An Epidemiological and Multidrug Resistance Study for *E. coli* Isolated from Urinary Tract Infection (Three Years of Study)

Mahde S. Assafi[1]   **Fawwaz F. Ali [2*]**   **Reem Fouad Polis[3]**
Nisreen Jawad Sabaly[4]   **Sozan Muhsin Qarani[5]**

[1]Department of Biology, College of Sciences, University of Duhok, Duhok, Iraq.
[2]Department of Animal Production, Northern Technical University, Mosul, Iraq.
[3]Department of Biology, Faculty of Science, University of Zakho.
[4]Zakho Emergency Hospital, Zakho, Iraq.
[5]University of Hawler, College ofDentistry, Erbil, Iraq
[*]Corresponding author: mahde.assafi@uod.ac. fawwaz@ntu.edu.iq*, biologyr84@yahoo.com, nisreen.jawad@gmail.com , suzan.qarany@hmu.edu.krd
[*]ORCID ID: https://orcid.org/0000-0002-4863-282X, https://orcid.org/0000-0003-1005-3694 *, https://orcid.org/0000-0002-6318-3831 , https://orcid.org/0000-0002-9871-9667 , https://orcid.org/0000-0001-7645-8315.

Abstract:

Uropathogenic *E. coli* (UPEC) is problematic and still the leading cause of urinary tract infections worldwide. It is developed resistance against most antibiotics. The investigation, surveillance system, and efficient strategy will facilitate selecting an appropriate treatment that could control the bacterial distribution. The present study aims to investigate the epidemiology and associated risk factors of uropathogenic *E. coli* and to study their antibiotic resistance patterns. 1585 midstream urine specimens were collected from symptomatic urinary tract infections (UTI) patients (225 males and 1360 females) admitted to Zakho emergency hospital, Zakho, Kurdistan Region, Iraq from January 2016 until the end of December 2018. Specimens were inoculated on blood and MacConkey plates and incubated at 37°C for 24 hours. Uropathogenic *E. coli* was diagnosed based on gram staining, colony characteristics, and standard biochemical tests in accordance with local standards and guidelines. All isolates were screened for their antibiogram pattern using the disk diffusion method based on the Clinical and Laboratory Standards Institute guidelines. The results showed that out of 1585 urine specimens, 1026 (64.7%) were UTIs positive with a statistically higher rate in 2016 (83.6%) (*P*< 0.0001). The UTIs frequency in females was significantly higher than males (*P*< 0.0001). Generally, the uropathogenic *E. coli* represented 21.1% with the highest level in 2016 (22.9%). The uropathogenic *E. coli* rate was higher, statistically not significant, in females (21.4%) than males (18.5%) (*P*=0.4946). Additionally, through the three years of study, uropathogenic *E. coli* (UPEC) was in high frequency in February and May 2016. The female's age group from 20 to 39 years was the most vulnerable (46%) form total infected females, while those from 70-74 years (1%) were the least susceptible in males and females. A high percentage (80.56 %) of multidrug resistance *E. coli* isolates was observed with high resistance against β-lactamase and macrolides antibiotics. However, higher sensitivity was towards imipenem and meropenem. In conclusion, the wrong and overuse of antibiotics will increase the resistance rate of *E. coli*. For this reason, proper use of available antibiotics is necessary. Also, the educational programs and periodic monitoring of antimicrobial susceptibility are essential for reducing the antibiotic resistance rate.

Introduction:

Escherichia coli (*E. coli*) is one of the main normal bacterial flora found in the intestinal lumen of humans and animals, and it is responsible for the most common diseases of the intestine and other organs. The infection caused by *E. coli* occurs by recruiting the bacterial virulence factors [1], such as bacterial capsule, fimbriae, flagella, iron scavenger receptors, lipopolysaccharide (LPS) and toxins that

disturb the host cellular process [2] Furthermore, all these factors are significantly associated with the disruption of the affectivity of the most used and known antibiotics used to treat uropathogenic *E. coli* (UPEC) infections [3]. Uropathogenic *E. coli* is linked with 70 to 95% of the urinary tract infections (UTI) worldwide [3, 4]. This bacterium can develop resistance against most discovered antibacterial therapy [5, 6]. Unfortunately, antibiotic resistance is remarkably increased among UTI patients suffering from UPEC infections [6]. Applying a robust surveillance system to investigate the antibiotic resistance bacteria could help to eliminate and/or control the antibiotic resistance bacteria [7]. Investigation of the ability of pathogenic bacteria to resist the current antibacterial treatments as well as their geographic distribution will facilitate choosing an appropriate treatment with the antibacterial drugs and design an efficient strategy to apply the antibiotic to control the bacterial infection [8]. This investigation is highly demanded, especially in areas or cities with the absence of control antibacterial prescription. Thus, the present research aims to study the epidemiology of UTI infections caused by uropathogenic *E. coli* and to investigate the antibiotic resistance among the *E. coli* isolated from UTI patients.

Materials and Methods:

This study was conducted in the microbiology laboratories at Zakho emergency hospital in Zakho city, Kurdistan Region, Iraq, from January 2016 until the end of December 2018. A total number of 1585 patients of both genders (225 males and 1360 females) were recruited (Table 1).

The patient's baseline data, such as gender, age (all ages were included) and the time of the year for the collected samples, were also recorded. All the included patients were symptomatic of UTI. Furthermore, frequency and percentages of UTIs and UPEC were evaluated along the three years of study as well as along the months of the indicated years of the study (2016, 2017, and 2018) (Table 1, Fig.1 and 2).

Table 1. Prevalence of UTIs and UPEC isolates among patients through the three years of study.

All participants[a]	Gender	2016	2017	2018	Total
	M	96	58	71	225
	F	521	403	436	1360
	Total	617	461	507	1585
UTI (%)[b]	M (%)	53 * (55.2)	23 (39.7)	32 (45.1)	108 * (48)
	F (%)	463 (88.9)	205 (50.9)	250 (57.3)	918 (67.5)
	Total (%)	516 (83.6)	228 (49.5)	282 (55.6)	1026 (64.7)
UPEC (%)[c]	M (%)	13 (24.5)	3 (13)	4 (12.5)	20 (18.5)
	F (%)	105 (22.7)	46 (22.4)	45 (18)	196 (21.4)
	Total (%)	118 (22.9)	49 (21.5)	49 (17.4)	216 (21.1)

M and F represent males and females, respectively. The differences between males and females were significant. *P* value < 0.00001. All other differences were not significant. [a] The total patients there were admitted over three years of study (2016, 2017 and 2018). [b] The UTI confirmed patients, the percentage values were calculated from the tottal admitted patients. [c] The UTI infection caused by UPEC, the percentage values were calculated from the UTI confirmed patients.
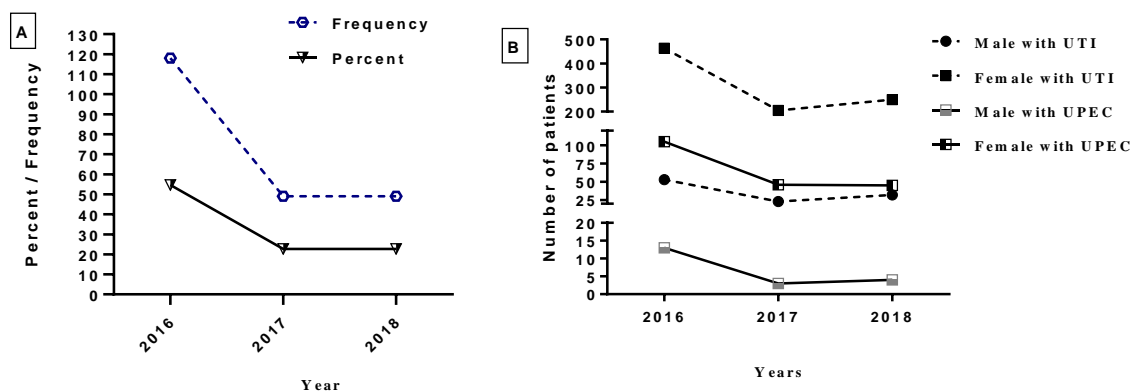

Figure 1. The prevalence of positive UPEC isolates (UTIs) through 2016, 2017, and 2018. A: the total confirmed positive UTIs with UPEC through the three years. B: the frequency of the overall UTIs infections and UPEC isolates (UTIS) infectiond spleted according to the gender of patients.
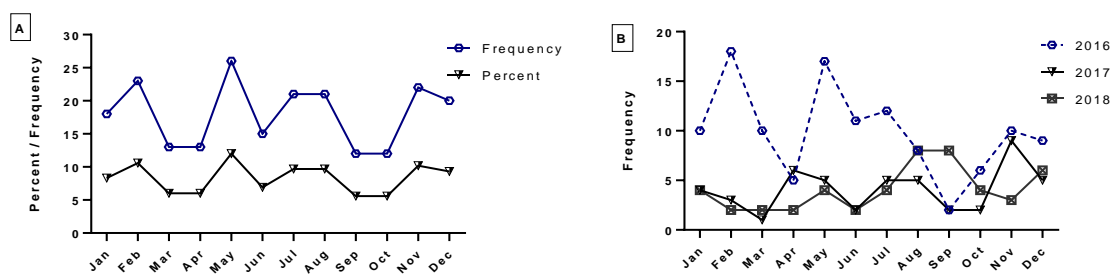
Figure 2. The monthly prevalence of positive UPEC isolates (UTIs). A: The monthly frequency and percentages of UPEC isolates from UTI of through three years of study, B: The monthly frequency of UPEC isolates from UTI in 2016, 2017 and 2018.

Specimens' collection

Urine specimens were collected from all UTI patients under sterile conditions. Clean catch midstream urine was obtained from the patients to avoid contamination. The collected specimens were directly sent to the microbiology laboratory, which inoculated them on blood and MacConkey plates and incubated at 37°C for 24 hours [9].

Isolation and identification of *E .coli*

The culture that yielded bacterial growth ($\geq 10^5$ colonies) was considered positive, and it was as microbiological evidence of a UTI. For identification, the bacterial colonies were classified by gram staining and then the bacteria were identified based on colony characteristics and standard biochemical tests including indole test,

methyl red test (M.R), Voges-Proskaur test (V.P), citrate utilization test, urease test. The identification of *E. coli* isolates was performed under local standards and guidelines [10].

Antimicrobial susceptibility test

All uropathogenic *E. coli* isolates were screened for their antibiogram pattern. The sensitivity to commonly used antimicrobial agents from different groups was determined. A range of antibiotics that belong to different classes were tested (Table 2). The susceptibility was investigated using the disk diffusion method on Mueller-Hinton agar. Each isolate was inoculated and incubated at 37°C for 24 hours. The results were recorded on the basis of Clinical and Laboratory Standards Institute (CLSI) guidelines 2015 [11].

Table 2. Antimicrobial sensitivity test results for isolated UPEC from urine spacemen.

Classes of Antibacterial drugs	Tested antibiotics (Disk content µg)	Antibiotic generations	Total analyzed specimens	Sensitivity n (%)	Resistance n (%)
B-lactamase	Ampicillin (10)	3rd	111	11 (9.91)	100 (90.09)
	Ampicillin/ Cloxacillin (10/10)	4th	64	2 (3.13)	62 (96.88)
	Cloxacillin (10)	2nd	22	1 (4.55)	21 (95.45)
	Amoxicillin (10)	3rd	45	5 (11.11)	40 (88.89)
	Amoxicillin Clavulanic acid (20/10)	4th	164	13 (7.93)	151 (92.07)
	Cephalothin (30)	1st	103	33 (32.04)	70 (67.96)
	Cephalexin (30)	2nd	28	2 (7.14)	26 (92.86)
	Ceftazidime (30)	3rd	71	9 (12.68)	62 (87.32)
	Ceftriaxone (30)	3rd	124	16 (12.90)	108 (87.10)
	Cefixime (30)	3rd	133	19 (14.29)	114 (85.71)
	Cefotaxime (30)	3rd	182	32 (17.58)	150 (82.42)
	Imipenem (10)	NCG	46	46 (100)	0 (0.00)
	Meropenem (10)	NCG	61	56 (91.80)	5 (8.20)
Tetracyclines	Tetracycline (30)	NCG	101	52 (51.49)	49 (48.51)
	Doxycycline (30)	2nd	95	37 (38.59)	58 (61.05)
Nitrofurans	Nitrofurantoin (300)	NCG	156	106 (67.95)	50 (32.05)
Fluoroquinolones	Nalidixic acid (30)	1st	167	25 (14.79)	142 (85.03)
	Norfloxacin (10)	2nd	50	24 (48.00)	26 (52.00)
	Ciprofloxacin (5)	2nd	149	78 (52.35)	17 (11.41)
	Ofloxacin (5)	2nd	36	10 (27.78)	26 (72.22)
Aminoglycosides	Gentamicin (10)	NCG	125	59 (47.20)	66 (52.80)
	Amikacin (30)	NCG	138	116 (84.06)	22 (15.94)
Rifamycins	Rifampicin (30)	NCG	37	12 (32.43)	25 (67.57)
Macrolide antibiotics	Erythromycin (15)	NCG	82	3 (3.66)	79 (96.34)
	Azithromycin (15)	2nd	113	32 (28.32)	81 (71.68)
	Clindamycin (2)	NCG	63	6 (9.52)	57 (90.48)
Others	Trimethoprim-Sulfamethoxazole (1.25/23.75)	NCG	82	29 (35.37)	53 (64.63)

NCG: No Classified Generation

Statistical analysis

All the recorded data were statistically analyzed using the SPSS and GraphPad prism 8. *P*-value of <0.05 was considered significant.

Ethics Statement

The scientific committee approved this research and method of attaining consent of the Department of Sciences, University of Zakho, Kurdistan, Iraq.

Results:

Uropathogenic *E. coli* (UPEC) were isolated from urine specimens among patients admitted to Zakho hospital, Kurdistan region, Iraq over three years of study (2016, 2017 and 2018). Among all 1585 participants through the period of study, UTIs were identified in 1026 (64.7%) patients (Table 1). The UTIs rate in 2016 (83.6%; 516/617) was higher and statistically significant ($P< 0.0001$) compared to those in the other years. The higher UTIs rate was significantly higher in females (88.9%) than males (55.2%) ($P< 0.0001$).

The prevalence of UPEC isolates from overall UTI patients admitted to the hospital during the three years was 21.1% (216/1026) with a higher level in 2016 (22.9%;118/516) than those of 2017 (21.5%; 49/228) and those of 2018 (17.4%; 49/282) (Table 1, Fig. 1). The difference between these three years was statistically insignificant ($P=0.1879$). Regarding gender, through the years, the %UPEC was insignificantly higher in females (196/918, 21.4%) compared to those of males (20/108, 18.5%) through 2017-2018 ($P=0.4946$). However, in 2016, the %UPEC was highest in males (13/53, 24.5%) compared to those of females (105/463, 22.7%) ($P=0.7612$).

By distributing the number of patients diagnosed with UTI infection caused by *E. coli,* as observed in Fig. 2, the results showed an apparent increase in the frequency of isolates in May and November (12% and 10%, respectively) of overall years of study (2016, 2017 and 2018). However, there were an obvious increase in frequency in February and May in 2016. The incidence of UPEC infection was also analyzed depending on the age group of the patients among all confirmed *E. coli* positive isolates. The prevalence of disease was shown to be increased from age five years and younger to reach the highest percentage of infection between 20 to 39 years old (98 patients, 47%), while the frequency of *E. coli* infection was decreased dramatically from patients aged 40 years and older to reach the lowest incidence in elderly patients70-74 years (2, 1%) (Fig. 3).
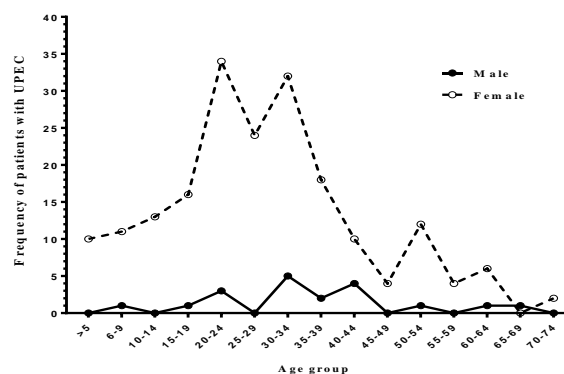

Figure 3. The occurrence of positive UPEC isolates (UTIs) in gender base distribution.

The overall isolates were distributed according to a patient's age and gender that entered the hospital. The total numbers of female patients with UPEC were 196 patients over the three years (2016, 2017and 2018), while the total number of male patients with UPEC isolates were 20 patients that were admitted to the hospital through three years.

All confirmed *E. coli* isolates were analyzed for antimicrobial drug resistance depending on the availability of theses tested antimicrobial drugs in the hospital at the time of the test. Furthermore, all moderate sensitive results to antibacterial medications were excluded from the analyzed data. Disk diffusion antibiotic sensitivity test was used as a routine procedure to identify the resistance to available antimicrobial drugs. As detailed in Table 2, the analyzed *E. coli* showed a variant level of resistance value to the tested antimicrobial medicines that were chosen for antimicrobial sensitivity. This study revealed that 174 (80.56%) *E. coli* isolates were resistant to three or more antibiotic categories (the antibiotic categories and multidrug resistance were described in Table 2 and 3. These results indicate that these isolates were multidrug resistance [12].

High percentages of antimicrobial resistance *E. coli* have been observed against most members of β-lactamase antibiotics. More than 90% of tested bacteria were found in classically used antibiotics, including ampicillin, ampicillin/ cloxacillin, and cloxacillin, and relatively newly introduced medicines, including amoxicillin/ clavulanic acid, cephalexin, and ceftazidime. Alongside β-lactamase antibiotics, the tested UPEC was exhibited a high level of resistance (90% or more) to erythromycin and clindamycin (macrolide antibiotics) (Table 2). The isolated UPEC also showed about 80-90% of resistance to another member of β-lactamase antibiotics, including amoxicillin, ceftazidime, ceftriaxone, cefixime, cefotaxime; and nalidixic acid. However, the high sensitivity of UPEC was

observed for *E. coli* isolates subjected to both imipenem and meropenem.

Table 3. The frequency of multidrug resistance UPEC isolated from UTI.

Year	*Frequency and percentages (%) of multidrug resistance						Total number of isolates
	Resistance to 7 antibacterial categories	Resistance to 6 antibacterial categories	Resistance to 5 antibacterial categories	Resistance to 4 antibacterial categories	Resistance to 3 antibacterial categories	Resistance 2 and less antibacterial categories	
2016	0 (0)	9 (7.63)	34 (28.81)	42 (35.59)	25 (21.19)	8 (6.78)	118
2017	1 (2.04)	3 (6.12)	8 (16.33)	11 (22.45)	13 (26.53)	13 (26.53)	49
2018	0 (0)	0 (0)	4 (8.16)	9 (18.37)	15 (30.61)	21 (42.86)	49
Overall three years	1 (0.46)	12 (5.56)	46 (21.30)	62 (28.70)	33 (15.28)	42 (19.44)	**216**
Multidrug resistance	**174 (80.56)** (isolates that showed resistance against at least one antimicrobial drug in three or more antimicrobial categories) [13]						

*The frequency and percentages were calculated separately for each years (2016, 2017 and 2018). The overall multidrug resistance was calculated based on the resistance of UPEC to three or more antibacterial categories (mentioned in Table 2). The isolates were considered as non-multidrug resistance when the resistance showed in two or less antibacterial category.

Discussion:

Urinary tract infections are inflammatory disorders caused by the abnormal growth of pathogens [14]. Annually, 150 million people worldwide are approximated to suffer from UTIs [15]. In the current study, the high rate of UTIs (64.7%) was identified in patients during the three years of the research with a higher frequency in 2016 (83.6%) (Table 1). A similarly high rate of UTIs was reported in other studies locally and worldwide [16-19]. Additionally, among the total positive UTIs, UPEC during the three years was 21.1% with a higher level in 2016 (22.9%). Many factors associated with the spread and distribution of UTIs, for example, socioeconomic, demographic data, hospitalization, age, gender, marriage status, clinical features, behaviors, practices, genitourinary abnormalities, and seasonal variation [14, 20].

Furthermore, one factor of this high rate of the infection in 2016 could be attributed to the high number of people displaced from other Iraqi cities (such as Mosul city) toward Zakho city, which is aligned to Turkey border. This internal displacement occurred when ISIS attacked many cities in Iraq in 2016. This large number of people put pressure on the healthcare system and its institutions in the local area [21]. By the end of 2015, around 200,000 internally displaced persons (IDPs) were living in camps sheltering in Duhok governorate [22]. In the following years, 2017-2018, IDPs started gradually to return to their original areas, and the healthcare centers were increased and supported by different organizations and became more available for persons [23]. This could explain the reduction of UTIs and UPEC in 2017 and 2018 compared to 2016.

This study showed a high incidence of UTIs and UPEC in females (Table 1). This incidence was in line with several pieces of research [24, 25]. It revealed that about 50% of women experience at least one episode of UTI at some point in their lifetime [26]. It is supposed that women are at high risk for UTI compared to men due to their anatomical and physiological characteristics [27]. For example, the proximity between the genital tract and the urethra/anus in women is one potential reason that could facilitate the auto-transmission of the pathogens and lead to increasing the rate of UTIs in women [28].

Regarding the seasonal risk factor, in Iraq, the average temperature ranges from 48°C in July and August to below freezing in January through a study that acquired temperature over 32 years (from 1980-2011) [29]. It was found that UPEC was at a higher rate during summertime (May) overall years of study (2016, 2017, and 2018) (Fig. 2a), and it was at a higher frequency in February and May 2016 (Fig. 2b). This finding was in agreement with other studies in Iraq and worldwide which found out that UPEC and most pathogens are seasonal diseases, with the majority of cases occurring in the summer months [30-33]. The primary associated risk factors for distributing UPEC in summer could contribute to different factors such as seasonal changes in human behavior such as eating locally prepared ice cream, travel, sexual activity, more consumption of water, and specific food contaminated with sewage, debris, and garbage [34]. Additionally, another critical factor

that explains this phenomenon could be the ability of E. coli to survive in the environment at higher temperatures [35]. Also, one possible risk factor may be as a result of seasonal disturbances in immune function that make the host more vulnerable to pathogens [36].

The incidence rates of UPEC were varied in different age groups (Fig. 3). It was observed that the highest rate of UPEC was prevalent among patients at the age of 20 to 39 years old, and the prevalence was reduced by increasing the age to reach the lowest rate at the age of 70-74 years. These observations were consistent with several studies in Iraq [24, 37, 38]. Habeeb [39] and Pirko and Ali [37] demonstrated that UPEC occurred mostly in patients aged between 20 to 35 years. Furthermore, a study performed in Pakistan revealed that 90% of Uropathogens belonged to the age group of 16–30 years [40]. The possible causes of the increased infection in this age group could be that this group is the most active in the society regarding the work, consumption of unhygienic food and water in working places, and colleges along with an increased number of social gatherings [32, 41]. Also, the sexual activities and hormonally induced changes in the vaginal flora of women could increase the UTI risks [40, 42, 43].

Recently, the efficacy of antimicrobial treatment of pathogenic bacteria has decreased because of the emergence of pathogenic isolates that are multidrug-resistant [16, 44, 45]. This study revealed that about 80% of UPEC isolates were multidrug resistance. There were variable susceptibilities of the UPEC toward the tested antibiotics. Generally, high resistance was observed against ampicillin, ampicillin/ cloxacillin, and cloxacillin, amoxicillin/ clavulanic acid, cephalexin, erythromycin, and clindamycin. However, the high sensitivity of UPEC was observed for both imipenem and meropenem (Table 2). It has been noted that the meropenem was shown to be effective against other gram-negative bacteria [46, 47].

The permanent investigation of antibiotic prescription is crucially essential to eliminate antimicrobial resistance of high virulent UPEC strains [7] that has developed progressively the ability to resist antimicrobial drugs over the past decade [8]. E. coli is a normal flora of animals and humans. However, its virulence is reportedly associated with various fatal infections that could infect the different organs and responsible for causing multiple diseases [1]. The resistance to nalidixic acid and cotrimoxazole was shown at a high level. However, the UPEC showed high resistance to Nitrofurantoin [48]. Rise the resistance against the fluoroquinolones, in particular, ciprofloxacin, could

be due to using this antimicrobial agent extensively. And this resistance seems to be more evident in developing countries than in European countries [4]. High resistance was shown against gentamicin in UPEC with biofilm formation strains.

Additionally, the previous study showed a high level of resistance to the cephalosporins, nalidixic acid, penicillins, and fluoroquinolones by E. coli isolated from UTI infections [8]. It is well established that wrong and overuse of these antibiotics will inevitably lead to selection pressure and increase the resistance rate [49, 50]. Also, the mistaken diagnosis of diseases may lead to proscribing wrong antibiotics to patients leading to resistance to pathogens.

Conclusion:

It was clear that the UPEC is at high frequency among patients with a higher percentage in females in the age group of 20 to 39 years. There is a high prevalence of resistance of UPEC isolates towards various groups of used antibiotics for UTI treatment. The highest antibiotic sensitivity of E. coli is observed for imipenem and meropenem. The wrong and overuse of these antibiotics will inevitably lead to selection pressure and increase the resistance rate. Therefore, awareness and education programs are necessary for the right diagnosis of diseases, proper selection, and wise use of available antibiotics. Hence, periodic monitoring of antimicrobial susceptibility pattern of UPEC will help guide the judicious use of antimicrobial agents and will help in reducing the bacterial vigor of resistance.

Authors' declaration:
- Conflicts of Interest: None.
- We hereby confirm that all the Figures and Tables in the manuscript are mine ours. Besides, the Figures and images, which are not mine ours, have been given the permission for re-publication attached with the manuscript.
- The author has signed an animal welfare statement.
- Ethical Clearance: The project was approved by the local ethical committee in Northern Technical University.

Authors' contributions statement:
Polis R.F. and Sabaly N.J. accomplished data acquisition, Assafi M.S. contributed in conception and design, Ali F.A. analyzed the data and drafted the MS; all authors contributed interpretation, revision, and approved the final manuscript.

References:

1. Kaper, J.B., J.P. Nataro, and H.L. Mobley, Pathogenic Escherichia coli. Nat Rev Microbiol, 2004. **2**(2): p. 123-140.

2. Asadi Karam, M.R., M. Habibi, and S. Bouzari, Urinary tract infection: Pathogenicity, antibiotic resistance and development of effective vaccines against Uropathogenic Escherichia coli. Mol Immunol, 2019. **108**: p. 56-67.

3. Karigoudar, R.M., et al., Detection of biofilm among uropathogenic Escherichia coli and its correlation with antibiotic resistance pattern. J Lab Physicians, 2019. **11**(1): p. 17-22.

4. Kot, B., Antibiotic Resistance Among Uropathogenic Escherichia coli. Pol J Microbiol, 2019. **68**(4): p. 403-415.

5. Tchesnokova, V., et al., The Uropathogenic Escherichia coli Subclone Sequence Type 131-H30 Is Responsible for Most Antibiotic Prescription Errors at an Urgent Care Clinic. Clin Infect Dis, 2019. **68**(5): p. 781-787.

6. Prasada, S., et al., Changing antibiotic susceptibility pattern in uropathogenic Escherichia coli over a period of 5 years in a tertiary care center. Infect Drug Resist, 2019. **12**: p. 1439-1443.

7. Paniagua-Contreras, G.L., et al., Multiple antibiotic resistances and virulence markers of uropathogenic Escherichia coli from Mexico. Pathog Glob Health, 2018. **112**(8): p. 415-420.

8. Shariff, V.A.A., et al., The antibiotic susceptibility patterns of uropathogenic Escherichia coli, with special reference to the fluoroquinolones. J Clin Diagn Res, 2013. **7**(6): p. 1027-1030.

9. Dadzie, I., et al., The Effectiveness of Dipstick for the Detection of Urinary Tract Infection. Canadian Journal of Infectious Diseases and Medical Microbiology, 2019. **2019**: p. 862-864.

10. MacFaddin, J.F., Biochemical Tests for Identification of Medical Bacteria. 3rd ed. 2000 Philadelphia, PA, USA: Lippincott Williams and Wilkins.

11. CLSI, Clinical and laboratory standards institute. Performance standards for antimicrobial susceptibility testing; Twenty-Fifth informational supplement. CLSI-NCCLS document M100-S25. Clinical and laboratory standards institute, wayne, PA. 2015.

12. Exner, M., et al., Antibiotic resistance: What is so special about multidrug-resistant Gram-negative bacteria? GMS hygiene and infection control, 2017. **12**: p. 1-24.

13. Basak, S., P. Singh, and M. Rajurkar, Multidrug Resistant and Extensively Drug Resistant Bacteria: A Study. Journal of pathogens, 2016. **2016**: p. 1-3.

14. Odoki, M., et al., Prevalence of bacterial urinary tract infections and associated factors among patients attending hospitals in Bushenyi district, Uganda. International journal of microbiology, 2019. **2019**(1): p. 1-8.

15. Karlowsky, J.A., et al., Trends in antimicrobial resistance among urinary tract infection isolates of Escherichia coli from female outpatients in the United States. Antimicrobial agents and chemotherapy, 2002. **46**(8): p. 2540-2545.

16. Assafi, M.S., et al., Urinary Bacterial Profile and Antibiotic Susceptibility Pattern among Patients with Urinary Tract Infection in Duhok City, Kurdistan Region, Iraq. Int. J. Pure Appl. Sci. Technol., 2015. **30**(2): p. 54-63.

17. Eriksson, I., et al., Prevalence and factors associated with urinary tract infections (UTIs) in very old women. Archives of gerontology and geriatrics, 2010. **50**(2): p. 132-135.

18. Fakhria, J., K. Salma, and A. Haydaite, Prevalence and associated factors of Urinary Tract Infection among female students in University of Babylon, Iraq. Research Journal of Pharmacy and Technology, 2017. **10**(6): p. 1976-1982.

19. Hussein, N.R., et al., Urinary Tract Infections and Antibiotic Sensitivity Patterns Among Women Referred to Azadi Teaching Hospital, Duhok, Iraq. Avicenna journal of clinical microbiology and infection, 2018. **5**(2): p. 27-30.

20. Stamm, W.E. and R. Raz, Factors contributing to susceptibility of postmenopausal women to recurrent urinary tract infections. Clin Infect Dis, 1999. **28**(4): p. 723-725.

21. Schweitzer, M., Iraq's Public Healthcare System in Crisis, in EPIC March. 2017: https://enablingpeace.org/healthcare-in-crisis/.

22. BRHA Report, Board of Relief and Humanitarian Affairs. Report on IDP camps in Duhok. BRHA https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0181028., 2016

23. IDPs, CORDAID Providing healthcare to minorities in North Iraq. 10 Sep 2018, Cordaid: https://reliefweb.int/report/iraq/cordaid-providing-healthcare-minorities-north-iraq.

24. Polse, R.F., S.Y. Yousif, and M.S. Assafi, Prevalence and antimicrobial susceptibility patterns of uropathogenic E. coli among people in Zakho, Iraq. Int. J. Res. Med. Sci., 2016. **4**(4): p. 1219-1223.

25. Almukhtar, S.H., Urinary Tract Infection Among Women Aged (18-40) Years Old in Kirkuk City, Iraq. The Open Nursing Journal, 2018. **12**(1): p. 248-260.

26. Ikähelmo, R., et al., Recurrence of urinary tract infection in a primary care setting: analysis of a I-year follow-up of 179 women. Clinical Infectious Diseases, 1996. **22**(1): p. 91-99.

27. Bashir, M., A.B. Umar, and M. Bilyaminu, Determination of Bacteria associated with Urinary Catheters from Patients Suffering from Urinary Tract Infections. Dr. Sulaiman Al Habib Medical Journal, 2020. **2**(1): p. 20-23.

28. Obiofu, E.N., O.H. Ige, and O. Iroro, Antimicrobial susceptibility pattern of urinary isolates from outpatients suspected for urinary tract infection. GSC Biological and Pharmaceutical Sciences, 2018. **5**(3): p. 001-011.

29. Şarlak, N. and O.M.A. Mahmood Agha, Spatial and temporal variations of aridity indices in Iraq. Theoretical and Applied Climatology, 2018. **133**(1): p. 89-99.

30. Wielders, C., et al., Seasonality in carriage of extended-spectrum β-lactamase-producing Escherichia coli and Klebsiella pneumoniae in the general population: a pooled analysis of nationwide cross-sectional studies. Epidemiology & Infection, 2020: p. 1-17.

31. Assafi, M.S., et al., The seroprevalence of human brucellosis in different age groups patients and other associated risk factors in Duhok, Iraq. Innovaciencia, 2019. **7**(2): p. 1-7.

32. Allu, M.A., et al., Present status of Salmonella Typhi in different age groups hospitalized patients in Duhok City, Iraq. . ZJPAS, 2019. **31**(6): p. 123-129.

33. Hussein, K.M., S.A. Fadhil, and S.A.-A.A. Salih, Assessing Water Quality for Al-Diwaniyah River, Iraq Using GIS Technique. Engineering and Technology Journal, 2019. **37**(7 A): p. 256-264.

34. Cabral, J.P., Water microbiology. Bacterial pathogens and water. International journal of environmental research and public health, 2010. **7**(10): p. 3657-3703.

35. Murata, M., et al., Molecular Strategy for Survival at a Critical High Temperature in Eschierichia coli. PLOS ONE, 2011. **6**(6): p. 1-9.

36. Freeman, J.T., D.J. Anderson, and D.J. Sexton, Seasonal peaks in Escherichia coli infections: possible explanations and implications. Clin Microbiol Infect, 2009. **15**(10): p. 951-954.

37. Pirko, E.Y. and M.R. Ali, The Relationship between Phylogenic Typing and Antimicrobial Susceptibility Patterns forEscherichia coliIsolatedfrom UTIs atMany Hospitals in Baghdad City. nursing national Iraqi specility, 2017. **30**(2): p. 1-12.

38. Aljebory, I.S. and K.A. Mohammad, Molecular Detection of Some Virulence Genes of Escherichia coli Isolated from UTI Patients in Kirkuk City, Iraq. Journal of Global Pharma Technology. **11**(3): p. 349-355.

39. Habeeb, A.A., Urinary Tract Infection Caused by Escherichia Coli and its Resistance to Antibiotics in Pregnant Women. Indian Journal of Public Health Research & Development, 2019. **10**(8): p. 2466-2469.

40. Fatima, S., et al., Incidence of multidrug resistance and extended-spectrum beta-lactamase expression in community-acquired urinary tract infection among different age groups of patients. Indian Journal of Pharmacology, 2018. **50**(2): p. 69-74.

41. Singer, R.S., Urinary tract infections attributed to diverse ExPEC strains in food animals: evidence and data gaps. Front Microbiol, 2015. **6**: p. 1-9.

42. Raz, R. and W.E. Stamm, A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. N Engl J Med, 1993. **329**(11): p. 753-759.

43. Marques, L.P., et al., Epidemiological and clinical aspects of urinary tract infection in community-dwelling elderly women. Braz J Infect Dis, 2012. **16**(5): p. 436-441.

44. Hussein, N.R., M.S. Assafi, and T. Ijaz, Methicillin-resistant Staphylococcus aureus nasal colonisation amongst healthcare workers in Kurdistan Region, Iraq. J Glob Antimicrob Resist, 2017. **9**: p. 78-81.

45. Polse, R.F., S.Y. Yousif, and M.S. Assafi, Prevalence and molecular characterization of extended spectrum beta-Lactamases-producing uropathogenic Escherichia coli isolated in Zakho, Iraq. Journal of Microbiology and Infectious Diseases, 2016. **6**(3): p. 163-167.

46. Maka G, et al., Antibiotic Susceptibility Profiling of Gram-Negative Bacteria Causing Upper Respiratory Tract Infections in Hyderabad, Sindh. JLBSR [Internet]. 2020. **1**(1): p. 12-17.

47. Sader, H.S. and R.N. Jones, Antimicrobial activity of the new carbapenem biapenem compared to imipenem, meropenem and other broad-spectrum beta-lactam drugs. European Journal of Clinical Microbiology and Infectious Diseases, 1993. **12**(5): p. 384-391.

48. Asadi, S., et al., The Association of Virulence Determinants of Uropathogenic Escherichia coli With Antibiotic Resistance. Jundishapur J Microbiol, 2014. **7**(5): p. 993-999.

49. Christaki, E., M. Marcou, and A. Tofarides, Antimicrobial resistance in bacteria: mechanisms, evolution, and persistence. Journal of molecular evolution, 2019: p. 1-15.

50. Assafi, M.S., et al., The Prevalence of S. aureus Nasal Colonisation and its Antibiotic Sensitivity Pattern amongst Primary School Pupils. Science Journal of University of Zakho, 2017. **5**(1): p. 7-10.

دراسة الوبائية والمقاومة للادوية المتعددة لجراثيم الايشيريشيا القولونية المعزولة من خمجات المسالك البولية (دراسة لثلاث سنوات)

مهدي صالح عسافي[1]   فواز فاضل علي[2]   ريم فؤاد بولص[3]   نسرين جواد سبالي[4]

سوزان محسن قرني[5]

[1] قسم البايولوجي، كلية العلوم، جامعة دهوك، دهوك، العراق.
[2] المعهد التقني في الموصل، الجامعة التقنية الشمالية، الموصل، العراق.
[3] قسم البايولوجي، كلية العلوم، جامعة زاخو، زاخو، العراق.
[4] مستشفى طوارئ زاخو، زاخو، العراق.
[5] كلية طب الاسنان، جامعة هولير، اربيل، العراق.

الخلاصة :

ان الاصابة بجراثيم الايشيريشيا القولونية ($E. coli$) هي احد المشاكل الرئيسة التي تؤدي الى اصابة الجهاز البولي في العالم. هذه البكتريا بامكانها من تطوير المقاومة ضد مجموعة واسعة من مضادات البكتريا. ان التقصي ونظام المراقبة والاستراتيجية الفعالة سوف يسهل بشكل كبير من اختيار العلاج المناسب للسيطرة على انتشار البكتريا. تهدف الدراسة الحالية الى الكشف عن وبائية الاصابة والعوامل الخطرة المتعلقة ببكتريا الايشيريشيا القولونية الممرضة للجهاز البولي وانماط المقاومة للمضادات الحيوية. تم جمع عينات من الادرار (من دفعة الادرار الوسطية) من 1585 مريض لديهم علامات سريرية للاصابة بالجهاز البولي (225 ذكور و 1360 اناث) دخلوا الى مستشفى زاخو للطوارئ في مدينة زاخو في اقليم كردستان العراق من تاريخ كانون الثاني 2016 ولغاية كانون الاول 2018. تم زرع العينات في اكار الدم والماكونكي وتم حضن اللاطباق المزروعة بدرجة حرارة 37 $^{\circ}$م لمدة 24 ساعة. ان تشخيص جراثيم الايشيريشيا القولونية تم بناءا على تفاعل التصبيغ بصبغة كرام والخصائص المستعمرية والفحوصات الكيميائية الحيوية وفقا للمعايير والتوجيهات المتبعة. تم فحص جميع العزلات لنمط المضادات الحيوية باستخدام طريقة نشر القرص بناء على إلارشادات والمعايير المختبرية والسريرية. بينت النتائج انه من بين 1585 عينة كانت 1026 عينة (64.7 %) ايجابية لاصابة جرثومية للجهاز البولي، وكانت باعلى مستوى خلال عام 2016 (83.6 %) ($P< 0.0001$). كما كان معدل الاصابة في الاناث بالايشيريشيا القولونية اعلى معنويا من الذكور ($P< 0.0001$) . وبشكل عام، كانت نسبة الاصابة بالايشيريشيا القولونية بمعدل 21.1% من مجموع الاصابات ونسبتها كانت اعلى خلال عام 2016 (22.9%). كما بينت الدراسة ان نسبة اصابة الاناث (21.4%) كانت اعلى مقارنة بالذكور (18.5%) ($P=0.4946$). بالاضافة الى ذلك ،خلال ثلاث سنوات من الدراسة (2016، 2017 و 2018)، فأن معدل الاصابة بالايشيريشيا القولونية كانت عند اعلى مستوى في الصيف (أيار) وكانت في اعلى مستوى في شهري شباط وايار من العام 2016، كما ان المجموعة العمرية من 20 الى 39 سنة كانت الاكثر اصابة بمعدل (46%) من مجمل اصابات الاناث، بينما كانت الفئة العمرية من 70 – 74 سنة هي الاقل بمعدل الاصابة (1%) لدى الذكور والاناث. لقد كشفت الدراسة ان نسبة عالية (80.56 %) من الايشيريشيا القولونية المقاومة لمضادات حيوية متعددة وبنسبة عالية لمجاميع المضادات الحيوية البيتا لاكتامز والماكروليدات. كانت نسبة حساسية عالية للمضادين الحيويين اميبنم و ميروبينم. في الختام، ان الاستخدام الخاطئ والمفرط للمضادات الحيوية ستزيد من معدل المقاومة لبكتريا الايشيريشيا القولونية، ولهذا السبب من الضروري الاستخدام الصحيح للمضادات الحيوية المتوفرة. كما أن البرامج التعليمية والمراقبة الدورية لحساسية المضادات الحيوية ضرورية لتقليل نسبة مقاومة المضادات الحيوية

الكلمات المفتاحية: المقاومة للمضادات الحيوية، الايشيريشيا القولونية، خمجات المسالك البولية.