

In Vitro Antibiotic-Sensitivity of Uro-Pathogenic Escherichia Coli (UPEC) Amongst Outpatient with Community-Acquired UTIs. A CrossSectional Study from Babylon Province.

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Abstract

Background: Urinary tract infections (UTIs) are the most common bacteriological infection that causes a significant illness and health burden all over the world. Escherichia coli (E. coli) is Gramnegative bacteria that has many serotypes. Only a limited serotype is in charge of infections, namely uropathogenic E. coli (UPEC). Antibiotic resistance (AR) is a big problem of great concern globally. The study aimed to evaluate the AR of UPEC among outpatient with community-acquired UTIs from Babylon Materials and methods: This study was a cross-sectional in vitro study carried out to evaluate the AR of UPEC among outpatient with community-acquired UTI. A total number of 247 outpatients (193 male) aging 41 ± 3.5 years, had been chosen randomly. The clinical presentation and the urinary signs and symptoms had recorded, and urine samples had collected for urinalysis and culture/sensitivity tests. **Results:** Out of the 247 patients studied, 180 undergo UCs. Those who have exhibited to have culturepositive urine samples were 98 patients. Out of the positive samples, 56-samples were positive for UPEC. Accordingly, the prevalence of UPEC culture-positive samples were 57.1% for E. coli. The remaining 42.9% of the total 89-samples, had revealed other types of bacteria. The sensitivity tests exposed that the E. coli resisting ABs like Nitrofurantoin, Cefazidime, and Ceftriaxone, ten-times more than other ABs like Amikacin, Ampicillin, and Imipenem. **Conclusions:** Among community-acquired patients with UTIs, UPEC signifies the commonest uropathogens isolated from urinary isolates. The AR of UPEC had steadily increased for ABs that frequently prescribed. Accordingly, the familiarity of AR among uropathogens is crucial to deliver proper cost-effective treatment

Keywords: Escherichia coli, urinary tract infection, uropathogens, and antibiotic sensitivity.

1. Introduction

Urinary tract infections (UTIs) are a most-common bacteriological infection that causes a significant illness and health burden all over the world [1]. Its assessed incidence reaches around 150 million new cases yearly [2]. It is well-known that UTI is principally a female disorder, owing to functional and anatomical variations [3]. Nevertheless, beyond the fifth decade of life, the incidence of UTI much increased among male owed to prostatic enlargement [3, 4].

The available evidence points to the fact that most UTIs are due to a single bacterial etiology that mainly existed in the gut and seldom caused by other microbes like virus or fungus [5]. Escherichia coli (E. coli) is one several Gram-negative bacteria that has various serotypes. Only a limited serotype is in charge of infections, namely uropathogenic E. coli (UPEC) [6].

There is overwhelming evidence corroborating the notion that aging had been linked with a higher vulnerability to the UTI owing to altered urethrovaginal vegetation and reduced estrogen levels from

menopausal females [7, 8].

There is a rapidly growing literature on UTI, which indicates increased UTI frequency and severity among diabetic patients due to glucosuria that enhances bacterial overgrowth and weakens leukocytes activities [9]. Of note, any obstruction to the urinary stream at any anatomic step produced by stone or any other obstacle is a crucial factor for increased vulnerability to UTI [10]. Furthermore, urinary catheterization may raise the risk of UTIs and be related to bacterial overgrowth [11].

The consensus view seems that bactericidal ABs to be are superior to bacteriostatic ABs in the treatment of recurrent infections [12]. Although some alternatives to the ABs for treating UTI, had been advised, still, the ABs are a very effective strategy for treating bacterial UTIs [13]. The incidence of antibiotic resistance (AR) arises principally from the uninhibited bacterial nature, since liable bacteria may attain AR genes from plasmids and additional horizontally transported genomic substances, ensuing in progression by leaps [14, 15].

Aim of the study

The study aimed to estimate the AR of UPEC among

outpatients with community-acquired UTIs from Babylon.

Methodology and Patients

Patients selection

This in vitro study, is a cross-sectional had conducted at a urology consultation clinic at Al-sadiq hospital in Babylon, the middle of Iraq. A total number of 247 outpatients (193 male), aging 22.5-86.7 years and randomly chosen that had been medically inspected and identified by nephrologists for manifestations of community-acquired UTI. An informed ethical-consent had attained from the local committee for research ethics. All applicants were not on prior antibiotics (ABs) and had the clinical manifestations of UTI with positive urine culture (UC) for E. coli. They were 56 patients out of the 247, the rest of the patient had excluded due to their negative UCs or for one of the following risk factors: diabetes mellitus, prostatic enlargement, pregnancy, recurrent UTI, congenital anomalies or catheterization of the urinary system, and elderly. The patients that had cultures negative for E. coli and positive for other bacterial spp. had excepted from this work (42 patients). All participants gave an oral permission to contribute to the study protocol.

Urine sampling and culturing

A mid-stream sample of urine for urinalysis had collected from all the participants, then examined according to the standard protocol [16, 17]. Antimicrobial sensitivity test had finalized according to the "clinical and laboratory standards institute (CLSI)" guidelines [18].

Antibacterial susceptibility test

The susceptibility test of the antibacterial agents had performed by "disc-diffusion technique" for ten antibiotics based on Bauer & Kirby [19].

Statistical analyses

All the patients' records had documented, processed, transformed into Microsoft Excel sheets, and scrutinized by means of SPSS-25 IBM software package.

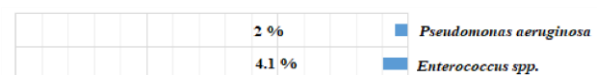
2. Results

The characteristics of all studied patients with UTI had presented in table-1. The mean of included patients was 38±7.3 years with a range of (25-65 years), 42 of them were females. A total of 180 UC had performed out of 247 total patients enrolled in the study. Those with negative UC had excluded from the study (82 patients) and 42 patients showed positive UC of other bacteria. Consequently, only 56 patients had included in this study for the detection of AR. The most common complaint was frequency, followed by dysuria, abdominal or flanks cramps, urgency, nausea/vomiting, fever, and diarrhea. The patients with any risk factors for UTI in terms of DM, older age, recurrent UTI, pregnancy, urinary catheterization, and prostatic enlargements had excluded also.

Table-1: characteristics of all studied patients with urinary tract infections

Total patients (247)	Number (%)	Included by the study (98) (% N)	Excluded from the study (149) (% N)
Age/years	35±41 (86.7-22.5)	73±38 (65-25)	
Escherichia			
Sex of the patients			
Males	(78) 193	coli positive (21.5) 12	Negative 82 (55)
Females	54 (22)	culture 56 (57.1)	(78.5) 42
Urine culture	180 (72.9)	Other bacteria, culture positive urine 42 (42.9)	
Signs and symptoms			
Frequency	(73.3) 18		
Dysuria	(73.3) 18		
Abdominal or flanks cramps	(66.7) 17		
Urgency	(53.3) 13		
Nausea/vomiting	(46.6) 12		
Fever	(46.7) 12		
Diarrhea	(20) 49		
Risk factors for UTI			
Diabetes mellitus	(16.2) 40		(26.8) 40
Elderly	(3.3) 8		(5.4) 8
Pregnancy	(0.8) 2		(1.3) 2
Prostate enlargement	(1.6) 4		(2.7) 4
Recurrent UTI	(44.9) 12		(8.1) 12
Urine catheter	(0.4) 1		(0.7) 1

Uropathogenic spreading among studied UTI patients figure-1 shows the spread of uropathogenic bacteria for UTI and their frequency in percentage after the results of UC. The commonest was E. coli, which represents 57.1% out of all positive UCs, followed by Staphylococcus aureus and other Staphylococcus spp., then both hemolytic Streptococcus and Klebsiela spp. equally, then Proteus spp. and Enterococci spp. equally, besides finally the Pseudomonas [12.2%, 8.1%, 6.2%, 4.1%, and 2%]



one-to-one.

Analysis of Antibiotic susceptibility test among UPEC infected patients

Based on the width of the inhibition-zone encircled the AB disc in the present study, E. coli has a widespread variety rang of AR against the different ABs. The highest resistance displayed against Nitrofurantoin (35.7%) followed by (28.6%) for each of Cefazidime and Ceftriaxone, (25%) for both Amoxycillin/Clavulanic acid and Ciprofloxacin. While (21.4%, 20%, and 10.7%) had been reported against Gentamicin, Trimethoprim-Sulfamethoxazole, and Amikacin, respectively. Meanwhile, the lowest resistance (3.6%) had found against each of Imipenem and Ampicillin. These outcomes indicated that E. coli isolated from urine samples have evident sensitivity for Imipenem & Ampicillin while lowest sensitivity for Nitrofurantoin (table 2).

Table 2: The percentages of antibiotic resistance(AR) in E. coli isolates from outpatients with UTI in the current study (N=56 isolates)

Antibiotic	Concentration	≤14	15-16	≥17	Total (%)
Nitrofurantoin	mcg 300				40 (35.7)
Cefazidime	mcg 30	≤14	15-17	≥18	32 (28.6)
Ceftriaxone	mcg 30	≤13	14-19	≥21	32 (28.6)
Amoxycillin/Clavulanic acid	mcg 10/20	≤13	14-17	≥18	28 (25)
Ciprofloxacin	mcg 5	≤15	16-20	≥21	28 (25)
Gentamicin	mcg 10	≤11	12-15	≥16	24 (21.4)
Trimethoprim-Sulfamethoxazol	mcg 23.8/1.25	≤14	11-15	≥16	22 (20)
Amikacin	mcg 30	≤13	14-17	≥18	12 (10.7)
Ampicilline	mcg 10	≤16	-	≥17	4 (3.6)
Imipenem	mcg 10	≤13	14-15	≥16	4 (3.6)

Examination of urine samples

Table-3 exhibited the variation of some findings detected by general urine examination in patients with UPEC urine infections compared with the normal levels. The data revealed an increment of the number of cellular blood elements (leukocytes and RBCs) detected in the urine (100% and 20%), respectively. Likewise, a similar 100%

increase of detectable bacteria per high power field examinations of the infected urine samples. Other urinary parameters showed minor and relative changes from the normal levels.

Table-3: Variation in the findings detected by general urine examination of 56 patients infected by Escherichia coli

Finding of general urine examination	Percentage of variation of patients from the normal finding
Number of leukocytes (pus cells) /HPF	%100
Bacteria /HPF	%100
Number of Red blood cells /HPF	%20
pH of the urine	%0.5
Amorphous	%2.5
Mucous	%5.
Color	%2.5
Albumin	2.5
Urobilinogen	%1
Bilirubin	%2
Specific gravity	%3.5
Others (casts, Crystals, uric acid, ketones, nitrates, glucose)	%1.5

3. Discussion

Universal transmission of AR amongst uropathogens triggering UTIs is alarming. This work reported the etiological bacteria of community-acquired UTI and antibiotic sensitivity of uropathogens isolated from outpatients in Babylon, the middle of Iraq. In the current study, a positive UC for UPEC had revealed. Our outcomes are relatively comparable to what had reported in more than a few other revisions [1, 20]. The subsequent most common uropathogens isolated in this work is the Staphylococcus aureus. The latter finding looks like that of a previous Iraqi study conducted in Diwaniya province [21]. The high proportion of Staphylococcus spp. as a causative agent for UTIs as it is the foremost organism that causes dermatological infection and can easily contaminate the urinary tract to cause UTI [22]. In our study, the fourth bacterial isolates from the urine, were Hemolytic streptococci (6.1%). It was more than (1.8% that is reported by Alós JI et al. study [23]. As well, the Proteus spp. had represented (4.1%), which looks a lot like the findings reported by Schaffer JN. et al. at 2013 [24]. Nevertheless, other uropathogens, including Enterococcus spp. and Pseudomonas aeruginosa signified (4.1% and 2%), respectively, which dislike the percentages from other works (14% and 3.4%) for Enterococci spp. and Pseudomonas aeruginosa, respectively [25]. These disparities might cause by different demographics and medications used among different societies that predominate some pathogens more than others.

A closer look at the data indicates that a high ratio of E. coli exhibited by females (78.5 %), although in males was (21.5 %). This ratio was unlike the outcome of other research [26], which may be due to differences in the marital age, the parity, contraceptive types, and educative health care services among the societies. The oral contraception consumption has as well augmented

the risks of infections, which might be related with the alerted vaginal microflora that promotes bacterial growth and ensuing infection [27].

The clinical presentation of the patients in this study revealed that the characteristic symptoms of lower UTI [28] had great prevalence rates. Then again, the manifestations of upper UTI [29] had presented with lower prevalence rates, which was similar to several other studies [26, 30].

Several risk factors for UTI with a higher proportion found in this study is undoubted, because the Iraqi affected patients do not ask medical consultation till the illness become problematic and affect their natural wellbeing, exclusively the aging groups who are somewhat accompanying more physical illness.

The variation in the urinalysis parameters reflects the presence of bacteriuria in patients with UTI. The presence of RBCs may specify the presence of urinary stones that evoke hemorrhage from the urinary tracts [31].

There have been studies that show lower rates of nitrofurantoin ranging from 0.5% to 35.7% in six European countries, including Russia, Iran, the USA, and Canada [25, 32, 34]. These outcomes appear to be much lower than what had confirmed by this study (35.7%). This wide discrepancy among the contemporary work and other reports may be owing to higher ABs usage rate in Iraqi society, which had recognized as robust risk factors for AR, particularly nitrofurantoin [35].

One of the additional ABs experienced in this study was ceftriaxone which also displayed a high AR rate (28.6%) compared with reports of other researchers which were ranging from (2.3% to 42.8%) [36, 37]. The dissimilarity in this issue was anticipated and may be a consequence of unwarranted ABs misuse, predominantly to ceftriaxone, which is used in great extents in base inpatients and outpatient levels.

For Amoxicillin/Clavulanic acid with Ciprofloxacin, the AR displayed in this study was 25%, which is differ from other studies from Venezuela [38] for Ciprofloxacin (79.66%) and (5.1%) for Amoxicillin/Clavulanic acid [39] from a Turkish study. The last results vary from the Iraqi study, possibly owing to the much usage of these two medicines as proposed empirical UTI therapy.

The current data showed that Gentamicin and Trimethoprim-sulfamethoxazole (TMP/SMX), have AR of (21.4% and 20%), respectively. Nevertheless, other researchers found a different value, which was ranging from (0% and 76.4%) for gentamicin [40, 41], and TMP-SMX [42, 43] were (14.2 and 20%). The higher AR of TMP-SMX had also observed among urinary' isolates from outpatient with E. coli in the USA, were the AR rates had ranged from 15% up to more than 40% in different regions of the USA and Canada [44].

The Amikacin resistance in our study was (10.7%), which is higher than what had reported (2%) by a Turkish survey [45], which might be attributed to the constraint use of Amikacin for management of UTI.

To finish, both Ampicillin and Imipenem revealed an AR in 3.6% of the cases, which had considered very low if compared with the results found in other studies, where

the AR was 42% for Ampicillin [46]. The high variation of AR among the two works might cause by the limited use of Ampicillin as a treatment for UTI in Iraq in the current era and consequently reduced AR. Of note, another study had exposed 100% sensitivity of Imipenem to UPEC [47]. The clarification for this result may be due to the irrational prescription of Imipenem in Iraq [23].

4. Conclusion

Among community-acquired patients with UTIs, UPEC signifies the commonest uropathogens isolated from urinary samples. The AR of UPEC had steadily increased for ABs that frequently prescribed. Accordingly, the familiarity of AR among uropathogens is crucial to deliver proper cost-effective treatment.

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