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Antimicrobial Sensitivities of Pathogens Causing Community Acquired Urinary Tract Infection in Adult Patients

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ABSTRACT

This retrospective analysis is intended to report the sensitivity rate of common pathogens causing community acquired UTIs in adult patients (age 19-59 years) to guideline-recommended antimicrobial agents. Similar to previous reports, *E. coli* and *Klebsiella pneumonia* were the commonest uropathogens isolated. Most of the isolated organisms showed a high sensitivity rate to Imipenem (93%), followed by Fosfomycin (86%), Amikacin (87%), Nitrofurantoin (81%), and finally Amoxicillin/K Clavulanate (74%). On the other hand, the susceptibility of all isolated organisms to Cotrimoxazole was only 50%. However, it was even lower for Cephalexin (35%), Ampicillin (25%), Nalidexic acid (15%), and PIP/TAZ (5.4%). The findings of this study show that the resistance rates of most of the uropathogens to most of the guideline-recommended antimicrobial agents are unacceptably high. This supports the notion that empirical antimicrobial selection should be based on a knowledge of the local prevalence of specific uropathogens and their antimicrobial sensitivities, rather than on universal guidelines.

KEYWORDS: UTI, Antimicrobial Sensitivity
Running head: Antibiotic Sensitivity of Pathogens Causing UTI

INTRODUCTION

Urinary tract infection (UTI) is the most common bacterial infection in both hospitals and community settings [1]. It affects about 150 million people worldwide every year and costs up to US$6 billion in treatment and management [2].

UTI is defined as the multiplication of microorganisms in the urinary tract, either in its upper part causing acute pyelonephritis or in its lower part causing cystitis or urethritis [3]. A clinical differentiation of the site of the infection is important. Pyelonephritis, or upper UTI, refers to an infection of the renal parenchyma, which manifests locally as a flank pain and systemically as fever, nausea, vomiting, or diarrhea. Patients with UTIs are at risk of renal scarring when the infection is recurrent, which may lead to chronic renal failure. In contrast, cystitis, or lower UTI, is due to an infection of the urinary bladder. Patients with this form of UTI usually experience symptoms of bladder irritation, such as dysuria, urinary frequency, urinary hesitancy, and low-grade abdominal pain, without the presence of systemic manifestations such as fever [4]. Women are more prone to UTIs than men; because in women, the urethra is much shorter and closer to the anus than it is in men [5].

Complicated UTI occurs in conditions where there is an increased risk of therapeutic failure, such as diabetes mellitus, pregnancy, instrumentation, renal failure, anatomic abnormality of the urinary tract, hospital acquired infection, or urinary tract obstruction. On the other hand, uncomplicated UTI occurs in a normal urinary tract with no prior instrumentation [6].

The commonly reported causative organisms of UTIs are *Escherichia coli (E. coli)*. Therefore, this occurs in as high as 85% of cases, while *Staphylococcus saprophyticus* occurs in 10% of cases. Furthermore, other common organisms are Klebsiella, Proteus, Pseudomonas, Enterococcus, and *Staphylococcus aureus*. Other uncommon organisms include Chlamydia, Fungal, and rare Viruses [7].

With outpatients, the treatment of uncomplicated UTI is often started empirically, and is based on history and a simple urinalysis [8]. Guidelines suggest the use of Nitrofurantoin monohydrate, Trimethoprim-Sulfamethaxazole (Cotrimexazole), Fosfomycin, Fluoroquinolones, and beta-Lactam agents such as Amoxicillin-Clavulanate as first line antimicrobial agents for empirical treatment [9]. Unfortunately, resistance to too many guideline-recommended antimicrobial agents is increasing because of many factors including indiscriminate use of antibiotics [10]. However, the changing pattern of antibiotic sensitivity emphasizes the

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importance of continuous research in updating relevant data to be used as a guideline for appropriate choice of antibiotics and for the optimum management of UTIs [11, 12].
Hence, this study was aimed at observing the prevalence of the different organisms causing uncomplicated UTI and their susceptibility to common antimicrobial agents. This study will help guide the proper empirical choice of antibiotics for uncomplicated UTI in Aseer Region.

MATERIALS AND METHODS

A retrospective analysis was performed on all adult (age: 19-59 years) urine specimens (394 patients) that were sent from ambulatory care facilities to the bacteriology laboratory at Aseer Central Hospital, Southwestern region of Saudi Arabia for culture and sensitivity analysis during the period of March, 2013 to March, 2015.

The collected data were based mainly on laboratory findings, which were limited to specimens from patients aged 19-59 years who were sent from ambulatory care facilities. Specimens from inpatient facilities were excluded. Thus, our aim is to study the pattern of antimicrobial sensitivities of common pathogens which are responsible for UTIs in ambulatory care settings in the selected age group.

Urine Collection Sample: A 10-20 ml of early morning midstream urine specimens were collected in sterile, dry, and wide mouth containers.

Bacterial Isolates: Qualitative microbiological wet amount analysis was done for all specimens, which were then cultured in MacConkey agar and 5% sheep blood agar that support the growth of most gram-negative bacilli and staphylococci [13]. Accordingly, inoculation on these media was done with pre-calibrated platinum loops to deliver a measured quantity (1.0 µl) of urine sample. The inoculation was done at a temperature of 37C° for 48 hours and a CFU count of 10^5/ml of urine was considered positive for UTI.

Antibiotics Susceptibility Testing: The minimum inhibitory concentration (MIC) of the antibiotics was determined by disc diffusion method on mueller-hinton agar plates (MHA). For streptococci organisms, blood ager plates were used. The antibiotics tested were Amox/K Clavulanate (20\10µg), Ampicillin (25µg), Amikacin (30µg), Gentamycin (10µg), Cotrimoxazole (1.25\23.75µg), Cephalexin (30µg), Ciprofloxacin (5µg), Nitrofurantoin (300µg), Nalidixic acid (30µg), Imipenem(10µg), Piperacillin/Tazobactam (100\10µg), Fosfomycin (200µg), and Levofloxacin (5µg). The results of the disc diffusion method were interpreted in accordance to the Clinical and Laboratory Stander Institute (CLSI, 2012) (M100-S20) [14].

In addition, SPSS software (Windows Version 22) was used for descriptive analysis.

RESULTS

Table 1 displays the gender distribution and frequency of isolated organisms. A Total of 394 patients aged between 19 to 59 years from ambulatory care facilities were included. Females represented 55.8% of the patients, while the rest were males. There was no statistically significant difference in the frequency of the different organisms among both sexes.

The commonest isolated organism among both sexes was *Escherichia coli*, though it was present in only 52.8% of cases. Other organisms, in descending order of prevalence, are *Klebsiella pneumonia* 67 (17%), *Enterococcus faecalis* 33 (8.4%), *Proteus mirabilis* 21 (5.3%), *Pseudomonas aeruginosa* 17 (4.3%), *Staphylococcus aureus* 16 (4.1%), Streptococcus species 11 (2.8%), and others 21 (5.3%). There was no statistically significant difference in the frequency of different organisms between both sexes.

Table 2 shows the details of the sensitivities of the different organisms to different antimicrobial agents. Most of the isolated organisms were sensitive to Imipenem (93%) followed by Fosfomycin (86%), Amikacin (87%), Nitrofurantoin (81%), and Amoxicillin/K Clavulanate (74%). On the other hand, the susceptibility of all isolated organisms to Cotrimoxazole was only 50%. It was even lower for Cephalexin (35%), Ampicillin (25%), Nalidexic acid (15%), and PIP/TAZ (5.4%).

E. coli, the commonest isolated organism, shows the highest sensitivity rate to Imipenem (97%), followed by Fosfomycin (92%), Nitrofurantoin (90.4%), Amikacin (90%), Amox/K Clavulanate (85%), and Gentamycin (75%). The sensitivity rate of isolated *E. coli* to Nalidixic acid and Ampicillin was 16% and 23%, respectively.

The sensitivity of the second commonly isolated organism, *Klebsiella pneumonia*, was highest for Imipenem (98%), followed by PIP/TAZ (93%), Amikacin (91%), Fosfomycin (86%), and Nitrofurantoin and Levofloxacin (70%). Similar to *E.coli*, the sensitivity rate of *Klebsiella pneumonia* to cotrimoxazole was 52% and is much lower with other tested antimicrobial agents.

Table 1: Gender distribution and frequency of different organisms isolated.

Organism	Gender		Total
	Female No. (%) 220 (55.8)	Male No. (%) 174 (44.2)	**394 (100%)**
Escherichia coli	114 (45.8)	94.0 (45.2)	208 (52.8)
Klebsiella pneumonia	42.0 (62.7)	25.0 (37.3)	67.0 (17.0)
Enterococcus faecalis	17.0 (51.5)	16.0 (48.5)	33.0 (08.4)
Proteus mirabilis	12.0 (57.1)	09.0 (42.9)	21.0 (05.3)
Pseudomonas aeruginosa	8.0 (47.1)	09.0 (52.9)	17.0 (04.3)
Streptococcus species	9.0 (81.8)	2.0 (18.2)	11.0 (02.8)
Staphylococcus aureus	6.0 (37.5)	10.0 (62.5)	16.0 (04.1)
Others	12.0 (57.1)	9.0 (42.9)	21.0 (05.3)

Table 2: The sensitivity rate of the isolated uropathogens to the tested antimicrobial agents.

Type of isolate	No. of isolates	Sensitivity to different antibiotics %												
		AMC/ CLAV	AMP	AMK	GM	SXT	CFX	CIP	NI	NA	IMP	PIP/TAZ	FOS	LEV
Escherichia coli	208	85	23	90	75	49	33	50	90	16	97	59	92	54
Klebsiella sp.	67	17	10	91	25	52	51	7	73	25	98	93	86	72
Enterococcus sp.	33	47	63	10	53	46	15	5	77	0.0	100	100	50	50
Proteus mirabilis	21	50	20	76	47	25	33	45	38	0.0	86	94	45	75
Pseudomonas sp.	17	0.0	0.0	60	55	28.5	0.0	60	43	0.0	85	90	0.0	86
Staphylococcus	16	39	33	50	64	79	0.0	73	90	0.0	42	0.0	0.0	83
Streptococcus sp.	11	83	67	0.0	0.0	33	75	0.0	0.0	50	100	100	0.0	100
Others	21	41	28	68	71	74	28.5	58	82	0.0	82	7.6	0.0	75
Total	394	74	25	87	69	50	35	56	81	15	93	5.4	86	61

AMC/CLAV: amox/K clavulanate, AMP: ampicillin, AMK: amikacin, GM: gentamycin, SXT: cotrimoxazole, CFX: cephalexin, CIP: ciprofloxacin, NI: nitrofurnatoin, NA: nalidixic acid, IMP: imipenem, PIP/TAZ: pipracillin/tazobactam, FOS: fosfomycin, LEV: levofloxacin.

DISCUSSION

In this study, the number of female patients with UTI was more than the number male patients, although the difference was not statistically significant. This lack of difference was because of the selection criteria and because it was a single center study. Hence, it does not reflect prevalence in the general population. The higher prevalence of UTIs among females is due to the factors that make females more predisposed to UTIs than males [15]. These factors include the close proximity of the urethral meatus to the anus, shorter urethra, sexual intercourse, incontinence, and bad toilets [16-18]. The most predominant urinary tract pathogen in both sexes in this study was *E. coli* followed by *Klebsiella pneumonia*. However, this finding is similar to previously published reports [1, 19, 20].

The resistance of *E. coli* and other members of the Enterobacteriaceae family to several commonly used antimicrobial agents is alarming. For example, the resistance of *E. coli* and Klebsiella, which are common UTI pathogens, to Ampicillin, Cloxacillin, Cephalexin, Ciprofloxacin, Nalidixic acid, and Cotrimoxazole is unacceptably high. These agents are of little prophylactic or empirical therapeutic use for the management of uncomplicated UTI in an outpatient setting.

Similar to other reports, in descending order, higher sensitivity rates of *E. coli* and *Klebsiella pneumonia* are observed for Imipenem, Amikacin, Fosfomycin, and Nitrofurantoin [9, 21, 22]. Imipenem and Amikacin are available only for parenteral use and should be reserved for patients with complicated UTI who require admission to the hospital.

Fosfomycin and Nitrofurantoin are the only oral agents tested in this study that remain relatively active against most of the isolated uropathogens with sensitivity rates of 86% & 81%, respectively. They can be used for empirical therapy in uncomplicated UTI. However, Nitrofurantoin is a bacteriostatic agent and has poor tissue penetration and low blood levels. Hence, it is not recommended for use in UTIs with significant tissue involvement, such as pyelonephritis, or in infections caused by *K. pneumonia* or *Proteus spp* [23]. Furthermore, nitrofurantoin causes dose-related nausea and vomiting. It also carries the serious risk of fatal hepatic failure, chronic active hepatitis, interstitial nephritis, pulmonary side effects (interstitial lung disease), hypersensitivity

lung disease, and non-cardiogenic pulmonary edema [24-26]. Patients receiving Nitrofurantoin were more likely to discontinue the antibiotic mainly due to gastrointestinal side effects [27].

The current data indicates that there is a higher resistance rate of common UTI pathogens to commonly used and readily available oral agents such as Ampicillin, Ciprofloxacin, Nalidixic acid, Cephalexin, and Cotrimexazole. This may reflect the overuse of these agents in our region to treat common infections, such as UTIs or respiratory tract infections. Unfortunately, misuse of antimicrobial agents in developing nations is still a major concern because of the failure to implement restriction policies concerning their use in the community and hospitals [28]. Overuse of these antimicrobial agents may lead to emergence of multidrug-resistant pathogens, which possesses the potential to disseminate within the region. Further antimicrobial consumption studies at the community level are needed to verify this assumption.

In this study, the resistance rate of common UTI pathogens to guideline-recommended first line oral antimicrobial agents such as Cotrimoxazole, Amoxicillin, and Fluoroquinolone was unacceptably high in Aseer region, Saudi Arabia. The data suggests the use of Fosfomycin or Nitrofurantoin as first line empirical therapy for uncomplicated UTI in ambulatory care settings. Consequently, this supports the notion that empirical antimicrobial selection should be based on a knowledge of the local prevalence of specific bacterial microorganisms and their antimicrobial sensitivities, rather than on universal guidelines. Against the background of a paucity of reports on UTIs in Aseer region, Saudi Arabia, this study provides valuable laboratory data to monitor the status of antimicrobial sensitivity among uropathogens. In addition, it also aims to improve treatment recommendations in a specific geographical region.

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