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Original Research Article

# Emerging trends in urinary tract infection pathogens: Insights from *K. oxytoca* and *M. morganii* in Indian settings

**Soni Gupta**[1], **Anju Dhar**[2]*, **Deepali Ghoel**[1], **Rupesh Dingankar**[1]

[1]*General Diagnostics International Private Limited,, Navi Mumbai, Maharashtra, India*
[2]*Dept. of Microbiology, The Mahatma Gandhi Mission (M.G.M) Hospital and Research Center, Navi Mumbai, Maharashtra, India*

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ABSTRACT

Urinary tract infections (UTIs) are a significant global health concern affecting millions annually. In India, UTIs linked to various bacterial pathogens, particularly *K. oxytoca* and *M. morganii,* present a formidable challenge. This study aimed to evaluate the occurrence of these bacteria in urine samples obtained from UTI patients in Indian settings. Our investigation identified a notable proportion of UTIs associated with *K. oxytoca* and *M. morganii,* highlighting the necessity for customized therapeutic approaches. Additionally, we conducted antibiotic susceptibility testing to guide appropriate antibiotic selection. Our findings revealed that 90% of *K. oxytoca* isolates exhibiting additional resistance to Azithromycin (AZK). These results emphasize the importance of judicious antibiotic use and continuous monitoring of antibiotic resistance in UTI-causing pathogens in Indian healthcare settings. This study contributes to UTI management strategies and the development of tailored treatment modalities for the Indian population.



## 1. Introduction

Urinary tract infections (UTIs) are among the most prevalent bacterial infections worldwide, posing significant challenges to healthcare systems and affecting individuals of all ages and backgrounds.[1] UTIs range from asymptomatic bacteriuria to severe systemic illness, reflecting the diverse clinical spectrum associated with microbial invasion of the urinary tract.[2] While females historically have had a higher susceptibility to UTIs due to anatomical factors, recent evidence suggests a rising incidence among males, indicating shifting epidemiological trends.[3] UTIs can occur in various settings, including community-acquired and healthcare-associated infections.[4]

The clinical presentation of UTIs varies widely, from uncomplicated cystitis, characterized by symptoms such as dysuria, frequency, and urgency, to severe pyelonephritis, which presents with fever, flank pain, and systemic symptoms.[5] Given the significant clinical and economic impact of UTIs, there is an urgent need for a comprehensive understanding of these infections, timely diagnosis, and effective management strategies.[5] The emergence of antibiotic resistance further complicates UTI management, with widespread antibiotic use contributing to the development of multidrug-resistant pathogens.[4] To address this challenge, it is essential to prioritize judicious antimicrobial use guided by local susceptibility patterns and resistance surveillance data.[1] By optimizing UTI management strategies, healthcare providers can mitigate the clinical and economic burden of these infections and reduce the emergence of antibiotic resistance, ultimately improving patient outcomes.[6]

Urinary tract infections (UTIs) are prevalent infectious conditions affecting individuals across diverse

* *Corresponding author*.
*E-mail address*: anjs09@gmail.com (A. Dhar).

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demographics, posing significant challenges in both community and hospital settings.[7] Among the causative agents, *Klebsiella oxytoca* and *Morganella morganii* stand out as noteworthy contributors, particularly due to their ability to colonize the gastrointestinal tract and ascend to the urinary tract, precipitating infection.[7] *K. oxytoca* and *M. morganii* are gram-negative bacteria commonly found in the human gastrointestinal tract. However, both species can cause UTIs, despite their lower prevalence compared to other UTI pathogens, their ability to form biofilms and develop antimicrobial resistance makes them clinically significant.

Significance of *K. oxytoca* and *M. morganii* in UTIs:

**Biofilm formation:** Both *K. oxytoca* and *M. morganii* have the capability to form biofilms on urinary catheters and mucosal surfaces of the urinary tract, leading to persistent infections and treatment challenges.[1]

**Antimicrobial resistance:** Increasing resistance to commonly used antibiotics, including beta-lactams, fluoroquinolones, and aminoglycosides, has been reported among *K. oxytoca* and *M. morganii* strains, necessitating targeted antibiotic therapy based on susceptibility testing.[8,9]

**Association with complicated UTIs:** These pathogens are frequently associated with complicated UTIs, including catheter associated UTIs, pyelonephritis, and UTIs in immunocompromised individuals, leading to increased morbidity and mortality if not promptly treated.[8,10]

**Nosocomial infections:** *K. oxytoca* and *M. morganii* are often implicated in nosocomial UTIs, particularly in healthcare settings where antibiotic pressure and invasive procedures are common.[11]

**Diagnostic challenges:** Due to their relatively low prevalence and overlapping phenotypic characteristics with other Enterobacterales, accurate identification of *K. oxytoca* and *M. morganii* in routine urine cultures requires specific laboratory methods.[12]

*Klebsiella oxytoca*, a gram-negative bacterium, is recognized for its role in UTIs, manifesting in symptoms ranging from frequent and painful urination to severe complications such as fever and flank pain.[12] Predisposing factors including urinary catheterization, structural urinary tract abnormalities, and recent antibiotic use heighten susceptibility to *K. oxytoca* UTIs.[1] Similarly, Morganella morganii, another gram-negative bacterium, acts as an opportunistic pathogen, capable of instigating UTIs, particularly in individuals with urinary tract anomalies or compromised immune systems.[8,10] Its ability to produce urease further complicates UTIs by contributing to urinary stone formation, exacerbating symptoms and potential complications.[10]

Antibiotic resistance adds a layer of complexity to UTI management, with both *K. oxytoca* and *M. morganii* demonstrating the acquisition of resistance mechanisms such as extended-spectrum beta-lactamase (ESBL) production and carbapenem resistance.[8,9] This necessitates a nuanced approach to treatment, considering the limited antibiotic options and the potential need for combination therapy.[11]

Understanding the epidemiology, pathogenesis, and antibiotic susceptibility profiles of *K. oxytoca* and *M. morganii* is imperative for effective UTI management and infection control measures. Here we delve into the intricacies of these bacterial pathogens, exploring their impact on UTIs and elucidating strategies for mitigating their clinical burden and combating antibiotic resistance from a tertiary care hospital of western India. This paper focus on UTI and its antibiogram.

## 2. Materials and Methods

The objective of this study is to provide a comprehensive description of the characteristics and prevalence of *K. oxytoca* and *M. morganii* isolates associated with urinary tract infections (UTIs). Another objective of this study is to assess the susceptibility of *K. oxytoca* and *M. morganii* isolates to various antibiotics commonly used for UTI treatment.

### *2.1. Study design*

This study employed a retrospective descriptive record-based approach to analyse data related to *K. oxytoca* and *M. morganii* isolates from UTI cases.

### *2.2. Duration of study*

The study spanned over a period of one year, from April 2022 to March 2023.

### *2.3. Study population*

The study included urine samples collected from all inpatients of the tertiary care hospital who were tested in the department of microbiology during the specified duration. Cultures that yielded contaminants or mixed bacterial growths were excluded from the analysis.

### *2.4. Processing of samples*

Urine samples were collected from patients upon the physician's recommendation, prior to the administration of any antibiotics. The patients' details were diligently recorded in registers. Upon receipt in the laboratory, the urine sample should be mixed well to ensure uniform distribution of bacteria. Using a calibrated loop, the sample is inoculated onto standard MacConkey agar media. The inoculated plates are streaked for isolation using the quadrant streaking method to obtain well-separated colonies. Passaging was done on MacConkey Agar to get isolated pure colonies. The inoculated plates are incubated aerobically at 35-37°C for 18-24 hours. Growth

is checked after 24 hours, and if no growth is observed, plates are rechecked after 48 hours. In cases where no growth was observed for 5 days in culture plates, the sample was reported as negative. For positive samples, the culture plates were again plated and incubated at 37°C aerobically. The growth obtained was identified by colony morphology, gram stain and standard biochemical identification tests. Antimicrobial susceptibility testing was performed by Kirby–Bauer disk diffusion method and interpreted using clinical laboratory standard institute (CLSI) guidelines 2019.[13] For bacteria from blood isolates following drugs were tested: Amikacin (AK), Augmentin (AG), Ampicillin-sulbactam (AS), Aztreonam (AC), Azithromycin (AZK), Cefazolin (CZ), Cefuroxime (CB), Ceftriaxone (RP), Ceftazidime (FG), Cefepime (ZX), Ciprofloxacin (RC), Chloramphenicol (CH), Gentamicin (GM), Imipenem (IM), Meropenem (MP), Nitrofurantoin (FD), Ceftriaxone-sulbactam (CL), Piperacillin-Tazobactam (PT), Trimethoprim-sulfamethoxazole (BA)) were tested. The susceptibility and resistance were interpreted as per CLSI guidelines 2019.

### 2.5. *Data analysis*

Data were entered and analysed using SPSS software.[14]

### 2.6. *Ethical clearance*

This is a retrospective study done with bacterial isolates and their susceptibility pattern. It's not interventional study, hence ethical clearance was not taken for the same.

## 3. Results

A total of 59 isolates were obtained and all were taken into the study, 37 were for *K. oxytoca* and 22 for *M. morganii* (Figure 1). The age group varied from 5 months to 85-year-old patient, and both genders were taken into the study.

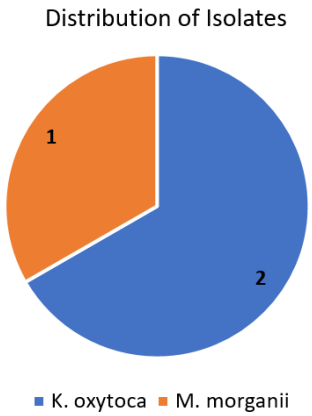


**Figure 1:** The number of isolates obtained and its distribution

We also looked at the gender distribution (ratio to male to female) and the ratio were high for *K. oxytoca* in females as shown in Figure 2.

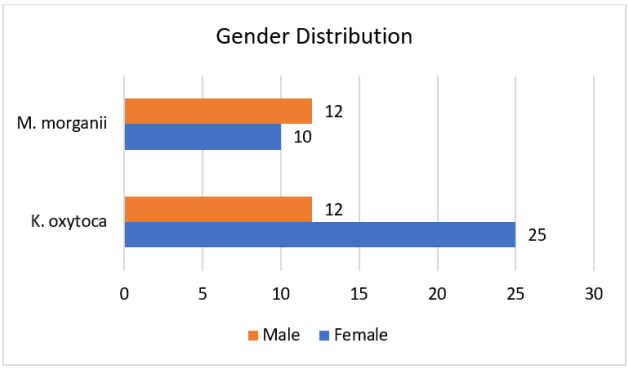


**Figure 2:** Gender distribution with the isolates of *K.oxytoca* and *M. morganii*

Further, the age distribution was also seen across the enrolled patients and found all the age groups. Children age group was found to be highest in blood infection while younger adults with least infection. The same has been shown in Figure 3.

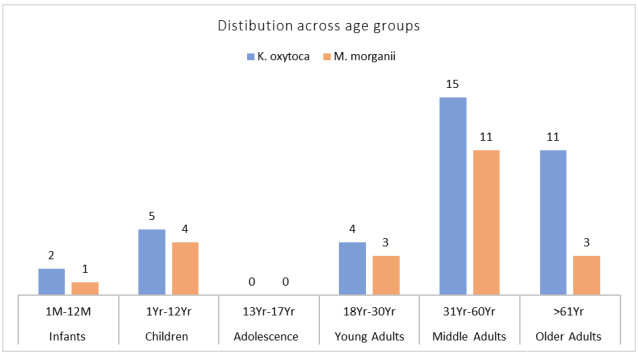


**Figure 3:** Distribution across age groups for *K. oxytocaand M. morganii*

Further, both bacteria *K. oxytoca* and *M. morganii* were plotted in bar graph for its resistance pattern against all antibiotics. Figures 4, 5, 6 and 7 represents the same.

A heat map was obtained for following culture and antibiotic and the same has been shown in the Figure 8. Most of the isolates of *K. oxytoca* and *M. morganii* were susceptible as seen in the heat map.

## 4. Discussion

Urinary tract infections (UTIs) represent a significant burden, with prevalence and incidence varying by age, sex, race, and other factors.[4,5] UTIs are most common in children under two years old, with a cumulative incidence of 2% in boys and 7% in girls within the first six years of life.[3]

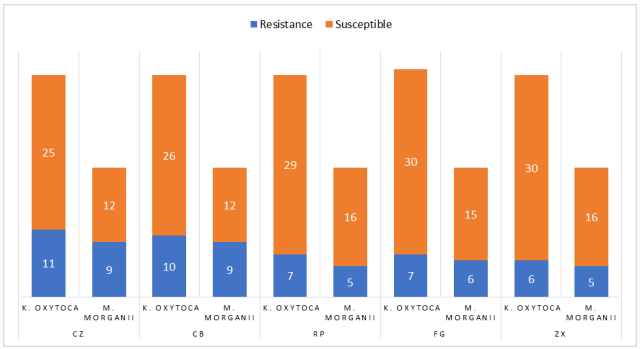


**Figure 4:** Antibiotic resistance pattern against: Cefazolin (CZ), Cefuroxime (CB), Ceftriaxone (RP), Ceftazidime (FG), Cefepime (ZX) for *K.oxytoca* and *M. morganii* respectively

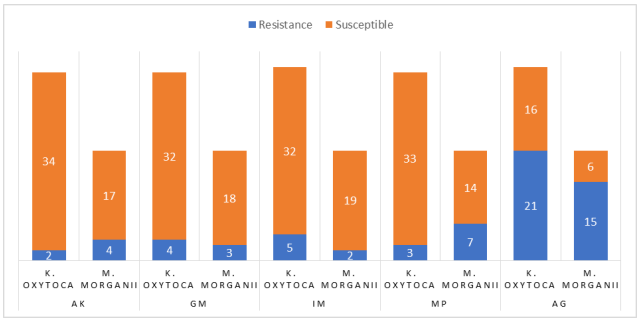


**Figure 5:** Antibiotic resistance pattern against: Amikacin (AK), Gentamicin (GM), Imipenem (IM), Meropenem (MP), Augmentin (AG) for *K.oxytoca* and *M. morganii* respectively

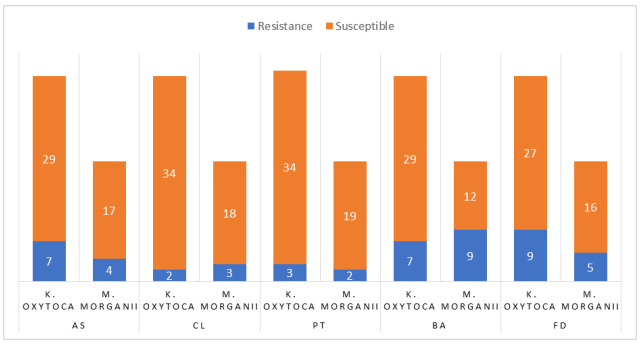


**Figure 6:** Antibiotic resistance pattern against: Ampicillin-sulbactam (AS), Ceftriaxone-sulbactam (CL), Piperacillin-Tazobactam (PT), Trimethoprim-sulfamethoxazole (BA), Nitrofurantoin (FD) for *K. oxytoca* and *M. morganii* respectively

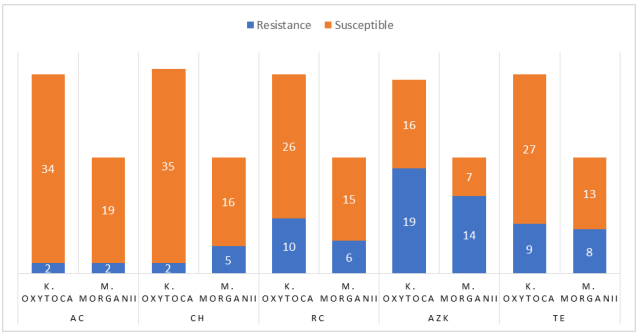


**Figure 7:** Antibiotic resistance pattern against: Aztreonam (AC), Chloramphenocol (CH), Ciprofloxacin (RC), Azithromycin (AZK), Tetracycline (TE) for *K. oxytoca* and *M. morganii* respectively

Globally, UTIs affect up to 9% of febrile children aged 1-60 months, with a higher prevalence in girls and malnourished children.[2] Recurrence rates are high, especially in the first 12 months after the initial infection, with risk factors including age <6 months, severe vesico-ureteric reflux, and abnormal renal scans.[1] While in adults it is one of the most common infections in local primary care. The incidence of UTIs in adult males aged under 50 years is low, with adult women being 30 times more likely than men to develop a UTI.[5]

*Escherichia coli* is the predominant pathogen in paediatric UTIs, accounting for about 80-90% of cases.[15] Other pathogens include Staphylococcus aureus, *Klebsiella pneumoniae*, and Proteus species.[16] Understanding the microbial spectrum is crucial for selecting appropriate antibiotics. An India-based study revealed *E. coli* as the most isolated bacterium in UTIs, followed by various other pathogens such as Staphylococcus aureus, *Klebsiella pneumoniae*, and *Morganella morganii*, among others.[17,18]

Prevalence of *Klebsiella oxytoca*- Studies have reported varying prevalence rates of *K. oxytoca* among UTI isolates, ranging from 0.5% to 10%. In a recent multicentre study done in 2020, *K. oxytoca* accounted for 4.5% of UTI isolates, highlighting its growing importance as a UTI pathogen. Certain populations, such as elderly patients in long-term care facilities or those with indwelling urinary catheters, may have higher rates of *K. oxytoca* UTIs due to increased exposure to healthcare settings and antimicrobial agents.[19]

Prevalence of *Morganella morganii* -*M. morganii* is less commonly isolated from UTIs compared to *K. oxytoca* and *E. coli*, with reported prevalence rates ranging from 0.1% to 2.5%. However, *M. morganii* is frequently associated with complicated UTIs, including catheter-associated UTIs, pyelonephritis, and UTIs in immunocompromised individuals. A study done in 2019 found that *M. morganii* accounted for 1.8% of UTI isolates, underscoring its clinical relevance in certain patient

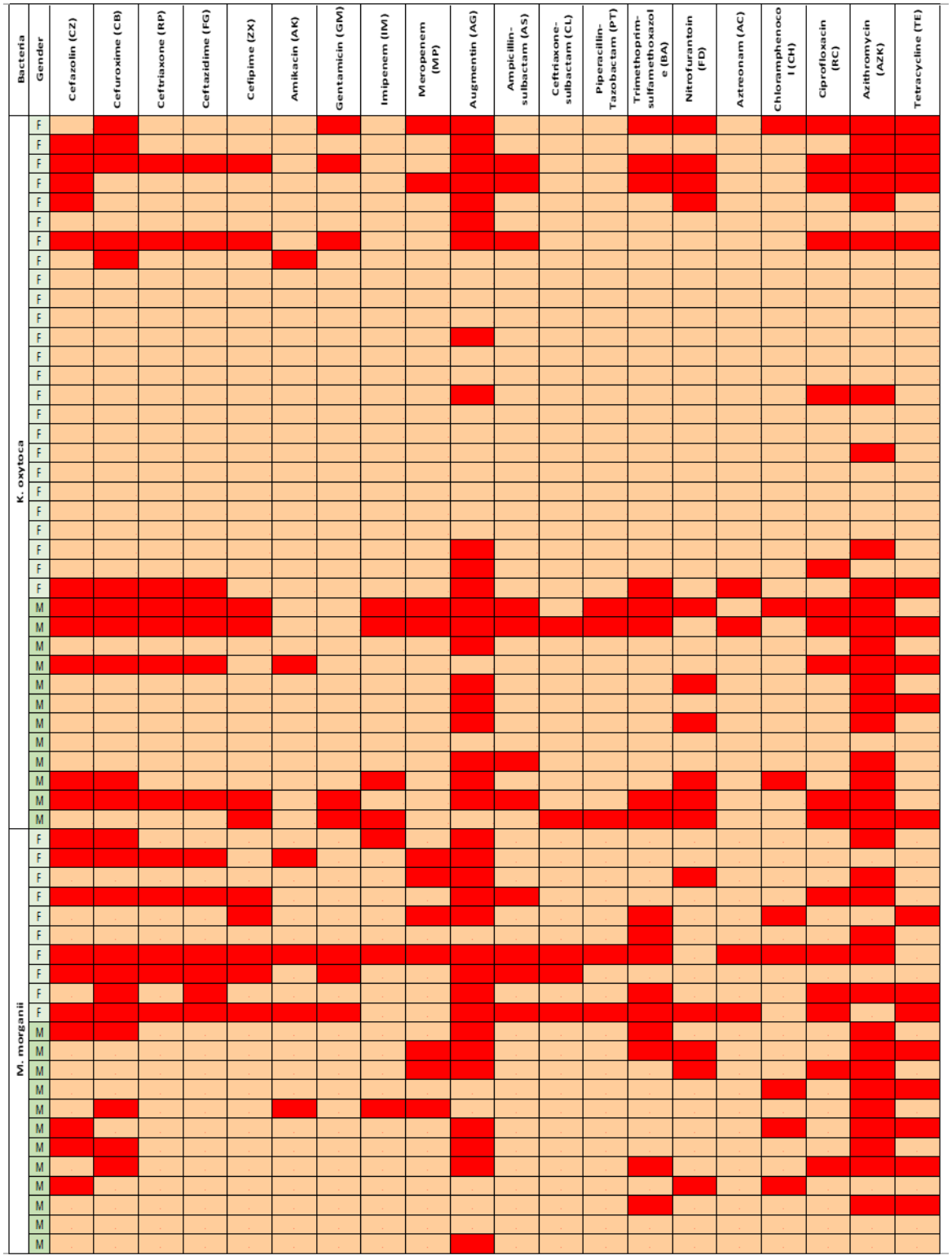


**Figure 8:** *K. oxytoca* and *M. morganii* culture against antibiotic resistance pattern in heat map

populations.[20]

Morganella morganii is typically a commensal organism, it can act as an opportunistic pathogen, causing various infections such as sepsis, abscesses, urinary tract infections (UTIs), chorioamnionitis, and cellulitis.[8,10] In certain populations, particularly postoperative patients, those in nosocomial environments, young children, and individuals with weakened immune systems, *M. morganii* infections can escalate to potentially fatal systemic infections.[10] UTIs, especially in children, are associated with significant short- and long-term morbidity, necessitating precise treatment decisions to prevent complications such as antibiotic resistance, renal scarring, and systemic illness.[10] The emergence of antimicrobial resistance in *M. morganii* poses a significant clinical challenge, complicating treatment strategies and potentially leading to multidrug-resistant infections. Recent clinical case reports have highlighted the importance of understanding the clinical manifestations and management of UTIs caused by *M. morganii*.[8] A study in Turkey marked the first investigation of community acquired UTIs caused by M. morganii in children, underscoring the need to explore risk factors, antimicrobial susceptibility patterns, and clinical characteristics to enhance treatment and prognosis for affected children.[20]

*Morganella morganii* is frequently detected in urine cultures from patients with prolonged indwelling urinary catheters.[18] Among 135 consecutive patients diagnosed with symptomatic, complicated, multidrug-resistant urinary tract infections, close to 10% were found to be infected with *M. morganii*.[20] Additionally, the presence of *M. morganii* in catheter-associated urinary tract infections may attenuate the severity of polymicrobial infections by potentially reducing urease activity, according to proposed mechanisms. Retrospective evaluation of children with *M. morganii* UTIs revealed a mean age of 4.2 years, with irritability and dysuria being the most common symptoms. Urinalysis showed positive leukocytes in 81.8% of patients, hematuria in 45.5%, and nitrite in 54.5%.[20] The pathogen exhibited high sensitivity to imipenem/meropenem and piperacillin-tazobactam. Hospitalization was required for 18.1% of patients, with antibiotic treatment adjusted accordingly. Repeat urine cultures post-treatment were negative. This study highlights *M. morganii* as a potential cause of community acquired UTIs in children and underscores the importance of antibiotic susceptibility profiles in guiding treatment decisions.[20]

A few studies showed the incidence of *Klebsiella oxytoca* in patients with urinary tract infections (UTIs) and its antibiotic sensitivity profile was identified.[19] Urine samples from 430 patients at Al-Shomally General Hospital, Babil, Iraq, and a private laboratory in Babil city were analyzed from January 2018 to December 2019 using routine bacteriological diagnosis and the VITEK® 2 system.[19] Of the 430 samples, 122 showed bacterial growth, with *K. oxytoca* isolated from 2 patients (11% of *Klebsiella species*).[19] *K. oxytoca* UTI isolates were sensitive to amikacin, trimethoprim, and ciprofloxacin but resistant to amoxicillin, cefotazidime, clindamycin, nitrofurantoin, and cefotaxime.[19] This study highlights the increasing burden of UTIs caused by *K. oxytoca* and emphasizes the importance of monitoring antimicrobial resistance patterns to guide treatment decisions effectively.

A research study conducted between January 2012 to March 2014 at a tertiary care hospital to assess the drug resistance pattern of *Klebsiella oxytoca*, an emerging cause of hospital-acquired infections in adults.[19] Out of 17,335 clinical samples processed, 654 yielded Klebsiella species, with 23 (3.52%) identified as *K. oxytoca*. All *K. oxytoca* isolates were sensitive to colistin and tigecycline but exhibited 58% resistance to imipenem and meropenem.[19] Resistance rates to gentamicin, amikacin, and ceftriaxone were higher at 72%, while resistance to ciprofloxacin and aztreonam was lower at 58%. Notably, all samples were from patients admitted to intensive care units (ICUs), suggesting an increasing prevalence of *K. oxytoca* infections in these critical settings. The study emphasizes the importance of Hospital Infection Control Committees monitoring the antibiotic resistance patterns of *K. oxytoca* to enhance patient care in ICUs.

## 5. Conclusions

In conclusion, the heightened susceptibility to urinary tract infections (UTIs) in adults over 30, attributed to factors like hormonal changes, weakened immunity, and structural alterations in the urinary tract, underscores the need for comprehensive prevention strategies across all age groups.[15,21] While older adults face additional risks such as hormonal fluctuations, decreased mobility, and catheter use, effective measures like hydration, hygiene, and prompt treatment of underlying conditions remain pivotal in maintaining urinary tract health.[6,22]

Our study contributes to understanding the prevalence and antimicrobial susceptibility patterns of bacterial pathogens like *Klebsiella oxytoca* and *Morganella morganii* in UTIs within our tertiary care facility in Western India. Notably, the emergence of antibiotic resistance, particularly against commonly prescribed antibiotics like Augmentin and Azithromycin, necessitates a shift towards more tailored and judicious antibiotic prescribing practices. Routine surveillance of UTIs and tracking hospital antibiograms are essential for guiding treatment decisions and minimizing resistance development.

Given the limited pipeline for new antimicrobials, the indiscriminate use of antibiotics poses a significant concern for the rise of pan drug resistance.[7] The urgent adoption of antibiotic consumption strategies is crucial to address urinary tract infections (UTIs) and combat antibiotic resistance effectively. This includes implementing measures

such as restricting antibiotic use, embracing combination therapy, and utilizing antimicrobial susceptibility testing results. These approaches have been recommended in numerous studies and are essential to mitigate the occurrence of UTIs and curb the development of antibiotic resistance.[7,23] Moreover, robust infection control measures and antibiotic stewardship programs are urgently required to safeguard public health and preserve the efficacy of existing antimicrobial agents. By prioritizing these efforts, we can work towards ensuring optimal patient care and preventing the escalation of antimicrobial resistance in the face of UTIs.[24]

## 6. Source of Funding

Nil.

## 7. Conflict of Interest

None.

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## Author biography


**Soni Gupta,** Technician https://orcid.org/0009-0008-0771-1135

**Anju Dhar,** Associate Professor (Microbiologist) https://orcid.org/0009-0008-4753-3601

**Deepali Ghoel,** Technician https://orcid.org/0009-0000-5788-1636

**Rupesh Dingankar,** Technician https://orcid.org/0009-0008-7259-2873


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