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Antibiotic Prescribing Pattern in Uncomplicated Urinary Tract Infection Patients at a Tertiary Care Hospital of North Gujarat.

Dr. Janki Patel*, Dr. Shrikalp Deshpande
Pharm.D Lecturer, Department of pharmacology and pharmacy practice, K.B Institute of Pharmaceutical Education and Research, Gandhinagar
B.Pharm, M.pharm, Ph.D I/C Principal, K.B Institute of Pharmaceutical Education and Research, Gandhinagar
Corresponding Author: Dr. Janki Patel

ABSTRACT: Background: *Urinary tract infection (UTI) is one of the most common infections in humans affecting all age groups and both genders in the community and hospital setup encountered and treated worldwide. There are an estimated 150 million urinary tract infections (UTIs) per annum worldwide and value the global economy in excess of 6 billion US dollars. UTI is the major cause of morbidity associated with high mortality. In order to achieve a satisfactory therapeutic effect, it is proposed that local information regarding the antimicrobial resistance of frequent pathogens should be established as a reference for the selection of empirical antimicrobial therapy.*
Aim: *"To check antibiotic prescribing pattern in uncomplicated urinary tract infection patients in tertiary care hospitals."*
Methodology: *It is a prospective, Observational study. Prescribing pattern of antibiotic has checked at three hospitals of North Gujarat. Patients' data regarding diagnostic parameter and medication during hospitalization were collected during the study period from March 2019 - May 2019 from medicine unit of hospitals.*
Results: *Total 120 patients diagnosed with uncomplicated UTI at medicine ward. Out of which 47 were male and 73 were female patients. To confirm uncomplicated UTI physicians checked with the clinical symptoms as well as urine sample has tested. E. coli has been found to be the major pathogen causing UTI. 10 patients were performed with culture sensitivity test before prescribing antibiotics. Physicians have been used Levofloxacin, Moxifloxacin and Amoxicillin were used in majority patients to treat UTI.*
Conclusion: *In our study, prevalence rate of UTI was found more in female at the age group of 31 to 40 years. Before starting antibiotic treatment antibiotic susceptibility pattern and antibiotic resistance pattern was not checked in majority patients.*
KEY WORDS: *Antibiotic Susceptibility pattern, Antibiotic Resistance pattern, E.coli, Uropathogens, Urinary Tract Infections.*

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I. INTRODUCTION

Urinary tract infection (UTI) is one of the most common infections which require medical care in humans affecting all age groups and both genders in the community and hospital setup encountered. Despite the widespread availability of antibiotics, the incidence of UTI increases with age and sexual activity.[1, 2, 3] There are an estimated 150 million urinary tract infections (UTI) per annum worldwide and value the global economy in excess of 6 billion US dollars.UTI is the major cause of morbidity associated with high mortality.[4, 5, 6] UTIs develop by either uphill or downhill bacterial invasion into the urinary tract. The most common mode of infection is the uphill pathway, where fecal flora gain access to the urinary tract via colonization of the urethra. Downhill infections are the result of hematogenous spread of bacteria from a primary source located elsewhere in the body and it's rare. The lower urinary tract infection is known as a simple cystitis (Bladder infection) and the infection in upper urinary tract or in kidney is known as pyelonephritis.[7]

The major causative and highly problematic antibiotic-resistant organisms are summarized by the ESKAPE mnemonic: Enterococcus, Staphylococcus, Klebsiella, Acinetobacter, Pseudomonas, and ESBL (Enterobacter and E. coli). ESKAPE indicates that these bacteria have developed defenses that permit them to escape the actions of available, effective therapies.[8, 9] Depending on whether the infection is occurring for the first time or a repeated event, the UTI is classified into two types, uncomplicated and complicated infections respectively. Uncomplicated UTI is common and easy to treat while complicated UTI is severe and difficult to treat. An acute uncomplicated UTI is one of the most common bacterial infections in women. It is estimated that as many as 60%of all women report having had a UTI at least once in their lifetime.[2, 7, 11] While it has been

estimated that nearly 10% of the human population will experience a UTI during their lifetime and the commonest bacterial agent involved in causation of UTIs is Escherichia coli, both in the community as well as in the hospital.[6, 11, 12] UTI was defined as the growth of a single pathogen of $>10^5$ colony forming units/ml by properly collected urine specimen (suprapubic aspiration, transurethral catheterization, or midstream specimen in circumcised boys) in humans with febrile disease or urinary symptoms.[12, 13] UTIs are the most common in women because of anatomic arrangement. Recently the UTI management is become more problematic due to the emergence of resistance to different antimicrobial agents. Bacterial resistance to different antimicrobial drugs is a serious health hazard worldwide. Reasonless or unconditional use of different antimicrobials is one of the major causes of bacterial resistance towards antimicrobial agents.[14]

In order to achieve a satisfactory therapeutic effect, it is proposed that local information regarding the antimicrobial resistance of frequent pathogens should be established as a reference for the selection of empirical antimicrobial therapy. Higher multidrug resistance rates were found to be common among hospital acquired UTI pathogens.[4, 12] β-lactam antimicrobial agents are most widely used antibiotics to treat those communities and hospital acquired infections.[7]

Amidst both outpatients and inpatients, Escherichia coli are the primary urinary tract pathogen, accounting for 75% to 90% of both sides - hospital acquired and community acquired UTI. UTIs are often treated with different broad-spectrum antibiotics when one with a narrow spectrum of activity may be appropriate because of concerns about infection with resistant organisms. Fluoroquinolones are preferred as initial agents for empiric therapy of UTI in area where resistance is likely to be of concern. This is because they have high bacteriological and clinical cure rates, as well as low rates of resistance, among the most common uropathogens.[15]

The extensive uses of antimicrobial agents have invariably resulted in the development of antibiotic resistance, which, in recent years, has become a major problem worldwide.[16] The Infectious Diseases Society of America also recommends that physicians obtain information on local resistance spectrum of organisms cause urinary tract infections and that ongoing surveillance be conducted to monitor changes in susceptibility of uropathogens.[8, 9]

Few authors have studied the risk factors associated with the UTI due to ESBL producing bacteria in hospitalized patients. Extended-spectrum β-lactamases (ESBLs) are a group of β-lactamases enzymes belongs to group 2, produced by Gram negative Enterobacteriaceae. Due to rapid emergence of ESBL producing Uropathogens over the last decade, the antimicrobial susceptibility profile has changed dramatically.[7]

II. MATERIALS AND METHODS

This prospective study was conducted at medicine ward with 3 hospitals to observe prescribing pattern for UTI patients. The study included 120 patients diagnosed with uncomplicated UTI over a period of 3 months, from March 2019 to May 2019. Uncomplicated UTI mostly affects healthy individuals with no structural or neurological urinary tract abnormalities; which includes cystitis and pyelonephritis. Consecutive patients who presented with dysuria, frequency, urgency and suprapubic tenderness associated with fever, chills and long pain during the study period were included in the study and total 120 patients were identified with uncomplicated UTI and for those patients' urine sample has collected to confirm UTI. Moreover, culture sensitivity test has suggested before prescribing antibiotics. Patients with pregnancy, urologic abnormality, urinary catheterization and hospitalized patients were excluded from the study. The age, sex, the organism isolated and the antimicrobial susceptibility profiles were collected. The data were entered into Excel for analysis and statistical analysis was done.

Culture and Identification: Urine specimens were collected in sterile wide mouth glass container as per the standard operating procedures. Urine samples were plated using calibrated wire loops (0.001ml) on Cystein Lactose Electrolyte-Deficient (CLED) medium, MacConkey agar and blood agar and then incubated aerobically at 37°C for 24 h. From positive cultures, isolates were identified according to the standard operating procedures. An isolate was considered significant if urine cultures having colony count $\geq 10^5$ CFU/ml.[17]

III. RESULTS

In the present study patients diagnosed with uncomplicated UTI were 120 at medicine ward in 3 hospitals. Patients admitted with complaints of fever, chills, dysuria**,** urinary frequency, urgency, suprapubic pain and haematuria. For detailed investigation and to cure symptoms, patients average stay at hospital was 5 days (Minimum stay at hospital was 3 days and maximum stay at hospital was 10 days). Patients enrolled in this study between the ages 20 to 65 years. 73(60.8%) were females and 47 (39.2%) were male. Patients had no co morbid conditions. Almost half of the studied population presented with dysuria alone and other patients had a complaint of fever, chills, urinary frequency. The prevalence of UTI was higher in females than-males and this was statistically significant Table 1.

Table 1: UTI and Associated Factors.

PARAMETERS	CATEGORIES	UTI PRESENT (NO)
Gender	Female	73(60.8%)
	Male	47(39.2%)
Age(in years)	20-30	27(22.5%)
	31-40	33(27.5%)
	41-50	19(15.8%)
	51-60	16(13.3%)
	>61	24(20%)

More cases of UTIs were recorded among 31 to 40 year (27.5%), Followed by 20 to 30 year (22.5%) and >61 year (20%) of patients. Least cases of UTIs were found in age of 41 to 50 year (15.8%) and age 51 to 60 year (13.3%) of patients. Uropathogens distribution among females and males varied significantly.

Urine routine examination report of pus cells more than five cells per high power field was considered as an indication for prescribing an antibiotic by the physicians. Accordingly, Fever and dysuria were also considered as an indication to prescribe antibiotic by the physicians. E.coli being the most common uropathogen to cause uncomplicated UTI that has been identified in our study. Culture sensitivity test suggested before starting empirical therapy but in our study 10 patients had performed. Of the total 10 patients, 4 patients are not showing bacterial growth, while other 6 patients found with E.coli resistance to following class of antibiotic: Penicillin, Cephalosporin, Carbapenem, Aminoglycoside, Macrolides, Tetracycline and Fluoroquinolones.

There is average drugs per day prescription were 13 and average antimicrobial agents prescribed were 4 (30.7%). Levofloxacin (75.8%) and Ceftriaxone (33.33%) were the most prescribed antibiotics in all age groups. Apart from Levofloxacin and Ceftriaxone, commonly prescribed antimicrobial agents were Amoxicillin (25.8%), Moxifloxacin (25.8%), Piperacillin/tazobactum (18.3%). Antimicrobial prescribing agents used in UTI patients shown in Table 2.

Table 2: Antibiotic Prescribed During Hospitalization.

SR. NO	ANTIBIOTIC USED	DOSE (MG)	ROUTE	AVERAGE UNITS	NO OF PATIENTS (%)
1	Levofloxacin	500	IV	11	91(75.8%)
2	Ceftriaxone	500	IV	7.9	40(33.33%)
3	Amoxicillin	500	IV	10.8	31(25.8%)
4	Moxifloxacin	400	IV/Oral	10	31(25.8%)
5	Piperacillin/tazobactum	4500	IV	8.5	22(18.3%)
6	Clarithomycin	250	IV/Oral	9	20(16.6%)
7	Ceftriaxone/salbactum	1500	IV	11.9	16(13.3%)
8	Cefotaxime	500	IV	6.6	15(12.5%)
9	Amikacin	500	IV	7.7	14(11.6%)
10	Amoxicillin/Clavulanic acid	1200	IV	6	5(4.16%)
11	Doxycycline	100	Oral	10.4	5(4.16%)
12	Metronidazole	500	IV	10	5(4.16%)
13	Cefixime	200	Oral	7	3(2.5%)
14	Ciprofloxacin	750	IV	15.6	3(2.5%)
15	Ofloxacin	400	Oral	8.5	2(1.6%)

It was found out that 51 (40.2%) out of 120 patients were wrongly managed, without urine culture they have been started with antibiotics. 14 (11.6%) out of 120 patients were over treated (treatment not needed but treated), after giving a dose of antimicrobial agents, on the third day observation complaints regarding uncomplicated UTI was not resolving in 26 (21..6%) patients, patients were requires culture sensitivity test but the test was not performed. All patients treated with antibiotics but, 6 (5%) were treated with the correct antibiotics and that include fluroquinolones, Aminoglycoside and Piperacillin/tazobactum class of drug for 5 days ,on observation it was found out patients got relief from UTI complaints after taking 5 days treatment. Almost, patients who did not require more than one antibiotic treatment for uncomplicated UTI were treated with more antibiotics. During hospital stay minimum units of one antibiotic prescribed were 3 and maximum units were 10. Overtreatment was not associated with age and gender. The presence of 6-15 pus cells was associated with over treatment.

IV. DISCUSSION

The study was tackled to determine the incidence of urinary tract infection in hospitalized patients as well as to analyze the prescribing pattern of antibiotics at different hospitals. UTI is one of the most frequently diagnosed diseases worldwide. In our study found out that females were more frequently affected than males. It has been widely revealed that women have a higher prevalence rate than males.[2, 10, 18] Effective treatment of patients with UTIs commonly relies on the identification of the type of organisms and the selection of an effective antibiotic agent to the organism. Availability of new antimicrobial improved the management of UTI.[17, 19] The most commonly isolated organism found in our study was Escherichia coli at three sites. The bacterial species isolated in the present study was similar to those described in several previous studies.[18, 20]

For selection of antibiotics culture sensitivity test is required and during the study period it was observed 10 patients were performed with the culture sensitivity test. Patients were treated with resistant drugs which could have been avoided if the physician has recommended for the culture report. The chance of treating with resistant antibiotic was higher when the physician started on cephalosporins (Cefixime, Ceftriaxone and Cefoperazone/Sulbactam). This was because most of the organisms were resistant to cephalosporins. This implies the importance of checking the culture report before starting on antibiotics. Because in culture test Penicillin, Cephalosporin, Carbapenem, Aminoglycoside, Tetracycline and Fluoroquinolones class were not sensitive against E.coli. The patient could have been managed by other symptom relieving drugs or by empirical therapy with nitrofurantoin.[2, 21]

There are no country specific guidelines for treating UTI; the Indian Society of Nephrology states that knowledge of local resistance pattern is needed to guide empirical therapy in the light of rising resistance to amoxicillin, sulfa drugs, Cotrimoxazole and Fluoroquinolones.[22] According to an update by the Infectious Diseases Society of America (IDSA) guidelines, a short-course therapy (3 day) with either nitrofurantoin or Trimethoprim-Sulfamethoxazole (if the local resistance prevalence less than 20%) is recommended.[23, 24]

According to guideline suggestion Nitrofurantoin (100mg), Cotrimoxazole(500/125 mg),Ciprofloxacin (500mg),Cefuroxime (250 mg), Cefixime (400mg), Piperacillin/tazobactam (4.5gm), Ertapenem (1gm), Imipenem (500mg), Amikacin (5mg/kg),Doxycycline (100mg),Cefoperazone/sulbactam (3gm) would be used for 3-5 days.[24, 25] 124 patients have been prescribed with fluoroquinolones class of drug, out of 124 patients 5 patients were performed with culture sensitivity test among them 4 patients were showing resistance towards fluoroquinolones class of drug that indicate before prescribing empirical therapy culture test should be performed.

V. CONCLUSION

Empirical treatment should be prescribed by using standard treatment guidelines; culture test is required to confirm prescribed antibiotic is effective or ineffective. According to result of culture sensitivity test change regarding prescribed antibiotics should be done. This study was a pilot study for giving interventions regarding antibiotics use with limited sample size and duration considering that further study will plan and result of that would be helpful in improving prescribing pattern.

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Ethical Clearance

Ethical approval has been taken from ethics Committee of K.B institute of pharmaceutical education and research, Gandhinagar.

Conflicts Of Interest

No.

Abbreviations

UTI - Urinary Tract Infection
E.coli - Escherichia coli
ESBLs - Extended-spectrum β-lactamases
CLED - Cystein Lactose Electrolyte-Deficient

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