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Bacteriological Profile of Catheter Associated Urinary Tract Infections in a Tertiary Care Hospital

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Abstract:
Background: *Antimicrobial Resistance and Hospital Acquired Infections are the modern hazards in the field of medicine. The most common of these infections is Catheter Associated Urinary Tract Infection (CAUTI), which amounts to almost 35%. CAUTI causes significant distress to patients, including risk of mortality, and increases healthcare costs. Bacteria causing CAUTIs show a high degree of antimicrobial resistance. Healthcare professionals must acquire knowledge of current local trend of causative organisms, and their resistance pattern, in any healthcare facility.*
Material and Methods: *This hospital-based cross-sectional study included urine samples from patients having an indwelling urinary catheter, and fever for more than two days. Bacterial identification and antibiotic susceptibility testing were done by conventional bacteriological techniques. Impact of empirical antibiotic therapy on development of CAUTI was assessed through detailed history.*
Results: *692 samples were included of which 249 produced bacterial isolates, with 216 of them being Gram-negative organisms. Fisher's exact test was used for statistical analysis; $p<0.05$ was considered significant. Antibiotic Susceptibility Test results showed resistance to Fluoroquinolones and Cephalosporins ranging from 78-93% ($p<0.05$).*
Conclusions: *Irrespective of the causative organism, the treatment of established CAUTI is a challenging task, as the organisms are highly resistant to most classes of antibiotics. Prevention strategies are more effective in case of CAUTI as compared to treatment options.*
Key Words*: Hospital Acquired Infections; Catheter Associated Urinary Tract Infections; Antimicrobial Resistance; Antibiotic Susceptibility Pattern.*

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I. Introduction

As the world enters the era of modern medicine, it has to contend with modern hazards like Antimicrobial Resistance (AMR) and Hospital Acquired Infections (HAI). AMR is responsible for approximately 23,000 deaths annually in the United States of America, and around 25,000 deaths across Europe[1,2]. However, the global scenario of AMR is not quantifiable, as many regions of the world simple lack the necessary epidemiological data[3]. HAI, on the other hand, have four major categories – Catheter Associated Urinary Tract Infection (CAUTI), Catheter Related Blood Stream Infection (CRBSI), Ventilator Associated Pneumonia (VAP), and Surgical Site Infection (SSI)[4]. CAUTI, which amounts to almost 35% of them, is the most common HAI[5]. It is well documented, that CAUTI causes significant physical distress, prolonged duration of hospitalization, increased costs, and increased risk of mortality. Furthermore, the plethora of complications caused due to CAUTI are not only common but are also considerably debilitating to the patient. Additionally, it has been proven that bacteria causing CAUTI have become increasingly resistant to urine-specific, and even broad-spectrum antibiotics[6].

Therefore, CAUTI poses a two-fold threat – the extensive occurrence and the ensuing debility to the patients, and the rapid rise in AMR. This necessitates healthcare professionals to acquire knowledge of current local trend of causative organisms, and their resistance pattern in any healthcare facility. To that effect, we aimed to analyze the bacteriological profile of CAUTI in our tertiary care hospital, in Western India. We believe this study would aid in updating guidelines for appropriate treatment, and consequently help reduce the development of multi-drug resistance among organisms.

II. Material And Methods

Study Design: Tertiary care teaching hospital-based cross-sectional Study
Study Duration: June 2021 to December 2022
Sample size: 692 patient samples (All urine samples from catheterized patients received in the department of Microbiology during the study period)
Inclusion criteria:

1. Patients admitted in the study institute
2. Patients having an indwelling urinary catheter in situ
3. Patients having fever for over two days
4. Patients with clinically suspected or diagnosed urinary tract infection after catheterization

Exclusion criteria:

1. Patients without an indwelling urinary catheter
2. Presence of fever and/or other urinary symptoms since before catheterization
3. Patients not giving a valid written informed consent

Procedure methodology:

Operational definition of Urinary Tract Infection for this study was infection involving any part of the urinary system, including urethra, bladder, ureters, and kidney. Date of Event was defined as the date on which the first element used to meet the NHSN-CAUTI criterion occurred for the first time. An infection was defined as CAUTI when the definition of HAI was met, and the Indwelling Urinary Catheter (IUC) was in place for over two calendar days on the date of event, or on the date of event and the day before[7,8].

This was a cross-sectional study, where all the included samples were subjected to the same processing. Details like age and sex were collected for all these patients from test requisition forms, and identity of the pathogen isolated from laboratory records. Only bacterial pathogens were considered for further processing and statistical analysis.

Samples collected from the indwelling urinary catheter, in situ in the patients admitted in the study institute, were sent for bacteriological processing within two hours of collection, where they were processed within an hour of receipt. Wet mount was prepared for microscopic examination using uncentrifuged samples, to note the number of pus cells and presence of bacteria in high-power magnification. The samples were then inoculated semi-quantitatively on Cystine Lactose Electrolyte Deficient (CLED) agar and incubated overnight at 37°C aerobically. After overnight incubation, colony count of the growth was performed to confirm its significance according to the Kass Concept of Significant Bacteriuria[9].

If a significant colony count was obtained, the bacterial etiological agents were provisionally identified by colony characteristics and microscopic examination of a Gram's-stained smear of the growth, which aided in choosing the antibiotic discs to be applied for antibiotic susceptibility testing. Antibiotic susceptibility testing was performed according to the Modified Kirby-Bauer Disk Diffusion method. Selection of antibiotic discs, as well as interpretation of patterns was done according to Clinical and Laboratory Standards Institute (CLSI) 2022 - M100 guidelines[10]. The catalase test was performed for all organisms, whereas Gram-negative organisms were additionally tested for motility. Final identification of organisms was made using Biochemical Tests as mentioned in Table 1[9,11].

Table 1: Biochemical Tests for Identification

For Gram-positive Organisms	For Gram-Negative Organisms
Catalase Test If positive ↓ Coagulase Test (Both Slide and Tube Test)	1. IMViC Tests: a. Indole Test b. Methyl Red Test c. Voges Proskauer Test d. Citrate Utilization Test
	2. Urea Hydrolyzation Test
	3. Triple Sugar Iron Test
	4. Oxidative - Fermentative Test
	5. Decarboxylation Tests: a. Lysine Decarboxylase b. Arginine Dehydrolase c. Ornithine Decarboxylase

Statistical analysis:

Data collection, data cleaning, preparation of the master-sheet, and data evaluation and tabulation were carried out in Microsoft ® Excel. Statistical analysis was done using OpenEpi online software. The Fisher exact test was performed to test for differences in proportions of categorical variables between two or more groups. A p-value of <0.05 was considered as statistically significant.

III. Results

Total number of samples included in the present study was 692. Of them 335 (48.41%) showed no growth on CLED Agar. Additionally, 108 samples grew *Candida* species, which were excluded. The remaining 249 isolates were processed further for determining their bacteriological profile. 216 isolates were Gram-negative organisms, divided into 143 from the *Enterobacteriaceae* family and 73 Non-Fermenting Gram-Negative Bacilli, while 33 were Gram-positive (Figure 1).

Demographic details were collected and classified according to the growth obtained on CLED Agar. As this study pertains to a device-associated infection, statistical analysis was not performed for these parameters (Figure 2).

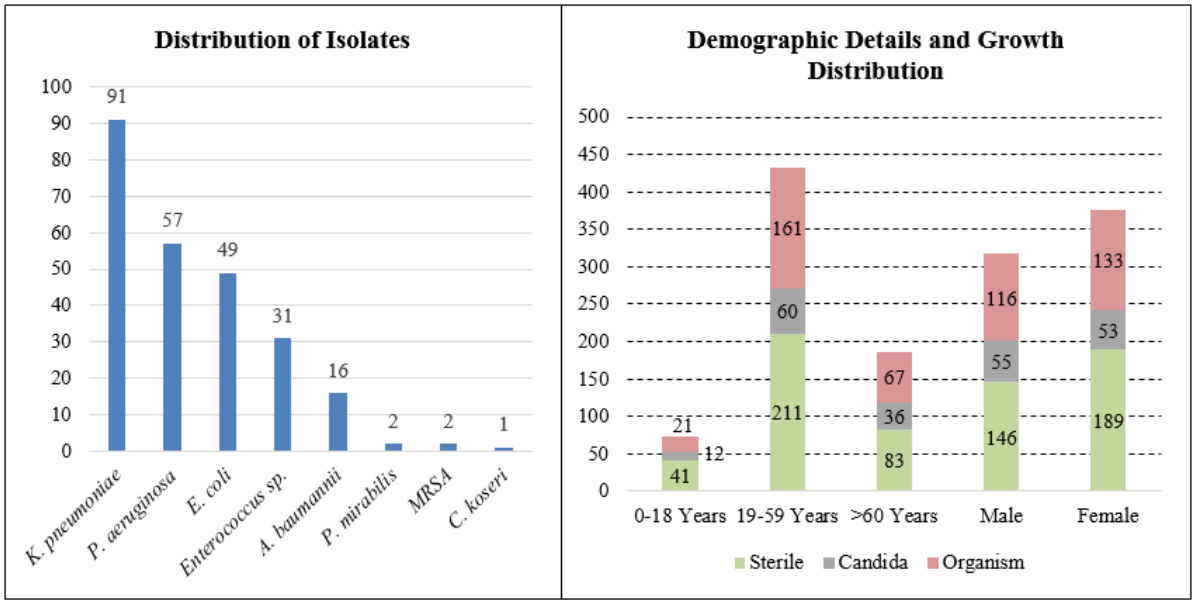

Figure 1: Shows the distribution of isolates in this study. Klebsiella pneumoniae was the most common isolate, followed by Pseudomonas aeruginosa and Escherichia coli. Gram-positive organisms constituted only 18 isolates.

Figure 2: Shows the demographic details and growth distribution. Most patients belonged to the age group of 19-59 years. A major proportion of the samples in all age groups were sterile. More samples were received from females, and a major proportion of the samples from both sexes were sterile as well.

The isolates were largely resistant to common antibiotics, especially those that concentrate in the urine. Determination of susceptibility was done according to CLSI 2022 M100 guidelines[10]. We analyzed the antibiotic susceptibility patterns according to the class of antibiotics (Table 2), as well as the individual organisms (Table 3).

Table 2: Antibiotic susceptibility patterns according to the class of antibiotics

Drug Class	Drug	%S	%I	%R	Cumulative		
					%S	%I	%R
Aminoglycosides	Amikacin	31.1	9.7	59.2	27.1	4.5	68.4
	Gentamicin	24.3	2.7	73			
	Tobramycin	27.4	5.4	67.2			
	High Level Gentamicin	25.8	0	74.2			
Beta Lactams	Ampicillin - Sulbactam	31.2	0	68.8	13.9	2.2	83.9
	Aztreonam	19.3	7	73.7			
	Cefazolin	6.3	0	93.7			
	Cefepime	9.3	4.6	86.1			
	Cefixime	6.3	0	93.7			
	Cefotaxime	4.9	0.7	94.4			
	Cefoxitin (Surrogate Marker)	0	0	100			
	Ceftazidime	15.1	1.4	83.5			
	Imipenem	22.2	5.6	72.2			
	Meropenem	21.8	4.2	74			
	Penicillin - G	6	0	94			
	Piperacillin - Tazobactam	23.6	3.2	73.2			
	Ciprofloxacin	8.4	1.2	90.4	13	3.2	83.8

Fluoroquinolones	Levofloxacin	17.5	5.3	77.2			
Lincosamide	Clindamycin	50	50	0	50	50	0
Macrolide	Erythromycin	6	9.1	84.9	6	9.1	84.9
Polymyxin	Colistin	85.6	0	14.4	85.6	0	14.4
Sulfonamide	Cotrimoxazole	9.6	0.5	89.9	9.6	0.5	89.9
Tetracyclines	Doxycycline	48.5	3	48.5	41.3	1	57.7
	Minocycline	50	0	50			
	Tetracycline	25.5	0	74.5			
Oxazolidinone	Linezolid	100	0	0	100	0	0
Nitrofuran	Nitrofurantoin	16.5	7.6	75.9	16.5	7.6	75.9
Glycopeptide	Vancomycin	83.9	3.2	12.9	83.9	3.2	12.9

Table 3: Organism wise susceptibility pattern according to antibiotic class

Organism		***AG**	***CS**	***PD**	***CP**	***FQ**	***CT**	***NT**	***TC**	***LZ**
Klebsiella pneumoniae	%R	71.34	78.36	73.68	80.71	80.70	94.74	91.23	[#]NA	
	p–value	**0.017**	**<0.001**	**<0.001**	**0.006**	**0.002**	0.583	**0.044**		
Pseudomonas aeruginosa	%R	45.92	90.31	59.18	56.12	93.88	91.84	63.27		
	p–value	**0.044**	**<0.001**	**<0.001**	**0.022**	**0.002**	0.182	**0.001**		
Escherichia coli	%R	72.53	95.33	84.62	80.00	93.41	90.11	82.42		
	p–value	**<0.001**	0.394	**0.009**	**<0.001**	**0.027**	0.444	**0.001**		
Acinetobacter baumannii	%R	66.67	78.13	65.63	62.5	81.25	68.75	81.25	53.12	NA[#]
	p–value	0.495	**0.041**	0.178	0.113	**0.0434**	**0.012**	0.462	**0.009**	
Enterococcus species	%R	NA[#]						51.61	83.87	100
	p–value							**<0.001**	**0.009**	**<0.001**

*AG -Aminoglycoside; CS-Cephalosporins; PD-Penicillin Derivatives; CP-Carbapenems; FQ-Fluoroquinolones; CT-Cotrimoxazole; NT-Nitrofurantoin; TC-Tetracyclines; LZ-Linezolid | [#]NA-Not Applicable as per CLSI 2022 M100[10]

IV. Discussion

Any infection developing more than two days after hospitalization can be labelled as Hospital Acquired Infection (HAI). The recognized definition of an HAI includes infections acquired by a patient hospitalized for a reason other than that infection, not present or incubating at the time of admission. Symptoms should appear at least 48 hours after admission, including those appearing after discharge. The definition also includes occupational infection among Health Care Workers[12]. Risk for developing Catheter Associated UTI is around 3-5% for each day of in-situ catheter, which rises to about 25% when catheter is in-situ for a week. The risk of developing CAUTI is 100% after completion of one month of catheterization[13]. As signs and symptoms of UTI in a catheterized patient are vague and non-specific, clinical suspicion is necessary for diagnosis.

We found that almost half (n=335 of 692; 48.41%) of the samples included were sterile, and the growth rate among samples was 51.59% (n=357 of 692. These findings were correspondent with an older study in central India (2017) which showed a growth rate of 47.71%[14]. Recently, the rate seems to have dropped considerably, both national and internationally, as a study in southern India (2022) showed the growth rate to be only 16.65%, while one in the Middle East (2021) showed it to be 35.85% [15,16]. This discrepancy could be ascribed to the fact that these studies were conducted in intensive care settings, where aseptic techniques are usually performed meticulously. Simultaneously, we observed the rate of isolating Gram-negative organisms was 86.74% (n=216 of 247) and that of Gram-positive organisms was 13.26% (n=33 of 247). These findings were comparable to various studies internationally and nationally. The rate of growing Gram-negative organisms was 83.27% in a study in Southern India (2022)[15] and 84.40% in a study from the Middle East (2021)[16]. These findings concur with various academic volumes as well[13,17-19].

As most of the isolates were Gram-negative organisms, the comparative analysis was done by making five groups and two individual drugs used for Gram-negative organisms. Additionally, due to the high frequency of isolation across studies over time, the AST patterns of *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Escherichia coli*, were compared with six other studies (Table 4).

Table 4: Antibiotic Susceptibility Pattern – Drug Wise (%R)

Author	**Organism**	**AG***	**CS***	**PD***	**CP***	**FQ***	**CT***	**NF***
Kulkarni *et al* (2014)[20]	*Escherichia coli*	33.33	88.88	40.74	44.44	59.25	81.48	40.74
	Klebsiella pneumoniae	54.50	100	45.40	18.20	81.80	99.90	54.50
	Pseudomonas aeruginosa	37.50	75.00	50.00	50.00	75.00	87.50	87.50
Kazi *et al* (2015)[21]	*Escherichia coli*	18.00	86.50	50.00	0.00	55.00	NA[#]	NA[#]
	Klebsiella pneumoniae	50.00	100	68.00	9.00	100	NA[#]	NA[#]
	Pseudomonas aeruginosa	22.30	100	100	75.50	50.00	NA[#]	NA[#]
Tomar *et al* (2017)[14]	*Escherichia coli*	35.50	84.30	73.13	3.75	82.50	27.50	11.25
	Klebsiella pneumoniae	75.00	98.44	75.00	0.00	93.75	68.75	43.75
	Pseudomonas aeruginosa	23.33	23.33	6.66	0.00	33.33	26.66	NA[#]

Singh *et al* (2018)[22]	*Escherichia coli*	50.00	NA#	100	0.00	100	NA#	NA#
	Klebsiella pneumoniae	100	100	100	0.00	NA#	NA#	NA#
	Pseudomonas aeruginosa	50.00	NA#	NA#	0.00	NA#	NA#	NA#
Liu *et al* (2020)[23]	*Klebsiella pneumoniae*	45.60	45.60	82.20	30.00	62.20	NA#	NA#
Khadim (2021)[16]	*Escherichia coli*	80.24	76.16	88.37	60.46	27.13	NA#	NA#
	Klebsiella pneumoniae	61.90	48.81	71.43	30.95	12.70	NA#	NA#
	Pseudomonas aeruginosa	100.00	75.00	85.11	63.33	44.44	NA#	NA#
Present Study (2023)	*Escherichia coli*	72.53	95.33	84.62	80.00	93.41	90.11	82.42
	Klebsiella pneumoniae	71.34	78.36	73.68	80.71	80.70	94.74	91.23
	Pseudomonas aeruginosa	45.92	90.31	59.18	56.12	93.88	91.84	63.27
* AG – Aminoglycosides, CS – Cephalosporins, PD – Penicillin Derivatives, CP – Carbapenems FQ – Fluoroquinolones, CT-Cotrimoxazole, NF – Nitrofurantoin | # – Not Applied								

In summary – irrespective of the organism causing CAUTI, the treatment of established infection is a wrought with difficulties. In addition to being highly resistant to commonly used antibiotics like Aminoglycosides, Cephalosporins, and even higher antibiotics like Carbapenems, the organisms also overcome antibiotics like Nitrofurantoin, which specifically concentrate in urine.

The studies (Table 4), both national and international, span over the course of almost a decade. We find that the varied geographical distribution and temporal factors have a diverse susceptibility pattern. It can, however, be presumed that resistance to common antibiotics shows a rising trend, irrespective of the causative organism. These findings further confirm our initial postulation that despite the generally characteristic of high degree of AMR, it is still essential to acquire knowledge of current local trend of causative organisms, and their resistance pattern in any healthcare facility.

V. Conclusion

CAUTI is predominantly caused by Gram-negative organisms, with *Klebsiella pneumoniae* as the primary organism. Irrespective of the causative organism, the treatment of established CAUTI is a challenging task. In addition to being highly resistant to most classes of antibiotics, it can also overcome those which concentrate in urine.

In conclusion, CAUTI, the most common HAI, not only leads to numerous local and systemic complications, but also caused by bacteria showing a high degree of antimicrobial resistance. All the findings and inferences in the present study emphasize that prevention strategies are more effective in case of CAUTI as compared to treatment options. Hence, Prevention is better than Cure.

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