

Etiology and risk factors of catheter associated urinary tract infections in ICU patients

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Abstract

Background: Catheter associated urinary tract infections (CAUTI) are common infections in ICUs patients. Unnecessary treatment of CAUTI causes economic burden on healthcare and contributes to antibiotic resistance.

Objectives: This study was planned to determine the incidence of CAUTI in ICU patients, to find the risk factors and to identify the causative agents and their antimicrobial susceptibility.

Materials and Method: This prospective study was performed over a period of one year, enrolling patients admitted and catheterised with indwelling urinary catheter for ≥ 48 hours in ICU of our hospital. Urine samples were collected from patients suspected of developing signs and symptoms suggestive of CAUTI after more than 48 hours of catheterisation and processed by semi-quantitative method. CAUTI was diagnosed using CDC definition.

Results: Out of 163, 26 patients (15.95%) were diagnosed with CAUTI. Risk factors identified for development of CAUTI were analyzed. Female gender, mechanical ventilation, duration of catheterization ≥ 5 days, Diabetes were independent risk factors while increasing age (≥ 65 years) was not found to be associated with CAUTI. 69.2% of CAUTIs were due to bacteria and 30.8% were due to yeast. The single most common organism isolated was *Candida* species (30.8%) followed by *Escherichia coli* and *Enterococcus faecalis* (19.2%) each. Incidence of drug resistance was high in CAUTI isolates.

Conclusion: CAUTI is common in ICU patients. Females, diabetics, patients on mechanical ventilation and with prolonged catheterization are independent risk factors for CAUTI. Majority pathogens were bacterial in origin and were resistant to multiple drugs.

Keyword: CAUTI, HAIs, Urinary catheterization in ICUs, Multi drug resistant uropathogens, *Candida* causing UTI

Introduction

Urinary tract infections (UTI) are the most commonly acquired healthcare infections with an estimated prevalence of 1-10%, representing 30-40% of all nosocomial infections. Approximately 10% of UTIs are associated with mortality, along with cost escalation and increased morbidity. In ICUs, presence of urinary catheterization is the most important independent risk factor for development of UTI.⁽¹⁾

Presence of indwelling catheter predisposes to a symptomatic infection because it provides a surface for attachment of microbial adhesion. Symptomatic infection can lead to ascending infection of bladder, ureter and kidney, with subsequent need for antimicrobial agents. Catheter Associated Urinary Tract Infections (CAUTI) are a huge reservoir of resistant pathogens with risk of cross infection of other patients.^(2,3)

CAUTI is defined by CDC as a UTI in a patient who was catheterized for more than 2 days with at least one of the following signs or symptoms: fever ($>38^{\circ}\text{C}$); urgency; frequency; dysuria; suprapubic tenderness; costovertebral angle pain or tenderness and a positive urine culture of $\geq 10^5$ colony-forming units (CFU)/ml with no more than 2 species of microorganisms. If an indwelling urinary catheter was in place for > 2 calendar days and then removed, the UTI criteria must

be fully met on the day of discontinuation or the next day.⁽⁴⁾

It has been recognized that the rates of CAUTI can be decreased by following proper protocols regarding need and duration of catheterization and catheter care. Different guidelines have been formulated to control and decrease the rates of CAUTI in hospitals.^(4,5)

However, due to lack of awareness, paucity of researches and financial constraints, there is dearth of hospital specific data on CAUTIs in India. The present study was planned to determine the incidence of Catheter Associated Urinary Tract Infections (CAUTI) in ICU patients, to find the risk factors for its development and to identify the causative agents and their antimicrobial susceptibility. This will help plan effective infection control policies and also prevent unnecessary antibiotic use in ICUs.

Materials and Method

Study design: This prospective study was conducted in M.S. Ramaiah Hospital, Bangalore from 1st January 2014 to 31st December 2014.

Inclusion criteria: All adult patients admitted to the Intensive Care Units, including both Medical and Surgical ICU and who were catheterized with an indwelling urinary catheter for ≥ 48 hours in the ICUs were included in this study. A urine sample was collected at the time of admission in ICU immediately

following catheterization to rule out pre-existing infection.

Exclusion criteria: The following patients were excluded from the study-

1. Patients whose sample taken on time of catheterization showed culture positivity.
2. Patients catheterized prior to admission in ICU
3. Patients who showed signs and symptoms of UTI within 2 calendar days of catheterization.
4. Patients with condom catheters, suprapubic catheters and percutaneous nephrostomy tubes.
5. Patients with renal anomalies.

Patients' demographic details, date of admission, date of catheterization, duration of catheterization, indication for catheterization, co-morbidities, antibiotic therapy etc. were obtained. Patients were monitored from the time of inclusion in the study to the date of removal of catheter and followed up till 1 day after removal of catheter to look for signs and symptoms suggestive of urinary tract infection. Second sample was collected if the patient developed signs and symptoms suggestive of urinary tract infection after ≥ 48 hours of catheterization. Using a calibrated nichrome wire loop of diameter of 4 mm, 10 μ l of the uncentrifuged specimen was transferred onto Cystine lactose-electrolyte-deficient (CLED) agar plate and streaked using the modified Mayo's technique without flaming the loop for isolation and incubated at 35–37°C for 24 hours. According to CDC guidelines, CAUTI is defined by the presence of symptoms or signs compatible with UTI along with $\geq 10^5$ CFU/mL of no more than 2 species of microorganisms in patients catheterized for more than 2 calendar days.⁽⁴⁾

Samples which showed growth $\geq 10^5$ CFU/ml were studied by colony morphology, Gram stain and identified using standard biochemical reactions. Susceptibility testing was performed by Kirby Bauer disc diffusion method according to CLSI guidelines. The Gram negative bacilli were tested with Ampicillin (10 μ g), Amikacin (30 μ g), Aztreonam (30 μ g), Ceftriaxone (10 μ g), Ceftazidime (30 μ g), Cefoxitin (30 μ g), Cephalexin (30 μ g), Cefuroxime (30 μ g), Cefipime(30 μ g), Ciprofloxacin (1 μ g), Doxycycline (30 μ g), Gentamicin (10 μ g), Imipenem (10 μ g), Meropenem (10 μ g), Netilmicin (30 μ g), Nitrofurantoin (300 μ g), Norfloxacin (10 μ g), Ofloxacin (5 μ g), Piperacillin (100 μ g), Piperacillin-Tazobactam (30+6 μ g), Tigecycline (15 μ g), Tobramycin (10 μ g), Trimethoprim/sulphamethazole (1.2 μ g/23.8 μ g), Colistin (10 μ g). Gram positive cocci were tested with Penicillin G (10units), Ampicillin (10 μ g), Ciprofloxacin (10 μ g), Linezolid (30 μ g), Vancomycin (30 μ g), Teicoplanin (30 μ g), Nitrofurantoin (300 μ g) and High level Gentamicin (120 μ g). The antifungal susceptibility was performed by Kirby Bauer disk diffusion method for Fluconazole (25 mcg/disc) and Amphotericin-B (100 U/disc) as per CLSI guidelines.⁽⁶⁾

The Enterobacteriaceae isolates were screened for extended spectrum beta lactamase (ESBL) production Ceftazidime (≤ 22 mm), Aztreonam (≤ 27 mm) and Ceftriaxone (≤ 25 mm). If the organisms showed a zone of inhibition lower than the minimum for any antibiotic disc, ESBL positivity was suspected. The phenotypic confirmation was done by testing the isolate against Ceftazidime and Ceftazidime/Clavulanic acid. A ≥ 5 -mm diameter of the zone of inhibition for Ceftazidime/Clavulanic acid in comparison to Ceftazidime was considered indicative of ESBL production.⁽⁶⁾

Result

The study was conducted in a 37 bedded general ICU including medical and surgical patients (excluding cardiac patients) of a 1050 bedded hospital. The study included 163 patients, who fulfilled the inclusion criteria, admitted to the ICU between 1st January 2014 and 31st December 2014. Out of 163 patients, 102 were male and 61 females. They were aged between 16 and 95 years (mean 54.21 \pm 8.62years) with 46 patients being older than 65 years. Mean APACHE score on admission and associated co-morbidities are listed in Table 1.

Out of 163 patients, CAUTI was identified in 26 (15.95%) patients according to CDC criteria. All these patients had CAUTI while urinary catheter was in situ. Fever was the sign noted in all cases and was the reason for requesting a urine culture. 8 patients had fever but their urine cultures were sterile and hence were not diagnosed as CAUTI.

Risk factors for development of CAUTI (gender, indication and duration of catheterisation, Diabetes mellitus and age) were analyzed. Female gender (Relative risk (RR) 1.67, $p=0.15$), mechanical ventilation (RR 7.95, $p= 0.003$), duration of catheterization ≥ 5 days (RR 6.11, $p= 0.03$), Diabetes (RR 1.18, $p=0.70$) were independent risk factors while increasing age (≥ 65 years) (RR 0.46, $p=0.11$) was not found to be associated with CAUTI. (Table 2)

Incidence of CAUTI was highest within 1 week of catheterization (61.54%). (Table 3)

All the urine cultures were monomicrobial. 69.2% (18/26) of CAUTIs were due to bacterial aetiologies and 30.8% (8/26) were due to yeast. Gram negative bacilli and Gram positive cocci were identified in 50% and 19.2% of CAUTI isolates respectively. The single most common organism isolated was *Candida* species (30.8%), isolated in pure cultures in all the instances. *Escherichia coli* and *Enterococcus faecalis* were the second most common organism isolated (19.2%) followed by 11.5% of *Klebsiella pneumoniae*, 7.7% each of *Pseudomonas aeruginosa* and *Acinetobacter baumannii* and 3.8% of *Citrobacter freundii* were isolated. (Table 4)

50% of *Candida* isolates (4/8) were sensitive to Fluconazole and all were sensitive to Amphotericin B.

77.8% of Enterobacteriaceae isolates were ESBL producers, 44.4% isolates were resistant to Nitrofurantoin, 88.9% isolates were resistant to Cotrimoxazole and 77.8% were resistant to Fluoroquinolones. All Enterobacteriaceae isolates were sensitive to Colistin.

Out of the 2 *Acinetobacter baumannii* isolates, 1 was resistant to all the tested antibiotics except Tigecycline. Both the *Pseudomonas aeruginosa* isolates were resistant to all the tested antibiotics except Colistin. All Non-fermenters were sensitive to Colistin.

All the 5 (100%) *Enterococcus faecalis* isolates were resistant to Ciprofloxacin and sensitive to Vancomycin and Teicoplanin. 1 isolate (20%) was resistant to Nitrofurantoin. (Table 5)

Table 1: Patients Characteristics (Data are Mean ± SD, range)

1. Age (years) Mean ±S.D Range	54.21 ± 8.62 16-95
2. Gender Males Females	102 61
3. Mean APACHE II score on admission (Range)	16.9 (12.5-17.8)
4. Duration of catheterization(days) Mean Range	7.96 ± 4.48 3-28
5. Co-morbidities Diabetes	53.8%
Neurological disorder	27%
Malignancy	6.13%
Chronic obstructive pulmonary disorder	9.81%
Chronic kidney disease	4.9%
Chronic liver disease	0.06%

Table 2: Risk Factor Analysis for CAUTI

Risk factor	Number of patients (%)	No. of CAUTI	Relative risk (RR)	p value
Female Gender	62 (38.04)	13	1.67	0.15
Diabetes	33 (20.25)	6	1.18	0.70
Indication for catheterization (mechanical ventilation)	98 (60.12)	24	7.95	0.0003
Duration of catheterization ≥ 5 days	131 (80.37)	25	6.11	0.03
Age ≥ 65 years	46 (28.22)	4	0.46	0.11

Table 3: Time interval between catheterization and symptoms of CAUTI

Interval (days)	No. of CAUTI (%)
1-7	16 (61.54)
8-14	7 (26.92)
15-21	2 (7.69)
22-28	1 (3.85)

Table 4: Microorganisms Isolated of Urine Cultures of CAUTI patients

Type	Number	Percentage
<i>Candida species</i>	8	30.8
<i>Escherichia coli</i>	5	19.2
<i>Klebsiella pneumoniae</i>	3	11.5
<i>Citrobacter freundii</i>	1	3.8
<i>Pseudomonas aeruginosa</i>	2	7.7
<i>Acinetobacter baumannii</i>	2	7.7
<i>Enterococcus faecalis</i>	5	19.2

Table 5: Antibiotic susceptibility of CAUTI isolates

Resistance to	Enterobacteriaceae n= 9	Non fermenting Gram negative bacilli n= 4	<i>Enterococcus faecalis</i> n= 5
3 rd generation Cephalosporins (ESBLs)	7/9 (77.8%)	-	-
Carbapenems	3/9 (33.3%)	3/4 (75%)	-
β lactam- β lactamase inhibitor combination	6/9 (66.7%)	4/4 (100%)	-
Aminoglycosides	3/9 (33.3%)	3/4 (75%)	4/5 (80%)
Cotrimoxazole	8/9 (88.9%)	-	-
Fluoroquinolones	7/9 (77.8%)	4/4 (100%)	5/5 (100%)
Nitrofurantoin	4/9 (44.4%)	-	1/5 (20%)
Colistin	0	0	-
Glycopeptides	-	-	0

Discussion

Incidence of CAUTI reported in literature varies from 8.7-59%.^(7,8) This variation could be attributed to difference in study protocols, type of patients included, number of centres where the study was performed and duration of study. In our study, 15.95% (26/163) patients were found to have CAUTI. Our incidence is more or less similar to many previous studies.⁽⁹⁻¹¹⁾

Though we predominantly had male patients (102 males, 61 females), it was observed that the incidence of CAUTI was more among the females (21.31%) as compared to males (12.75%) although the difference did not reach statistical significance ($p=0.15$). Many authors have failed to find female gender a risk factor for CAUTI. Our finding is in strong disagreement with the findings of other researchers that females have a stronger predilection for CAUTI compared to males.⁽¹²⁻¹⁵⁾ Less number of female patients in our study could be a possible reason for this result.

In our study, increased duration of catheterization was found to be significantly associated with CAUTI. Catheterization beyond 5 days increased the risk of CAUTI by 6 times and was found to be statistically significant ($p=0.03$). Study by Tasseau et al found that the risk of developing CAUTI rises from 19% to 50% if duration of catheterization increases from 5 days to 14 days.⁽¹⁶⁾ The risk of developing CAUTI increases 5% with each day of catheterization and virtually all patients are colonized by day 30.⁽¹⁶⁾ The urinary catheter disrupts host defence mechanisms and provides surface for the attachment of microbes eventually leading to biofilm formation.⁽¹⁸⁻²⁰⁾

Studies suggest the number of CAUTI cases increase with advancing age.⁽²¹⁻²³⁾ But we failed to find any correlation of CAUTI with advanced age.

The patients requiring ventilator support were at 8 times higher risk of acquiring CAUTI and it was also found to be statistically significant.

Diabetes has been identified as a risk factor for the development of CAUTI.^(1,22-26) Our results confirm the

previous reports that Diabetes increases the risk of developing CAUTI by 1.18 times.

In our study, incidence of CAUTI was highest within 1 week of catheterization (61.54%) which was similar to results of various other studies.^(8,27)

69.2% of CAUTIs were found to be of bacterial aetiologies and 30.8% were due to yeast. Bacterial agents were predominant causes of CAUTI in the 1st week (81.3%) while yeast and bacteria caused equal cases of CAUTI after a week of catheterization.

Candida species was the single most common organism isolated amongst the CAUTI isolates (30.8%) followed by *Escherichia coli* (19.2%), *Enterococcus faecalis* (19.2%), *Klebsiella pneumoniae* (11.5%), 7.7% of *Pseudomonas aeruginosa* and *Acinetobacter baumannii* each and 3.8% of *Citrobacter freundii*. Enterobacteriaceae are the most common organisms isolated from CAUTI cases with *Escherichia coli* being the most commonly isolated species.^(1,5,28) *Candida* emerged as the single most common organism causing CAUTI. Though not included in the CDC list of CAUTI pathogens, the high percentage of *Candida* causing CAUTI cannot be ignored.^(10,21,29,30) Repeat samples taken with freshly inserted catheters also grew *Candida* confirming it as a cause of CAUTI.

Antimicrobial susceptibility pattern of the isolates obtained in the present study showed that most of the Gram negative bacilli were multidrug resistant. Enterobacteriaceae isolated showed a high level of resistance to beta-lactam antibiotics and Carbapenems. *Acinetobacter baumannii* and *Pseudomonas aeruginosa* were found to be resistant to most of the classes of antibiotics in current use including Carbapenems. Previous studies have suggested that the selective pressure from the use of antimicrobial agents is a major determinant for the emergence of resistant strains.⁽³¹⁾ In our study, all the Enterobacteriaceae were found to be resistant to Ampicillin. 4 out of 5 *Escherichia coli* isolates and all 3 *Klebsiella pneumoniae* isolates were ESBL producers making the use of 3rd generation

Cephalosporins like Cefotaxime, Ceftriaxone and Ceftazidime ineffective in these patients.

High resistance rates to Ciprofloxacin- a drug considered highly effective in the treatment of UTIs was another finding of our study. In our study, 77.8% of Enterobacteriaceae were found to be resistant to Ciprofloxacin. All the *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Enterococci* isolates were found to be resistant to Ciprofloxacin. Similar results are described by Xie et al who found that 88% of *Escherichia coli* were resistant to Ciprofloxacin and all *Pseudomonas aeruginosa* isolates showed absolute resistance to Ciprofloxacin.⁽¹⁰⁾ The very high rate of Ciprofloxacin resistance observed among the isolates in our study warrants special attention and possibly is explained by the fact that in our setting, Ciprofloxacin constitutes one of the commonly prescribed drugs. Overuse of Fluoroquinolones in the last few years has contributed to this rise in resistance.

Cotrimoxazole is another commonly used drug for treatment of UTIs. In our study, 88.9% of Enterobacteriaceae isolates were resistant to Cotrimoxazole. Studies have also found resistance rates as high as 86% in uropathogens to Cotrimoxazole.^(27,32)

44.4% of Enterobacteriaceae and 20% of *Enterococci* isolates were found to be resistant to Nitrofurantoin, another commonly used drug for treatment of urinary tract infections. Similar results were shown by Poudel et al, Kulkarni et al who found 22-44.7% of Nitrofurantoin resistant Enterobacteriaceae isolates.^(27,28)

High incidence of Carbapenem resistance in the isolates was obtained in present study. 44.4% of Enterobacteriaceae and 100% of Non-fermenting Gram negative bacilli isolates were resistant to Meropenem thus limiting therapeutic options. Rising Aminoglycoside resistance across all organisms was also observed with 33.3% of Enterobacteriaceae isolates being resistant to both Gentamicin and Amikacin. All the isolates of *Pseudomonas aeruginosa* and *Acinetobacter baumannii* were resistant to Amikacin while 75% of them were resistant to Gentamicin. Amongst the *Candida* isolates, 7 were *Candida tropicalis* and 1 *Candida albicans* was isolated. All the *Candida* isolates were sensitive to Amphotericin B while 50% were sensitive to Fluconazole. The results of anti-fungal susceptibility were found to be consistent with similar studies.⁽²¹⁾

Conclusion

This study provides a baseline data on incidence of CAUTI in our set up. It also gives us knowledge on risk factors of CAUTI and its causative microbial flora along with information on the susceptibility patterns of the organisms. This will help in selection of the appropriate antibiotic for therapeutic use and also prevent indiscriminate and irrational use of antibiotics

which contribute to emergence of drug resistance strains in the environment.

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