ORIGINAL ARTICLE

Culture and Sensitivity pattern of Urinary Tract Infections among Women of Reproductive Age Group

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ABSTRACT

Aim: To identify the culture and sensitivity pattern of microorganisms in urinary tract infection (UTI) among women of reproductive age group.

Methods: A retrospective study was conducted in the Microbiology department, Services Institute of Medical Sciences, where patient's records of all positive culture for UTI during the one year period from November, 2017 to October 2018 were retrieved. The inclusion criteria were; patients with confirmed diagnosis of UTI, women with age 18 to 44 years and culture positivity. Patients with history of prior antibiotic therapy, incomplete records, recent surgery and steroid therapy were excluded. The freshly voided midstream urine samples were analyzed for urine culture and Antibiotic Sensitivity Test (ABS). The research was initiated after the ethical approval was granted by the Institutional Review Board (IRB) of Services Institute of Medical Sciences, Lahore.

Results: The records of 96 urine samples from females of reproductive age were analyzed for isolation of the bacterial isolates. The age range was 18 to 44 years with mean (SD) as 28.54 (7.63) years. The most common urinary tract pathogen identified was Escheraecia coli (49%), followed by Staphylococcus Aureus (24%), Klebsiella pneumoniae (17.7%) and Enterobacter spp. (4.2%). There were sixty six (68.8%) females having severe UTI infection. Against E. coli highest sensitivity was observed for Meropenem (100%), Fosfomycin (100%), Nitrofurantoin (100%), Imipenim (97.9%), Amikacin (91.5%) and Cefaparazone/ Sulbactam (72.3%). Moreover, against Staphylococcus Aureus highest antibiotics sensitivity was identified for Imipenim (95.7%), Meropenem (95.7%), Tetracycline (91.3%), Cefaparazone/ Sulbactam (87%), Augmentin (87%) and Nitrofurantoin (78.3%),

Conclusion: Most common urinary tract pathogens in females of reproductive age group were E. coli and Staphylococcus Aureus. Meropenem, Fosfomycin, Nitrofurantoin, Imipenim and Amikacin were the most effective antibiotics against E. coli. However, against Staphylococcus Aureus the most sensitive antibiotics were identified as Imipenim, Meropenem and Tetracycline.

Keywords: Anti-microbial susceptibility, Escheraecia coli, Reproductive age, Staphylococcus Aureus, UTI

INTRODUCTION

Urinary Tract Infection (UTI) has been defined as the diverse spectrum of conditions that affects the urinary tracts, thereby causing multiple clinical complaints[1]. UTI has been classified as upper UTI and lower UTI, depends the involvement of upper or lower urinary tract and at times it involved both; thereby classification depends on the anatomical part involvement[2-5]. Acute pyelonephritis (APN) affecting kidney is being described as upper UTI with patients presenting with complaints of high grade fever, flank pain, vomiting, nausea and rigors[6-7]. However, the lower UTI presents with the symptoms of urinary urgency, dysuria, nocturia, urinary incontinence, bladders infection (cystitis) and urethral inflammation.[8] Importantly, The UTI etiology is microbial, where in most cases bacterial pathogens has been the cause of UTI[1].

UTI are either acquired from community or from the hospital setting[2]. The prevalence of UTI has been considerably high and estimated that it affects 150 million of the global population annually[3]. In the year 1997, the National Hospital Ambulatory Medical Care Survey reported that UTI affects around 7 million outpatient visits annually, thus ranked second most prevalent infection being encountered by clinicians practicing the community

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medicine.[3] The most common organism causing UTI has been identified as *E. coli* followed by other gram negative bacteria; Klebsiella, Pseudomonas aeruginosa and Proteus[7]. The gram negative organisms causing UTI has been identified as Enterococcus, Staphylococci, and Streptococci accounting for 5 to 10% infections[9]. Though a wide range of antibiotics are available for the treatment of UTI, it continues to remain highly prevalent infection and cause for significant morbidity among women. The UTI significantly affects the quality of life among infected females and have serious health consequences as infection may lead to renal damage. This calls for more attention towards the reproductive health need of women i.e. health education. Moreover, resistance developing against antibiotic is also a serious concern. The resistance has developed on account of the misuse of antibiotics prescription and the resistances for different antibiotics are increasing[10].

Evidence from the literature suggested that the two most common organisms causing UTI are Escherichia coli, Klebsiella pneumonia[11]. The study conducted in Pakistan, that recruited seventy women of reproductive age group with confirmed diagnosis of UTI reported that the most common pathogen isolated was Escherichia coli, followed by Klebsiella pneumonia, Streptococcus faecalis, Acinetobacter, Staphylococcus aureus, Candida, Pseudomonas and Proteus[11]. The similar study further highlighted that among fourteen antibiotics tested against

E. coli; Amikacin was identified as being the most effective antibiotic (97.6%) followed by Nitrofurantoin (90%)[12]. In recent years the response of uropathogen to different antibiotics have been changing rapidly and alteration of resistance of these causative organisms acquired from the community has also increased. Therefore, it is deemed essential to retrospective analysis in each community to gain understanding and knowledge of antibiotic susceptibility. The aim of the study is to identify the culture and sensitivity pattern of microorganisms in UTI among reproductive age women.

METHODS

A retrospective study was conducted in the Microbiology department, Services Institute of Medical Sciences, Lahore, Pakistan. The patient's records of all positive culture for UTI during the one year period from November, 2017 to October 2018 were retrieved. The inclusion criteria were; patients with confirmed diagnosis of UTI, women with age 18 to 44 years and culture positivity (10^{4-5} CFU/ml or greater than 10^5 CFU/ml growths of bacteria on the culture medium). Patients with history of prior antibiotic therapy, incomplete records, recent surgery and steroid therapy were excluded. The freshly voided midstream urine samples were analyzed for urine culture and Antibiotic Sensitivity Test (ABS). Bacterial pathogens were isolated and identified by gram staining, morphology and biochemical characters. For the positive cultures, antibiotic sensitivity discs were placed on the Muller Hinton agar plates with incubation at 37 ^{0}C for 18-24 hours and sensitivity plates results were read after 24 hours. The sensitivity and resistance of antibiotics tested were Amikacin, Gentamicin, Tabromycin, Amoxcil/ Ampicillin, Augmentin, Ciprofloxacin, Enoxacin, Nalidixic Acid, Ofloxacin, Pipemidic Acid, Sparfloxicin, Cephradine, Cefuraxime, Ceflexime, Cefotaxime, Cefatazidime, Ceftriaxone, Cefaparazone/ Sulbactam, Imipenim, Meropenem, Doxycycline, Tetracycline, Co-trimaxole, Fosfomycin and Nitrofurantoin. All laboratory investigations were performed in the single laboratory to ensure calibration.

The study was conducted according to the ethical guidelines of Pakistan Medical research Council (PMRC) and Helenski declaration. Confidentiality and anonymity of patient's data were ensured. The research initiated once ethical approval was granted by the Institutional Review Board (IRB) of Services Institute of Medical Sciences, Lahore.

Data Analysis: Data was analyzed using SPSS version 21 (IOBM). Descriptive statistics was performed. Categorical variables (i.e. age categories, organism isolated, sensitivity and resistance) were presented as frequency and percentage while continuous variable (i.e., age) was presented as mean ± Standard deviation (SD).
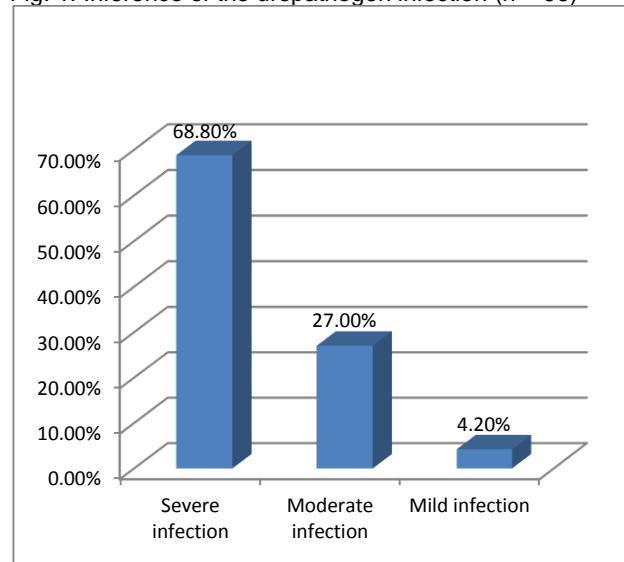
RESULTS

The records of 96 urine samples from females of reproductive age were analyzed for bacterial isolates. These samples satisfied the inclusion and exclusion criteria and documented positive bacteriuria. The sample was positive for urine culture thus antibiotic sensitivity and resistance pattern for these specimens were only included for the analysis.

Table 1: Distribution of isolated urinary tract pathogens (n=96)

Organism isolated	n
Escheraecia coli	47 (49)
Staphylococcus Aureus	23 (24)
Klebsiella pneumoniae	17 (17.7)
Enterobacter spp.	4 (4.2)
Pseudomonas Aeruginosa	2 (2.1)
Proteus spp.	1 (1)
Salmonella Group D	1 (1)
Staph saprophyticus	1 (1)

Fig. 1: Inference of the uropathogen infection (n = 96)

The study participants age range was 18 to 44 years with mean (SD) as 28.54 (7.63) years. Majority of females were in the age range of 18 to 25 years (40.6%), followed by 26 to 35 years (39.6%) and least in age category 36 to 44 years (19.8%).

The table 1 gives details of the isolated pathogens. Escheraecia coli was being identified as the most common causative microorganism for UTI. Among ninety six isolated pathogens the most common was Escheraecia coli (49%), followed by Staphylococcus Aureus (24%), Klebsiella pneumoniae (17.7%), Enterobacter spp. (4.2%), Pseudomonas Aeruginosa (2.1%), Proteus spp. (1%), Salmonella Group D (1%) and Staph saprophyticus (1%).

The figure 1 entails details of the inference of the uropathogen infection. There were sixty six (68.8%) females of reproductive age having severe UTI infection. Moreover, twenty six (27.1%) females had moderate UTI and four (4.2%) had mild infection.

The table 2 gives details of the antimicrobial susceptibility pattern of uropathogens (Escheraecia coli, Staphylococcus Aureus and Klebsiella pneumoniae). The sensitivity and resistance pattern for these three uropathogens were tested against the antibiotics. The highest sensitivity of different antibiotics against Escheraecia coli were Meropenem (100%), Fosfomycin (100%), Nitrofurantoin (100%), Imipenim (97.9%), Amikacin (91.5%), Cefaparazone/ Sulbactam (72.3%), Cefotaxime (66%), Cefatazidime (66%), Ceftriaxone (66%), Augmentin (63.8%), Ciprofloxacin (63.8%), Ceflexime (63.8%). The remaining antibiotics tested had sensitivity less than sixty percent against Escheraecia coli. Moreover, against

Staphylococcus Aureus highest antibiotics sensitivity was identified for Imipenim (95.7%), Meropenem (95.7%), Tetracycline (91.3%), Cefaparazone/ Sulbactam (87%), Augmentin (87%), Nitrofurantoin (78.3%), Cefuraxime (73.9%), Amikacin (69.6%), Cefotaxime (60.9%), Cefatazidime (60.9%) and Fosfomycin (60.9%). The remaining antibiotics tested had sensitivity less than 60% against Staphylococcus Aureus. Finally, for the seventeen isolates of Klebsiella pneumoniae the highest antibiotic sensitivity was observed for Imipenim (100%), Meropenem (100%), Amikacin (88.2%), Fosfomycin (76.5%), Cefotaxime (70.6%), Cefatazidime (70.6%), Ceftriaxone (70.6%), Cefaparazone/ Sulbactam (70.6%), Ciprofloxacin (64.7%), Enoxacin (64.7%), Ofloxacin (64.7%) and Sparfloxicin (64.7%). The remaining antibiotics tested had sensitivity less than 60% against Klebsiella pneumoniae.

Table 2: Antimicrobial Susceptibility pattern of uropathogens (Escheraecia coli, Staphylococcus Aureus and Klebsiella pneumoniae)

Antibiotics	Organisms Isolated					
	Escheraecia coli (n = 47)		Staphylococcus Aureus(n= 23)		Klebsiella pneumoniae(n = 17)	
	Sensitive(%)	Resistant(%)	Sensitive(%)	Resistant(%)	Sensitive(%)	Resistant(%)
Amikacin	43 (91.5)	4 (8.5)	16 (69.6)	7 (30.4)	15 (88.2)	2 (11.8)
Gentamicin	26 (55.3)	21 (44.7)	12 (52.2)	11 (47.8)	10 (58.8)	7 (41.2)
Tabromycin	26 (55.3)	21 (44.7)	12 (52.2)	11 (47.8)	10 (58.8)	7 (41.2)
Amoxcil _ Ampicillin	0 (0)	47 (100)	10 (43.5)	13 (56.5)	0 (0)	17 (100)
Augmentin	30 (63.8)	17 (36.2)	20 (87)	3 (13)	6 (35.3)	11 (64.7)
Ciprofloxacin	30 (63.8)	17 (36.2)	9 (39.1)	14 (60.9)	11 (64.7)	6 (35.3)
Enoxacin	24 (51.1)	23 (48.9)	9 (39.1)	14 (60.9)	11 (64.7)	6 (35.3)
Nalidixic Acid	13 (27.7)	34 (72.3)	1 (4.3)	22 (95.7)	9 (52.9)	8 (47.1)
Ofloxacin	24 (51.1)	23 (48.9)	9 (39.1)	14 (60.9)	11 (64.7)	6 (35.3)
Pipemidic Acid	16 (34)	31 (66)	4 (17.4)	19 (82.6)	9 (52.9)	8 (47.1)
Sparfloxicin	24 (51.1)	23 (48.9)	9 (39.1)	14 (60.9)	11 (64.7)	6 (35.3)
Cephradine	22 (46.8)	25 (53.2)	10 (43.5)	13 (56.5)	8 (47.1)	9 (52.9)
Cefuraxime	28 (59.6)	19 (40.4)	17 (73.9)	6 (26.1)	9 (52.9)	8 (47.1)
Ceflexime	30 (63.8)	17 (36.2)	0 (0)	23 (100)	9 (52.9)	8 (47.1)
Cefotaxime	31 (66)	16 (34)	14 (60.9)	9 (39.1)	12 (70.6)	5 (29.4)
Cefatazidime	31 (66)	16 (34)	14 (60.9)	9 (39.1)	12 (70.6)	5 (29.4)
Ceftriaxone	31 (66)	16 (34)	13 (56.5)	10 (43.5)	12 (70.6)	5 (29.4)
Cefaparazone- Sulbactam	34 (72.3)	13 (26.7)	20 (87)	3 (13)	12 (70.6)	5 (29.4)
Imipenim	46 (97.9)	1 (2.1)	22 (95.7)	1 (4.3)	17 (100)	0 (0)
Meropenem	47 (100)	0 (0)	22 (95.7)	1 (4.3)	17 (100)	0 (0)
Doxycycline	9 (19.1)	38 (80.9)	3 (13)	20 (87)	6 (35.3)	7 (64.7)
Tetracycline	5 (10.6)	42 (89.4)	21 (91.3)	2 (8.7)	3 (17.6)	14 (82.4)
Co-trimaxole	16 (34)	31 (66)	8 (34.8)	15 (65.2)	5 (29.4)	12 (70.6)
Fosfomycin	47 (100)	0 (0)	14 (60.9)	9 (39.1)	13 (76.5)	4 (23.5)
Nitrofurantoin	47 (100)	0 (0)	18 (78.3)	5 (21.7)	1 (5.9)	16 (94.1)

DISCUSSION

The results of the retrospective analysis highlighted that Escheraecia coli was most common uropathogen followed by Staphylococcus Aureus and Klebsiella pneumoniae for causing UTI. Moreover, more than two third of females of reproductive age had severe UTI, while more than one quarter had moderate UTI. The highest sensitivity of different antibiotics against Escheraecia coli were observed for Meropenem (100%), Fosfomycin (100%), Nitrofurantoin (100%), Imipenim (97.9%) and Amikacin (91.5%). Moreover, against Staphylococcus Aureus highest antibiotics sensitivity was identified for Imipenim (95.7%), Meropenem (95.7%) and Tetracycline (91.3%). Finally, for the seventeen isolates of Klebsiella pneumoniae the highest antibiotic sensitivity was observed for Imipenim (100%), Meropenem (100%) and Amikacin (88.2%).

The Centre of Disease Control and Prevention (CDC) had reported that UTI is accountable to around 13,000 deaths each year thus a disease of significant public health concern.[13] Evidence from the literature reported that UTI is more prevalent among females[14]. Women are approximately six times more likely to be affected by UTI as compared to men.[15] Though, most UTI resolved with treatment, but around one third of women have recurrent UTI and around one fifth suffer multiple recurrances.[16] Apart from deaths patients with recurrent UTI infection may suffer from pyelonephritis, renal disease, pre-term birth and even Clostridium difficile colitis from the use of antibiotics.[17] Thus, antimicrobial susceptibility reporting is of extremely clinical significance, rather than treating the patients simply on the basis of classic UTI symptoms[18].

Evidence from the literature has highlighted that bacteria causing UTI included; Klebsiella pneumoniae, Enterococcus sp., and Staphylococcus saprophyticus.[19] As these bacteria were capable of developing resistance thus new antibiotics have been developed since last decade and also the change in prescription practice to combat bacterial resistance[20] This is also significant to note that among 15% of all prescribed antibiotics are for the treatment of UTI[21].

The Infectious Diseases Society of America (IDSA) guidelines consider Nitrofurantoin and Co-trimoxazole as current standard therapy for uncomplicated UTI in women[22]. The study conducted almost fifteen year back recruited female patients reported that Trimethoprim-Sulfamethoxazole was first line empiric agent for UTI, showed relatively poor activity against E. coli isolates (73.5% susceptibility). However, alternative empiric drugs such as Nitrofurantoin, Ciprofloxacin and Ofloxacin showed good activity against E. coli (98.1%, 93.7% and 92.9% susceptibility, respectively)[23]. A multicenter international study of 4734 women presenting with symptoms of acute UTI reported that E. coli resistance was highest for Ampicillin (29.8%) and Sulfamethoxazole (29.1%), followed

by trimethoprim (14.8%), trimethoprim/Sulfamethoxazole (14.1%) and Nalidixic acid (5.4%)[24]. Another study that recruited only female patients reported that the antibiotic susceptibility for E. coli ranged from 97% for Floroquinolone to 48% for Cefaclor[25]. A recent study has reported that top antimicrobial activity against UTI were demonstrated by Imipenim, and Amikacin (>90%) and resistance rates to Floroquinolone and Ampicillin/ Sulbactam were high[26].

The study has few limitations. Firstly, being the secondary analysis, there were missing values for laboratory data. Secondly, the data was retrieved from only one hospital that was the microbiology laboratory of Services Institute of Medical Sciences, Lahore. This would have limited the generalisibility of the study findings. Thirdly, the data was retrieved from laboratory records of one year which have limited the sample. Moreover, being a retrospective analysis the study had its own limitations in the form of non-availability of co-morbidities, pregnancy, marital status, and socioeconomic conditions. Though, this has highlighted the recent antibiotic sensitivity pattern, but retrieval of laboratory data from last five years would have helped in giving a detailed and more precise insight of antimicrobial sensitivity pattern against UTI. Thus, in future studies with larger sample from multiple hospital labs would be worthwhile to better identify the culture isolates and antimicrobial sensitivity against specific microorganisms.

CONCLUSION

Most common urinary tract pathogens in females of reproductive age group are E. coli and Staphylococcus Aureus. Meropenem, Fosfomycin, Nitrofurantoin, Imipenim and Amikacin are the most effective antibiotics against E. coli. However, against Staphylococcus Aureus the most sensitive antibiotics were identified as Imipenim, Meropenem and Tetracycline. It is therefore recommended that females of reproductive age with UTI infection should be examined and treated by clinicians after proper laboratory investigations.

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