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ANTIMICROBIAL RESISTANCE DEMONSTRATED BY UROPATHOGENIC *ESCHERICHIA COLI* AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Urinary tract infection (UTI) is one of the most common bacterial infections encountered by clinicians in developing countries. *Escherichia coli* is the most common causative organism of UTI. Development of resistance by *E.coli* towards different antimicrobial agents is alarming. Hence, our study was planned to analyze the antimicrobial resistance pattern of *E.coli* isolates at a tertiary care teaching hospital.

Materials and method: Culture sensitivity reports of all urine samples sent to microbiology department of a tertiary care teaching hospital during the period of July 2010-June 2013 were screened. Detailed reports were collected for all the samples in which *E.coli* was identified as a causative organism. Culture sensitivity testing was done by modified Kirby-Bauer disk diffusion (high media) method.

Result: *E.coli* was isolated in total 1155 urine samples during the period of three years. Majority of patients belonged to pediatric age group (823/1155, 71.25%). 52.21% samples were of female patients. Thirty-one antimicrobial agents were tested for 13048 times for their sensitivity towards *E.coli*. Antimicrobial resistance ranging from 14.58% to 100% was noted among various antimicrobials. *E.coli* showed 38.23% resistance towards aminoglycosides, 52.27% resistance towards quinolones, 54.95% resistance towards beta-lactams and 67.33% resistance towards miscellaneous group of antimicrobials.

Conclusion: Proper selection and wise use of available antibiotics will help in reducing the rate of increase in resistance. Periodic monitoring of antimicrobial susceptibility pattern of causative agent in a particular setting will be helpful in guiding judicious use of antimicrobial agents limiting the spread of resistant strains.

Key Words: Aminoglycosides, Antimicrobial susceptibility, *Escherichia coli*, Urinary tract infection.

INTRODUCTION

Urinary tract infections (UTI) is one of the most common bacterial infections encountered by clinicians in developing countries[1] and constitute a great proportion of prescription of antibiotics [2]. It has been estimated that symptomatic urinary tract infections (UTI) occurs in as many as 7 million visits to emergency units and 100,000 hospitalizations annually. UTI has become the most common hospital-acquired infection, accounting for as many as 35% of nosocomial infections, and it is the second most common cause of bacteraemia in hospitalized patients [3].

Escherichia coli is the most common causative organism of urinary tract infections.[4] The emergence of drug resistance to trimethoprim-sulfamethoxazole, the penicillins, cephalosporins, and fluoroquinolones by Uropathogenic *Escherichia coli* (UPEC) has limited the options for selecting the appropriate antibiotic for the treatment of urinary tract infections [4].

As resistance to commonly prescribed antimicrobial agents is increasing significantly, there is a need of periodic analysis of the pattern and sensitivity of organisms isolated and the results need to be communicated to doctors [5].

Hence, this study was carried out with an aim to analyze the antimicrobial resistance pattern of *E.coli* towards commonly prescribed antimicrobial agents.

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MATERIALS AND METHODS

Culture sensitivity reports of all urine samples sent to microbiology department of a tertiary care teaching hospital during the period of July 2010-June 2013 were screened. Detailed clinic- epidemiological data were collected for all the samples in which *E.coli* was identified as a causative organism and the data was entered into Microsoft excel spreadsheet 2007.

Antimicrobial susceptibility testing was done by modified Kirby Bauer disc diffusion method [6].

Statistical analysis

Data has been presented as percentage of resistance or Mean (SD). Chi square test was performed as a test of significance whenever necessary using GraphPad InStat software version 3.10 (trial version).

P value < 0.05 was considered statistically significant.

RESULTS

Amongst 33,000 samples of positive urine culture received at the Microbiology Department in a tertiary care teaching hospital during the period of 3 years (July 2010- June 2013), *E.coli* isolates were obtained from 1155 urine samples.

Out of 1155 urine samples, 603 samples (52.21%) were of female patients while 552 samples (47.79%) were of male patients. The age of the patients ranged from 1 day to 87 years with mean age of 16.33± 20.05 years. Maximum numbers of samples (823/1155, 71.25%) were obtained from pediatric age group followed by patients belonging to adult age group (270/1155, 23.38%). Only 62 (5.37%) samples belonged to the patients of geriatric age group.

E.coli isolates were tested for their susceptibility towards 31 different antimicrobial agents with each *E.coli* isolate being tested for its susceptibility towards 5 to 17 different antimicrobial agents (Mean 11± 3.89), out of which it showed resistance towards at least 0 to 10 antimicrobials (Mean 5± 3.32).

Out of total 13,048 times for which different antimicrobials were tested for their susceptibility towards *E.coli*, 6824 (52.30%) times resistance was observed while 6188 (47.42%) times sensitivity was observed and for 36 times (0.28%) intermediate sensitivity was observed.

Group wise resistance pattern of E.coli isolates.

E.coli isolates were tested for their susceptibility towards four different groups of antimicrobial agents including aminoglycosides, quinolones, beta lactams and miscellaneous (which includes nitrofurantoin, doxycycline, tetracycline etc.).

Aminoglycosides were tested for 3071 times for their susceptibility towards *E.coli* out of which resistance was shown towards them for 1174 times (38.23%). (Table1)

Among the four different aminoglycosides tested, amikacin was the most commonly tested antimicrobial agent (1084/1155, 93.85%) followed by gentamicin (950/1155, 82.25%). Percentage of resistance amongst aminoglycosides ranged from 77.45% to 27.21% with amikacin sowing least resistance.

Total seven quinolones were tested for 3046 times for their susceptibility towards *E.coli* out of which resistance was observed for 1592 times (52.27%). (Table2) Marked difference in resistance was observed among quinolones with lomefloxacin and levofloxacin exhibiting 100% resistance while gatifloxacin showed 14.58% resistance towards *E.coli*.

Total 14 beta-lactams were tested for total 4719 times for their susceptibility towards *E.coli* out of which resistance was observed for 2593 (54.95%) times. (Table3)

Amongst beta-lactams, piperacillin (1073/1155, 92.90 %) was the most commonly tested antimicrobial agent while ceftriaxone showed highest resistance (100%, 5/5) towards *E.coli*. Out of 1249 times for which 3rd generation cephalosporins were tested, 841 times (67.33%) resistance was observed towards them. 86.96% resistance (20/23) was observed towards 4th generation cephalosporin.

Among the six miscellaneous antimicrobials tested for their susceptibility towards *E.coli* for 2176 times, resistance was observed for 1465 times (67.33 %). Chloramphenicol (987/1155, 85.45%) was most commonly tested antimicrobial agent as shown in table 4. Highest resistance was observed towards doxycycline (100%, 4/4) followed by cotrimoxazole (76.71%, 56/73).

Out of 1155 samples where *E.coli* was isolated, 925 (80.1%) samples showed resistance to atleast one agent from three or more antimicrobial families and hence was identified as MDR.

The pattern of resistance among samples obtained from male and female patients appeared similar for all the antimicrobial agents tested, except for nitrofurantoin. In case of nitrofurantoin higher resistance (p=0.025) was observed among male patients (69.94%, 328/469) as compared to samples obtained from female patients (63.12%, 315/499).

Except for amikacin (p=0.013), piperacillin (p<0.0001) and combination of piperacillin and tazobactam (p=0.01) which showed significant increase in percentage of resistance from the year July 2010 to June 2013, overall percentage of resist-

ance remained similar for rest of the antimicrobials over the period of three years.

DISCUSSION

Urinary tract infections (UTI), being the most common infections diagnosed in community and hospital, are to be treated scrupulously considering the type of infecting organism and its antibiotic resistance pattern [7].

The prevalence of antimicrobial resistance in urinary pathogens is increasing worldwide.[8] The consequences of resistance are severe as infection caused by resistant microbes fail to respond to standard treatment, resulting in prolonged illness and greater risk of death [9].

Escherichia coli is the most common causative organism of urinary tract infections.[4] According to a WHO report, *E.coli* has acquired resistance to many different groups of antimicrobials [10], and the prevalence of antimicrobial resistance varies greatly between and within countries and between different pathogens.[11]

Treatment of UTI cases is often started empirically and therapy is based on information determined from the antimicrobial resistance pattern of the urinary pathogens [8]. Accurate bacteriologic records of culture results may provide guidance on empirical therapy before sensitivity patterns are available [8].

Hence, keeping this in mind, our study was planned to analyze the antimicrobial resistance pattern of *E.coli* isolates towards commonly prescribed antimicrobial agents in a tertiary care hospital.

1155 urine samples where *E.coli* was isolated as a causative organism were collected during the period of 3 years (July 2010- June 2013) from different clinical departments of the hospital. Total 31 antimicrobial agents were tested for their susceptibility towards *E.coli* using disc diffusion method (Hi Media).

Majority of the samples were of female patients (603/1155, 52.21%) while 552 samples (47.79%) were of male patients. This data was similar to a study conducted by Abdul Rahaman Shariff V A *et al.*[4] , Shamataj Razak *et al.*[8] and Patel S *et al.*[3] where majority of urine samples were obtained from female patients.

In our study, percentage of resistance ranged from 38.23% towards aminoglycosides to 67.33% towards miscellaneous group of antimicrobial agents.

Resistance observed towards amikacin, gentamicin and norfloxacin was 27.21% (295/1084), 40.53% (385/950) and 68.68% (658/958) respectively. A comparable finding with our study for resistance towards amikacin was demonstrated by Shamataj R *et al.*[8] where resistance observed was 30.12%, while resistance demonstrated towards gentamicin and norfloxacin was 73.5% and 93.98% which was not in accordance to our study. However, the sample size was smaller (i.e. 156) than our study.

In our study, *E.*coli showed 100% resistance towards levofloxacin (tested for lesser number (i.e. 9) of times), while contrast results were obtained in a study conducted by Patel S *et al* [3].

Among the beta lactams tested for their susceptibility towards *E.coli*, 51.54% (553/1073) and 70.65% (657/930) resistance was observed towards piperacillin and combination of ampicillin and sulbactam respectively. On the contrary, resistance observed towards piperacillin and combination of ampicillin and sulbactam was 74.9% (968/1292) and 37.7% (487/1292) respectively, in a study conducted by Abdul Rahaman Shariff V A *et al.*[4]

Another study conducted by Patel S *et al.* [3] showed 24% resistance towards combination of ampicillin and sulbactam which was in contrast to our study.

Resistance observed towards nitrofurantoin was 66.43% (643/968) in our study, while in a study conducted by Shamataj R *et al.*[8] and Patel S *et al.*[3], *E.coli* showed lesser resistance (18.08% and 20% respectively) towards nitrofurantoin. However, sample size was smaller in case of study conducted by Shamataj R *et al.* (i.e.156) than our study.

A study conducted by Abdul Rahman Shariff V A *et al.*[4] reported 0% (0/2584) resistance of *E.coli* towards carbapenems, while in our study resistance observed towards carbapenem group of antimicrobials was 33.58% (90/268) but carbapenems were tested for lesser number of times (i.e. 268 times) in our study.

In our setting the resistance observed towards cotrimoxazole, 3rd generation cephalosporins and fluoroquinolones was worrisome.

Antimicrobial agents were viewed as miracle cures when first introduced into clinical practice. However, it became evident rather soon after the discovery of penicillin that resistance developed quickly, terminating the miracle. This serious development is ever present with each new antimicrobial agent and threatens the end of the antimicrobial era. Today every major class of antimicrobial is associated with the emergence of significant resistance [12].

Proper selection of antimicrobial agent is the most crucial step in successful management of urine infection. This data provides useful information not only for clinicians in determining the appropriate antimicrobial regimen [13] but also for microbiologists to procure appropriate antimicrobial suscep-

tibility discs. That will lead to judicious use of antimicrobials and providing of effective antimicrobial therapy which will help in limiting the emergence of drug resistance and spreading of multidrug resistant strains.

Limitations of the study were: (1) As this was an in vitro study hence results cannot be directly applied to clinical setting as multiple factors play a role in actual response of the antimicrobial agent.

(2) The study period (i.e. three years) was not longer enough to analyze the trend in antimicrobial resistance pattern of *E.coli* towards different antimicrobial agents tested.

(3) As 90% of the isolates were obtained from in-patient department, comparison could not be done with isolates obtained from out-patient department.

CONCLUSION

In our setting, overall there was high prevalence of resistance of *E.coli* isolates towards various groups of antimicrobial agents. Hence, periodic monitoring of antimicrobial susceptibility pattern of causative agent in a particular setting will be helpful in guiding judicious use of antimicrobial agents and limiting the spread of resistant strains.

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Table 1: Resistance pattern of *E.coli* towards aminoglycosides.

Antimicrobial	Resistance	Total	% Resistance
Amikacin	295	1084	27.21
Gentamicin	385	950	40.53
Netilmicin	79	102	77.45
Tobramycin	415	935	44.39
Total	1174	3071	38.23

Table2: Resistance pattern of *E.coli* towards quinolones

Antimicrobial	Resistance	Total	% Resistance
Ofloxacin	564	977	57.73
Ciprofloxacin	185	248	74.60
Gatifloxacin	113	775	14.58
Norfloxacin	658	958	68.68
Levofloxacin	9	9	100
Lomefloxacin	6	6	100
Nalidixic acid	57	73	78.08
Total	1592	3046	52.27

Table3: Resistance pattern of *E.coli* towards beta lactam group of antimicrobial agents

Antimicrobial	Resistance	Total	% Resistance
Cefotaxime	681	934	72.91
Ceftriaxone	5	5	100
Cefepime	20	23	86.96
Cefoperazone+ sulbactam	22	77	28.57
Ceftazidime	126	221	57.01
Cefixime	7	12	58.33
Ampicillin+ sulbactam	657	930	70.65
Piperacillin	553	1073	51.54
Piperacillin+ tazobactam	309	953	32.42
Carbenicillin	53	77	68.83
Ticarcillin+ clavulanic acid	3	4	75
Aztreonam	67	142	47.18
Imipenem	84	249	33.73
Meropenem	6	19	31.58
Total	2593	4719	54.95

Table 4: Resistance pattern of *E.coli* towards miscellaneous antimicrobial agents

Antimicrobial	Resistance	Total	% Resistance
Nitrofurantoin	643	968	66.43
Chloramphenicol	663	987	67.17
Doxycycline	4	4	100
Polymyxin-B	2	4	50
Cotrimoxazole	56	73	76.71
Tetracycline	97	140	69.29
Total	1465	2176	67.33