DOI: 10.21088/ijpm.2321.5917.13125.2

Indian Journal of Preventive Medicine
Volume 13 Number 1, January - June 2025

Original Article

E. Coli and Klebsiella Pneumoniae are Major Culprits in Catheter-Associated Urinary Tract Infections, Exhibiting an Increasing Trend in Drug Resistance

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How to cite this article:

Lalfakmawia Benjamin, Upendra Baitha, Piyush Ranjan, et al. E. Coli and Klebsiella Pneumoniae are Major Culprits in Catheter-Associated Urinary Tract Infections, Exhibiting an Increasing Trend in Drug Resistance. J Prev Med. 2025; 13(1): 09-16.

ABSTRACT

Background and Objective: Catheter-Associated Urinary Tract Infections (CAUTI) are a primary concern in healthcare, leading to increased mortality and morbidity among critically ill patients. This study aimed to identify uropathogens causing CAUTI and assess their antibiotic sensitivity/resistance.

Methods: This study was conducted on 100 patients, all aged 18 or above, admitted for more than 48 hours with Foley catheters in place. Microbiologically, we classified the patients confirmed (mCAUTI) and clinically suspected (cCAUTI) based on urine culture results.

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Received: 05-04-2025 **Revised:** 25-05-2025

Results: Out of 100 patients, 21 had positive urine cultures (mCAUTI), while 79 clinically suspected CAUTI cases were culture-negative (cCAUTI). Fever was the most prevalent symptom (67 patients), followed by genitourinary complaints, shock, and altered sensorium. Escherichia coli was the primary isolate among mCAUTI cases, followed by Klebsiella pneumoniae, Acinetobacter baumannii, Enterococcus spp., Enterobacter, and Pseudomonas aeruginosa. Imipenem demonstrated the highest sensitivity against gram-negative isolates, while gram-positive isolates exhibited significant drug resistance.

Conclusion: The study highlights E. coli and emerging Klebsiella pneumoniae as major CAUTI culprits with rising drug resistance. Urgent, cautious antibiotic practices are vital. Limiting catheter use, stringent aseptic measures, and timely removal are key to reducing CAUTI. Imipenem stands out as the most effective antibiotic, urging its careful use against CAUTI-causing pathogens.

KEYWORDS

• Catheter-associated Urinary Tract Infections • Enterobacteriaceae • Antibiotic resistance • Catheterization • Imipenem

INTRODUCTION

Catheter-associated urinary tract infections (CAUTI) stand as a significant challenge in healthcare, representing more than 30% of reported healthcare-associated infections.[1] These infections, acquired during hospital stays due to urinary catheterization, exert considerable toll on patient outcomes, escalating morbidity, mortality rates,[2-5] healthcare expenses, and prolonging hospital stays.[4]

The risk factors contributing to CAUTI encompass a spectrum of demographic and procedural elements. Studies underscore the influence of gender, [6] age,[7] and comorbidities such as diabetes.[8] Immunosuppression[9] and inadequate catheter insertion techniques are crucial contributors to CAUTI development. [9] Understanding the pathogenesis of CAUTI unveils complex mechanisms differentiating between extraluminal and intraluminal sources of infection. Extraluminal infections mainly happen because of biofilm buildup on the walls of catheters,[10] while intraluminal infections occur due to urine being trapped inside the catheter system or not having a closed drainage system.[11]

Escherichia coli (E. coli) emerges as the predominant uropathogen in CAUTI cases, supported by research highlighting the significance of other pathogens, such as Pseudomonas aeruginosa, Enterococci, and Staphylococci in contributing to the CAUTI landscape.[12] Comprehending the multifaceted nature of CAUTI, its prevalence, and associated risk factors, pathogenesis and prevalent uropathogens serve as a crucial foundation for development. Effective preventive measures and targeted treatment strategies are crucial. Addressing CAUTI not only enhances patient outcomes but also reduces the significant healthcare expenses associated with these infections.

Based on this knowledge gap, we hypothesised that the spectrum of uropathogens contributing to CAUTI would exhibit a diverse range, including prevalent strains such as Escherichia coli (E. coli), alongside other significant pathogens including Pseudomonas aeruginosa, Enterococci, and Staphylococci. These identified uropathogens exhibit varying degrees of antibiotic sensitivity and resistance. This could potentially highlight specific antibiotics as more effective against certain strains. Others may exhibit heightened resistance, thus guiding the selection of appropriate therapeutic interventions.

METHODOLOGY

Study Design: This study was conducted at the tertiary care hospital, All India Institute of Medical Sciences, New Delhi, India. Institutional ethical approval was obtained and informed written consent was also taken.

Participant Selection Criteria: We enrolled a total of 100 patients, comprising both male and female individuals aged 18 years or older. Inclusion criteria required patients to have a Foley catheter inserted for a minimum duration of 48 hours post hospital admission. Patients with admitting diagnoses of UTI, complicated UTI (cUTI), or urosepsis were excluded from the study.

Data Collection: Comprehensive clinical history was meticulously recorded for all enrolled patients, capturing any underlying comorbidities as delineated in *Table 1* of the study. Foley catheter insertion for all patients was post-admission, ensuring uniformity in catheterization protocols.

Urine Specimen Collection and Analysis: Aseptic urine specimen collection was performed via sterile syringe aspiration from clamped catheters upon clinical suspicion of CAUTI. The collected urine specimens underwent detailed analysis for routine, biochemical parameters, and microscopy to detect any pathological abnormalities.

Microbiological Analysis: For microbiological assessment, 0.001 mL of uncentrifuged urine samples were used to inoculate nutrient agar, sheep blood agar, and MacConkey agar plates. These inoculated plates underwent aerobic incubation at 37°C for 18 to 24 hours. Isolated microorganisms were identified based on colony morphology, gram-stain characteristics, and biochemical tests.

Subsequently, antibiotic susceptibility tests (AST) were conducted to ascertain the sensitivity and resistance patterns of the identified uropathogens against a panel of antibiotics.

Statistical Analysis: The statistical analysis employed a comprehensive array of tests to dissect various facets of CAUTI within the cohort. Chi-square tests were pivotal in comparing comorbidities between clinically suspected and microbiologically confirmed cases. Age distribution differences were examined through T-tests and non-parametric tests. Correlation and regression analyses delved into the relationships between symptoms, lab parameters, and CAUTI presence. For antibiotic resistance profiling, the Antibiotic Sensitivity Test (AST) elucidated sensitivity percentages against distinct uropathogens. These diverse statistical approaches provided nuanced insights into CAUTI, its associated factors, and the microbial landscape, aiding in comprehensive understanding and targeted management strategies. Statistical analysis was conducted utilizing Stata 12 software (Stata Corp 2011, College Station, TX). A significance level of $p < 0.05$ was considered statistically significant.

RESULTS

The studied cohort, comprising 100 participants aged 18 years or older with Foley catheters inserted post-admission for at least 48 hours, showcased a diverse age distribution with a mean age of 42.93 ± 14.96 years. Fever (>100.4°F) was prevalent in 67% of patients. accompanied by varied genitourinary complaints, shock in 35 patients, and altered sensorium in 36 patients. In 21 cases where cultures showed infection (mCAUTI), Escherichia coli was the most common, followed by Klebsiella pneumoniae, Acinetobacter baumannii, Enterococcus spp., Enterobacter, and Pseudomonas aeruginosa. Antibiotic sensitivity highlighted imipenem as most effective (55.6%) against gram-negative isolates, while linezolid exhibited 100% sensitivity in gram-positive isolates. The group's details, such as an average of 23.76 ± 19.60 catheter days and normal vital signs, provide a basic understanding of CAUTI and its related factors in this situation. (*Table 1*)

Table 1: Comparison of c-CAUTI and m-CAUTI based on comorbidities

Comorbidities	cCAUTI (n = 79)	mCAUTI (n = 21)	P value
Comorbidity (pooled)	73 (92.4%)	18 (85.7%)	0.392
Diabetes	22 (27.8%)	10 (47.6%)	0.084
Hypertension	28 (35.4%)	9 (42.9%)	0.532
CKD (Present)	19 (24.1%)	8 (38.1%)	0.198
Cardiovascular	10 (12.7%)	7 (33.3%)	0.045
CLD	6 (7.6%)	1 (4.8%)	1.000
COPD/OSA/OHS	10 (12.7%)	2 (9.5%)	1.000
Hypothyroid	3 (3.8%)	3 (14.3%)	0.105
TB	9 (11.4%)	1 (4.8%)	0.684
HIV	3 (3.8%)	0 (0.0%)	1.000
Hematological Disorder	5 (6.3%)	2 (9.5%)	0.635
Malignancy	6 (7.6%)	3 (14.3%)	0.392
CTD	13 (16.5%)	3 (14.3%)	1.000
Immunosuppression	4 (5.1%)	1 (4.8%)	1.000

(Abbreviations: CKD – *Chronic kidney disease,* ***CLD*** *– Chronic liver disease,* ***COPD*** *– Chronic obstructive pulmonary disease,* ***OSA*** *– Obstructive sleep apnoea,* ***OHS*** *–Obesity hypoventilation syndrome,* ***TB*** *– Tuberculosis, HIV – Human Immunodeficiency Virus,* ***CTD*** *– Connective tissue disease)*

The comparison of clinically suspected CAUTI (cCAUTI) and microbiologically confirmed CAUTI (mCAUTI) showed some interesting patterns based on other health conditions. Among the combined health conditions, 92.4% were seen in cCAUTI and 85.7% in mCAUTI (p = 0.392). We observed 92.4% of the pooled comorbidities in cCAUTI and 85.7% in mCAUTI (p = 0.392). Diabetes exhibited higher prevalence in mCAUTI compared to cCAUTI (p = 0.084). Cardiovascular comorbidities were significantly more prevalent in mCAUTI than cCAUTI (p=0.045). Other health issues like chronic kidney disease (CKD), high blood pressure, chronic liver disease (CLD), chronic obstructive pulmonary disease (COPD), obstructive sleep apnoea (OSA), obesity hypoventilation syndrome (OHS), low thyroid hormone levels (hypothyroidism), tuberculosis (TB), and cancer did not show any meaningful differences between the two groups (p > 0.05). (*Table 2*)

Table 2: Baseline details of recruited patients

Baseline Details	Mean ± SD/ Frequency (%)
Age (in years)	42.93 ± 14.96
Age distribution	
≤20 Years	6 (6.0%)
21-30 Years	19 (19.0%)
31-40 Years	23 (23.0%)
41-50 Years	21 (21.0%)
51-60 Years	15 (15.0%)
61-70 Years	14 (14.0%)
71-80 Years	2 (2.0%)
Gender	
Male	54 (54.0%)
Female	46 (46.0%)
Number of catheter days	23.76 ± 19.60
Pulse rate	87.51±15.20
SBP	117.21±20.01
DBP	70.49±10.67
Temperature	99.05±1.40

(**Abbreviations:** ***SD*** *– Standard deviation,* ***SBP*** *- Systolic Blood Pressure,* ***DBP*** *– Diastolic Blood Pressure)*

The mean ages for cCAUTI and mCAUTI were 41.84 ± 14.06 years and 47.05 ± 17.74 years, respectively. The distribution across age groups did not show statistically significant differences between the two groups (p > 0.05), although a slight variation in the distribution of cases was observed in some age brackets (*Figure 1*). Further, fever (>100.4°F) was prevalent in 63.3% of cCAUTI and 81.0% of mCAUTI cases (p = 0.126).

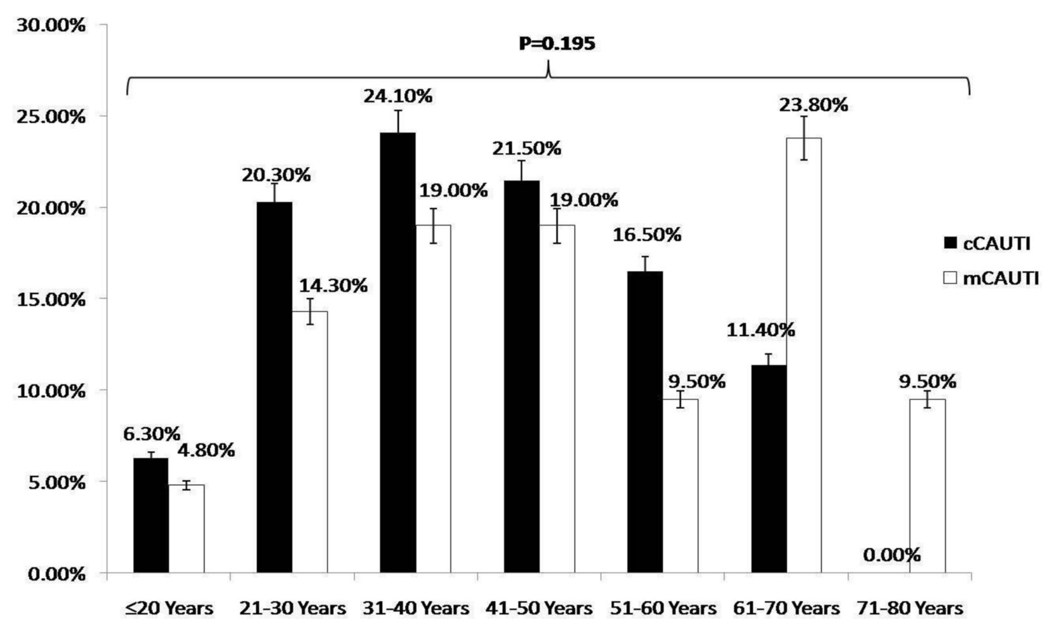

Figure 1: Age-Stratified comparison of clinical suspected and microbiologically confirmed catheter-associated urinary tract infections

For instance, E. coli exhibited seven discharged and two expired cases out of nine total, while K. Pneumonia had three discharged and two expired cases out of five total. A. baumannii resulted in one discharge and two expired cases out of three total cases. Enterococcus demonstrated none discharges and two expired cases out of two total cases, and Enterobacter had no discharges and one expired case out of one total case. P. aeruginosa resulted in one discharge out of one total case.

Table 3 shows the summary of ASTs for all the uropathogens. The AST against various uropathogens revealed differing resistance and sensitivity profiles across antibiotics. For instance, piperacillin- tazobactam showed a high resistance rate of 77.8% and a sensitivity rate of 22.2%. Imipenem exhibited a resistance rate of 44.4% and a sensitivity rate of 55.6%. Meropenem showed a resistance rate of 66.7% and a sensitivity rate of 33.3%. Similar variations in antibiotic susceptibility were observed across multiple antibiotics tested against the uropathogens isolated in the study.

Table 3: Antibiotic Resistance and Sensitivity Profiles of Uropathogens

Antibiotics	Resistant (%)	Sensitive (%)	P value
Piperacillin-Tazobactam	14 (77.8%)	4 (22.2%)	0.123
Meropenem	12 (66.7%)	6 (33.3%)	0.214
Imipenem	8 (44.4%)	10 (55.6%)	0.035
Cefoperazone-Sulbactam	11 (61.1%)	7 (38.9%)	0.297
Gentamicin	2 (66.7%)	1 (33.3%)	0.722
Amikacin	14 (77.8%)	4 (22.2%)	0.172
Nitrofurantoin	9 (52.9%)	8 (47.1%)	0.461
Ciprofloxacin	14 (73.7%)	5 (26.3%)	0.081
Netilmicin	10 (71.4%)	4 (28.6%)	0.134
Penicillin	4 (100.0%)	0 (0.0%)	0.001
Vancomycin	1 (50.0%)	1 (50.0%)	0.899
Linezolid	0 (0.0%)	2 (100.0%)	**0.003**
Teicoplanin	1 (50.0%)	1 (50.0%)	0.764

DISCUSSION

In our study, females had over double the likelihood of culture-proven CAUTI compared to males (61.9% vs. 38.1%), a contrast to previous research.[13-15] Comorbidities were prevalent in 85.7% of mCAUTI patients, notably diabetes (47.6%) and hypertension (42.9%). Cardiovascular comorbidity was over two times more likely in mCAUTI versus cCAUTI cases (33.3%vs.12.7%), aligning with Kakaria *et al.*'s (2018) identification of female sex, diabetes, and longer catheterization as key CAUTI risk factors.[15]

In our study, 90.48% of microbial isolates were gram-negative, primarily the Enterobacteriaceae group accounting for 66.7% of the cases, which is consistent with prior CAUTI research.[14-16] E. coli (42.9%) was the most prevalent organism, followed by Klebsiella pneumoniae (23.8%), Acinetobacter baumannii (14.3%), Enterobacter (4.8%), and Pseudomonas aeruginosa (4.8%). Gram-positive isolates were minimal (9.48%), both identified as Enterococcus spp., which aligns with earlier CAUTI studies.[14-15]

CAUTI is the leading cause of healthcare-associated infections due to widespread use of catheterization.[17-18] It is an important cause of morbidity and mortality in hospitalised patients and increases the healthcare financial burden.[19-20] A total of a hundred patients with clinical suspicion of CAUTI were recruited for this study out of which 21 were culture positive (mCAUTI = microbiologically proven CAUTI). The study included both patients admitted to the general ward and critically ill patients from the ICU/HDU. The mean age of patients with CAUTI was 47.05 ± 17.74.

The number of catheter days in recruited patients varied widely, ranging from 3 to 125 days. The data did not follow a normal distribution. The mean number of catheter days overall was 23.76 ± 19.60. In cCAUTI patients it was 23.03 ± ±19.96 and in mCAUTI patients it was 26.52 ±18.36. The difference in the number of catheter days in mCAUTI and cCAUTI was not significant. This was probably due to the inclusion of patients admitted to the general ward and also critically ill patients in ICU/HDU. A study conducted by Garg *et al.* (2010) at Maulana Azad Medical College (MAMC), another hospital in New Delhi found much lower mean catheter days of 4.8 days in CAUTI. This might be due to the non-inclusion of critically ill patients in the ICU, and the study looked at patients catheterised in the casualty and general medical wards only.[21] A prospective multi-centre study by Venkataraman R (2018) across various ICUs in India reported a mean Foley day of 17.7 days.[22]

In our study, fever prevailed as the most common symptom overall (67%) among CAUTI patients, consistent with prior research.[23] No significant variance was observed in other symptom distributions between culture-negative and culture-positive groups. The mCAUTI group showed genito-urinary symptoms in 38.1% of cases, shock in 42.9% of cases, and altered sensorium in 33.3%. Leukocytosis was noted in 52.4% of mCAUTI patients.

Elevated inflammatory markers (ESR and CRP) were widespread among mCAUTI cases, while higher urea and creatinine levels were notable, possibly indicating associated AKI or a bias due to recruited CKD patients.

Urine routine microscopic examination revealed a comparable mean urine WBC count between culture-positive and culture-negative patients. However, mCAUTI cases showed a higher likelihood of increased bacteria in urine RME, significantly different from cCAUTI cases (p=0.046). Antibiotic exposure, predominantly Piperacillin-Tazobactam, was higher at baseline, with Imipenem having the least exposure. In the mCAUTI group, Piperacillin-Tazobactam was administered to 61.9%, Cefoperazone-Sulbactam to 38.1%, and Meropenem to 28.6% at baseline.

In our AST for CAUTI organisms, imipenem exhibited the highest sensitivity among Gram-negative isolates (55.6%). Following closely was Cefoperazone-Sulbactam. However, other antibiotics displayed weaker sensitivities, notably Meropenem (33.3%), Nitrofurantoin (47.1%), Amikacin (22.2%), and particularly Piperacillin-Tazobactam (22.2%). These findings contrast with Sandhu R *et al.* (2018), where Amikacin was found to be the most sensitive antibiotic in CAUTI.[24]

Within the small cohort of Gram-positive isolates, linezolid demonstrated perfect sensitivity (100%), while Teicoplanin and Vancomycin exhibited 50% sensitivity. Similar sensitivity patterns were reported in studies by Sandhu *et al.* and Bhani *et al.*, indicating high susceptibility of Gram-positive bacteria to Vancomycin and Linezolid.[24-25]

In examining specific uropathogens, imipenem maintained superior sensitivity compared to other antibiotics. E. coli, the most prevalent isolate, exhibited the highest sensitivity to Imipenem (62.5%) and the lowest to Piperacillin-Tazobactam and Amikacin (25% each). Similarly, Klebsiella pneumoniae, the second most common uropathogen, showed the highest sensitivity to Imipenem (80%), while other commonly used antibiotics displayed weaker efficacy at 20% sensitivity.

Although Piperacillin-Tazobactam and Meropenem are commonly used as first-line CAUTI treatments, their suboptimal sensitivity in this study suggests reconsideration. Imepenem and Cefoperazone-Sulbactam displayed much higher sensitivity and are recommended as primary therapies, especially for severe cases. Nitrofurantoin emerged as a potential alternative for selected patients due to relatively preserved sensitivity. Cefoperazone-Sulbactam and Nitrofurantoin could serve as Impenem-sparing agents, while cautious use of Impenem is advised as a last-resort treatment in our healthcare setup.

CONCLUSION

CAUTI remains predominantly caused by Enterobacteriaceae, notably E. coli and emerging Klebsiella pneumoniae, exhibits concerning patterns of drug resistance. Catheter duration significantly influences CAUTI risk. Piperacillin-tazobactam and meropenem exhibit declining sensitivity, whereas imipenem emerges as the most effective antibiotic. Minimising catheter use and judicious antibiotic selection, favouring imipenem where suitable, are vital strategies to combat CAUTI.

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