

# Emerging Carbapenemase *Klebsiella oxytoca* with Multidrug Resistance Implicated in Urinary Tract Infection

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## Abstract

**Background:** At present, *Klebsiella oxytoca* is emerging as a crucial persisted bacterial pathogen in urinary tract infection (UTI), which causes true public health problems worldwide. This study aimed to detect the incidence of *K. oxytoca* in patients severe from UTI with antibiotic sensitivity tests that assist urologist doctors for appropriate empirical antimicrobial therapy for this bacterium. **Methods:** *K. oxytoca* isolated clinically from urine samples during the period from January 2018 to December 2019 at the Al-Shomally General Hospital, Babil, Iraq, and a private laboratory in Babil city. A total of 430 patients were involved in this study; urine samples were processed at the hospital laboratory during this period; and a diagnosis has been done by the routine bacteriological diagnosis as well as VITEK® 2 system. **Results:** Of these 430 urine samples, 122 had bacterial growth; two types of *Klebsiella* species have been isolated in 18 patients (14.75%) of total specimens; *K. pneumonia* detected in 16 patients (89%); and *K. oxytoca* in 2 patients (11%) of the total *Klebsiella* species. *Escherichia coli* was the most prevalent bacteria (56; 45.90%). *K. oxytoca* UTI isolates were sensitive to amikacin, trimethoprim, and ciprofloxacin. However, these isolates showed resistance to amoxicillin, cefotazidime, clindamycin, nitrofurantoin, and cefotaxime. **Conclusion:** The current study showed an increasing burden of UTI caused by *K. oxytoca*. Multidrug resistance is associated with *K. oxytoca* implicated in UTI that causes changeable sensitivity to various antimicrobial agents.

**Keywords:** Carbapenemase, *Klebsiella oxytoca*, *Klebsiella* species, multidrug resistance, urinary tract infection

## INTRODUCTION

Urinary tract infections (UTIs) are considered the most common bacterial infection globally; every year, more than 150 million people suffering from acute or chronic UTI caused by various bacteria.<sup>[1]</sup>

*Klebsiella oxytoca* can cause community-acquired and hospital-acquired infection resembling those caused by *Klebsiella pneumonia* with less common frequently,<sup>[2]</sup> but in recent years, some types of causative agents bacterial UTI became more prevalent clearly with high antibiotic resistance that never seen before, *K. oxytoca* one of these emerging bacteria.

*K. oxytoca* is Gram-negative bacilli, nonmotile bacteria, and commensal in the intestinal tract in about 2%–10% of the population.<sup>[3]</sup> The main clinically habitats regions in the human body for *K. oxytoca* are the gastrointestinal and respiratory tract.<sup>[4]</sup> *K. oxytoca* as other enterobacteria can acquire antimicrobial agents resistance by producing lactamases and carbapenemase.<sup>[5]</sup> *K. oxytoca* antibiotic resistance outbreaks

have been observed in many hospitals and other places throughout the world and also environment reservoirs play an essential role in infection.<sup>[6]</sup> Few studies in Iraq observed *K. oxytoca* as a causative agent of UTI and emerging of carbapenemase-producing bacteria, and hence, the prevalence of this bacteria with antibiotic sensitivity tests presented in this study highlights the multidrug resistance (MDR) *K. oxytoca* associated with Iraqi patients severe from UTI.

## MATERIALS AND METHODS

The study protocol has been approved according to the Ethical Committee in the Babil Health Directorate on January 2, 2018.

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Besides, verbal approval was obtained from the patients before obtaining the sample. Health safety was obtained during the sampling. Furthermore, this work was done according to the Ethics Committee of the Iraqi Ministry of Health and was performed and agreed with all national regulations.

A total number of 430 patients with UTI were evolved in this study from January 2018 to December 2019. These patients have attended the Al-Shomally General Hospital, Babil, Iraq, and a private laboratory in Babil city. Every patient was suffering from the clear symptoms of UTI as a complaint of frequent urge to urinate and painful and also a questionnaire survey has been taken from the patients.

All nonrepetitive midstream urine samples were included in the study. A urine sample for direct examination and basic bacterial-cultured methods have been done. Urine samples were directly inoculated on Blood agar and MacConkey Agar. The bacterial diagnosis of suspected *Klebsiella* spp was identified by VITEK 2 (Biomerieux). Further identification was done as per the routine laboratory protocols. Mix growth of *K. oxytoca* and other bacteria were excluded from this study.

Antimicrobial susceptibility investigation was done as to Kirby–Bauer’s disc-diffusion method<sup>[7]</sup> included ceftriaxone (30 mg), ceftazidime (30 mg), cefotaxime (30 mg), gentamicin (10 mg), amikacin (30 mg) ciprofloxacin (5 mg), imipenem (10 mg), meropenem (10 mg), and clindamycin. Bacteria considered MDR when they resist more than two classes of antibiotics.

## RESULTS

*K. oxytoca* isolated from the urine samples during the period from January 2018 to December 2019 at the Al-Shomally General Hospital, Babil, Iraq. Out of these 430 urine samples, 122 had bacterial growth. The two types of *Klebsiella* species have been isolated in 18 patients (14.75%) of total specimens; the first was *K. pneumonia* in 16 patients (89%) and *K. oxytoca* in 2 patients (11%) of the total *Klebsiella* species. *Escherichia coli* were the most prevalent bacteria in this study (56; 45.90%) [Figures 1 and 2].

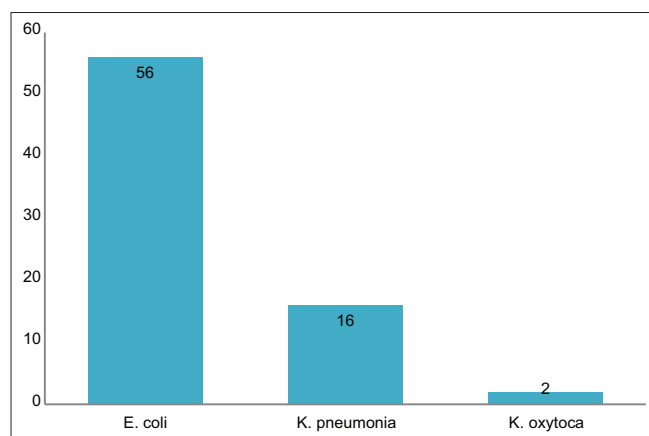


Figure 1: Distribution of bacterial urinary tract infection

Biochemical tests of *K. oxytoca* revealed a positive indole test, whereas *K. pneumonia* showed a negative indole test; both species have positive results to catalase, urease, and capsule tests [Table 1].

Antibiotic sensitivity pattern was studied, and it was found that all the *K. oxytoca* isolates were sensitive to trimethoprim, ciprofloxacin, and amikacin. However, these isolates showed resistance to amoxicillin, cefotazidime, clindamycin, nitrofurantoin, and cefotaxime. Multidrug-resistant *K. oxytoca* has been detected in the current study [Table 2].

## DISCUSSION

*Klebsiella* species are becoming a crucial pathogen of all populations and are being implicated in increasing morbidity among the patients. Infections with *Klebsiella* species regarding cause to prolonged stays in hospitals and compromised immune persons along with exposures to multiple antibiotics are the main factors that increase the risks for infections and MDR.

Table 1: Biochemical tests of *Klebsiella pneumoniae* and *Klebsiella oxytoca*

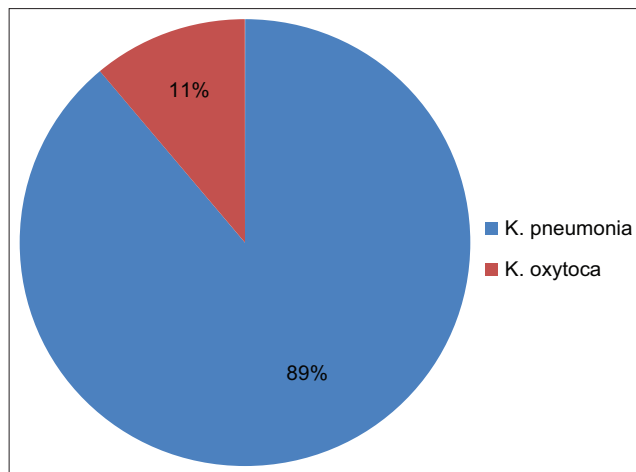
Biochemical test	<i>K. oxytoca</i>	<i>K. pneumonia</i>
Motility test	–	–
Urease	+	+
Citrate	+	+
Voges-Proskauer test	+	+
Methyl red	–	–
Catalase	+	+
Oxidase test	–	–
Indole	–	+
Capsule	+	+

*K. pneumonia*: *Klebsiella pneumoniae*, *K. oxytoca*: *Klebsiella oxytoca*

Table 2: Antibiotic pattern of *Klebsiella oxytoca* clinically isolated from urinary tract infection

Antibiotic	<i>K. oxytoca</i> 1	<i>K. oxytoca</i> 2
Amoxicillin	Resistance	Resistance
Ciprofloxacin	Sensitive	Sensitive
Imipenem	Sensitive	Resistance
Meropenem	Sensitive	Resistance
Tetracycline	Sensitive	Resistance
Ceftriaxone	Resistance	Resistance
Cefotaxime	Resistance	Resistance
Cefotazidime	Resistance	Resistance
Gentamicin	Sensitive	Sensitive
Amikacin	Sensitive	Sensitive
Trimethoprim	Sensitive	Sensitive
Nalidixic acid	Sensitive	Sensitive
Chloramphenicol	Sensitive	Resistance
Azithromycin	Sensitive	Sensitive
Clindamycin	Resistance	Resistance
Tobramycin	Sensitive	Resistance
Nitrofurantoin	Resistance	Resistance

*K. oxytoca*: *Klebsiella oxytoca*



**Figure 2:** Distribution of *Klebsiella oxytoca* to *Klebsiella pneumoniae*

In the current search, the prevalence of *K. oxytoca* was 11% of total 18 *Klebsiella* species isolated in Iraqi UTI patients; some studies detected predominance of *K. oxytoca* in urine samples as 8% of all patients with UTI.<sup>[8]</sup> Another study in elderly adults severing from UTI revealed 32 *K. pneumoniae* and 7 *K. oxytoca*.<sup>[9]</sup> Furthermore, *K. oxytoca* isolates from four patients (0.7%) in the United Kingdom.<sup>[10]</sup> Some studies showed a high prevalence of *K. oxytoca* reached (34%) in Ghana.<sup>[11]</sup>

In the last decades, *K. oxytoca* showed many reports of the outbreak, one report in Austria when five patients in 2011 infected by *K. oxytoca* that capable of producing many enzymes as carbapenemase,<sup>[5]</sup> in this study, carbapenemase is also detected.

*E. coli* was the most common prevalent pathogen isolated from UTI patients in the current study. *E. coli* have been implicated in 56 samples (45.90%), and this finding accords many studies<sup>[12]</sup> that mentioned *E. coli* prevalence was 42.2% in patients with UTI, and also agree with.<sup>[13-15]</sup>

Biochemical tests of *K. oxytoca* revealed a positive indole test, whereas *K. pneumoniae* showed a negative indole test; both species have positive results to catalase, urease, and capsule tests. *K. pneumoniae* and *K. oxytoca* can be distinguished from each other by indole presentation by *K. oxytoca* but not produced by *K. pneumoniae*.<sup>[2]</sup> This study revealed the sensitivity of *K. oxytoca* to trimethoprim, ciprofloxacin, and amikacin. Resistance to amoxicillin, cefotazidime, clindamycin, nitrofurantoin, and cefotaxime is observed. Multidrug-resistant *K. oxytoca* has been detected in the current study.

All *K. oxytoca* in this search revealed resistance to amoxicillin because most strains of *K. oxytoca* produce a chromosomally mediated beta-lactamase (K1).<sup>[2]</sup>

In this work, *K. oxytoca* was resistant to cephalosporin as ceftriaxone, cefotazidime, and cefotaxime. Almost all isolates of *Klebsiella* species were initially considered to be susceptible to cephalosporin; studies over the last two decades have shown variable susceptibility to this antibiotic class; this

resistance is mediated by plasmid-mediated extended-spectrum beta-lactamases.<sup>[2]</sup>

## CONCLUSION

*K. oxytoca* with MDR considered serious public health challenges to patients and to clinicians, especially carbapenemase bacteria that emerged in recent years, so this need to direct more attention to antimicrobial resistance monitoring and surveillance. This would be critical for creating and fine-tuning effective antimicrobial resistance control strategies and for informing the accurate antibiotic prescriptions in clinical settings.

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## Conflicts of interest

There are no conflicts of interest.

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