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Original Article

Spectrum of Antimicrobial Susceptibility Pattern of Urinary Tract Infection in Adults

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ABSTRACT

Patients of all ages and genders regularly experience urinary tract infections. Antibiotic misuse has caused organisms to develop drug resistance, creating a treatment problem. **Objective**: To uncover risk variables and relationships, as well as the antibiotic susceptibility in UTI patients. **Methods:** Diabetes and non-diabetes with UTI were compared within groups using the Chi-square test, with a significant P-value of 0.05. **Results:** 32 (21.2%) were given empirical treatment with ciprofloxacin (11%), cefixime (5%), ceftriaxone (2.6%), cefoparazone-sulbactum (1.30%), amoxicillin-clavulanic acid (1.30%), ampicillin (1.30%), and co-trimoxazole (0.60%), respectively. *E. coli* was the most prevalent pathogen, with an isolation rate of 84%, followed by pseudomonas aeruginosa (6%), Serratia (3.3%), klebsiella (2.6%), Enterobacter cloacae (2.6%), Sternotophomus (0.7%), and MRSA (each in 0.7%). Ampicillin, Cefixime, Ceftriaxone, Co-Trimoxazole, Ciprofloxacin, Amoxicillin-Clavulanic Acid, Tetracycline, and Levofloxacin were all often resistant to, respectively, 87 percent, 83 percent, 78 percent, 78 percent, and 51 percent of these antibiotics. **Conclusions:** MDR prevalence is highest in gram-negative bacteria. The presence of diabetes mellitus and being a woman are significant risk factors for UTI, according to tests. Escherichia coli (84%) is the most common uropathogen. Carbapenems, piperacillin-tazobactam, Amikacin, Gentamicin, and cefoparazone-sulbactam (parenteral) as well as Nitrofurantoin are the preferred empirical treatments (oral). Hospitals and the nation at large should constantly examine and reassess their antimicrobial policies.

INTRODUCTION

One of the most typical infectious disorders seen in medical practise, urinary tract infections (UTIs) affect persons of all ages. Around 150 million people get UTIs each year in the world, according to estimates [1]. People with diabetes mellitus experience UTIs more frequently than people without the condition [2], and they also experience UTIs that are more severe and are more likely to result in complications, such as dysuria (pain or burning when urinating), organ dysfunction, and occasionally even death from complicated UTI (pyelonephritis). UTIs are brought on by viruses, bacteria, and fungus that colonise and proliferate in the urinary tract. The frequency of viral and fungal UTI, however, is extremely low [3]. Gram negative bacteria are the most frequent ones to cause UTIs, but gramme positive bacteria infections have also been documented [4]. Escherichia coli, Staphylococcus saprophyticus, Klebsiella pneumoniae, Proteus mirabilis, Enterococcus species, Pseudomonas aeruginosa, and group B streptococcus are the most prevalent uropathogens [5]. Although some studies imply a reduced incidence of E. coli linked UTI in diabetics as compared to age matched non-diabetics, E. coli is the most frequent bacterium causing UTI in both diabetic and non-diabetic people [6]. Normally, the urinary tract works to prevent

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long-term colonisation of infections. This results from the repeated flushing out of dangerous organisms and bladder emptying." Innate immunity and a high concentration of urea in the urinary tract are additional elements that offer defence against pathogen colonisation [7]. The risk of UTI increases if the host's defences are weakened or any morphological or pathological abnormalities in the urinary tract blocks the passage of urine. E. coli and other uropathogens colonise the urinary system when this kind of damage takes place as a result of the presence of specific virulent elements that allow them to infiltrate the uroepithelium [8]. The anatomical and physiological differences between men and women make UTI more prevalent in women [9]. This infection affects about half of all women at some point in their lives [10]. In accordance with earlier research, 1 in 5 women will develop a UTI at some point in their lives [11], making it a very widespread issue. One of the factors contributing to females experiencing UTIs more frequently is the proximity of the urethra to the anus. This anatomical characteristic makes the perineal area vulnerable to contamination by stomach bacteria, which can subsequently spread to the urine bladder and result in infection. Other significant risk factors that raise the likelihood of UTI include diaphragm use, catheterization, diabetes mellitus (DM), and birth control tablets, spermicidal substances, advanced age, missed micturition, antibiotic misuse, and other immune suppressing diseases [12]. In patients with diabetes compared to non-diabetics, asymptomatic bacteriuria (ASB) and symptomatic UTI are more common, and these conditions more frequently result in consequences [13]. Changes in host immunity, delayed bladder emptying, and an increase in the concentration of glucose in urine are factors that contribute to a higher prevalence of UTI and a significantly increased risk of complications in diabetes. This is the host component that raises the likelihood of infection, which is more significant than changes in the bacterium. Uropathogens like E. coli are more likely to stick to the bladder surface because of changes in the uro epithelium cells. Theoretically, these alterations are attributed to the infected cells' glycosylation. UTI is more frequent, severe, and results in more disastrous outcomes in individuals with DM, according to research [14]. The empirical treatment of suspected UTIs in the emergency room and outpatient department is a relatively prevalent procedure. On the one hand, it is wise to treat the UTI right once to avoid complications like sepsis, but on the other hand, it is also crucial to use antibiotics when necessary to avoid the development of drug resistance. With common urinary bacterial infections, resistance to trimethoprim-sulfamethoxazole (TMP-SMX) and fluoroquinolone antibiotics has been on the rise. Extended-spectrum - lactamase and other multi-drug resistant pathogens are also becoming more common [15]. Given the inappropriate use of antibiotics whether due to inappropriate prescription by health professionals, self-medication, quackery or availability of antibiotics over the counter, antibiotic resistance is on the rise. It is deemed necessary that physicians or other health care workers should prescribe appropriate treatment for suspected UTI. Infectious Diseases Society of America (IDSA) and the American Academy of Pediatrics (AAP) have provided some international guidelines for this purpose [16]. However, local factors influence the resistance pattern, and this should be studied and reviewed locally time to time. Internationally antibiograms are used in hospitals to provide local guidelines in management of UTI and other infections empirically." These antibiograms can be used by doctors, along with worldwide standards, to adjust prescriptions based on local conditions. There are issues with UTI prescribing practices, namely the overuse of broad-spectrum antibiotics and treatment in the absence of a real illness [17].

METHODS

This cross-sectional study was conducted at the Rawal Institute of Health Sciences in Islamabad, Pakistan, from February 1, 2021, to June 30, 2021, after getting ethical permission. Patients who showed signs of a urinary tract infection and are above the age of 18 (i.e., burning, urgency, hematuria supported by urine routine examination findings of pyuria, positive nitrite, and bacteriuria) were included. Patients with critical illnesses, septic shock, terminal illnesses (from cancer), those who had recently started antibiotic therapy, hospital acquired UTIs, and those who were catheterized (with indwelling or suprapubic catheters) were all disqualified. Informed consent was obtained before selecting 151 cases overall through successive sampling. Their demographic information, medical history, symptoms, co-morbid conditions, self-medication history, and clinical findings were recorded. Patients with symptoms of a UTI were encouraged to undergo routine urine testing, including HbA1c, culture and sensitivity tests, and random blood sugar checks. After sending a urine culture, drugs were begun for patients who needed empirical therapy. In order to evaluate the isolated organisms and the pattern of treatment resistance and susceptibility, reports were examined during the follow-up visit. According to ADA guidelines, patients were classified as diabetes based on their HbA1c levels. On a unique proforma, the specifics were recorded. SPSS version 22 was used to analyse the data. Age has a mean and standard deviation determined; frequencies and percentages are used for qualitative characteristics (gender, micro-

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organism isolated, anti-microbial sensitivity and resistance). Diabetes patients and non-diabetics with UTI were compared within groups. The connection between age, gender, isolated organism, and sensitivity between two groups was investigated using the Chi-square test. P-value under 0.05 is regarded as significant. Information is provided as a table, pie chart, and bar graph.

RESULTS

There were 151 patients in this study that had UTI symptoms overall. 46 (31%) were men and 105 (69.5%) women were present. Hypertension was present in 56 patients (22%) and was followed by chronic kidney disease (CKD) (6.6%), ischemic heart disease (6.6%), benign prostatic hypertrophy (4.6%), chronic liver disease (4.6%), tuberculosis (2%), cerebrovascular accident (1.3%), and lymphoma (1.3 percent). The patients' ages ranged from 13 to 91, with a mean age of 48 and a standard deviation of 19. Of these 56 patients, 37 percent had diabetes (0.60 percent). 14.7% of the patients in the research had no other co-morbid conditions that were known to them (Figure 1).

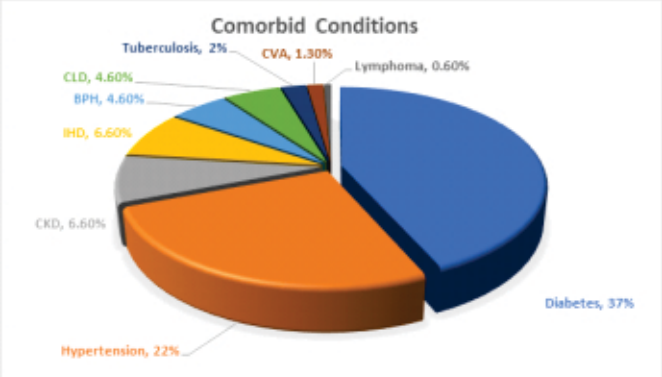

Figure 1: Pie chart presenting Various Co-morbid conditions Observed in patients presenting with Urinary Tract infection (n=151)

40 (26.5%) of the patients were found to be self-medicating, with 18 (32%) having diabetes and 22 (23%) not. Thirty-two patients (21.2%) who underwent empirical treatment did not respond; 13 of these had diabetes and 19 did not. After sending urine for culture sensitivity testing, ciprofloxacin was the drug that was most usually administered. Following Ciprofloxacin (11%), patients were given Cefixime (5%), Ceftriaxone (2.6%), Cefoparazone-Sulbactum (1.30%), Amoxicillin-Clavulanic Acid (1.30%), Ampicillin (0.60%), and Co-trimoxazole (0.60%). (Figure 2).

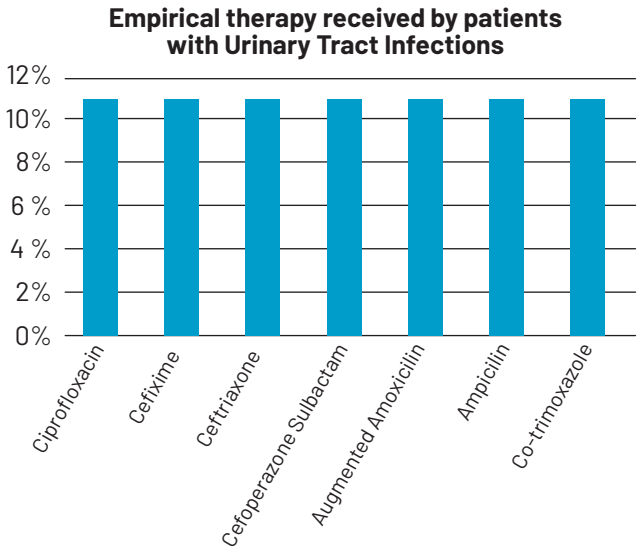

Figure 2: Bar graph presentation of Medications received by Patients with Urinary tract infection after sending the culture and sensitivity report (n=151)

100 percent of the 151 individuals showed some UTI symptoms. The most common clinical symptom, occurring in 144 (95.4 percent) of the patients, was urinary urgency. Of the patients, 140 (92.7%) reported dysuria as the second most common symptom. Following this, 88 patients (58.3%) experienced hematuria, and 4 patients (2.6%) experienced fever. In 95 (62.9%) instances, there was a prior history of UTI (Table 1). Each patient had bacteriuria, according to the urine analysis result for 151 patients who had a positive UTI culture. 55 (98%) of the 113 total individuals who had hematuria also had diabetes. After that, nitrite was found in 143 (94.7%) people, 88 (92.6%) of whom had diabetic mellitus. All people with positive cultures showed the tendency of pyuria in the following order. 39 (41%) of the 69 patients (45.7%) with many pus cells had diabetes mellitus. 11 (7.3%) of the diabetics had 20–25 pus cells/HPF in 6 (3.9%) (Table 1). Seven different pathogens were isolated from urine culture. E. coli was the isolate that was found 127 times (84%) the most frequently. The next most frequent species were Pseudomonas aeruginosa (9%) followed by Serratia (5%) Klebsiella (4%) Enterobacter cloacae (4%) Sternotophomus (0.7%), and Methicillin-resistant Staphylococcus aureus (0.7%). All bacterial cultures were tested with 16 different antibiotics. Meropenem had the highest sensitivity to isolates (97.4%), Imipenem was second (94.4%), then Piperacallin-Tazobactum was third (94.74%), Amikacin was seventh (77.5%), Tobramycin was eighth (76.8%), Nitrofurantoin was seventh (74.2%), and Gentamicin was sixth (61.6%) (Table 1).

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Demographic variables and Culture and sensitivity report	Amongst all n=151	Diabetics n=56	Non-diabetics n=95	p-value
Age (range13-91years)	48±17	59±14	41±19	0.023
Gender				
Female	105(69.3%)	42(75.1%)	63(64.5%)	0.262
Male	46(30.1%)	14(25.2%)	32(37.3%)	
Self-medication				
Yes	40(26.2%)	18(32.4%)	22(27.2%)	0.225
No	111(73..4%)	38(68.4%)	73(75.1%)	
Empirical therapy				
Yes	32(21.7%)	13(25.4%)	19(27.9%)	0.644
No	119(78.3%)	43(75.4%)	76(83.6%)	
Urine Analysis Results				
blood	113(74.8%)	55(91.5%)	58(61.9%)	<0.0001
bacteria	151(199.5%)	56(100%)	95(100%)	-
Nitrite	143(94.1)	55(98.5%)	88(92.6%)	0.139
Pus cells				
<5	5(3.3%)	0(0%)	5(5.7%)	
6-10	11(7.6%)	2(3%)	9(9.4%)	
11-15	29(19.2%)	11(19.7%)	18(17.3%)	0.018
16-19	25(16.1%)	13(22.6%)	12(12.2%)	
20-25	11(7.4%)	0(0%)	11(11.2%)	
Numerous	69(45.9%)	30(53.1%)	39(42.7%)	
Urine Culture and Sensitivity Results				
Organism isolated				
E-coli	127(85%)	47(81%)	80(84%)	0.93
Pseudo-monas	9(7%)	7(12.6%)	2(2%)	0.09
Serratea	5(3.4%)	0(0%)	5(5.2%)	0.01
Klebsilla	4(2.7%)	2(3.7%)	2(2%)	0.58
Enterobactar Cloaca	4(2.5%)	0(0%)	4(4.2%)	0.10
Strenotophomas	1(0.8%)	0(0%)	1(1%)	0.41
MRSa	1(0.9%)	0(0%)	1(1%)	0.41
Sensitivity				
Imipinam	142(94.1%)	52(92.3%)	90(95%)	0.67
Cefoperazon-sulbactum	103(68.6%)	31(54.3%)	72(76%)	0.09
Tazobacatm-piperacillin	143(94.2%)	54(95.2%)	89(94%)	0.47
Meropenm	147(97.9%)	55(97.5%)	92(97%)	0.62
Tobramysin	116(76.8%)	44(78.7%)	72(76%)	0.66
Amikasin	117(77.6%)	37(66.1%)	80(84%)	0.00
Nitrofurantoen	112(74.2%)	39(70.5%)	73)77%)	0.39
Gentamisin	93(61.4%)	27(48.5.9%)	66(69.5%)	0.09
Levofloxasin	74(48.7%)	25(44.1%)	49(51.6%)	0.41
Augmented amoxicillin	54(35.7%)	17(30%)	37(39%)	0.28
Ciprofloxacin	50(32.7%)	16(28%)	34(36%)	0.36
Ceftriaxone	33(21.5%)	06(10%)	27(28%)	0.01
Cefixime	26(17.4%)	04(7.1%)	22(23%)	0.01
Co-trimoxazole	40(26.47%)	11(19%)	29(30.5%)	0.14
Tetracycline	56(37.14%)	16(28%)	40(42%)	0.09
Ampicillin	19(12.71%)	4(7.6%)	15(15.8%)	0.12

Table 1: Presenting demographic variables, self-medication, empirical therapy, urine routine examination and culture and sensitivity and diabetics vs non- diabetics with UTI(n=151)

With resistance rates of 87 percent, 83 percent, 78 percent, 73.5%, and 51 percent, respectively, to commonly used antibiotics like ampisillin, cefizime, ceftriaxon, co-trimoxazol, ciprofloxasin, amoxicillin-clavulanic acid, tetracyclin, and levofloxasin, the majority of the organisms showed resistance to these drugs. The MDR frequency were found to be 100% in all gram-negative bacteria.

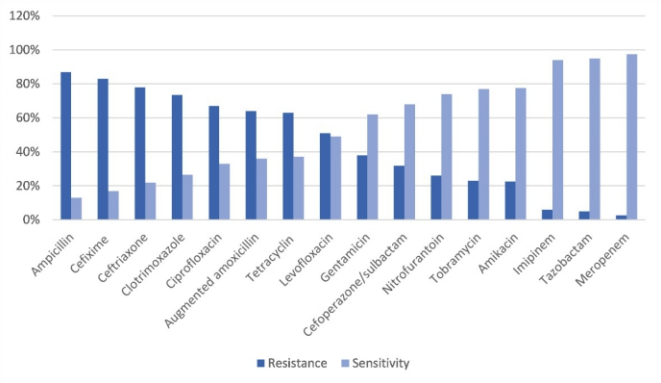

Figure 3: Bar Graph representing the trends of culture proven organism's resistance and susceptibility to specific antibiotics (n=151)

DISCUSSION

In the practise of medicine, urinary tract infections are fairly typical. Numerous patients develop urosepsis as a result of fatally inadequate initial treatment. In order to comprehend the new issues in UTI management that can be addressed, we want to determine the most recent pattern of antibiotic susceptibility in UTIs. In this investigation, regardless of accompanying morbidities, E. coli was the most frequently isolated pathogen in both genders and across all age categories. 84 percent of cases of infection were linked to E. coli. This is like a study from India where E. coli was the main pathogen in both CA-UTI (68%) and HA-UTI (45%) [18]. According to studies from Mekelle(83%), observation of high Gram-negative bacterial isolates in patients is consistent and is also in accordance with Sudan (87.2%) [19], India (92%) [20]. However, comparatively lower incidence rates in Ethiopia, such as in Bahir Dar(61.9%), were reported from comparable research [21]. E. coli was the most often isolated uropathogen, according to several additional research from India (67.6 percent) [22], Dessie (63 percent) [23], Sudan (54.6 percent) [21], and Romania (68.9 percent) [24]. A significant proportion of all urinary tract infections (UTIs) are caused by Escherichia coli, a common gastrointestinal pathogen that penetrates the urine tract via its highly powerful virulence factors. Pseudomonas aeruginosa ranked as the second most common bacterial pathogen in our survey(6 percent). Another study in Bahir Dar observed the same trend, and further investigations revealed that proteus and Coagulase negative staphylococci were the second-most prevalent uropathogens in Addis Abeba [25,26]. Serratia(3.3 percent), Klebsiella(2.6 percent), and Enterobacter cloacae were the three isolates that were most frequently found in the current investigation (2.6 percent). Methicillin-resistant Staphylococcus aureus and Sternotophomus maltophilia were found in 0.7 percent of patients, indicating that gram-positive bacteria rarely

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cause UTI in this location. While gram-positive bacteria, such as those found in Bahir Dar, are one of the main causes of UTI in several other parts of the world [25]. In our investigation, certain significant risk variables, such as diabetes mellitus, female gender, and prior UTI history, were found. The Diabetic mellitus was found in 37% of patients with culture positive UTIs, which isn't surprising given that the genitourinary system (neuropathy) can be adversely affected by diabetes, leading to bladder dysfunction and micturition abnormalities, both of which are necessary conditions for the development of UTIs. In fact, earlier investigations from Egypt [14] and India [27] came to the same conclusion: UTI incidence increases with DM duration. In our study, women (69.5 percent) were more likely than men (30.5 percent) to get a urinary tract infection (UTI). According to RD Harrington's study, UTI affects women more frequently than males, even though as people get older, the prevalence is the same for both sexes [28]. In this study, 63 percent of patients had a prior history of UTI. An important risk factor for recurrent infection, considerably higher rates of bacteriuria have been observed in certain other investigations in people with a history of urinary tract infections [29]. According to the results of the antibiotic sensitivity tests, the Gram-negative uropathogens E. coli, Pseudomonas, Klebsiella, and Enterobacter cloacae were extremely sensitive to Meropenem (97.4%), Piperacallin-Tazobactum (97.4%), Imipenem (94%), Amikacin (77.5%), Tobramycin (76.8%), Nitrofurantoin (74.2%), and (61.6 percent). A study from India found that urine-derived bacterial isolates were highly susceptible to Imipenem (96.7 percent), Piperacallin-Tazobactum (80.7 percent), and Gentamicin (59.4 percent) [30]. No organism demonstrated complete antibiotic sensitivity. Contrarily, Gram-negative isolates, particularly E. coli, showed high levels of resistance to several tested antibiotics that are frequently used to treat bacterial UTIs: Ampicillin (87%) Cefixime (83%) Ceftriaxone (78%) Co-Trimoxazole (73.5%) Ciprofloxacin (67%) Amoxicillin-clavulanic acid (64%) Tetracycline (63%) and Levofloxacin (63%) (51 percent). Research from Korea and India revealed a similar trend of resistance to third generation Cephalosporins and Amoxicillin-clavulanic acid [31]. The majority of fluoroquinolone prescriptions are for the treatment of UTI, particularly for the empirical management of female uncomplicated acute cystitis. In our study, 67 percent of the isolates were susceptible to Ciprofloxacin. Between 0.5 and 7.6 percent of E. coli isolates were susceptible in European nations [32], whereas in Turkey, this prevalence was 50 percent [33]. Globally, fluroquinolone resistance is a growing problem [33]. All Gram-negative organisms in this investigation displayed multidrug resistance, and one instance of E. coli displayed pan resistance. More research has confirmed that Gram negative uropathogens are frequently found to have high MDR in other nations as well [23,24,29]. It is possible that the significantly higher prevalence of resistance to these commonly prescribed antibiotics, including MDR, is due to their greater accessibility and affordability outside of treatment centers, which might also lead to careless use of the medication without a prescription, the widespread availability in the market of subpar or expired medications that are likely to be used for self-treatment (26.5 percent in our study), the frequent use of antibiotics were empirically used by 21.2 percent of the participants in our research due to a lack of culture sensitivity testing. Guidelines issued by the French Infectious Disease Society in 2017 that advised against using fluroquinolones to treat cystitis without first doing antibiotic susceptibility testing [33] brought attention to the rise in fluroquinolone resistance.

CONCLUSIONS

The most common Uropathogen was Escherichia coli. It was discovered that having diabetes mellitus and being a woman were significant contributors to the higher occurrence of lab-verified urinary tract infections among all individuals. In the present investigation, both Gram-positive and Gram-negative bacterial uropathogens were successfully treated with carbapenems, piperacillin-tazobactam, amikacin, gentamicin, and Cefoperazone-sulbactam, all of which are accessible as parenteral preparations. A substantial prevalence of drug resistance to popular antimicrobials was also revealed by this investigation, particularly to co-trimoxazole, ciprofloxacin, doxycycline, ampicillin, amoxicillin-clavulanate, and ceftriaxone. The prevalence of MDR was also high for Gram-negative bacteria.

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