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Differences in Clinical Features, Microbial Profiles, And Treatment Outcomes Between Catheter-Associated and Non-Catheter-Associated Complicated UTIS

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Abstract

Background: Complicated urinary tract infections (cUTIs) lead to numerous hospital admissions, influencing both patient outcomes and healthcare costs. Regional data on the clinical and microbiological distinctions between catheter-associated and non-catheter-associated cUTIs are scarce.

Aims & Objectives: This study addresses the gap by exploring the clinical features, microbial profiles, and treatment outcomes of cUTIs in a Pakistani hospital, differentiating between catheter-associated and non-catheter-associated infections.

Methods: In this cross-sectional study, adult patients with cUTIs were analyzed for clinical symptoms, microbial cultures, and resistance patterns, adhering to the European Association of Urology's guidelines. SPSS version 21 was used for statistical evaluation.

Results: Out of 390 patients, most of whom were female (55.13%), the prevalent diagnosis

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was pyelonephritis (72.05%). Immunosuppression was present in a third, while urinary abnormalities were found in nearly half of the patients. The study found higher rates of abnormalities and recurrent UTIs in catheter-associated cases, which also tended to have longer hospital stays and increased ICU admissions and 30-day mortality.

Conclusion: The findings shed light on the local clinical and resistance patterns of cUTIs, particularly in patients with catheter usage, emphasizing the need to reassess empirical treatments like ertapenem or fourth-generation cephalosporins for CAUTI.

INTRODUCTION:

Complicated urinary tract infections (cUTIs) are a diverse group of conditions marked by symptoms of UTIs alongside risk factors such as structural abnormalities in the urinary tract, the use of catheters or devices, and underlying health issues like diabetes, cancer, immune system disorders, or the presence of drug-resistant bacteria.[1] These infections account for 1.8% of hospital admissions in the United States, with each stay costing approximately $10,000.[2,3] cUTIs also have a notable impact on patient outcomes, including a 26.6% rate of treatment failure[4], about a 9% chance of hospital readmission[3], and a 30-day mortality rate of 8.7%.[4] The significant expenses and demands these infections place on healthcare systems highlight their importance. In Pakistan, research has primarily focused on identifying the types of bacteria responsible for community-acquired UTIs and UTIs in healthcare settings[5–9], particularly among patients using bladder catheters.[10–12] Nevertheless, both in Pakistan and the wider region, there is a notable gap in data regarding the clinical signs, complications, and resistance patterns of cUTIs, especially comparing infections associated with catheter use to those without. This study's purpose is to examine the clinical and microbiological profiles, treatment methods, and patient outcomes for cUTIs, specifically comparing cases with and without catheter use, within a major teaching hospital in Pakistan.

MATERIAL AND METHODS:

This descriptive cross-sectional study conducted with patients diagnosed with complicated urinary tract infections (UTIs) at a hospital in Abbottabad between ---- & ____. The study focused on individuals over the age of 18, regardless of gender, who had documented cases of complicated UTIs, were diagnosed with UTIs upon discharge, and exhibited symptoms such as urgency, dysuria, flank pain, frequent urination, a positive percussion test, hospitalization for at least 48 hours, fever, or suprapubic pain. Additionally, their urine cultures needed to show $\geq 10^5$ colony-forming units per milliliter with no more than two types of microorganisms present. Specimens were collected using clean-catch methods from patients not using catheters. For those with catheters or similar devices due for replacement, samples were obtained through the new catheter. The inclusion criteria also extended to patients with neurogenic bladders, provided there was no suspicion of other infection sites, following the European Association of Urology's guidelines [9]. Exclusions were made for pregnant women, individuals transferred to other hospitals, and patients who completed their care via home services. The study received approval from the institutional research ethics committee.

Data collection was thorough, drawing from the hospital's electronic medical records for sociodemographic information, which is routinely recorded during patient care. The

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study also compiled data on clinical symptoms, treatments with antibiotics, any comorbidities, the duration of hospital and intensive care unit stays, rates of hospital readmission within 30 days of discharge, and mortality within 30 days post-discharge, utilizing standardized documentation methods.

We classified catheter-associated urinary tract infections (UTIs) as complicated UTIs found in patients using suprapubic cystostomy, nephrostomy, or indwelling catheters. Complicated UTIs not linked to the use of external devices were categorized as non-catheter-associated. We defined immunosuppression based on criteria including the use of prednisolone at doses of 10 mg/day or higher, HIV infection, active cancer, or history of organ transplantation. The study analyzed culture isolates and resistance patterns based on reports from the microbiology laboratory. We identified several resistance phenotypes :

Natural pattern: Isolates of Salmonella enterica, Escherichia coli, P. mirabilis, Shigella, and Klebsiella spp., which are sensitive to beta-lactams.

AMPc pattern: The AmpC pattern of resistance refers to bacterial resistance mechanisms against certain antibiotics, particularly β-lactam antibiotics. AmpC β-lactamases are enzymes produced by some bacteria that can break down a wide range of β-lactam antibiotics, including penicillins and cephalosporins, rendering them ineffective. Isolation of certain species (*Enterobacter spp*., *Citrobacter freundii*, *Morganella morganii*, etc.) showing confirmed resistance to first-, second-, and third-generation cephalosporins.

Penicillinase-producing pattern: Enterobacteria showing resistance to carboxypenicillin and aminopenicillin and having low to intermediate resistance to ureidopenicillins.

Extended-spectrum beta-lactamase pattern: Identified by resistance to cephalosporins (excluding cephamycin), but sensitivity to carbapenems and amoxicillin-clavulanate, as confirmed by the laboratory.

Penicillinase-hyperproducing pattern: Isolation of amalonaticus and Citrobacter koseri or enterobacteria resistant to the above penicillins, with variable resistance to amoxicillin-clavulanic acid and first- and second-generation cephalosporins (except cephamycin), showing decreased sensitivity.

Carbapenemase production pattern: Isolations that are resistant or show decreased sensitivity to carbapenems, confirmed through tests such as EDTA, Hodge test, or boronic acid test. Non-enzymatic resistance, though possible, was identified based on carbapenem resistance and a negative confirmatory test.

Others: This category includes Candida, as well as other gram-positive and gram-negative organisms that do not fit the above patterns, exhibiting alternative resistance characteristics.

We analyzed the sociodemographic characteristics of our participants through both absolute and relative frequencies. For those variables that followed a normal distribution, we calculated the mean and standard deviation. Conversely, for variables not following a normal distribution, we used the median and interquartile range. To determine the normality of these variables, the Kolmogorov-Smirnov test was applied, with a significance level set at 5% ([$p < 0.05$).

We classified complicated urinary tract infections (UTIs) into two categories: those not

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associated with catheter use (Non catheter associated complicated UTI) and those associated with catheter use (Catheter associated complicated UTI). To compare these two groups, we employed various statistical tests depending on the type of variable in question. Specifically, the chi-square test, t-test, or Mann-Whitney U test were utilized. All statistical analyses were conducted using SPSS version 21.

RESULTS

In our cohort of 390 patients, the mean age was approximately 51 years, with a standard deviation of 7.23. Among these patients, 55.13% were female, and 44.87% were male. The majority presented with pyelonephritis, accounting for 72.05%. A significant portion of the participants, 34.10%, had immunosuppression, while 46.67% had urinary tract malformations. Recurrent UTIs were reported in 26.92% of the cases. Prior antibiotic use within the last 90 days was documented for 45.90% of the patients, and 17.69% had bacteremia.

When comparing non-catheter-associated UTIs (262 patients) with catheter-associated UTIs (128 patients), the former group showed a higher proportion of females (59.92% vs. 45.31%) and a slightly higher mean age (52±5.48 years vs. 50±6.32 years). Significant differences were noted in the prevalence of malformations and recurrent UTIs, with catheter-associated UTI patients showing higher percentages (67.19% and 44.53% respectively). Antibiotic use was more common in the catheter-associated group (54.69%).

Hospitalization data indicated that the mean length of stay was 6±4.31 days. Within the non-catheter group, this was slightly shorter at 5.3±3.79 days, compared to the catheter group's 9.78±2.45 days. Hospital readmission within 30 days occurred in 15.38% of the total patients, with the catheter group experiencing a slightly lower rate (13.28%). The mean intensive care unit (ICU) stay was similar across groups, with an overall mean of 5.4±2.34 days. ICU admissions were significantly higher in the catheter group at 16.41% versus 8.97% in the non-catheter group. Mortality within 30 days of hospitalization was reported in 5.38% of the total patient population, with a higher incidence in the catheter-associated group (7.81%).

These data reflect the clinical and demographic features of the study population, highlighting the significant associations between catheter use and increased rates of certain complications and outcomes.

Analyzing the p-values from the study data reveals that gender distribution ($p = 0.09$) and age ($p = 0.09$) did not show significant differences between non-catheter and catheter-associated UTI groups, suggesting similar demographic profiles. Significant disparities were observed in the presentation as pyelonephritis ($p = 0.004$), urinary tract malformations ($p = 0.001$), recurrent UTI ($p = 0.001$), and more frequent antibiotic use within the past 90 days in the catheter group ($p < 0.001$). No significant differences were found for rates of sepsis ($p = 0.078$), bacteremia ($p = 0.102$), previous renal transplant ($p = 0.34$), stroke ($p = 0.305$), and heart failure ($p = 0.775$). Notably, chronic kidney disease ($p = 0.001$) and diabetes mellitus ($p = 0.001$) were significantly more prevalent in the catheter-associated UTI group. Furthermore, the duration of hospital stay was notably longer ($p = 0.001$), and the rates of ICU hospitalization ($p = 0.001$) and 30-day mortality ($p = 0.001$) were higher in the catheter-associated group, while the length of ICU stay did not differ significantly ($p = 0.83$). The marginal significance in 30-day hospital readmission rates ($p = 0.04$) also indicates a

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slightly higher tendency for catheter-associated UTI patients to be readmitted (Table-1).

Variable	Total patients (390)		Non-catheter associated UTI (262)		Catheter Associated UTI (128)		*p*
	Number	%	Number	%	Number	%	
Age (Mean±SD)	51±7.23		52±5.48		50±6.32		0.09
Female Sex	215	55.13	157	59.92	58	45.31	
Male sex	175	44.87	105	40.08	70	54.69	0.001
Pyelonephritis as presentation	281	72.05	188	71.76	93	72.66	0.004
Immunosuppression	133	34.10	92	35.11	41	32.03	0.5
Urinary tract malformations	182	46.67	96	36.64	86	67.19	0.001
Recurrent UTI	105	26.92	48	18.32	57	44.53	0.001
Sepsis	124	31.79	76	29.01	48	37.5	0.078
Used antibiotics in past 90 days	179	45.90	109	41.60	70	54.69	< 0.001
Bacteremia	69	17.69	37	14.12	32	25	0.102
Previous renal transplant	32	8.21	18	6.87	6	4.69	0.34
Stroke	24	6.15	17	6.49	7	5.47	0.305
Heart failure	2	0.51	1	0.38	1	0.78	0.775
Chronic Kidney Disease	59	15.13	20	7.63	39	30.47	0.001
Diabetes Mellitus	103	26.41	78	29.77	25	19.53	0.001
Length of Hospitalization (days; Mean±SD)	6±4.31		5.3±3.79		9.78±2.45		0.001
30-Day hospital readmission	60	15.38	43	16.41	17	13.28	0.04
ICU stay (days; Mean±SD)	5.4±2.34		4.3±3.82		5.5±3.12		0.83
ICU hospitalization	35	8.97	14	5.34	21	16.41	0.001
30-Day mortality	21	5.38	11	4.20	10	7.81	0.06

Table 1 Clinical, laboratory and demographic data of study participants

The microbiological analysis of 390 patients with complicated urinary tract infections (UTIs) yielded 480 isolates. Escherichia coli was the most commonly isolated microbe, present in 66.88% of cases. The occurrence of other microbes, including Proteus, Klebsiella, Pseudomonas, and Enterococci, varied, with Proteus and Klebsiella being significantly more common in catheter-associated UTIs ($p = 0.00$ for both). A second microbe was identified in 11.67% of the overall cases, with a higher incidence in non-catheter associated UTIs (6.45%).

Regarding antibiogram sensitivity profiles, natural penicillinases were produced by 27.29% of the isolates, with ESBL and AMPC producers present in 22.92% and 11.46%, respectively. Carbapenemases resistance was noted in 3.96% of cases. Non-catheter associated UTIs showed a higher proportion of natural penicillinases production, while catheter-associated UTIs had a significantly

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higher rate of carbapenemases resistance (p = 0.00).

All patients were administered antibiotics, with first-generation cephalosporins given to 24.10%, and second-generation cephalosporins to 22.31%. Third- and fourth-generation cephalosporins, quinolones, meropenem, ertapenem, piperacillin/tazobactam, ampicillin/sulbactam, and carbapenems combined with another antibiotic were also used but to a lesser extent. Noteworthy differences in antibiotic administration were observed between non-catheter and catheter-associated UTIs, such as a higher usage of first-generation cephalosporins in the former (p = 0.02) and a greater use of meropenem (p = 0.01) and carbapenemases resistance (p = 0.00) in the latter (Table-2).

	Total patients (390)		Non-catheter associated UTI (262)		Catheter Associated UTI (128)		*p*
	N	%	N	%	N	%	
Total isolated Microbes		480		310		173	
Isolated Microbes							
E. coli	321	66.88	221	71.29	71	41.04	0.00
Proteus	33	6.88	17	5.48	22	12.72	0.00
Klebsiella	48	10.00	33	10.65	21	12.14	0.31
Pseudomonas	18	3.75	8	2.58	16	9.25	0.00
Enterococci	13	2.71	7	2.26	5	2.89	0.02
Enterobacter	9	1.88	5	1.61	8	4.62	0.08
Estafilococci	3	0.63	3	0.97	3	1.73	0.26
Morganella	7	1.46	2	0.65	7	4.05	0.01
Serratia	7	1.46	2	0.65	5	2.89	0.00
Candida	2	0.42	1	0.32	2	1.16	0.65
Citrobacter	8	1.67	1	0.32	9	5.20	0.00
Others	11	2.29	10	3.23	4	2.31	0.73
Second germ isolated	57	11.87	20	6.45	50	28.91	0.00
Antibiotic sensitivity profile		480		310		173	
Penicillinase production	140	29.17	101	32.58	38	21.97	0.01
Natural Pattern	131	27.29	91	29.35	34	19.65	0.00
ESBL production	110	22.92	72	23.23	36	20.81	0.11
AMPc	55	11.46	23	7.42	39	22.54	0.00
Carbapenemase production	19	3.96	9	2.90	14	8.09	0.00
Others	25	5.21	14	4.52	12	6.94	0.03
Antibiotic administered to Patients		390		262		128	
1st Gen. Cephalosporins	94	24.10	66	25.19	22	17.19	0.02

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2nd Gen. Cephalosporins	87	22.31	64	24.43	19	14.84	0.01
3rd Gen. Cephalosporins	5	1.28	6	2.29	1	0.78	0.57
4th Gen. Cephalosporins	9	2.31	4	1.53	6	4.69	0.00
Quinolones	7	1.79	5	1.91	1	0.78	0.21
Meropenem	10	2.56	8	3.05	4	3.13	0.51
Ertapenem	126	32.31	84	32.06	52	40.63	0.03
Piperacillin/tazobactam	13	3.33	10	3.82	6	4.69	0.95
Ampicillin/sulbactam	6	1.54	5	1.91	3	2.34	0.75
Carbapenems associated with another antibiotic	14	3.59	3	1.15	10	7.81	0.00
Others	19	4.87	7	2.67	4	3.13	0.87

Table 2 antimicrobial culture and sensitivity pattern in study population

DISCUSSION

The current study offers an examination of the clinical and microbiological profiles, therapeutic interventions, and health outcomes among patients with complicated urinary tract infections (UTIs) treated at a key hospital in Abbottabad, Pakistan. The findings highlight a notably high rate of recurrent UTIs, recent antibiotic usage, and unplanned readmissions within 30 days. Moreover, a substantial portion of these patients exhibited resistance to AMPc and carbapenems, necessitating the use of advanced treatment options such as fourth-generation cephalosporins, ertapenem, and combinations of carbapenems with other antibiotics.

When compared to global data, the demographics of patients with complicated UTIs in this study were largely consistent, though certain differences were noted. A median age between 65-73 years has been reported in literature[13,14], however, the average age of our study population was much less, corresponding to the generally reduced life expectancy observed regionally. The prevalence of sepsis or septic shock in our patients was 31.79%, surpassing the 16-27% range reported in other studies.[14,15] Antibiotic use within the preceding three months was found to be higher at 45.90% than figures cited in other publications.[4] The need for intensive care unit (ICU) admissions was lower at 8.97% than the 18.6% indicated by some U.S. data[15], aligning with or exceeding figures from various other sources.[16]

In this study, the average hospital stay was 6 days, with a standard deviation of 4.31, which aligns with the median stay observed in the United States (5 days, with an interquartile range of 3–8 days).[14] The 30-day hospital readmission rate in our cohort was 15.38%, markedly higher than the 4.53% reported in Europe[14], and the mortality rate of 5.38% also exceeded that of the USA (2.78%)[14,16] and matched the European figure (5%).[14,16]

Clinical characteristics for patients with catheter-associated UTIs (CAUTIs) in our study differed from those in the international context.

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For instance, the proportion of male patients with CAUTIs in the USA was reported to be 66.39%[13], whereas our study found a slightly lower percentage of 54.69%.

The predominant microorganisms identified in patients with complicated UTIs in our study were *Enterococcus spp*. (2.7%), *Proteus spp*. (6.88%), *Klebsiella spp*. (10%), and *E. coli* (66.8%). These findings are consistent with patterns reported in global studies.[1,15,17] However, when comparing patients with catheter-associated versus non-catheter-associated UTIs, a distinct microbial distribution was observed. Catheter-associated UTIs showed a decreased incidence of E. coli and an increased presence of AMPc-producing organisms, such as *Enterobacter spp., Pseudomonas spp*., *Citrobacter freundii*, and *Serratia marcescens*. This mirrors the proportions found in European research, which reported 25.8% constitutive AMPc producers [16], and aligns with findings from a systematic review of ICU-managed patients, where 22% were AMPc producers.[18]

The resistance patterns observed in patients with complicated urinary tract infections (cUTIs) indicated a significant occurrence of Extended Spectrum Beta-Lactamase (ESBL) producing organisms, accounting for 20.81% of cases. This prevalence did not show a marked difference between catheter-associated UTIs (CAUTI) and non-catheter-associated cUTIs (NC-cUTI), with ESBL rates of 20.81% and 23.23%, respectively ($p = 0.11$). Contrastingly, research conducted in 2010 across nine Colombian hospitals identified a lower prevalence of ESBL in Escherichia coli (between 3.4% and 6.3%) and Klebsiella pneumoniae (between 3.4% and 17.2%).[19] In 2017, GREBO highlighted resistance to ceftriaxone in E. coli and Klebsiella spp. at 18.7% and 44.9%, respectively, when ESBL was confirmed.[16] Our study delineates an intermediate resistance profile, with ESBL found in 36% of E. coli and 12% of Klebsiella spp. cases. These figures point to a regional uptick in ESBL prevalence among E. coli and Klebsiella spp. Therefore, it is critical to maintain vigilant epidemiological monitoring of these pathogens in the context of cUTIs.

Our research identified a 3.96% rate of resistance to carbapenems, which exceeds figures reported from China, where E. coli and Klebsiella spp. showed imipenem resistance rates of 0.5% and 1.3%, respectively.[17] Compared to a 2013 Colombian study that found no ertapenem resistance in E. coli and a 6.9% resistance rate in Klebsiella spp.[18], our figures more closely align with the GREBO 2017 findings, which reported ertapenem resistance rates of 1.5% in E. coli, 23.3% in Klebsiella spp., and 6.2% in Pseudomonas spp..[16] Our figures for carbapenem resistance stood at 1% for E. coli and 18% for Klebsiella spp., underscoring the need for ongoing epidemiological monitoring.

In patients with catheter-associated UTIs (CAUTIs), we noted a particularly high prevalence of carbapenem resistance at 8.09%. This includes a 29% resistance rate in Klebsiella spp., which, while high, is still below the 11% resistance observed in Pseudomonas spp. This is in contrast to data from US ICUs, where Klebsiella spp. and Pseudomonas spp. resistance rates are reported at 13% and 36%, respectively.[18] These resistance patterns, particularly concerning AMPc and carbapenems, likely contribute to the observed higher administration rates of ertapenem (40.63%), combined carbapenems and other antibiotics (7.81%), and fourth-generation cephalosporins (4.69%) in CAUTI patients. The

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data indicates that CAUTI patients require more intensive monitoring and regular evaluation of the need for continued catheterization.

This investigation is the initial report from our area to examine the clinical features, bacterial types, and resistance patterns in complicated urinary tract infections (cUTIs), differentiating between cases with and without catheter or external device usage. It contributes valuable insights into the local microbial patterns found in our patient population and supplies critical data for ongoing epidemiologic monitoring. The research uses established clinical diagnostic standards for cUTIs, aiding in the practical application of its findings.

The study is not without its limitations. It acknowledges the potential for selection bias in the cUTI patient group due to the varying definitions of the condition when diagnosed at discharge by different physicians. Despite this, patient classification was conducted using widely recognized international criteria. The research was carried out in a single institution, raising questions about the applicability of its results to other settings, particularly less complex hospitals, which should be assessed in the future. Additionally, it did not differentiate between community-acquired or healthcare-related cUTIs, nor did it consider the timing of catheter or external device use due to incomplete medical record data, rendering this research preliminary and supportive of future confirmatory studies.

The study identifies that patients with catheter-associated UTIs (CAUTIs) had higher rates of recurrent UTIs, antibiotic usage in the preceding three months, 30-day hospital readmissions, a greater frequency of AMPc resistant profiles, and increased administration of carbapenems and fourth-generation cephalosporins in combination with other antibiotics. The study suggests that the empirical use of ertapenem or fourth-generation cephalosporins in CAUTI patients warrants further investigation.

Authors' contributions:

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