BAU Journal - Health and Wellbeing

Volume 3 | Issue 1
ISSN: 2617-1635

Article 5

October 2020

SURVEILLANCE OF MULTIDRUG-RESISTANT UROPATHOGENIC ESCHERICHIA COLI IN HOSPITALIZED PATIENTS AND COMMUNITY SETTINGS IN THE SOUTH OF LEBANON

Nourhan Darwich
Infection Control Graduate, Master Student, Infection Control, Faculty of Health Sciences, Beirut Arab University, Beirut, Lebanon, nourhandarwish7@gmail.com

Ali Samaha
Assistant Professor, Department of Biomedical Sciences, Lebanese International University, Beirut, Lebanon, ali.samaha@bau.edu.lb

Hanan Al Nuqaidan
Head of Studies and Information Office, Nursing Department, Ministry of Health, Kuwait, Kuwait, dr.hanan75@yahoo.com

Ahmad Tassi
Assistant Professor, Nursing Department, Faculty of Health Sciences, Beirut Arab University, Beirut, Lebanon, a.tassi@bau.edu.lb

Mirna Fawaz
Associate Professor, Nursing Department, Faculty of Health Sciences, Beirut Arab University, Beirut, Lebanon, mirna.fawaz@bau.edu.lb

SURVEILLANCE OF MULTIDRUG-RESISTANT UROPATHOGENIC ESCHERICHIA COLI IN HOSPITALIZED PATIENTS AND COMMUNITY SETTINGS IN THE SOUTH OF LEBANON

Abstract

Urinary Tract Infection (UTI) is one of the common infectious diseases in both hospitals as well as community settings; they are recognized to be among the most serious worldwide bacterial infections impacting 150 million people globally every year. The purpose of this study was to assess the changing antibiotics resistance profile for uropathogenic Escherichia coli isolated from community and hospital setting over a period of time (2018–2019) with a special emphasis on ESBL/MDR producing Escherichia coli. A descriptive retrospective study was conducted among patients with uropathogenic Escherichia coli from both community and hospital settings in south Lebanon. Out of 863 patients with positive uropathogenic Escherichia coli, 451 (52.25 %) comes from the community while 412 (47.74 %) came from the hospital settings. Almost 60.83 % are not Extended Spectrum Beta-Lactamases (ESBL), 31.4 % ESBL, and 7.76 % Multiple drug resistance (MDR). The majority of urinary tract infections are related to the female population (78.21 %). The most vulnerable age for both gender to develop UTI belong to elderly population (>64 years) which account 37.19 % of all isolates. Statistically, we observed a high resistance rate toward all antibiotics using in the treatment of urinary tract infections such as Cefixime (45.30 %), Sulfamethoxazole (44.95 %), Ciprofloxacin (38.23 %) and Augmentin (38.93 %). A statistically significant association was observed between risk factors for hospitalized patients and all age categories with ($P < 0.05$). Susceptibility profiles are critical to be evaluated in countries such as Lebanon where excessive use of antibiotics is observed at all levels. Therefore, this finding is useful for the determination of appropriate antimicrobial treatment in UTI patients that are caused by Escherichia coli and to follow the antimicrobial stewardship program to reduce the rate of resistance toward antibiotics.

Keywords

Urinary tract infection, Escherichia coli, Multidrug resistance, Antimicrobial resistance.

1. INTRODUCTION

Urinary Tract Infections (UTIs) constitute the main cause of morbidity and mortality worldwide (Foxman, 2010). The key cause of UTIs is reported to be Escherichia coli (E. coli) (Farajnia et al., 2009), and the uropathogenic E. coli (UPEC), a subset of pathogenic extra-intestinal E. coli (ExPEC) group, is associated with causing more than 80% of all UTIs (Ronald, 2002). It has been guesstimate that 150 million UTIs occur per year globally (Stamm & Norrby, 2001). UTI happens eight times more often in females than in males, and about 50-60% of women report at least one UTI in their lifespan (Foxman et al., 2000; Rahn, 2008; Al-Badr and Al-Shaikh, 2013). In the US, UTIs are accountable for >7 million physician visits yearly and 15% of all community-prescribed antibiotics, with similar statistics in some European countries (Bonkat et al., 2017). E. coli causes the majority of UTIs and pyelonephritis, where the host vaginal or fecal microbiota is the most common source for these strains—termed Uropathogenic E. coli—although UPECs are not necessarily the predominant clones from these reservoirs.

However, there is a frightening level of antimicrobial resistance developing in UTI pathogens as a consequence of random and global use of antibiotics. Bacteria producing extended-spectrum beta-lactamases (ESBLs), exhibiting resistance to most antibiotics except for the carbapenem group, are steadily increasing in the population (Bonkat et al., 2017; Oteo et al., 2010). ESBLs are enzymes that break down commonly used antibiotics, such as penicillins and cephalosporins, making them ineffective. ESBL-producing Enterobacteriaceae often cause infections in otherwise healthy people. Over the past twenty years, the antimicrobial resistance of ExPEC to first-line antibiotics, such as amoxicillin and ciprofloxacin has escalated markedly (Foxman, 2010). Additionally, an increased extended-spectrum β-lactamase (ESBL) carriage has been announced among ExPEC strains (Pitout et al., 2005b). As reported in 2008, E. coli sequence type 131 (E. coli ST131) was described among ESBL-producing E. coli in many *continents* throughout the world, and it has distributed to become the preponderant ExPEC clone that drives multidrug resistance (MDR) universally (Nicolas-Chanoine et al., 2014). MDR is when a single bacterium is resistant to more than one antibiotic it is said to be multidrug-resistant. Antimicrobial resistance is currently one of the main issues in public health (Cassini et al., 2019). The prevalence of multidrug-resistant (MDR) bacteria has risen significantly in recent decades, and the World Health Organization (WHO) has incorporated antimicrobial resistance in its list of 10 world threats to public health. Infections by MDR organisms are especially important in health care settings. However, they have also increased in frequency in community settings (Kaarme et al., 2018). These infections have a poorer prognosis because of the delay in the initiation of suitable antibiotic therapy and the need for alternative antibiotics, which are usually less effective and are less secure (Chiotos et al., 2016; Folgori et al.,2017).

The increase of antibiotic resistance and development of multi-drug resistant (MDR) pathogens in the course of UTI is correlated with high rates of inadequate antibiotic empirical therapies prescribed without checking for antibiotic susceptibility testing and finally result in an ineffective UTI treatment (Adamus-Białek 2018). As a consequence, surveillance and antimicrobial stewardship programs have been directed to optimize the prevention and control of infections by lowering antibiotic resistance rates in hospitals (CDC, 2013).

According to a study previously carried out in Beirut (Daoud & Afif, 2011), E. coli was the most recurrent isolate (60.64% of the total isolates) and an increase in the production of ESBL was noticed between the years 2000 and 2009 (2.3% to 16.8%). Unfortunately, very limited data concerning UTIs is obtainable from other regions of the country. The purpose of this study was to assess the changing antibiotics resistance profile for uropathogenic Escherichia coli isolated from community and hospital setting over a period of time (2018–2019) with a special emphasis on ESBL/MDR producing Escherichia coli. The findings of this study will redound to the benefit of the Lebanese healthcare society by showing the real fact of the antibiotics' resistance in the hospital and community setting and make it the first step for improvement later through the infection control program.

2. METHODOLOGY

The aim of this study was to assess the changing antibiotics resistance profile for uropathogenic Escherichia coli isolated from community and hospital setting over a period of time (2018–2019) with a special emphasis on ESBL/MDR producing Escherichia coli. A descriptive cross-sectional research design was adopted. This study was conducted in laboratory department of one hospital in South, Lebanon. An official permission to conduct this study was obtained from the responsible authorities referred to institutional review board (IRB) at Beirut Arab University, and the ethical committee at the relevant clinical site after explaining the aim of the study, where the anonymity and confidentiality of the data have been guaranteed to be maintained. All Patients (863) who have positive UPEC belong to any age group and gender were included in the study. Patient that have urinary tract infection caused by other bacteria than Escherichia coli were excluded. Hospital based UTI was defined to be prevalent after 48 hours of admission. Data was collected retrospectively for the two years 2018/2019. Nine hundred and thirteen cases were recorded to be eligible to be included in the research, however the researchers were able to access the files of 863 patients therefore a rate of 94.52%. The Statistical Package for Social Science (Corp, 2013) was used to analyze the data. Descriptive statistics were utilized to describe the characteristics of the patients that suffer from positive UPEC. The inferential statistics were used to test the relationship between variables.

3. RESULTS

3.1. Socio-Demographic Characteristics Of Patient With Positive UPEC

The study included eight hundred thirty-six patients (N= 863), where 675 (78.21 %) of them were females while 188 (21.78 %) of them were males. With regard to the age categories of patients, a total of 321 (37.19 %) samples were collected from the elderly, 305 (35.34 %) samples belong to adults population, and 237 (27.46 %) were obtained from children. In addition, 412 (47.74 %) are hospitalized admitted patient (inpatient) while 451 (52.25 %) came from the community setting (outpatient). The demographics characteristics of the patient are shown in table 1

Table 1: Sociodemographic characteristics

Variables	Category	Total n (%)
Gender	Male	188(21.78)
	Female	675(78.21)
Age	<18	237(27.46)
	18-64	305(35.34)
	>64	321(37.19)
Setting	Inpatient	412(47.74)
	Outpatient	451(52.25)

Moreover, with respect to setting or location, inpatients females are at higher risk for the development of UTIs than males respectively (295, 71.60 %; VS 117, 28.39 %).Also, outpatient is higher in female than male respectively (380, 84.25 %; VS 71, 15.74 %).On the other hand, a total of 197 (83.12 %) were collected from female children, 251 (82.29 %) collected from adult females, and 227 (70.71 %) collected from an elderly female. While, 40 samples (16.87 %) collected from male children, 54 (17.70 %) from adult males and 94 (29.28 %) from the elderly males (Table 2).

Table 2: Distribution of UPEC by age category and setting with respect to gender

Gender	Male	Female
Setting		
Inpatient	117(28.39)	295(71.60)
Outpatient	71(15.47)	380(84.25)
Age		
<18	40(16.87)	197(83.12)
18-64	54(17.70)	251(82.29)
>64	94(29.28)	227(70.71)

3.2. Prevalence Of ESBL and MDR Production Among UPEC

A descriptive analysis was carried out to assess the prevalence of MDR and ESBL production among UPEC. From 863 patients with positive uropathogenic Escherichia coli, we have 525(60.83 %) samples are non ESBL, 271(31.4 %) ESBL & 67(7.76 %) sample are MDR. Also, the most associated group for both ESBL and MDR are from the female population (200 samples, 73.8 % VS; 47 samples, 70.14 %) compared to male (71 samples, 26.19%, VS; 20 samples, 29.85 %) respectively with P-value = 0.011 which is significantly associated with a P value less than 0.05. On the other hand, ESBL and MDR are significantly higher in the hospitalized patient (inpatient) (156 samples, 37.86%; 43 samples, 10.43%) compared to outpatient (115 samples, 25.49%; 24 samples, 5.32%) respectively with P value=0.000* (Table 3).

Table3.Prevalence of ESBL and MDR producing among UPEC

Variables	Category	ESBL	MDR
Gender	M	71(26.19)	20(29.85)
	F	200(73.8)	47(70.14)
Age	>18	75(27.67)	20(29.85)
	18-64	78(28.78)	18(26.86)
	>64	118(43.54)	29(43.28)
Setting	Inpatient	156(57.56)	43(64.17)
	Outpatient	115(42.43)	24(35.82)

3.3. Antimicrobial Profile

A descriptive analysis was also carried out to determine antimicrobial susceptibility for UPEC strains. The results of antibiotic susceptibility showed that the highest resistance rate was against amoxicillin (73.58%) followed by cefuroxime (55.38%), tetracycline (50.28%), Cefixime (45.3 %), Sulfamethoxazole (44.95 %) and Norfloxacin (40.55 %). On the other hand, the highest susceptibility was toward Colistin (99.07 %), Imipenem (99.18 %), Meropenem (98.95 %), Nitrofurantoin (98.95 %), Fosfomycin (98.72 %), Pipracillintazobactam (91.42 %), Amikacin (91.19 %) and Gentamicin (66.85 %) (Table 4).

Table 4: Antimicrobial susceptibility for UPEC strains

Antibiotics	Resistance	Intermediate	Susceptible
Amoxicillin	636(73.69)	69(7.99)	158(18.30)
Augmentin	336(38.93)	239(4.51)	28(33.37)
Cefixime	391(45.30)	30(3.47)	441(51.10)
Cefotaxime	339(39.28)	5(0.57)	519(60.13)
Cefoxitine	89(10.31)	82(9.50)	692(80.18)
Ceftriaxone	339(39.28)	2(0.23)	522(60.48)
Ceftazidime	342(39.26)	7(0.81)	514(59.55)
Cefuroxime	478(55.38)	4(0.46)	381(44.14)
Ciprofloxacin	330(38.23)	40(4.63)	493(57.12)
Norfloxacin	350(40.55)	38(4.40)	475(55.04)
Levofloxacin	324(37.54)	30(3.47)	509(58.98)
Amikacin	32(3.70)	44(5.09)	787(91.19)
Gentamicin	187(21.66)	99(11.47)	577(66.85)
Nitrofurantoin	9(1.04)	0(0)	854(98.95)
Fosfomycin	22(2.54)	0(0)	852(98.72)
PipracillinTazobactam	33(3.82)	41(4.75)	789(91.42)
Colistin	8(0.92)	0(0)	855(99.07)
Imipenem	6(0.69)	1(0.11)	856(99.18)
Meropenem	8(0.92)	1(0.11)	854(98.95)
Sulfamethoxazole	388(44.95)	2(0.23)	473(54.80)
Tetracycline	434(50.28)	19(2.2)	410(47.5)

3.4. Comparison of Antimicrobial Resistance Pattern Among UPEC for Year 2018 and 2019

Descriptive analysis was made to make a comparison between the years 2018 and 2019. For the year 2018, we have 384 patients with uropathogenic Escherichia coli while in 2019 we have 479 patients with uropathogenic Escherichia Coli. Based on the resistance profile for the year 2018 and 2019, we see an increase resistance toward all antibiotics that's used to treat urinary tract infection such as Cefixime (41.66 %, VS 48.22 %) ,Augmentin (36.45 % ,VS 40.9 %), Sulfamethoxazole (42.18 %, VS 47.18 %), Gentamicin (16.92 %, VS 25.05 %), Nitrofurantoin (0.78 %, VS 1.25 %), Fosfomycin (2.08 %, VS 2.92)and Levofloxacin (36.97 %, VS 37.99 %) respectively (Table 5).

Table 5: Comparison of Antimicrobial profile for the years 2018 and 2019

	2018			2019		
Antibiotics	Resistance	Intermediate	Susceptible	Resistance	Intermediate	Susceptible
Amoxicillin	278(72.39)	31(8.07)	75(19.53)	357(74.53)	38(7.93)	83(17.32)
Augmentin	140(36.45)	107(27.86)	137(35.67)	196(40.90)	132(27.55)	151(31.52)
Cefixime	160(41.66)	12(3.12)	211(54.94)	231(48.22)	18(3.75)	230(48.01)
Cefotaxime	141(36.71)	1(0.26)	242(63.02)	198(41.33)	4(0.83)	277(57.82)
Cefoxitine	38(9.89)	32(8.33)	314(81.77)	51(10.64)	50(10.43)	378(78.91)
Ceftriaxone	140(36.45)	4(1.04)	240(62.5)	199(41.54)	2(0.41)	278(58.03)
Ceftazidime	142(36.97)	3(0.78)	239(62.23)	200(41.75)	4(0.83)	275(57.41)
Cefuroxime	169(51.04)	2(0.52)	186(49.21)	282(58.87)	2(0.41)	195(40.70)
Ciprofloxacin	147(38.28)	18(4.68)	219(57.03)	182(37.99)	22(4.59)	274(57.20)
Norfloxacin	162(42.18)	15(3.90)	207(53.90)	188(39.24)	23(4.80)	268(55.94)
Levofloxacin	142(36.97)	14(3.64)	228(59.37)	182(37.99)	16(3.34)	281(58.66)
Amikacin	10(2.60)	13(3.38)	361(94.01)	22(4.59)	31(6.47)	526(88.93)
Gentamicin	65(16.92)	34(8.85)	285(74.21)	120(25.05)	65(13.56)	292(60.96)
Nitrofurantoin	3(0.78)	0(0)	381(99.21)	6(1.25)	0(0)	473(98.74)
Fosfomycin	8(2.08)	0(0)	376(97.91)	14(2.92)	0(0)	464(96.86)
PipracillinTazobactam	13(3.38)	23(5.98)	348(90.62)	20(4.17)	18(3.75)	439(91.64)
Colistin	0(0)	0(0)	384(100)	8(1.67)	0(0)	471(98.32)
Imipenem	0(0)	0(0)	384(100)	6(1.25)	1(0.20)	472(98.53)
Meropenem	0(0)	0(0)	284(100)	8(1.67)	1(0.20)	470(98.12)
Sulfamethoxazole	162(42.18)	2(0.52)	220(57.29)	226(47.18)	0(0)	253(52.81)
Tetracycline	196(51.04)	16(4.16)	172(44.79)	238(49.68)	3(0.62)	238(49.68)

3.5. Susceptibility Profile For ESBL And NON-ESBL Escherichia Coli Isolated From Urine

A descriptive analysis was also carried out to determine the susceptibility profile of ESBL Escherichia coli isolated from the urinary tract. Among all antibiotics tested in this study for extended-spectrum beta-lactamase (ESBL), Carbapenem, Nitrofurantoin, and Fosfomycin was the most active against Escherichia coli isolates, also 90.77 % to piperacillin-tazobactam, 83.02 % to Amikacin and 53.87 % to gentamicin. Out of 271 ESBL producing Escherichia .coli isolates, 98.52% were resistant to amoxicillin, 66.05 % to Norfloxacin, 64.20% to Ciprofloxacin, 63.09% to Levofloxacin, 62.36% to Augmentin, and 34.68% to Gentamicin (Table 6).

Table 6: Antimicrobial profile for ESBL producing UPEC

Antibiotics	Resistance	Intermediate	Susceptible
Amoxicillin	267(98.52)	0(0)	4(1.47)
Augmentin	169(62.36)	94(34.68)	8(2.95)
Cefixime	267(98.52)	1(0.36)	3(1.10)
Cefotaxime	266(98.15)	1(0.36)	4(1.47)
Cefoxitine	2(0.73)	42(15.49)	227(8.11)
Ceftriaxone	267(98.52)	0(0)	4(1.47)
Ceftazidime	267(98.52)	0(0)	4(1.47)
Cefuroxime	268(98.89)	0(0)	3(1.10)
Ciprofloxacin	174(64.20)	10(3.69)	87(32.10)
Norfloxacin	179(66.05)	11(4.05)	81(29.88)
Levofloxacin	171(63.09)	10(3.69)	90(33.21)
Amikacin	17(6.27)	29(10.70)	225(83.02)
Gentamicin	94(34.68)	31(11.43)	146(53.87)
Nitrofurantoin	2(0.73)	0(0)	269(99.26)
Fosfomycin	9(3.32)	0(0)	262(96.67)
PipracillinTazobactam	6(2.21)	19(17.01)	246(90.77)
Colistin	1(0.36)	0(0)	270(99.63)
Imipenem	1(0.36)	0(0)	270(99.63)
Meropenem	1(0.36)	0(0)	270(99.63)
Sulfamethoxazole	153(56.45)	1(0.36)	106(39.11)
Tetracycline	170(62.73)	8(2.95)	93(34.31)

3.6. Distribution Of Antimicrobial Profile For MDR Escherichia Coli Isolates From Urine

A descriptive analysis was also carried out to determine the Distribution of Multi-drug resistant (MDR) Escherichia coli isolates among urine. The results show that Multidrug-resistant isolates were resistant 100% to Cephalosporin's & amoxicillin, 77.61% to Trimethoprim-sulfamethoxazole, 71.64% to Norfloxacin, and 67.16 % to Ciprofloxacin & levofloxacin. Moreover, the distribution of ciprofloxacin (231 samples, 70.21 %) and levofloxacin (227 samples, 70.06 %) resistance was significantly higher among female than male gender with P-value =0.000*. Also, UPEC isolates from hospital-acquired infection was associated with Ceftazidime (P=0.000*) and MDR phenotype in a hospitalized patient more than in the community-acquired infection respectively (64.17% VS 35.82%, P= 0.000*) (Table 7).

Table 7: Antimicrobial profile for MDR Escherichia coli isolated from urine

Antibiotics	Resistance	Intermediate	Susceptible
Amoxicillin	67(100)	0(0)	0(0)
Augmentin	67(100)	0(0)	0(0)
Cefixime	66(98.50)	0(0)	1(0.19)
Cefotaxime	66(98.50)	0(0)	1(0.19)
Cefoxitine	63(94.02)	3(0.57)	1(0.19)
Ceftriaxone	66(98.50)	0(0)	1(0.19)
Ceftazidime	64(95.52)	2(0.38)	1(0.19)
Cefuroxime	66(98.50)	0(0)	1(0.19)
Ciprofloxacin	45(67.16)	5(0.95)	17(3.23)
Norfloxacin	48(71.64)	2(0.38)	17(3.23)
Levofloxacin	45(67.16)	3(0.57)	19(11.23)
Amikacin	4(5.97)	4(5.97)	59(5.90)
Gentamicin	30(44.77)	6(1.14)	31(5.90)
Nitrofurantoin	3(4.47)	0(0)	64(12.19)
Fosfomycin	2(2.98)	0(0)	65(12.38)
PipracillinTazobactam	19(28.35)	11(2.09)	37(7.04)
Colistin	4(5.97)	0(0)	63(12)
Imipenem	3(4.47)	1(0.19)	63(12)
Meropenem	4(5.97)	0(0)	63(12)
Sulfamethoxazole	52(77.61)	0(0)	15(2.85)
Tetracycline	45(67.16)	2(0.38)	20(3.80)

3.7. Results of Chi-square

A Chi-Square test was carried out to determine if there is an association between age and gender on one hand and the location on the other. During the study, females (675 samples, 78.21 %) were the most affected group of patients with P-value <0.05 as compared to males (188 samples, 21.78 %). Moreover, most of the urinary tract infection was detected in a community setting (451 samples, 52.25 %) while 412 were obtained from hospital-acquired infection (47.74 %). Also, females of age group 18-64 years (251 samples, 37.18 %) are more prone to develop urinary tract infections than males (54 samples, 28.72 %) with highly significant P value (< 0.05). However, females were correlated with community-acquired urinary tract infection of both age groups (<18 & 18-64) and with hospital-acquired infection of age group (>64) with P-value < 0.05. Therefore, the results showed that there is a significant relationship between the age and gender where a significant-value of p = 0.000* was recorded. In addition, another highly significant association was noted between the age and location of where a p-value of p = 0.000*was recorded (Table 8).

Table 8: Results of association between age with gender and setting

Age	All patient N=863	Male N=188	Female N=675	P	HAI N=412	CAI N=451	P
<18	237(27.46)	40(21.27)	197(29.18)	0.000	73(17.71)	164(36.36)	0.000
18-64	305(35.34)	54(28.72)	251(37.18)	0.000	100(24.27)	205(45.45)	0.000
>64	321(37.19)	94(50)	227(33.62)	0.000	239(58)	82(18.18)	0.000

Another chi-Square test was carried out to determine if there is an association between antibiotic resistance and gender on one hand and the location on the other. High frequency of resistance was observed toward Amoxicillin (73.69 %), cefuroxime (55.38 %), tetracycline (50.98 %), cefixime (45.30 %), TM/SMX (44.95 %), and norfloxacin (40.55 %). From twenty-one different antibiotics tested, highly susceptible isolates were toward imipenem, meropenem, colistin, nitrofurantoin, fosfomycin, and amikacin with low resistance rate respectively (0.69 %, 0.92 %, 0.92 %, 1.04 %, 2.54 %, and 3.7 %). Among 863 we have 67 isolates were related to multidrug-resistant organisms MDR (7.76 %). MDR organisms were highly resistant toward amoxicillin and cephalosporin, TM/SMX (77.61 %), tetracycline (67.67 %) and gentamicin (44.77 %). Moreover, the fluoroquinolone-resistant strain showed MDR. And the percentage for resistance toward these families was 71.64 % to norfloxacin 67.16 % to ciprofloxacin and, 67.16 % to levofloxacin. Moreover, the distribution of quinolones family that includes (ciprofloxacin, norfloxacin, and levofloxacin) resistance was significantly higher among male than female gender (52.12 %, 53.19 %, 51.59 %, P=0.000*, VS 34.37 %, 37.03%, 33.62%) and also, these quinolones antibiotics are higher in hospitalized patient than in community-acquired infection respectively (53.88 %, 54.61 %, 53.15 %, P=0.000* VS, 23.94 %, 27.71 %, 23.28 %). Therefore, the results showed that there is significant association between gender and antibiotics include: cefotaxime (p=0.009), cefoxitine (0.000*), ceftriaxone (p=0.012), ceftazidime (p=0.012) and quinolones family with p value =0.000*, amikacin (p=0.047) and gentamicin (p= 0.000*). Also, the results of this analysis showed that there is a significant relationship between location and antibiotics that include: Augmentin (p=0.004), cefixime (0.000*), cefotaxime (p=0.000*), cefoxitine (p=0.002), ceftriaxone, ceftazidime, cefuroxime, tetracycline ciprofloxacin, norfloxacin and levofloxacin with p value =0.000*, gentamicin (p=.008) (Table 9).

Table 9: Results of association between antibiotics with gender and setting

Antibiotics	All patient N=863	MDR N=67	Male N=188	Female N=675	P	CAI N=451	HAI N=412	P
Amoxicillin	636 (73.69)	67(100)	144(76.59)	492(72.88)	0.58	321(71.17)	315(76.45)	0.091
Augmentin	336(38.93)	67(100)	76(40.42)	260(38.51)	0.278	155(34.36)	181(43.93)	0.004
Cefixime	391(45.30)	66(98.5)	101(53.72)	290(42.96)	0.068	172(37.13)	219(53.15)	0.000
Cefotaxime	339(39.28)	66(98.5)	91(48.40)	248(36.74)	0.009	139(30.82)	200(48.54)	0.000
Cefoxitine	89(10.31)	63(94.02)	26(13.82)	63(9.33)	0.000	35(7.76)	54(13.10)	0.002
Ceftriaxone	339(39.28)	66(98.5)	91(48.40)	248(36.74)	0.012	139(30.82)	200(48.54)	0.000
Ceftazidime	342(39.26)	64(95.52)	92(48.93)	250(37.03)	0.012	139(30.82)	203(49.27)	0.000
Cefuroxime	478(55.38)	66(98.5)	116(61.70)	362(53.62)	0.095	223(49.44)	255(61.89)	0.000
Ciprofloxacin	330(38.23)	45(67.16)	98(52.12)	232(34.37)	0.000	108(23.94)	222(53.88)	0.000
Norfloxacin	350(40.55)	48(71.64)	100(53.19)	250(37.03)	0.000	125(27.71)	225(54.61)	0.000
Levofloxacin	324(37.54)	45(67.16)	97(51.59)	227(33.62)	0.000	105(23.28)	219(53.15)	0.000
Amikacin	32(3.70)	4(5.97)	8(4.25)	24(3.55)	0.047	15(3.32)	17(4.12)	0.369
Gentamicin	187(21.66)	30(44.77)	71(37.76)	116(17.18)	0.000	79(17.51)	108(26.21)	0.008
Nitrofurantoin	9(1.04)	3(4.47)	2(1.06)	7(1.03)	0.974	7(1.55)	2(0.48)	0.123
Fosfomycin	22(2.54)	2(2.98)	2(1.06)	20(2.96)	0.144	11(2.43)	11(2.66)	0.830
PipracillinTazobactam	33(3.82)	19(28.35)	8(4.25)	25(3.70)	0.673	13(2.88)	20(4.85)	0.279
Colistin	8(0.92)	4(5.97)	1(0.53)	7(1.03)	0.523	4(0.88)	4(0.97)	0.898
Imipenem	6(0.69)	3(4.47)	1(0.53)	5(0.74)	0.830	4(0.88)	2(0.48)	0.451
Meropenem	8(0.92)	4(5.97)	2(1.06)	6(0.88)	0.849	4(0.88)	4(0.97)	0.573
Sulfamethoxazole	388(44.95)	52(77.61)	85(45.21)	303(40.88)	0.756	183(40.57)	205(49.75)	0.025
Tetracycline	434(50.28)	45(67.16)	95(50.53)	339(50.22)	0.815	196(43.45)	238(57.76)	0.000

3.8. Risk factor for UPEC in Hospitalized Patient

Descriptive and inferential analysis chi-square was also carried out to determine the risk factors for acquiring uropathogenic Escherichia coli in hospitalized patients according to gender and age group. Out of N=412 hospitalized patients (inpatient), where 294 (71.35 %) of them were female while, 118 (28.64 %) of them belong to a male. With regard to gender, females are more prone to develop urinary tract infection than males as see in table menopausal female (204 samples, 69.38 %, P=0.000*) which is significantly associated with urinary tract infection. Also, another risk factor such as diabetic patient was higher in female than male (34.01 %, VS 16.10 %) with p value=0.000* also the previous hospitalization is significantly associated with UTI development especially in the female population than male respectively (64.28 %, VS 50.84 %) with P-value =0.012. While there is no association between gender and previous antibiotics use with (P Value=0.861). On the other hand, with regard to the age category, there is a significant association between older age category (>64 years) and menopause (166 samples, 70.33 %), diabetic (98 samples, 41.52 %), previous hospitalization (166 samples, 70.33 %) & previous antibiotics (169 samples, 71.61 %) however, all of them with P-value =0.000* which is less than 0.05 and therefore it's strongly associated (Table 10).

Table10: Risk factor for UPEC in hospitalized patient

Category	Menopause	P	Diabetic	P	Previous hospitalization	P	Previous antibiotics	P
Gender								
Male	0(0)		19(16.10)		60(50.84)		74(62.71)	
Female	204(69.38)	0.000	100(34.01)	0.000	189(64.28)	0.012	187(63.6)	0.865
Age								
<18	0(0)		2(2.73)		32(43.83)		34(46.57)	
18-64	38(36.89)		19(18.44)		51(49.51)		58(56.31)	
>64	166(70.33)	0.000	98(41.52)	0.000	166(7.33)	0.000	169(71.61)	0.000

4. DISCUSSION

This chapter provides a general discussion of the study findings, which compares our results to that of various other studies that have to investigate to evaluate UPEC. However, in south Lebanon, there are no studies on microbiological surveillance of multidrug-resistant UPEC at hospitals and community settings or related topics. Because urinary tract infection is one of the most common medical problems affecting the population. This retrospective study aim to describe the prevalence of uropathogenic Escherichia coli (N=863 isolates) from the community (451 isolates) and hospital-acquired (412 isolates) urinary tract infections and their antibiotics resistance profile between the years 2018 and 2019 at the capital hospital (Alnajdi hospital) in the Nabatieh area at the south of Lebanon.

In the present study, 863 patients with positive uropathogenic Escherichia coli were reported, 675 cases (78.21%) were female, while 188 cases (21.78%) were male (P<0.05). Gender and urinary tract infections were found to have a major correlation. This result is consistent with Mahesh et al (Mahesh et al., 2010), demonstrating that female urinary tract infection was higher than males (65 %, 35% respectively). With regard to the age category, the female population was higher than the male population throughout all age groups, studies have demonstrated that the higher prevalence of urinary tract infection in females can be attributed to many factors, such as the anatomical factor suggesting that urethra in females is shorter than in males and closer to anus, increasing the probability that Escherichia coli bacteria can be easily translatable to the bladder (Ghanbari et al. 2017; Tabasi et al., 2015) Poor hygiene and sexual activity as well as contraception use (John et al., 2016). This finding is consistent with previous studies in Lebanon and other countries that in our study, the prevalence of urinary infection toward females was higher than those of males within all age groups (Daoud, 2011; Tajbakhsh et al., 2015; Ghanbari et al., 2017; Tabasi et al., 2015). In addition, UTIs in our sample are more prevalent throughout the older age group (> 64 years), which is 37.19 %; increasing risk of prostate problem prevalence in males and diabetes mellitus are willing to increase the incidence of UTI in elderly patients (Mahesh et al., 2010).

The diagnosis and treatment of diseases in this age group (>64 years) have become more important because of the growing elderly population worldwide. UTI is a major cause of mortality and morbidity in older patients. Urinary tract infection is amongst the most considerable causes of sepsis in elderly patients, with a mortality rate of 33 percent associated with urosepsis. (Gbinigie et al., 2018). Visits to the outpatient clinic by the elderly population due to Urinary tract infection were noted to be three times greater than those in the younger population (Cortes-Penfield et al., 2017). This was typically associated with age-related bladder malfunction, urethral catheterization, and blood vessel obstruction related to benign prostatic hyperplasia, especially in males. Additionally, due to repeated antibiotic therapies, resistance to antibiotics is higher in older patients along with young patients (Gbinigie et al., 018).

The study revealed the prevalence of UPEC's broad spectrum beta-lactamase phenotype was (31.4 %) but was low in this study for multidrug-resistant (8 %) like other Mexican studies recording (16.4 percent) of MDR strain (Ochoa et al., 2016). While (Paniagua –Contreras et al., 2017)'s research has shown 97 percent of multidrug-resistant strains. The burden of ESBL in community-acquired infections is also increasing (Rodríguez-Bano et al., 2008) noted that older age, men, DM existence, and fluoroquinolone utilization over the last two months are risk factors in community-acquired ESBL-producing E. coli infection. In response, serious adverse effects such as fluoroquinolone-induced QT prolongation, delirium, and seizures were recorded by the United States Food and Drug Administration in May 2016 (Gbinigie et al., 2018). Therefore the use of fluoroquinolone must be restricted in patients who are at high risk. The involvement of ESBL in this research was greater than in other studies (Coskun USS, Coskun G, 2015; Asgin & Satilmis, 2019; Duman et al., 2010). This may be attributable to our patient group comprising of elderly patients and fluoroquinolone being unnecessary prescribed.

In this study, all species of Escherichia coli (N=863) were resistant to amoxicillin (73.58 percent) suggesting a careful use of these antibiotics to treat urinary tract infection. Resistant Escherichia coli to the family penicillin community was on a higher side in different parts of the world, and it is growing day by day (Olowe et al., 2007). Resistance to the combination amoxicillin-CA (Augmentin 38.93 percent) was also high like other studies that posted similar findings (Drawz & Bonomo, 2010). The degree of resistance in E.coli strains to amoxicillin-clavulanic acid in elderly patients was 39.58 %. In agreement with the research by Ulug et al. (Ulug &Gul, 2012), this incidence was stated to be 33 percent in elderly patients. In addition, the resistance rates to third-generation cephalosporins include cefixime in E. coli strains were 37%, high resistance to cefixime may be explained by the fact that our research group composed of elderly patients. In general, antibiotic resistance in the elderly population is perceived to be higher relative to that in the young. It could be due to excessive antibiotic (Palacios-Ceña et al., 2017).

For this research project, the rate of TMP-SMX resistance in E. coli was 35%. Likewise, high resistance rates were recorded in the Brazilian (35 percent) (Marques, 2012) and the US (60 percent) studies (Das et al., 2009). In contrast, Fagan et al.'s analysis (Fagan et al., 2015) (Norway) noticed resistance levels to be 24 percent. However, Over 44 percent of isolates displayed TM-SMX resistance, which is prescribed as the first option for UTI treatment (Ali et al., 2014). Similar results have been recorded in recent studies (Pniagua-Contreras et al., 2017). In particular, TM-SMX's resistance rate increased from 2018 (42.18%) to 2019 (47.18%) in my study so, the rise in resistance indicates that great caution should be exercised when deciding to use this antibiotic.

The rise in fluoroquinolone usage (Ciprofloxacin, Levofloxacin & Norfloxacin), increases the probability of global resistance to these antibiotics in uropathogens (Fasugba et al., 2015). With respect to this phenomenon, the increase in resistance of fluoroquinolones among UPEC isolates are now leading to demands to counter their use as agents of the first choice (Stewardson et al., 2018) in agreement with Hoban et al.(2012). In this study, more than 37% of UPEC isolates were resistant to ciprofloxacin and levofloxacin antibiotics. Also, the rate of antimicrobial resistance towards these antibiotics was higher for males than for female patients (Linhares et al., 2017). In agreement with (Ali et al., 2019; Wagenlehner et al., 2007), we noticed older men (> 64 years) had increased risks of FQ-resistant (fluoroquinolones) UTIs. Interestingly, fluoroquinolones are commonly used in male patients for treating UTI. Thus, it may be more difficult for male infections to eliminate due to the higher level of antibiotic resistance found in male-isolated strains, which can lead to persistent infection. Such findings were similar to earlier papers (Tabasi et al., 2015; Ali et al., 2016; Ibrahim et al., 2012).

Moreover, the prevalence of ciprofloxacin resistance in E. coli strains was 42%. We agree that the misuse of fluoroquinolones in the treatment of infections other than UTI in our hospital has resulted in high resistance to fluoroquinolone. The levels of resistance to ciprofloxacin in a multi-center study performed on elderly patients, Escherichia Coli strains were estimated to be 30% in Canada and 44% in the US (Lob et al., 2016). Sanchez et al. (Sanchez et al., 2013) documented resistance rates of 11% in adults, and 30% in aging patients while, Fagan et al. (Fagan et al., 2015) recorded relatively low resistance levels toward UPEC which is 8 %. Furthermore, research carried out in Spain has shown that fluoroquinolone-resistant for E.coli is prevalent in older age groups (Nicolle et al., 2016). Also, a history of hospitalization and the use of fluoroquinolones are independent risk factors for developing this resistance toward antibiotics (Das et al., 2009; Smithson et al., 2012).On the other hand, Ciprofloxacin and co-trimoxazole resistance associations with past UTI diagnosis are compatible with existing literature (Denheijer et al., 2013; Briongos-figuero et al., 2012), and the relationship between ciprofloxacin resistance and hospitalization could be due to a significantly increased prevalence of resistance in hospital settings (Fasugba et al., 2015).

The usage of nitrofurantoin is prevalent in the treatment of ESBL-positive UPEC. However, in uncomplicated UTI, nitrofurantoin is prescribed only (Cortes-Penfield et al., 2017; Nicolle, 2016). The rate of nitrofurantoin resistance for E.coli in the current study was 1.04 %. However, Nitrofurantoin resistance levels were stated to be 2 percent in Fagan et al. (Norway) study (Fagan et al., 2015) and 7 percent in Das et al. (USA) study (Das et al., 2009). Generally, the vast majority of isolates remained susceptible to fosfomycin and nitrofurantoin, in terms of empirical therapy. Both of these are recommended antibiotics in international recommendations for uncomplicated UTIs (over amoxicillin-clavulanate, which is assumed to have weaker effectiveness, more adverse effects, and a wider cover spectrum (Gupta et al., 2010).

It is well established that patterns of susceptibility can differ from country to country geographic regions and can change with time (Ali et al., 2016). As a result, UPEC's rate of resistance to commonly used antimicrobials has grown over the years. As we see in this study resistance rate from the year 2018 to 2019 toward trimethoprim-sulfamethoxazole increases from (42.18 % to 47.18%), cefixime (41.66 % to 48.22 %) and for augmentin (36.45 % to 40.90%) (Gupta et al., 2001). On the other hand, antimicrobial resistance among UPEC was growing in both community and hospital settings (Bonadio et al., 2001). However, carbapenems stay as the last line of treatment against infection caused by varieties of drug resistance that are strongly against the hydrolysis of beta-lactamase. The reason for the increasing antibiotic resistance identified in this study may, therefore, be linked to the inappropriate use of antibiotics (Frère & Rigali, 2016). The other is prescribing inaccurate and irrational antibiotics. Thus, over-treatment with antibiotics can lead to antibiotic resistance and increase the persistence of extended-spectrum beta-lactamase and thus increase the rate of multidrug-resistant organisms.

Our study results indicate that in postmenopausal women with positive uropathogenic Escherichia coli and type 2 diabetes UTIs are typical and occur in every 1 in 3 patients. In our research, the prevalence of UTI observed in postmenopausal women with type 2 diabetes is equivalent to a study done by (Al-Rubeaan et al., 2013) or higher than that recently reported studies (Hirji et al., 2012). In addition to the range of postmenopausal status, the number of variations in the comorbidities of patients and other variables, such as age, may explain the discrepancy. Post-menopausal loss of estrogen is related to deregulate immunity mechanisms that are required to protect against E. coli adhesion to cells in the vagina. The lack of estrogen also makes the walls thinner and reduces the ability of the urinary tract to resist bacteria. As for diabetes itself, the clinical post-menopausal status can contribute to other UTI-related problems, such as neuropathy leading to incomplete voiding of the clinical bladder and glycosuria (Funfstuck et al., 2012). Based on the results reported from this study antimicrobial stewardship program needs to be enforced to control antibiotic use and specifically decrease antibiotic resistance. Similarly, understanding of patterns of bacterial resistance in Escherichia coli is very relevant in the selection of empirical antimicrobial therapy to reduce urinary tract infection incidence.

5. CONCLUSION

A- The study revealed that uropathogenic Escherichia coli (UPEC) is the most common infectious disease in both the hospital and community settings and its affect a member of patients with different risk factors.

B- The study detects that higher rate of resistance toward commonly used antibiotics family that includes Penicillin, Cephalosporin's, Fluor quinolones, and Trimethoprim-sulfamethoxazole. These increase the development of AMR that has faced physicians with limited options to choose the correct antibiotics to treat the infections caused by MDR organisms.

C- The study also suggests that judicious use of antibiotics, proper culture, and drug susceptibility monitoring and regulation of empiric antibiotics by culture and sensitivity is global conflict-ridden in order to stop the growth of drug resistance, especially MDR, in order to limit complication associates with ESBL/MDR organisms related to urinary tract infection.

6. ACKNOWLEDGEMENTS

I take time to acknowledge the people in my life who have been supportive during this journey. First, all praise and thanks to Allah, for giving me the power, guidance, strength, and patience to complete this work.I want to express my deepest gratitude to my supervisor Dr. Mirna Fawaz and to professor Dr.Ali smaha, M.D, medical science and Dr.Ahmad Tassi for continuous guidance, detailed comments, encouragement, insightful suggestions, time, and support. I must also thank the administration of Beirut Arab University and the hospital (ALnajdi hospital) who shared in the study for their approval to conduct this research and special thanks to Dr. Nadia Fayad the director of the laboratory department and Miss. Fawazieh Najem, a supervisor at Alnajdi hospital for showing their encouragement toward conducting this research study. My continuous source of strength has been my family and friends. I am thankful for their faith and love, which inspired my ambition and passion to complete this journey.

REFERENCES

- Adamus-Białek, W., Baraniak, A., Wawszczak, M., Głuszek, S., Gad, B., Wróbel, K., & Parniewski, P. (2018). The genetic background of antibiotic resistance among clinical uropathogenic Escherichia coli strains. *Molecular Biology Reports, 45*(5), 1055-1065.
- Al-Badr, A., & Al-Shaikh, G. (2013). Recurrent urinary tract infections management in women: A review. *Sultan Qaboos University Medical Journal, 13*(3), 359.
- Ali, I., Kumar, N., Ahmed, S., & Dasti, J. I. (2014). Antibiotic resistance in uropathogenic E. coli strains isolated from non-hospitalized patients in Pakistan. *Journal of Clinical and Diagnostic Research*: *JCDR, 8*(9), DC01.
- Al-Rubeaan, K. A., Moharram, O., Al-Naqeb, D., Hassan, A., & Rafiullah, M. R. M. (2013). Prevalence of urinary tract infection and risk factors among Saudi patients with diabetes. *World Journal of Urology, 31*(3), 573-578.
- Asgin, N., & Satilmis, Ş. (2019). Which antibiotics should we prefer empirical treatment of urinary tract infections in elderly patients.*Journal of Surgery and Medicine, 3*(12), 856-860.
- Bonadio, M., Meini, M., Spitaleri, P., & Gigli, C. (2001). Current microbiological and clinical aspects of urinary tract infections. *European Urology, 40*(4), 439-445.
- Bonkat, G., Pickard, R., Bartoletti, R., Bruyère, F., Geerlings, S. E., Wagenlehner, F., & Wullt, B. (2017). EAU guidelines on urological infections. *European Association of Urology*, 22-26.
- Briongos-Figuero, L. S., Gómez-Traveso, T., Bachiller-Luque, P., Domínguez-Gil González, M., Gómez-Nieto, A., Palacios-Martín, T., & Pérez-Castrillón, J. L. (2012). Epidemiology, risk factors and comorbidity for urinary tract infections caused by extended-spectrum beta-lactamase (ESBL)-producing enterobacteria. *International Journal of Clinical Practice, 66*(9), 891-896.
- Cassini, A., Högberg, L. D., Plachouras, D., Quattrocchi, A., Hoxha, A., Simonsen, G. S., & Ouakrim, D. A. (2019). Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: A population-level modelling analysis. *The Lancet Infectious Diseases, 19*(1), 56-66.
- Centres for Disease Control and Prevention (US). (2013). Antibiotic resistance threats in the United States, 2013. Centres for Disease Control and Prevention, US Department of Health and Human Services.

- Chiotos, K., Han, J. H., & Tamma, P. D. (2016). Carbapenem-resistant Enterobacteriaceae infections in children. *Current Infectious Disease Reports, 18*(1), 2.
- Corp, I. B. M. (2013). IBM SPSS statistics for windows, version 22.0. Armonk, NY: IBM Corp.
- Cortes-Penfield, N. W., Trautner, B. W., & Jump, R. L. (2017). Urinary tract infection and asymptomatic bacteriuria in older adults. *Infectious Disease Clinics, 31*(4), 673-688.
- Coşkun, U. S. Ş., & Coşkun, G. (2015). Bir devlet hastanesinde poliklinik hastalarına ait idrar örneklerindenizole edilen genişlemiş spektrumlu Beta-Laktamaz pozitif escherichia coli suşlarının prevalans ve antibiyotik duyarlılıklarının belirlenmesi. *Kocatepe Tıp Dergisi, 16*(1), 25-30.
- Daoud, Z., & Afif, C. (2011). Escherichia coli isolated from urinary tract infections of Lebanese patients between 2000 and 2009: epidemiology and profiles of resistance. *Chemotherapy Research and Practice, 2011*.
- Das, R., Perrelli, E., Towle, V., Van Ness, P. H., & Juthani-Mehta, M. (2009). Antimicrobial susceptibility of bacteria isolated from urine samples obtained from nursing home residents. *Infection Control & Hospital Epidemiology, 30*(11), 1116-1119.
- Den Heijer, C. D., Penders, J., Donker, G. A., Bruggeman, C. A., & Stobberingh, E. E. (2013). The importance of gender-stratified antibiotic resistance surveillance of unselected uropathogens: A Dutch Nationwide Extramural Surveillance study. *PloS One, 8*(3).
- Drawz, S. M., & Bonomo, R. A. (2010). Three decades of β-lactamase inhibitors. *Clinical Microbiology Reviews, 23*(1), 160-201.
- Duman, Y., Güçlüer, N., Serİndağ, A., & Tekerekoğlu, M. S. (2010). Antimicrobial susceptibility of E. coli strains and presence of extended-spectrum beta lactamase. *Firat Tip Dergisi, 15*(4), 197-200.
- Fagan, M., Lindbæk, M., Grude, N., Reiso, H., Romøren, M., Skaare, D., & Berild, D. (2015). Antibiotic resistance patterns of bacteria causing urinary tract infections in the elderly living in nursing homes versus the elderly living at home: an observational study. *BMC Geriatrics, 15*(1), 98.
- Farajnia, S., Alikhani, M. Y., Ghotaslou, R., Naghili, B., & Nakhlband, A. (2009). Causative agents and antimicrobial susceptibilities of urinary tract infections in the northwest of Iran. *International Journal of Infectious Diseases, 13*(2), 140-144.
- Fasugba, O., Gardner, A., Mitchell, B. G., & Mnatzaganian, G. (2015). Ciprofloxacin resistance in community-and hospital-acquired Escherichia coli urinary tract infections: A systematic review and meta-analysis of observational studies. *BMC Infectious Diseases, 15*(1), 545.
- Folgori, L., Bielicki, J., Heath, P. T., & Sharland, M. (2017). Antimicrobial-resistant Gram-negative infections in neonates: burden of disease and challenges in treatment. *Current Opinion in Infectious Diseases, 30*(3), 281-288.
- Foxman, B. (2002). Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. *The American Journal of Medicine, 113*(1), 5-13.
- Foxman, B. (2010). The epidemiology of urinary tract infection. *Nature Reviews Urology, 7*(12), 653.
- Frère, J. M., & Rigali, S. (2016). The alarming increase in antibiotic-resistant bacteria. *Drug Targets Rev, 3*, 26-30.
- Fünfstück, R., Nicolle, L. E., Hanefeld, M., & Naber, K. G. (2012). Urinary tract infection in patients with diabetes mellitus. *Clinical Nephrology, 77*(1), 40.
- Gbinigie, O. A., Ordóñez-Mena, J. M., Fanshawe, T. R., Plüddemann, A., & Heneghan, C. (2018). Diagnostic value of symptoms and signs for identifying urinary tract infection in older adult outpatients: systematic review and meta-analysis. *Journal of Infection, 77*(5), 379-390.
- Ghanbari, F., Khademi, F., Saberianpour, S., Shahin, M., Ghanbari, N., Naderi, K., & Motalebi-Rad, T. (2017). An epidemiological study on the prevalence and antibiotic resistance patterns of bacteria isolated from urinary tract infections in central Iran. *Strategies, 4*(7), 12.
- Gupta, K., Hooton, T. M., & Stamm, W. E. (2001). Increasing antimicrobial resistance and the management of uncomplicated community-acquired urinary tract infections. *Annals of Internal Medicine, 135*(1), 41-50.
- Gupta, K., Hooton, T. M., Naber, K. G., Wullt, B., Colgan, R., Miller, L. G., & Soper, D. E. (2011). International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the

European Society for Microbiology and Infectious Diseases. *Clinical Infectious Diseases, 52*(5), e103-e120..

- Hoban, D. J., Lascols, C., Nicolle, L. E., Badal, R., Bouchillon, S., Hackel, M., & Hawser, S. (2012). Antimicrobial susceptibility of Enterobacteriaceae, including molecular characterization of extended-spectrum beta-lactamase–producing species, in urinary tract isolates from hospitalized patients in North America and Europe: results from the SMART study 2009–2010. *Diagnostic Microbiology and Infectious Disease*, 74(1), 62-67.
- Ibrahim, M. E., Bilal, N. E., & Hamid, M. E. (2012). Increased multi-drug resistant Escherichia coli from hospitals in Khartoum state, Sudan. *African Health Sciences, 12*(3), 368-375.
- Kaarme, J., Riedel, H., Schaal, W., Yin, H., Nevéus, T., & Melhus, Å. (2018). Rapid increase in carriage rates of Enterobacteriaceae producing extended-spectrum β-lactamases in healthy preschool children, Sweden. *Emerging Infectious Diseases, 24*(10), 1874.
- Linhares, I., Raposo, T., Rodrigues, A., & Almeida, A. (2013). Frequency and antimicrobial resistance patterns of bacteria implicated in community urinary tract infections: A ten-year surveillance study (2000–2009). *BMC Infectious Diseases, 13*(1), 19.
- Lob, S. H., Nicolle, L. E., Hoban, D. J., Kazmierczak, K. M., Badal, R. E., & Sahm, D. F. (2016). Susceptibility patterns and ESBL rates of Escherichia coli from urinary tract infections in Canada and the United States, SMART 2010–2014. *Diagnostic Microbiology and Infectious Disease, 85*(4), 459-465.
- Mahesh, E., Ramesh, D., Indumathi, V. A., Punith, K., Kirthi, R., & Anupama, H. A. (2010). Complicated urinary tract infection in a tertiary care center in South India. *Al Ameen Journal of Medical Sciences, 3*(2), 120-127.
- Nicolas-Chanoine, M. H., Bertrand, X., & Madec, J. Y. (2014). Escherichia coli ST131, an intriguing clonal group. *Clinical Microbiology Reviews, 27*(3), 543-574.
- Ochoa, S. A., Cruz-Córdova, A., Luna-Pineda, V. M., Reyes-Grajeda, J. P., Cázares-Domínguez, V., Escalona, G., & Parra-Ortega, I. (2016). Multidrug-and extensively drug-resistant uropathogenic Escherichia coli clinical strains: phylogenetic groups widely associated with integrons maintain high genetic diversity. *Frontiers in Microbiology, 7*, 2042.
- Olowe, O. A., Eniola, K. I. T., Olowe, R. A., & Olayemi, A. B. (2007). Starch paper technique is easy to detect beta lactamase detection from cases of diarrheagenic Escherichia coli in Osogbo. *Life Sci J, 4*.
- Oteo, J., Pérez-Vázquez, M., & Campos, J. (2010). Extended-spectrum β-lactamase producing Escherichia coli: changing epidemiology and clinical impact. *Current Opinion in Infectious Diseases, 23*(4), 320-326.
- Palacios-Ceña, D., Hernández-Barrera, V., Jiménez-Trujillo, I., Serrano-Urrea, R., Fernández-de-las-Peñas, C., & Carrasco-Garrido, P. (2017). Time trends in antibiotic consumption in the elderly: Ten-year follow-up of the Spanish National Health Survey and the European Health Interview Survey for Spain (2003–2014). *Plos one, 12*(11), e0185869.
- Paniagua-Contreras, G. L., Monroy-Pérez, E., Rodríguez-Moctezuma, J. R., Domínguez-Trejo, P., Vaca-Paniagua, F., & Vaca, S. (2017). Virulence factors, antibiotic resistance phenotypes and O-serogroups of Escherichia coli strains isolated from community-acquired urinary tract infection patients in Mexico. *Journal of Microbiology, Immunology and Infection, 50*(4), 478-485.
- Pitout, J. D., Laupland, K. B., Church, D. L., Menard, M. L., & Johnson, J. R. (2005). Virulence factors of Escherichia coli isolates that produce CTX-M-type extended-spectrum β-lactamases. *Antimicrobial Agents and Chemotherapy, 49(*11), 4667-4670.
- Rahn, D. D. (2008). Urinary tract infections: contemporary management. Urol Nurs, 28(5), 333-341.
- Rodríguez-Baño, J., Alcalá, J. C., Cisneros, J. M., Grill, F., Oliver, A., Horcajada, J. P., & Esteve, M. (2008). Community infections caused by extended-spectrum β-lactamase–producing Escherichia coli. *Archives of Internal Medicine, 168*(17), 1897-1902.
- Ronald, A. (2002). The etiology of urinary tract infection: traditional and emerging pathogens. *The American Journal of Medicine, 113*(1), 14-19.
- Sanchez, G. V., Adams, S. J., Baird, A. M., Master, R. N., Clark, R. B., & Bordon, J. M. (2013). Escherichia coli antimicrobial resistance increased faster among geriatric outpatients compared with adult outpatients in the USA, 2000–10. *Journal of Antimicrobial Chemotherapy, 68*(8), 1838-1841.

- Smithson, A., Chico, C., Ramos, J., Netto, C., Sanchez, M., Ruiz, J., & Bastida, M. T. (2012). Prevalence and risk factors for quinolone resistance among Escherichia coli strains isolated from males with community febrile urinary tract infection. *European Journal of Clinical Microbiology & Infectious Diseases, 31*(4), 423-430.
- Stamm, W. E., & Norrby, S. R. (2001). Urinary tract infections: disease panorama and challenges. *The Journal of Infectious Diseases, 183*(1), 1-4.
- Stewardson, A. J., Vervoort, J., Adriaenssens, N., Coenen, S., Godycki-Cwirko, M., Kowalczyk, A., & Harbarth, S. (2018). Effect of outpatient antibiotics for urinary tract infections on antimicrobial resistance among commensal Enterobacteriaceae: A multinational prospective cohort study. *Clinical Microbiology and Infection, 24*(9), 972-979.
- Tabasi, M., Karam, M. R. A., Habibi, M., Yekaninejad, M. S., & Bouzari, S. (2015). Phenotypic assays to determine virulence factors of uropathogenic Escherichia coli (UPEC) isolates and their correlation with antibiotic resistance pattern. *Osong Public Health and Research Perspectives, 6*(4), 261-268.
- Tajbakhsh, E., Tajbakhsh, S., & Khamesipour, F. (2015). Isolation and molecular detection of Gram negative bacteria causing urinary tract infection in patients referred to Shahrekord hospitals, Iran. *Iranian Red Crescent Medical Journal, 17*(5).
- Ulug, M., & Gul, I. (2012). Investigation of the Results of Urine Cultures and Approaches to Empirical Antibiotic Treatment of Community-Acquired Urinary Tract Infections in Elderly Patients. *Klimik J*, 25(2), 71-76.
- Wagenlehner, F. M., Weidner, W., & Naber, K. G. (2007). Therapy for prostatitis, with emphasis on bacterial prostatitis. *Expert Opinion on Pharmacotherapy, 8*(11), 1667-1674.