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Antimicrobial Susceptibility Patterns of *Escherichia coli* from Urine Isolates

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Abstract: Urinary tract infections (UTIs) are predominantly caused by *Escherichia coli* (*E. coli)*. Increasing *E. coli* resistance to antibiotics is a major concern worldwide. Since UTIs are often treated by trial and error, measuring antimicrobial resistance (AMR) is important. However, there isn't much information about the rate of antimicrobial resistance to *E. coli* in the Libyan community. To determine rate of antimicrobial susceptibility patterns of *E. coli* urine isolates, in Al-Bayda, Libya. A retrospective study, in which 104 *E. coli* urine isolates were conducted using the antimicrobial susceptibility profile (antibiogram) of six different antibiotics against *E. coli*, isolates, were collected from several medical laboratories. Out of the 104 *E. coli* urine isolates, the MDR was 39.4%. The overall frequency of isolates resistant to ceftriaxone was 62.5%, trimethoprim-sulfamethoxazole (TMP-SMZ)(54.8%), Amoxicillin-Clavulanic acid (47.11%), ciprofloxacin (26%), nitrofurantoin (18.26%), and levofloxacin (15.4%). Prevalence of AMR among Libyan outpatient urine-isolated *E. coli* was high, with a high incidence of multidrug-resistance. The knowledge of antibiotic resistance rates in the region helps inform empiric treatment of community-onset UTI and highlights the antibiotic resistance profile to clinicians.

أنماط حساسية مضادات الميكروبات لعزلات بول الإشريكية القولونية

الكلمات المفتاحية :
ع . دوى المس . الك البولية؛
مقاوم .ة مض .ادات الميكروبات؛
الإشريكية القولونية؛
الأنتيبيوجرام (تحسس الجراثيم للمضادات).

المستخلص : إن التهابات المسالك البولية تسببها في الغالب الإشريكية القولونية، زيادة مقاومة الإشريكية القولونية للمضادات الحيوية هو مصدر قلق كبير في جميع أنحاء العالم، نظرًا إلى أن عدوى المسالك البولية تُعالَج غالبًا عن طريق التجربة واحتمالية الخطأ، فمن المهم قياس مقاومة مضادات الميكروبات؛ بما أنه لا تتوافر الكثير من المعلومات حول معدل مقاومة مضادات الميكروبات للإشريكية القولونية في عدوى المسالك البولية التي تظهر في المجتمع الليبي. تم تحديد تواتر وأنماط الحساسية لمضادات الميكروبات لعينات الإشريكية القولونية من عينات البول خلال جائحة فيروس كورونا في مدينة البيضاء، ليبيا. حيث أُجريت دراسة بأثر رجعي لـ 104 من عزلات الإشريكية القولونية المعزولة من البول جُمعت من عدة مختبرات طبية وذلك باستخدام بيانات التحسُّس لمضادات الميكروبات (الأنتيبيوجرام) لستة مضادات حيوية مختلفة. حيث أظهرت النتائج أنه من بين 104 عزلة من الإشريكية القولونية، كان معدل المقاومة المتعددة للأدوية 39.4٪. وكان الإجمالي للعزلات المقاومة للإشريكية القولونية على النحو الآتي: للسيفترياكسون 62.5٪، تريميثوبريم–سلفاميثوكسازول (54.8٪)، حمض أموكسيسيلين–كلافولانيك (47.11)، سيبروفلوكساسين (26٪)، نتروفورانتوين (18.26٪) و ليفوفلوكساسين (15.4٪). حيث كانت للمضادات الحيوية الآتية أعلى مقاومة لمضادات الميكروبات: سيفترياكسون، سلفاميثوكسازول / تريميثوبريم، أموكسيسيلين + حمض الكلافولانيك، وسيبروفلوكساسين، بهذا الترتيب. على الرغم من أن الليفوفلوكساسين والنيتروفورانتوين كانا أكثر المضادات الحيوية حساسية، فإن العمر عامل كبير في مدى حساسية عزلات بكتريا القولونية تجاه المضادات الحيوية.

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INTRODUCTION

Urinary tract infections (UTIs) are considered the most common community-acquired and nosocomial infections. It has been reported that 150 million cases of UTI occur each year worldwide (Medina & Castillo-Pino, 2019). The prevalence of UTI varies with age and gender. About 40–60% of women will get an UTI in their lifetime, which is more than the 12% of men who will get one (Kot, 2019; Medina & Castillo-Pino, 2019). It is the second most common infection after respiratory tract infections (Elsayah et al., 2017).

E. coli accounts for up to 80% of isolated bacteria causing UTIs (Niranjan & Malini, 2014; van Driel et al., 2019). Additionally, *E. coli* is also capable of infecting the lungs, surgical sites, bloodstream, and meninges (Forsyth et al., 2018). A local study performed by (Ismail et al. 2018) in Eastern Libya to determine the incidence of UTIs found that the most prevalent uropathogen was *E. coli* (48%). Another national study enrolled 1,790 patients with UTIs, *E. coli* was the predominant uropathogen, being isolated at 55.8% (Abujnah et al., 2015). Amongst bacteria detected in 2209 urine specimens from patients with UTI in Tripoli, Libya, *E. coli* was the major positive isolate (24%) followed by Staphylococcus spp. (8%) (Ghenghesh et al., 2003).Uncomplicated UTIs are commonly treated by empirical antibiotics without prior antibiotic susceptibility testing. These include: Nitrofurantoin, fosfomycin, trometamol, and TMP-SMZ are recommended as first-line therapy for uncomplicated cystitis. Amoxicillin-clavulanic acid is recommended as first line-therapy for mild and moderate pyelonephritis or complicated UTI, as well as alternative empiric therapy for uncomplicated UTIs. In the treatment of uncomplicated cystitis, ciprofloxacin should not be considered as a first-line antibiotic, but as an alternative (Kot, 2019).

Many studies have reported that antimicrobial resistance in *E. coli* has been increasingly observed and reported worldwide due to several factors, such as the use of empirical antibiotics to treat UTIs without antibiotic sensitivity testing as the international protocols recommend (Kot, 2019; Shuaib et al., 2021). The development of multidrug resistance (MDR), which is the resistance to one or more classes of antimicrobials against *E. coli* strains, has caused increasing concern over the empirical treatment options in the case of UTIs with *E. coli*. Fluoroquinolones (levofloxacin and ciprofloxacin), cephalosporins (Cefixime and Ceftriaxone), sulfonamides (TMP-SMX), penicillin (Amoxicillin-Clavulanic acid), and nitrofurantoin are among the MDR classes reported (Abduzaimovic et al., 2016). During the COVID-19 pandemic in May 2021, a WHO report shows worrying trends, especially in low- and middle-income countries like Libya, where more reports are being sent to the Global Antimicrobial Resistance and Use Surveillance System (GLASS), which was the first global effort to standardize AMR surveillance (WHO, 2021).

The WHO reported over 3 million laboratory-confirmed bacterial infections resistant to WHO priority list pathogens in 70 countries. Although it is too early to link the higher resistance rates to the COVID-19 pandemic. Resistance rates have increased six-fold since sites began sharing AMR surveillance data in 2017 (WHO, 2020, 2021). Prior to the COVID-19 epidemic, the Arab world had already experienced alarming levels of AMR (Dandachi et al., 2019) Recognizing the scarcity of research on the topic, this study studied the impact of COVID-19 on *E.coli* AMR and antimicrobial stewardship (AMS) in Libya as an Arab League country .

This study aimed to determine the prevalence of antimicrobial susceptibility profile (Antibiogram) of *E. coli* isolates collected from urine samples of outpatients suffering from UTIs.

MATERIALS AND METHODS

Study design and participants: This study was a retrospective study conducted in the medical laboratories at Al-Bayda, Libya, from January 2021 to April 2022. Outpatients with UTI infections caused by *E.coli* of all ages and both sexes were tested for sensitivity to 5 antibiotics. Excluding incomplete patient records, comorbid cases, and cases with a recurrent history of UTIs.

Sample size, and collection techniques
The sample size was calculated using the Epi-info software program to be 104 urine samples. The urine specimens and their age and sex were labeled.

Urine culture; The standard loop method, which is semi-quantitative, was used to cultivate urine. Standard procedures, such as gram stain, blood agar, MacConkey agar, and API (Analytical Profile Index) 20E, were used to identify isolated *E. coli*

Procedures: The antibiotic sensitivity test was done on Mueller-Hinton agar by the Kirby-Bauer disc diffusion test as per Clinical and Laboratory Standard Institute (CLSI) guidelines (Clinical & Institute, 2012). The following antimicrobial agents were tested for their resistance and susceptibility: amoxicillin/clavulanic acid (30 µg), TMP/SXT (25 µg), ciprofloxacin (5 µg), nitrofurantoin (300 µg), Levofloxacin (5 µg) and ceftriaxone (30 µg). An isolate was considered an MDR if it was found resistant to three or more antimicrobial classes belonging to different classes/groups of antimicrobials.

Statistical Analysis: The data was analyzed using SPSS version 25 (IBM Corp., Armonk, NY, USA). Differentials were considered statistically significant at $p< 0.05$. The qualitative and discrete sociodemographic variables were presented as frequency and percent. The Chi-square test was performed to test the relationship between sociodemographic factors and antibiotic resistance and susceptibility. The predictors of antibiotic resistance and susceptibility of *E. coli* isolates were identified using multinomial logistic regression analysis.

RESULTS

The majority of the studied samples were females 99 (95.5%). Out of the 104 *E. coli* urine isolates, Augmentin resistance was 49 (47.1%). The susceptibility patterns of *E. coli* strains were significantly ($p = 0.03$*) affected by the patient age, especially the age group 18–25 y. The OR (95% C.I] was 2.28 (-4.12-0.44) with $p = 0.02$* compared to participants ≥65 y (Table 1)**.**

ciprofloxacin resistance was 27 (26. 0%).There was a statistically significant relationship between it and the age ($p = 0.01$*), especially the age group 18–25 y, and ≥65 y. The OR (95% C.I] was 3.18(1.62-56.7) and 2.95(1.9-81.9) in order with $p <0.05$ compared to participants aged less than 18 y (Table 2).

Nitrofurantoin resistance was 19(18.3%). There was a statistically significant (P value less than 0.05) relationship between it and the age and sex of participants. Among males, the OR (95% C.I] was -2.05 (-3.92/-0.18), and had significantly lower resistance ($p = 0.03$). Compared to participants aged more than 65 years, nitrofurantoin resistance was significantly lower ($p<0.05$) among the age groups of 18–35 years and less than 10 years**.** As shown in (Table 3)**.**

Levofloxacin resistance was 16(15.4%). There was a statistically significant ($p< 0.05$) relationship between it and the age and sex of participants. Among males, the OR (95% C.I] was 2.29(4.18-0.41), and had significantly lower resistance ($p = 0.02$). Compared to participants aged more than 65 years, Levofloxacin resistance was significantly lower ($p<0.05$) among the age groups of 18–<25 years and less than 10 years. (Table 4).

Table (1). Background information, and Frequency, Determinants., and Predictors of Augmentin susceptibility patterns to *E. coli* strains urine isolates

Age groups (y)	Total T=104	Augmentin		X^2 (P)	Predictors of Augmentin resistance OR[95% C.I]	P
		Sensitive 55(52.9) F (%)	Resistance 49(47.1) F (%)			
1-<10	19(18.3)	11(20.0)	8(16.3)	15.1 (0.03*)	-1.29(-2.90-0.310)	0.11
10-<18	5(4.8)	4(7.3)	1(2.0)		-2.37(-4.93-0.19)	0.07
18-<25	14(13.5)	11(20.0)	3(6.1)		-2.28(-4.12-0.44)	0.02*
25-<35	32(30.8)	19(34.5)	13(26.5)		-1.36(-2.86-0.14)	0.08
35-<45	10(9.6)	3(5.5)	7(14.3)		-0.13(-2.02-1.76)	0.89
45-<65	13(12.8)	4(7.3)	9(18.4)		-0.17(-1.94-1.60)	0.85
≥65	11(10.6)	3(5.5)	8(16.3)		Reference	
Sex						
Male	5(4.8)	1(1.8)	4(8.2)	2.28 (0.13)	-1.6(0.02-1.93)	0.17
Female	99(95.2)	54(98.2)	45(91.8)			

*p <0.05 there was a statistical significant difference

Table (2). Patterns of ciprofloxacin susceptibility of isolated *E. coli* at different age groups

Age groups (y)	Ciprofloxacin		X^2 (P)	Predictors of ciprofloxacin resistance OR[95% C.I]	P
	Sensitive 77(74.0) F (%)	Resistance 27 (26.0) F (%)			
1-<10	17(22.1)	2(7.4)	18.1 (0.01*)	Reference	
10-<18	2(2.6)	3(11.1)		2.77(0.5-44.1)	0.11
18-<25	13(16.9)	1(3.7)		3.18(1.62-56.7)	0.02*
25-<35	26(33.8)	6(22.2)		0.21(0.07-21.6)	0.89
35-<45	7(9.1)	3(11.1)		1.30(0.41-33.5)	0.25
45-<65	7(9.1)	6(22.2)		2.62(1.38-55.9)	0.12
≥65	5(6.5)	6(22.2)		2.95(1.9-81.9)	0.03*
Sex					
Male	2(2.6)	3(11.1)	3.17 (0.08)	Reference	
Female	75(97.4)	24(88.9)		-1.54(0.03-1.35)	0.10

*p <0.05 there was a statistical significant difference

Table (3). Patterns of Nitrofurantoin susceptibility of isolated *E. coli* at different age groups

Age groups (y)	Nitrofurantoin		X^2 (P)	Predictors of Nitrofurantoin resistance OR[95% C.I]	P
	Sensitive 85(81.7) F (%)	Resistance 19 (18.3) F (%)			
1-<10	17(20.0)	2(10.6)	15.9 (0.04*)	-1.96(-3.84/-0.72)	0.04*
10-<18	4(4.7)	1(5.3)		-1.20(-3.69-1.29)	0.34
18-<25	14(16.5)	0(0.0)		-2.38(-4.74/-0.03)	0.047*
25-<35	27(31.8)	5(26.3)		-2.52(-4.38/-0.67)	0.008*
35-<45	6(7.1)	4(21.1)		-2.02(-4.39-0.37)	0.097
45-<65	11(12.9)	2(10.5)		-0.63(-2.30/1.04)	0.46
≥65	6(7.1)	5(26.3)		Reference	
Sex					
Male	2(2.4)	3(15.8)	6.12 (0.013*)	-2.05(-3.92/-0.18)	0.03*
Female	83(97.6)	16(84.2)		Reference	

*p <0.05 there was a statistical significant difference

Table 4; Patterns of Levofloxacin susceptibility of isolated *E. coli* at different age groups

Age groups (y)	Levofloxacin		X^2 (P)	Predictors of Levofloxacin resistance OR[95% C.I]	P
	Sensitive 88(84.6) F (%)	Resistance 16 (15.4) F (%)			
1-<10	17(19.3)	2(12.6)		-1.96(3.84- 0.07)	0.04*
10-<18	4(4.5)	1(6.3)		-1.20(3.69-1.29)	0.34
18-<25	13(14.8)	1(6.3)		-2.38(2.7-0.03)	0.047
25-<35	30(34.1)	2(12.5)	16.1	-2.53(4.38-0.67)	0.008*
35-<45	9(10.2)	1(6.3)	(0.024*)	-2.01(4.39-0.37)	0.097
45-<65	9(10.2)	4(25.0)		-0.63(2.30-1.04)	0.46
≥65	6(6.8)	5(31.3)		Reference	
Sex					
Male	2(2.3)	3(18.8)	8.03	-2.29(4.18-0.41)	0.02*
Female	86(97.7)	13(81.3)	(0.005*)	Reference	

Ceftriaxone resistance was 65(62.5 %). There was a statistically significant (p less than 0.05) relationship between Ceftriaxone resistance and the age of participants. Compared to participants aged more than 65 all age groups except the age group between 45 and less than 65y are significant (p<0.05) risky to Ceftriaxone resistance (Table 5).

TMP-SMZ resistance was (57,54.8%). There was a statistically significant (p less than 0.05) relationship between TMP-SMZ resistance and the age and sex of participants. Among females, the OR (95% C.I) was 17.2 (16.8/-17.9) and had significantly lower resistance (p = 0.00). Compared to participants aged more than 65 years, nitrofurantoin resistance was significantly lower (p<0.05) The OR (95% C.I] was 2.35 (4.429-0.42) among the age groups of 18–<25 years (Table 6).

Table (5). Patterns of ceftriaxone susceptibility of isolated *E. coli* at different age groups

Age groups (y)	Ceftriaxone		X^2 (P)	Predictors of ceftriaxone resistance OR[95% C.I]	P
	Sensitive 39(37.5) F(%)	Resistance 65 (62.5) F(%)			
1-<10	10(25.6)	9(13.8)		2.41(4.65-0.16)	0.035*
10-<18	4(10.3)	1(1.5)		3.69(6.69-0.68)	0.016*
18-<25	8(20.5)	6(9.2)		2.59(4.90-0.28)	0.028*
25-<35	13(33.3)	19(29.2)		1.92(4.09-0.25)	0.083
35-<45	3(7.7)	7(10.8)	22.12	1.45(3.92-1.001)	0.246
45-<65	0(0.0)	13(20.0)	(0.002*)	19.9(17.1-20.2)	0.03*
≥65	1(2.6)	10(15.4)		References	
Sex					
Male	0(0.0)	5(7.7)	3.15	References	
Female	39(100.0)	60(92.3)	(0.19)	17.1(16.1-18.9)	0.00*

*p <0.05 there was a statistical significant difference

Table: (6) Patterns of TMP-SMZ susceptibility of isolated *E. coli* at different age groups

	TMP-SMZ		X^2 (P)	Predictors of Septrin resistance OR[95% C.I]	P
	Sensitive 47(47.2) F (%)	Resistance 57 (54.8) F (%)			
Age groups (y)					
1-<10	4(8.5)	15(26.3)		0.76(0.88-2.41)	0.37
10-<18	2(4.3)	3(5.3)		0.15(2.23-2.02)	0.89
18-<25	12(25.5)	2(3.5)		2.35(4.29-0.42)	0.017*
25-<35	19(40.4)	13(22.8)		0.94(2.35-0.46)	0.194
35-<45	3(6.4)	7(12.3)	20.65 (0.004*)	0.29(1.53-2.12)	0.758
45-<65	3(6.4)	10(17.5)		0.64(1.13-2.43)	0.48
≥65	4(8.5)	7(12.3)		References	---
Sex					
Male	0(0.0)	5(8.8)	4.33	Reference	0.00*
Female	47(100.0)	52(91.2)	(0.04*)	-17.2(16.8/17.9)	

*p <0.05 there was a statistical significant difference

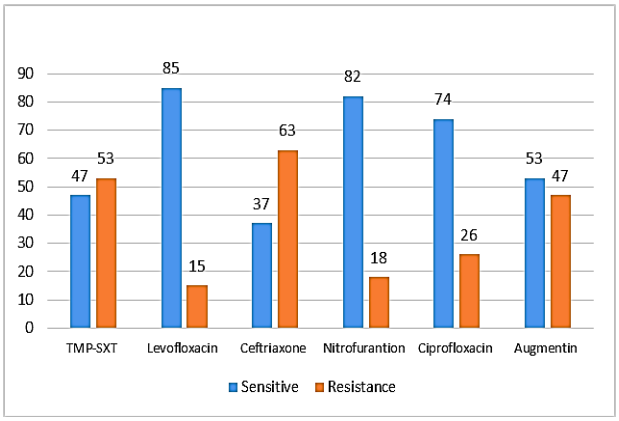

Figure (1). Antimicrobial susceptibility patterns of *E. coli* strains to different antimicrobial agents

All *E. coli* isolates (104) were tested for their susceptibility using a panel of antibiotics. The *E. coli* isolates were resistant mostly to the tested antibiotics as follows: Ceftriaxone (65,62.5%), TMP-SMZ (57/104; 54.8%), amoxicillin + clavulanic acid (49/104; 47.11%), and ciprofloxacin (27/104; 26.8%) were all found to have high rates of resistance. While the antibiotics of higher sensitivity were levofloxacin (88,84.6%), nitrofurantoin (85.81.7%).

DISCUSSION

Uropathogenic *Escherichia coli* (UPEC) is one of the main bacteria causing UTIs. The rates of UPEC with high resistance to antibiotics and MDR *E. coli* have increased dramatically in recent years and could complicate the treatment (Ramírez-Castillo et al., 2018),. This emergence of global concern poses a major challenge to physicians and public health worldwide (Paterson, 2000). The choice of empirical antimicrobial therapy is based on antibiogram patterns that show resistance trends among pathogens. Because antibiotic resistance patterns change over time, it is important for clinicians to learn about the information they have seen (Kumarasamy et al., 2010).

Limited studies show the resistance rate to antibiotics used in treating UTIs against *E. coli* in other areas and cities in Libya during the COVID-19 pandemic, studies carried out between 2002 and 2008 reported an increase in *E. coli* resistance rates to Ciprofloxacin and other fluoroquinolones (Ghenghesh et al., 2013). High rates of resistance to TMP-SMZ were also observed from 1990 to 1999 for *E. coli* from UTIs in Tripoli and Benghazi (Ghenghesh et al., 2013). AMR patterns of *E. coli* from patients with UTIs who attended Zawiya Teaching Hospital in Zawiya city between November 2012 and June 2013 were (37%), (23.1%) and (19.2%) for TMP-SMZ, Ciprofloxacin, and Levofloxacin. MDR (resistance to 3 antimicrobial groups) was

found in (33.2%) (Abujnah et al., 2015).

As regards the sex; According to the findings (95.2 %), between January 2021 and April 2022 in Al-Bayda, Libya, the *E. coli* urine isolates in outpatients were detected more frequently in women. These findings are in line with prior research (Deshpande et al., 2011; Haque et al., 2015; Keah et al., 2007). Furthermore, male patients' isolates had higher antimicrobial drug resistance than female patients' isolates, male infections may be more difficult to treat since male strains have higher rates of antibiotic resistance, which could lead to repeated infections. These findings were consistent with previous research (Ali et al., 2016; Tabasi et al., 2015; Wagenlehner et al., 2007). Isolates should be screened for antibiotic susceptibility before deciding on a treatment.

As regards the MDR; we found the MDR of the UPEC was 39.4%. This result is similar to other previous studies that indicated an increasing resistance to three or more classes of antibiotics, especially in developing countries (Sanchez et al., 2014).

As regards the Ceftriaxone resistance; Ceftriaxone resistance was shown to be the most common in the current study (62.25 percent). This can be explained by the recent emergence of ß-lactam resistance in nosocomial Enterobacteriaceae, which has become a severe problem worldwide, notably the increasing resistance to third-generation cephalosporins (Ceftriaxone) (Pfeifer et al., 2010). Ceftriaxone is therefore a less common first-line medication for UTIs, but it is essential for treating more serious infections (Abernethy et al., 2017).

Different resistance rates have been recorded in different geographical courtiers in studies of ceftriaxone resistance status. Pakistan (90 %) and Ethiopia (73 %) showed higher ceftriaxone resistance (Gashe et al., 2018; Kathia et al., 2020). Mexico (27.3%) and Jordan (55.1%), on the other hand, have lower resistance patterns for *E. coli* isolates against ceftriaxone (Ramírez-Castillo et al., 2018; Shakhatreh et al., 2019). Others, have identified lesser resistant *E. coli* isolates (20%) in Saudi Arabia (Aabed et al., 2021), (7.8%) in northern Brazil from 2007 to 2010 (Cunha et al., 2016), and 6.7 percent in 2013 in Zawiya, Libya (Abujnah et al., 2015; Cunha et al., 2016).

As regards TMP-SMZ**;** TMP-SMZ resistance was the second most common in this study (54.8%). It is used in practice a lot, and (Jancel & Dudas, 2002) say it should be the first choice for treating a simple UTI (cystitis).

Susceptibility patterns vary across geographical regions and alter over time, as previously mentioned (Prakash & Saxena, 2013). For example, approximately equal frequencies of UPEC isolates resistant to TMP-SXT were found (2018) (Alqasim et al., 2018; Cunha et al., 2016; Raeispour & Ranjbar, 2018). While Mongolia had more TMP-SMZ resistance in 2017, Mexico had 72.7 percent in 2018, while Jordan had 73.1 percent in 2019 (Munkhdelger et al., 2017; Ramírez-Castillo et al., 2018; Shakhatreh et al., 2019). Certain European countries reported a lower frequency of between 14.6 and 60 percent in 2019 (Kot, 2019); Switzerland reported 24.5 percent from 2012 to 2015 (Erb et al., 2018); 37.1 percent in France in 2016 (Lavigne et al., 2016). In different Libyan cities, *E. coli* isolates showed varying rates of resistance to TMP-SMZ throughout time, for example, 1994-1995/Tripoli (45%), 1996/Benghazi (81%), 2002- 005/ Sirte (36%), 2006-2008/ Benghazi (31%) (Ghenghesh et al., 2003).

According to (Abujnah et al., 2015), resistance to TMP-SMZ was 24.6 percent in 2013. Due to increased resistance to TMP-SMZ that has recently been documented in numerous countries, TMP-SMZ should not be used in empiric UTI treatment and the

maximum resistance that can be tolerated is 20% (Bartoletti et al., 2016).

As regards Nitrofurantoin resistance; Because nitrofurantoin's activity against commonplace causes of UTIs, such as *E. coli*, is well-documented, so in this study the resistance was found to be (18.26 percent). Nitrofurantoin resistance is uncommon in principle, and many MDR species remain vulnerable (Sanchez et al., 2014) These findings support the European Association of Urology (EAU) (Grabe et al., 2015) and International Clinical Practice Guidelines' recommendations that nitrofurantoin be used first-line for the treatment of uncomplicated UTIs (Grabe et al., 2015; Rowe & Juthani-Mehta, 2013).

This result was similar in low rate of resistance to nitrofurantoin as in Mexico (2013–2017) by (Ramírez-Castillo et al., 2018), in India was (12.7%). by (Prasada *et al*., 2019) and in Saudi Arabia found that the prevalence of nonsusceptible *E. coli* to nitrofurantoin was 15% (Alqasim et al., 2018). While in Tripoli, Libya 2003 was (25%) (Ghenghesh et al., 2003).

As regards* fluoroquinolones *resistance; The fluoroquinolones resistance rates in this study (ciprofloxacin 26% and levofloxacin 15.4%) suggest that fluoroquinolones antibiotics, such as ciprofloxacin and levofloxacin, are recommended for empirical oral antimicrobial treatment in uncomplicated UTIs (pyelonephritis) and are widely used in clinical practice against UTI pathogens such as *E. coli* (Bonkat et al., 2018; Drago et al., 2001), whereas various countries reported significant levels of fluoroquinolone-resistant *E. coli* (Drago et al., 2001). It is thought that the widespread use of fluoroquinolones in outpatients is the reason for the persistent increase in resistance to this medication. Thus, the use of ciprofloxacin as empirical therapy for UTI should be avoided, and the application of policy that restricts ciprofloxacin use should be enhanced, particularly in developing countries (Fasugba et al., 2015; Karam et al., 2019).

In agreement with our results, what was found in previous studies, which showed that fluoroquinolone resistance rates are always less than 20%, with a few cases of much higher resistance rates of 49% to 72% (Walker et al., 2016). For example, nearly similar results were found in Benghazi, Libya between 2006 and 2008; 17% were resistant to ciprofloxacin (Buzayan et al., 2010; Ghenghesh et al., 2003); in Switzerland, 17.4% were resistant to ciprofloxacin (Erb et al., 2018); in Brazil, 18.8% were resistant to ciprofloxacin (da Silva et al., 2017); in Zawiya city between 2012 and 2013; 23.1% were resistant to ciprofloxacin; and 19.2% to levofloxacin (Abujnah et al., 2015). In developed countries, the rates were much lower (5.1% in the USA, 10.5% in Germany, and 24.8% in France) than in developing countries (64.6% in Nepal, 58.1% in Mongolia, and 55.5% in Jordan) (Khatri et al., 2017; Munkhdelger et al., 2017; Shakhatreh et al., 2019).

While higher frequencies were reported in Saudi Arabia. 40% was resistance to ciprofloxacin (Alqasim et al., 2018). In Mexico, 47.3% was resistance to ciprofloxacin and 43.6 to levofloxacin (Ramírez-Castillo et al., 2018); in Pakistan, 60% was resistance to ciprofloxacin and 61.4% to levofloxacin (Ali et al., 2016).

As regards Amoxicillin-Clavulanic acid resistance; In our study, the percentage of *E. coli* resistance to Amoxicillin-Clavulanic acid was 47.11%. For this reason, amoxicillin-clavulanic acid is not indicated for empirical treatment due to the high prevalence of bacterial resistance (Bartoletti et al., 2016). Therefore, its treatment should be based on the susceptibility results of UPEC (Kot, 2019).The variance level of *E. coli* isolates resistant to amoxicillin-clavulanic acid among patient groups or geographical regions is unknown. For example, it was

reported higher in Jordan, where 2019 was 83.2% (Shakhatreh et al., 2019), in Pakistan, 2016 was 71% (Ali et al., 2016), and in Saudi Arabia it was 55% (Abernethy et al., 2017; Alqasim et al., 2018; Kot, 2019; Lavigne et al., 2016; Ramírez-Castillo et al., 2018) reported low resistance in France (36.6%), England (30%), Mexico (23.6%), and Poland (13.9%).

Strength: To best of our knowledge, this is the first study in Libya that study this topic during the COVID-19 pandemic, to cover large period of time more than 18 months (January 2021 to April 2022) in order to evaluate the rate of *E. coli* resistance to the chosen antimicrobial agents.

Limitations: Being a retrospective study and record based study may affect the quality of the collected data, and we cannot calculate the incidence and cannot prove. As a single city study, may limit the generalizability of the results. in other Libyan cities.

CONCLUSION

In Libya's Al-Bayda, during the COVID-19 pandemic, the following antibiotics had the highest antimicrobial resistance patterns: ceftriaxone, TMP-SMZ, amoxicillin + clavulanic acid, and ciprofloxacin, in that order. While levofloxacin and nitrofurantoin were the antibiotics with the highest sensitivity, age is a significant determinant of antimicrobial sensitivity patterns in E. coli urine isolates, while sex is only a significant determinant of antimicrobial sensitivity patterns in the TMP-SMZ, ceftriaxone, and nitrofurantoin treatments. Antibiotic resistance in UPEC is a severe concern in Libya that requires immediate attention from health officials.

RECOMMENDATIONS

1. The results of the current study demonstrates clearly that the problem of antibiotic resistance in *E. coli* treatment in Libya is a very serious problem that needs urgent attention by the health authorities.
2.For setting up a basis for clinical treatment of *E. coli* infections, readily available data (Antibiogram profiling) on antibiotic resistance patterns from annual reports of clinical laboratories should be used for the choice of appropriate antimicrobial therapy in patients with suspected UTI.
3.Alternatives to the commonly used antimicrobial for the treatment of UTI in Libya should be considered, particularly those with high resistance (ceftriaxone, TMP-SMZ and Amoxicillin + Clavulanic acid)**.** Thus, selection of appropriate antibiotics for the UTIs should start after establishing monitoring systems based on antibiotic susceptibility pattern of the causative isolate obtained (Karam *et al*., 2019; Sifaw Ghenghesh, 2003).
4.Further multicenter, and prospective research should be conducted either on the *E. coli* or other types of bacteria on a regular basis.

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