Prevalence of Escherichia Coli in the Urine Samples of the Community with Estimation of Effective Antibiotic Therapy in a Tertiary Care Hospital

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Abstract:

Background: Urinary tract infection (UTI) is one of the most common infections encountered and treated worldwide. The spectrum of etiologic agents causing urinary tract infections and their antimicrobial resistance pattern has been continuously changing over the years, both in community and in hospitals. No data concerning the antimicrobial resistance of bacteria isolated from UTI in and around Dehradun region of Uttarakhand has been published to date. Hence an evaluation may also be useful to detect emerging trends of antimicrobial resistance and serve as an indicator for change in antimicrobial prescriptions.

Material & Methods: Study was conducted on all patients who came to the laboratory for urine culture & sensitivity and 100 Escherichia coli isolates were included in the study over a period of 10 months. Minimal inhibitory concentrations were calculated on Vitek 2 compact automated system with emphasis on different enzyme resistance mechanisms.

Results: These isolates had predilection primarily for females except in older age group wherein males were more affected. Different enzyme resistance mechanisms responsible for antibiotic resistance included ESBL, carbapenemase, etc were statistically evaluated.

Conclusion: Importance of excessive water intake and alkalisers should be stressed upon before starting the antibiotic therapy to minimize the emergence of multidrug resistance.

Keywords: Carbapenemase, ESBL, MDR, UTI, MIC.

I. Introduction

Urinary tract infection (UTI) is one of the most common infections encountered and treated worldwide. The spectrum of etiologic agents causing urinary tract infections and their antimicrobial resistance pattern have been continuously changing over the years, both in community and in hospitals.(1) Paul Ehrlich described the concept of antimicrobial agents as "magic bullets" for killing microbes. This impression of antimicrobial agents as magic bullets was thoroughly reinforced when penicillin and other antibiotics came into clinical use in the 1940s. However, shortly after the introduction of these magic bullets in clinical practice, it was discovered that the bacteria were capable of developing resistance to the antimicrobials.

Inappropriate use of antibiotics, use of broad-spectrum antibiotics, insufficient hygiene, immunosuppressants and prolonged hospitalization may promote antimicrobial resistance. Use of antimicrobials of poor quality may contribute to emerging resistance and is a huge problem in countries with poor regulatory capacities. While antimicrobial resistance affects all countries, it has potential for doing more harm in developing countries since second-line antimicrobial drugs are often neither available nor affordable to those who need it.

For rational empirical therapy of community associated UTI, it is necessary to consider the spectrum of uropathogens and their antimicrobial susceptibility pattern time to time, as it may vary institutionally, temporally and geographically. (2-5) There are many unresolved questions regarding antimicrobial resistance in general, including regarding its impact on patient outcome.

II. Study Design

In this prospective study, 100 Escherichia coli isolates from urine samples of all the patients coming to the laboratory were taken.

Selection criteria for Subjects:

Inclusion criteria: All patients coming to the laboratory with chief complaints of dysuria, frequency, flank pain, fever and other co morbid conditions were included in the study.

Exclusion criteria: Patients already on antibiotic treatment were excluded from the study.

Informed consent from all the patients was obtained, before collection of clinical samples.

III. Material and Methods

Vitek 2 compact automated culture system was used for identification and antibiotic sensitivity on isolates from urine cultures. Urine was cultured on cysteine lactose electrolyte deficient agar (CLED agar) and culture plates incubated aerobically at 37°C for 16-18 hrs. After 18 hours plates were observed for growth and colonies were processed according to standard Microbiological procedures.(10)Isolates were first of all identified on basis of Gram staining, followed by identification by GN card and AST N280 for antibiotic sensitivity.

IV. Statistical Analysis

Results were analysed statistically and p-values were calculated to establish the relationship between different enzyme resistance mechanisms and resistance to particular antibiotics.

V. Results

A total of 100 Escherichia coli isolates were cultured from urine samples over a period of 10 months from Sept 2015 -June 2016. 67 % were females and 33 % were males which clearly depicted that females were more commonly affected in our study except in age group of 71-80 years where males were more affected. Increase in frequency and dysuria were found to be the chief symptoms associated with almost every age group while hypertension and DM were chiefly present after the middle age. Nephropathy led to the chronicity of symptoms at a later age [Figure 9].

High level of resistance was seen to Amoxicillin, Ampicillin, Ampi-Sulbactam, Cotrimoxazole, Cefotaxime, Ceftriaxone, Cefepime & Ciprofloxacin ranging from 70-95% whereas Imipenem, Amikacin, Nitrofurantoin, Tigecycline & Piperacillin, showed low level of resistance. (Table 1)

Most of the urinary isolates of Escherichia coli showed resistance to commonly used antibiotics due to the production of Extended spectrum β lactamase group of enzymes followed by amino acyl carboxylase enzymes. (7) (Figure 1)

ESBL production as a mode of resistance was found to be highly significant for ceftriaxone and cefepime. This mode of resistance was also found statistically significant for all other β-lactam drugs tested. (Table 2)

AAC production as a mode of resistance was found to be highly significant for amikacin. This mode of resistance was also found to be statistically significant for gentamicin. (Table 3)

Of all the isolates tested, inhibitor resistant penicillinase production as a mode of resistance contributed to all β-lactam drugsexcept cephalosporin group of drugs.(Table 4)

Table 1: % Resistance of Isolates to Different Drugs

% RESISTANCE	ANTIBIOTICS
96	AMOXYCILLIN
95	AMPICILLIN
75	AMPICILLIN-SULBACTAM
50	PIPERACILLIN
77	CEFOTAXIME
77	CEFTRIAXONE
74	CEFEPIME
3	IMIPENEM
12	AMIKACIN
38	GENTAMICIN
91	CIPROFLOXACIN
1	TIGECYCLINE
28	NITROFURANTOIN
74	COTRIMOXAZOLE

Fig 1. Enzyme-wise Distribution of Isolates
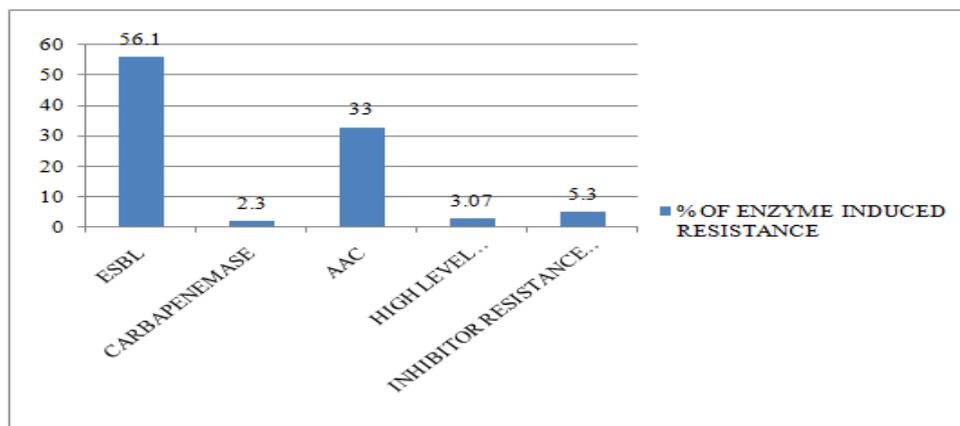
Table 2: Correlation between B-Lactam Drugs andESBL Production

ANTIBIOTICS	ESBL Negative	ESBL Positive	P-value
AMOXYCILLIN	23 (85.2)	73 (100)	0.004
AMPICILLIN	22 (81.5)	73 (100)	0.001
AMPISULBACTAM	13 (48.1)	62 (84.9)	0.001
PIPERACILLINTAZOBACTAM	7 (25.9)	43 (58.9)	0.003
CEFOTAXIME	5 (18.5)	72 (98.6)	0.001
CEFTRIAXONE	5 (18.5)	72 (98.6)	0.0001
CEFEPIME	3 (11.1)	70 (95.9)	0.0001

p-Value: highlySignificant for Ceftriaxone and Cefepime

Table 3: Correlation between Aminoglycosides and Amino Acyl Carboxylase (AAC) production

ANTIBIOTICS	AAC Negative(N= 57)	AAC Positive (N=43)	P-value
AMIKACIN	1 (1.8)	11 (25.6)	0.0001
GENTAMICIN	14 (24.6)	24 (55.8)	0.001

Table 4: Correlation between β-lactam drugs and Inhibitor resistant Penicillinase production

ANTIBIOTICS	INHIBITOR RESISTANT PENICILLINASE Negative (N= 93)	INHIBITOR RESISTANT PENICILLINASE Positive (N=7)	P-value
CEFOTAXIME	77 (82.8)	0 (0)	0.00001
CEFTRIAXONE	77 (82.8)	0 (0)	0.0001
CEFEPIME	73 (78.5)	0 (0)	0.0001

p-value: Highly Significant

VI.   Discussion

The objective of this retrospective analysis was to determine resistance patterns among *E. coli* isolates from community, irrespective of the age and then delineating the most prominent age group. All urinary isolates in this study were processed at Microbiology Division of Central Lab, SMIH, Dehradun. The records of persons presenting with symptoms of UTI and who had urine culture and sensitivity results positive for *E. coli* were examined retrospectively.

Frequency and dysuria were the chief symptoms encountered in each age group followed by diabetes in our study, which correlated with the findings of other studies from south India . (6) Diabetes mellitus produces a number of long-term effects on the genitourinary system. Diabetic nephropathy is one of the many factors that make these patients more susceptible to UTIs than the non diabetics.

In India, most uncomplicated urinary tract infections are treated in the community with short courses of empirical antibiotics and over the counter availability of the broad spectrum antibiotics. This relies on susceptibility data from local surveillance schemes as in many cases urine samples are only sent for microbiological evaluation following treatment failure, recurrent or relapsing infection. Although the levels of resistance we observed amongst community isolates may therefore overestimate the true rate of resistance in the community, the high levels of resistance to ampicillin and trimethoprim raise concerns over the use of these agents.

High level of resistance was seen to Amoxicillin, Ampicillin, Ampi-Sulbactam, Cotrimoxazole, Cefotaxime, Ceftriaxone, Cefepime & Ciprofloxacin ranging from 70-95% whereas Imipenem, Amikacin, Nitrofurantoin, Tigecycline & Piperacillin, showed low level of resistance. Although fluoroquinolones are among the most effective drugs in treating UTI, diverse studies have revealed increasing resistance to fluoroquinolones. (9)

Our study shows Imipenem and Amikacin 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 nitrofurantoin may be influenced by their narrow spectrum of activity, limited indication (treatment of acute cystitis),narrow tissue distribution and limited contact with bacteria outside the urinary tract . There is a reluctance to prescribe nitrofurantoin due to its side effect profile but it stands as an important first – line drug against UTI before culture and sensitivity.When divided for age groups, most *E.coli* resistance was seen in older population (age more than 61 years). Nitrofurantoin showed low level resistance at all ages.

In our study we encountered five different enzyme resistance mechanisms possessed by the isolates, responsible for showing resistance to different classes of drugs. These were extended spectrum β lactamase group of enzymes, amino acyl carboxylase enzymes, inhibitor resistant penicillinase, high level cephalosporinase followed by carbapenemase group of enzymes in descending order of their occurrence. Out of these mechanisms production of extended spectrum β lactamases was the chief mechanism responsible for resistance to different classes of drugs followed by amino acyl carboxylase production.

43% isolates were resistant to aminoglycosides due to production of amino acyl carboxylase group of enzymes. Out of which 11 had positive association with resistance to amikacin and 24 had positive association with resistance to gentamicin.

Inhibitor resistant penicillinase production was evident in 7 isolates that contributed towards resistance to all β-lactam drugsexcept cephalosporin group of drugs. Only 3 isolates were found positive for carbapenemase production which had a highly significant correlation with resistance to imipenem.

Thus we came to observe that various enzyme resistance mechanisms are responsible for resistance to different classes of drugs thus giving rise to MDR pathogens difficult to treat but there elucidation is extremely important to limit our drug use and irrational prescribing.

VII.   Conclusion

Urinary tract infections are one of the common infections which are encountered in the clinical practice. The present study has revealed that UTIs are caused commonly by the organisms who belong to the Enterobacteriaceae family, Escherichia coli being the commonest aetiological agent of uncomplicated, community acquired UTIs. The emergence of drug resistance has left the clinicians with limited options for selecting the appropriate antibiotics for the treatment of the infections which are caused by these multi-drug resistant organisms.

The emergence of ESBL producing organisms among both the hospital and community isolates has forced the clinical microbiology laboratories to check for their presence compulsorily. Apart from this, treating the infections which are caused by these multi-drug resistant isolates by administering carbapenems, is not feasible for the common man in a developing country like ours. The judicious use of antibiotics and the proper implementation of an antibiotic policy in hospitals, will not only help in limiting the emergence of drug resistance, but also in limiting the spread of multidrug resistant strains.

Through our study we came to the conclusion that the clinicians should wait for the culture report before giving the empirical treatment and in the meanwhile excessive water intake and alkalisers can be given to minimize the symptoms of the patient. Moreover, it was also seen that Amikacin and Nitrofurantoin still hold a strong position to curtail the infection if used judiciously.

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