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***Original Article***

# Assessment of ß-lactams and Carbapenems Antimicrobials Resistance in *Klebsiella Oxytoca* Isolated from Patients with Urinary Tract Infections in Najaf, Iraq

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**Abstract**

Antimicrobial resistance is becoming an arising global issue. Until recent years, more than 50% of commercially available antibiotics were ß-lactam. Pathogenic bacteria which are resistant to antibiotics include all ß-lactams except for cephamycin and carbapenems. This study aimed to evaluate some ß-lactams and carbapenems antimicrobials resistance in *Klebsiella oxytoca.* In total, 177 urinary tract infection samples were collected for the purposes of the study. Isolates were identified using morphological features and routine biochemical testing. All isolates were tested for susceptibility to 11 antibiotics using the usual disc diffusion method. The result showed that 155 (87.57%) and 20 (11.29%) out of 177 collected urine samples were gram-negative bacterial isolates and gram-positive bacterial isolates, respectively. The findings also showed that there were two samples (1.12 %) with no growth. The results proved no susceptibility to Ampicillin, Cloxacillin, Ceftazidime, Penicillin, Piperacillin with a resistance rate of 100%.

**Keywords:** Antibacterial, B-lactam, ESBL, UTI

## 1. Introduction

Emergence of bacterial antimicrobial resistance is becoming a global issue. Until recent years, more than 50% of commercially available antibiotics were ß-lactam. Pathogenic bacteria which are resistant to antibiotics included all ß-lactams except for cephamycin and carbapenems. The common mechanisms for antibiotic resistance work by hydrolyzing the ß-lactam ring with the production of ß-lactamase enzymes. This is considered the common mechanism in resistance to ß-lactam antibiotics.

ß-lactamase enzymes are generally inhibited by clavulanate, sulbactam, or tazobactam which is determined a ß-lactamase inhibitor substance (1, 2). Extended-spectrum beta-lactamases (ESBL) belong to the family of ß-lactamase enzymes. Enterobacteriaceae are most ESBLs-producing members, especially *Klebsiella pneumonia* and *Escherichia coli* (3). The first incidence of ESBL production was in Germany in 1983. These isolates were responsible for the prevalence of various infection outbreaks worldwide (4).

It should be mentioned that *Klebsiella oxytoca* can cause a serious infection (5). One type of infection causes pneumonia-like symptoms (6). It should be noted that *K. oxytoca* can also lead to various disorders, such as urinary tract infections (UTIs) and wound infections. Moreover, the intense ESBL-mediated resistance of *K. oxytoca* isolates is determined as a major public health threat. The rise of these enzymes is leading to therapeutic failure and limitation of the antimicrobials used in therapy; hence, the infection is becoming hard to eradicate (7).

The most frequent bacterial infection in humans is UTI (7, 8). The UTIs caused by *K. oxytoca* happen when the pathogen passes into the urinary tract. It can also happen by the overgrowth of pathogenic bacteria resulting from the long use of a urinary catheter (9). Likewise, multidrug-resistant bacteria frequently result from resistance plasmids that are co-transferred by antibacterial agents, such as aminoglycosides, fluoroquinolones, tetracyclines, and chloramphenicol (10).

Carbapenems are the most effective treatment for severe infections (11). As gaps in the identification and reporting of ESBL production are linked to longer hospital admissions, higher morbidity, mortality, and healthcare expenses, the National Committee for Clinical Laboratory Standards (NCCLS) recommends ESBL screening protocols and confirmatory testing. This study aimed to evaluate some ß-lactams and carbapenems antimicrobials resistance in *K. oxytoca*.

## 2. Materials and Methods

The present research was conducted at the Microbiology Laboratory of the University of Alkafeel, which is part of the Department of Medical Laboratory Techniques, Najaf, Iraq. Patients at Al-Sadr Hospital provided a total of 177 UTI samples. Isolates were identified using morphological features and routine biochemical testing; all isolates were tested for susceptibility to 11 antibiotics using the usual disc diffusion method. After inoculation of all tested isolates of *K. pneumonia* on Muller Hinton Agar plates and application of antimicrobial discs, the plates were incubated at $37^0$ C for 24 h, and the inhibition zone diameter of each disc was measured and compared to the control measure. Ampicillin (30 µg), Cloxacillin (30 µg), Penicillin (10 U), Ceftazidime (5 µg), Cefixime (5 µg), Ceftriaxone (30 µg), Piperacillin (30 µg) Cefoxitin (30 µg), Cefotaxime (10 µg), Imipenem (10 µg), and Meropenem (10µg) (Bioanalyses, Turkey) were used. The results were clarified according to NCCLS guidelines.

## 3. Results

### 3.1. Total Bacterial Isolates

Based on the results, 155 (87.57%) and 20 (11.29%) out of 177 collected urine samples were gram-negative bacterial isolates and gram-positive bacterial isolates, respectively. Moreover, the results showed that there were two samples (1.12 %) with no growth as shown in figure 1.

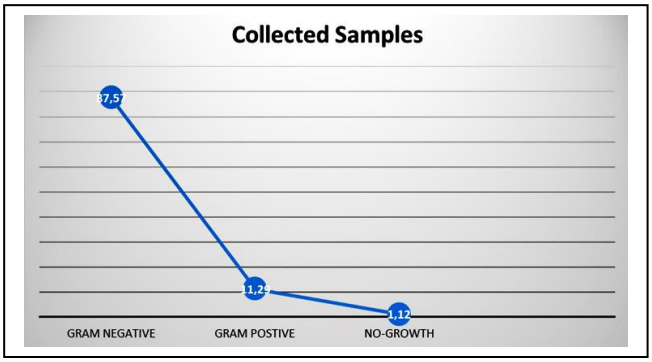


**Figure 1.** Percentage of total samples isolated from unhealthy with urinary tract infections

The results proved that the gram-negative bacteria isolates included 97 (62.58%) *E. coli* isolates, 43 (27.74%) *K. pneumonia* isolates, 11 (7.09%) *K. oxytoca* isolates, 3 (1.93%) *Pseudomonas aeruginosa* isolates, and 1 (0.64%) *Proteus* spp. isolate. While gram-positive bacteria isolates included 11 (55%) *S. aureus* isolates and 9 (45%) *E. faecalis* isolates as shown in figure 2.

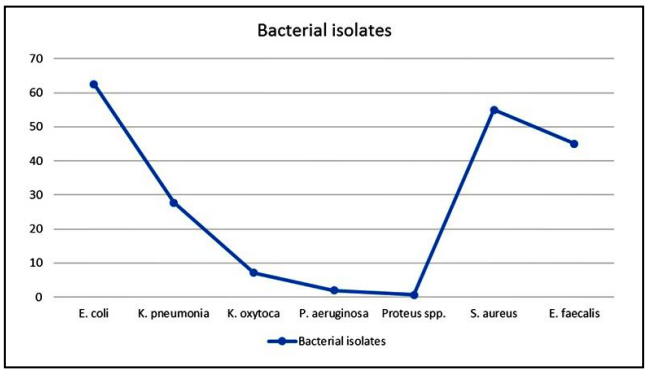


**Figure 2.** Number and percentage of total bacterial from unhealthy urinary tract infections

### 3.2. Antimicrobial Sensitivity Testing

In this study, there were 11 different antimicrobials. Based on the results, 11 (100%) isolates exhibited a high resistance rate to Ampicillin, Cloxacillin, Ceftazidime, Penicillin, Piperacillin, followed by Cefotaxime and Ceftriaxone (n=10, 90.90%) as well as Cefixime and Cefoxitin (n=9, 81.81%). Furthermore, the *K. oxytoca* was affected by Imipenem and Meropenem (n=9, 81.81%) and (n=8, 72.72%) (Figure 3).

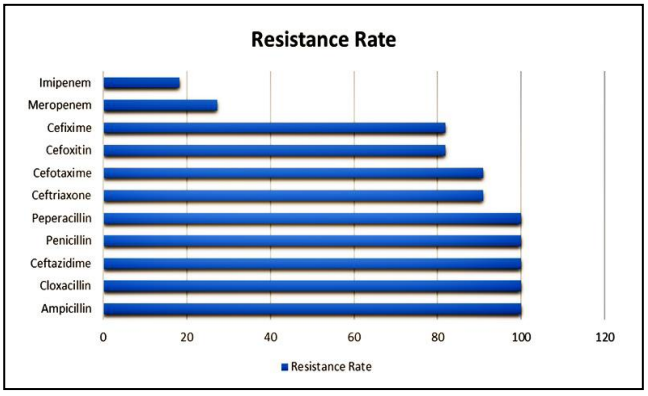


**Figure 3.** Number and percentage of total *Klebsiella oxytoca* isolate that was resistant to seven antimicrobials isolated collected from unhealthy urinary tract infections in Al-Najaf province of Iraq

## 4. Discussion

Beta lactamases enzymes are a major issue that has been identified worldwide and play a major role in drug resistance in many Enterobacteriaceae (12). The *K. oxytoca* in the present study was observed in (7.09%) of gram-negative bacterial isolates, which varies from the results of other research which was within the range of 3.52-5.88% (13). The resistance pattern may guide the selection of the antibiotic of choice for this type of multidrug-resistant bacteria (1). Antimicrobial susceptibility profiles of individual isolates should be used to guide treatment (14).

Penicillins are antibiotics that inhibit the formation of bacterial cell walls. The sensitivity of isolated *K. oxytoca* to penicillin and ampicillin was absent in this study. Other investigations, particularly among ß-lactamase producers, revealed similar findings (15). The prolonged administration of penicillins at random for years may be the cause of such high penicillin resistance (16). In addition, additional investigations have found that ampicillin is no longer effective against infections of the urinary tract. In contrast, cephalosporins of the second and third generations are routinely used to treat *K. oxytoca* infections (17).

Ceftriaxone resistance was found in 90.9 % of cases in this study, which was higher than the results of the earlier investigations (20% and 22.2%) (18, 19). In the present research, the rate of resistance to cefotaxime was 90.9% which agrees with the findings of the study performed by Chayakulkeeree, Junsriwong (20). This low susceptibility to cephalosporins could be highlighted by the fact that these antibiotics are commonly available without a doctor's prescription and are available at relatively low prices at any local drugstore (21). The rates of resistance to Imipenem and Meropenem were 18.19 and 27.28 %, respectively which was in line with the findings of the research performed by Razzaque (22) and Pérez-Vazquez, Oteo-Iglesias (23).

The *K. oxytoca* isolates obtained from clinical samples in this region developed a high resistance rate to penicillins and the majority of cephalosporins. The resistance to carbapenems has been arising. In hospitals, a tight antibiotic strategy should be maintained to monitor the impact of rising bacterial resistance and to take actions to prevent this resistance. Knowledge of the resistance pattern in a given location

will aid in the successful use of antibiotics. Moreover, the screening for the generation of ESBL as a standard technique in medical laboratories may provide clinicians with vital information on the antibiotics to use.

## Authors' Contribution

Study concept and design: A. S. Y. A.
Acquisition of data: T. H. H.
Analysis and interpretation of data: I. A. J. A.
Drafting of the manuscript: A. A. J. A.
Critical revision of the manuscript for important intellectual content: A. S. Y. A.
Statistical analysis: T. H. H.
Administrative, technical, and material support: A. S. Y. A.

## Ethics

The study protocol was approved by the medical ethics board of the University of Alkafeel, Najaf, Iraq. Written informed consents were provided by all the subjects participated in the study

## Conflict of Interest

The authors declare that they have no conflict of interest.

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