Antibiotic Resistance among Patients with Urinary Tract Infections in Kandahar, Afghanistan

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Abstract

Background: Antimicrobial resistance is a global public health threat. Highest burden of resistance is reported from low- and middle-income countries. **Objectives:** To investigate and report the current scenario of increased antibiotic resistance of uropathogens among symptomatic urinary tract infection patients in Kandahar, Afghanistan. **Methods:** From January 2018 to December 2021, this retrospective study was carried out at two main hospitals in Kandahar City, Afghanistan. Here, culture and sensitivity profiles of uropathogens were studied among symptomatic Bacteriuria in the presence of genitourinary symptoms (i.e., dysuria, suprapubic pain or tenderness, frequency, or urgency) (UTI) patients. **Results:** Among urine samples of 1589 patients, 1047 (65.9%) were culture positive and included in this study. Most of these patients (626/1047 [59.8%]) were females, with majority (818 [78.1%]) having age between 19 and 39 years. Gram-negative bacteria were the most prevalent (840/1047 [80.2%]), with *E. coli* (653/1047 [62.4%]) as the most common isolated uropathogen. Overall gram-negative bacteria had higher resistance against commonly used antibiotics of cotrimoxazole (62.8%), ciprofloxacin (56.0%), levofloxacin (47.5%), cefixime (44.5%), fosfomycin (41.5%), and even ceftriaxone (48.3%). **Conclusions:** Kandahar province has higher resistance rates against commonly used empirical antibiotics like norfloxacin, ciprofloxacin, levofloxacin, and cefixime. Nitrofurantoin should be used as the first-line antibiotic in treating UTI patients. Public health authorities should make strict regulations and policies to reduce irrational use, inappropriate prescription, and over-the-counter availability of antibiotics in Kandahar.

Keywords: Afghanistan, antibiotics, bacteria, Kandahar, resistance, uropathogens

Introduction

Antimicrobial resistance is a global public health threat.[1] Highest burden of resistance is reported from low- and middle-income countries due to several factors, including lack of surveillance capacity and systematic data collection of antimicrobial resistance.[2,3]

Currently, UTI represents one of the most common diseases encountered in clinical practice, affecting people of all age groups, from neonatal to geriatric age groups.[4] The most commonly reported bacterial cause of UTI is *Escherichia coli*, followed by others such as *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Pseudomonas aeruginosa*.[5,6] UTI due to multidrug resistance (MDR) bacteria treated with inappropriate empirical antibiotics is related to serious complications (like sepsis and increased mortality), increased treatment cost and hospital stay, and loss of working days.[7,8] Antibiotic resistance mostly differs by geographical location.[9] Therefore, local susceptibility studies are crucial to determine the most effective antibiotics to improve empirical prescription and minimize the treatment cost and duration.[10]

Unfortunately, we could not find any published research from Kandahar and even whole Afghanistan that investigates the antibiotic resistance against uropathogens in UTI patients.

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Objectives

Main objective of this study was to investigate and report the current scenario of increased antibiotic resistance of uropathogens among symptomatic urinary tract infection patients in Kandahar, Afghanistan.

Materials and Methods

Design, population, and demography

This was a retrospective study carried out at outpatient departments (OPDs) of Mirwais Regional Hospital (a government hospital) and Sidal Hospital (a private hospital) in Kandahar, Afghanistan. In this study, culture and sensitivity profiles of uropathogens were studied in clinically suspected symptomatic UTI patients during a period of 4 years (January 2018 to December 2021). Culture and sensitivity profiles were carried out at Mirwais Regional Hospital and Lemar Laboratories. The most common uropathogens and their antibiotic resistance rates were identified in different age groups (5–18, 19–29, 30–39, 40–49, 50–59, and ≥60 years) and with respect to gender. All the patients received care as usual, i.e., diagnostic tests and empirical therapy according to the daily practice.

Inclusion and exclusion criteria

The inclusion criteria of this study were patients presenting with symptoms of UTI and permanent residents of Kandahar province. The exclusion criteria were patients who refused to participate, immunocompromised, patients suffering from phimosis or paraphimosis, uncircumcised males, and patients who had taken antibiotics within the past 24 hours.

Sample size calculation

Sample size calculation was not required, as records of all the UTI patients who attended the hospitals' OPDs during the 4-year period were included in this study.

Ethical issues

In the present study, an effort was made to protect the health, privacy, and secrecy of personal information and the rights to self-determination of all the participants. All ethical issues were considered and the study was conducted after approval from the Kandahar University Ethics Committee (code number KDRU-EC-2021.75) and written permissions from Mirwais Regional Hospital and Sidal Hospital. The name, personal, and medical information of all the participants were kept secret. Before entering into the computer for analysis, the collected data were coded and de-identified.

Urine sampling and determination of antimicrobial susceptibility

Uropathogens were isolated from a total of 1589 clinically suspected UTI patients' early morning midstream "clean-catched" urine samples. Urine samples were cultured on blood agar and MacConkey agar by using a standard calibrated loop (0.01 mL), and the plates were incubated at 37°C for 24 hours. If a patient had >1 positive urine culture, only the first positive urine culture result was included in the results. After the identification of bacteria, antibiotic susceptibility test was performed by the Kirby–Bauer disk diffusion technique based on the Clinical and Laboratory Standards Institute (CLSI) 2013.[11] Susceptibility of isolates to antibiotics was tested against the disks of 16 antibiotics, namely ampicillin, amoxicillin, cephradine, cefixime, ceftriaxone, imipenem, norfloxacin, ciprofloxacin, levofloxacin, amikacin, gentamicin, cotrimoxazole (trimethoprim/sulfamethoxazole [TMP-SMX]), doxycycline, fosfomycin, vancomycin, and nitrofurantoin.

Statistical analysis

All the collected data were double-entered into Microsoft Excel software. Later, data were entered into Statistical Package for the Social Sciences (SPSS) version 25 (Chicago, IL, USA) for the statistical analysis. Descriptive statistics were used to calculate organisms' prevalence rate, frequency distributions, and susceptibility patterns. *P*-value less than 0.05 was considered statistically significant.

Results

During the period of 4 years (January 2018 to December 2021), nonduplicative urine cultures and antibiotic susceptibility results of 1589 UTI patients were retrospectively reviewed. A total of 1047 (65.9%) samples came up with a positive urine culture and were included in the study. Among the 1047 samples, 626/1047 (59.8%) were females, while 103/1047 (9.8%) were ≤18 years of age. Most (818/1047 [78.1%]) of these patients were between 19 and 39 years of age [Figure 1, Table 1].

Isolated uropathogens

Among the uropathogens, gram-negative bacteria were the most prevalent (840/1047 [80.2%]). The most common isolated uropathogens were *E. coli* (653/1047 [62.4%]), followed by *Enterococcus* spp. (119/1047 [11.4%]) and *Klebsiella* spp. (114/1047 [10.9%]). *E. coli*, *Pseudomonas* spp., and *Enterococci* spp. were present in statistically significant numbers (*P* value <0.001) among females, whereas *Staphylococcus* spp. were mostly present among males (*P* value <0.001) [Table 2].

Table 1: Age- and gender-wise distribution of culture-positive UTI patients

Variable	Frequency, *n* (%)	Gram-negative bacteria	Gram-positive bacteria
Gender			
Male	421 (40.2)	288 (68.4)	133 (31.6)
Female	626 (59.8)	562 (89.7)	64 (10.3)
Total	1047 (100)	850 (81.2)	197 (18.8)
Age (years)			
5–18	103 (9.8)	76 (74.2)	27 (25.8)
19–29	402 (38.4)	356 (88.6)	46 (11.4)
30–39	416 (39.7)	351 (84.3)	65 (15.7)
40–49	64 (6.1)	39 (60.9)	25 (39.1)
50–59	33 (3.2)	11 (33.6)	22 (66.4)
≥60	29 (2.8)	7 (24.7)	22 (75.3)
Total	1047 (100)	840 (80.2)	207 (19.8)

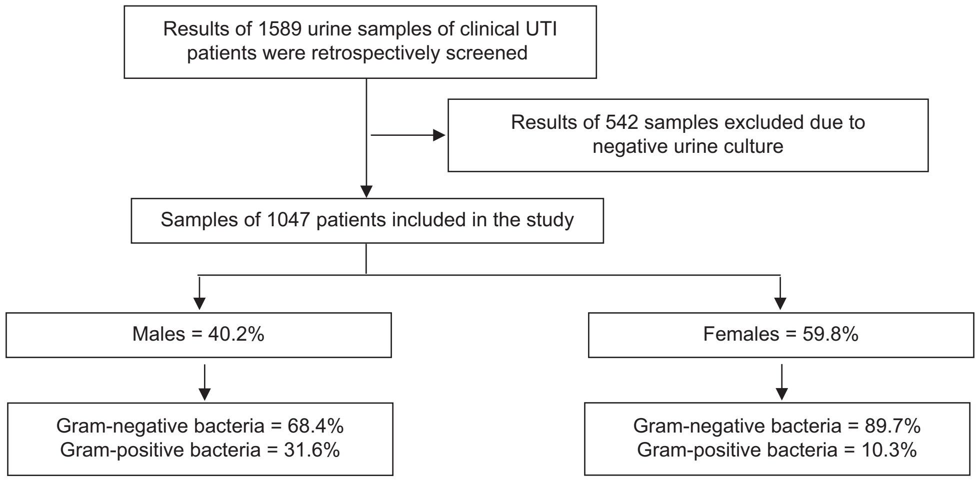

Figure 1: Flowchart of the study

Table 2: Distribution and frequency of bacterial isolates from the urine samples of UTI patients

Gram stain	Bacteria isolated	Total frequency, *n* (%) (*n*=1047)	Males, *n* (%) (*n*=421)	Females, *n* (%) (*n*=626)	*P*
Gram-negative bacteria	*E. coli*	653 (62.4)	170 (26.0)	483 (74.0)	<0.001
	Klebsiella spp.	114 (10.9)	49 (43.0)	65 (57.0)	0.522
	Pseudomonas spp.	60 (5.7)	6 (10.0)	54 (90.0)	<0.001
	Serratia spp.	13 (1.2)	3 (23.1)	10 (76.9)	0.205
Gram-positive bacteria	*Enterococcus* spp.	119 (11.4)	30 (25.2)	89 (74.8)	<0.001
	Staphylococcus spp.	88 (8.4)	68 (77.3)	20 (22.7)	<0.001

spp., species

Resistance against gram-negative bacteria

For *E. coli*, the highest resistance was present against ampicillin (91.7%), amoxicillin (88.4%), and cephradine (86.1%), whereas the least resistance was seen against imipenem (4.4%), nitrofurantoin (15.2%), and amikacin (26.9%). *Klebsiella* spp. showed increased resistance to ampicillin (99.1%), amoxicillin (98.2%), and norfloxacin (64.0%), whereas revealed the least resistance to imipenem (8.8%), nitrofurantoin (16.7%), and fosfomycin (27.2%). *Pseudomonas* spp. revealed highest resistance against ampicillin (100%), cotrimoxazole (100%), and amoxicillin (98.3%), whereas showed the least resistance to nitrofurantoin (21.7%), amikacin (36.7%), and ceftriaxone (43.3%). Overall gram-negative bacteria had higher resistance against commonly used antibiotics of cotrimoxazole (62.8%), ciprofloxacin (56.0%), levofloxacin (47.5%), ceftriaxone (48.3%), cefixime (44.5%), and fosfomycin (41.5%) [Table 3].

Resistance against gram-positive bacteria

Enterococcus spp. had the highest resistance to cotrimoxazole (88.2%), fosfomycin (79.8%), and ciprofloxacin (76.5%), whereas decreased least resistance to imipenem (5.0%), vancomycin (9.2%), and nitrofurantoin (11.8%). *Staphylococcus* spp. showed highest resistance to ampicillin (98.9%), amoxicillin (92.1%), and cefixime (89.8%), whereas least resistance was revealed to vancomycin (4.6%), imipenem (11.4%), and nitrofurantoin (15.9%) [Table 3].

Overall resistance

Overall antibiotic resistance pattern of bacterial isolates is shown in Table 4. Highest resistance was observed to ampicillin (88.0%), amoxicillin (80.7%), and cotrimoxazole (69.8%). Contrary, least resistance was observed to nitrofurantoin (14.8%), imipenem (16.4%), and amikacin (23.7%). Norfloxacin, ciprofloxacin, cefixime, levofloxacin, and ceftriaxone had resistance rate of 66.7%, 61.4%, 54.9%, 52.0%, and 45.6%, respectively.

Discussion

We are living in an era of increasing antibiotics resistance. So, to keep an eye on the changes in the efficacy of the antibiotics against uropathogenic bacteria, there is a need for continuous surveillance of antibacterial susceptibility of the clinical isolates. Antibiotics resistance is expected to be even more than in the other provinces of Afghanistan. This situation is sensed by many health workers in the clinical practice.

In our study, the most common uropathogen was *E. coli*, present in 62.4% of UTI patients. Similarly, in the neighboring country Pakistan, various urine culture studies have reported *E. coli* as the most common uropathogen, ranging from 52 to 77.4%.[12-17] Also, studies from Iraq (50.0%),[18] Ethiopia (52.7%),[19] India (59.8%),[20] Saudi Arabia (27%),[21] and Ivory Coast (28.7%)[22] have reported *E. coli* as the most common uropathogen among UTI patients.

Table 3: Antibiotic resistance pattern of various bacteria to various antibiotics

Antibiotic class	Antibiotic	Resistance, *n* (%), *n*=1047							
		Gram-negative bacteria					Gram-positive bacteria		
		E. coli, *n*=653	*Klebsiella* spp. (*n*=114)	*Pseudomonas* spp. (*n*=60)	*Serratia* spp. (*n*=13)	Overall resistance (%)	*Enterococcus* spp. (*n*=119)	*Staphylococcus* spp. (*n*=88)	Overall resistance (%)
Beta-lactams	Ampicillin	599 (91.7)	113 (99.1)	60 (100)	8 (61.5)	88.1	91 (76.5)	87 (98.9)	87.7
	Amoxicillin	577 (88.4)	112 (98.2)	59 (98.3)	6 (46.1)	82.7	73 (61.3)	81 (92.1)	75.6
	Cefixime	341 (52.2)	53 (46.5)	43 (71.7)	1 (7.7)	44.5	73 (61.3)	79 (89.8)	75.6
	Cephradine	562 (86.1)	64 (56.1)	40 (66.7)	5 (38.5)	61.9	21 (17.6)	19 (21.6)	19.6
	Ceftriaxone	456 (69.8)	56 (49.1)	26 (43.3)	4 (30.8)	48.3	44 (37.0)	37 (42.1)	79.1
	Imipenem	29 (4.4)	10 (8.8)	32 (53.3)	2 (15.4)	20.5	6 (5.0)	10 (11.4)	8.2
Fluoroquinolones	Norfloxacin	372 (57.0)	73 (64.0)	55 (91.7)	4 (30.8)	60.9	86 (72.3)	74 (84.1)	78.2
	Ciprofloxacin	492 (75.3)	60 (52.6)	53 (88.3)	1 (7.7)	56.0	91 (76.5)	60 (68.2)	72.4
	Levofloxacin	295 (45.1)	63 (55.3)	49 (81.7)	1 (7.7)	47.5	64 (53.8)	60 (68.2)	61.0
Aminoglycosides	Gentamicin	281 (43.0)	59 (51.7)	35 (58.3)	1 (7.7)	40.2	30 (25.2)	38 (43.2)	34.2
	Amikacin	176 (26.9)	32 (28.1)	22 (36.7)	1 (7.7)	24.9	17 (14.3)	25 (28.4)	11.4
Others	Cotrimoxazole	452 (69.2)	67 (58.8)	60 (100)	3 (23.1)	62.8	105 (88.2)	70 (79.6)	83.9
	Fosfomycin	258 (39.5)	31 (27.2)	55 (91.7)	1 (7.7)	41.5	95 (79.8)	78 (88.6)	84.2
	Doxycycline	337 (51.6)	49 (43.0)	29 (48.3)	3 (23.1)	41.5	90 (75.6)	38 (43.2)	59.4
	Vancomycin	226 (34.6)	67 (58.8)	43 (71.7)	5 (38.5)	50.9	11 (9.2)	4 (4.6)	6.9
	Nitrofurantoin	99 (15.2)	19 (16.7)	13 (21.7)	1 (7.7)	15.3	14 (11.8)	14 (15.9)	13.9

spp., species

Table 4: Chi-square test of overall antibiotic resistance pattern of bacterial isolates in males and females

Antibiotic class	Antibiotic name	Resistance, *n* (%) (*n*=1047)	Males, *n* (%) (*n*=421)	Females, *n* (%) (*n*=626)	*P*
Beta-lactams	Ampicillin	921 (88.0)	398 (43.2)	523 (56.8)	<0.001
	Amoxicillin	845 (80.7)	370 (43.8)	475 (56.2)	<0.001
	Cefixime	575 (54.9)	207 (36.0)	368 (64.0)	0.002
	Cephradine	500 (47.8)	206 (41.2)	294 (58.8)	0.532
	Ceftriaxone	477 (45.6)	199 (41.7)	278 (58.3)	0.362
	Imipenem	172 (16.4)	69 (40.1)	103 (59.9)	0.978
Fluoroquinolones	Norfloxacin	698 (66.7)	251 (36.0)	447 (64.0)	<0.001
	Ciprofloxacin	643 (61.4)	155 (24.1)	488 (75.9)	<0.001
	Levofloxacin	544 (52.0)	203 (37.3)	341 (62.7)	0.047
Aminoglycosides	Gentamicin	400 (38.2)	159 (39.8)	241 (60.3)	0.811
	Amikacin	248 (23.7)	108 (43.5)	140 (56.5)	0.220
Others	Cotrimoxazole	731 (69.8)	291 (39.8)	440 (60.2)	0.687
	Fosfomycin	584 (55.8)	233 (39.9)	351 (60.1)	0.817
	Doxycycline	497 (47.5)	180 (36.2)	317 (63.8)	0.012
	Vancomycin	379 (36.2)	177 (46.7)	202 (53.3)	0.001
	Nitrofurantoin	155 (14.8)	45 (29.0)	110 (71.0)	0.002

UTI was most commonly present among females (59.8%) in our study. Similar results have been reported in studies from Iraq (62.7%),[18] Pakistan (68.0%),[23] Saudi Arabia (73%),[21] India (76.6%),[20] Ethiopia (81.2%),[19] and South Africa (67.6%).[24] The increased prevalence of UTI among females might be due to the anatomical differences in urogenital organs between the two sexes.[5,25]

In our study, higher resistance was observed against commonly prescribed antibiotics of ciprofloxacin (75.3%), ceftriaxone (69.8%), cotrimoxazole (69.2%), cefixime (52.2%), levofloxacin (45.1%), fosfomycin (39.5%), and nitrofurantoin (15.2%).

In a study conducted in the Balochistan province of Pakistan, *E. coli* was the major multidrug-resistant organism. Among the commonly prescribed broad-spectrum antibiotics, higher resistance was observed against cefotaxime (76.5%), levofloxacin (71.3%), amoxicillin/clavulanate (70.3%), ceftriaxone (64.3%), cefepime (53.4%), and ceftazidime (49.4%).[23] A study in Iran reported less resistance to *E. coli* with commonly used antibiotics.[26] They reported that *E. coli* was resistant against cefixime (68.2%), ceftriaxone (37%), cotrimoxazole (33.6%), and ciprofloxacin (31.9%).[26] A study from Haryana, India, reported higher *E. coli* resistance against levofloxacin (79.3%), ciprofloxacin

(73.6%), ceftriaxone (69.8%), cotrimoxazole (69.8%), nitrofurantoin (15.1%), and fosfomycin (13.2%).[27]

However, a study in South Africa revealed less resistance of *E. coli* against ciprofloxacin (18.5%), cotrimoxazole (11.0%), ceftriaxone (8.8%), and nitrofurantoin (3.9%).[24]

Conclusions

As the pattern of bacterial sensitivity to antibiotics varies over time and in different geographical regions, antibiotic treatment of UTI should be based on local experience of sensitivity and resistance patterns. This high level of antibiotic resistance against uropathogens in Kandahar may be attributed to irrational use, inappropriate prescription, and over-the-counter availability of antibiotics. In Kandahar province, all antibiotics can be purchased in private pharmacies without a medical prescription.

In Kandahar province, *E. coli* is the most frequent cause of UTI, which mostly affects females. Higher resistance rates are present in Kandahar province against commonly used empirical antibiotics like amoxicillin, norfloxacin, ciprofloxacin, levofloxacin, cefixime, and ceftriaxone. So, based on our results, nitrofurantoin should be used as the first-line antibiotic in treating UTI patients. High rates of antibiotic resistance in Kandahar could be due to the widespread and injudicious use of broad-spectrum antibiotics, as well as the over-the-counter availability of all the antibiotics in pharmacies. There is an intense need to formulate guidelines for preventing antibiotic resistance evolution among urinary tract infection. Thus, it is highly recommended to regulate the continuous supervision of pharmacies in Kandahar province. Instead of blind prescription of antibiotics, physicians should judiciously prescribe antibiotics and practice the culture and sensitivity of urine samples. Health authorities should make strict regulations and policies to reduce irrational use, inappropriate prescription, and over-the-counter availability of antibiotics in Kandahar. Afghanistan Ministry of Public Health and other health-related national and international bodies should focus on a continuous surveillance of uropathogens prevalence and resistance in Kandahar.

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Conflicts of interest

There are no conflicts of interest.

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