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Evaluation of urine culture: common organisms and their antimicrobial susceptibility patterns in a tertiary care hospital of Peshawar

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ABSTRACT

Introduction: Urinary Tract Infections (UTIs) have great clinical significance because they are a major cause of morbidity and antibiotic use among older adults. Considering the high recurrence rates and emergence of antibiotic resistance in uropathogens, knowledge about the area-specific prevalence of these pathogens and their antimicrobial resistance patterns is necessary.

Objective: To document the common bacterial microorganisms causing UTI and their antimicrobial resistance patterns based on reported urine samples from a tertiary care hospital of Peshawar, KP, Pakistan.

Materials & Methods: This was an observational cross-sectional study, conducted at Rehman Medical Institute, Peshawar, on archival urine samples of UTI patients reported from January 2016 to March 2017. Antimicrobial sensitivity tests were performed according to the guidelines of Clinical and Laboratory Standards Institute (CLSI).

Results: A total of 626 samples were tested. The samples tested for urine cultures had 34.9% (n=218) males and 65.1% (n=408) females. Mean age of all subjects was 41.19 ± 27.06 years. *Escherichia coli* and *Enterococcus* were the most commonly isolated pathogens. *E. coli* showed highest resistance to Ampicillin and *Enterococcus* was highly resistant to Ciprofloxacin.

Conclusion: Antimicrobial resistance is high in urine samples from a tertiary care hospital of Peshawar, KP, and seen against drugs which are routinely prescribed to treat urinary tract infections.

Keywords: Anti-bacterial agents; *Escherichia coli*; Drug Resistance; Microbial Sensitivity Tests; Urinary Tract Infections.

The authors declared no conflict of interest. All authors contributed substantially to the planning of research, data collection, data analysis, and write-up of the article, and agreed to be accountable for all aspects of the work.

INTRODUCTION

Urinary Tract Infections (UTIs) are of great clinical significance because they cause considerable morbidity and antibiotic use among older adults. A study in England estimated at least 21% of older adults had been diagnosed with UTI once.[1] Antibiotic resistance of urinary tract pathogens has increased worldwide. The extensive use of antimicrobial agents have invariably resulted in the development of antibiotic resistance, which, in recent years, has become a major problem worldwide.[2-3] The incidence of UTI is greater in women (25-35% of women aged 20-40 years)[4] compared to men, which may be either due to anatomical predisposition, adherence to the urothelial mucosal mucopolysaccharide lining, or other host factors.[5] Sexual activity, pregnancy, and obstruction also increase the frequency of UTI.[6]

Due to rising antibiotic resistance among uropathogens, it is important to have local hospital-based knowledge of the organisms causing UTI and their antibiotic sensitivity patterns. Extended-Spectrum Beta-Lactamase (ESBL) producing bacteria may not be detected by routine disk diffusion susceptibility test, leading to inappropriate use of antibiotics and treatment failure.[7]

Considering the high recurrence rates and emergence of antibiotic resistance in uropathogens, knowledge about the area-specific prevalence of these pathogens and their antimicrobial resistance patterns is necessary.[8] Antibiotic resistance in specific geographical locations is an important factor for choosing an appropriate empirical antimicrobial treatment. In almost all cases of UTI, empirical antimicrobial treatment initiates before the laboratory results of urine culture are available; thus, antibiotic resistance may increase in uropathogens due to frequent misuse of antibiotics.[9.]

Treatment of UTI has become challenging due to the emergence of pathogens with increasing resistance to antimicrobial agents. Early and effective antimicrobial therapy for UTI significantly reduces renal scars and their consequences, such as renal failure and hypertension.[10]

The present study was conducted to determine the antimicrobial susceptibility patterns of commonly used antibiotics among community-acquired uropathogens during one-and-a-half-year period from Jan 2016 to March 2017 at a tertiary care hospital of Peshawar, Khyber Pakhtunkhwa (KP), Pakistan.

MATERIALS & METHODS

An observational cross-sectional study was conducted at Rehman Medical Institute (RMI), Peshawar, on data collected from the archival laboratory database of the hospital for the period of January 2016 to March 2017.

Urine specimens were collected from patients who presented to RMI with symptoms of UTI. Specimens were collected in wide mouth sterile containers. Mid-stream clean-catch method was used to collect specimens from most of the patients; suprapubic aspiration was used in patients who were unable to provide the former. The urine samples were inoculated on Sheep Blood Agar and MacConkey Agar and the incubated at 37^0C for 24 hrs. Culture plates yielding pathogens at concentration of more than 105 colony forming units/ml were considered significant. Standard biochemical reactions were used to further identify Gram-negative and Gram-positive organisms.

Antimicrobial susceptibility testing was performed using the Kirby-Bauer disk diffusion method as described by the National Committee for Clinical Laboratory Standards (presently called as Clinical Laboratory Standard Institute).[11] The antibiotics tested were Amikacin, Imipenem, Vancomycin, and Third Generation Cephalosporins.

There were no exclusion criteria. Data were analyzed through entry in the excel spreadsheets and pivot tables were formulated to give percentages of the resistance of the antibiotics to each isolated urine culture.

RESULTS

A total of 626 samples were tested. The sample reports that were tested for blood cultures had 34.8% (n=218) males and 65.2% (n=408) females (Female: Male ratio of 1.87:1). Mean age of all subjects was 41.19 ± 27.06 years.

Table 1 shows the pathogens isolated from urine cultures. Gram negative isolates made up 90% of the microbes isolated and out of those *Escherichia Coli* made up the major bulk (83%) followed by *Klebsiella* (6.5%), *Pseudomonas* (5.1%), *Citrobacter* (1.4%), *Enterobacter* (1.06%), *Proteus mirabilis* (1.06%), *Serratia* (0.8%), *Acinetobacter* (0.5%) and *Morganella morganii* (0.3%). The most common Gram-positive pathogen isolated out of 61 Gram-positive bacteria cultured was *Enterococcus* (63.9%) followed by *Staphylococcus aureus* (36%).

Table 1: Urine Culture Isolates

Gram Negative isolates (565)	
Organism	**Frequency**
Escherichia coli	469
Klebsiella species	37
Pseudomonas species	29
Citrobacter species	8
Enterobacter species	6
Proteus mirabilis	6
Serratia species	5
Acinetobacter species	3
Morganella morganii	2
Gram positive isolates (61)	
Enterococcus	39
Staphylococcus aureus	22
Total	**626**

Table 2 shows the antimicrobial resistance patterns of the Gram-negative bacteria isolated from urine samples. The most common pathogen isolated was *Escherichia coli*. The pathogen showed highest resistance towards Ampicillin (94%) Ciprofloxacin (87%) Cefazolin (82.9%) and Cefipime (80%) Around half of the isolates were resistant to Doxycycline (49.7%) Ceftriaxone (51.2%) and Ampicillin / Clavulanic Acid (65.5%). The microbe was highly susceptible to Meropenem (0.6%), Imipenem (3.2%) and Cefoperazone / Sulbactam (1.7%).

The other Gram-negative bacteria isolated included *Klebsiella* species, *Citrobacter* species, *Enterobacter* species, *Proteus mirabilis*, *Serratia* species, *Citrobacter* species and *Morganella morganii*. These pathogens were highly resistant to Ampicillin (86.1%) and Cefazolin (83.9%). Ciprofloxacin was ineffective against 60% of these pathogens and 45% of the isolates were resistant to Doxycycline and 39.18% were resistant to Piperacillin / Tazobactam. *Pseudomonas* species were moderately resistant to Ciprofloxacin (65%) Gentamicin (55.2%) and Levofloxacin (55.2%).

Table 2: AntibioGram of Epidemiologically Important Gram-Negative Urine Culture Isolates									
Antimicrobial Agent	**Gram negative urine culture isolates n(%resistance)**								
	Esch. coli (n=469)	Klebsiella species (n=37)	Pseudomonas species (n=29)	Citrobacter species (n=8)	Enterobacter species (n=6)	Proteus mirabilis (n=6)	Serratia species (n=5)	Acinetobacter species (n=3)	Morganella morganii (n=2)
Amikacin	29(6.2)	2(5.4)	10(34.5)				2(40.0)	1(33.3)	
Amoxicillin/Clavulanic Acid	307(65.5)	20(54.1)		3(37.5)	3(50.0)	3(50.0)	5(100)		2(100)
Ampicillin	441(94.0)	35(94.6)		6(75.0)	6(100)	6(100)	5(100)	1(33.3)	2(100)
Amoxil	238(50.7)	17(46.0)		1(12.5)	6(100)	1(16.7)	2(40.0)		2(100)
Ampicillin/Sulbactam	99(21.1)	6(16.2)		2(25.0)	2(33.3)	2(33.3)	1(20.0)	1(33.3)	
Azithromycin									
Aztreonam	343(73.1)	14(37.8)	11(37.9)	4(50.0)	2(33.3)		4(80.0)		1(50.0)
Cefaclor	215(45.8)	10(27.0)		3(37.5)	5(83.3)		4(80.0)		2(100)
Cefoperazone	5(1.1)				1(16.7)				
Cefoperazone/Sulbactam	8(1.7)	1(2.7)							
Cefodoxime	117(24.9)	6(16.2)		2(25.0)			2(40.0)		2(100)
Colistin/Polymixin B									1(50.0)
Co-triamoxazole	190(40.5)	13(35.1)		2(25.0)	4(66.7)	3(50.0)			
Ceftizoxime				3(37.5)					
Cefazolin	389(82.9)	23(62.2)		6(75.0)	6(100)	4(66.7)	5(100)		2(100)
Cefoxitin	75(16.0)	4(10.8)		2(25.0)	3(50.0)		1(20.0)	3(100.0)	
Cefipime	375(80.0)	19(51.4)	12(32.4)	4(50.0)	4(66.7)	2(33.3)	4(80.0)	2(66.6)	
Cefixime	112(23.9)	7(18.9)		1(12.5)	1(16.7)		2(40.0)		
Cefuroxime	184(39.2)	6(16.2)		4(50.0)	5(83.3)		2(40.0)		2(100)
Cefotaxime	204(43.5)	6(16.2)	1(3.4)	5(62.5)	1(16.7)	2(33.3)	2(40.0)	2(66.6)	
Cafotetan	8(1.7)	1(2.7)			1(16.7)				
Ceftazidime	340(72.5)	16(43.2)	11(37.9)	5(62.5)	4(66.7)		4(80.0)	3(100.0)	1(50.0)
Ceftriaxone	240(51.2)	13(35.1)			5(83.3)			2(66.6)	
Cephalexin	162(34.5)	6(16.2)		1(12.5)	4(66.7)		2(40.0)		2(100)
Cephradine	4(0.9)								
Chloramphenicol									
Cephodoxime					1(16.7)				
Ciprofloxacin	408(87.0)	15(40.5)	19(65.5)	4(50.0)	3(50.0)	5(83.3)	4(80.0)		
Clarithromycin									
Clindamycin									
Doxycycline	233(49.7)	14(37.8)		3(37.5)	3(50.0)	2(33.3)	4(80.0)	1(33.3)	
Erythromycin									
Fosfomycin	21(4.5)	4(10.8)				3(50.0)			
Gentamicin	196(41.8)	12(32.4)	16(55.2)		1(16.7)	1(16.7)	3(60.0)	1(33.3)	
Imipenem	15(3.2)		8(27.6)		2(33.3)		2(40.0)		
Levofloxacin	147(31.3)	6(16.2)	16(55.2)	1(12.5)	1(16.7)		1(20.0)		
Loracarbef	105(22.4)	4(10.8)		1(12.5)	1(16.7)		2(40.0)		2(100)
Linezolid									
Meropenem	3(0.6)		4(13.8)		1(16.7)				
Minocycline	5(1.1)								
Moxifloxacin									
Nitrofurantoin	56(11.9)	12(32.4)		2(25.0)	2(33.3)	6(100.0)	1(20.0)		1(50.0)
Norfloxacin	139(29.6)	3(8.1)	10(34.5)	2(25.0)	1(16.7)	3(50.0)	2(40.0)	1(33.3)	
Penicillin									
Piperacillin									
Piperacillin/Tazobactam	170(36.2)	13(35.1)	7(24.1)	3(37.5)	2(33.3)	3(50.0)	2(40.0)		
Rifampicin									
Tobramycin	25(5.3)	5(13.5)				1(16.7)		1(33.3)	
Teicoplanin									
Vancomycin									

Table 3 demonstrates the susceptibility patterns of Gram-positive bacteria isolated. *Enterococcus* is the most common pathogen isolated and it showed complete resistance to Ciprofloxacin and Norfloxacin. It was also highly resistant to Gentamicin (69.2%) and Penicillin (76.9%) but showed least resistance to Ampicillin / Clavulanic Acid (5.1%) and Clindamycin (2.6%). *Staphylococcus aureus* was also 100% resistant to Ciprofloxacin and 95% to Cefoxitin. It was highly susceptible to Minocycline (95.5%) and Moxifloxacin (91.9%).

Table 3: AntibioGram of Gram-positive bacteria isolated from urine cultures

Antimicrobial Agent	Enterococcus (n=39) n (%resistance)	Staphylococcus aureus (n=22) n (%resistance)
Amikacin	1 (2.6)	7 (31.8)
Amoxicillin/Clavulanic Acid	2 (5.1)	11 (50.0)
Ampicillin	10 (25.6)	17 (77.2)
Amoxil		13 (59.1)
Ampicillin/Sulbactam		12 (54.5)
Azithromycin		13 (59.1)
Cefaclor		12 (54.5)
Cefaperazone/Sulbactam		8 (36.4)
Cefphodoxime		9 (40.1)
Co-triamoxazole		10 (45.5)
Ceftizoxime		8 (36.4)
Cefazolin		13 (59.1)
Cefoxitin		21 (95.5)
Cefuroxime		13 (59.1)
Cephradine		1 (4.5)
Ceftriaxone		12 (54.5)
Cephalexin		12 (54.5)
Chloramphenicol	7 (17.9)	4 (13.8)
Ciprofloxacin	39 (100)	22 (100)
Clarithromycin		9 (31.0)
Clindamycin	1 (2.6)	7 (24.1)
Doxycycline	19 (48.7)	9 (40.2)
Erythromycin	21 (53.8)	16 (72.7)
Fosfomycin	15 (38.5)	
Gentamicin	27 (69.2)	16 (72.7)
Imipenum		11 (50.0)
Levofloxacin		5 (22.7)
Meropenem		4 (13.8)
Minocycline	24 (61.5)	1 (4.5)
Moxifloxacin		2 (9.1)
Nitrofurantoin	17 (43.6)	
Norfloxacin	39 (100)	3 (13.6)
Penicillin	30 (76.9)	13 (59.1)
Piperacillin		6 (27.3)
Piperacillin/Tazobactam		11 (50.0)
Rifampacin	16 (41.0)	4 (13.8)
Teicoplanin	8 (20.5)	

DISCUSSION

This study was conducted to evaluate the susceptibility patterns of the most common uropathogens. In this study, *Escherichia coli* was the most common pathogen isolated from urine cultures followed by *Enterococcus* and *Klebsiella* species. Data collected from around the world shows that *Escherichia coli* and *Klebsiella* are the most common uropathogens isolated from patients with community acquired UTI. A study on uropathogens in Iran[12] reported *Escherichia coli* as the most common pathogen isolated. Other studies showed that frequency of UTIs are higher in women than men, similar to the current study with female to male ratio of 1.87:1.[13] Similar findings were seen in studies done in India, United States and Singapore.[14-16]

Second Generation Fluoroquinolones tested against *Escherichia coli* in the present study showed variable resistance. Almost 87% were resistant to Ciprofloxacin and 30% were resistant to Norfloxacin. These findings are different from the results of a study done in Iran,[12] where around 32% of the isolates were resistant to Ciprofloxacin. These findings may be due to shifting of antibiotic prescription trend towards Fluoroquinolones and indicate reconsidering usage of Fluoroquinolones in empiric therapy.

A study done on susceptibility pattern on *Escherichia coli* in obstetric patients[17] demonstrated 90% resistance towards Ampicillin; these findings are similar to the current results where 94% of pathogens were resistant to Ampicillin. Carbapenems showed highest rates of susceptibility towards *Escherichia coli* in the present study and similar patterns of susceptibilities were seen against Imipenem in another study.[14]

Antimicrobials such as Ampicillin and Third Generation Cephalosporins were highly ineffective against *Klebsiella* species in this study. A study analyzing the changing patterns of *Klebsiella* against these antimicrobials showed similar pattern of increasing resistance against Cephalosporins.[18] Nearly 100% resistance was seen against Tetracyclines in the present study; these findings are consistent with those of another study done in Pakistan on Klebsiella pneumonia.[19]

A study done in Kerala on uropathogens isolated *Enterococcus* as the third most common pathogen whereas in the current study *Enterococcus* was the second most common pathogen.[20] Results of the present study demonstrated complete resistance against Fluoroquinolones and high resistance against Penicillin and Gentamicin by the *Enterococcus* species. Similar findings were observed in another study,[21] but around 20% of pathogens were sensitive to fluoroquinolones. In current study, 75% of the isolates were sensitive to Ampicillin; these results were different from another study where Ampicillin was effective against *Enterococcus* but to a lesser extent.[21]

CONCLUSION

Antimicrobial resistance is high in urine specimens obtained from patients of Urinary Tract Infections attending a tertiary care hospital of Peshawar, Khyber Pakhtunkhwa, Pakistan. Resistance is seen

against drugs which are usually used to treat infections routinely. This rise in resistance may be attributed to empirical prescription of antibiotics by physicians.

RECOMMENDATIONS

Empirical therapies to treat UTIs should be carefully chosen to prevent prescribing unnecessary and ineffective antibiotics. Urine culture and antimicrobial susceptibility testing is important in establishing a diagnosis and selecting appropriate therapy for UTIs. Pathogens should be regularly tested for susceptibility patterns and these tests should form the basis on which therapeutic guidelines are formed.

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