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STUDY ON ANTIMICROBIAL DISTRIBUTION AND SUSCEPTIBILITY PATTERN OF UROPATHOGENS CAUSING URINARY TRACT INFECTION IN A TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Urinary tract infection (UTI) is one of the commonest infections encountered by clinicians and despite the widespread availability of antimicrobial agents UTI has become difficult to treat because of appearance of pathogens with increasing resistance to antimicrobial agents. The study is to analyse the bacteriological pattern in lower UTI in a specific geographical region and antibiotic susceptibility pattern of isolated uropathogens from urology outpatient department of a tertiary care hospital. This is prospective observational study conducted at department of urology in Karuna medical college hospital Chittur, Palakkad during a period of 6months from November 2017-April 2018. Females were more prevalent for urinary tract infection and the most prevalent organism is found to be E.coli, followed by pseudomonas aeruginosa. The antibiotic sensitivity pattern of both gram negative and gram positive cocci revealed maximum sensitivity for fosfomycin (98%), followed by imipenem (79%). of the study shows that uropathogens have shown decreased susceptibility to most of the available antibiotics for the treatment of UTI while fosfomycin shows high sensitivity to most of the uropathogens isolated. Hence it is now necessary to use these antibiotics with utmost care and also develop new antimicrobials having high effectiveness with minimal side effect, freely available and less expensive.

Key words: Urinary Tract Infection, Antimicrobial Pattern, Uropathogens.

INTRODUCTION

Sterculia foetida L is a tropical plant belonging to the Urinary Tract Infection (UTI) remains the most common bacterial infection in human population and is also one of the most frequently occurring nosocomial infections [1]. Its annual global incidence is of almost 250 million [2, 3]. UTIs refer to the presence of microbial pathogens within the urinary tract and it is usually classified by the site of infection as bladder (cystitis), kidney or urine. They are asymptomatic or symptomatic. UTIs that occur in a normal genitourinary tract with no prior instrumentation are considered as “uncomplicated” whereas “complicated” infections are diagnosed in genitourinary tracts that have structural or functional abnormalities including instrumentation such as indwelling urethral catheters, and are frequently asymptomatic [4, 5]. Many different microorganisms can cause UTIs though the most common pathogens causing the simple ones in the community are Escherichia coli and other entero bacte riacae, which accounts for approximately 75% of the isolates [6]. Treatment of UTI is often started empirically and therapy is based on information determined from the antimicrobial resistance pattern of the urinary pathogens [7].

The spectrum of bacteria causing complicated UTI ismuch broader than of those causing uncomplicated UTI. However, the most commonly encountered micro organismsare Gram negative bacteria including Escherichia coli, Citrobacter spp., Enterobacter aerogenes, Pseudomonas aeruginosa, and Proteus vulgaris whereas Klebsiella spp., Staphylococcus aureus, and Salmonella spp. are found rarely [8]. Increasing multidrug resistance in bacterial uropathogens is an important and emerging public health problem. The Infectious Disease Society of

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America (IDSA) identified some microorganisms for new effective therapies. Those microorganisms were called "ESKAPE pathogens" which include Enterococcus faecium, S.Aureus, Klebsiellaspp., Acinetobacterspp., Pseudomonas spp., and Entero bacterspp. Increasing drug resistance in UTI needs regular monitoring of the antibiotic susceptibility of uropathogens in a particular area. Various factors such as the type of UTI (complicated or uncomplicated), gender, age, and previous history of antibiotic therapy of each UTI patient should also be considered to find out the correct global data on susceptibility [9]. The distribution of antimicrobial susceptibility data of UTI-causing microorganisms changes from time to time and from place to place [10]. The susceptibility data provided by regional microbiology laboratories helps to choose the empirical choice of antimicrobials to treat UTI; however, these conditions are limited to complicate UTI as the samples of uncomplicated UTI are rarely sent to laboratories [11, 12]. Generally, the antimicrobial treatment is initiated before the laboratories results which may lead to the frequent misuse of antibiotics [13]. The resistance pattern of community acquired uropathogens has not been extensively studied in India [14, 15].

Methodology

A prospective drug utilization study was conducted in Type 2 diabetes mellitus patients in the department of urology at Karuna Medical College Hospital (KMCH), Kerala for 6 months - between from November 2017 to April 2018. Ethical approval for this study (SDAT / KMC/12-2017/84) was provided by Institutional Ethics Committee in Karuna Medical College, which permits and confirms that the institute gives approval to release the data.

Bacterial Isolates

The present observational study was performed on UTI cases who were referred to outpatient department of urology, Karuna medical college hospital, Palakkad from November to April .Patients those who were clinically diagnosed with UTI and those for whom urine microscopy culture and sensitivity has been ordered as a part of routine medical test were included in the study. Paediatric population of patients with UTI symptoms, patients with symptoms of acute pyelonephritis and female population on their menstrual phase. Urine specimen showing ESBL and MRSA were also excluded in the study. A total of 107 clinical isolates were obtained from the urine specimens of patients with lower UTI. Urine samples were obtained from the study subjects. UTI refers to the existence of microbial pathogens in the urinary tract and is defined as the growth of a single pathogen of > 105 colony-forming units per millilitre (CFU/ml) from properly collected midstream urine specimens. Proper specimen collection was instructed to all patients. All samples were processed on Muller Hinton agar using calibrated loops. The inoculated plates were aerobically incubated at 37◦C for 48 hours. The specimen was considered positive and negative for UTI if a single organism is at a concentration of $\geq 10^5$ CFU/ml and $<10^2$ CFU/ml respectively. Negative cultures were maintained in incubator up to 2 days. Bacterial isolates were identified on the basis of their cultural and biochemical characteristics. Identification of gram positive isolates was performed by gram staining.

Antibiotic Susceptibility Testing

Antibacterial susceptibility of isolates were tested by Kirby-Bauer disk diffusion .For gram-negative and gram- positive bacteria, following discs were tested with their respective concentration. The following antimicrobial agents were used in the study: amikacin, ampicillin, ampicillin-sulbactam, azithromycin, cefotaxime, cefotaxime clavunalic acid, ceftazidime, ceftriaxone, cefuroxime, cotrimoxazole, doxycycline, fosfomycin, gentamycin , imipenem, levofloxacin, linezolid, meropenem, netilmycin, nitrofurantoin, norfloxacin, ofloxacin, piperacillin + tazobactam. Diameter of inhibition zones was measured after incubation at 35 ◦C for 18-24 hours, and data were reported as Sensitive, Intermediate and Resistant.

RESULTS

The total of 107 symptomatic patients was included in the study. Out of 107 urine samples examined in our study, 100(93.4%) showed significant bacteriuria and 7(6.5%) showed negative bacterial growth.

A total 107 symptomatic patients in the age group of 18 years to 100 years, 69(64.48%) were females and 38(35.51%) were male patients. Female and male patient ratio was 1.81:1.

The study reveals that out of the 69 females (64.48%) tested, 65 were found to be positive samples(65%) and out of 38 males (35.51%) tested, 35 were found to be positive samples(35%). Out of 107 urine samples processed 93.4 %(n=107) had significant bacterial growth.

The isolates included both gram positive and gram negative organisms. Of the 100 isolates, gram negative accounts for 94(94%) while gram positive organisms accounts for 6(6%). Escherichia coli showed highest prevalence of 77% followed by pseudomonas aeruginosa (6%), acinetobacter (4%), enterococcus species(4%), klebsiella species(3%), enterobacter species (3%), coagulase negative Staphylococci (2%), citrobacter (1%). Escherichia coli was the predominant isolate among the gram negative organism and enterococcus species among the gram positive organisms.

The antibiotic sensitivity pattern of both gram negative bacilli and gram positive cocci revealed that the maximum sensitivity for fosfomycin (98%) followed by imipenem (85.7%), nitrfurantoin (67.7%), meropenem (60.8%), cotrimoxazole (58.1%) and netilmycin (59%). The maximum resistance was seen against cefotaxime (62.2%), ampicillin (59.1%), cefuroxime (57.1%), norfloxacin (54.4%) ceftriaxone (54%), ceftazidime (52%). (Table4).

The antimicrobial potency and spectrum for 23 selected antimicrobial agents of different classes against the 6 most frequent gram negative UTI pathogens and 2 frequent gram positive UTI pathogens are summarized in table 5 and table 6.Sensitivity to Aztreonam to klebsiella species, acinetobacter, and citrobacter were not tested as they have intrinsic resistance to that drug. Sensitivity to linezolid to acinetobacter, klebsiella species, citrobacter, pseudomonas species, enterobacter. Among most frequently isolated gram negative and gram positive pathogens, 98% were found to be highly sensitive to fosfomycin. E.coli showed high sensitivity to fosfomycin (97.4%) followed by imipenem (69%), nitrofurantoin (51%), meropenem (47%), cotrimoxazole (46%).

Table 1. Growth of Urine Culture among the Study Population

Growth	No : Of Patient(N =107)	Percentage %
Positive	100	93.4%
Negative	7	6.5%

Table 2. Frequency of Isolated Bacterial Agents among the Study Patients

Isolated Bacteria	No : Of Patient	(%)	Male	Female
Gram Negative Organism				
E.Coli	77	77%	25	52
Klebsiella Species	3	3%	2	1
Acinetobacter	4	4%	2	2
Citrobacter	1	1%	-	1
Pseudomonas Species	6	6%	3	3
Enterobacter	3	3%	1	2
Gram Positive Organism				
Enterococcus Species	4	4%	1	3
Coagulase –ve Staphylococcus Species	2	2%	1	1
Total Bacterial Growth	**100**	_	**35**	**65**
No Bacterial Growth	**7**	_	**3**	**4**
Total	**107**	_	**38**	**69**

Table 3. Antibiotic sensitivity and resistance pattern of isolated organism in lower UTI

Antibiotic	Total No Isolates	S	%	I	%	R	%	Not Tested Samples
Amikacin	100	37	37.4	26	26.2	36	36.3	1
Ampicillin	100	21	21.4	19	19.4	58	59.1	2
Ampicillin /Sulbactam	100	41	41.8	27	27.5	30	30.6	2
Azithromycin	100	41	41.8	27	27.5	30	30.6	2
Cefotaxime	100	21	21.4	16	16.3	61	62.2	2
Cefotaxime Clavulanic Acid	100	33	35.9	35	38.0	24	26	8
Ceftazidime	100	33	33.7	14	14.2	51	52	2
Ceftriaxone	100	18	18.4	27	27.5	53	54	2
Cefuroxime	100	30	30.6	12	12.2	56	57.1	2
Ciprofloxacin	100	11	33.3	5	15.1	17	51.5	67
Cotrimoxazole	100	57	58.1	5	5.1	36	36.7	2
Doxycycline	100	46	47.4	21	21.6	30	30.9	3
Fosfomycin	100	98	98	2	2	0	0	0
Gentamicin	100	57	58.7	14	14.4	26	26.8	3
Imepenem	100	79	85.7	3	3.3	10	10.8	8
Levofloxacin	100	30	33.7	22	24.7	37	41.5	11
Meropenem	100	59	60.8	10	10.3	28	28.8	3
Nitrofurantoin	100	65	67.7	12	12.5	19	19.7	4
Ofloxacin	100	38	38.7	13	13.2	47	47.9	2
Piperacillin +Tazobactam	100	33	35.5	36	38.7	24	25.8	7
Norfloxacin	100	27	30	14	15.5	49	54.4	10
Netilmycin	100	56	59	15	15.7	24	25.2	5

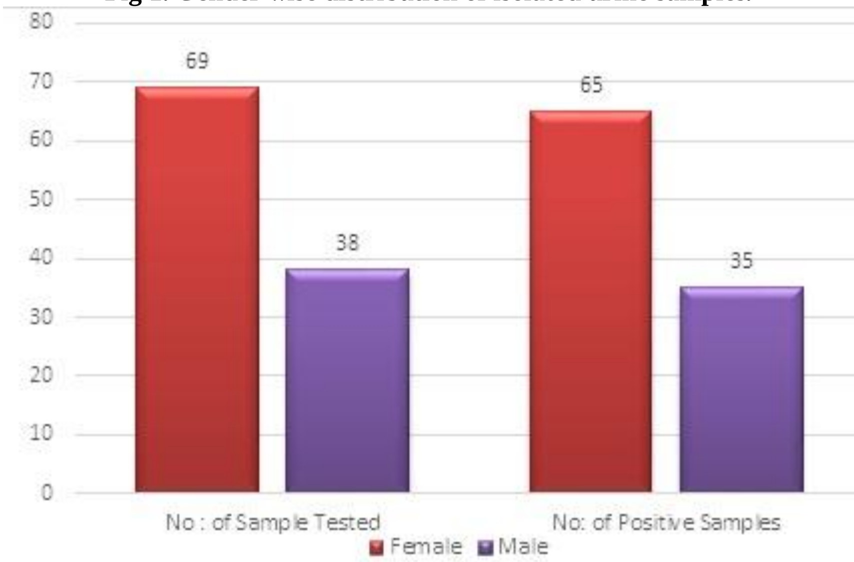
Table 4. Anti bigram pattern of most frequently isolated gram negative urinary pathogens

Antibiotics	E .coli (n=77)			Klebsiella species (n=3)			Acinetobacter (n=4)			Citrobacter (n=1)			Pseudomonas species (n=6)			Enterobacter (n=3)		
	S	I	R	S	I	R	S	I	R	S	I	R	S	I	R	S	I	R
Amikacin	29	21	27	0	0	3	3	1	0	1	0	0	2	2	2	1	1	1
Ampicillin	14	20	43	0	0	3	0	2	2	0	0	1	0	0	4	1	1	1
Ampicillin sulbactam	35	19	23	0	2	1	2	1	1	0	0	1	1	2	3	2	1	0
Azithromycin	18	20	36	2	0	1	0	2	2	1	0	0	3	0	2	0	2	1
Aztreonam	0	0	4	0	0	0	0	0	0	0	0	0	2	0	0	0	1	0
Cefotaxime	19	12	46	0	0	3	1	1	2	0	0	1	0	0	5	0	3	0
Cefotaxime clavulanic acid	25	8	18	0	1	0	3	1	0	0	0	1	2	0	2	0	1	0
Ceftazidime	25	12	39	0	1	2	2	1	1	0	0	1	1	0	2	3	0	0
Ceftriaxone	22	12	42	0	1	2	2	1	1	0	0	1	0	1	5	1	1	1
Cefuroxime	24	11	42	0	0	3	4	0	0	0	0	1	0	0	6	1	1	1
Cotrimoxazole	46	3	28	2	1	0	2	0	1	0	0	1	3	0	2	2	0	1
Doxycycline	36	19	22	1	0	2	3	0	0	0	1	0	1	1	4	1	0	2
Fosfomycin	75	2	0	3	0	0	4	0	0	1	0	0	6	0	0	3	0	0
Gentamycin	43	13	18	3	0	0	2	0	2	1	0	0	3	0	2	1	0	1
Imipenem	69	2	6	3	0	0	3	1	0	1	0	0	2	0	3	3	0	0
Levofloxacin	21	20	31	0	0	3	0	2	1	1	0	0	3	0	2	3	0	0
Linezolid	2	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Meropenem	47	10	20	1	0	2	3	0	1	1	0	0	2	0	3	3	0	0
Netilmycin	45	13	18	2	1	0	2	0	2	1	0	0	3	0	3	2	1	0
Nitrofurantoin	51	14	11	1	0	2	3	0	1	1	0	0	3	0	2	0	0	2
Norfloxacin	20	14	38	0	0	3	3	1	0	1	0	0	2	0	3	3	0	0
Ofloxacin	26	12	38	0	0	3	2	1	1	1	0	0	3	0	3	3	0	0
Piperacillin Tazobactam	28	29	16	0	0	3	1	2	1	1	0	0	3	1	2	0	1	0

Table 5. Anti bigram pattern of most frequently isolated gram positive urinary pathogens

Antibiotics	Enterococcus species(n=4)			Coagulate negative staphylococcus(n=2)		
	S	I	R	S	I	R
Amikacin	0	2	2	1	0	0
Ampicillin	3	0	1	0	0	0
Ampicillin sulbactam	2	1	1	0	0	0
Azithromycin	2	1	0	0	0	0
Aztreonam	0	0	1	0	0	0
Cefotaxime	2	1	1	0	0	0
Cefotaxime clavulanic acid	3	0	0	0	0	0
Ceftazidime	2	0	2	0	0	1
Ceftriaxone	2	1	1	0	0	0
Cefuroxime	1	0	3	0	0	0
Cotrimoxazole	1	0	3	1	0	0
Doxycycline	2	1	1	0	0	0
Fosfomycin	4	0	0	2	0	0
Gentamycin	2	1	1	0	0	0
Imepenem	3	0	1	0	0	0
Levofloxacin	3	0	0	0	0	0
Linezolid	1	0	0	2	0	0
Meropenem	2	0	2	0	0	0
Netilmicin	1	1	2	0	0	0
Nitrofurantoin	4	0	0	1	0	0
Norfloxacin	1	0	2	0	0	0
Ofloxacin	2	0	2	1	0	0
Piperacillin Tazobactam	1	2	1	0	0	1

Fig 1. Gender wise distribution of isolated urine samples.



DISCUSSION

The study observes that the prevalence of UTI is high among females (65%) than males (35%). It has been reported that adult women have a higher prevalence of UTI than men, principally due to anatomical and physical factors [14]. Bacterial uropathogens have the potentiality to change tissues of urinary tract adjacent structures [16]. Early detection and selection of an appropriate effective antimicrobial agent is highly essential for effective management of patients suffering from UTIs to prevent any further complications. Diagnosis and adequate management is only possible by close association between the clinicians and microbiologist [17]. In the present study infection rate is higher in females (65%) than male patients (35%), which is consistent with study by Razak SK et al., [17]. The study demonstrates that Escherichia coli is the most common isolated organism (77%) followed by pseudomonas species (6%) among gram negative uropathogens, which is consistent with many other studies by Razak SK et al., [17], Sibi et al., [18]. Among gram positive isolates enterococcus (4%) followed by coagulase negative staphylococcus species (2%), which is consistent with the study done by Das RN et al [19].

The antimicrobial sensitivity and resistance pattern varies from community to community and from hospital to hospital. This is because of emergence of resistant strains as a result of indiscriminate use of antibiotics. In our study gram negative organism E. coli showed following sensitivity pattern – fosfomycin (97.4%), imipenem (89.6%), nitrofurantoin (66.23%), meropenem (61.03%), cotrimoxazole (59.74%), netilmycin (58.44%). According to Das RN et al [19], susceptibility pattern showed amikacin (87.2%), ciprofloxacin (74.8%), ceftazidime (71.5%), gentamicin (70.4%), nitrofurantoin (35%) and ampicillin (50.5%). According to Supriya et al [20] susceptibility pattern showed, nitrofurantoin (62.5%), cefotaxime (58.7%), norfloxacin (44.9%), ampicillin (21.4%) and cotrimoxazole (18%).

In our study gram positive organism showed following sensitivity pattern fosfomyc in (100%), nitrofurantoin (83.3), ampicillin (50%), ofloxacin (50%), levofloxacin (50%). In our study fosfomycin was found to be most sensitive followed by imipenem, nitrofurantoin, cotrimoxazole, meropenem, gentamycin, netilmycin, and doxycycline. Amoxicillin clavulanic acid, erythromycin and polymyxin is found to be least sensitive. Among other oral antibiotics, fosfomycin was found to be more effective in the treatment of UTI,only after the culture and sensitivity testing studies were done. This finding is analogous with the study conducted by Smitha et al [21] that concludes fosfomycin in a single 3-4 gram dose is as effective as 7 day regimen of nitrofurantoin for the treatment of uncomplicated lower UTI in women. Continuous analysis of the antibiotic resistance pattern act as a guide in initiating the empirical treatment of UTI and the therapy must be started only after the urine culture and the sensitivity testing has been done. This acts as a gold standard test and it helps in avoiding the treatment failure. So the rapid dissemination of the antibiotic resistance and its mechanism can be prevented.

CONCLUSION

Present study showed that uropathogens have shown decreased susceptibility to most of the available antibiotics for the treatment of UTI while fosfomycin shows high sensitivity to most of the uropathogens isolated. Hence it is now necessary to use these antibiotics with utmost care and also develop new antimicrobials having high effectiveness with minimal side effect, freely available and less expensive.

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Nil

CONFLICT OF INTEREST

No interest

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