PREVALENCE OF EXTENDED SPECTRUM ß-LACTAMASE PRODUCING *E. COLI* ISOLATED FROM IN-PATIENTS AND OUT-PATIENTS IN ZAGAZIG UNIVERSITY HOSPITALS

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Abstract

This study was done on 143 patients (75 in-patients and 68 out-patients) in Zagazig University Hospitals who were suspected to have urinary tract infections (UTIs). Their ages ranged from 12 to 61years. One hundred and twenty four of urine samples that collected from patients yielded positive culture on MacConkey's agar. The identification of isolates was done by biochemical tests and confirmed by automated Vitek 2 system. The results showed that *E. coli* was the most causative organisms of UTIs 44 isolates (35.4%). Antimicrobial susceptibility test by modified Kirby-Bauer disc diffusion method was performed to select multi drugs resistant (*ESβL*) production according to the Clinical and Laboratory Standards Institute (CLSI) recommendation. The PCR technique was applied to detect the *ESβL* genes that responsible for the resistance, it was found that the *TEM* gene was the predominate gene (100%) amongst *ESβL E. coli* followed by *SHV* (90%) but *CTX-M* gene was absent. The coexistence of more than one type of β-lactamase enzymes was detected and represented (30%) of *ESβL E. coli*. From these results we can concluded that the Prevalence of *ESβL* producing *E. coli was* (22.7%) among *E. coli* isolates. *TEM* and *SHV* genes were the most frequent genes and the coexistence of *ESβL*, *AmpC*, *OXA-1* was detected in (30%) of isolates.

Keywords: *ESBL*, UTI, *E. coli*.

Introduction

Urinary tract infections (UTIs) are the most common human bacterial infections. Each year about 150 million people developed UTIs [1]. UTI

clinically identified as a bacterial colonization on any part of the urinary tract, including the kidneys, ureters, bladder, or urethra.

The organisms that known to cause UTIs, including *Pseudomonas aeruginosa*, *Staphylococcus saprophyticus*, *Enterococcus spp.*, *Proteus mirabilis*, *Klebsiella spp*., *Citrobacter spp* and *E.coli* is considered as the most common causative agent [2, 3, 4].

E. coli is an enteric Gram-negative bacillus found in the large intestine of all healthy individuals, Uropathogenic *E. coli* (UPEC) are certain serogroups of *E. coli* which capable of adhering and colonizing to the urinary tract. It differed from commensals by the presence of special virulence factors, involving adhesins and toxins, which improved their ability to cause infection and evade host responses. About75-95% of all cases of uncomplicated cystitis and pyelonephritis are caused by UPEC [5].

Extended spectrum β-lactamase (*ESβL*) enzymes are usually plasmid-mediated, have the ability to hydrolyze, inactivate a wide variety of β-lactams, including third-generation cephalosporins, penicillins and aztreonam [6]. These enzymes are sensitive to β-lactamase inhibitors such as clavulanate, sulbactam and tazobactam [7, 8].

Many *ESBL* encoding plasmids also carry genes which encode resistance to other classes of antibiotics such as fluoroquinolones, aminoglycosides and sulfonamides [9]. Such resistances minimizing the probabilities of selection of applicable drug [10].

Defeat in detection of *ESβL* -mediated resistance represented a disaster as it leads to treatment failure, an increase in hospital costs, length of stay, and patient mortality [11].

The present study aims to determine the prevalence of *ESβL* producing *E. coli* isolated from in-patients and out patients in Zagazig University Hospitals and extend to detect *ESβL* genes among *E. coli* isolates.

Materials and Methods

Sample collection and *E. coli* identification

Urine samples were collected from in-patients and out-patients in Urology Department, Intensive Care Unit and External lab of Zagazig University Hospitals during the period from March 2015 to February 2016, who were suspected to have UTIs. A total of 143 specimens were cultured on MacConkey's agar to specify lactose fermenters and non-lactose fermenters isolates then the lactose fermenters isolates recultured on EMB media to differentiates between *E. coli* and *Klebsiella*. Finally, *E. coli* isolates were identified manually by biochemical tests and automatically by vitek® 2 system.

Antimicrobial susceptibility test

Antimicrobial susceptibility was determined using th**e** Kirby-Bauer disc diffusion method [12] that modified by the Clinical and Laboratory Standards Institute (CLSI) [13]. The antibiotic disks used were β-Lactams: Amoxicillin, Amoxicillin / Clavulanate (20/10 µg), Ceftriaxone (30 µg), Ceftazidime (30 µg), Aztreonam (30 µg), Imipenem (10 µg), Meropenem (10 µg). Aminoglycosides: Amikacin (30 µg), Gentamicin (30 µg). Quinolones: Ciprofloxacin (5 µg). Others: Nitrofurantoin (300 µg), Trimethoprim / Sulfamethoxazole (1.25/23.75 µg)**.**

Detection of Extended Spectrum β-lactamases

Phenotypic studies

A) Screening for *ESβL* production using Disc Diffusion method

This screening method is based on measuring the specific zone diameters for the antibiotic discs cefpodoxime (CPD, 10 µg), ceftazidime (CAZ, 30 µg), aztreonam (ATM, 30 µg), ceftriaxone (CRO, 30 µg) and cefotaxime (CTX, 30 µg). CLSI recommends a zone diameter of ≤ 17 mm for cefpodoxime, ≤ 22 mm for ceftazidime, ≤ 27 mm for aztreonam, ≤ 25 mm for ceftriaxone and ≤ 27 mm for cefotaxime. [14]. When the most of these diameters were obtained, this indicated suspected *ESβL* production; there after a phenotypic confirmation test was done to ensure the diagnosis [14].

B) Phenotypic confirmatory tests for *ESβL* production

1- Combined disc method

Cephalosporin / clavulante combination discs were used to confirm the suspected *ESβL* strains by the combination discs diffusion method. [15]. Briefly, the overnight growth in broth of Gram negative bacteria was adjusted to 0.5 McFarland Standard. By using a sterilized cotton swab the bacterial suspension was spread on Muller Hinton agar (Oxoid, UK). After incubation at room temperature for 15 min, four discs were placed on the plates: Ceftazidime (30 µg), ceftazidime / clavulanic acid (30/10 µg), cefotaxime (30 µg), cefotaxime / clavulanic acid (30/10 µg). An increase in zone size > 5 mm than zone size once tested alone was accepted as confirmation of *ESβL* production.

2- *ESβL* -E-test

The *ESβL* -E-Test strips were obtained from (Liofilchem) including ceftazidime / ceftazidime + clavulanic acid (CAZ/CAL) and cefotaxime and cefotaxime + clavulanic acid (CTX/CTL) in accordance with the manufacturer's instructions. One end of each strip contains a gradient concentration of either ceftazidime (CAZ) (MIC range 0.5 to 32 µg/ml) or cefotaxime (CTX) (MIC range of 0.25 µg to 16 µg). The other end of the strip with a gradient of ceftazidime plus a constant concentration of clavulanate

CAZ/CAL (0.064-4 µg/ml plus 4 µg/ml of clavulanic acid) or with a gradient of cefotaxime plus a constant concentration of clavulanate CTX/CTL (0.25 µg- 16 µg plus 4 µg of clavulanic acid) [16, 17] .After overnight growth, the organism was emulsified in saline solution to a turbidity of 0.5 McFarland standard. The suspension was spread on a Muller Hinton agar plate with a cotton swab. The plates were left for 5-15 min to dry, then the E-Test strips were placed on them and incubated at 35˚C for 18 h. According to the manufacturer, if the ceftazidime (CAZ) MIC/ceftazidime clavulanic acid (CAL) MIC ratio and the ratio for cefotaxime (CTX) MIC/cefotaxime clavulanic acid (CTL) MIC ≥ 8 indicates the presence of *ESβL*. Also, the presence of an *ESβL* is confirmed either by the appearance of a phantom zone or deformation of the cefotaxime or ceftazidime ellipse or when the MIC of cefotaxime or ceftazidime is reduced by $\geq 3\log_2$ dilutions in the presence of clavulanic acid.

Molecular studies

Molecular studies were done in the Animal Health Research Institute in GIZA for determination of the genetic type of β-lactamase by polymerase chain reaction (PCR). All phenotypically confirmed *ESBL* producing strains were investigated to determine the probable type of β-lactamase enzyme which was responsible for resistance. According to QIAprep Spin Miniprep kits hand book, the extraction of plasmid DNA was done as follows, the pelleted bacterial cells were resuspended in 250 µl Buffer P1 then they were transfered to a microcentrifuge tube. 250 µl Buffer P2 was added and the tube was gently inverted 4-6 times to mix. After this 350 µl buffer N3 was added and the tube was inverted immediately but gently 4-6 times then centrifuged for 10 min at 13,000 rpm (~17,900 x g) in a table-top microcentrifuge, the supernatants were applied to the QIAprep spin column by decanting or pipetting, then centrifuged for 30–60 sec.

The flow-through was discarded and the QIAprep spin column was washed by adding 0.5 ml buffer PB and centrifuged for 30-60 sec.the last step was repeated but by using of 0.75 ml Buffer PE, centrifuged for 30–60 sec, the flow-through was discarded, and centrifuged for an additional 1 min. to remove residual wash buffer. Finally, the QIAprep column was placed in a clean 1.5 ml microcentrifuge tube. To elute DNA, 50 µl Buffer EB(10 m MTris·Cl, pH 8.5) was added or water to the center of each QIAprep spin column, let stand for 1 min., and centrifuge for 1 min after extraction step preparation of PCR master mix occured according to Emerald Amp GT PCR mastermix (Takara) Code No. RR310A, The cycling conditions of the primers during cPCR [18, 19, 20, 21] . according to specific authors and Emerald Amp GT PCR mastermix (Takara) kit. [22].

Then the ladder was mixed gently by pipetting up and down. 6 µl of the required ladder were directly loaded. Finally, Agarose gel electrophoreses were prepared [22].

Results

Out of one hundred and forty three urine samples collected from patients suspected to have UTIs at Zagazig University Hospitals, One hundred and twenty four of urine samples showed positive growth on MacConkey agar, included 60 samples from in-patients and 64 from out-patients, the patients involved 76 females and 48 males. After the detection of cultured organisms, *E. coli* was represented (35.4%), *Klebsiella* was represented (30.6%) and other non-lactose fermented organisms were represented (33.8%). Among 44 *E. coli* isolates 20 isolates (33.33%) were obtained from UTI in-patients and 24 isolates (37.5%) from UTI out-patients. The distribution of urinary isolates among in-patients and out-patients in Zagazig Hospitals are shown in the Table (1).

Antimicrobial susceptibility test

Antibiotics sensitivity of *E. coli* isolates showed that the isolates were mostly sensitive to Meropenem and Imipenem (97.7%), while they were sensitive to Cefotaxime (63.7%), Ceftazidime, Gentamicin, Trimethoprim/ Sulfamethoxazole (56.8%), Nitrofurantoin (50%), Ceftriaxone (43.1%), Amoxicillin/ Clavulanate (36.3%) and Ciprofloxacin (20.4%).

Screening of ESBL production

Preliminary screening tests showed that 27.2% (12/44) of *E. coli* isolates were potential *ESβL* producers. Confirmatory tests (Combined Disc method and *ESβL*-E-Test) were carried out to confirm the production of *ESβL* (Figuers1, 2). Results confirmed that 83.3% (10/12) of *E. coli* isolates were *ESBL* producers.

Determination of the genotype of β-lactamase by PCR

All confirmatory screened isolates were analyzed by PCR to determine the probable type of *ESβL* gene which is responsible for resistance. It was found that *TEM* gene was the mostly distributed genes among *E. coli* isolates (100%) as shown in Figure (3a), while *SHV* gene was (90%) as shown in Figure (3b) and *CTX-M* was abscent as shown in Figure (3c).

Three isolates exhibited resistance to combination of cephalosporine with clavulanic acid and by PCR analysis it was found that all of three isolates contained *DHA* and *OXA-1*, two of them contained *CIT* where no one contained *FOX* as shown in Figure (3d). Only one isolate was resistant to carbapenem group included (impenem and meropenem) and the PCR analysis

demonstrated that this isolate contained KPC and NDM and VIM as shown in Figure (3e).

The present results showed that all strains produced more than one type of β-lactamase expect isolate no (59) that produced only *TEM* enzyme while there were nine strains produced both enzymes *TEM* and *SHV* (90%), two of them produced *TEM*, *SHV*, *OXA-1*, *DHA* and *CIT* enzymes (20%), only one strain produced *TEM*, *SHV*, *OXA-1*, *DHA*, *NDM*, *VIM*, *KPC* enzymes (10%) as shown in Table (2).

Table (1) Distribution of urinary isolates among in-patients and out-patients in Zagazig Hospitals.

Isolates (n=124)	In-patients (n=60)	Out-patients (n=64)
E. coli (n=44)	20 (33.3 %)	24 (37.5 %)
Klebsiella (n=38)	21 (35.0 %)	17 (26.56%)
Non–lactose fermented organisms (n=42)	19 (31.66 %)	23(35.9%)

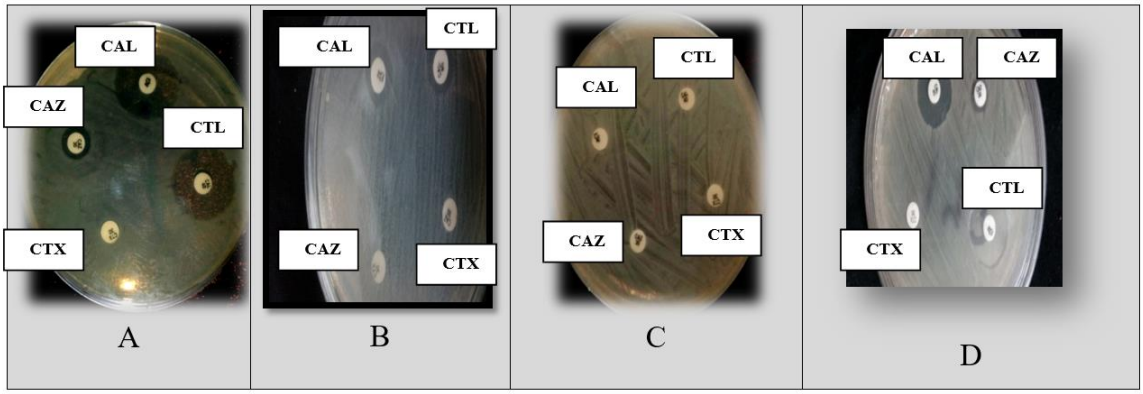


Fig. (1) Combined disc method, CTX) cefotaxime, (CTL) cefotaxime/clavulanate. (CAZ) ceftazidime, (CAL) ceftazidime/clavulanate, (R; resistant). A: showed isolate no (142).{CTX; R, CAZ; 1.4, CTL; 2.4, CAL; 1.9}, B: showed isolate no (121) {CTX; R, CAZ; R, CTL; 1.8, CAL; 1.7}, Combined disc method, C: showed isolate no (92).{CTX; R, CAZ; R, CTL; R, CAL; R}, D: showed isolate no (102) {CTX; R, CAZ; 1, CTL; 1.8, CAL;1.7}.

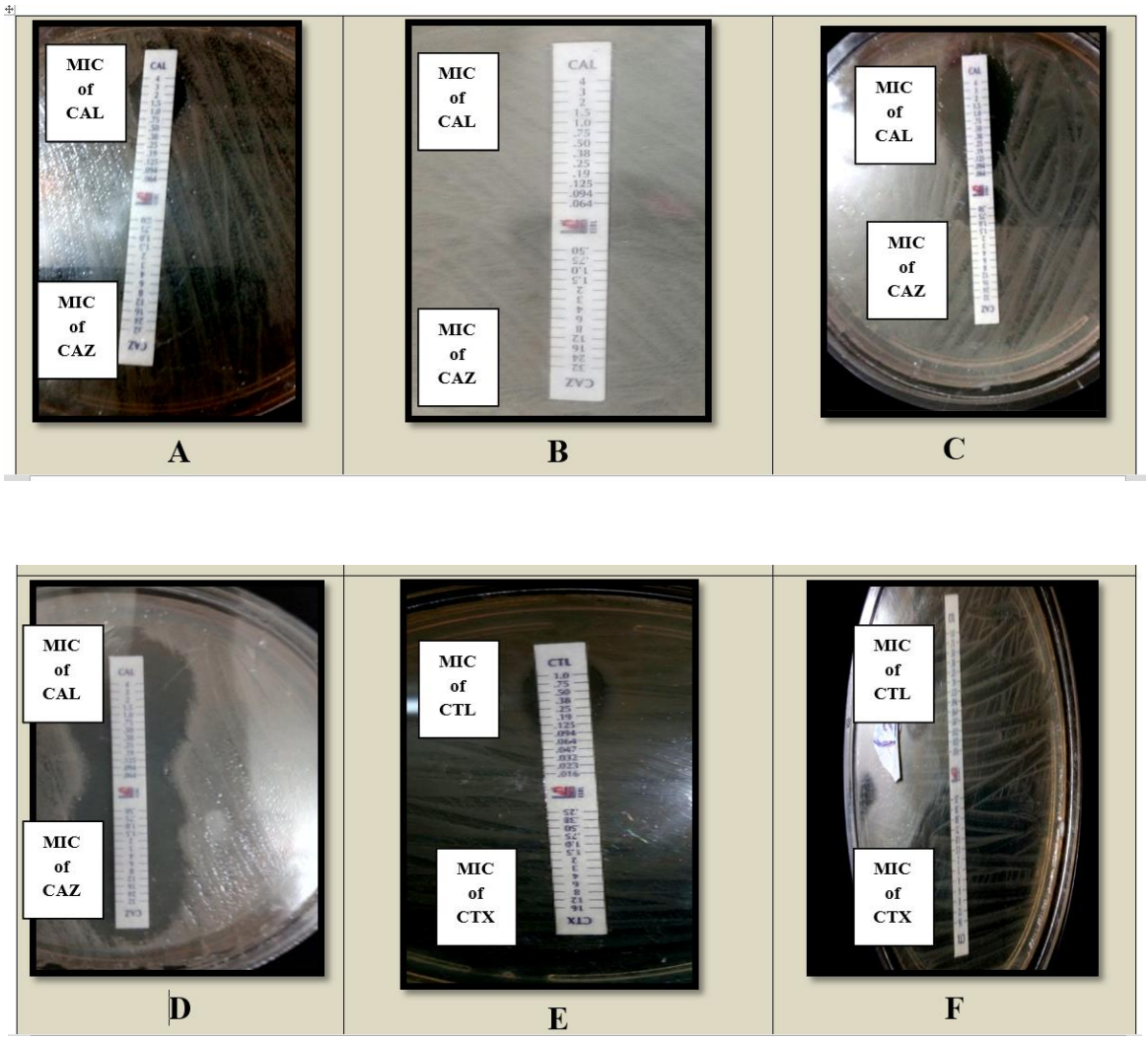
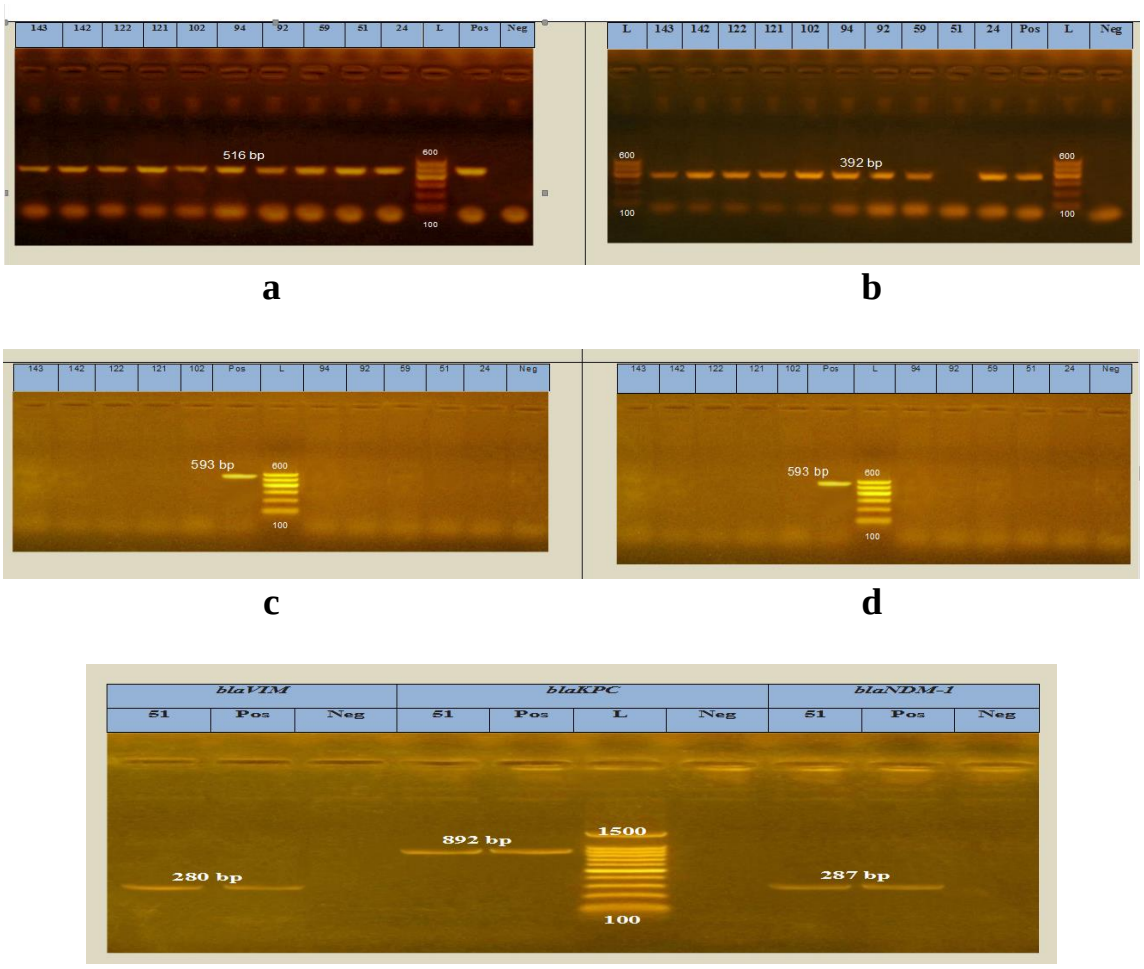


Fig. (2) *ESβL* -E-Test method (MIC and MIC ratio of CAZ, CAL). A: showed isolate no (122), {CAZ; >32 and CAZ/CAL;>42}, B: showed isolate no (143), {CAZ; >32 and CAZ/CAL; ND}, C: showed isolate no (59), {CAZ; appearance of around zone }, D: showed isolate no (24), {CAZ; appearance of deformation of the CAZ ellipse}, E: showed isolate no (59), {CTX; >16 and CAZ/CAL;>170}, F: showed isolate no (122), {CTX; >16 and CTX/CTL; ND}



a **b**

c **d**

e

Fig. (3) Agarose gel electrophoresis of amplified DNA of (a) bla *TEM*, (b) bla *SHV*, (c) bla *CTX*, (d) bla *CIT*, *DHA*, *FOX* and *OXA-1* and (e) bla *KPC*, *VIM* and *NDM-1*.

Table (2): Incidence of the bla genes among *E. coli* isolates.

I	*TEM*	*SHV*	*CTX*	*CIT*	*DHA*	*FOX*	*OXA-1*	*KPC*	*VIM*	*NDM*	No of Genes
24	+	+	-	-	-	-	-	-	-	-	2
51	+	+	-	-	+	-	+	+	+	+	7
59	+	-	-	-	-	-	-	-	-	-	1
92	+	+	-	+	+	-	+	-	-	-	5
94	+	+	-	-	-	-	-	-	-	-	2
102	+	+	-	-	-	-	-	-	-	-	2
121	+	+	-	-	-	-	-	-	-	-	2
122	+	+	-	-	-	-	-	-	-	-	2
142	+	+	-	-	-	-	-	-	-	-	2
143	+	+	-	+	+	-	+	-	-	-	5

Discussion

Urinary tract infections (UTIs) influence a large proportion of the human population. Every year regarding 150 million people worldwide develop UTI. [1, 23]. As UTIs are common conditions in the world and therefore the manner of antimicrobial resistance varies in several regions, this lead to increase the necessity for research on bacterial drug resistance day by day. The transfer of drug resistance among bacterial strains creates issues within the treatment of bacterial diseases. The increasing resistance pattern to a drug creates pressure to switch to a different more potent drug as prescription. It is also mentionable that just as drug resistance is mainly an acquired property; it can also be lost in course of time. This explain why the resistance manner of some drugs towards a particular infectious agent shows rises and downfalls with course of time. Therefore, vigil is required in screening the drug resistance pattern of various antibiotics that ought to be a continual method [24].

There are several organisms known to cause UTIs, including *Pseudomonas aeruginosa*, *Staphylococcus saprophyticus*, *Enterococcus spp.*, *Proteus mirabilis*, *Klebsiella spp.*, *Citrobacter spp.*, and the most importantly *E. coli*.

The present study concluded that the lactose fermenters *E. coli* and *Klebsiella* were the most common pathogens causing UTIs by (66.1%) while non-lactose fermenters by (33.8%). This result is in accordance with the observation of other studies from different parts of worldwide which announced that the lactose fermenters *E. coli* and *Klebsiella* were the most causative pathogens associated with UTIs [25, 26]. Our results were supported also by those results that obtained by Akram *et al* [27], who found that non-lactose fermenters were the least dominant uropathogens causing UTIs.

Through the biochemical and morphological tests that administrated to detect the causative uropathogens we found that *E. coli* was the dominant organism 44(35.8%) among the isolates. These results were in agreement with these obtained from alternative studies conducted worldwide which approved that *E. coli* is the major pathogen that cause UTIs[28, 29]. And in accordance with many previous studies conducted in Bangladesh those also considered *E. coli* to be the most prevalent pathogen associated with UTI [30, 31]. This could as a result of *E. coli* is amajor normal flora in the gut however within the presence of poor hygiene will lead to cross contamination and then urinary tract infection. UTIs are usually caused by UPEC strains which accounts for around 90% of all UTIs [32].

E coli causes several infections and is frequently associated with urinary tract infections in both nosocomial and community settings [27, 33]. In the present study the leading pathogens of UTIs among out-patients were *E. coli* 36.9% and *K. pneumoniae* 26.1%. These results were nearly matching with the

results of North American Urinary Tract Infection Collaborative Alliance (NAUTICA) [3], which approved that the common pathogen causing community settings was *E. coli* 57.5% followed by *K. pneumoniae* 23.5%. on the other hand, we found that the leading pathogen causing UTIs among in-patients was *K. pneumoniae* (35.6%) which, outnumbered *E. coli* (33.8%) for overall prevalence of nosocomial UTI. These results were compatible with what was observed by Taher and Ali [34] in Iran who found that the rate for *K. pneumoniae* 46% and *E. coli* 25%, and also similar to Mirsalehian *et al*. [35]. Who reported that the rate of nosocomial UTI caused by *K. pneumoniae* was 36.66% which was higher than those caused by *E. coli* 20%.

Antimicrobial therapy remains the standard treatment for UTIs, and therefore the most active of those agents being third-generation cephalosporins and carbapenem drugs [36]. However, the worldwide emergence of *ESβL*, *AmpC* β-lactamases and carbapenemase producing *E. coli* poses a great challenge for the clinical therapy of infections caused by these organisms leading to increased morbidity and mortality [36, 37]. The prompt detection of those multi-resistant organisms eventually enhances patient diagnosis and limits potential abuse of antimicrobial agents [36].

In the present study the preliminary screening of ESBL production led to 12 isolates that were suspected as ESBL producer and by using of confirmation methods including combined disc diffusion and E-tests methods and we found that about 10 isolates (83%) were *ESβL* producer.

The results also showed that there were 7 isolates that inhibited by the combination of cephalosporine with clavulanic acid but the isolates that resistant to this combination were suspected as *ESβL* and *AmpC* co-producer. As, Clavulanic acid may induce expression of high-level *AmpC* production and may then antagonize rather than protect the antibacterial activity of the partner β-lactam [38]. Thus, the presence of an ESBL can be masked by the expression of an AmpC-type enzyme in the same strain (by masking any synergy with *ESβL*) [39].

During this work the results that were obtained by using the Combined Disc method were similar to that revealed by using E-tests method expect in isolates no 102, 121. As, those isolates responded to the inhibition with combined disc of cefotaxime with clavulanic acid and provide no reaction with E-tests strips which contained MIC cefotaxime with clavulanic it might occur due to the concentration gradient is not as extensive as that recommended by CLSI, they yield more inconclusive results than CLSI phenotypic confirmatory test.

These findings showed that TEM (100%) gene predominated, the *SHV* (90%) and *CTX-M* not detected. These genes responsible for *ESβL* production. These results are in accordance with the results of a study that obtained by Yazdi *et*

al. [40]. who found that *TEM* was 87.1% and *SHV* was 70.6%. On other hands, our results were disagreed with those results of Eftekhar *et al* [41] study, which suggested that *SHV* percentage (43.1%) exceeded that of *TEM* (35.2%), and also in contrast with the results declared by Shahid *et al* [42], in which *CTX-M* (28.8%) exceeded SHV (13.7%), and the results obtained by Ahmed *et al* [43], which found that *CTX-M* exceeded *TEM*., and also contrasted with previous research from North Palestine, which accounted that the occurance of *CTX-M*-type and *TEM*-type *ESβL* was 100% and 32%, respectively, among *ESβL* -producing *E. coli* detected by PCR [44].

Several alternative studies performed throughout the world demonstrated variable results. The differences between our study results and those of other authors indicated that the prevalence and type of *ESβL* genes may vary from one geographical region to another. or may be due to different races in different studies. [45].

In this study detection of *OXA-1* and *AmpC* β-lactamases genes among the isolates showed that the *DHA*, *OXA-1* are the predominant genes followed by *CIT* subtype of *AmpC* genes Whereas, several other studies from various parts of the world announced the presence of different subtypes among isolates of *E. coli* [46, 47].

In this work the co-production of both *AmpC* and *ESβL* in the isolates was observed. It was represented by 30% of all isolates which in contrasted with the study by Mathur *et al* [48] who found that the co-production was 1.25%. The coexistence of different classes of β-lactamases in a single bacterial pathogen may pose treatment challenges, and this will seriously restricted treatment options. In addition, may pose diagnostic challenge, such as high-level expression of *AmpC* β-lactamases may prevent the recognition of the *ESβL*, it may lead to the using of an unsuitable antimicrobial therapy and the result may be fatal [49]. The expression of both *AmpC* β-lactamases and *ESβL* enzymes in a single isolate decreases the efficacyof the β-lactam/β-lactamase inhibitor combinations [50].

It was observed through this work that ESBL isolates were significantly associated with carbapenemase producers. Notably, one of *E. coli* isolates (10%) co-expressed *ESβL* and carbapenemases. The co-existence of different *ESβL* enzymes in *E. coli* isolates has similarly been declared elsewhere, such as in Taiwan (40.6%). Infections with such highly resistant organisms may lead in repeated hospitalization or increase the mortality. Hence, it is basic to apply better screening conventions to detect these isolates and to devise an exact treatment policy for patient at high risk of infection by such isolates [51].

Results also, revealed that the rate of *ESβL* producing *E coli* was 22.7% that consistent with the findings of other studies which showed low rates of *ESβL*

producing *E coli* that have been reported within the Middle East 12%in Turkey, 11.7% in Kuwait, 16.8% in Lebanon and 33.3% in Iran [52, 53, 54, 55]. On other hand results of study in China showed that 55% of *E. coli* isolates were *ESβL* positive [56].

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دراسة مدى إنتشار بكتيريا الإيشيريشيا كولاى ذات الطيف الممتد المقاومة للمضادات الحيوية والمعزولة من مرضى سريريين وخارجيين فى مستشفيات جامعة الزقازيق

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أُجريت هذه الدراسة على 143 مريضاً منهم75مريضا بالقسم الداخلى و 68 مريضاَ من المترددين على العيادات الخارجية بمستشفيات جامعة الزقازيق والتى تتراوح أعمارهم بين 12الى 61 عاماَ وقد تم عمل مزارع بكتيرية لعينات البول التى تم جمعها من هؤلاء المرضى على وسط الماكونكى أجار أظهرت.124عينة نتائج إيجابية على هذا الوسط ثم تم التعرف على البكتريا بواسطة الإختبارات البيوكيمائية والتأكد منها أليا بواسطة جهاز2 Vitek والتى أظهرت أن بكتيريا الإيشيريشيا كولاى الأكثر شيوعاَ بين الكائنات المسببة لعدوى المسالك البولية بنسبة (35.4%) ثم تم إجراء إختبار الحساسية للمضادات الحيوية لعزلات الإيشيريشيا كولاى وإختيار المقاوم منها و تم عمل فحص أولى لها لمعرفة مقاومة هذه العزلات لمجموعة البيتالاكتام ذات الطيف الممتد وفقاَ للمعايير التى وُضعت بمختير المعايير السريرية وبإستخدام تقنية تفاعل البلمرة المتسلسل أكدت النتائج أن جين (*TEM*) هو الجين السائد بين العزلات بنسبه 100% يليه جين (*SHV*) بنسبة 90% وأتضح الغياب التام لجين (*CTX*) خلال تلك الدراسة وتبين أن بعض العزلات أنها تنتج أكثر من نوع من إنزيمات البيتالاكتام ومثلت 30% من عزلات الإيشيريشيا كولاى ذات الطيف الممتد المقاومة للمضادات الحيوية. وخلصت هذه الدراسة إلى أن معدل إنتشار بكتيريا الإيشيريشيا كولاى ذات الطيف الممتد المقاومة للمضادات الحيوية يمثل 22.7% من بين عزلات الإيشيريشيا كولاى المسببة لعدوى المسالك البولية وأن الجينين TEMو*SHV* هما الأكثر شيوعا.