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Antibiotics susceptibility profile of *Escherichia coli* isolated from patients with urinary tract infection in Misan, Iraq

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Abstract

Background: Urinary tract Infection is one of the most frequently diagnosed infections among inpatients and outpatients with an annual incidence of 150 million cases. The aim of current study was to determine the distribution and antimicrobial susceptibility of *Escherichia coli* isolated from inpatients with urinary tract infections.

Methods: Over the period from February/ 2017 to January/ 2018, a total of 110 urine samples were collected from inpatients.

Results: *E.coli* was spotted in approximately two thirds of the specimens and very high resistance rates were found among the isolates. Antibiotic resistance rates ranged from 100% for ampicillin to 0% for imipenem. All of the isolates showed resistance to multiple antibiotics. In conclusion: UTI treatment guidelines may need to be modified based on the local antimicrobial susceptibility data reported in this study.

Keywords: Antibiotic resistance, *Escherichia coli*, Multi-drug resistance, Urinary Tract Infection, Imipenem.

INTRODUCTION

Urinary tract infection (UTI) is defined as urinary system infection involving either the upper or lower urinary tracts or both [1]. UTI is one of the most frequently diagnosed infections among patients of different age groups and it has been reported to be the second most common infection worldwide in hospital practices [2, 3]. In each year throughout the world, about 150 million people develop UTI [4].

Among the main causative bacteria of UTI is *Escherichia coli*, which is responsible for 70-80% of cases [4, 5]. Other Gram-negative bacteria, such as *Proteus mirabilis* and *Klebsiella* species, also can cause UTI, but less frequently than E. coli. On the other hand, Gram-positive bacteria, such as *Staphylococcus aureus* and *Enterococci*, might also be a cause for UTI, but with less incidence [6-8].

One of the most serious health-related problems in the era of infectious diseases is antibiotics resistance [9]. UTI, in most of the cases as other infectious diseases, is treated empirically with antibiotics based on the predictable causative bacteria before obtaining the results of culture and sensitivity [10]. Additionally, one of the most common indications for prescription of antibiotics is UTI[1]. Consequently, such an overuse of antimicrobial drugs had led to the development of resistance to antibiotics and the appearance of multi-drug resistant (MDR; resistance to 3 or more antibiotics) species which in turn increased the health-related costs and morbidity rates worldwide [1, 11].

Antimicrobial resistance among patients with UTI is increasing and it is variable in different geographical locations [11]. Several studies have been conducted to determine the patterns of antibiotic resistance among *E.coli* isolates in different countries and at different times and all these studies have shown variable resistance trends [6, 7, 9, 10, 12-14]. Therefore, the aim of this research was to study antibiotic sensitivity profile among patients with UTIs from Al-Sadder Teaching Hospital at Misan city, Southern Iraq.

MATERIALS AND METHODS

Study design

A retrospective study conducted from February, 2017 to January, 2018 at Al-Sadder Teaching Hospital, Misan city, Southern Iraq.

Urine samples culture and identification

All urine specimens were collected by midstream clean-catch catheterization or from urine bags. These samples were processed on blood agar and MacConkey media with a standard loop and were incubated at 37 °C for 24-48 hr. Significant growth was determined as ≥105 colony-forming units (CFU)/mL of midstream urine and urine bag samples, and ≥102 CFU/mL of a catheter specimen. Isolates were identified by Gram staining and conventional biochemical methods [15].

Antibiotic susceptibility testing

Antibiotic susceptibility tests were done on Mueller-Hinton agar using disk diffusion method as described by Bauer [16]. Antibiotic discs used in current study and their concentrations are shown in Table (1).

RESULTS

A total of one hundred and ten specimens were collected over the study period and investigated for the isolation of etiologic bacteria and then antimicrobial susceptibility test was done on E.coli isolates. As shown in Table (2), E.coli was identified in eighty one samples (73.6 %) while in the remaining 29 samples (26.3 %) other bacteria were spotted. In addition, Table (3) shows that all isolated E.coli were subjected to antimicrobial sensitivity testing to expose the pattern of resistance among these isolates. All of the isolated uropathogenic E.coli were shown to be resistant to ampicillin (100%) while no resistance was detected for imipenem. Other penicillins tested in this study were augmentin and piperacillin with resistant rates of 83.9 % and 51.8%, respectively. On the other hand, cephalosporins also included in the study and the results shown that 34.5 % of isolates were resistant to ceftriaxone, 91.3 % were resistant to cefazoline, 1.2% were resistant to cefoxitin, 38.2% were resistant to cefepime and 62.9% were resistant to cefixime. Additionally, some of the quinolones and aminoglycosides also tested and the results were as follows; 17.2%, 25.9% and 23.4% of isolates showed resistance to norfloxacin, nalidixic acid and ciprofloxacin, respectively. The resistance rates to amikacin, tobramycin, gentamicin, and kanamycin were 11.1%, 30.8%, 11.1% and 45.6% respectively. Furthermore, 19.7% of isolates were resistant to aztreonam, 13.6% resistant to chloramphenicol, 23.4% resistant to cotrimoxazol and 79% resistant to nitrofurantoin.

Regarding the MDR isolates, all of E.coli isolates collected for this study showed resistance to four or more antibiotics. As shown in table (4), twelve isolates were resistant to four different antibiotics, eighteen isolates were resistant to five antibiotics, nine isolates were resistant to six antibiotics and nine isolates were resistant to seven antibiotics. The remaining thirty three isolates showed resistance to eight or more antibiotics as described with details in Table (4) and Figure (1).

DISCUSSION

The present study provides useful information to the health-care professionals about the main cause and antibiotics sensitivity profile in patients with UTI. A large pool of studies had been published about UTI and the trends of antibiotics resistance

among the most frequently encountered uropathogens [3, 6, 9, 12]. E.coli has been reported to be the uropathogen responsible for 70-80% of UTI[17] which is in accordance with the result of the present study.

Antibiotics resistance has been reported since the beginning of using these agents for treating infections and it is a growing problem around the world [18, 19]. Here, the results of the study showed a very high resistance rate among E.coli isolated from urinary tract infected patients. The highest resistance was to ampicillin (100%). Similarly, other studies have also reported high resistant rate to ampicillin [9, 12]. All bacteria, particularly the Gram-negative species, can easily develop resistance to multiple antibiotics [20]. Additionally, Gram-negative bacteria can have several resistance mechanisms to antimicrobial agents. One of these mechanisms is the production of Extended-Spectrum Beta Lactamases (ESBL) that makes the bacteria resistant to beta lactam antibiotics and also prone to developing resistance to other antibiotic classes, including quinolones, aminoglycosides and cotrimoxazole [21]. Accordingly, the findings of resistance to other antibiotics was expected in this study, where the results showed the following resistance rates; Aztreonam (19.7%), augmentin (83.9%), ceftriaxone (34.5%), cefazoline (91.3%), piperacillin (51.8%), cefixime(38.2%), cefixime (62.9%), cotrimoxazole(23.4%), ciprofloxacin (25.9%), norfloxacin (17.2%), nalidixic acid (23.4%), gentamicin (11.1%), amikacin(11.1%), tobramycin (30.8%), and kanamycin (45.6%). Based on cotrimoxazole resistance reported here, it should no longer be recommended for empiric therapy of UTI [22]. Resistance to nitrofurantoin was found in 79% of the isolates which contradicts other studies [4, 11]. According to the American infectious disease society, bacterial resistance rates exceeding 10% has been set as the cut-off at which antibiotic is no longer recommended for empirical therapy[23]. Based on this, most of the abovementioned antibiotics are no longer recommended for empirical UTI therapy in our city. All of E.coli isolates were susceptible to imipenem which agrees other studies [24]. The contradictions or agreements of the current study results may be due to the fact that antimicrobial sensitivity may vary from patient to patient and from country to country [4].

Table (1) Antibiotic discs

Antibiotics	Concentration	Antibiotics	Concentration	Antibiotics	Concentration
Ampicillin	10 µg	Imipenem	10 µg	Cefoxitin	30 µg
Augmentin	10 µg	Cefazoline	30 µg	Piperacillin	100 µg
Aztreonam	30 µg	Nalidixic acid	30 µg	Nitrofurantoin	30 µg
Norfloxacin	10 µg	Ciprofloxacin	5 µg	Cefepime	30 µg
Ceftriaxone	30 µg	Chloramphenicol	30 µg	Cefixime	30 µg
Amikacin	10 µg	Gentamicin	10 µg	Kanamycin	30 µg
Tobramycin	10 µg	Co-trimoxazol	25 µg		

Table (2) Frequency of E.coli and other bacteria as a cause of UTI

Number of samples	E. coli		Others	
110	Number	Percent	Number	Percent
	81	73.6	29	26.3

Table (3) Susceptibility of clinical isolates of E.coli to 20 different antibiotics

Antibiotic	Resistant		Intermediate		Sensitive	
	Number	Percent	Number	Percent	Number	Percent
Ampicillin (AM)	81	100	0	0	0	0
Aztreonam (ATM)	16	19.7	12	14.8	53	65.4
Augmentin (AMC)	68	83.9	13	16	0	0
Norfloxacin (NOR)	14	17.2	0	0	67	82.7
Ceftriaxone (CRO)	28	34.5	5	6.2	48	59.2
Amikacin (AK)	9	11.1	14	17.2	58	71.6
Cefazoline (CZ)	74	91.3	7	8.6	0	0
Nalidixic acid (NA)	19	23.4	3	3.7	59	72.8
Chloramphenicol (C)	11	13.6	2	2.4	68	83.9
Imipenem (IPM)	0	0	2	2.4	79	97.5
Ciprofloxacin (CIP)	21	25.9	1	1.2	59	72.8
Nitrofurantoin (F)	64	79	9	11.1	8	9.8
Co-trimoxazol (COT)	19	23.4	17	20.9	45	55.6
Cefoxitin (FOX)	1	1.2	15	18.5	65	80.2
Piperacillin (PRL)	42	51.8	14	17.3	25	30.8
Tobramycin (TOB)	25	30.8	12	14.8	44	54.3
Gentamicin (CN)	9	11.1	12	14.8	60	74
Cefepime (FEP)	31	38.2	11	13.6	39	48.1
Cefixime (CEF)	51	62.9	9	11.1	21	25.9
Kanamycin (K)	37	45.6	32	39.5	12	14.8

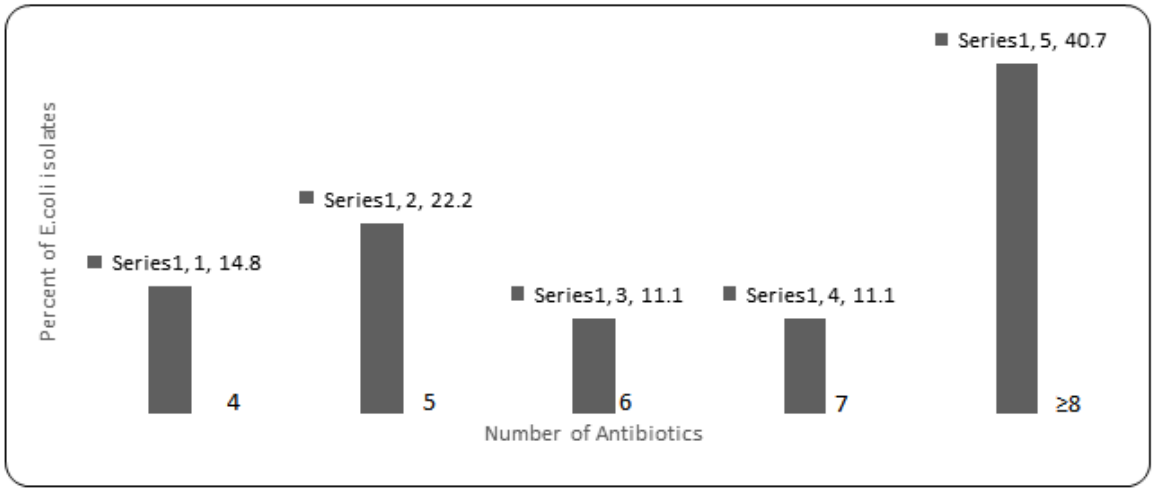

Figure (1) Multidrug resistance rates among *E.coli* isolates.

Table (4) Antibiogram patterns of MDR isolates

Number of Antibiotics	Number of Isolates	Patterns of Antibiotic Resistance
4	6	AM, AMC, CZ, F
4	2	AM, AMC, CZ, K
4	4	AM, AMC, K, F
5	5	AM, AMC, CZ, K, F
5	3	AM, AMC, CZ, F, CEF
5	2	AM, AMC, CZ, K, PRL
5	2	AM, AMC, CZ, F, TOB
5	3	AM, AMC, CZ, F, PRL
5	3	AM, AMC, C, FEP, CN
6	1	AM, AMC, CZ, K, F, TOB
6	1	AM, AMC, CZ, F, PRL, TOB
6	2	AM, AMC, CZ, F, PRL, CEF
6	2	AM, CZ, CRO, PRL, FEP, CEF
6	3	AM, CZ, AK, K, F, CEF
7	2	AM, CZ, CRO, NA, PRL, FEP, CEF
7	1	AM, CZ, K, CIP, F, PRL, CEF
7	1	AM, AMC, CZ, CRO, F, PRL, FEP
7	2	AM, CZ, K, F, CIP, PRL, CEF
7	1	AM, AMC, CZ, F, PRL, CN, CEF
7	2	AM, AMC, CZ, F, PRL, TOB, CEF
8	1	AM, AMC, CZ, CRO, NA, FOX, FEP, CEF
8	1	AM, AMC, CZ, C, K, F, COT, CEF
8	1	AM, AMC, CZ, F, PRL, FEP, CEF, COT
8	1	AM, AMC, CZ, CRO, PRL, TOB, FEP, CEF
9	4	AM, AMC, CZ, F, CIP, PRL, TOB, CEF, C
9	3	AM, CZ, K, F, NA, PRL, TOB, FEP, CEF
9	3	AM, AMC, CZ, CRO, AK, F, PRL, FEP, CEF
10	2	AM, AMC, CZ, CRO, K, F, PRL, FEP, CEF, ATM
10	2	AM, AMC, CZ, CRO, K, F, COT, PRL, TOB, CEF
11	3	AM, AMC, CZ, CRO, F, NOR, NA, CIP, COT, CEF, ATM
12	2	AM, AMC, CZ, CRO, F, NOR, PRL, CIP, COT, CEF, FEP, ATM
13	1	AM, AMC, CZ, CRO, F, NOR, NA, CIP, COT, CEF, PRL, FEP, ATM
14	3	AM, AMC, CZ, CRO, K, F, NOR, NA, CIP, COT, CEF, TOB, FEP, ATM
14	1	AM, AMC, CZ, F, NA, K, AK, COT, PRL, TOB, FEP, CN, CEF, ATM
15	2	AM, AMC, CZ, CRO, K, NOR, NA, CIP, CN, COT, CEF, TOB, FEP, PRL, ATM
15	1	AM, AMC, CZ, CRO, K, F, NOR, NA, CIP, C, COT, CEF, TOB, FEP, PRL
16	2	AM, AMC, CZ, CRO, K, NOR, NA, AK, CN, COT, CEF, CIP, TOB, FEP, ATM, C

Regarding multiple-antibiotic resistance, all E.coli isolates investigated in current study showed resistance to four or more antibiotics. This can partly be explained by the fact that genes for antibiotics resistance can be carried on the same plasmid where studies have shown that quinolones resistance genes have the ability to transfer on the same plasmid used by ESBL genes [25]. In most of the isolates, co-resistance to quinolones and beta-lactam antibiotics had been found which might be in accordance with the findings of [13], however, this needs to be confirmed by further local polymerase chain reaction studies which is one of the limitations in this study. Additionally, E.coli is one of the bacteria that are known of rapidly developing resistance to antibiotics [26]. Some studies had suggested that physicians' prescription habits can also be a factor in increasing resistance to some antibiotics [26, 27]. Using antibiotics without prescription has been postulated as one of the causes of reducing bacterial sensitivity to the antibiotics [28] and in Iraq antibiotics can be easily obtained without prescription. All of the previous factors might be responsible for such high prevalence of resistance.

CONCLUSIONS

To our knowledge, this is the first study investigating E.coli resistance trends in UTI patients over the specified period mentioned above in Misan, Southern Iraq. The findings of current study opens the gate for a pool of antibiotic-related problems and warrants the urgent need for further efforts to perform nationwide multi-center study to update the local antibiogram profiles and the infectious disease treatment guidelines. Further studies are recommended to test all antibiotics that can be used for treating UTI and to genetically determine the distribution of E. coli strains. Imipenem, with 100% sensitivity rate, is the most effective antibiotic for empiric therapy of UTI according to the current findings. Last, but not least, all healthcare professionals must pay attention to this study and strictly adhere to the culture and sensitivity results and the international guidelines to minimize further MDR development, cost-related and health-related consequences.

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Conflict of Interest: None to declare.

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