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# Identification of Carbapenem-Resistant *Enterobacteriaceae* and Extended Spectrum Beta-Lactamase *E. Coli* and *K. Pneumoniae* in Some Iraqi Hospitals

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**Abstract**

*Enterobacteriaceae* is a large family of Gram-negative. The carbapeneme antibiotics are used as a last line of defense against multi-drug resistant (MDR) bacteria.The carbapenem resistance in Enterobacteriaceae can be caused by a variety of methods, including the synthesis of Carbapenemase enzymes. This study aims to estimate the anti-microbial susceptibility, mechanisms of carbapeneme-resistant *ESBLs* in two genera of the *E. coli* and *K. pneumoniae.* A total 380 clinical specimens were collected from patients attending hospitals / health centers and outpatient clinics including urine (165), swab (100), sputum (100), wound infection of diabetic foot (50), stool (50) and blood (10), during November (2022) to April (2023). Bacterial colonies were Gram stained and microscopically examined. Biochemical tests were done to identify pathogen species and Vitek- 2 system, and detect the antimicrobial susceptibility to different antibiotic. In the current study, as a general the results revealed that all isolates of *E. coli* were 100% resistant to lincomycin, In the current study, the results revealed that all isolates of *K. pneumoniae* were resistant to lincomycin were 100%, with high significant $P<0.001$.the Vitek-2 system utilized for the detection of ESBL of *E. coli* and *K. pneumoniae*. The phenotypic of ESBL results of E. coli in UTIs was 58.9% positive, while the results of phenotypic of carbenem for E. coli were 24.1% in UTIs. In conclusion, all isolates of *E. coli* resistant to lincomycin, by ampicillin, ceftazidime and cefozolin.

**Keywords**: Carbapenem-Resistant *Enterobacteriaceae*, Extended spectrum Beta-Lactamase, *E. coli*, *K. pneumoniae*, and antibiotic susceptibility.

## Introduction

*Enterobacteriaceae is* a large family of Gram-negative bacteria. It was the first proposed by Rahn in 1936 *Enterobacteriaceae* includes, along with many harmless symbionts, many of the more familiar pathogens, such as *Salmonella* spp., *Escherichia coli* (*E. coli*), *Klebsiella* spp., and *Shigella* spp. Members of this family are normal with gut microbiota in humans and other animals (Adeolu *et al*., 2016). The bacterium *E. coli* constitute about 0.1% of gut microbiota, produce carbapenemases, enzymes that hydrolyze carbapenems. The resistance to carbapenem in *E. coli* bacteria is attributable to their ability to produce carbapenemase enzymes (Ding *et al*., 2019). In addition, *Klebsiella*

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*pneumoniae* (*K. pneumoniae*)member of *Enterobacteriaceae* and normal flora of the mouth, the skin/ and intestines, it can cause destructive changes to human and animal lungs if aspirated, specifically to the alveoli, *Klebsiella* spp., are often resistant to multiple antibiotics. Current evidence implicates that plasmids as the primary source of the resistance genes. Furthermore, it's has the ability to produce extended-spectrum beta-lactamases (*ESBL*) are resistant to virtually all beta-lactam (β- lactam) antibiotics (Ghaith *et al*., 2019).

On the other hands, the carbapeneme antibiotics are used as a last line of defense against multi-drug resistant (MDR) bacteria. The carbapenems are usually considered as last-line drugs, especially for the treatment of critically ill patients or those having a Gram-negative infection which is resistant to the majority of antibiotics (Mustafai *et al*., 2023). In hospitals throughout Southeast and South Asia, Gram-negative bacteria have high rates for carbapenem resistance (Idrees and Saeed, 2021). So, the polymyxins may be chosen for treatment, but there are also some reports which showed polymyxin resistance by a *mcr*-1 gene, making the problem worse. The rapid rise in the prevalence of resistance to carbapenem among the *Enterobacteriaceae* is connected with health care, particularly *K. pneumoniae* and *E. coli* which are significant causes for infection and the antibiotic resistance burden, such as *K. pneumoniae* and *E. coli* (Mustafai *et al*., 2023). Moreover, the emergence of *ESBL* is frequently associated with prolonged hospital stay, increased treatment cost, and limited treatment options especially wide-spectrum antibiotics. As well as, *ESBLs* have been reported in India most frequently in *Enterobacteriaceae* and cause difficulty in the management of infections in intensive critical care settings (Verma *et al*., 2022).

## Material and method

### *Specimen collection and culture*

A total 380 clinical specimens were collected from patients attending hospitals / health centers and outpatient clinics, and from the inpatient department in the halls ICUs and RCU, that include urine (165), swab (100), sputum (100), diabetic foot (wound infection) (50), stool (50) and blood (10), with age 5 days–75 years during the period from 13$^{th}$ November, 2022 to 1$^{st}$ April, 2023 that admitted to Al- Karama teaching hospital in Wasit province, Al-Zahra teaching hospital in Wasit province, Al-Nu'man teaching hospital in the capital Baghdad, Al- Jadiriyah private hospital in the capital Baghdad, Al-Zahrawi surgical hospital in Maysan province, Al-Basra general hospital in Basra province, Al- Najaf Al- Ashraf teaching hospital in Al- Najaf Al-Ashraf province, and private clinics in Wasit province. Samples were taken by sterile disposable cotton swabs and transport swab. They were, then, cultured onto (Blood agar base, EMB agar, Brain heart infusion broth, Motility medium, MacConkey agar, Muller-Hinton agar, Nutrient agar, Simmons' citrate agar) Himedia/India, plates before incubating aerobically at 37ºC for (24h). After that, identified based on colony morphology, microscopic Gram stain investigation, standard biochemical tests, Vitek 2 system and antibiotic susceptibility to (Amikacin, Amoxicillin-Clavulanate, Ampicillin, Azitreonam, Cefepime, Cefixime, Cefozolin, Ceftazidime, Ciprofloxacin, Colistin, Gentamicin, Imipenem, Levofloxacin, Lincomycin, Meropenem, Nalidixic Acid, Nitrofurantoin, Pipracacilin, Pipracacilin–Tazobactam, Tobramycin, Trimethoprim-Sulfamethoxazole, Vancomycin.

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### *Antimicrobial susceptibility test*

The Kirby-Bauer disc diffusion method was used to test the antibiotic sensitivity of isolates on Mueller Hinton agar in accordance with the clinical and laboratory criteria institute (CLSI, 2022) criteria (Sharma and Srivastava, 2016). Using the CLSI, 2022 standards, bacteria pathogens were classified as either resistant to treatment or sensitive to it based on their zone of inhibition and Vitek-2 AST system.

### *Statistical analyses*

Statistical-Package-for-Social-Science, version 25.0 was used to do statistical analysis on all data. All findings with a significant level ($P \leq 0.05$) were analyzed using Chi Square (Gharban *et al*., 2023).

## Results and discussion

### *Isolation and identification*

During the present study period from 13th November, 2022 to 1st November, 2023. The current study was conducted on total 380specimens, Bacteremia 30(7.9%), dietetic foot 26(6.8%), RTI 55(14.5%), and high rate of UTI = 269(70.8%). The results were distributed according to the patient age between age 5days–75 years old. Male specimens were 141(37.1%) and Female were 239(62.9%). the highest incidence was among 51–75-year age groups (21.8%), with high significant *P*-value <0.001, asshowed in the Table 1.

**Table 1: Distribution of patients according to demographic factors**

| Variables | Categories | No. (%) |
|---|---|---|
| Age groups(Mean ± SE) | 5day-1 year | 33(8.7) |
| | 1-10 (4.77±0.34) | 69(18.2) |
| | 11-20 (15.39±0.46) | 46(12.1) |
| | 21-30 (26.17±0.47) | 47(12.4) |
| | 31-40 (35.82±0.36) | 57(15.0) |
| | 41-50 (46.93±0.43) | 45(11.8) |
| | > 51-75 (57.8±0.34) | 83(21.8) |
| Gender | Male | 141(37.1) |
| | Female | 239(62.9) |
| Diseases | Bacteremia | 30(7.9) |
| | Dietetic foot | 26(6.8) |
| | RTI | 55(14.5) |
| | UTI | 269(70.8) |
| Patients | Out patient | 330(86.8) |
| | Inpatient | 50(13.2) |
| Residence | Urban | 351(92.4) |
| | Rural | 29(7.6) |
| Taken drugs | Yes | 41(10.8) |
| | No | 339(89.2) |
| Smoking | Yes | 40(10.5) |

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| | | |
|---|---|---|
| | No | 340 (89.5) |
| Province | Wasit | 313(82.4) |
| | Baghdad | 25(6.6) |
| | Al-Basra | 13(3.4) |
| | Missan | 18(4.7) |
| | Al-Najaf | 11(2.9) |
| Total | | 380(100) |
| *P* value | | <0.001* |

* Significant differences at *P*-value <0.05.

In the present study, the results of identification revealed that the number of patients with significant culture growth among 380 bacteremia, diabetic foot, RTI, UTI specimens with positive culture was 300/380(79 %) and the negative culture was 80/380(21%), these results may be return due to other infection i.e. viral infections or fungal infections or other bacteria need more incubation period and growth condition or indicates no evidence of infection (asymptomatic infection) as showen in the Figure 1.

The results in the current study of positive culture of all specimen isolates give elevated rate of *E. coli* 128/380(33.7%), *K. pneumonia* 47/380(12.4%) as summarized in the Figure 2.

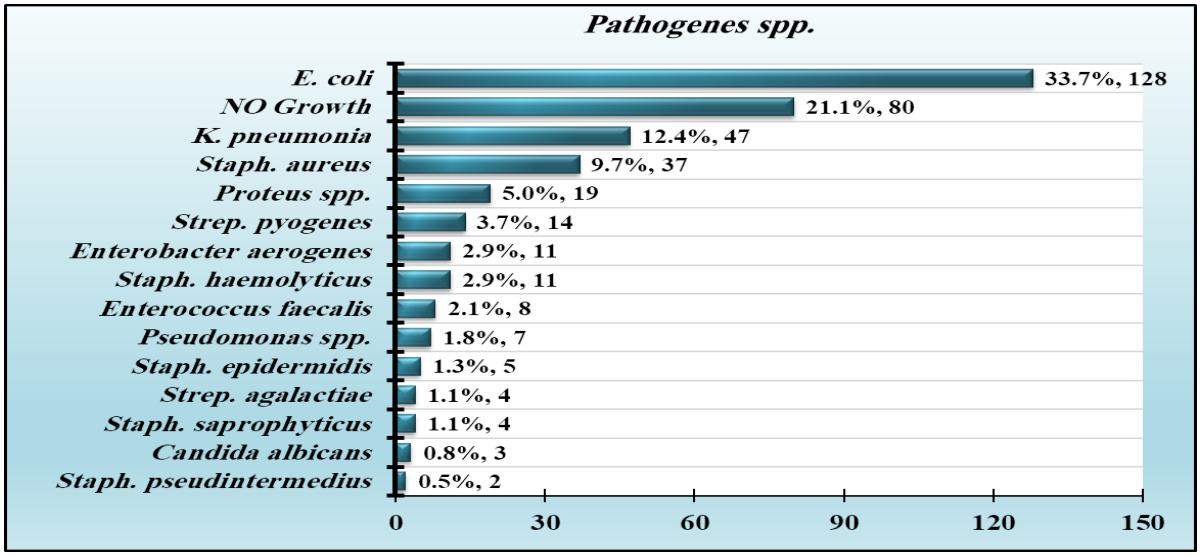


**Figure 1: Result of positive culture all specimen isolates n=380 (*P*-value <0.001)**

These results in the present study were appeared that the patients had a higher significant infection (*P*<0.001) with UTIs and uropathogenic bacteria than the other cases with *E. coli* 112(41.6%), and *K. pneumonia* 26(9.7%). These results agreed with results that conducted by Mofolorunsho *et al*. (2021), and by Koirala *et al*. (2021), who demonstrated that the *E. coli* were 227/879 (25.82%) and 118/879 (13.42%) were *K. pneumoniae* indicating that *E. coli* as a predominant bacterium from the total of different clinical specimens that included urine, sputum, pus, blood, and body fluids. Similar results

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conducted by Zubair *et al*. (2019), who demonstrated that the *E. coli* was the most frequent pathogen (71%), followed by *K. pneumoniae* (7.48%), isolated from UTIs.

***Antibiotic susceptibility***

According to CLSI 2023, guidelines and by Kirby-Bauer disk diffusion method, on Muller-Hinton agar a total of *E. coli* (128) isolates and *K. pneumoniae* (47) were exposed to susceptibility testing using different antibiotics mentioned above.

***Antibiotic susceptibility test of E. coli isolates***

In the current study, as a general the results revealed that all isolates of *E. coli* were (100%) resistant to lincomycin, followed by ampicillin, ceftazidime and cefazolin with 88%, 79% and 78% respectively ($P$<0.001) as show in the Table 2.

**Table 2**: **The percentage resistance of *E. coli* isolates against different antibiotics n= 128**

| Antibiotic | R | I | S | p-value |
|---|---|---|---|---|
| Amikacin | 4(3) | 4(3) | 120(94) | <0.001* |
| Amoxicillin-Clavulanate | 88(69) | 2(2) | 38(30) | <0.001* |
| Ampicillin | 113(88) | 7(5) | 8(6) | <0.001* |
| Azitreonam | 97(76) | 0(0) | 31(24) | <0.001* |
| Cefepime | 92(72) | 0(0) | 36(28) | <0.001* |
| Cefixime | 48(38) | 0(0) | 80(63) | 0.005* |
| Cefazolin | 100(78) | 0(0) | 28(22) | <0.001* |
| Ceftazidime | 101(79) | 0(0) | 27(21) | <0.001* |
| Ciprofloxacin | 79(62) | 9(7) | 40(31) | <0.001* |
| Colistin | 71(55) | 0(0) | 57(45) | 0.216 NS |
| Gentamicin | 45(35) | 7(5) | 76(59) | <0.001* |
| Imipenem | 18(14) | 7(5) | 103(80) | <0.001* |
| Levofloxacin | 78(61) | 3(2) | 47(37) | <0.001* |
| Lincomycin | 128(100) | 0(0) | 0(0) | N.A000 |
| Meropenem | 47(37) | 0(0) | 81(63) | 0.003* |
| Nalidixic Acid | 44(34) | 0(0) | 84(66) | <0.001* |
| Nitrofurantoin | 26(20) | 21(16) | 81(63) | <0.001* |
| Pipracacilin | 40(31) | 0(0) | 88(69) | <0.001* |
| Pipracacilin– Tazobactam | 44(34) | 15(0) | 69(54) | <0.001* |
| Tobramycin | 70(55) | 0(0) | 58(45) | 0.289 NS |
| Trimethoprim-Sulfamethoxazole | 91(71) | 0(0) | 37(29) | <0.001* |
| Vancomycin | 2(2) | 0(0) | 126(98) | <0.001* |

*Significant differences at *p*-value <0.05. NS: non-significant. *N.A:* non applicated. Chi-square test

These results in the current study agreed with results in the a study was conducted by Hozzari *et al*. (2020), in Tehran/Iran, who observedthat *E. coli* as the most frequent uropathogen showed high

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resistance to trimethoprim was 37 (56.9%), cefozolin were 45 (69.2%), ciprofloxacin 26 (40%), nalidixic acid were 46 (70.8%). Furthermore, these results agreed with results achieved by Mehrabi (2020). Individuals with Diabetes mellitus (DM) are more susceptible to resistant bacterial pathogens due to their complicated UTIs, including vancomycin-resistant enterococci, fluoroquinolone-resistant uropathogens, extended-spectrum β-lactamase-positive Enterobacteriaceae and carbapenem-resistant *Enterobacteriaceae* (Nasser *et al*., 2019).

In the current study, the results of antibiotic heights resistance of *E. coli* in UTIs (N=112) were high to lincomycin 112(100%), ampicillin 97(86.6%) and azitreonam 97(86.6%) with high significant ($P\leq$ 0.001). The higher resistance level in the present study of *E. coli* for diabetic foot (n=14) were to ampicillin, ciprofloxacin, lincomycin with 100% for each and Levofloxacin, Cefozolin were 85% and 92%, respectively ($P\leq$ 0.001). Moreover, the resistance level in the current study of *E. coli* for RTIs (n=2) were 100% for all antibiotic such as ampicillin, cefozolin, ceftazidime, ciprofloxacin, levofloxacin, lincomycin, meropenem, pipracacilin, tobramycin, trimethoprim-sulfamethoxazole with high significant $P\leq$ 0.001, as outlined in the Table 3.

**Table 3: The percentage resistance of *E. coli* isolates against different antibiotics to UTI=112, Diabetic foot n=14 and RTI n =2**

| Antibiotic | | UTI | Diabetic foot | RTI |
|---|---|---|---|---|
| | | **No. %** | **No. %** | **No. %** |
| Amikacin | **R** | 4(3.6) | 0(0.0) | 0(0.0) |
| | **S** | 104(92.8) | 14(100) | 2(100) |
| | **I** | 4(3.6) | 0(0.0) | 0(0.0) |
| Amoxicillin-Clavulanate | **R** | 78(69.6) | 9(64.3) | 1(50) |
| | **S** | 32(28.6) | 5(35.7) | 1(50.0) |
| | **I** | 2(1.8) | 0(0.0) | 0(0.0) |
| Ampicillin | **R** | 97(86.6) | 14(100.0) | 2(100.0) |
| | **S** | 8(7.1) | 0(0.0) | 0(0.0) |
| | **I** | 7(6.3) | 0(0.0) | 0(0.0) |
| Azitreonam | **R** | 97(86.6) | 0(0.0) | 0(0.0) |
| | **S** | 15(13.4) | 14(100.0) | 2(100.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Cefepime | **R** | 81(72.3) | 10(71.4) | 1(50.0) |
| | **S** | 31(27.7) | 4(28.6) | 1(50.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Cefixime | **R** | 48(42.9) | 0(0.0) | 0(0.0) |
| | **S** | 64(57.1) | 14(100.0) | 2(100.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Cefozolin | **R** | 86(76.8) | 12(85.7) | 2(100.0) |
| | **S** | 26(23.2) | 2(14.3) | 0(0.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |

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| | | | | |
|---|---|---|---|---|
| Ceftazidime | **R** | 87(77.7) | 12(85.7) | 2(100.0) |
| | **S** | 25(22.3) | 2(14.3) | 0(0.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Ciprofloxacin | **R** | 63(56.3) | 14(100.0) | 2(100.0) |
| | **S** | 40(35.7) | 0(0.0) | 0(0.0) |
| | **I** | 9(8.0) | 0(0.0) | 0(0.0) |
| Colistin | **R** | 60(53.6) | 11(78.6) | 0(0.0) |
| | **S** | 52(46.4) | 3(21.4) | 2(100.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Gentamicin | **R** | 39(34.8) | 5(35.7) | 1(50.0) |
| | **S** | 66(58.9) | 9(64.3) | 1(50.0) |
| | **I** | 7(6.3) | 0(0.0) | 0(0.0) |
| Imipenem | **R** | 18(16.0) | 0(0.0) | 0(0.0) |
| | **S** | 91(81.3) | 10(71.4) | 2(100.0) |
| | **I** | 3(2.7) | 4(28.6) | 0(0.0) |
| Levofloxacin | **R** | 63(56.3) | 13(92.9) | 2(100.0) |
| | **S** | 46(41.0) | 1(7.1) | 0(0.0) |
| | **I** | 3(2.7) | 0(0.0) | 0(0.0) |
| Lincomycin | **R** | 112(100.0) | 14(100.0) | 2(100.0) |
| | **S** | 0(0.0) | 0(0.0) | 0(0.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Meropenem | **R** | 35(31.2) | 10(71.4) | 2(100.0) |
| | **S** | 77(68.8) | 4(28.6) | 0(0.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Nalidixic Acid | **R** | 44(39.3) | 0(0.0) | 0(0.0) |
| | **S** | 68(60.7) | 14(100.0) | 2(100.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Nitrofurantoin | **R** | 21(18.8) | 4(28.6) | 1(50.0) |
| | **S** | 75(67.0) | 5(35.7) | 1(50.0) |
| | **I** | 16(14.2) | 5(35.7) | 0(0.0) |
| Pipracacilin | **R** | 35(31.2) | 3(21.4) | 2(100.0) |
| | **S** | 77(68.8) | 11(78.6) | 0(0.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Pipracacilin– Tazobactam | **R** | 37(33.0) | 7(50.0) | 0(0.0) |
| | **S** | 63(56.3) | 5(35.7) | 1(50.0) |
| | **I** | 12(10.7) | 2(14.3) | 1(50.0) |
| Tobramycin | **R** | 68(60.7) | 0(0.0) | 2(100.0) |
| | **S** | 44(39.3) | 14(100.0) | 0(0.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |

| | | | | |
|---|---|---|---|---|
| Trimethoprim-Sulfamethoxazole | **R** | 78(69.6) | 11(78.6) | 2(100.0) |
| | **S** | 34(30.4) | 3(21.4) | 0(0.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Vancomycin | **R** | 2(1.8) | 0(0.0) | 0(0.0) |
| | **S** | 110(98.2) | 14(100.0) | 2(100.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |

($P$<0.001)

These results agreed with the result, which founded in study conducted by Abed and Mutter (2023) that revealed the antibiotic resistance profile of UPEC isolated in Ramadi/Iraq, the gentamicin were 28(68.2%), trimethoprim/sulfamethoxazole were 33(80.4 %), and ciprofloxacin were 34(82.9%). Another result that be in close compatible with study achieved which by Al-Khfaji *et al*. (2023) in Karbala/Iraq. Similar finding in Duhok/Iraq by Ibrahim *et al*. (2023) who showed that phenotypic testing of the isolates were most resistant to ciprofloxacin with (70%) and levofloxacin with (63%). In addition, UPEC as the most important bacterial agent of UTIs encompasses a wide treasure of virulence genes and factors (Hozzari *et al*., 2020). Also, UPEC isolates were highly resistant to β-lactamase antibiotics, followed by quinolones, sulfonamides, aminoglycosides, and carbapenems. The high percentage of resistance could be self-medication, as in our region, there are no strict roles for prescriptions and pharmacists, and even patients, can prescribe drugs and consume it without medicinal prescription. Also, the high percentage of genetic transfer between isolates increased the resistance to antibiotics (Abed and Mutter, 2023). The present study of *E. coli* for diabetic foot (n=14) were disagreed with the results conducted by Sannathimmappa *et al*. (2021) who predominant that the antibiotic susceptibility rate of *E. coli* isolated from diabetic foot infections (DFIs) were ampicillin (24%), ciprofloxacin (51%), amikacin (92%), , cefixime (59%), and vancomycin (0%). Furthermore, dissimilar results conducted by Shi *et al*., 2023, who observed that the ampicillin, levofloxacin and amikacin were 52%, 56%, 32%, respectively. Moreover, in DFIs, the diversity of microbial profile and ever-changing antibiotic-resistance patterns emphasize accurate characterization of microbial profile and antibiotic susceptibility pattern (Sannathimmappa *et al*., 2021). In the current study, the result with *E. coli* for RTIs (n=2) were close similarity to the results of Mohammed *et al*. (2023) in Kirkuk/Iraq, who conducted that The resistance level of *E. coli* for RTIs were ampicillin (80%), ceftazidime (41.7%) and ciprofloxacin (66.7%), respectively. These results agreed with result founded by Taqi and Hadi (2023) Karbala/Iraq that revealed the resistance level of *E. coli* for RTIs were ampicillin (100%), ceftazidime (65%), ciprofloxacin (76%), and trimethoprim-sulfamethoxazole (66%).

***Antibiotic susceptibility test against K. pneumoniae isolates***

In the current study, the results revealed that all isolates of *K. pneumoniae* were resistant to lincomycin were (100%), followed by ampicillin (98%), cefozolin (98%), with high significant $P$<0.001. as outlined in the Table 4. These results in the present study agreed with results in study conducted by Al-Khfaji *et al*. (2023) in Karbala City, Iraq, who observed that resistance of *K.*

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*pneumonia* isolated from clinical sample were nitrofurantoin (70%), amikacin (10%) and amoxicillin-clavulanate (100%). Similar study achieved by Mohamed and Al-Taai (2023) in Diyala/Iraq.

**Table 4**: **The percentage resistance of *K. pneumonia* isolates against different antibiotics n= 47**

| Antibiotic | **R No. (%)** | **I No. (%)** | **S No. (%)** | ***P*-value** |
|---|---|---|---|---|
| Amikacin | 19(40) | 4(9) | 24(51) | 0.001* |
| Amoxicillin-Clavulanate | 28(60) | 0(0) | 19(40) | 0.189 $^{NS}$ |
| Ampicillin | 46(98) | 1(2) | 0(0) | <0.001* |
| Azitreonam | 21(45) | 0(0) | 26(55) | 0.466 $^{NS}$ |
| Cefepime | 37(79) | 0(0) | 10(21) | <0.001* |
| Cefixime | 32(68) | 0(0) | 15(32) | 0.013* |
| Cefozolin | 46(98) | 0(0) | 1(2) | <0.001* |
| Ceftazidime | 38(81) | 7(15) | 2(4) | <0.001* |
| Ciprofloxacin | 43(91) | 0(0) | 4(9) | <0.001* |
| Colistin | 26(55) | 0(0) | 21(45) | 0.466 $^{NS}$ |
| Gentamicin | 31(66) | 0(0) | 16(34) | 0.029* |
| Imipenem | 21(45) | 4(9) | 22(47) | 0.001* |
| Levofloxacin | 27(57) | 7(15) | 13(28) | 0.001* |
| Lincomycin | 47(100) | 0(0) | 0(0) | N.A |
| Meropenem | 8(17) | 0(0) | 39(83) | <0.001* |
| Nalidixic Acid | 13(28) | 0(0) | 34(72) | 0.002* |
| Nitrofurantoin | 37(79) | 9(19) | 1(2) | <0.001* |
| Pipracacilin | 27(57) | 0(0) | 20(43) | 0.307 $^{NS}$ |
| Pipracacilin– Tazobactam | 35(74) | 0(0) | 12(26) | 0.001* |
| Tobramycin | 11(23) | 0(0) | 36(77) | 0.001* |
| Trimethoprim-Sulfamethoxazole | 24(51) | 0(0) | 23(49) | 0.884 $^{NS}$ |
| Vancomycin | 0(0) | 0(0) | 47(100) | N.A |

*Significant differences at *P*-value <0.05. NS: non-significant. N.A: non applicable

In the current study, the results of antibiotic heights resistance of *K. pneumoniae* in UTIs (N=26) were high to ampicillin, cefixime, colistin, lincomycin with 26(100%).with high significant ($P\leq$ 0.001). as outlined in the Table 5. The result conducted by Hasan and Mustafa, 2023 in North of Iraq, who revealed that similar result of the *K. pneumoniae* isolated from UTIs were resist to ampicillin (90%), trimethoprim-sulfamethoxazole (40%), ceftazidime (20%) and ciprofloxacin (30%). Another study in close agreed founded by Ali and Aljanaby, (2023) in Babylon City in Iraq. The higher resistance level in the present study of *K. pneumoniae* for diabetic foot (n=2) were 2(100%) to ampicillin, cefepime, cefozolin, ceftazidime, ciprofloxacin, levofloxacin, lincomycin, pipracacilin–tazobactam, while the sensitivity rate ranging from 50% to 100% for remain antibiotic ($P\leq$ 0.001).
These results in the current study was compatible with result in a study conducted by Mohsin and Jasim (2023) in Karbala/Iraq, who observe that the *K. pneumoniae* was shown highest resistance

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100% for gentamycin and levofloxacin, followed by resistance toward ciprofloxacin (96%) and resistance toward amikacin (92%). Furthermore, similar results reported by study in Saharan Africa by Wada *et al*. (2023),who observed that the results of antibiotic sensitivity of *K. pneumoniae*was highest resistance to amoxicillin (62.67%), ampicillin (94.29%), ceftriaxone (86.86%).
Moreover, the resistance level in the current study of *K. pneumoniae* for RTIs (n=19) were cefozolin and lincomycin (100%), and to ampicillin and ciprofloxacin (94.7%). ($P< 0.001$), as outlined in the Table 5. Similar result founded with Aziz and Khider (2023) in Erbil, Iraq, who observed that the resistance to ampicillin 28(100%), ciprofloxacin 21(75%) and levofloxacin 21(75%). Furthermore, Shakir *et al*. (2022), who revealed that *K. pneumoniae* isolated from RTIs were showed high resistance rate 100% to ampicillin, ciprofloxacin, amikacin, and sensitive to imipenem (100%).

**Table 5: The percentage resistance of *K. pneumonia* isolates against different antibiotics to UTI=26, Diabetic foot n=2 and RTI n =19**

| Antibiotic | | UTI | Diabetic foot | RTI |
|---|---|---|---|---|
| | | **No. %** | **No. %** | **No. %** |
| Amikacin | **R** | 10(38.5) | 1(50.0) | 8(42.1) |
| | **S** | 14(53.8) | 1(50.0) | 9(47.4) |
| | **I** | 2(7.7) | 0(0.0) | 2(10.5) |
| Amoxicillin-Clavulanate | **R** | 12(46.2) | 1(50.0) | 15(78.9) |
| | **S** | 14(53.8) | 1(50.0) | 4(21.1) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Ampicillin | **R** | 26(100.0) | 2(100.0) | 18(94.7) |
| | **S** | 0(0.0) | 0(0.0) | 0(0.0) |
| | **I** | 0(0.0) | 0(0.0) | 1(5.3) |
| Azitreonam | **R** | 11(42.3) | 0(0.0) | 10(52.6) |
| | **S** | 15(57.7) | 2(100.0) | 9(47.4) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Cefepime | **R** | 20(76.9) | 2(100.0) | 15(78.9) |
| | **S** | 6(23.1) | 0(0.0) | 4(21.1) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Cefixime | **R** | 26(100.0) | 0(0.0) | 6(31.6) |
| | **S** | 0(0.0) | 2(100.0) | 13(68.4) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Cefozolin | **R** | 25(96.2) | 2(100.0) | 19(100.0) |
| | **S** | 1(3.8) | 0(0.0) | 0(0.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Ceftazidime | **R** | 20(76.9) | 2(100.0) | 16(84.2) |
| | **S** | 2(7.7) | 0(0.0) | 0(0.0) |
| | **I** | 4(15.4) | 0(0.0) | 3(15.8) |
| Ciprofloxacin | **R** | 23(88.5) | 2(100.0) | 18(94.7) |
| | **S** | 3(11.5) | 0(0.0) | 1(5.3) |

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| | | | | |
|---|---|---|---|---|
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Colistin | **R** | 26(100.0) | 0(0.0) | 0(0.0) |
| | **S** | 0(0.0) | 2(100.0) | 19(100.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Gentamicin | **R** | 17(65.4) | 1(50.0) | 13(68.4) |
| | **S** | 9(34.6) | 1(50.0) | 6(31.6) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Imipenem | **R** | 12(46.2) | 0(0.0) | 9(47.4) |
| | **S** | 13(50.0) | 1(50.0) | 8(42.1) |
| | **I** | 1(3.8) | 1(50.0) | 2(10.5) |
| Levofloxacin | **R** | 13(50.0) | 2(100.0) | 12(63.2) |
| | **S** | 8(30.8) | 0(0.0) | 5(26.3) |
| | **I** | 5(19.2) | 0(0.0) | 2(10.5) |
| Lincomycin | **R** | 26(100.0) | 2(100.0) | 19(100.0) |
| | **S** | 0(0.0) | 0(0.0) | 0(0.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Meropenem | **R** | 8(30.8) | 0(0.0) | 0(0.0) |
| | **S** | 18(69.2) | 2(100.0) | 19(100.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Nalidixic Acid | **R** | 13(50.0) | 0(0.0) | 0(0.0) |
| | **S** | 13(50.0) | 2(100.0) | 19(100.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Nitrofurantoin | **R** | 22(84.6) | 1(50.0) | 14(73.7) |
| | **S** | 0(0.0) | 0(0.0) | 1(5.3) |
| | **I** | 4(15.4) | 1(50.0) | 4(21.0) |
| Pipracacilin | **R** | 21(80.8) | 0(0.0) | 6(31.6) |
| | **S** | 5(19.2) | 2(100.0) | 13(68.4) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Pipracacilin– Tazobactam | **R** | 18(69.2) | 2(100.0) | 15(78.9) |
| | **S** | 830.8) | 0(0.0) | 4(21.1) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Tobramycin | **R** | 6(23.1) | 1(50.0) | 4(21.1) |
| | **S** | 20(76.9) | 1(50.0) | 15(78.9) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Trimethoprim-Sulfamethoxazole | **R** | 12(46.2) | 0(0.0) | 12(63.2) |
| | **S** | 14(53.8) | 2(100.0) | 7(36.8) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |
| Vancomycin | **R** | 0(0.0) | 0(0.0) | 0(0.0) |
| | **S** | 26(100.0) | 2(100.0) | 19(100.0) |
| | **I** | 0(0.0) | 0(0.0) | 0(0.0) |

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***Phenotypic of ESBL and phenotypic of carbenem resistant of E. coli and K. pneumoniae isolates***

In the current study, the Vitek-2 system utilized for the detection of ESBL of *E. coli* and *K. pneumoniae.* The phenotypic of ESBL and carbenem results of *E. coli* in UTI, Diabetic foot, and RTI were outlined in the Table 6.

**Table 6: The percentage resistance of carbenem and ESBL for *E. coli* isolates to UTI=26, Diabetic foot n=2 and RTI n =19**

| ***E. coli*** | | **UTI No. %** | **Diabetic foot No. %** | **RTI No. %** | ***P*-value** |
|---|---|---|---|---|---|
| phenotypic of ESBL | **Negative** | 46(41.1) | 6(42.9) | 1(50.0) | 0.962 |
| | **Positive** | 66(58.9) | 8(57.1) | 1(50.0) | |
| phenotypic of carbenem | **Negative** | 85(75.9) | 10(71.4) | 1(50.0) | 0.667 |
| | **Positive** | 27(24.1) | 4(28.6) | 1(50.0) | |

In the present study, the phenotypic of ESBL and carbenem resultsof *K. pneumoniae* for UTIs, Diabetic foot and RTIs were outlined in the Table 7.

**Table 7: The percentage resistance of carbenem and ESBL for *K. pneumonia* isolates to UTI=26, Diabetic foot n=2 and RTI n =19**

| ***K. pneumonia*** | | **UTI** | **Diabetic foot** | **RTI** | ***P*-value** |
|---|---|---|---|---|---|
| Phenotypic of ESBL | Negative | 14(53.8) | 1(50.0) | 11(57.9) | 0.953 |
| | Positive | 12(46.2) | 1(50.0) | 8(42.1) | |
| Phenotypic of carbenem | Negative | 19(73.1) | 1(50.0) | 16(84.2) | 0.453 |
| | Positive | 7(26.9) | 1(50.0) | 3(15.8) | |

The results in the current study agreed with found Guclu *et al*. (2021) who founded that the ESBL rate was in *K. pneumoniae* and *E.coli* (62.5% and 53.1%) which isolated from clinical sample. Also, these results disagreed with Sakaeda *et al*. (2023) in Japan, who founded that of the 911 *E. coli* strains isolated from urine samples identified, 158(17.3%) were ESBL-producing.The results in current study were agreed with the results study conducted by Rajendran *et al*. (2023), who observed that out of 81 *E. coli* isolates, 15 (18.51%) isolates, 8 (25%) isolates of the 32 *Klebsiella* species, were found to be ESBL-positive. The frequency of bacteria producing ESBL was recently been increasing worldwide, and antibiotic resistance is becoming a larger problem. The frequency of occurrence of UTIs caused by ESBL-producing *Enterobacterales* has been increasing globally. Among ESBL-producing *Enterobacterales*, ESBL-producing *E. coli* is considered the greatest concern (Sakaeda *et al*., 2023).

Close similar percentage conducted by Dwomoh *et al*. (2022) who revealed that the phenotypic confirmation of carbapenem resistance, 75% (6/8) of the isolates that were resistant to carbapenems for *E. coli* and *K. pneumonia*. In addition, regarding the phenotypic characteristics of carbapenem-resistant *E. coli* isolates collected from hospitalized patients and outpatients in Ardabil province, Iran. (Khavandi *et al*., 2022) Results revealed that out of *E. coli* (200) isolates, and 34% were resistant to

carbapenem antibiotics. The results of current study were disagreed to Taha *et al*. (2023), who appeared that the detection of phenotypic carbapenem resistance in 31.3% (50/160) in*K. pneumonia* isolates from different clinical samples.Finally, the organisms that hydrolyze carbapenems frequently resist other antibiotics, such as aminoglycosides, fluoroquinolones, and sulfonamides. Therefore, treating these infections is very difficult due to the increasing resistance to carbapenem antibiotics (Khavandi *et al*., 2022).

## Conclusion

All isolates of *E. coli* resistant to lincomycin, by ampicillin, ceftazidime and cefozolin. The results revealed that all isolates of *K. pneumoniae* were resistant to lincomycin. The phenotypic of ESBL results of *E. coli* in UTIs was 66(58.9%) positive.

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