



## Assessment of antimicrobial resistance of *Klebsiella oxytoca* isolated from pregnant women with UTIs in Najaf, Iraq

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**SUMMARY.** Background: Urinary tract infections (UTIs) are common in pregnant women and if untreated maternal fetal health is threatened if untreated or caused by multidrug-resistant (MDR) bacteria. We identified a resistant model resistance in Iraqi pregnant women with UTI to *Klebsiella oxytoca*, an important uropathogen. Methods: *Klebsiella oxytoca* were (n=34) from pregnant women urine samples (n=34) diagnosed with UTI in a hospital in Najaf, Iraq during October 2022-January were tested using the CLSI disc diffusion method 2023 between ensured that 12 drugs will be monitored. Antimicrobial susceptibility testing against Multidrug resistance (MDR) was defined as insensitivity to  $\geq 3$  antimicrobial classes. Results: High resistance rates were observed for ampicillin (91.2%), oxacillin (67.6%), nalidixic acid (52.9%), and ciprofloxacin (38.2%). 73.5% of isolates showed MDR, including 23% resistance to extended-spectrum cephalosporins. All MDR isolates remained susceptible to imipenem and amikacin. Conclusion: This study demonstrates severe MDR, especially against oral medications commonly used to treat urinary tract infections of UTI in pregnant women. Imipenem and amikacin have the greatest activity, emphasizing the importance of antimicrobial management and prevention of suppression. Timely management will improve the management of UTI, the leading cause of pregnancy complications in Najaf, Iraq.

### INTRODUCTION

Females are more likely to get urinary tract infections (UTIs) because of their shorter urethra and closer anatomical closeness to the anus<sup>1</sup>. The most frequent bacterial illness that affects pregnancy is urinary tract infection<sup>2</sup>. Numerous hormonal and physical changes occur in the body during pregnancy, starting in the sixth week and reaching its highest frequency in

Ninety percent of pregnant women have the syndrome between weeks 22th and 24th<sup>3</sup>. Urinary stasis and vesicoureteral reflux are risks that are increased by urethral dilation<sup>4</sup>. Furthermore, two other conditions that increase the risk of bacterial infections during pregnancy are glycosuria and aminoaciduria<sup>5</sup>. Urinary tract infections during pregnancy cause morbidity and mortality in both the mother and the fetus if

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left untreated<sup>6</sup>. Uropathogens have been known to acquire resistance to previously effective antibiotics in recent years, according to reports from all around the world<sup>7</sup>. Pregnancy-related UTI treatment presents two main challenges: preserving the fetus and fostering a resistance to urinary infections<sup>8</sup>.

The gram-Negative bacteria are the most prevalence organisms that causing UTI, *E. coli* and *Klebsiella sp.* are the most prominent among the organism's causing this infection<sup>9</sup>.

*Klebsiella sp.* is a notorious group of pathogens that pose a significant threat to human health. These bacteria are responsible for a wide array of infections, ranging from lungs to urinary tracts, surgical sites, and soft tissues<sup>10</sup>. These infections are prevalent in hospitals, long-term care facilities, and communities globally, and they can even cause blood infections<sup>11</sup>.

The emergence of *Klebsiella oxytoca* as a significant bacterial strain causing hospital-acquired infections in adults is causing concern<sup>11</sup>. This bacterium is becoming increasingly resistant to commonly used antibiotics, making it difficult to treat especially between pregnant women<sup>12</sup>.

The study aimed to investigation of antimicrobials sensitivity of *Klebsiella oxytoca* in urinary tract infection pregnant women.

## METHODOLOGY

Between October 2022 and January 2023, a total of 194 urine samples from expectant mothers with or without UTI symptoms were taken. Participants in the study ranged in age from 20 to 45 years.

Urine samples from clean catch midstream were collected using a normal procedure and placed into a sterile screw-capped universal container<sup>13</sup>. To stop the growth of bacteria in the urine samples, 0.2 mg of boric acid was applied along with labelling the samples<sup>14</sup>.

Using a sterile 4 mm loop, the samples were cultivated on blood agar and cysteine-lactose electrolyte deficient agar in order to isolate microorganisms<sup>15</sup>. After an overnight incubation period at 37 °C, the samples proved positive if an organism could be cultivated at a concentration of 104 CFU/mL, which could be calculated by multiplying the isolated colonies by 1000. Using common biochemical tests, the isolates were identified to the species level<sup>16,17</sup>.

All of *Klebsiella oxytoca* isolates performed to antibiotics sensitivity test using the modified disc diffusion method. All inoculums adjusted to standard of McFarland (0.5), then swabbed to Muller Hinton Agar plates to preparing for antibiotics sensitivity test<sup>18</sup>. Twelve type of antibiotics was performed, these antibiotics selected due to usual prescription by physicians.

These antibiotics were amoxicillin (10 µg), oxacillin (10 µg), cefotaxime (10 µg), ceftriaxone (30 µg), nalidixic acid (30 µg), ciprofloxacin (5 µg), norfloxacin (10 µg), amikacin (30 µg), gentamycin (10 µg), erythromycin (10 µg), clindamycin (2 µg), vancomycin (30 µg).

The study results subjected to statical analysis using (Chai square), the values less than 0.05 were determined statically significant.

## RESULTS

Among 194 urine samples from pregnant mothers, 93 samples (48%) tested positive for bacterial growth at  $\geq 104$  CFU/mL. *Klebsiella oxytoca* was isolated from 34 samples (13.4% of total, 36.6% of positive cultures).

Resistance screening of 34 *Klebsiella oxytoca* isolates revealed precursor resistance to several drugs (Figure-1). Resistance to amoxicillin (91.2%) was most common, followed by oxacillin (67.6%), nalidixic acid (52.9%), and ciprofloxacin (38.2%). Moderate resistance to cefotaxime (29.4%), ceftriaxone (23.5%), and norfloxacin (20.6%) was observed. Resistance to amikacin (11.8%), gentamicin (8.8%), erythromycin (5.9%), clindamycin (2.9%), and vancomycin (0%) was rare.

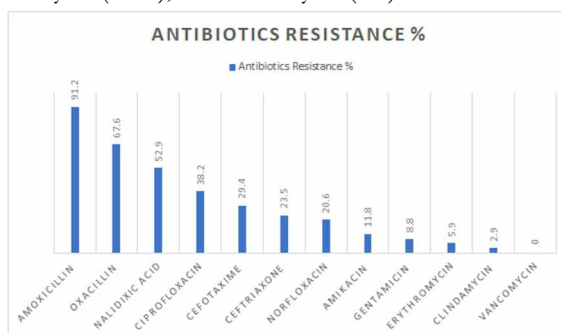


Figure-1 Showing antibiotics resistance rate of *Klebsiella oxytoca* isolated from UTI pregnant women

Multidrug resistance (MDR), defined as resistance to  $\geq 3$  antimicrobial classes, was evident in 73.5% of isolates. The highest number of antibiotic resistances per isolate was 9/12 (25.0%). All MDR isolates remained susceptible to amikacin and vancomycin.

This study highlights the resistance of *Klebsiella oxytoca* strains isolated from the urine of pregnant women, especially to drugs commonly used in primary care settings. The 73.5% prevalence of MDR observed here is high and consistent with recent field reports from Pakistan and India describing an increase in multidrug resistance in *Klebsiella spp.* Mechanisms of resistance in *Klebsiella oxytoca* such as extended-spectrum beta-lactamases and plasmid-mediated quinolones. Genetic immunity may explain the observations. Meanwhile, amikacin and vancomycin re-

mained reliably effective against most MDR isolates.

Certain limitations must be acknowledged. Bacterial resistance does not necessarily represent a cause of UTI compared with asymptomatic bacteriuria because some patients had no signs/symptoms. In addition, the resistant phenotype was no longer shown. However, statistically significant increases in sensitive and nonsensitive exclusion rates were significant for several key parameters. Detailed research, including genetic analysis, can provide deeper insights.

At the end, study findings emphasize the importance of ongoing local surveillance to effectively treat infected UTIs in pregnant populations considering antibiotic use plan. Which is prudent to prevent further spread of resistance through prophylactic practices also considering maternal and fetal outcomes.

## DISCUSSION

The high prevalence of MDR *Klebsiella oxytoca* observed in this study is of concern, and has important implications for pregnant women with UTIs cared for in Najaf, Iraq. The MDR rate of 73.5% exceeds the average reported in previous regional studies in Iraq, Iran, Pakistan and India<sup>19-23</sup> on a large scale. 1-3 antimicrobial resistance in this setting highlights the rapid development and spread.

*Klebsiella oxytoca* is well known for its ability to acquire early and widespread genetic resistance through genetic movements such as plasmids and transposons<sup>24</sup>. Four to six common first-line drugs. High prevalence of UTI in pregnant women including ampicillin, TMP-SMX and fluoroquinolones,<sup>7-9</sup> suggest that these by overuse of antimicrobial classes<sup>25-26</sup>. Strong selective pressure has been applied to local *Klebsiella oxytoca* populations inducing resistance develops and spreads. Although some medications remain expensive options in primary care settings with limited resources, they are worthy of a smart prophylaxis if they are used by the mouth<sup>27-29</sup>.

Current carbapenems retain reliable *in vitro* activity against the majority of MDR isolates in this study. However, carbapenemases have now emerged worldwide<sup>10-12</sup> and it is important to continue to use them judiciously to preserve this class as a treatment of last resort, especially in light of emerging reports of resistance in the field<sup>30-34</sup>. In addition to antimicrobial resistance modification, standardized infection control practices can also help reduce the spread and further spread of resistant clones<sup>35-38</sup>.

Several restrictions were acknowledged. Since resistance profiles are inconsistent with their causes, careful monitoring is required<sup>39</sup>. The mechanism of molecular resistance has yet to be further demonstrated but will provide deeper insights. Strengths include an under-

studied pathogen and population screening<sup>40-42</sup>.

At the end, this study highlights the need for timely targeted antimicrobial therapy with customized guidelines consistent with local epidemiology. Caution a promotion and infection prevention are essential to achieve evidence-based management of UTIs in this vulnerable group of patients, and to prevent compromised treatment efficacy<sup>43-45</sup>.

## CONCLUSION

In this study, the causes of UTI among pregnant women in Najaf, Iraq, were investigated. The high prevalence of identified MDR isolates, if not addressed promptly, creates a stalemate in terms of clinical implications. Key findings point to the need for judicious use of antibiotics and increased infection prevention practices. Timely monitoring will help optimize treatment interventions and delay emerging resistance. Prudent management and adherence to guidelines developed for local epidemiology may achieve the goal of improved pregnancy outcomes while maintaining limited treatment for these complex patients. Research a continuation of resistance markers to inform sustained multidrug prevention strategies against multidrug-resistant uropathogens in this population. Will provide a deeper understanding.

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