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ORIGINAL ARTICLE

Multidrug Resistant E-Coli in Patients with Urinary Tract Infections Presenting to Internal Medicine Clinics of Two Tertiary Care Hospitals in Lahore, Tip of the Iceberg

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ABSTRACT

Background: The commonly presenting infections in medical outpatients' department are that of Urinary tract. If not treated properly these can lead to hospitalization and can increase the morbidity and mortality. *Escherichia coli* is found to be the most frequent bacterium causing these infections. The available literature may not under representing the prevalence of *E. Coli* which is multi drug resistant and is seen in general medical outdoor and internal medicine clinics of our local population, because urine sample is usually sent for culture only in complicated patients.

Objective: To determine the prevalence of multi drug resistant *E. Coli* and its resistance to the most commonly used antimicrobial agents in Internal Medicine Clinics of Bahria International Hospital, and Farooq Hospital, West wood branch, Lahore.

Study Design: This is an observational study done retrospectively carried out at Internal Medicine Clinics of Bahria International Hospital Lahore and Farooq Hospital, Lahore from 1st January 2019 to 31st December 2020.

Methodology: One hundred and ninety adult patients with urinary symptoms and suspected UTI were enrolled. We analyzed the available urine culture reports and susceptibility against the pathogens. The testing was interpreted according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards.

Results: The most common microorganism was *E. Coli* (70%) followed by klebsiella (17.9%), enterococcus (8.9%) and Acinetobacter (3.2%) in both complicated and uncomplicated urinary tract infections. 75 % females were *E. coli* positive as compared to the male (58.6%). Patients aged greater than 60 and less than 20 years were mostly affected with E. coli. Most of the isolated pathogens were highly resistant to ampicillin, cotrimoxazole, and cephalexin (70%–95.5%).

Conclusion: E. coli is found highly resistant to antimicrobial agents used to treat UTI at family medicine practice. No difference could be appreciated in the apportioning of resistant *E. coli* in both complicated and uncomplicated UTIs. This study emphasizes that we should collect data at National level and prepares a proper guideline for choosing appropriate antibiotics in patients with UTI presenting to general medical clinics.

Key words: *E. coli*, Multidrug resistance, Urinary tract infection, Antibiotics, Pyelonephritis

INTRODUCTION

Most common presentation among infectious diseases are Urinary tract infections (UTIs) both in family practice and in tertiary care hospital settings.[1,2] UTIs can be grouped into two types: hospital acquired urinary tract infection (HAUTIs) acquired during hospital stay of a patient, and community-acquired urinary tract infection written sometimes as CAUTIs.[3] Most common cases are females and they predominantly present with CAUTIs.[1-3] If we read the statistics of United States UTIs were reported to show 100,000 hospitalizations, 7 million clinic visits and 1 million admissions to the emergency services. This poses severe burden on economy and affects the markedly the sense of wellbeing and quality of life of infected individuals.[4,5] Although our data is limited but the leading cause of infections in women seeking medical attention has been reported to be UTIs. International literature shows that E. Coli is the leading pathogen causing Urinary tract infection, followed by others like Enterobacteriaceae, Proteus spp., Staphylococcus saprophyticus, Klebsiella spp. and others.[6,7] Commonly prescribed antibiotics for treatment of UTIs include Ciprofloxacin, Co-trimoxazole (trimethoprim/sulfamethoxazole), Nitrofurantoin, Levofloxacin and Ampicillin. However, it is a common observation that antibiotic resistance among urinary tract pathogens has been rising globally, which has limited the treatment options.[8,9]

Evidence has proved a causal relationship between development of antibiotics resistance and extensive and irrational use of antimicrobials. Therefore, judicious antibiotic usage is warranted to reduce the load of disease and reduce both its costs and complications. That's why, antibiotics stewardship programs and a close watch on development of resistance against antimicrobials is important to find the patterns and develop the guidelines for using the empirical therapy.[10] Our study tried to find the pervasiveness and sensitivity to ampicillin, Co-Amoxiclave (amoxicillin/clavulanate), co-trimoxazole (trimethoprim / sulfamethoxazole), nitrofurantoin, cefazolin, and ciprofloxacin amongst all E. coli isolates obtained from the study patients with urinary tract infections. Study focused on any relationship between patients' demography and E. coli isolates resistance as well.

MATERIALS AND METHODS

This is a retrospective study of patients presented with Urinary Tract Infections in the outpatient's departments of Bahria International Hospital and Farooq Hospital, Lahore over a period of 2 years from January 2019 to December 2020. Urine samples which showed growth of >105 CFU/mL colony-forming units per millilitre with a single type of bacterium from a "clean catch" urine sample, were considered as urinary tract infection and subjected further for microbiological identification and antimicrobial susceptibility testing.

VITEK test method measuring minimum inhibitory concentration (MIC) was used to check sensitivity and resistance of E. coli isolates against multiple antibiotics including Ampicillin, Co-amoxiclav, Co-trimoxazole (Trimethoprim/sulphamethoxazole), Ciprofloxacin, Nitrofurantoin, Cefazolin, and other commonly used antibiotics. According to the Clinical Laboratory Standards Institute (CLSI) guidelines the susceptibility results were interpreted. The

age categories were divided into four groups, starting from 14 years to greater than 60 years. UTIs were classified as uncomplicated if the patient was without any co-morbidities and not having an acute complicated cystitis or suspected pyelonephritis, a woman who was not pregnant, or patients under 60 years of age, while UTIs were grouped as complicated for patients who were male, or women who were pregnant, women of 60 years of age or more or with any co-morbidity or if patient had cystitis or pyelonephritis. Proportions of resistant E. coli isolates between complicated and uncomplicated UTI cases were compared. The data was entered and analyzed through SPSS-23. Significance of the differences between the independent samples was performed by using the Pearson's Chi-Square test, and Fisher exact test where appropriate.

RESULTS

We reviewed a total of two hundred patients' medical records who presented with features of urinary tract infections in both hospitals. From two hundred files, we excluded 10 patients due to incomplete medical record (Table 1).

75% females were found to be E. coli positive as compared to males (58.6%). Patients aged greater than 60 and less than 20 years were mostly affected with E. coli. Most of the isolated pathogens were highly resistant to ampicillin, cotrimoxazole, and cephalexin (70%–95.5%).124(65%) cases of UTIs were classified as uncomplicated UTI (uUTI) while 66 (34%) were grouped as complicated UTI (cUTI). E. c*oli* was isolated as most prevalent bacterium in both complicated (cUTI) and uncomplicated (uUTI) urinary tract infections (70%) of total positive urine cultures followed by klebsiella (17.9%), enterococcus (8.9%) and Acinetobacter (3.2%).86 (69%) cases out of 124 uncomplicated UTI and 47 (71%) among complicated urinary tract infections were caused by *E. Coli* (Table 2). Culture and sensitivity test showed that ampicillin is the most resistance drug in UTI caused by the *E. coli.* The other drugs resistance is summarized in Table 3.

Table 1: Prevalence of *E. coli* in different age groups, genders and type of UTI

Variable	No.	E. Coli +ve	E. Coli –ve	Prevalence	P. Value
Gender					
Male	58	34	37	58.6	0.08
Female	132	99	20	75	
Age (years)					
14-20	10	8	4	80	0.99
21-40	41	24	17	58.5	
41-60	88	61	27	69.3	
>60	51	40	9	78.4	
Type					
Complicated	66	47	19	71.2	0.69
Uncomplicated	124	86	38	69.3	

Table 2: Prevalence of different microorganism in UTI

Species	No.	%
E. Coli	133	70.0
Klebsiella	34	17.9
Enterococcus	17	8.9
Acineto	6	3.2

Table 3: Resistance of E. coli in both complicated and non-complicated UTI

Drug	*E. coli*		P value
	Uncomplicated (86)	Complicated (47)	
Ampicillin	93.2%	95.5%	0.19
Cotrimoxazole	70.3%	81.1%	0.07
Cephalexin	67.4%	75.4%	0.06
Gentamicin	35.9%	44.2%	0.05
Ciprofloxacin	35.5%	40.6%	0.64
Nalidixic acid	32.1%	40.9%	025
Ceftazidime	26.1%	32.1%	0.54
Ceftizoxime	24.1%	34.1%	0.14
Ceftriaxone	20.3%	30.4%	0.08
Cefotaxime	20.5%	25.1%	0.06
Cefixime	22.9%	25.4%	0.07
Nitrofurantoin	14.7%	20.5%	0.09

DISCUSSION

This study pointed that even uncomplicated cases had high antimicrobial resistance to the commonly used drugs in our routine clinical practices and in primary care settings. Resistance to the common antibiotics is a major danger faced by the medical community and several measures are being taken worldwide to manage and address this threat.[11-13] Family physicians around the world attend and treat a significantly large number of urinary tract infections both in adults and children. They have also found the most common pathogens i.e., E coli causing UTI have become resistant to many routinely used antibiotics.[14,15] The available literature shows that previously uncomplicated UTIs had been underestimated and the focus stayed on the treatment of complicated UTIs only. The results of the current study encourage that the primary health care physicians need to be guided about the prevalence of UTIs and the resistance to commonly used antibiotics in our community. Proper knowledge and awareness should also be given to the family physicians for the selection of appropriate drugs to be used empirically, because their usual practice is to send urine samples for microbiology only in cases of complicated UTIs or treatment failure.[16]

The spectrum of resistance in our study is quite similar to the resistance reported in previous literature from other countries where Ampicillin is the highest resistant drug while Nitrofurantoin has lowest reported resistance.[17-19] The increasing levels of resistance can be due to the extensive and non-evidence based used of antibiotics. Extended Spectrum Beta Lactamase (ESBL) producing E coli has emerged as a major concern and has surfaced the literature as it has potential to spread outside the hospital environment. This has posed a major threat in our observation as well.[20] Major limitations to our study is the sample size which still is small for the large population of the city thus lacks the power to handle the type II error. We emphasize that the physicians should interpret the results considering clinically important relevance. As there is debate on classifying a case as uUTI or cUTI, it is possible that we might have misclassified few cases depending upon the clinical judgment of our clinicians working at the Internal Medicine Clinics.[21] This is the need of the hour that the cases of UTIs presenting to the primary health care centres should get classified into uncomplicated and complicated and the treatment for complicated UTIs should be culture-based while that of the uncomplicated ones should follow a uniform and updated guideline or policy.

CONCLUSION

This is obvious that the burden of UTIs on economy and public health of a society is enormous and it affects the quality of life of the affected individual. E. coli is the causative agent in majority of cases followed by Klebsiella and other species of Enterobacteriaceae. Commonly used antibiotics are becoming ineffective with an increase in the resistance among the encountered pathogens.

Recommendations: Antibiotics stewardship and development of guidelines according to local flora is the need of the hour. Teaching and training of primary health care physicians should be carried out at regular intervals with repeated audits or surveillance of cases. Hopefully it will improve the situation and reduce the disease burden. This can help the clinicians in developing guidelines for empiric therapy by determining the infections and resistance patterns in a specific community.

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