Detection of Class 1 Integron and Antibiotic Resistance of β-Lactamase-Producing *Escherichia coli* Isolated from Four Hospitals in Babylon, Iraq

Mohammed Jasim Khulaif, Alaa H. Al-Charrakh

Department of Microbiology, College of Medicine, University of Babylon, Babylon Province, Hilla, Iraq

Abstract

Background: The emergence of multidrug-resistant *Escherichia coli* is a major public health threat worldwide. **Objectives:** This study was conducted to determine the sensitivity pattern and class 1 integron of *E. coli* isolated from various clinical sources in Babylon, Iraq. **Materials and Methods:** A total of 1874 clinical samples were collected from patients between February and June 2022. Antimicrobial susceptibility of *E. coli* to different antibiotics was determined using the Vitek-2 compact system. Class 1 integron was detected genetically. **Results:** From 1874 clinical samples, 231 (12.3%) isolates belonged to *E. coli*. Isolates from urine were more frequent in females than in males. All isolates were resistant to ampicillin, amoxicillin, and amoxicillin/clavulanate. *Escherichia coli* isolates showed high sensitivity to meropenem, ertapenem, imipenem, amikacin, and isepamicin. Isolates from vaginal discharge were resistant to cephazolin, ciprofloxacin, levofloxacin, sparfloxacin, nalidixic acid, and aztreonam. Isolates from diabetic foot ulcer showed high resistance to ciprofloxacin, levofloxacin, sparfloxacin, nalidixic acid, norfloxacin, and ceftazidime. All *E. coli* isolates were multidrug-resistant (MDR) and 67% of them were extended-spectrum β-lactamase (ESBL) producers, most prevalent in urine and vaginal discharge. Approximately 99.1% of *E. coli* isolates carried class 1 integron. **Conclusions:** *Escherichia coli* isolated from various clinical specimens showed differences in antibiotic susceptibility patterns, with high resistance to commonly used antibiotics. The most effective antibiotics against *E. coli* isolates were ertapenem, imipenem, meropenem, amikacin, and isepamicin. However, MDR *E. coli* isolates showed high resistance rates to most of the antibiotics tested. ESBL-producing *E. coli* showed high prevalence. Class 1 integron is the leading cause of antibiotic resistance.

Keywords: Antibiotic resistance, class 1 integron, *E. coli*, ESBL, β-lactamase

Introduction

Escherichia coli is a gram-negative, rod-shaped bacterium that typically resides in the lower intestinal tract of humans. It is also found in hospital environments and can cause nosocomial infections.[1] *Escherichia coli* is the most common bacteria in the human gastrointestinal tract and lacks virulence in this setting. However, when found outside of the intestinal tract, *E. coli* can cause urinary tract infections (the most common pathogen leading to uncomplicated cystitis), pneumonia, bacteremia, and spontaneous bacterial peritonitis.[2,3] *Escherichia* is found most frequently in the genital tract of women. These microorganisms possess several virulence factors that allow them to cause vaginal and/or endocervical colonization and have been implicated in different infections in pregnant women, as well as in intra-amniotic, puerperal, and neonatal infections both early and late neonatal sepsis, presenting sometimes with meningitis.[4]

The increase in multidrug resistance (MDR) among pathogenic bacteria responsible for infectious diseases has led to a lack of effectiveness of some antibiotics. The

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Address for correspondence: Dr. Alaa H. Al-Charrakh, Department of Microbiology, College of Medicine, University of Babylon, Babylon Province, Hilla, Iraq.
E-mail: ahani67@gmail.com

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ability of *E. coli* to harbor resistant genes has made the treatment of infections a major challenge.[5]

Extended-spectrum β-lactamases (ESBLs) and AmpC enzymes have been observed in virtually all species of the family Enterobacteriaceae.[6] Both ESBLs and AmpC β-lactamases confer resistance to a broad spectrum of β-lactams that include penicillins and cephalosporins. But, unlike ESBLs, plasmid-encoded AmpC β-lactamases are effectively active against cephamycins and are not inhibited by a β-lactamase inhibitor such as clavulanic acid. Harboring these enzymes is usually associated with multiple antibiotic resistance (MDR) means that there are fewer antibiotic options available to treat.[7]

ESBL-producing bacteria are one of the more recent bacterial evolutions observed in the ongoing antibiotic-resistant pandemic. Since the first detection of these organisms, an increasing prevalence of ESBL-producing bacteria has been described worldwide.[5] ESBLs pose a serious therapeutic challenge to clinicians due to limited therapeutic options.[6] *Escherichia coli* and *Klebsiella pneumoniae* have been described as the two predominant groups of bacteria associated with ESBL production.[8]

Carbapenems possess broad-spectrum antibacterial activity and have a unique structure that is defined by a carbapenem coupled to a β-lactam ring which confers protection against most β-lactamases such as metallo-β-lactamase (MBL) as well as ESBLs.[9] Consequently, carbapenems are considered one of the most reliable drugs for treating bacterial infections, and the emergence and spread of resistance to these antibiotics constitute a major public health concern.[10]

Horizontal gene transfer (HGT) has an important role in spreading resistance genes among bacteria through mobile genetic elements such as plasmids, transposons, and integrons.[11] Integrons are genetic elements that are capable of integration of resistance gene cassettes in their structure and subsequently denote resistance phenotype to their bacterial host.[12] Integrons can be located within transposons or conjugated plasmids and transfer along with them, facilitating the dissemination of antibiotic-resistance genes between bacteria.[13]

This study was conducted to determine the antibiotic susceptibility pattern and class 1 integron of *E. coli* isolated from various clinical sources in Babylon province, Iraq.

Materials and Methods

Study design and patients

A cross-sectional study was accomplished in four hospitals in Babylon province: Marjan Teaching Hospital, Alamam Al-Sadeq Hospital, Al-Hilla General Teaching Hospital, and Babylon Hospital, for 5 months from February to the end of June 2022. Patients include males and females, all ages; variable samples include urine, stool, burn swabs, diabetic foot swabs, vaginal swabs, sputum, blood, ear swabs, and CSF.

Bacterial identification and antibiotic susceptibility testing

Escherichia coli isolates were initially identified by their morphological characteristics on blood agar, MacConkey, eosine Methylene blue agar, and biochemical tests based on CLSI guidelines.[14] Identification of *E. coli* was then confirmed using Vitek-2 system (bioMerieux, France). Antibiotic susceptibility testing was performed using Vitek-2 system (bioMerieux), AST GN76 kit, and Kirby–Bauer disk diffusion methods (Becton Dickinson, Germany), and interpretation was done according to CLSI guidelines.[14]

Susceptibility testing was performed on Mueller Hinton agar (bioMerieux), using overnight cultures at a 0.5 McFarland standard followed by incubation at 35°C for 16–18 h. The antimicrobial tests include ampicillin, piperacillin/tazobactam, cefazolin, cefoxitin, ceftazidime (CAZ), ceftriaxone, cefepime (PEP), ertapenem, imipenem, merpenem, amikacin, gentamicin, isepamicin, ciprofloxacin, levofloxacin, sparfloxacin, tigycycline, nitrofurantoin, trimethoprim/sulfamethoxazole, azithromycin, doxycycline, piperacillin, amoxicillin/clavulanate, aztreonam, colistin, nalidixic acid, norfloxacin, fosfomycin, and chloroamphenicol.

Phenotypic testing for β-lactamase production

Nitrocefin disk (Hardy Diagnostic, Santa Maria, California) was used for detecting β-lactamase production; nitrocefin is a chromogenic cephalosporin that changes from yellow to red when the amide bonds in the β-lactamase hydrolyzed by β-lactamase.

Phenotypic testing for AmpC β-lactamase and extended-spectrum β-lactamase

A total of 112 *E. coli* isolates were screened for phenotypic AmpC β-lactamase production by Vitek-2 compact system (bioMerieux) using ASTGN 76, depending on cefoxitin resistance. All isolates were also screened for ESBL production by recording to Virek-2 compact system using ASTGN 76 that is compatible with CLSI-recommended conditions.[14] ESBL screening also included the following criteria for *E. coli*, a PEP 1, cefotaxime (CTX) 0.5, CAZ 0.5, PEP/clavulanic acid (CA) 1/10, CTX/CA 0.5/4, CAZ/CA 0.5/4.

DNA extraction and polymerase chain reaction protocol

From pure overnight cultures, plasmid DNA templates of isolates were extracted and prepared by Plasmid Extraction Mini Kit (FAVORGEN Comp., Taiwan, Cat. Number FAPDE 100) according to the manufacturer's protocol. Concentrations and purity of DNA were determined by

NanoDrop one (Thermo Scientific NanoDrop) at 260 nm and used as a template in polymerase chain reaction (PCR) technique.

Detection of class 1 integron was performed by PCR using specific primers INT-1F 5 CAGTGGACATAAGCCTGTTC 3, INT-1R 5 CCCGAGGCATAGGCTGTA 3, with product size 160 bp. The PCR reactions were prepared in 25-µL total reaction mixture volume by comprising 12.5 µL of Taq DNA Polymerase Master Mix green (Promega, UK), primers, 2 µL (10 pmol/µL) from each one with 6 µL (50 ng) of extracted DNA, and sterile deionized water to achieve a final volume of 25 µL. The amplifications were carried out in a thermocycler (C1000 Touch, Bio-Rad), with the following conditions: initial denaturation at 95°C for 1 min, followed by 35 cycles of denaturation at 94°C for 30 s, annealing at 55°C for 40 s, and extension at 72°C for 90 s with a final extension at 72°C for 5 min.

Statistical analysis

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS) software program, version 25.0 (SPSS, IBM Company, Chicago, Illinois). Categorical variables were presented as frequencies and percentages.

Ethical approval

All subjects involved in this work are informed and the agreement was obtained verbally from each one before the collection of the samples. This study was approved by a local committee of publication ethics at Babil Health Directorate, Iraq, under reference number BMS 0322/016 on January 11, 2022.

Results

During the 5-month period, a total of 1874 clinical samples were collected from four main hospitals in Babylon province, Marjan Teaching Hospital, Al-Hilla General Teaching Hospital, Babylon Hospital, and Alamam Al-Sadeq Hospital; the number and percentage of samples from each hospital were 590 (31.5%), 189 (9.9%), 483 (25.8%), and 615 (32.8%), respectively.

The clinical sample types collected during the study period included 642 (34.3%) urine samples from patients suspected with UTIs, 422 (22.5%) burn exudate, 253 (13.5%) vaginal discharge, 240 (12.8%) sputum samples, 118 (6.3%) diabetic foot ulcer, 62 (3.3%) stool samples, 57 (3%) CSF, 53 (2.9%) blood specimens, and 27 (1.4%) ear swabs.

The distribution of *E. coli* isolates according to the origin: urine samples 118 (51.1%), burn exudate 30 (13%), and vaginal discharge 27 (11.6%) as shown in Table 1.

Escherichia coli isolates screened for production of β-lactamase by nitrocefin (chromogenic cephalosporine). The results revealed that 112 (48.5%) *E. coli* isolates were positive for nitrocefin. *Escherichia coli* isolates from vaginal discharge revealed a high percentage of 63%. The percentages for each isolates types are mentioned in Table 2.

Escherichia coli resistance to β-lactam antibiotics revealed ampicillin (100%), amoxicillin (100%), amoxicillin/CA (100%), piperacillin (99.1), ceftriaxone (78.5%), and aztreonam (67.9%), whereas the highest frequency of susceptibility was associated with meropenem (100%), ertapenem (96.5%), imipenem (95.5%), and others, as mentioned in Figure 1.

Bacteria isolated from diabetic food ulcer were resistant to cephazolin (100%), aztreonam (100%), and ceftriaxone (100%), while those isolated from vaginal discharge were resistant to cephazolin (100%), aztreonam (100%), and ceftriaxone (76.5%), as mentioned in Table 3.

Table 1: The distribution of *E. coli* according to origin

Sample types	Total *E. coli* isolates (%)
Urine	118 (51.1%)
Burn exudate	30 (13%)
Vaginal discharge	27 (11.6%)
Sputum samples	2 (0.9%)
Diabetic foot ulcer	13 (5.6%)
Stool samples	38 (16.5%)
Ear swabs	3 (1.3%)
Total	231 (100%)

Table 2: Clinical sample types and nitrocefin results

Samples types	Total *E. coli* isolate	*E. coli* produce β-lactamase (nitrocefin positive)
Urine	118	56 (47.5%)
Burn exudates	30	16 (53.3%)
Vaginal discharge	27	19 (70.4%)
Sputum samples	2	–
Diabetic foot ulcer	13	7 (53.8%)
Stool samples	38	13 (34.2%)
Ear swabs	3	1 (33.3%)
Total	231	112 (48.5%)

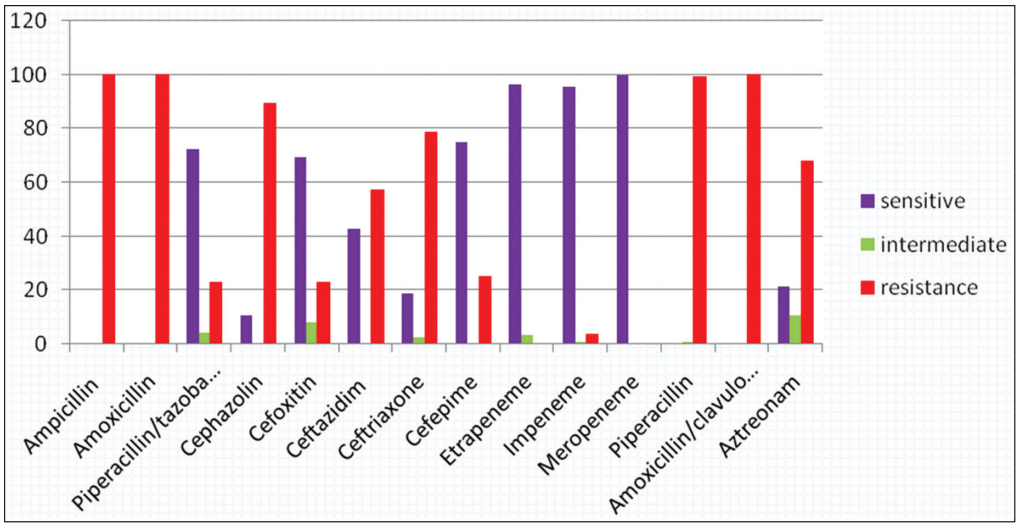

Figure 1: Antibiotics susceptibility to β-lactam drugs of *E. coli* isolate ($n = 112$)

Table 3: β-Lactam antibiotic resistance profiles of *E. coli* isolated from various clinical sources

β-Lactam antibiotics	Number of isolates recovered from clinical sources (percent (%) of resistance)					
	Urine ($N = 418$)	Burn exudate ($N = 16$)	Stool ($N = 15$)	Vaginal discharge ($N = 17$)	Diabetic foot ulcer ($N = 7$)	Ear swab ($N = 1$)
Ampicillin	56 (100)	16 (100)	15 (100)	17 (100)	7 (100)	1 (100)
Amoxicillin	56 (100)	16 (100)	15 (100)	17 (100)	7 (100)	1 (100)
Piperacillin/Tazobactam	16 (28.5)	1 (6.2)	2 (13.3)	1 (5.9)	5 (71.4)	–
Cephazolin	53 (94.6)	9 (60)	17 (100)	7 (100)	7 (100)	1 (100)
Cefoxitin	14 (25)	2 (12.5)	4 (26.7)	1 (5.9)	5 (71.4)	–
Ceftazidime	38 (67.8)	5 (31.2)	5 (33.3)	10 (58.8)	6 (85.7)	–
Ceftriaxone	52 (92.8)	11 (68.7)	4 (26.7)	13 (76.5)	7 (100)	1 (100)
Cefepime	24 (42.8)	–	–	2 (11.8)	2 (28.6)	–
Ertapenem	–	–	–	–	–	–
Imipenem	2 (3.5)	–	–	1 (5.9)	1 (14.3)	–
Meropenem	–	–	–	–	–	–
Piperacillin	56 (100)	16 (100)	15 (100)	17 (100)	7 (100)	1 (100)
Amoxicillin-clavulanate	56 (100)	16 (100)	15 (100)	17 (100)	7 (100)	1 (100)
Aztreonam	42 (75)	5 (31.2)	5 (33.3)	17 (100)	7 (100)	–

Resistance to non-β-lactam resistance includes nalidixic acid (90.5%), norfloxacin (70.5%), trimethoprim/sulfamethoxazole (68%), whereas high-rate susceptibility to tigecycline (100%), isepamicin (98.2%), amikacin (92%), nitrofurantoin (82.2%), and others, as illustrated in Figure 2.

Escherichia coli isolates recovered from vaginal discharge revealed high resistance to ciprofloxacin (100%), levofloxacin (100), sparfloxacin (100), nalidixic acid (100), and trimethoprim/sulfamethoxazole (94.1%). *Escherichia coli* was isolated from diabetic foot ulcer resistance to many antibiotics. The resistance of *E. coli* isolated from different sources to non-β-lactam antibiotics is illustrated in Table 4.

All 112 *E. coli* isolates showed MDR, 25 (22.3%) isolates were resistant to 7 classes, 24 (21.4%) isolates were resistant to 8 classes, 19 (17%) isolates were resistant to 9 classes, 8 (7.1%) isolates showed resistant to 10 classes, and 4 (3.6%) isolates were resistant to 11 classes [Table 5].

ESBL-producing *E. coli* were 75 (67%). *Escherichia coli* isolates from vaginal discharge showed the highest frequency in 14 (82.4%), whereas *E. coli* from diabetic food ulcer showed the highest frequency 1 (14.3%) among carbapenemase-producing isolates [Table 6].

PCR results for amplification and electrophoresis of class 1 integron revealed that 111 (99.1%) of β-lactamase-producing *E. coli* isolates carried class 1 integron [Figure 3].

Discussion

Trends of resistance to β-lactam antibiotics in Gram-negative bacteria isolated from clinical samples have

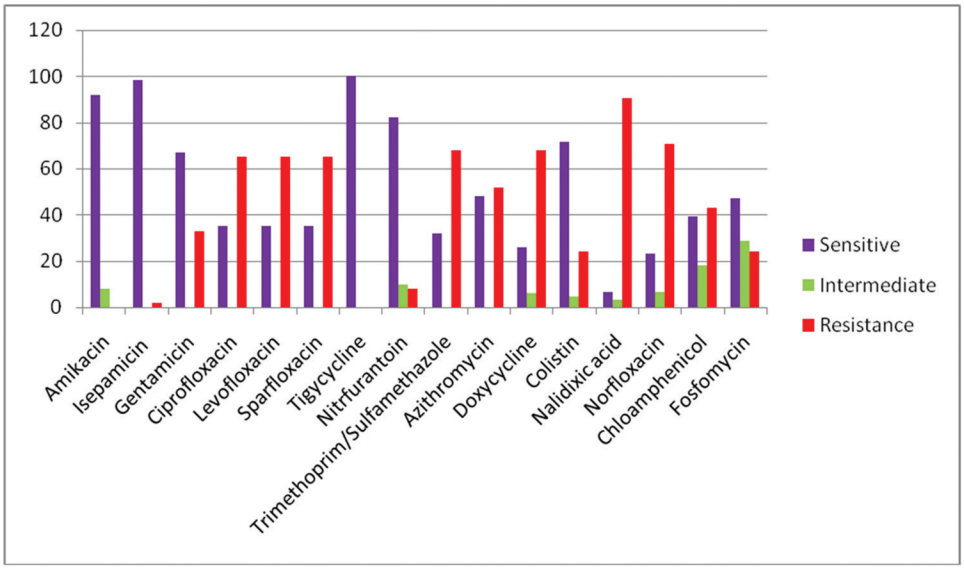

Figure 2: Antibiotics susceptibility of *E. coli* isolate (n = 112) to non-β-lactam drugs

Table 4: Non-β-lactam antibiotic resistance profiles of *E. coli* isolated from various clinical sources

Non-β-lactam antibiotics	Number of isolates recovered from clinical sources (percent (%) of resistance)					
	Urine (*N* = 56)	Burn exudate (*N* = 16)	Stool (*N* = 15)	Vaginal discharge (*N* = 17)	Diabetic foot ulcer (*N* = 7)	Ear swab (*N* = 1)
Amikacin	–	–	–	–	–	–
Isepamicin	–	–	–	–	–	–
Gentamicin	19 (33.9)	5 (31.2)	3 (20)	10 (58.8)	–	–
Ciprofloxacin	32 (57.1)	9 (56.2)	8 (53.3)	17 (100)	6 (85.7)	1 (100)
Levofloxacin	32 (57.1)	9 (56.2)	8 (53.3)	17 (100)	6 (85.7)	1 (100)
Sparfloxacin	32 (57.1)	9 (56.2)	8 (53.3)	17 (100)	6 (85.7)	1 (100)
Tigecycline	–	–	–	–	–	–
Nitrofurantoin	–	2 (12.5)	3 (20)	-	4 (57.1)	–
Trimethoprim/Sulfamethoxazole	31 (55.3)	10 (62.2)	12 (80)	16 (94.1)	6 (85.7)	1 (100)
Azithromycin	30 (53.5)	5 (31.2)	5 (33.3)	14 (82.4)	4 (57.1)	–
Doxycycline	45 (80.3)	10 (62.2)	7 (46.7)	12 (70.6)	2 (28.6)	–
Colistin	9 (16.0)	6 (37.5)	3 (20)	5 (29.4)	4 (57.2)	–
Nalidixic acid	50 (89.3)	15 (93.7)	13 (86.7)	17 (100)	6 (85.7)	–
Norfloxacin	38 (67.8)	12 (56.2)	10 (66.7)	12 (70.6)	6 (85.7)	–
Chloroamphenicol	22 (39.3)	9 (75)	6 (40)	6 (35.3)	5 (71.4)	–
Fosfomycin	21 (37.5)	3 (18.7)	3 (20)	–	–	–

Table 5: Frequency of MDR *E. coli* isolates from various origins to different antibiotic classes

Samples types	MDR									Total
	Number of classes									
	3 cl.	4 cl.	5 cl.	6 cl.	7 cl.	8 cl.	9 cl.	10 cl	11 cl.	
Urine samples	–	1	6	12	8	13	10	4	2	56
Stool samples	–	1	3	-	2	3	2	1	1	13
Vaginal discharge	–	–	1	2	6	5	2	2	1	19
Burn exudate	1	–	3	1	8	2	–	1	–	16
Diabetic foot ulcer	–	–	–	1	–	1	5	–	–	7
Ear swabs	–	–	–	–	1	–	–	–	–	1
Total	1 (0.9%)	2 (1.8%)	13 (11.5%)	16 (14.3%)	25 (22.3%)	24 (21.4%)	19 (17%)	8 (7.1%)	4 (3.6%)	112

Table 6: Frequency of ESBL and carbapenemase-producing *E. coli* isolated from various origins

Samples types	Total no.	No. (%) of ESBL-producing isolates	No. (%) of carbapenemase-producing isolates
Urine	56	45 (80.4%)	2 (3.6%)
Burn exudates	16	10 (62.5%)	–
Vaginal discharge	17	14 (82.4%)	1 (5.9%)
Sputum samples	–		
Diabetic food ulcer	7	2 (28.6%)	1 (14.3%)
Stool samples	15	3 (20%)	–
Ear swabs	1	1 (100%)	–
Total	112	75 (67%)	4 (3.6%)

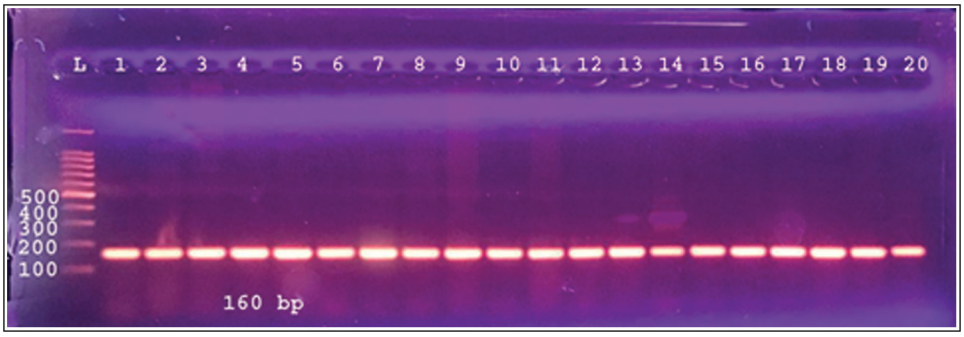

Figure 3: 1.5% Agarose gel with red-safe stained of monoplex PCR-amplified product from extract DNA of *E. coli* isolates with class 1 integron (*intI1*) gene primer. The electrophoresis was performed at 65 V for 120 min. Lane (L) is a DNA molecular size marker (1000 bp ladder). Lanes 1–20 show positive results with *intI-1* gene (160 bp)

increased over recent years.[7] Production of β-lactamase enzymes such as AmpC and ESBLs is among the main mechanisms for resistance expanded-spectrum cephalosporins.[15,16] Nitrocefin is used as substrate for the rapid and quantitative detection of β-lactamase-producing *E. coli*.[14] In this study, out of 231 *E. coli* clinical isolates, 112 (48.5%) isolates produced β-lactamases (nitrocefin positive). This result is compatible with resistance to β-lactam antibiotics that found each *E. coli* isolate positive to nitrocefin was resistant to one or more β-lactam antibiotics.

In this study, the results of antibiotic resistance of *E. coli* isolates to β-lactam drugs revealed that isolates were resistant to ampicillin (100%), amoxicillin (100%), piperacillin (99.1%), amoxicillinclavulanate (100%), cephazolin (89.3%), ceftriaxone (78.5), and aztreonam (67.9%) [Figure 1]. Regarding the antibiotic resistance of the isolates to non-β-lactam drugs, the results revealed that isolates were resistant to nalidixic acid (90.5%), norfloxacin (70.5%), trimethoprim–sulfamethoxazole (68%), doxycycline (67.8%), and ciprofloxacin (65%) [Figure 2].

A study reported in Iran was consistent with our study which found that clinical *E. coli* isolates were resistant to ampicillin (100%), ciprofloxacin (61.7%), and ceftriaxone (85.1%).[17] Naqid *et al.*[18] in Duhok city, Kurdistan region of Iraq, reported that ampicillin resistance was 88.3%.

Resistance to ceftriaxone in this study was compatible with several authors worldwide[17-25]; Medugu *et al.*[19] revealed that *E. coli* isolates were resistant to ceftriaxone (80.4%), whereas Bahramian *et al.*[17] from Iran reported that the resistance rate to ceftriaxone was 85.1%.

Jain *et al.*[26] in Bangladesh reported *E. coli* resistance to amoxicillin (98%) and resistance to amoxicillin-clavulanate. Khatun *et al.*[27] from Bangladesh reported 75% of *E. coli* isolates were resistant to amoxicillin-clavulanate. The high resistance rate to this antibiotic in Khatum *et al.*'s study was nearly compatible with the results in our study.

Liu and Liu[28] revealed that *E. coli* resistance to carbapenem antibiotics including meropenem, ertapenem, and imipenem in this study because high stability of these drugs against β-lactamase and reported that there is no resistance to imipenem (0%). Halaji *et al.*[29] revealed that *E. coli* resistance to imipenem and meropenem (0%) is consistent with our study, but Lin *et al.*[30] found that *E. coli* resistance to meropenem, ertapenem, and imipenem were 81.5%, 100%, and 72.2%, respectively, and they also found that no resistance was detected against tigecycline, as in our study. There was resistance to trimethoprim–sulfamethoxazole (77.8%), fosfomycin (22.2%), gentamicin (40.7%), amikacin (11.1%), and aztreonam (66.7%), all these results were consistent with our study. Khatun *et al.*[27] revealed that 70% of *E. coli* isolates were resistant to ciprofloxacin, relatively similar to our study.

Escherichia coli isolated from vaginal discharge were more resistant to antibiotics than the other types of clinical

samples, as mentioned in Tables 4 and 5. Several studies in Iraq reported that vaginal *E. coli* was resistant to ampicillin, ceftriaxone, trimethoprim/sulfamethoxazole, and cephazolin.[31-33] Atia[34] in Libya reported that *E. coli* isolated from vagina were sensitive to more antibiotics and no resistance was detected for ceftriaxone, ciprofloxacin, and gentamicin; in contrast with our study, there was resistance to ceftriaxone (76.5%), ciprofloxacin (100%), and gentamicin (58.8%).

Escherichia coli isolated from diabetic food ulcer showed high resistance to several antibiotics as shown in Tables 3 and 4; a study in Ethiopia for *E. coli* isolated from diabetic foot ulcer reported high resistance to cephalosporins, doxycycline, and trimethoprim/sulfamethoprim,[35] Shi *et al.*[36] in China reported moderate resistance to several antibiotics in contrast with our study which showed high resistance (100%) to cefazolin, ceftriaxone, aztreonam, and 85.7% for ciprofloxacin, nalidixic acid, and norfloxacin.

This study showed a high prevalence of class 1 integron among *E. coli* isolates. This result was consistent with several authors, who found that class 1 integron-associated gene cassettes were predominant among *E. coli* strains.[37,38]

Conclusions

Escherichia coli isolated from various clinical specimens showed differences in antibiotic susceptibility patterns, with high resistance to commonly used antibiotics. The most effective antibiotics against *E. coli* isolates were ertapenem, imipenem, meropenem, amikacin, and isepamicin. However, the clinical isolates of *E. coli* showed high resistance rates to ampicillin, amoxicillin, piperacillin, nalidixic acid, ceftriaxone, cephazolin, and piperacillin/clavulanate. ESBL-producing *E. coli* isolates showed high prevalence (67%). Class 1 integron is the leading cause of antibiotic resistance.

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Conflicts of interest
There are no conflicts of interest.

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