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# Comparative Antimicrobial Susceptibility Profiles of Uropathogenic Extended-Spectrum ß-Lactamase Producing Strains of *Klebsiella pneumonia* and *Escherichia coli* by the CLSI and EUCAST methodologies

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## ABSTRACT

**Aims**: The lack of information about the inter variability of the test results obtained by CLSI and EUCAST requires further clarifications to interpret antimicrobial susceptibility patterns better. This study aimed to compare the CLSI and EUCAST interpretations of the antimicrobial susceptibility test results of the ESBL–producing uropathogenic Escherichia coli and *Klebsiella pneumonia* strains.

**Methods**: After obtaining 157 ESBL-producing *E. coli* and 95, ESBL-producing K. pneumonia isolates from the urine specimens of the patients, Kirby-Bauer's disc diffusion method was used for conducting antimicrobial susceptibility test. The test procedures and the interpretation of the results were carried out according to the year 2017 versions of both of the two guidelines. For the statistical comparison of concordance between the two guidelines, the Kappa coefficients and the concordance rates were calculated.

**Results:** The results were graded in the range from perfect to poor agreement. For E. coli, interpretations of the AST results revealed a moderate to perfect agreement between both methods. Weighted Kappa agreement scores in the range from 0.42 to 1. The agreement for AMC, TPZ30/6, ceftazidime 10, meropenem, and aztreonam was poor without any inconsistencies. For *Klebsiella*, the kappa agreement score was in the range from 0.25 to 1. It was incompatible with AMC, TPZ 30/6, ceftazidime 10, aztreonam; there was poor agreement for cefepime, amikacin and ertapenem.

**Conclusions:** Our results showed agreement between the two guidelines for uropathogenic extended-spectrum ß-lactamase producing Escherichia coli and Klebsiella pneumoniae but also showed inconsistencies between two guidelines. Therefore, the results of our study contribute to the comparison of these guidelines for interpreting antibiotic susceptibilities.

**Key words;** CLSI, EUCAST, ESBL Urinary tract infections, Escherichia coli, Klebsiella pneumoniae, Kappa coefficient

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## 1.Introduction

Urinary tract infections (UTIs) are the most common form of bacterial infection worldwide, and they are associated with high costs and morbidity. The treatment of UTIs has become problematic, and the treatment options are limited due to the common use of antibiotic medications leading to increased antibiotic resistance rates [1, 2]. The extended-spectrum beta-lactamase (ESBL) synthesis was first published in 1983 in the members of the Enterobacteriaceae family, and it is currently one of the most critical health problems worldwide [2]. Following the identification of ESBL strains of *Klebsiella pneumonia*, those strains of E. coli were demonstrated. Both of these pathogens are mainly involved in UTIs [2, 3]. The synthesis of ESBL leads to resistance development to all types of beta-lactam antibiotics, excluding cefamicins and carbapenems. The ESBL synthesis is most commonly seen in *Klebsiella pneumoniae* and *Escherichia coli* strains. Since ESBL-encoding plasmids often carry other resistance genes too, resistance to sulfonamides, aminoglycosides, and fluoroquinolones is common [1,3]. The most crucial problem here is the worldwide geographical variability in the frequency of ESBL-producing strains, which are usually resistant to a wide variety of antibiotics. High resistance rates lead to several unfavorable consequences, including treatment failures, recurrent or chronic infections, increased treatment costs, prolonged hospital stay, development of permanent complications, and high morbidity and mortality rates [4]. To avoid treatment failures associated with antibiotic resistance, standardization should be ensured in conducting, interpreting, and reporting antimicrobial susceptibility tests (AST). Standardization is essential for determining the resistance profiles at the national level, comparing resistance profiles on international platforms, and taking part in global surveillance systems. For this purpose, two widely-known standards for AST have been developed, and they are used globally. One of these standards is the "Clinical Laboratory Standards Institute" (CLSI), which has been used in our country for many years. The other is the "European Committee on Antimicrobial Susceptibility Testing" (EUCAST) recommendations, which have been used in many European Union member countries since 2015 [5,6]. Our laboratory has been using the CLSI guidelines for conducting AST and interpreting the results for many years. However, the increasing number of countries adopting the EUCAST guidelines led us to use the EUCAST methodology in our laboratory frequently. Therefore, our study aimed to investigate the extent of agreement between the AST results obtained by CLSI and EUCAST methodology by examining the antibiotic susceptibility of uropathogenic ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae*. It is aimed to evaluate the zone diameters to be yielded, compare the interpretations of test results made according to both of the CLSI and EUCAST guidelines, and to determine possible differences.

## 2.Materials and methods

### 2.1. Ethical Consideration

Before commencing the study, approval of the ethics committee of Ankara Numune Research and Training Hospital (Ref 2017/001) was obtained.

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### 2.2. Study Setting, Design and Population

This cross-sectional study was conducted prospectively in Ankara Numune Research and Training Hospital. ESBL-producing *Escherichia coli* and *Klebsiella pneumonia* strains obtained from the urine samples of patients were included in the study to evaluate zone diameters according to the standards of both CLSI and EUCAST to determine possible differences between the two methods. The ESBL-producing strains were excluded from the study when colonization was identified or when the ESBL producing strains were isolated from the same site of infection in the same patient. The uropathogenic strains of ESBL–producing *K. pneumonia* and *E. coli*, isolated from the hospital- or community-acquired infections were included in the study.

### 2.3. Bacterial Isolate Collection

MALDI-TOF mass spectrometry (BD, Sparks, USA) and the combined disc method were used for identifying the isolates and their ESBL characteristics, respectively. The quality control of the media used in the study, the bacteria identification tests, and AST were performed according to both of the CLSI and EUCAST recommendations about the *E.coli* ATCC 25922 and *K. pneumoniae* ATCC 700603 strains.

### 2.4. Confirmation of ESBL-Producing Strains

The phenotypic confirmation of ESBL synthesis in the isolates was performed using the combined disc method. The Mueller Hinton agar medium (Oxoid LTD, Hampshire, England) was used for the cultivation of the bacterial suspension prepared according to a 0.5 McFarland standard. After placing the discs (BD BBL) 25 mm apart from center to center and incubating the plates at 37°C for 24 hours, the zone inhibitions of the ceftazidime [30µg] and cefotaxime [30µg] discs were compared to the zone inhibitions observed with the clavulanic acid (10µg) containing discs of ceftazidime (30µg) and cefotaxime (30µg). A difference of ≥5 mm between the zone diameters around either of the clavulanic acid-containing discs compared to those of the only antibiotic discs was accepted to the indicate the ESBL synthesis in that specific bacterial isolate [7].

### 2.5. Antimicrobial Susceptibility Testing [AST]

After inoculating the Muller-Hinton Agar (Oxoid LTD, Basingstoke, Hampshire, United Kingdom) plates with 0.5 Mc Farland turbidity inoculums, the antimicrobial discs [Abtek Biologicals, Liverpool, United Kingdom] were applied to the plates. Then, they were incubated at 37°C for 24 hours. Discs of ampicillin, amoxicillin-clavulanic acid (AMC), ampicillin/sulbactam (SAM), piperacillin/tazobactam 30/6 (TPZ), cefuroxime, cefepime, ceftazidime 10, cefoxitin, cefotaxime 5, ceftriaxone, gentamicin, tobramycin, amikacin, imipenem, meropenem, ertapenem, trimethoprim/sulfamethoxazole (TMP/SMX), chloramphenicol, aztreonam, ofloxacin, ciprofloxacin, norfloxacin, levofloxacin, and nitrofurantoin were used in the study. The Kirby-Bauer disc diffusion method was used for conducting AST. The zone diameters formed after the incubation period were measured and recorded. Finally, the inhibition zone diameters were interpreted according to the 2017

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guidelines of CLSI and EUCAST. The interpreted results were assigned to one of the susceptible, intermediate, or resistant categories [8,9]. The AST results of the *Escherichia coli* and *Klebsiella pneumonia* isolates were evaluated according to both of the CLSI and EUCAST standards. The susceptibility rates of the isolates and the results of the comparative statistical analyses are shown in Table 1 and Table II.

### 2.6. Statistical analysis

Statistical analyses were carried out by using R (Psych package of R software /cohen. kappa function). The Kappa (**κ**) coefficient was calculated to compare the study parameters. The concordance rates between the CLSI and EUCAST guidelines were calculated and presented in percentages. The susceptibility to the antimicrobial agents was calculated in percentages for both of the *Escherichia coli* and *Klebsiella pneumonia*. Weighted kappa values were calculated to find the level of absolute agreement between the two guidelines. Cohen's kappa statistics were used for determining the level of agreement between the AST results found according to both of the CLSI 2017 and EUCAST 2017 guidelines. The results were categorized in the range from a perfect to poor agreement. In practice; to determine the level of agreement with Cohen's Kappa statistics, two independent observations are made. Then, the agreement level above chance is found out. The level of agreement can numerically be in the range from −1 to 1, and a p-value of less than 0.05 but not equal to zero indicates a significant difference occurring not by chance. The calculated Kappa coefficient values in the study were interpreted as follows [10,11], No agreement: $0 \leq \kappa < 0.20$, Poor agreement: $0.20 \leq \kappa < 0.40$,Moderate agreement: $0.40 \leq \kappa < 0.60$,Good agreement: $0.60 \leq \kappa < 0.80$,Perfect agreement: $0.80 \leq \kappa < 1.00$,A p-value of $\leq 0.05$ was accepted to indicate a statistically significant difference for all inferential statistics.

## 3.Results

The study included 157 ESBL-producing *E. coli* and 95 ESBL-producing *K. pneumonia* strains that were collected consecutively in Ankara Numune Research and Training Hospital in the period from April 2014 to November 2018. Table 1 summarizes the AST results obtained for *E. coli* and the respective concordance rates and kappa statistics results comparing the CLSI and EUCAST methods. The concordance between these two methods ranged from 56.4% to 100%. The comparisons revealed that AST results of *E.coli*, found by both methods, were in moderate to perfect agreement for most of the antibiotics tested. The weighted Kappa agreement scores for the AST results of *E.coli* for these antibiotics ranged from 0.42 to 1. However, the level of agreement between these two methods was poor for the following antibiotics: AMC: $\kappa = 0.37$ [95% CI: 0.27-0.47], $p < 0.000$, TPZ 30/6: $\kappa = 0.39$ [95% CI: 0.30-0.47], $p < 0.000$, Ceftazidime 10: $\kappa = 0.29$ [95% CI:0.22-0.37], $p < 0.000$, Meropenem: $\kappa = 0.33$ [95% CI: 0.11-0.55], $p < 0.000$, Aztreonam: $\kappa = 0.33$ [95% CI: 0.26-0.41], $p < 0.000$. The comparative evaluation of the AST results obtained by using the two guidelines was presented as the kappa agreements in Table 2. The comparisons of the CLSI and EUCAST interpretations made for the AST results for *K. pneumonia* revealed moderate to perfect agreement for most of the antibiotics. The Kappa agreement scores for these AST results ranged from 0.15 to 0.96 for these antibiotics, and

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their concordance rates ranged from 42.3% to 100 %. The antibiotic susceptibility patterns interpreted according to both guidelines were found out to be similar. However, the kappa analysis showed that the agreement was hardly present for the following antibiotics: AMC: κ = 0.20 [95% CI: 0.01-0.39], p < 0.000, TPZ 30/6: κ = 0.15 [95% CI: 0.04-0.27], p < 0.000, Ceftazidime 10: κ =0.06 [95% CI: -0.05-0.18], p < 0.000, Aztreonam: κ = 0.20 [95% CI: 0.05-0.36], p < 0.000. Also, the agreement was poor for the following antibiotics: Cefepime: κ = 0.29 [95% CI: 0.09-0.50], p < 0.000, Amikacin: κ = 0.35 [95% CI: 0.11-0.58], p < 0.000, Ertapenem κ = 0.25 [95% CI: 0.13-0.38], p < 0.000. The comparative evaluation of the interpretations of the AST results according to both of the guidelines is presented in Table 2. The comparative evaluation of the Kappa agreement scores between the two guidelines is shown in Table 4.

## 4.Dıscussıon

Extended-spectrum β-lactamases [ESBLs] are responsible for resistance development against β-lactam-antibiotics. This group of antibiotics includes penicillins, cephalosporins, and aztreonam. The ESBL enzymes are usually inhibited by beta-lactamase inhibitors, including clavulanic acid, sulbactam, and tazobactam [12,13]. ESBLs are most commonly produced by *Escherichia coli* and *Klebsiella pneumonia; which are* Gram-negative bacteria of the family Enterobacteriaceae [13,14]. Resistance to more than one type of antibiotics is common with ESBL-producing *Klebsiella pneumonia* and *E.coli* strains, limiting the available treatment options and leading the researchers to look for new therapeutic alternatives [15]. β-lactam antibiotics are the main antimicrobial agents used for the treatment of UTI; however, the rates of resistance to β-lactams are on the rise, affecting the treatment effectiveness unfavorably. The most commonly identified microorganisms in UTI are *E. coli* and *Klebsiella* species, which are currently resistant to more than one antibiotic recommended for use in the treatment. There has been an observed increase in the incidences of ESB-producing E. coli and *Klebsiella spp* in recent years [12,15]. In a multicenter study conducted in Spain, antibiotic susceptibility test results of ESBL-producing *E.coli* blood isolates were compared according to the 2009-2010 CLSI, and 2011 EUCAST guidelines and the study reported a significant difference only between the AMC sensitivity test interpretations [16]. Polsfuss et al. reported no significant differences in the sensitivity of EUCAST 2011 and CLSI 2011 guidelines in detecting ESBL-producing *Enterobacteriaceae* [17]. However, in a different study conducted by Hombach et al., significant differences were reported in the susceptibility rates to cephalosporins for the ESBL-producing *Enterobacteriaceae* isolates when the test results were obtained according to both of the CLSI 2013 and EUCAST 2013 criteria [18]. In a study conducted in Turkey, antibiotic susceptibility test zone diameters for uropathogenic *Escherichia coli* isolates were evaluated according to both CLS 2014 and EUCAST 2014 standards. The results obtained separately by each method showed that amikacin and trimethoprim-sulfamethoxazole susceptibility rates were the same. However, the susceptibility rates were significantly different for gentamicin, cefuroxime axetil, and levofloxacin [19]. Kassim et al. reported that the AST patterns of *E. coli* obtained according to the EUCAST 2015 and CLSI 2015 guidelines were similar, excluding AMC, nitrofurantoin, and amikacin. A moderate

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agreement was noted with AMC; a fair agreement was reported with nitrofurantoin, and a poor agreement was noted with amikacin [6]. In a similar study comparing the 2017 guidelines of CLSI and EUCAST, the agreement between these two methods in the AST results of uropathogenic *E. coli* isolates was the highest with trimethoprim and cephalexin with rates of 100% agreement. However, the same study reported that the agreement levels for AMC and ciprofloxacin were the lowest [20]. Batista et al. evaluated the clinical isolates of E. coli and Klebsiella according to both guidelines. The authors reported that the kappa match for amikacin indicated a poor agreement between the guidelines for both microorganisms. Kappa statistics for other antibiotics were found to be consistent [21]. In our study, the susceptibility patterns for ESBL-producing *E.coli* were found similar between both EUCAST 2017 and CLSI 2017 guidelines excluding AMC, TPZ, ceftazidime 10, meropenem, and aztreonam. The weighted Kappa agreement scores for these antibiotics indicated a poor agreement between EUCAST 2017 and CLSI 2017 guidelines. For the ESBL-producing *K. pneumonia* isolates in our study; when the interpretations of the AST results made by both CLSI and EUCAST guidelines were compared, the kappa analysis revealed almost no agreement for AMC, TPZ, ceftazidime 10, and aztreonam, and a poor agreement with cefepime, amikacin, and ertapenem. The guidelines recommend that the ESBL-producing isolates can be treated with cephalosporins based on the categorization of the AST results. Compared to the CLSI 2009 guidelines and partly to the EUCAST 2010 guidelines, the 2013 versions of EUCAST and CLSI classify an increased number of isolates as resistant and recommend higher zone diameter breakpoints, intending to ensure that correct treatment practices are implemented. These recommendations particularly aim for the treatment with cephalosporins [22-25]. Recommending cephalosporin therapy for infections caused by ESBL-producing bacteria provides an additional treatment option alternative to the reserve medications, including carbapenems, relieving the pressure felt by treatment providers. However, the data about antibiotic susceptibility patterns of specific ESBL-producing isolates are limited, and there is a scarcity of information in the EUCAST and CLSI guidelines [26]. The role of antibiotics becomes critical, especially when the susceptibility of the bacteria is high and when the treatment is given timely. Therefore, selecting the most appropriate antibiotic for the treatment is of major importance based on the interpretation of the phenotypic AST in treatment-resistant infections [27]. AST results play a critical role in guiding critical treatment decisions. Two leading organizations setting standards for AST to be used by clinical microbiology laboratories have used different strategies to overcome these challenges. With our study, we have demonstrated that an acceptable level of agreement exists between the EUCAST 2017 and CLSI 2017 guidelines in the interpretation of AST results of *Escherichia coli* and *Klebsiella pneumoniae*. Our findings indicate that a comparison of susceptibility rates can only be considered in the treatment provider if the discordance generated by the use of different guidelines is established. We would like to see consistency between the recommendations of CLSI and EUCAST to bring standardization to the international reports. The free provision of EUCAST guidelines provides a significant advantage in maintaining the current standards for interpreting antibiotic susceptibility test results.

## 5.Conclusıons

We compared the AST result interpretations of the guidelines using only two different bacteria species. Therefore, the results may not be generalized and may not represent the comparison of two guidelines for the whole spectrum of clinically relevant gram-positive and negative bacteria. However, the two ESBL-producing bacteria species used in our study represent a significant population of uropathogenic bacteria. Adopting the updated limits in the current recommendations is vital for consistency in reporting the AST results. However, we are still concerned about the inconsistencies between the two guidelines in resistance screening. We recommend the use of the more conservative breakpoints for antibiotics because of the inconsistencies obtained with the kappa analysis results regarding the ESBL-producing uropathogenic strains of E. Coli and K. pneumonia.

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**Table 1.** Susceptibility of uropathogenic extended-spectrum beta-lactamase-producing *Escherichia coli* to various antibiotics; respective concordance rates and kapa statistics comparing the CLSI 2017 and EUCAST 2017guidelines

| | CLSI( %) n=264 | | | EUCAST %( %) n=264 | | | Concordance (%) | Kappa, κ (95 % CI)* |
|---|---|---|---|---|---|---|---|---|
| | S | I | R | S | I | R | | |
| **Ampicilline** | 0 | 2 | 98 | 1 | 0 | 99 | 98.5 | 0.42 (0.29-0.56) |
| **AMC** | 15.9 | 20.5 | 63.6 | 10.2 | 0.4 | 89.4 | 74.6 | 0.37(0.27-0.47) |
| **SAM** | 56.8 | 17.8 | 25.4 | 64 | 0 | 36 | 82.2 | 0.67(0.60-0.74) |
| **TPZ 30/6** | 79.5 | 11.4 | 9.1 | 61 | 11 | 28 | 70.8 | 0.39(0.30-0.47) |
| **Cefuroxime** | 0 | 0.4 | 99.6 | 0 | 0 | 100 | 99.6 | 1 |
| **Cefepime** | 8 | 37.1 | 54.9 | 9.5 | 8.3 | 82.2 | 71.2 | 0.44(0.34-0.53) |
| **Ceftazidime 10** | 31.1 | 20.1 | 48.9 | 11 | 8.7 | 80.3 | 60.6 | 0.29(0.22-0.37) |
| **Cefoxitin** | 92.4 | 3.8 | 3.8 | 90.2 | 0 | 9.8 | 93.9 | 0.63(0.50-0.76) |
| **Cefotaxime 5** | 0 | 0.4 | 99.6 | 0 | 0 | 100 | 99.6 | 1 |
| **Ceftriaxone** | 0 | 0.8 | 99.2 | 0 | 0 | 100 | 99.2 | 1 |
| **Gentamicin** | 69.3 | 3.4 | 27.3 | 54.9 | 15.2 | 29.9 | 83.0 | 0.68(0.60,0.76) |
| **Tobramycin** | 45.1 | 14.8 | 40.2 | 31.4 | 16.7 | 51.9 | 75.4 | 0.60(0.53,0.67) |
| **Amikacin** | 95.5 | 4.5 | 0 | 89.8 | 8.3 | 1.9 | 92.4 | 0.46(0.29-0.62) |
| **Imipenem** | 98.5 | 1.1 | 0.4 | 98.5 | 0.8 | 0.8 | 99.2 | 0.75(0.41-1.00) |
| **Meropenem** | 98.5 | 0.8 | 0.8 | 99.2 | 0.8 | 0 | 98.5 | 0.33(0.11-0.55) |
| **Ertapenem** | 75.8 | 11.4 | 12.9 | 58.0 | 15.2 | 26.9 | 70.8 | 0.43(0.35-0.51) |
| **TMP/SMX** | 38.6 | 0.4 | 61 | 38.6 | 0.4 | 61 | 100 | 1 |
| **Chloramphenicol** | 91.7 | 1.5 | 6.8 | 91.7 | 0 | 8.3 | 98.5 | 0.90(0.82-0.99) |
| **Aztreonam** | 30.7 | 32.2 | 36.4 | 19.7 | 8.3 | 71.2 | 56.4 | 0.33(0.26-0.41) |
| **Ofloxacin** | 34.5 | 6.1 | 59.5 | 31.4 | 1.9 | 66.7 | 90.9 | 0.82(0.75-0.88) |
| **Ciprofloxacin** | 31.4 | 6.1 | 62.5 | 31.1 | 1.9 | 67 | 95.1 | 0.90(0.85-0.95) |
| **Norfloxacin** | 32.2 | 2.7 | 65.2 | 30.3 | 1.5 | 68.2 | 95.5 | 0.90(0.85-0.95) |
| **Levofloxacin** | 33.3 | 4.9 | 61.4 | 30.7 | 1.5 | 67.4 | 92.1 | 0.84(0.78-0.90) |
| **Nitrofurantoin** | 92.0 | 3.0 | 4.9 | 95.5 | 0 | 4.5 | 95.8 | 0.65(0.46-0.84) |

EUCAST = European committee for antimicrobial susceptibility testing, CLSI = Clinical and Laboratory Standards Institute,
IS =Intermediate susceptibility, S = Susceptible, R = Resistant, * =Weighted Kappa agreement score, AMC=amoxicillin-clavulanic acid
SAM= ampicillin/sulbactam, TPZ= piperacillin/tazobactam 30/6, TMP/SMX= trimethoprim/sulfamethoxazole.

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**Table 2**. Susceptibility of uropathogenic extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* to various antibiotics, concordance rates and kapa statistics, comparing the CLSI 2017 and EUCAST 2017 guidelines

| | CLSI( %) n=264 | | | EUCAST ( %) n=264 | | | Concordance (%) | Kappa, κ (95 % CI) |
|---|---|---|---|---|---|---|---|---|
| | S | I | R | S | I | R | | |
| **Ampicilline** | 0 | 0 | 100 | 0 | 0 | 100 | 100 | 1 |
| **AMC** | 5.1 | 24.4 | 70.5 | 3.8 | 0 | 96.2 | 74.36 | 0.20 (0.01-0.39) |
| **SAM** | 35.9 | 32.1 | 32.1 | 44.9 | 0 | 55.1 | 67.95 | 0.52 (0.40-0.63) |
| **TPZ 30/6** | 69.2 | 20.5 | 10.3 | 32.1 | 26.9 | 41 | 42.31 | 0.15 (0.04-0.27) |
| **Cefuroxime** | 1.3 | 0 | 98.7 | 1.3 | 0 | 98.7 | 100 | 1 |
| **Cefepime** | 2.6 | 24.4 | 73.1 | 3.8 | 2.6 | 93.6 | 78.21 | 0.29 (0.09-0.50) |
| **Ceftazidime 10** | 3.8 | 10.3 | 85.9 | 0 | 1.3 | 98.7 | 85.9 | 0.06 (-0.05-0.18) |
| **Cefoxitin** | 85.9 | 3.8 | 10.3 | 83.3 | 0 | 16.7 | 91.03 | 0.66 (0.46-0.86) |
| **Cefotaxime 5** | 0 | 0 | 100 | 0 | 1.3 | 98.7 | 98.72 | 1 |
| **Ceftriaxone** | 0 | 0 | 100 | 0 | 0 | 100 | 100 | 1 |
| **Gentamicin** | 59 | 5.1 | 35.9 | 43.6 | 15.4 | 43.6 | 76.92 | 0.61 (0.47-0.74) |
| **Tobramycin** | 30.8 | 20.5 | 48.7 | 21.8 | 15.4 | 62.8 | 76.92 | 0.61 (0.47-0.75) |
| **Amikacin** | 94.9 | 5.1 | 0 | 88.5 | 7.7 | 3.8 | 89.74 | 0.35 (0.11-0.58) |
| **Imipenem** | 96.2 | 2.6 | 1.3 | 97.4 | 1.3 | 1.3 | 98.72 | 0.80 (0.40-1) |
| **Meropenem** | 96.2 | 1.3 | 2.6 | 97.4 | 0 | 2.6 | 98.72 | 0.79 (0.40-1) |
| **Ertapenem** | 64.1 | 19.2 | 16.7 | 37.2 | 19.2 | 43.6 | 51.28 | 0.25 (0.13-0.38) |
| **TMP/SMX** | 21.8 | 1.3 | 76.9 | 21.8 | 0 | 78.2 | 98.72 | 0.96 (0.89-1) |
| **Chloramphenicol** | 76.9 | 5.1 | 17.9 | 76.9 | 0 | 23.1 | 94.87 | 0.86 (0.74-0.98) |
| **Aztreonam** | 12.8 | 25.6 | 61.5 | 5.1 | 2.6 | 92.3 | 66.67 | 0.20 (0.05-0.36) |
| **Ofloxacin** | 50 | 6.4 | 43.6 | 35.9 | 12.8 | 51.3 | 79.49 | 0.65 (0.52-0.78) |
| **Ciprofloxacin** | 33.3 | 16.7 | 50 | 33.3 | 3.8 | 62.8 | 87.18 | 0.77 (0.65-0.90) |
| **Norfloxacin** | 46.2 | 3,8 | 50 | 29.5 | 6.4 | 64.1 | 79.49 | 0.62 (0.48-0.76) |
| **Levofloxacin** | 48.7 | 7.7 | 43.6 | 33.3 | 11.5 | 55.1 | 76.92 | 0.61 (0.47-0.74) |
| **Nitrofurantoin** | 35.9 | 21.8 | 42.3 | 53.8 | 0 | 46.2 | 73.08 | 0.56 (0.43-0.69) |

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EUCAST = European committee for antimicrobial susceptibility testing, CLSI = Clinical and Laboratory Standards Institute, IS = Intermediate susceptibility, S = Susceptible, R = Resistant * = Weighted Kappa agreement score, AMC= amoxicillin-clavulanic acid SAM= ampicillin/sulbactam, TPZ= piperacillin/tazobactam 30/6, TMP/SMX= trimethoprim/sulfamethoxazole.

**Table-3**. Interpretation of the comparative evaluations of the Kappa agreement scores by the two guidelines for uropathogenic extended-spectrum ß-lactamase producing *Escherichia coli*

| **Agreement (Kappa)** | | | | |
|---|---|---|---|---|
| **No agreement** (0.01–0.20) | **Fair** (0.21– 0.40) | **Moderate** (0.41–0.60) | **Substantial** (0.61–0.80) | **Perfect** (0.81–1) |
| - | AMC | Ampicilline | SAM | Cefuroxime |
| - | TPZ 30/6 | Cefepime | Cefoxitin | Cefotaxime 5 |
| - | Ceftazidime 10 | Tobramycin | Gentamicin | Ceftriaxone |
| - | Meropenem | Amikacin | Imipenem | TMP/SMX |
| - | Aztreonam | Ertapenem | Nitrofurantoin | Chloramphenicol |
| | | | | Ofloxacin |
| | | | | Ciprofloxacin |
| | | | | Norfloxacin |
| | | | | Levofloxacin |

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**Table-4**. Interpretation of the comparative evaluation of the Kappa agreement scores by the two guidelines for uropathogenic extended-spectrum ß-lactamase producing *K. pneumonia*

| **Agreement (Kappa)** | | | | |
|---|---|---|---|---|
| **No Agreement** (0.01–0.20) | **Fair** (0.21– 0.40) | **Moderate** (0.41–0.60) | **Substantial** (0.61–0.80) | **Perfect** (0.81–1) |
| AMC | Cefepime | SAM | Cefoxitin | Ampicilline |
| TPZ 30/6 | Amikacin | Nitrofurantoin | Gentamicin | Cefuroxime |
| Ceftazidime 10 | Ertapenem | | Tobramycin | Cefotaxime 5 |
| Aztreonam | | | Imipenem | Ceftriaxone |
| | | | Meropenem | TMP/SMX |
| | | | Ofloxacin | Chloramphenicol |
| | | | Ciprofloxacin | |
| | | | Norfloxacin | |
| | | | Levofloxacin | |