Prevalence of ESBL genes in ESBL producing *Klebsiella pneumoniae* isolated from patients with urinary tract infections in Baghdad, Iraq

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*Klebsiella pneumoniae* is one of the main causes of urinary tract infections (UTIs). The uropathogens are becoming increasingly resistant to different classes of antibiotics and their resistance to new generations of cephalosporins due to the production of extended-spectrum beta-lactamases (ESBLs). The aim of this study was isolation of *K. pneumoniae* from patients with UTI also investigates the antibiotic resistance patterns and determines their association with ESBL genes. CHROM agar Orientation medium was used for rapid detection of *K. pneumoniae* from urine specimens and the identification was confirmed by VITEK 2 system. Out of 77 of *K. pneumoniae* isolated from UTI patients, sixty-six (85.7 %) were considered ESBL producing based on phenotyping ESBL detection by ESBL E-strip test. These isolates were then tested by polymerase chain reaction (PCR) for the presence or absence of *bla* TEM, *bla* CTX-M, and *bla* SHV beta-lactamase genes. The *bla* SHV gene was present in all isolates (100 %) followed by *bla* TEM (56 %) and *bla* CTX-M (4.5 %) genes. The most common ESBL genotype among our isolates was *bla* SHV and *bla* TEM (56 %). The most of ESBL-producing *K. pneumoniae* isolates were susceptible to Meropenem and Imipenem, 85.7 % and 75 % respectively, and showed 100 % resistance to Ampicillin, Cephalexin, and Ceftazidime. Also high resistance was recorded for the antibiotics; Doxycycline (90.9 %), Cefotaxime (85.7 %), Cefipime (85.7 %), Ciprofloxacin (83.1 %) and Kanamycin (77.9 %). In conclusion, most of ESBL-producing *K. pneumoniae* were multidrug resistant and the most prevalent gene was SHV-type. Investigation of ESBL-producing strains and the predominant ESBL genes in UTI patients are important for the selection of the most appropriate antibiotic for treatment and also infection control.

Keywords: *K. pneumoniae*, ESBL, UTI, Antibiotic Resistance.

INTRODUCTION

UTIs are among the most prevalent community-acquired and hospital-acquired infections, affecting almost 50% of the population at least once in their lifetime has an associated with a high mortality rate among UTI patients. The majority causative agents of UTIs are Gram-negative pathogens, primarily from the Entero bacteriaceae family including *Escherichia coli*, *Proteus mirabilis*, and *Klebsiella pneumoniae* (Tenney et al., 2018). *K. pneumoniae* has the mechanisms of natural resistance against some antibiotic groups, but a constant increasing frequency of acquired multidrug resistant *K. pneumoniae* which possess Extended-Spectrum Beta-Lactamases (ESBL) enzymes activity (Paterson and Bonomo, 2005). Multiple drug resistance has significantly increased among bacteria of nosocomial infections and there is a growing concern for multidrug resistant Gram-negative bacteria which produce extended-spectrum β-lactamases (ESBLs) (Coque et al.,
2008). ESBLs are Class A β-lactamases that hydrolyse penicillin, oxyimino-cephalosporins, and monobactams. ESBLs are often plasmid-mediated enzymes and have various genotypes. The most common are the SHV, TEM, and CTX-M types. ESBLs are primarily produced by the Enterobacteriaceae family of Gram-negative organisms, in particular Klebsiella pneumoniae, K. oxytoca and E. coli (Paterson and Bonomo, 2005). Some of the local studies indicated to increasing of the antibiotics resistance among ESBL-producing uropathogenic strains to most common cephalosporins which used in our hospitals (Al-Janaby et al., 2017; Khalid et al., 2017). The various ESBL encoding genes in bacteria may reveal characteristic differences in relation to antimicrobial resistance expression and the genetic characterization of ESBL-producing organisms is essential for epidemiological use. The aim of the present study is investigating the distribution of Extended-Spectrum Beta-Lactamases (ESBLs) producing K. pneumoniae strains isolated from patients with UTIs and determining the antibiotics resistance patterns, also, surveying the presence of ESBL enzymes in K. pneumoniae isolates and investigating their prevalence among ESBL-producing clinical isolates.

MATERIALS AND METHODS

Isolation and identification of K. pneumoniae

This study was performed at Hospitals in Baghdad, Iraq, between January and June 2018. Out of 310 Urine sample, a total of 77 isolates of K. pneumoniae were collected from patients with Urinary Tract Infections. Blood agar and McConkey agar were used for isolation uropathogenic K. pneumoniae and CHROM agar Orientation medium for the rapid detection. These isolates were identified using traditional bacteriological methods and biochemical testing, with VITEK 2 system (bioMerieux, France), according to the manufacturer’s recommendations.

Antibiotic Susceptibility Test

Antimicrobial susceptibility test was conducted by using disc diffusion method. Briefly, K. pneumoniae overnight growth were prepared on McConkey agar and then re suspended in Mueller-Hinton broth (Oxoid). The turbidity of the suspension is adjusted to an equivalent 0.5 McFarland and this suspension was used to inoculate on Mueller-Hinton agar (Oxoid) plates. The antibiotics discs used in this study as the following: Kanamycin (K), Gentamicin (GM), Imipenem (IPM), Meropenem (MEM), Ceftazidime (CAZ), Cefotaxime (CTX), Ciprofloxacin (CIP), Doxycycline (DO), Tetracycline (TE), Ampicillin (AM), Aztreonam (ATM), Amoxicillin-clavulanic acid (AMC), Cephalexin (CL), Piperacillin (PI), Cefipime (FEP), Trimethoprim / Sulfamethoxazole (TS) and Cefoxitin (FOX). (MAST, UK) were placed on the medium. The agar plates were incubated at 35°C for 24 h, and then the inhibition zone was measured and interpreted by the percent of susceptible, intermediate, or resistant isolates as defined by CLSI breakpoint interpretative Criteria (CLSI, 2012).

Screening ESBL producing isolates by phenotypic method (ESBL E-strip test)

The ESBL E-strip test (Ezy ?) is based on two gradients: one end of the strip is impregnated with Ceftazidime (0.5–32 µg/mL), and the opposite end is impregnated with Ceftazidime (0.125–8 µg/mL) and Clavulanate (4 µg/mL). The test was performed following the manufacturer's instructions. Briefly, an overnight culture of K. pneumoniae on brain heart infusion agar was suspended in saline to match the turbidity to that of a 0.5 McFarland standard. This suspension was then used to inoculate a Muller Hinton agar plate by swabbing the plates with a sterile cotton swab. After drying, the E-test strip was placed on the plate, and the plate was incubated overnight at 37°C. For both ends of the strip, the point of intersection between the inhibition eclipse and the edge of the E-test strip was considered the MIC. According to the manufacturer, a Ceftazidime MIC/Ceftazidime-Clavulanate MIC ratio ≥8 indicates the presence of ESBL enzymes (Cormican et al., 1996).

DNA extraction and identification of ESBL genes by PCR

Bacterial DNA was extracted from all K. pneumoniae ESBLs producer isolates using ready kits (Promega, USA). Purity of the isolated DNA was monitored by Nano Dropper 2000 (Thermo Scientific, USA). The PCR reactions for detection bla CTX-M, bla SHV and bla TEM genes were done within a total volume of 25 µL. The mixture of reaction contained 1x buffer (10 mM Tris-HCl, 50 mM KCl), 0.2µM of each deoxynucleoside triphosphate, 1 mM MgCl2, 0.5 µM of forward and reverse primers.
The confirmation of the identification of K. pneumoniae was completed by using VITEK 2 system. The confirmation of the identification of K. pneumoniae was completed by using VITEK 2 system. Seventy-seven (24.8 %) of the isolated bacteria identified as K. pneumoniae from all collected bacterial cultures. Most of the patients were of the females 52/77(67.5%), while the percentage of the males was 25/77 (32.5 %).

Table 1. Primer sequences for PCR detection of extended-spectrum beta-lactamases genes in K. pneumoniae.

<table>
<thead>
<tr>
<th>Target gene</th>
<th>Oligonucleotide primer sequence 5’ to 3’</th>
<th>Amplicon size (bp)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bla SHV-F, Bla SHV-R</td>
<td>AGCCGCTTGAGCAAATTTAAC, ATCCCGGAGATAAAATCACCAC</td>
<td>713</td>
<td>Diagbouga et al., 2015</td>
</tr>
<tr>
<td>Bla CTX-M-F, Bla CTX-M-R</td>
<td>ATGGTGACAAAGAGAGTGCA, CCCCCTGCGGTAGTCTC</td>
<td>869</td>
<td>Peerayeh et al., 2016</td>
</tr>
<tr>
<td>Bla TEM-F, Bla TEM-R</td>
<td>TCGCCGCATACTATTCTCAGATGA, ACGCTACCGGGCTCAGATTAT</td>
<td>445</td>
<td>Ali Akbar et al., 2016</td>
</tr>
</tbody>
</table>

For multiplex PCR, PCR conditions for amplification of ESBL gene was carried out by the thermocycler (Applied Biosystems, Malaysia) as follows: initial denaturation at 94°C for 5 min, denaturation at 95°C for 30 sec, annealing at 60 °C for 30 sec, and extension at 72°C for 1 min, was repeated for 30 cycles; a final extension at 72°C for 5 min. Agarose gel electrophoresis was done a 1.2 % agarose gel at 80V for 2 hours. After electrophoresis fragments were stained by ethidium bromide, and then visualized with ultraviolet light.

RESULTS AND DISCUSSION

Out of the 310 urine samples, 146 (47.1 %) of the patients had significant bacterial growth. Due to the specificity of CHRO Magar Orientation medium with the differentiation of bacterial colonies of uropathogens from urine samples, the colonies of K. pneumoniae on this medium were obtained as metallic blue as showed in Figure 1. The confirmation of the identification of K. pneumoniae was completed by using VITEK 2 system.

The confirmation of the identification of K. pneumoniae was completed by using VITEK 2 system. Seventy-seven (24.8 %) of the isolated bacteria identified as K. pneumoniae from all collected bacterial cultures. Most of the patients were of the females 52/77(67.5%), while the percentage of the males was 25/77 (32.5 %).

The Primer sequences, which were used for detection of ESBL genes in this study, were as in Table 1. PCR conditions for amplification was according to the reference of Table 1.

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workload in the microbiology laboratory compared to that for Blood agar and MacConkey agar, and should be considered as an alternative to conventional culture methods for detecting and reporting uropathogens (Qaiser et al., 2011; Kanchana et al., 2013).

Many of the studies indicated to the predominant of E. coli and Klebsiella isolates as infectious agents in urinary tract infections because of these strains can bind to the glycol-conjugate receptor of the uroepithelial cells of human urinary tract so it can initiate infection (Raza et al., 2011; Tayal et al., 2015). The results of Rimal et al., 2017 demonstrated that the most of causative agents of bacteriuria were E. coli and Klebsiella spp. and the most of these isolates were multidrug resistant and extended spectrum beta-lactamases producers. Our results revealed that the rate of infection in female patients was higher than males, similar results was obtained by Thakur et al., (2013) where 56.64% female were infected. The pathogenicity of K. pneumoniae in UTIs is related to a multitude of virulence factors such as biofilm formation, serum resistance and ability to readily acquire multiple antibiotic resistances (Aljanaby and Alhasani, 2016; Gharrah et al., 2017).

Of the 77 K. pneumoniae isolates tested for the production of ESBL by uropathogenic strains according to the ESBL E-test, the results revealed that 66 (85.7 %) isolates were ESBL-producing K. pneumoniae and 11 (14.3 %) isolates were non-ESBL-producing K. pneumoniae (Figure 2).
Several studies revealed that the ESBL production is more frequent in Latin America and Asia than in Europe (Coque et al., 2008; Leylabadlo et al., 2017). The frequency of ESBL-producing K. pneumoniae was 85.7 % in our study, which was higher than the findings of the local study conducted by Aljanaby et al. (2016) who found that the rate of ESBL-producing K. pneumoniae was 62.5 %. Another study from Iran indicated to the presence of ESBL-producing K. pneumoniae isolated from UTIs in Tehran at the percentage 50.7 % (Ghafourian et al., 2012). This may be due to the differences in the time of sample's collection and random consumption of antibiotics. The incidence of ESBL-producing strains among UTI isolates resulting in limitations to the therapeutic options and the presence of ESBL producers is a significant problem in hospitalized patients throughout the world (Tenney et al., 2018). Table 2. Explain patterns of susceptibility and resistance among ESBL and non-ESBL K. pneumoniae to 17 commonly used antibiotics. The antibiogram for studied isolates revealed high level resistance of K. pneumoniae clinical isolates to most of the antibiotics under test. It was found that all isolates of K. pneumoniae (100 %) were resistant to Ampicillin, Cephalexin and Ceftazidime. The present study showed a high resistance to Piperacillin (97.4 %), Amoxicillin-clavulanic acid (97.4 %), also high resistance was recorded for the antibiotics; Doxycycline (90.9 %), Cefotaxime (85.7 %), Cefipime (85.7 %), Ciprofloxacin (83.1 %) and Kanamicin (77.9 %). The moderate resistance was observed for Trimethoprim/Sulfamethoxazole, Gentamicin, Tetracycine and Cefoxitin.
Table 2. Percentages of antimicrobial susceptibility rate of 77 K. pneumoniae isolates against 17 antimicrobial agents.

<table>
<thead>
<tr>
<th>Antibiotic*</th>
<th>Resistant</th>
<th>Intermediate</th>
<th>Sensitive</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST</td>
<td>51 (66.2 %)</td>
<td>0 (0 %)</td>
<td>26 (33.8 %)</td>
</tr>
<tr>
<td>CIP</td>
<td>64 (83.1 %)</td>
<td>6 (7.8 %)</td>
<td>7 (9.1 %)</td>
</tr>
<tr>
<td>TE</td>
<td>35 (45.5 %)</td>
<td>13 (16.9 %)</td>
<td>29 (37.6 %)</td>
</tr>
<tr>
<td>DO</td>
<td>70 (90.9 %)</td>
<td>5 (6.5 %)</td>
<td>2 (2.6 %)</td>
</tr>
<tr>
<td>K</td>
<td>60 (77.9 %)</td>
<td>10 (13 %)</td>
<td>7 (9.1 %)</td>
</tr>
<tr>
<td>MEM</td>
<td>2 (2.6 %)</td>
<td>9 (11.7 %)</td>
<td>66 (85.7 %)</td>
</tr>
<tr>
<td>IPM</td>
<td>4 (5.2 %)</td>
<td>16 (20.8 %)</td>
<td>57 (75 %)</td>
</tr>
<tr>
<td>AM</td>
<td>77 (100 %)</td>
<td>0 (0 %)</td>
<td>0 (0 %)</td>
</tr>
<tr>
<td>PI</td>
<td>75 (97.4 %)</td>
<td>0 (0 %)</td>
<td>2 (2.6 %)</td>
</tr>
<tr>
<td>ATM</td>
<td>54 (70.1 %)</td>
<td>0 (0 %)</td>
<td>23 (29.9 %)</td>
</tr>
<tr>
<td>AMC</td>
<td>75 (97.4 %)</td>
<td>0 (0 %)</td>
<td>2 (2.6 %)</td>
</tr>
<tr>
<td>CL</td>
<td>77 (100 %)</td>
<td>0 (0 %)</td>
<td>0 (0 %)</td>
</tr>
<tr>
<td>CTX</td>
<td>66 (85.7 %)</td>
<td>1 (1.3 %)</td>
<td>10 (13 %)</td>
</tr>
<tr>
<td>FEP</td>
<td>66 (85.7 %)</td>
<td>2 (2.6 %)</td>
<td>9 (11.7 %)</td>
</tr>
<tr>
<td>FOX</td>
<td>34 (44.2 %)</td>
<td>10 (13 %)</td>
<td>33 (42.8 %)</td>
</tr>
<tr>
<td>CAZ</td>
<td>77 (100 %)</td>
<td>0 (0 %)</td>
<td>0 (0 %)</td>
</tr>
<tr>
<td>CN</td>
<td>45 (58.4 %)</td>
<td>4 (5.2 %)</td>
<td>28 (36.4 %)</td>
</tr>
</tbody>
</table>

Kanamycin (K), Gentamicin (GM), Imipenem (IPM), Meropenem (MEM), Ceftazidime (CAZ), Cefotaxime (CTX), Ciprofloxacin (CIP), Doxycycline (DO), Tetracycline (TE), Ampicillin (AM), Aztreonam (ATM), Amoxicillin-clavulanic acid (AMC), Cephalexin (CL), Piperacillin (PI), Cefipime (FEP), Trimethoprim / Sulfamethoxazole (TS) and Cefoxitin (FOX).

The current study demonstrated that K. pneumoniae possessed a low-level resistance against Meropenem (2.6 %) and Imipenem (5.2 %). Among 77 isolates of K. pneumoniae, 73(94.8 %) were resistant to more than 3 classes of selected antibiotics, in other words, Multi-Drug Resistant (MDR) K. pneumoniae. In the present study, there was obvious high resistance to beta-lactam antibiotics, especially in ESBL producing strains; this resistance pattern is often correlated with the presence of ESBL enzymes (Roshan et al., 2011). The high percentage resistance to third- and fourth-generation cephalosporins such as Cefotaxime and Ceftazidime were concordant with the results of Mishra et al., (2013) who referred that the resistance of uropathogens to cephalosporins reached to 75%. The local study in the Kurdistan region of Iraq showed that all K. pneumoniae isolates were 100 % resist to Ampicillin, Cefipime, Cefotaxime, Ceftazidime and Aztreonam (Khalid et al., 2017). The increasing of K. pneumoniae resistance to Ceftazidime was detected by many researchers (Calfee, 2017; Heidary et al., 2018), suggesting that Ceftazidime may not be active against organisms with this particular combination of beta-lactamases, and mutations in outer-membrane porins (Calfee, 2017). Also, in the current study more than half of K. pneumoniae isolates were resistant to important antibiotics such as Gentamicin (58.4%) and Trimethoprim/Sulfamethoxazole (66.2 %); we recommend that antimicrobial test should be performed prior to any antibiotic prescription in K. pneumonia infections. High resistance of ESBL producers was observed among antibiotics belonging to different families including Kanamicin, Ciprofloxacin, and Doxycycline, and these findings were similar to reports of different studies (Reis et al., 2016; Yasin et al., 2017). In the present study, Meropenem and Imipenem have been found to be the most effective antibiotics and the results indicated that most of isolates were susceptible to these antibiotics; this is consistent with the findings of many previous studies (Alzahrani and Akhtar, 2005; El Nekidy et al., 2017).

In order to detect the presence of Extended-Spectrum Beta-Lactamase genes (bla TEM, bla SHV and bla CTX-M) and determination the prevalence of each gene among K. pneumoniae clinical isolates, uniplex and multiplex polymerase chain reaction (PCR) for each DNA extracted...
sample have been used. The PCR reaction included 66 of ESBL-producing isolates for detection the sets of ESBL genes. The PCR products have been confirmed by analysis of the bands on gel electrophoresis and by comparing their molecular weight with 100 bp DNA Ladder. The results of uniplex PCR reaction for ESBL genes showed in Figures (3), (4), and (5), and these genes also detected by multiplex PCR reaction (Figure 6). Each DNA extracted sample was subjected to uniplex and multiplex PCR reaction with three primer sets of bla SHV (713 bp), bla TEM (445 bp), and bla CTX-M (869 bp). The results of their distribution in the ESBL-producing isolates with their genotypes demonstrated in the Table 3. The results of PCR reaction (Figures, 3 to 6) and Table 3 revealed the detection and genotypes of ESBL genes among K. pneumoniae clinical studied isolates, which exhibited production of ESBL enzymes. Extended Spectrum β-Lactamase-producing K. pneumoniae isolates were characterized for bla TEM, bla SHV and bla CTX-M genes. All K. pneumoniae (100 %) of the ESBL genotypes expressed bla SHV genes followed by 56 % bla TEM and 4.5 % bla CTX-M. About 3 % (n=2) of the isolates harbored all three genes (bla TEM, bla SHV and bla CTX-M). The predominant genotype was the presence of the tow genes (bla SHV + bla TEM) in 56 % of the isolates. Our results were in agreement with the local study of Aljanaby and Alhasnawi (2017) who revealed that K. pneumoniae strains isolated from inpatients with UTI in Al-Kufa hospital in Al-Najaf province, Iraq, gave high resistant rate toward Amoxicillin+clavulanic acid (97.67 %) while the lowest resistance rate was observed for Imipenem and the most common resistance genes were blaSHV (86.04 %). In the present study, majority of the isolates expressed blaSHV genes. Similar findings were reported in a study conducted in Turkey among patients with ESBL-producing carbapenem-resistant K. pneumoniae strains, where the most prevalent ESBL gene was blaSHV (97%), followed by blaTEM (92%), and blaCTX-M-1 (62%)(Iraz et al., 2015). In Brazil, The results of Flores et al., (2016) found that ESBL and carbapenemase producing K. pneumoniae strains isolated from patients in intensive care units showed high resistance rates to Cefepime (94%), Ceftazidime (96%), and Ciprofloxacin (69%) with high percentage of SHV and TEM genes. In K. pneumoniae, A multidrug-resistant transferable plasmid encoding the SHV-5 β-lactamase, causing unusually high resistance to Ceftazidime and Aztreonam, and the combination of AAC(6′)-I + AAC(3)-I, producing resistance to aminoglycosides (Galani et al., 2002). The risk of developing infections caused by ESBL-producing organisms is due to use of invasive medical devices (endotracheal tubes, urinary catheters, central venous lines) and prolonged hospital stays (Paterson and Bonomo, 2005).
Figure 4. Agarose gel electrophoresis of PCR products for the resistance gene *bla*TEM (445 bp). Lane M: 100bp DNA ladder; lanes 1-12: *K. pneumoniae* isolates; lane C: Negative control. (80V for 2hr).

Figure 5. Agarose gel electrophoresis of PCR products for the resistance genes *bla*CTX-M (869bp). Lane M: 100bp DNA ladder; lanes 1: *K. pneumoniae* K5 isolate; lane C: Negative control. (80V for 2hr).
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Figure 6. Agarose gel electrophoresis for detection the resistance genes *bla* SHV, *bla* TEM, and *bla* CTX-M by multiplex PCR. Lane M: 100bp DNA ladder; lanes 2-13: *K. pneumoniae* isolates; lane 1: Negative control. (80V for 2hr).


<table>
<thead>
<tr>
<th>Genotypes</th>
<th><em>K. pneumoniae</em> (n=66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>One genotype</td>
<td></td>
</tr>
<tr>
<td><em>bla</em> SHV</td>
<td>66 (100 %)</td>
</tr>
<tr>
<td><em>bla</em> TEM</td>
<td>37 (56 %)</td>
</tr>
<tr>
<td><em>bla</em> CTX-M</td>
<td>3 (4.5 %)</td>
</tr>
<tr>
<td>Tow or thee combination genes</td>
<td>No. (%)</td>
</tr>
<tr>
<td><em>bla</em> CTX-M + <em>bla</em> TEM + <em>bla</em> SHV</td>
<td>2 (3 %)</td>
</tr>
<tr>
<td><em>bla</em> CTX-M + <em>bla</em> TEM</td>
<td>3 (4.5 %)</td>
</tr>
<tr>
<td><em>bla</em> CTX-M + <em>bla</em> SHV</td>
<td>2 (3 %)</td>
</tr>
<tr>
<td><em>bla</em> SHV + <em>bla</em> TEM</td>
<td>37 (56 %)</td>
</tr>
</tbody>
</table>

Also, heavy antibiotic use has been recorded as a factor for acquisition of ESBL-producing enterobacteria, especially with *E. coli* and *K. pneumoniae* (Lautenbach et al., 2001). Very low prevalence of *bla*CTX-M in our results (4.5 %) don’t agree with the findings reported from other parts of the world, where, CTX-M was found to be the most dominant gene in Saudi Arabia (74.1%) (Elhassan et al., 2016), Isfahan, Iran (92 %) (Maleki et al., 2018) and also, CTX-M-producing *K. pneumoniae* isolates demonstrated rapid emergence and spread at the 2000s in the United States (Wang et al., 2013). While the local study in the Kurdistan region of Iraq revealed the high prevalence of *bla*SHV (87 %) in comparison with the percentages of *bla* TEM (60 %) and *bla* CTX-M (58 %) (Khalid et al., 2017). The present findings was in contrast to the results Diagbouga et al. (2016), who found that the predominant genotype in *K. pneumoniae* was TEM/SHV/CTX-M (61.90%), followed by (TEM/SHV 20.63%) and ESBL genes occur more by combination than singularly, where, these strains exhibited high resistance to quinolones and trimethoprim-sulfamethoxazole. *Bla*TEM type had the tendency of hydrolysing Ceftazidime more than CTX-M types among ESBL producers, this gives credence to that exposure to Ceftazidime is the...
cause of the selective pressure leading to the emergence of TEM-ESBL genes (Bush et al., 1995). SHV-producing K. pneumoniae strains are currently a problem in Iraq which may be related to the misuse of third generation cephalosporins, especially Cefotaxime. Therefore, isolation and detection of ESBL-producing strains in UTI patients are essential for the selection of the most appropriate antibiotic for treatment and also infection control.

CONCLUSION

The present study showed that ESBL positive uropathogenic K. pneumoniae are resistant to most classes of antibiotics, not only beta-lactams and pose challenges for determining the suitable antibiotic for treatment the complicated UTI infections. ESBL SHV-producing K. pneumoniae strains are currently a problem in Iraq which may be related to the misuse of third-generation cephalosporins. Therefore, isolation and detection of ESBL-producing strains in UTI patients are essential for the selection of the most appropriate antibiotic for treatment and also infection control. The present study demonstrated the need for control of the use of non-prescribed antibiotics and continuous monitoring of antibiotic susceptibility profiles of uropathogenic isolates.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

ACKNOWLEDGEMENT

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AUTHOR CONTRIBUTIONS

KKG contributed to the design of the experiments and performed the experimental work. RAS carried out laboratory tests. KKG wrote the manuscript, all authors revised and approval the final version.

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