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MICROBIAL ETIOLOGY OF CATHETER-ASSOCIATED URINARY TRACT INFECTIONS IN HOSPITALIZED PATIENTS

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Abstract

Background: *Catheter-associated urinary tract infection (CAUTI) is a healthcare-associated infection that leads to morbidity, longer hospital stay, healthcare costs, and antimicrobial resistance. The purpose of this study was to identify the microbial profile, resistance pattern, and risk factors for CAUTI that were multidrug resistant (MDR).*

Methodology: *This study (n=160) included culture-confirmed CAUTI following at least 48 hours of catheterization, over a period of six months. Data on demographic information, catheter history, comorbidities, hospitalizations, and prior antibiotic use were gathered from a form and medical records. Microbiological methods were used for culture of urine samples, and antimicrobial susceptibility was determined by Kirby–Bauer disk diffusion according to CLSI. MDR was considered resistance to three or more classes of antimicrobial agents. Data were analysed using SPSS version 26.0, Chi-square and Fisher's exact test, and multivariable logistic regression, with $p<0.05$ considered significant.*

Results: *The mean age was 58.9 ± 16.4 years, and 56.9% were male. 81.3% of isolates were Gram-negative. The predominant bacteria were Escherichia coli (35.0%), Klebsiella pneumoniae (23.1%), and Pseudomonas aeruginosa (15.0%). The highest levels of resistance were for ampicillin (57.5%), ciprofloxacin (46.3%), ceftriaxone (43.1%) and trimethoprim–sulfamethoxazole (41.3%). Overall, 43.8% of the isolates were MDR. The factors that were independent predictors were as follows: prior antibiotic use (AOR=3.61), admission to the ICU (AOR=3.08), prior hospitalization (AOR=2.09), diabetes mellitus (AOR=2.21), and catheterization for >14 days (AOR=2.84).*

Conclusion: *Resistant Gram-negative bacteria were the main cause of CAUTI, and there was a high load of MDR. Improved catheter care practices, surveillance, culture-based treatment, and antimicrobial stewardship may help to decrease the rate of MDR CAUTI and enhance outcomes.*

Keywords: *Catheter-related infections, Drug resistance, Escherichia coli infections, Microbial sensitivity tests, Urinary catheters, Urinary tract infections*

INTRODUCTION

Catheter-associated urinary tract infection (CAUTI) is one of the most common device-associated healthcare-associated infections and is an important contributor to morbidity, length of hospital stay, secondary bloodstream infection, and excess healthcare costs (1). An indwelling urinary catheter is a disruption of the normal host defenses, and it allows for ascending microorganisms and facilitating bacterial adhesion to the catheter surface (2). Longer catheterisation time is associated with an increased risk of bacteraemia and colonisation, so avoiding unnecessary catheterisation and early removal are integral parts of the prevention strategy (3).

One of the significant features of the pathogenesis of CAUTI is biofilm formation (4). Biofilms on catheters form a protective barrier for organisms, which can sometimes be less susceptible to antimicrobial treatment and lead to persistent or recurring infections (5). The distribution of microorganisms in hospitals is variable, but the most common ones are Gram-negative bacilli, especially and Candida species (6). Empirical treatment of CAUTI has been complicated by the significant antimicrobial resistance that has been observed in recent surveillance studies of CAUTI pathogens (7).

In hospitalized patients, multidrug-resistant (MDR) urinary pathogens are becoming a growing issue (8). Other factors reported for resistant urinary infections include previous antibiotic use, previous hospital admission, intensive care unit (ICU) stay, prolonged use of a urinary catheter, diabetes mellitus and other comorbidities (9). Standardized susceptibility testing and local surveillance are thus crucial for antimicrobial stewardship and successful planning of infection control (10). Microbial profiles and resistance patterns vary across institutions and regions, and there is limited local evidence to identify predictive factors of MDR-CAUTI (11). Empirical therapy and targeted prevention strategies need institution-specific data.

The purpose of this study was to identify the microbial cause of CAUTI in hospitalized patients. It also evaluated the prevalence of MDR isolates and the pattern of their antimicrobial resistance. Finally, it sought to define clinical and catheter-related risk factors that were independent of MDR CAUTI.

METHODOLOGY

The current study aimed to determine the causative microorganisms of CAUTI and associated factors with hospital-acquired multi-drug resistant (MDR) infections. This study was carried out in the Department of Microbiology of a tertiary care hospital Authors' affiliated diagnostic lab, in association with the Department of Medicine and Surgery and Intensive Care from January 2022 to June 2022. The required sample size was calculated using OpenEpi software (12). Consecutive sampling was used, and a total of 160 hospitalized patients were included who were diagnosed with CAUTI. Patients 18 years old or older who were catheterized for at least 48 hours and who developed signs and/or symptoms of a UTI after catheterization were eligible. CAUTI was diagnosed with the use of standard clinical and microbiological definitions (i.e., urinary symptoms and a positive urine culture). Patients with community-acquired UTI's, positive urine culture before catheterisation, intermittent catheterisation, and those with incomplete microbiological records or contaminated urine specimens were not included in the study.

A structured data collection form was used for data collection, along with hospital medical records, and demographic and clinical data were collected. Catheterization duration, intensive care unit admission and prior antibiotic use for the last three months, age, and gender were considered as variables. Urine samples were aseptically taken from the catheter sampling port before beginning or changing an antimicrobial therapy. The samples were grown on standard microbiological media, and bacterial identification was done using conventional laboratory techniques per institutional protocol. The antimicrobial susceptibility testing was accomplished by the Kirby–Bauer disk diffusion method in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines. By definition, three- or more- antimicrobial class-resistant organisms were defined as multidrug resistant (MDR).

The results of continuous variables were presented as mean ± standard deviation, and the results of categorical variables were presented as frequencies and percentages (SPSS v. 26.0). The associations of clinical variables with MDR infection were assessed by the Chi-square test or Fisher's exact test if applicable. The variables that showed statistical significance in univariate analysis were then added to a multivariable logistic regression model to determine independent predictors of MDR CAUTIs. The odds ratios (ORs) were adjusted, and 95% confidence intervals (CI) were computed; and p value <0.05 was taken as statistically significant (two-tailed analysis). The confidentiality of patients was maintained, and all microbiological and clinical information was anonymized before statistical analysis.

RESULTS

There were 160 CAUTIs in hospitalized patients. The mean age was 58.9 ± 16.4 years, and 56.9% were male. The isolates consisted of Gram-negative (81.3%) and Gram-positive (18.7%) bacteria, of which *Escherichia coli* was the most frequent (35.0%), and *Klebsiella pneumoniae* was the second most frequent (23.1%). A multidrug-resistant organism was found in 43.8% of the cases. ICU admission, long-term catheterization and diabetes mellitus (DM).

Demographic and catheter-related characteristics of patients with CAUTIs. There were 160 bedbound UTI patients with a mean age of 58.9 ± 16.4 years included. Half of the patients (50.0%) were aged

≥60 years, and 56.9% were male. Medical wards had the highest proportion of infections (38.1%), and the ICU had the most (35.0%). The most frequent length of time was 8-14 days (39.4%) (Table I).

Table I. Demographic and catheter-related characteristics of patients with CAUTIs (n=160)

Variable	Frequency (n)	Percentage (%)
Age group (years)		
<40	24	15.0
40–59	56	35.0
≥60	80	50.0
Gender		
Male	91	56.9
Female	69	43.1
Hospital Unit		
Medical ward	61	38.1
Surgical ward	43	26.9
ICU	56	35.0
Duration of Catheterization		
≤7 days	54	33.8
8–14 days	63	39.4
>14 days	43	26.8
Mean age (years)	58.9 ± 16.4	

Table II shows the distribution and antimicrobial resistance pattern of the microorganisms isolated from CAUTIs. Gram-negative bacteria were the predominant organisms, with *E. coli* (35.0%) being the most common organism isolated, followed by *K. pneumoniae* (23.1%) and *P. aeruginosa (15.0%)*. Ampicillin (57.5%), ciprofloxacin (46.3%), ceftriaxone (43.1%) and trimethoprim–sulfamethoxazole (41.3%) had the highest resistance. Overall, 43.8% of the isolates were multidrug resistant.

Table II. Distribution of microorganisms and antimicrobial resistance profile among patients with catheter-associated urinary tract infections (n=160)

Microorganism isolated	n (%)	Antibiotic/Resistance category	Resistant isolates, n (%)
Escherichia coli	56 (35.0)	Ampicillin	92 (57.5)
Klebsiella pneumoniae	37 (23.1)	Ciprofloxacin	74 (46.3)
Pseudomonas aeruginosa	24 (15.0)	Ceftriaxone	69 (43.1)
Enterococcus faecalis	18 (11.3)	Trimethoprim sulfamethoxazole	66 (41.3)
Proteus mirabilis	14 (8.8)	Piperacillin–tazobactam	24 (15.0)
Candida spp.	11 (6.8)	Nitrofurantoin	18 (11.3)
—	—	Meropenem	12 (7.5)
—	—	Multidrug-resistant isolates	70 (43.8)

E. coli was the predominant CAUTI pathogen, followed by *K. pneumoniae* and *P. aeruginosa*. High resistance was observed to ampicillin, ciprofloxacin, and ceftriaxone, while 43.8% of isolates were multidrug resistant (Fig. 1).

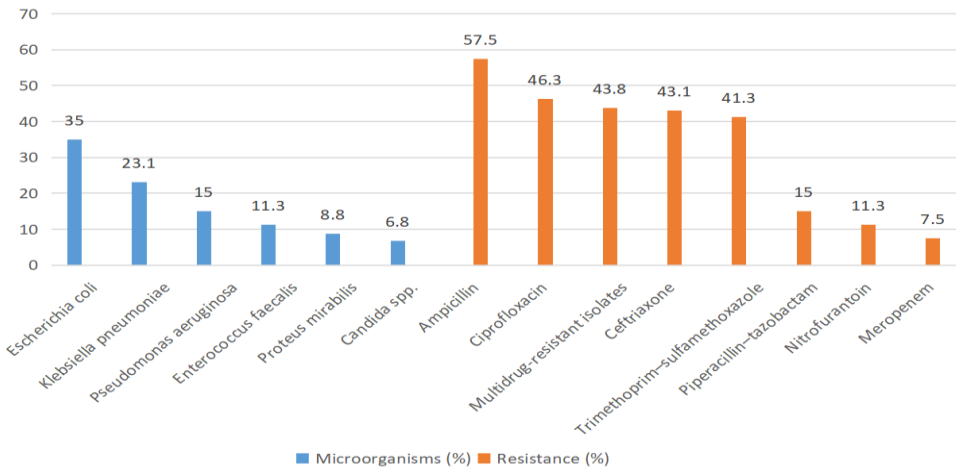

Fig. 1. Distribution of microorganisms and antimicrobial resistance profile in CAUTIs

MDR/non-MDR comparison of the use of CAT-UTI was carried out. Patients with multidrug-resistant (MDR) infections were significantly more likely to have been previously admitted to the intensive care unit (ICU) (50.0% vs. 23.3%, p<0.001), to have had antibiotic use in the preceding 30 days (65.7% vs. 32.2%, p<0.001), prolonged hospitalization over 14 days (40.0% vs. 16.7%, p=0.001), diabetes mellitus (44.3% vs. 25.6%, p=0.012), and previous hospitalization (54.3% vs. 31.1%, p=0.003) compared with patients with non-MDR infections Table III.

Table III. Comparison between MDR and non-MDR catheter-associated UTIs

Variable	MDR (n=70)	Non-MDR (n=90)	p-value
ICU admission	35 (50.0%)	21 (23.3%)	<0.001
Catheter >14 days	28 (40.0%)	15 (16.7%)	0.001
Diabetes mellitus	31 (44.3%)	23 (25.6%)	0.012
Previous antibiotic use	46 (65.7%)	29 (32.2%)	<0.001
Previous hospitalization	38 (54.3%)	28 (31.1%)	0.003
Chronic kidney disease	18 (25.7%)	12 (13.3%)	0.046

Multivariable logistic regression applied to determine predictors of MDR UTIs related to urinary catheter. After adjustment for potential confounders, previous exposure to antibiotics was the most important independent factor associated with MDR infection (AOR=3.61, 95% CI: 1.74–7.47, p<0.001). Other factors independently associated with an increased risk of MDRO-CAUTIs were admission to ICU (AOR=3.08, p=0.002), more than 14 days of catheterization (AOR=2.84, p=0.007), diabetes mellitus (AOR=2.21, p=0.036), and prior hospital admissions (AOR=2.09, p=0.047) Table IV.

Table IV. Multivariable logistic regression for predictors of MDR catheter-associated UTIs

Predictor	Adjusted OR	95% CI	p-value
Previous antibiotic exposure	3.61	1.74–7.47	<0.001
ICU admission	3.08	1.49–6.37	0.002
Catheterization >14 days	2.84	1.33–6.05	0.007
Diabetes mellitus	2.21	1.05–4.64	0.036
Previous hospitalization	2.09	1.01–4.33	0.047

Previous antibiotic exposure was the strongest independent predictor of MDR CAUTI. ICU admission, prolonged catheterization, diabetes mellitus, and previous hospitalization also significantly increased the risk (Fig. 2).

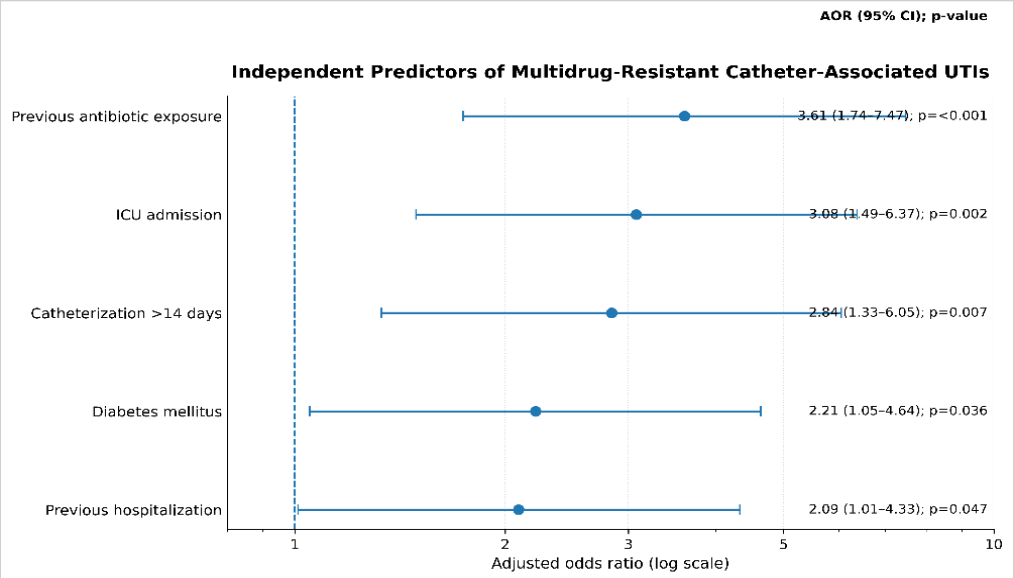

Fig. 2. Forest plot of adjusted odds ratios and 95% confidence intervals for independent predictors of multidrug-resistant catheter-associated urinary tract infections

There was a different clinical response according to the microorganism. Hospital stay and admission to the intensive care unit (ICU) were the longest for *Pseudomonas aeruginosa* and *Candida spp.* patients. The highest percentage of MDR isolates was *Klebsiella pneumoniae* (10.0%) and *Pseudomonas aeruginosa* (15.0%),

suggesting that these were associated with more severe infections and were more likely to cause larger healthcare problems Table V.

Table V. Clinical outcomes according to infecting organism

Organism	Mean hospital stay (days)	ICU admission n (%)	MDR isolates n (%)
Escherichia coli	11.6 ± 4.2	14 (25.0)	20 (35.7)
Klebsiella pneumoniae	13.8 ± 5.1	17 (45.9)	22 (59.5)
Pseudomonas aeruginosa	15.2 ± 6.3	15 (62.5)	16 (66.7)
Enterococcus faecalis	10.9 ± 3.8	5 (27.8)	6 (33.3)
Proteus mirabilis	11.8 ± 4.1	3 (21.4)	4 (28.6)
Candida spp.	16.1 ± 5.7	7 (63.6)	—

DISCUSSION

The present study showed that Gram-negative organisms were responsible for the majority of the cases of CAUTIs, and almost half of the organisms were identified as multidrug-resistant. *E. coli* was the most common pathogen, followed by *K. pneumoniae* and *P. aeruginosa*, and was highly resistant to ampicillin, ciprofloxacin, ceftriaxone, and trimethoprim–sulfamethoxazole. This microbial distribution was similar to long-term surveillance in Lebanon, where *E. coli, P. aeruginosa*, and *K. pneumoniae* were predominant among CAUTIs (13). Antibiotic exposure history, admission to an intensive care unit, catheterization for >14 days, diabetes mellitus, and previous hospitalization were independent risk factors for MDR infection. In other ICU cohorts, such as those from Ethiopia and Saudi Arabia, similar high susceptibility to Gram-negative bacteria and high levels of resistance were reported (14, 15).

The higher prevalence of *E. coli* is attributed to its capacity to colonize the periurethral area, ascend the surface of the catheter, and to adhere via adhesins and form biofilms (16). However, the high percentage of *K. pneumoniae* and *P. aeruginosa* suggests that although there is an important contribution from nosocomial isolates, there are also a large number of opportunistic pathogens adapted to the health care setting among patients admitted for longer periods (17). Other studies from Somalia and India have also found Enterobacterales and non-fermenting Gram-negative bacilli to be the common pathogens of CAUTI, but with differing proportions (18)(19). Other hospital-based studies have also reported high-level resistance to fluoroquinolones, cephalosporins and trimethoprim–sulfamethoxazole (20). This is encouraging as the meropenem resistance is relatively low; however, the use of carbapenems should be restricted as it could be contributing to the selection of carbapenem-resistant Enterobacterales and difficult-to-treat Pseudomonas infections (21).

The identified predictors support the high prevalence of MDR, which is 43.8% in this study. Previous antibiotic use was the most important risk factor, with adjusted odds of MDR CAUTI> 3-fold. Other multicenter studies of complicated UTI and studies of resistant urinary infections have also shown a relationship between recent antimicrobial use and resistant organisms (22). ICU admission could exacerbate this risk by means of critical illness, broad-spectrum prescriptions, cross-transmission, and heavy use of devices (23). Long-term catheterization also allows the growth of biofilm and multiple handling of the drainage system, and these two factors were also shown as significant risk factors in other studies carried out in ICUs (24). Diabetes can play a role in impaired host defenses, glycosuria, increased health care system exposure, and repeated antibiotic exposure, and hospital research has also found diabetes to be a predictor of resistance (25). Hospitalization in the past may also signal for current colonization/reacquisition of HAROs (26).

The clinical outcomes varied according to the organism, with the organism *P. aeruginosa* and Candida spp. having the longest hospital stays and proportions of patients with ICU admission. This finding is broadly consistent with an ICU-based CAUTI study in which *P. aeruginosa* was associated with adverse clinical outcomes (27). The highest proportion of MDR was for *P. aeruginosa*, followed by *K. pneumoniae*, highlighting the challenge of treating these pathogens. Comparable studies have reported extensively drug-resistant *P. aeruginosa* and ESBL-producing *K. pneumoniae* as important causes of complicated UTIs, although the relative resistance rates vary across settings (28). That suggests a culture-

guided approach to therapy and appropriate stewardship and careful review and/or replacement of the catheter at regular intervals, but not indiscriminate antimicrobial escalation.

There are some limitations to this study. It is an observational design with a single center, which limits causal inference and restricts generalizability to other hospitals hosting patients who are different, have different catheter practices, and exhibit different resistance patterns. There may be residual confounding due to severity of illness, indication for catheterization, duration of antimicrobial therapy, and adherence to the use of the catheter. These predictors should be further validated with multicenter prospective studies with catheter-day denominators, organism-specific antibiograms, molecular resistance characterization, and longitudinal outcomes, and tested to inform targeted antibiotic- and catheter-removal interventions through antimicrobial stewardship.

CONCLUSION

In this study, Gram-negative organisms, mainly *Escherichia coli, Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, were found to be the primary causes of CA-UTI, with 43.8 % of the isolates demonstrating multidrug resistance. Antibiotic history, admission to the intensive care unit, long-term catheterization, diabetes mellitus, and previous hospitalization were independent risk factors for MDR. The results contribute to the detection of local surveillance, culture-guided treatment, antimicrobial stewardship, and timely removal of the catheter. Multicenter prospective studies of organism-specific resistance and targeted infection-prevention across various hospital environments and patient populations should be conducted in the future.

Conflict of interest:

Authors declared no conflict of interest.

Authors' contribution:

AGMP, KT, HA & ME Substantial contributions to the conception and design, data analysis, drafting the work and revising it critically for important intellectual content and final approval of the version to be published.

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