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ANTIMICROBIAL SUSCEPTIBILITY TRENDS IN CATHETER ASSOSCIATED URINARY TRACT INFECTIONS: INSIGHTS FROM A TERTIARY CARE CENTRE

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ABSTRACT

Background: Catheter associated Urinary Tract Infections (CAUTI) is associated with various risk factors such as older age, diabetes. There is an increased occurrence of antimicrobial resistance among CAUTI cases.
Objectives: The current study was undertaken to know the antimicrobial resistance pattern of bacterial isolates from CAUTI, and the risk factors for CAUTI.
Materials and Methods: This cross-sectional study was conducted among catheterised in-patients who met the CAUTI criteria. Urine samples were collected, and culture, gram staining, identification and antibiotic susceptibility tests were performed. Data was entered in MS Excel sheet and analyzed by using Epi-info software.
Results: Among the total 120 urine samples collected, 64 (53.3%) of them showed growth. A statistically significant association of CAUTI was found with increasing age, diabetes mellitus and prior antibiotic therapy. Majority of the isolates were *E.coli* (33.3%). The Gram-positive isolates showed an increased resistant pattern to Norfloxacin, Clindamycin, Erythromycin while Gram-negative isolates were more resistant to Norfloxacin, Ampicillin, Amoxicillin clavulanate, Cefepime, and Ceftriaxone.
Conclusion: It is better to start CAUTI treatment, initially with higher antibiotics empirically, based on the local hospital antibiogram and de-escalating/ escalating later, based on the susceptibility pattern of pathogens to antibiotics, especially in case of older diabetic patients
Keywords: Catheterization, Uropathogen, CAUTI, Antimicrobial resistance.

INTRODUCTION

Globally, Urinary Tract Infections (UTI) make up to 40% of all Health-care Associated Infections (HAI), of which 80% is associated with the presence of an indwelling urinary catheter.[1,2]The vulnerability of an individual to Catheter associated UTI (CAUTI) is because of various risk factors, including older age, female gender, diabetes, and impaired immunity.[3]The etiological agents of CAUTI are usually the microbial flora from the patient, health-care providers and the environment[4]. Bacteria usually seen in CAUTI are Escherichia coli, Klebsiella pneumoniae, other Enterobactericeae and Staphylococcus species, while Pseudomonas aeruginosa have a higher prevalence in a health care setting.[1,5-7] The increased occurrence of antimicrobial resistance among CAUTIs has significant economic implications especially in developing countries with limited resources as patient recovery is difficult.[2]

Therefore, early detection of antimicrobial susceptibility pattern is mainstay in managing CAUTI and overcoming antimicrobial resistance.[8] The awareness about the pathogen, the antibiotic resistance pattern and risk factors would be helpful for effective management and prevention of CAUTI. Since no study of this kind was done in our tertiary care center previously, the current study was undertaken to know the antimicrobial resistance

pattern of bacterial isolates from CAUTI and the risk factors of CAUTI, with the aim to improve patient care.

MATERIALS AND METHODS

This hospital based cross-sectional study was conducted in KH Patil Institute of Medical Sciences (KHPIMS), Mallasamudra, Gadag, Karnataka from August 2022- August 2024 for a duration of 2 years. The study population consisted of all catheterized in-patients in the wards and Intensive Care Units of KHPIMS, Gadag, who met the CAUTI criteria[9]. Random sampling method was used to select the study samples. According to the study conducted by Vishwajeet. B,[10] the proportion of patients with biofilm production in CAUTI isolates is 60.72%=p. Sample size was calculated using the formula n= z^2 pq/e^2 as 120.

Inclusion Criteria: All catheterized in-patients who satisfy the CDC, National Healthcare Safety Network (NHSN) CAUTI criteria[9] and are aged 18 years and above.

Exclusion Criteria: patients with hydronephrosis, pyelonephritis, urinary tract abnormalities, pregnant subjects, patients on diuretics, samples for which the urine culture yields non-bacterial isolates, samples which show contamination on culture were excluded from the study.

Ethical consideration: The letter of Academic& Scientific Review Committee Approval (GIMS/ASRC/06/22-23) for the study was obtained on 29.06.2022, from the Academic& Scientific Review Committee. The letter of Approval (GIMS/IEC/19/22/2022-23) was obtained from the Institutional Ethical Committee, on 22.07.2022. Informed consent was obtained from all the study participants.

Patient Data and sample collection method: Sociodemographic and clinical data were collected with the help of a proforma. 3-5ml of urine sample was collected from the catheter, as per standard microbiological guidelines.[11-13].

Culture: Physical nature of samples was evaluated initially, following which semi-quantitative culture was done by inoculating on Cysteine Lactose Electrolyte Deficient (CLED) medium (Microxpress, Goa) using a standard calibrated loop (Microxpress-Steriloop-10) of which delivers 0.001mL of urine.[11]. The plate was incubated at 37°C for 24 hours.

Identification of isolated organisms: The organisms isolated in significant numbers were identified by standard microbiological procedures including morphological characteristics, Gram's stain, and biochemical tests.[12,13,14].

Antimicrobial susceptibility testing: Antibiotic Sensitivity Testing was done on Mueller Hinton agar (Microxpress, Goa) by Kirby-Bauer disc-diffusion method. About 6 disks (Microxpress, Goa) per 100 mm plate were placed at least 24 mm apart, under sterile precautions. Then the plates were incubated at 37°C for 24 hours and interpreted as per CLSI 2022, M100 guidelines. Detection of methicillin resistance and ESBL production were performed according to CLSI guidelines.[15].

Data Analysis: Data was entered in MS-Excel sheet and analyzed by using Epi-info software. Frequencies, percentages, Chi-square tests were used. P value <0.05 was considered as significant.

RESULTS

In this study, a total of 120 urine samples were collected from the in-patients with the symptoms of CAUTI, in KHPIMS, Gadag. From table-1, it can be seen that, there is a statistically significant relationship between incidence of CAUTI with increasing age of patients, prior antibiotic treatment, diabetes mellitus and hypertension. Multivariate logistic regression analysis was done for understanding the significance of Diabetes mellitus and hypertension (Table2). The culture positivity was 53.3% with a total of 66 isolates. Majority of them were E. coli (33.3%), followed by S.aureus (13.6%), C.freundii (13.6%), P.aeruginosa(12.1%), Coagulase negative staphylococcus (10.6%), A.baumannii (6.1%), K.pneumoniae (6.1%), C.koseri (4.5%).

Both S.aureus and CoNS showed a predominant sensitive pattern for Nitrofurantoin, High level Gentamycin, Ciprofloxacin, Linezolid, Teicoplanin, Cotrimoxazole, Doxycycline and Tetracycline. On the other hand, these isolates showed an increased resistant pattern to Norfloxacin, Clindamycin, Erythromycin (table-3). On evaluating the antibiotic sensitivity pattern of Gram-negative bacilli, it can be seen that, E.coli, Klebsiella and Citrobacter show predominant sensitive pattern to Amikacin & Gentamicin, and a variable sensitivity to Nitrofurantoin, Meropenem, Piperacillin-tazobactam. P.aeruginosa gives a predominantly sensitive pattern to Aztreonam and Netilmicin, while A.baumannii shows susceptibility to Ciprofloxacin and Amikacin (Table-4). E.coli show a predominant resistant pattern against Norfloxacin, Ampicillin, Amoxicillin clavulanate, Cefepime, and Ceftriaxone. Meanwhile K.pneumoniae isolates show resistance to Ampicillin and Amoxicillin clavulanate. C. freundii show more resistance towards Ciprofloxacin, Ampicillin, Amoxicillin-clavulanate, Cefepime and Ceftriaxone. On the other hand, C.koseri show predominant resistance pattern against Norfloxacin, Cotrimoxazole, Ampicillin, Amoxicillin-clavulanate, Cefepime, Ceftriaxone and Piperacillin-tazobactam. P.aeruginosa and A.baumannii display more resistance against Nitrofurantoin, 62.5% and 100% respectively. 62.5% of the Staphylococcus isolates showed methicillin resistance among the total 16 isolates. Among the bacterial isolates, 70.3% were ESBL producers and 29.7% did not show ESBL production. [Table 5]

Table 1: Baseline characteristics of study participants

		CAUTI positive	CAUTI negative	Total	χ^2	p-value
Age group	**Upto 40years**	8(6.7%)	16(13.3%)	**24(20%)**	4.89	0.0270
	41-70years	45(37.5%)	33(27.5%)	**78(65%)**		
	Above 70years	11(9.2%)	7(5.8%)	**18(15%)**		
	Total	**64(53.3%)**	**56(46.7%)**	**120(100%)**		
Gender	Male	35(29.2%)	31(25.8%)	66 (55%)	0.005	0.9436
	Female	29(24.2%)	25(20.8%)	54 (45%)		
	Total	**64(53.3%)**	**56(46.7%)**	**120(100%)**		
Location	**Ward**	22(18.3%)	27(22.5%)	**49(40.8%)**	2.368	0.1238
	ICU	42(35%)	29(24.2%)	**71(59.2%)**		
	Total	**64(53.3%)**	**56(46.7%)**	**120(100%)**		
Department	**General Medicine**	39(32.5%)	37(30.8%)	**76(63.3%)**	2.53	0.1117
	General Surgery	7(5.8%)	7(5.8%)	**14(11.7%)**		
	Orthopaedics	9(7.5%)	3(2.5%)	**12(10%)**		
	Obstetrics & Gynaecology	9(7.5%)	9(7.5%)	**18(15%)**		
	Total	**64(53.3%)**	**56(46.7%)**	**120(100%)**		
Duration of hospital stay (in days)	**1-5 days**	33(27.5%)	31(25.8%)	**64(53.3%)**	0.251	0.6164
	6-10 days	28(23.3%)	22(18.3%)	**50(41.7%)**		
	11-15 days	3(2.5%)	3(2.5%)	**6(5%)**		
	Total	**64(53.3%)**	**56(46.7%)**	**120(100%)**		
Duration of catheterization (in days)	**1-5 days**	42(35%)	35(29.2%)	**77(64.2%)**	1.339	0.2472
	6-10 days	21(17.5%)	18(15%)	**39(32.5%)**		
	11-15 days	1(0.8%)	3(2.5%)	**4(3.3%)**		
	Total	**64(53.3%)**	**56(46.7%)**	**120(100%)**		
Co-morbidities	**Hypertension**	26(21.7%)	13(10.8%)	39(32.5%)	4.127	0.0422
	Type 2 Diabetes mellitus	37(30.8%)	20(16.7%)	57(47.5%)	5.849	0.0156
	Hypertension &Type 2 Diabetes mellitus	16(13.3%)	4(3.3%)	20(16.7%)	6.858	0.0088
	Dyslipidemia	2(1.7%)	2(1.7%)	4(3.3%)	0.018	0.8933
History of antibiotic therapy	**On prior antibiotic therapy**	56(46.7%)	40(33.3%)	**96(80%)**	4.821	0.0281
	Not on antibiotic therapy	8(6.7%)	16(13.3%)	**24(20%)**		
	Total	**64(53.3%)**	**56(46.7%)**	**120(100%)**		

The p-value is significant at $p < 0.05$

Table 2: Results of multivariate logistic regression

Co-morbidities	N(%)	OR	p-value
Diabetes mellitus	39(32.5%)	2.42	0.020
Hypertension	57(47.5%)	2.12	0.069

OR: Odds ratio; p-value is significant at $p<0.05$

Table 3: Antibiotic sensitivity pattern of Gram-positive isolates

Antibiotic	Susceptible isolates		Resistant isolates	
	S. aureus (n=9)	CoNS (n=7)	*S. aureus*(n=9)	CoNS(n=7)
Nitrofurantoin	6 (66.7%)	4(57.1%)	3(33.3%)	2(28.6%)
Norfloxacin	4(44.4%)	3(42.9%)	4(44.4%)	2(28.6%)
Azithromycin	3 (33.3%)	4(57.1%)	4(44.4%)	2(28.6%)
Chloramphenicol	4(44.4%)	5(71.4%)	3(33.3%)	2(28.6%)
Clindamycin	3(33.3%)	2(28.6%)	4(44.4%)	3(42.9%)
Erythromycin	2(22.2%)	2(28.6%)	4(44.4.%)	4(57.1%)
High level Gentamycin	6(66.6%)	4(57.1%)	1(11.1%)	2(28.6%)
Ciprofloxacin	5(55.5%)	4(57.1%)	4(44.4%)	3(42.9%)
Linezolid	6(66.6%)	6(85.7%)	1(11.1%)	1(14.3%)
Teicoplanin	6(66.6.%)	6(85.7%)	1(11.1%)	1(14.3%)
Cotrimoxazole	6(66.6%)	5(71.4%)	3(33.3%)	1(14.3%)
Doxycycline	7(77.7%)	5(71.4%)	2(22.2%)	1(14.3%)
Tetracycline	7(77.7%)	5(71.4%)	2(22.2%)	1(14.3%)

Table 4: Antibiotic Sensitivity Pattern of Gram-Negative Isolates

Antibiotics	E.coli (n=22)	K. pneumoniae (n=4)	C.freundii (n=9)	C.koseri (n=3)	P.aeruginosa (n=8)	A.baumannii (n=4)
Nitrofurantoin	15(68.2%)	2(50%)	4(44.4%)	3(100%)	3(37.5%)	0
Norfloxacin	6(27.3%)	3(75%)	4(44.4%)	1(33.3%)	4(50%)	2(50%)
Ciprofloxacin	5(22.7%)	3(75%)	2(22.2%)	1(33.3%)	1(12.5%)	3(75%)
Cotrimoxazole	(22.7%)	3(75%)	0	1(33.3%)	0	0
Ampicillin	3(13.6%)	0	0	1(33.3%)	0	0
Amoxicillin-clavulanate	2(9.1%)	0	0	1(33.3%)	-	0

Amikacin	17(77.3%)	4 (100%)	8(88.9%)	3(100%)	4 (50%)	3(75%)
Cefepime	5(22.7%)	1(25%)	2 (22.2%)	1(33.3%)	-	0
Ceftazidime	2(9.1%)	0	1(11.1%)	0	2 (25%)	1(25%)
Ceftriaxone	5(22.7%)	1(25%)	0	1(33.3%)	-	1(25%)
Doxycycline	2(9.1%)	0	2(22.2%)	0	0	0
Gentamicin	15(68.2%)	4(100%)	4(44.4%)	1(33.3%)	1(12.5%)	1(25%)
Imipenem	4(18.2%)	0	3(33.3%)	1(33.3%)	4(50 %)	2(50%)
Meropenem	9(40.9%)	3 (75%)	4(44.4%)	2(66.7%)	1(12.5%)	2(50%)
Piperacillin Tazobactam	6 (27.3%)	3 (75%)	2(22.2%)	1(33.3%)	3(37.5%)	0
Aztreonam	4(18.2%)	0	2(22.2%)	0	5(62.5%)	0
Tetracycline	1(4.5%)	0	1(11.1%)	0	1(12.5%)	0
Netilmycin	0	0	-	-	5(62.5%)	-
Tobramycin	11(50%)	4 (100%)	1(11.1%)	1(33.3%)	4(50%)	0
Levofloxacin	0	0			2(25%)	0

Table 5: Methicillin resistance and ESBL production among the isolates

Antimicrobial resistance	Present	Absent	Total
Methicillin resistance	10(62.5%)	6(37.5%)	16(100%)
ESBL production	26(70.3%)	11(29.7%)	37(100%)

DISCUSSION

CAUTI is a major HAI, which can lead to prolonged hospital stay and financial burden to the patients. The culture positivity rate in our study (53.3%) was compared with the study conducted by Vinoth M et al,[16] that reported 70% of culture positivity and Sayal P et al,[17] who documented, 82% significant growth. However, 90% culture positivity was observed in a study conducted by Majumder M.I. et al,[18] while in another study by Amuthamani R et al,[19] showed only 12% of culture positivity. This difference in incidence could be because of the demographic and geographical variability, as well as to the variance in the bacterial species involved in nosocomial infections and hospital infection control practices.

In the current study, significant association between occurrence of CAUTI and increasing age is present. Similarly, S.G.Kulkarni et al,[20] and N.Bhatia et al,[21] found that CAUTI was more common in age group of more than 40 years. There are numerous reasons for increased incidence of UTI in elderly, such as, age associated changes in immune function, exposure to multidrug resistant nosocomial pathogens and increased incidence of co-morbidities. Moreover, old age contributes to increased and prolonged hospital admission for various ailments, some of which may require catheterization.

In the present study, 54.2% of the CAUTI positive cases were males and rest were females. This was in concordance with the demographic characteristics of the studies, conducted by Sandhu R et al,[3] and Verma et al.[22] On the other hand, a study conducted by Mangukiya JD et al concluded that females were more commonly affected than males.[23] This is likely because of the easier access of the perineal flora to the bladder, through the shorter urethra. The slightly increased prevalence of CAUTI in males in the current study could be due to the presence of comorbidities, increased age and small sample size.

65.6% of the CAUTI cases were from ICUs, in the present study. Contrary to this finding, 82.5% patients were in the wards while 17.5% were in ICU, in a study conducted by Omer S.A et al.[24] This could be because of increased catheterization rates in ICUs as compared to wards. Majority of the CAUTI cases in this study, were from General Medicine department, which is in line with the results of study done by Sandhu R et al.[3] Elderly patients admitted for various conditions such as acute cerebrovascular accidents, other acute illness with previous history of paralysis, other ailments requiring catheterization, were the majority of patients from General Medicine department. Even though catheterization is done routinely in other departments, the duration of catheterization is usually less, often not meeting the CAUTI criteria.

There was no statistically significant association of incidence of CAUTI with either duration of hospital-stay or duration of catheterisation in the current study. While in the research done by Al-Hazmi H,[25] there was a statistically significant association between length of hospital stay and occurrence of CAUTI and also between duration of catheterization and CAUTI incidence. In general, the incidence of CAUTI increases with the duration of hospital stay and duration of catheterization,[5] which was not observed in our study because of smaller sample size and as majority of the participants had lesser duration of hospital stay.

57.8% of CAUTI cases had Type 2 Diabetes mellitus, which was correlated with the study by Eshwarappa et al.[26] Diabetes mellitus produces a number of long-term effects on the genitourinary system along with weakened immunity, which contributes as a risk factor for CAUTI. 16.7% of the study subjects had hypertension along with Type 2 Diabetes mellitus. The multivariate logistic regression analysis gave a statistically significant output for the correlation of Diabetes mellitus and CAUTI, meanwhile for hypertension no statistical significance was shown.

87.5% of CAUTI cases were on antibiotic treatment, while showing symptoms of CAUTI. Similar to these findings, Opatowski et al,[27] found that prior use of antibiotics is associated with increased odds of UTI

with antibiotic resistant bacteria. More over in our study, antibiotics such as cephalosporins, amoxicillin-clavulante and fluoroquinolones, were started for their presenting illness or as prophylactic treatment, which may have led to the emergence of resistance to these drugs, among the isolates.

In the current study, E.coli (33.3%) was the most frequently isolated organism, followed by C.freundii (13.6%) and S.aureus (13.6%). E.coli was the commonly isolated organism in many other studies.[17,19,28] The isolation of S.aureus in this study was similar to that of Sayal P et al,[17] while the presence of P.aeruginosa was correlating with the research of Amuthamani et al.[19] Uropathogenic E.coli (UPEC), is the most common etiologic agent of CAUTI, because of its various virulence factors such as adhesins, cytotoxic necrotizing factor and iron acquisition systems,[6] and its presence among the perineal flora. Meanwhile, fibrinogen-binding proteins present in S. aureus strains, aids in colonization of the catheter.[29] The virulence factors which assist Citrobacter could be the adhesins and cytotoxins.[11] Citrobacter species are generally multidrug resistant especially when isolated from hospital acquired infections, which is being reflected in our study.

Based on our study, the most effective antibiotics against Gram negative bacilli other than Pseudomonas and Acinetobacter were aminoglycosides. Similar results were observed in a study conducted by Sandhu R et al,[3] where most of the Gram negative isolates were sensitive to Amikacin (77.78%) followed by Cefazolin and Ceftazidime (66.67%). Jafari et al,[30] observed Amikacin (91%) as one of the most effective drugs against uropathogens in his study. The infection due to non-fermenters requires the use of antibiotics such as aminoglycosides or carbapenems, rather than the routinely used antibiotics for treatment of UTI. Because these bacteria are usually multidrug resistant and they also exhibit intrinsic resistance along with acquired resistance.[14]

Lower sensitivity pattern was observed for the Ampicillin, Amoxicillin clavulanate, Cephalosporins, Fluoroquinolones, Tetracycline in our study, which was correlated with the study conducted by Sujatha et al,[31] that showed higher resistance for the drugs ampicillin, fluoroquinolones and cephalosporins. In the study by Sandhu R et al,[3] decreased sensitivity was observed to Nitrofurantoin, Cefuroxime, and Cefotaxime (55.56%).

This can be due to indiscriminate use of these drugs for all type of infections and emergence of newer drug-resistant strains. Some studies from Europe, USA and many other countries had showed better susceptibility pattern for pathogens isolated from UTI against cotrimoxazole.[32,33] But, in our study, Co-trimoxazole had poor response for Gram negative isolates, except for K.pneumoniae. Extensive and uncontrolled use of this drug could be a reason for this.

Both S.aureus and CoNS showed a predominant sensitive pattern for Nitrofurantoin, High level Gentamicin, Ciprofloxacin, Linezolid, Teicoplanin, Cotrimoxazole, Doxycycline and Tetracycline and an increased resistant pattern to Norfloxacin, Clindamycin and Erythromycin. This is in line with the findings of Tayebi et al,[34] which showed higher sensitivity of Gram-positive isolates to Tetracycline (76%) and Nitrofurantoin (76%). The lower sensitivity was observed for Norfloxacin, was similar with the study conducted by Sujatha et al,[31] which additionally showed reduced sensitivity to Cotrimoxazole which was absent in our study.

Among the Gram-positive isolates, 62.5% were methicillin resistant. Similar results were observed in the study conducted by Ando et al.[35] As CAUTI is a nosocomial infection, and MRSA mainly spreads through the hands of health care workers and thrive in a hospital environment, the increased percentage can be explained. 70.3% of Gram-negative isolates were showing ESBL production. 56.7% and 35.16% of isolates were ESBL producers in the studies conducted by Sheik G B et al,[36] and Oberoi L et al,[37] respectively. Due to the enhanced and extensive use of penicillins and cephalosporins, the emergence of ESBL producers is no longer a surprise. The escalated and unmonitored use of prophylactic antibiotics, extensive use of cephalosporins, aminopenicillins and fluoroquinolones, has led to the origin of many multidrug resistant strains, which show sensitivity to higher antibiotics only, making the eradication of infection a challenging process.

Although this study provides valuable insights, its small sample size may limit the generalizability of the results. The absence of an observable association between CAUTI and female gender, duration of catheterization or hospital stay, underscores the need for studies with larger sample size.

CONCLUSION

The study reveals that, CAUTI show a significant association to the increasing age of the patient, presence of Type2 Diabetes mellitus and prior antibiotic therapy. As hypertension and Type 2 Diabetes mellitus can occur in the same individual, careful interpretations of statistical significance is required.

E.coli was found to be the predominant isolate in our study and Staphylococcus was the only Gram-positive isolate. The study highlights that Gram negative isolates show higher sensitivity to Amikacin and Gentamicin, while the sensitivity to Piperacillin-tazobactam, Nitrofurantoin and carbapenems were variable. A predominant resistance pattern is shown to aminopenicillins and cephalosporins, which should be avoided from the empirical treatment. The Staphylococcus isolates, show an increased resistant pattern to Norfloxacin, Clindamycin, Erythromycin and a predominant sensitive pattern for Nitrofurantoin, Ciprofloxacin, Linezolid,

Teicoplanin, Cotrimoxazole, Doxycycline and Tetracycline.

In conclusion, elderly and diabetic patients require heightened clinical vigilance due to their increased susceptibility to CAUTI and it is better to start CAUTI treatment, at the earliest, by the removal of the catheter and starting the patient on higher antibiotics empirically, based on the local hospital antibiogram and de-escalating/ escalating later, based on the susceptibility pattern of pathogens to antibiotics.

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