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Original Article

The Antibiotic Resistance and Multidrug Resistance Pattern of Uropathogenic *Escherichia coli* at Soba University Hospital: A Descriptive Retrospective Survey

Hagir Mohamed Eezzeldin[1], Safaa Badi[2], and Bashir Alsiddig Yousef[3*]

[1]Department of Clinical Pharmacy, Faculty of Pharmacy, University of Khartoum, Al-Qasr Ave, Khartoum, Sudan
[2]Department of Clinical Pharmacy, Faculty of Pharmacy, Omdurman Islamic University, Aboseid Street, Khartoum, Sudan
[3]Department of Pharmacology, Faculty of Pharmacy, University of Khartoum, Al-Qasr Ave, Khartoum, Sudan
ORCID:
Bashir Alsiddig Yousef: https://orcid.org/0000-0001-7832-4556

Corresponding Author: Bashir Alsiddig Yousef; email: bashiralsiddiq@gmail.com

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Abstract

Background: The irrational use of antibiotics for the treatment of urinary tract infections (UTIs) may lead to increased antimicrobial resistance among uropathogenic *Escherichia coli* (*E. coli*), as well as multidrug resistance worldwide, which will limit available treatment options for UTIs caused by these organisms. This study aimed to determine the resistance pattern of *E. coli* causing UTIs in out-patients and in-patients of Soba University Hospital.

Methods: Data were collected from the laboratory records in the Department of Microbiology in Soba Teaching Hospital by using a predesigned checklist and then analyzed using the statistical package for social sciences. Bivariate analysis (Chi-square test) was used to compare between variables.

Results: Out of the 231 *E. coli* urine cultures, 160 (69.3%) were collected from females. The results showed high resistance to ampicillin (92.4%), amoxicillin-clavulanic acid (83.3%), cephalexin (90.6%), cefuroxime (72%), ceftazidime (71%), ceftriaxone (72%), ciprofloxacin (68%), and co-trimoxazole (75.3%). Collectively, around 188 (81.4%) were multidrug-resistant. On the other hand, the sensitivities of *E. coli* isolates were 68.8%, 93.1%, 89.4%, and 100% to gentamicin, amikacin, nitrofurantoin, and carbapenems, respectively.

Conclusion: The rate of *E. coli* resistance was observed to be high to the commonly prescribed drugs for UTIs, including ampicillin, amoxicillin/clavulanic acid, different cephalosporins, fluoroquinolones, and co-trimoxazole. However, *E. coli* showed lower resistance rates to nitrofurantoin, amikacin, and carbapenems. Thus, these drugs can be reserved for the empirical treatment of UTIs caused by *E. coli*.

Keywords: *Escherichia coli*, urinary tract infection, multidrug resistance, Soba University Hospital

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1. Introduction

Urinary tract infections (UTIs) are one of the most frequent infectious diseases that affect humans and is considered a critical public health problem [1, 2]. In United States, UTIs are responsible for around 7 million clinic visits per year and cost $2 billion annually [1]. The main etiology of UTIs is the microbial invasion to different tissues of the urinary tract system [3]. Among bacteria causing UTIs, *Escherichia coli* (*E. coli*) is considered as the most predominant cause of both community and nosocomial UTIs. Other UTI-causing bacteria include *Proteus spp, Staphylococcus Saprophyticus, Klebsiella spp*, and other *Enterobacteriaceae* [2, 4]. Clinically, *E. coli* can cause uncomplicated and complicated UTIs. In uncomplicated UTIs, individuals develop infection without any structural or neurological abnormalities in the urinary tract; it can either be upper UTIs (pyelonephritis) or lower UTIs (cystitis) [5]. Many risk factors are associated with UTIs, including a previous UTI, female gender, vaginal infection, obesity, diabetes, and genetic susceptibility [6]. In complicated UTIs, other factors such as compromised immune system, urinary obstruction, neurological disease, renal failure, and foreign bodies can predispose to UTI [7, 8].

Treatment of UTIs requires assessment of the patient by evaluating the symptoms or signs, determining the type of UTI, and knowing the previous antimicrobial therapy in case of recurrent infection [9]. Many antibiotics commonly prescribed for the treatment of UTIs include ciprofloxacin, nitrofurantoin, co-trimoxazole, and ampicillin [10]. According to clinical practice guidelines, fluoroquinolones have been recommended for lower UTIs, whereas intravenous cephalosporins are commonly administered for upper UTIs. Moreover, the recommended first-line antimicrobial for acute uncomplicated bacterial infection is nitrofurantoin or fosfomycin or co-trimoxazole; the second-line options include fluoroquinolones and β-lactams antibiotics, while for β-lactamase-producing organisms, it recommends using fosfomycin or fluoroquinolones or piperacillin-tazobactam or carbapenems. Whereas, for multi-drug resistance (MDR), the recommended antibiotics are fluoroquinolones, ceftazidime, piperacillin-tazobactam, carbapenems, aminoglycosides, and colistin [11]. However, extensive use of antibiotics in treating UTIs is highly correlated to antimicrobial resistance [1, 12] and the emergence of MDR that is defined as organisms being resistant to at least three classes of antimicrobial agents [13]. Moreover, antibiotic resistance is a public health problem, which may result in treatment failure and poor clinical outcomes such as development of complications, prolonged hospitalization, and need for intravenous therapy [14, 15].

Knowledge of the causative organisms and their sensitivity pattern is crucial for empirical therapy for various infections. Since *E. coli* is the most predominant causative agent for UTIs, regular antibiogram of *E. coli* strains at different hospitals is crucial for better adaptation of empirical antibiotic therapy. Hence, our study aimed to explore the pattern of antibiotic resistance by uropathogenic *E.coli* isolate from urine samples at Soba University Hospital in Khartoum State.

2. Materials and Methods

2.1. Study setting

This retrospective cross-sectional hospital-based survey used medical records of the patients visiting Soba Hospital in Khartoum, Sudan between January and December 2017, who underwent the antibiotic sensitivity test (disc-diffusion method) for the *E. coli* isolates.

2.2. Inclusion and exclusion criteria

All medical records of patients for whom *E. coli* antibiogram was done were included, while patient records with incomplete information were excluded.

2.3. Sample size and sampling method

A total of 231 patients met the inclusion criteria and were included in the study.

2.4. Data collection tool

Data were collected retrospectively from patient records using a data collection sheet, which consisted of the sociodemographic data of the patient, and the list of used medications with the sensitivity findings (sensitive or resistant).

2.5. Data analysis

Data were analyzed by the International Business Machines (IBM) Statistical Package for Social Sciences [SPSS] for Windows, v.22.0 software [Armonk, NY: IBM Corp]. Descriptive statistics (frequency tables) and bivariate analysis (Chi-square) was done. *P*-value $\leq$ 0.05 was considered significant in comparative data.

3. Results

Of the 231 urine culture samples, 160 (69.3%) were of females and 71 (30.7%) of males. Additionally, while 159 (68.8%) samples were of adults, 72 (31.6%) were of pediatric patients. Regarding patient age, 20.8% of the participants were aged 1–6 years, and 28.6% were >60 years (Table 1)

Regarding the antibiotics sensitivity pattern for different antibiotics, as shown in Table 2, the pattern to β-lactams antibiotics were varied, *E. coli* was resistant to ampicillin in 91.5% of the participants, and it was resistant to amoxicillin-clavulanic acid in 84.6%. Furthermore, the resistance rates for *E. coli* strains against cephalexin, cefuroxime, ceftazidime, and ceftriaxone were 69%, 73.1%, 71.7%, and 71.8%, respectively. Moreover, *E. coli* bacteria were resistant to ciprofloxacin in around two-thirds (65.9%) of the participants, and to gentamicin in about one-third (32.2%) of them. However, it was resistant to nitrofurantoin in only 10.6% of the samples. Interestingly, 99.6% of *E. coli* samples were sensitive to carbapenems (Table 2). On the other hand, the frequency of *E. coli* stains with MDR (with resistance to at least three classes of the antimicrobial agents) were 188 (81.4%) (Figure 1). Furthermore, *E. coli* samples from pediatric or adult patients showed different resistance and sensitivity patterns toward various antibacterial agents (Tables 3 and 4).

When chi-square was performed to determine the association of the antibiotic resistance and sociodemographic characteristics of the participants, the study showed no significant association between the sensitivity to antibacterial drugs and the gender or the age groups. However, the admission status (in- or outpatient) was significantly associated with the sensitivity to cephalexin, cefuroxime, ceftazidime, ceftriaxone, ciprofloxacin, gentamicin, and nitrofurantoin (0.041, 0.009, 0.003, 0.006, 0.000, 0.042, 0.012), respectively.

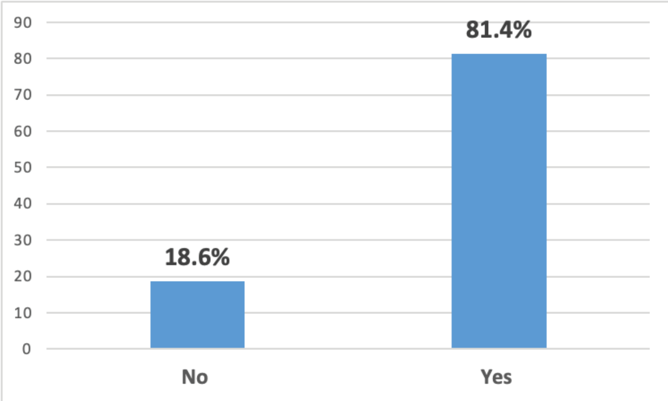

Figure 1: Distribution of study sample according to multiple antibiotics resistance.

TABLE 1: Demographic characteristics of the participants (n = 231).

Variable		Number (frequency %)
Gender	Male	71 (30.7%)
	Female	160 (69.3%)
Age category	Adult	159 (68.8%)
	Pediatric	72 (31.2%)
Age group (yr)		
	1–6	48 (20.8%)
	7–12	20 (8.6%)
	13–18	4 (1.7%)
	19–30	13 (5.6)
	31–40	19 (8.4)
	41–50	29 (12.5)
	51–60	32 (13.8)
	>60	66 (28.6)
Admission unit	Inpatient	160 (69.3%)
	Outpatient	71 (30.7%)

4. Discussion

The emergence of antibiotic resistance in *E. coli* and other microorganisms that cause UTIs is increasing day by day, making it a critical health problem. Thus, in order to provide proper treatment for UTIs, it is crucial to measure the antibiotic resistance patterns in *E. coli* isolates [16]. In the present study, the total *E.coli* samples isolated within the study period were 231. We found that the occurrence of Uropathogenic *E. coli* frequency was higher in females than in males; this may occur due to the difference in the anatomy of the urinary tract of the females, and the hormonal effects, pregnancy, certain type of birth control, and behavioral patterns [17–20]. Regarding the resistant pattern, 91.5%

TABLE 2: Distribution of study sample according to sensitivity pattern (n = 231).

Antibiotic class	Antibiotic	Sensitivity test		*N* (%)
β-lactams	Ampicillin	NRST† (n = 43)		
		RST* (n = 188)	Resistance	172 (91.5%)
			Sensitive	16 (8.5%)
	Amoxicillin + Clavulanic acid	NRST (n = 10)		
		RST (n = 221)	Resistance	187 (84.6%)
			Sensitive	34 (15.4%)
Cephalosporin	Cephalexin	NRST (n = 173)		
		RST (n = 58)	Resistance	40 (69%)
			Sensitive	18 (31%)
	Cefuroxime	NRST (n = 8)		
		RST (n = 223)	Resistance	163 (73.1%)
			Sensitive	60 (26.9%)
	Ceftazidime	NRST (n = 8)		
		RST (n = 223)	Resistance	160 (71.7%)
			Sensitive	63 (28.3%)
	Ceftriaxone	NRST (n = 4)		
		RST (n = 227)	Resistance	163 (71.8%)
			Sensitive	64 (28.2%)
Flouroquinolones	Ciprofloxacin	NRST (n = 8)		
		RST (n = 223)	Resistance	147 (65.9%)
			Sensitive	77 (34.1%)
Aminoglycosides	Gentamycin	NRST (n = 60)		
		RST (n = 171)	Resistance	55 (32.2%)
			Sensitive	116 (67.8%)
	Amikacin	NRST (n = 4)		
		RST (n = 227)	Resistance	20 (8.8%)
			Sensitive	208 (91.2%)
Carbapenems	Meropenem and imipenem	NRST (n = 2)		
		RST (n = 229)	Resistance	1 (0.4%)
			Sensitive	228 (99.6%)
Sulphonamides	Co-trimoxazole	NRST (n = 4)		
		RST (n = 227)	Resistance	169 (73.2%)
			Sensitive	58 (26.8%)
Others	Nitrofurantoin	NRST (n = 5)		
		RST (n = 226)	Resistance	24 (10.6%)
			Sensitive	202 (89.4%)

*RST: Requested sensitivity test; †NRST: Not requested sensitivity test.

Table 3: Distribution of pediatric patients' sample according to sensitivity pattern (n = 72).

Antibiotic class	Antibiotic	Sensitivity test		N (%)
β-lactams	Ampicillin	NRST† (n = 14)		
		RST* (n =58)	Resistance	55 (94.8%)
			Sensitive	3 (5.2%)
	Amoxicillin + Clavulanic acid	NRST (n = 2)		
		RST (n = 70)	Resistance	59 (84.3%)
			Sensitive	11 (15.7%)
Cephalosporin	Cefuroxime	NRST (n = 4)		
		RST (n = 68)	Resistance	51 (75%)
			Sensitive	17 (25%)
	Ceftazidime	NRST (n = 4)		
		RST (n = 68)	Resistance	48 (70.6%)
			Sensitive	20 (29.4%)
	Ceftriaxone	NRST (n = 0)		
		RST (n = 72)	Resistance	51 (70.8%)
			Sensitive	21 (29.2%)
Flouroquinolones	Ciprofloxacin	NRST (n = 1)		
		RST (n = 71)	Resistance	46 (64.8%)
			Sensitive	25 (35.2%)
Aminoglycosides	Gentamycin	NRST (n = 16)		
		RST (n = 56)	Resistance	19 (33.9%)
			Sensitive	37 (66.1%)
	Amikacin	NRST (n = 0)		
		RST (n = 72)	Resistance	7 (9.9%)
			Sensitive	65 (90.1%)
Carbapenems	Meropenem and imipenem	NRST (n = 2)		
		RST (n = 70)	Resistance	1 (1.4%)
			Sensitive	69 (98.6%)
Sulphonamides	Co-trimoxazole	NRST (n = 1)		
		RST (n = 71)	Resistance	56 (78.9%)
			Sensitive	15 (21.1%)
Others	Nitrofurantoin	NRST (n = 2)		
		RST (n = 70)	Resistance	11 (15.7%)
			Sensitive	59 (84.3%)

*RST: requested sensitivity test; † NRST: not requested sensitivity test.

and 84.6% of *E.coli* samples were resistant to ampicillin and co-amoxiclav, respectively, which indicated a cautious use of these antibiotics for the treatment of UTIs. Similar findings were seen in India and Pakistan [21–23]. The resistance rates were also high for cephalosporin antibiotics, including cephalexin (90.6%), ceftazidime (71%), cefuroxime

Table 4: Distribution of adult patients' sample according to sensitivity pattern (n = 159).

Antibiotic class	Antibiotic	Sensitivity test		N (%)
β-lactams	Ampicillin	NRST† (n = 29)		
		RST* (n = 130)	Resistance	117 (90%)
			Sensitive	13 (10%)
	Amoxicillin + Clavulanic acid	NRST (n = 8)		
		RST (n = 151)	Resistance	128 (84.7%)
			Sensitive	23 (15.3%)
Cephalosporin	Cephalexin	NRST (n = 113)		
		RST (n = 46)	Resistance	32 (69.6%)
			Sensitive	14 (30.4%)
	Cefuroxime	NRST (n = 4)		
		RST (n = 155)	Resistance	112 (72.3%)
			Sensitive	43 (27.7%)
	Ceftazidime	NRST (n = 4)		
		RST (n = 155)	Resistance	112 (72.3%)
			Sensitive	43 (27.7%)
	Ceftriaxone	NRST (n = 4)		
		RST (n = 155)	Resistance	112 (72.3%)
			Sensitive	43 (27.7%)
Flouroquinolones	Ciprofloxacin	NRST (n = 7)		
		RST (n = 152)	Resistance	101 (66.4%)
			Sensitive	52 (33.6%)
Aminoglycosides	Gentamycin	NRST (n = 44)		
		RST (n = 115)	Resistance	36 (31.3%)
			Sensitive	79 (68.7%)
	Amikacin	NRST (n = 3)		
		RST (n = 156)	Resistance	13 (8.3%)
			Sensitive	143 (91.7%)
Carbapenems	Meropenem and imipenem	NRST (n= 0)		
		RST (n = 159)	Resistance	0 (0%)
			Sensitive	159 (100%)
Sulphonamides	Co-trimoxazole	NRST (n = 3)		
		RST (n = 156)	Resistance	113 (72.4%)
			Sensitive	43 (27.6%)
Others	Nitrofurantoin	NRST (n = 3)		
		RST (n = 156)	Resistance	13 (8.3%)
			Sensitive	143 (91.7%)

*RST: Requested sensitivity test; †NRST: Not requested sensitivity test

(72%), and ceftriaxone (72%), which renders them inefficient as empirical therapy against UTIs. The main reason for that is the irrational prescribing of these classes of drugs in different hospitals in Sudan [24–26]. However, in United States, due to the rational prescribing of antibiotics, the resistance rates to penicillin and cephalosporins were comparatively low [27].

Trimethoprim-sulfamethoxazole (co-trimoxazole) has been widely used for the treatment of UTIs, but our results showed high resistance (74.4%), this result is inconsistent with other studies [21, 27]. Among aminoglycosides, the observed resistance rate for gentamicin and amikacin were 32.2% and 8.8%, respectively, with a significant association with the kind of admission ($p < 0.05$). Similar results were observed in a hospital in Tamil Nadu, India, where gentamicin and amikacin resistance rates were 30.4% and 10.5%, respectively [19]. However, even with high sensitivities for these antibiotics, the utilization of aminoglycosides is low, due to their nephrotoxicity and ototoxicity [28]. On the other hand, fluoroquinolones, especially ciprofloxacin, have been the most frequently used antibiotic for UTIs in the recent past [29]. In the present study, *E. coli* strains were highly resistant (65.9%) to ciprofloxacin, this finding is concerning, as fluoroquinolones are frequently used empirically to treat UTIs, especially complicated infections. Interestingly, the resistance to nitrofurantoin was very low (10.6%) in comparison to other antibiotics, which suggest using this drug as the first-line option in the empirical treatment of uncomplicated cystitis and other lower UTIs. This low rate of resistance may be due to the limited use of nitrofurantoin in the last years. These findings were also observed worldwide [21, 30].

Among the carbapenems class of antibiotics, this study demonstrated there was only one resistant case for all tested isolates, as these drugs are restricted for severe infections. In contrast to another study done in a tertiary care hospital in India that showed relatively high resistance (43.3%) to carbapenems, these may have resulted due to misuse and overuse of this class in the hospital [31]. In addition, the current study showed a high rate (81.4%) of MDR of *E. coli* in comparison to another study done in the United States that showed only 7.1% of MDR [32]. A high occurrence of MDR could result from many factors including hospitalization, diabetes, chronic renal disease, and catheterization [33, 34].

Limitations

The limitations of the current study are: firstly, the cross-sectional design in one hospital may not allow generalization of the findings to all hospitals in Sudan. Secondly, many incomplete and missed data were also reported. Despite these limitations, this surveillance is essential, as it demonstrates the situation of the *E. coli* resistance to antibiotics which will help a lot in the proper selection of empirical therapy to treat UTIs. However, prospective studies are urgently needed in other Sudanese Hospitals in order to determine the resistance and sensitivity patterns for *E. coli* and microorganisms.

5. Conclusion

The uropathogenic *E.coli* are highly resistant to the majority of antibiotics commonly used in the clinical practice in inpatients and outpatients. The *E. coli* resistance rate was observed to be high for ampicillin, combination B-lactamase inhibitor (amoxicillin/clavulanic acid), and cephalosporin (cefuroxime, ceftazidime, and ceftriaxone), fluoroquinolones, and co-trimoxazole. However, *E. coli* showed lower resistance to nitrofurantoin, amikacin, and carbapenems; this can be reserved for empirical treatment of UTIs. According to our findings, we recommend using nitrofurantoin as an empirical therapy for the treatment of lower UTIs.

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Ethical Considerations

The ethical clearance was obtained from the Ethical Committee of the Faculty of Pharmacy, University of Khartoum. Additional approval was taken from the administration of Soba University Hospital and the Department of Microbiology in the hospital before starting data collection. All collected data were coded while ensuring confidentiality throughout the study.

Competing Interests

There are no conflicts of interest.

Availability of Data and Material

All relevant data of this study are available to any interested researchers upon reasonable request to the corresponding author.

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