Bauer *et al.*, 1966; Clinical and Laboratory Standards Institute, 2017). Antibiotic discs were procured from HiMedia, Mumbai, India. ESBL screening and phenotypic confirmation was done by testing the strain against ceftazidime and ceftazidime/clavulanic acid, cefotaxime and cefotaxime/clavulanic acid. A difference of >5 mm diameter of the zone of inhibition for combination disc in comparison to the ceftazidime/cefotaxime alone was considered as indicative of ESBL production. *Escherichia coli* ATCC 25922 for ESBL negative and *Klebsiella pneumoniae* 700603 for ESBL positive was used as reference strains. (Clinical and Laboratory Standards Institute 2017)

Discs of the following antimicrobial agents, were put up: ampicillin (10 µg), amoxicillin-clavulanic acid (20 µg/10 µg), amikacin (30 µg), cefazolin (30 µg), ceftazidime (30 µg), cefuroxime (30 µg), cefotaxime (30 µg), piperacillin-tazobactam (100/10 µg), ceftazidime-clavulanic acid (30/10 µg), ciprofloxacin (5 µg), norfloxacin (10 µg), meropenem (10µg), trimethoprim-sulfamethoxazole (1.25 µg/23.75 µg), aztreonam (30 µg), tetracycline (30 µg), Tobramycin (10 µg) and nitrofurantoin (300 µg).

The diameter of the zones of complete inhibition (as judged by unaided eye) was measured to the nearest whole millimeter using a scale, which was held on the back of the inverted petridish. Any presence of small colonies (>1 colony) or a light film of growth

within the zone of inhibition indicated resistance of the isolate to that antimicrobial agent.

The zones of inhibition were measured and were interpreted as sensitive (S), intermediate sensitive (IS) or resistant (R) according to the disc manufacturer information tables. An isolate was considered as multidrug resistant (MDR) if it was resistant to at least three classes of antimicrobial agents viz. all penicillins and cephalosporins (including inhibitor combinations), fluoroquinolones, and aminoglycosides. Isolate was considered extensively drug resistant (XDR) if it was resistant to the three classes of antimicrobials described above (MDR) and also resistant to carbapenems (Manchanda *et al.*, 2010)

The collected data was entered in Microsoft excel and then imported to SPSS. The collected data was analyzed using appropriate statistical methods.

Results and Discussion

In the present study 73 isolates (18.15%) were obtained from 402 inpatient urine specimens. Table 1 shows the percentage distribution of IP samples in relation to age and sex. The females (55.22%) had higher prevalence of UTI in comparison with males (44.77%) Proximity of the female urethral meatus to anus, short urethra, and sexual intercourse have been stated as factors which influence the higher prevalence in women (Omoriegie *et al.*, 2008). The age group analysis showed that young female patients in the range of 21-40 years had highest prevalence rate of symptomatic UTI (69.17%). Incidence of symptomatic UTI is high among patient with a history of recurrent UTIs, sexually active young women, and the risk is strongly associated with recent sexual intercourse, (Das RN *et al.*, 2006). In present study males (≥ 60 years) had a higher incidence of UTI (56.6%)

when compared with the elderly females (43.94%) similar to study conducted by Sood *et al.*, (2001) The rate of UTIs increases in men with advanced age, prostate enlargement and neurogenic bladder.

Total of 4167 (IP+OP) urine samples were received for culture and sensitivity during the study period. Among these, 717 samples (17.21%) yielded significant bacteriuria; 2381 samples (57.1%) showed no growth, 1026 (24.6%) reported insignificant growth and 43 samples (1.03%) showed mixed growth (Table 2).

In our study out of 402 urine samples from inpatients (n=73) 18.15% were reported positive. The various organisms isolated from urine culture are shown in figure 1. Gram negative aerobic rods (61.64%) dominated among which *E. coli* was the commonest uropathogen accounts for 37.5% followed by *Klebsiella* sp (16.6%), MS-CNS (15.27%), MRSA (8.33%), MSSA & MR-CNS accounts for (6.9%), *Proteus* (4.16%), *Pseudomonas* (2.7%) *Citrobacter* sp. (1.3%).

Out of 4167 samples, 117 (IP+OP) *E. coli* were isolated. 27 *E. coli* (23.8%) were isolated from in-patients, which were considered for the study. Of these 27 *E. coli* isolates, 15 (55.55%) were multi drug resistant (MDR). The overall susceptibility

patterns of *E. coli* isolates from various clinical sources is displayed in figure 2. The isolates showed high levels of resistance to Ampicillin (81.48%), amoxycylav (70.3%) cefuroxime (74.07%), cefazolin (70.37%), cefotaxime (62.96%), cefoxitin (59.26%) Ciprofloxacin (74.07%), norfloxacin (66.67). The isolates were sensitive to piperacillin-tazobactam (96.30%), Meropenem (100%), tobramycin (96.30%), aztreonam (74.07%), amikacin (74.07%), nitrofurantoin (74.07%) ceftazidime-clavulanic acid (70%), co-trimoxazole (74.07%), Tetracycline (55.56%). Among 27 *E. coli* isolates, 17 (62.96%) were ESBL producers (Fig. 3).

Of the 15 patients with UTI due to MDR *E. coli*, 14 (93.33%) patients improved after the treatment, 1 case did not respond to the treatment and was referred to higher centres.

The most common risk factors associated with MDR *E. coli* were diabetes mellitus (7 patients, 46.66%) followed by catheterisation (3, 20%). The other risk factors were renal calculi (2, 13.33%) and renal pathologies (1 patients, 6.66%). 2 patients did not have any of the risk factors. Studies from India have reported *E. coli* as one of the commonest organisms causing UTI. In our study also *E. coli* was the commonest organism followed by *Klebsiella* species (Fig. 3 and Table 3).

Table.1

AGE	GENDER				TOTAL	
	MALE		FEMALE		M+F	%
	NO	%	NO	%		
<20 Yrs	49	55.68%	39	44.32%	88	21.89%
21-40 Yrs	41	30.83%	92	69.17%	133	33.08%
41-60 Yrs	53	46.09%	62	53.91%	115	28.61%
>60 Yrs	37	56.06%	29	43.94%	66	16.42%
	180		222		402	100.00%

Table.2

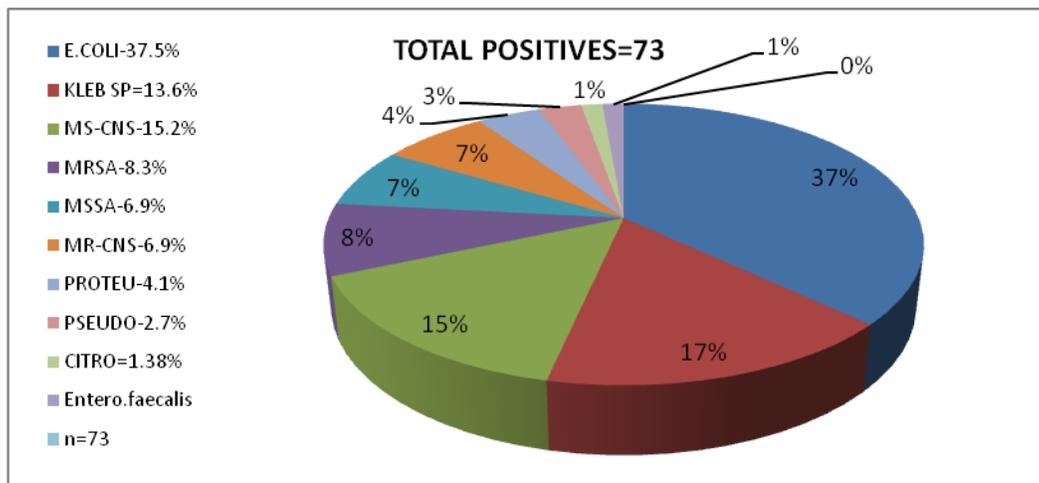
CULTURE DATA	OUT PATIENT (OP)		IN PATIENT (IP)		
Urine Culture Data	Number	%	Number	%	Total
No Of Samples	3765	90.35	402	9.65	4167
No of Significant Bacteriuria	644	17.01	73	18.3	717
No Of Insignificant	970	26.29	56	13.9	1026
Culture Sterile/No Growth	2120	56.3	261	64.9	2381
Mixed Growth	31	0.87	12	2.99	43

Table.3 Comparison with other studies

Study year	name,	location	Organisms	β-lactam	Fluoro-quinolones	Nitro-furantoin	Amino-glycosides	Cotri maxazole
Dash <i>et al.</i> , (2013)		East	<i>E Coli</i>	58–94	47–53	10	6–16	51.9
Shakya <i>et al.</i> , (2013)		Central	<i>E Coli</i>	29–41	5–16	nd	nd	nd
Niranjanetal. (2014)		South	<i>E Coli</i>	22–88	75	18	18	48.5
Dugal <i>et al.</i> , (2013)		West	gram negative uro pathogens	5–80	70–80	15	10–50	nd
Jayanthi ray <i>et al.</i> , (2015)		East	<i>E Coli</i>	19–84	19–62	34	12–25	31
Present study		south	<i>E Coli</i>	59-81	66-74	26	26	25.93

nd: not done

Fig.1 The various pathogens isolated were listed in



CPS= Coagulase Positive Staphylococci, CNS= Coagulase Negative Staphylococci, MSSA=Methicillin Sensitive *Staphylococcus aureus*, MRSA= Methicillin Resistant *Staphylococcus aureus*

Fig.2 Antibiogram of *E. coli* isolates

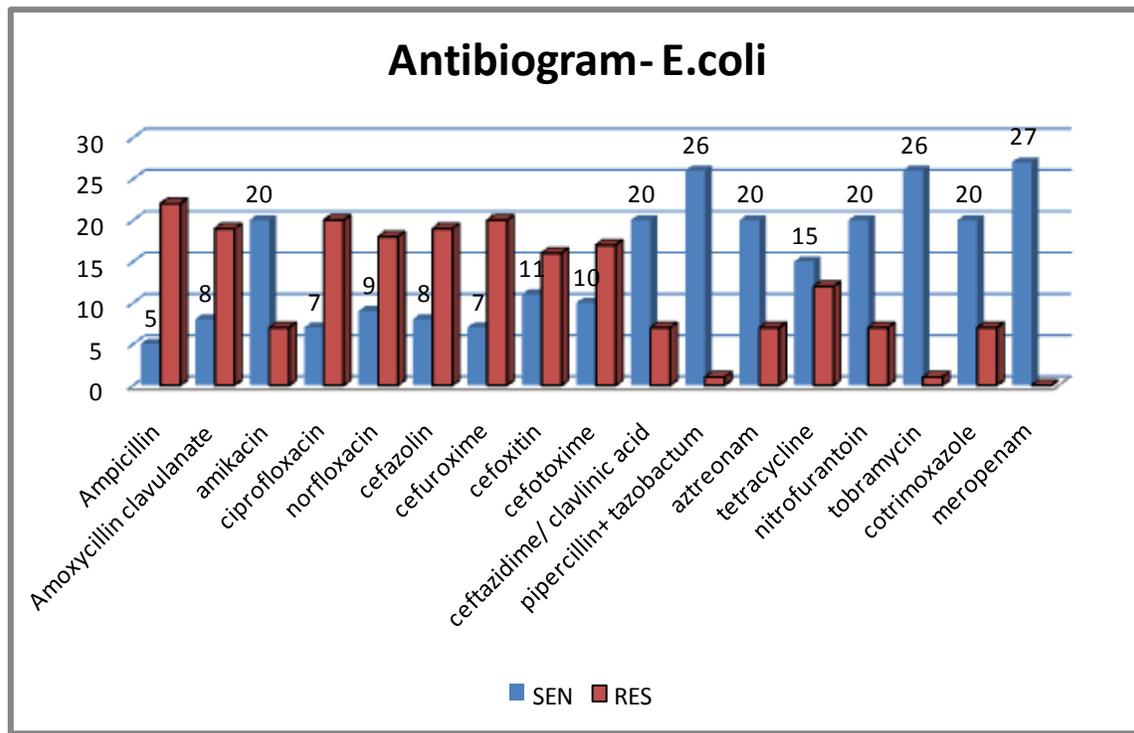
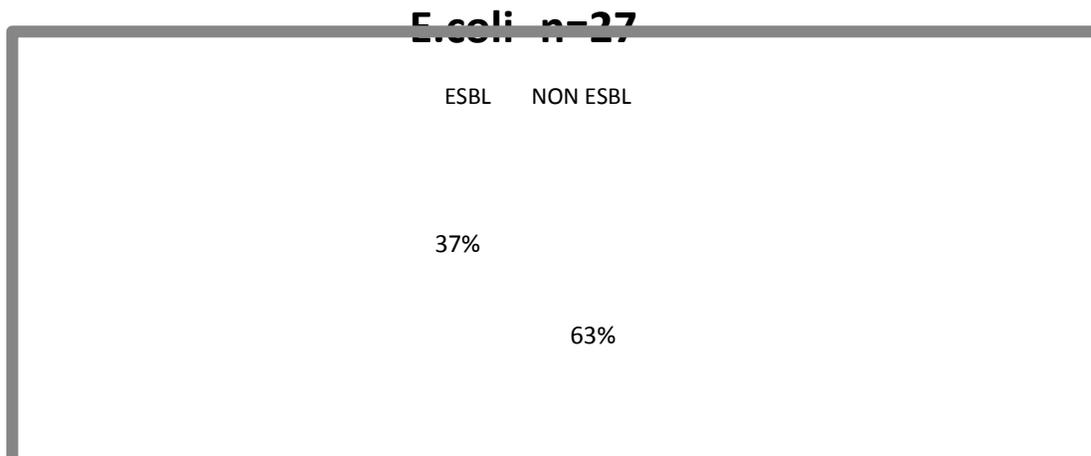


Fig.3 Showing ESBL producers



In our study, 55.55% isolates of *E. coli* were MDR. This is high when compared to other studies. Prevalence of MDR *E. coli* was about 52.9 per cent in a study done by Hasan *et al.*, (2007) in a tertiary care Indian hospital and 7.1 per cent in a study done by Sahm *et al.*, (2007) in USA. Study by Mathai *et al.*,

(2008) in southern India has showed that 8.4 per cent of commensal *E. coli* was MDR.

The antimicrobial sensitivity pattern of the *E. coli* isolates in our study was similar to previous studies done in India. The comparison of resistance patterns of

uropathogenic *E. coli* in various studies is shown in Table 3. Dash *et al.*, (2013), Shakya *et al.*, (2013), Niranjana *et al.*, (2014), Dugal *et al.*, (2013), Jayanthi ray *et al.*, (2015)

To conclude, this study showed high resistance among uropathogenic *E. coli* to ampicillin, fluoroquinolones and cephalosporins. The increased occurrence of UTI due to MDR *E. coli* could be due to increased prevalence of MDR strains in the community and due to common risk factor associated with MDR *E. coli* observed in our study

The limitations of the study were that it included only the inpatients, as a result of which the resistance rates could be high. The reason for this resistance is that ESBLs are encoded by plasmids, which also carry resistance genes for other antibiotics leading onto multidrug resistance. Multidrug resistance may be due to a number of factors like inappropriate self-medication, lack of prescribing regulations, substandard or falsified medicines and agricultural use of antibiotics.

ESBL producing *E. coli* has become the most causative agent in UTI. Other worrisome aspects of ESBL positive *E. coli* concern the high rate of resistance to non-beta lactam antibiotics, particularly quinolones and cotrimoxazole. The rising trend of ESBL production in *E. coli* is quite alarming as it limits the choices and outcome of antimicrobial treatment indicating the requirement of continuous monitoring systems and effective infection control measures.

This study concluded that multidrug resistant *E. coli* isolates are on rise and susceptibility to various antibiotics which is a matter of concern. Drug-resistance surveillance programmes should be run in hospitals to

keep a check on antimicrobial resistance. Policies should be implemented to curb over the counter sale of antibiotics and stringent measures should be undertaken to limit the spread of antibiotic resistance.

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