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Profile of Urinary Tract Infections in Catheterised Patients in the Critically Ill Population in a Tertiary Care Hospital

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Abstract

Urinary tract infection (UTI) is commonly seen in women, diabetics, immune-compromised individuals, anatomic abnormalities, and history of instrumentation for surgical or medical conditions. Catheter-associated bacteriuria is commonly encountered in the medical health care system especially with prolonged catheterisation.

Objective: The main objective of the study was to do risk stratification of patients requiring urinary catheterisation, correlate it with the clinical profile and study the microbiological profile of catheterised adult patients with Catheter-associated Urinary tract infections (CAUTI) in a tertiary care hospital.

Material and Method: This was a cross-sectional, hospital based, observational study done at a tertiary care hospital in New Delhi on critically ill patients requiring indwelling urinary catheters for medical or surgical illness.

Results: A total of 200 patients formed the study population, and amongst them 139 were males and 61 were females. CAUTI was diagnosed in patients with indwelling catheters for at least 48 hours who developed symptoms or signs of infection. It was observed that E. Coli was the most common pathogen involved in infection followed by Enterococcus spp, Pseudomonas spp. and Klebsiella pneumoniae. There was very high level of resistance to various broad spectrum antibiotics.

Conclusion: A universal definition of CAUTI needs to be accepted as the present criteria emphasize too much on the presence of symptoms. High-risk patients need to be identified and a guarded approach towards catheterization in critical patients needs to be followed. Hospital policies need to be more stringent towards the catheter insertion and its maintenance.

Introduction

Urinary tract infection (UTI) is an infection that affects part of the urinary tract. When it affects the lower urinary tract (urinary Bladder and urethra), it is known as cystitis and urethritis respectively; and when it affects the upper urinary tract (kidneys and ureters) it is known as pyelonephritis.

Patients at an increased risk for UTI include women, diabetics, immune-compromised patients, those with anatomic abnormalities, impaired mobility, incontinence, advanced age, and a past history of instrumentation[1].

Catheter-associated bacteriuria accounts for almost 40% of all nosocomial infections. It appears to be a result of the widespread use of urinary catheterisation, most of which is inappropriate (in hospitals and long-term care facilities). Early studies , along with recently published reports estimate the incidence of healthcare associated urinary tract infection at around 2 - 3 patients per 100 admissions (anywhere between 15% to 25% of patients admitted to a general hospital have a urethral catheter inserted at one time or another during their stay). Urinary catheter use is more common in acute care and referral hospitals, with approximately 1 in 5 patients admitted receiving an indwelling catheter once during their hospital stay. Bacteriuria and funguria are acquired in up to 25% of patients with indwelling urinary catheters left in place for more than 7 days. Urinary catheterisation for more than 6 days is by far the most important risk factor for acquisition of a urinary tract infection UTI; each day of catheter use is associated with approximately 5% increase in bacteriuria[2]. By one month, nearly all patients with an indwelling catheter will be bacteriuric and/or funguric. Catheter- associated urinary tract infections (CAUTI) remains a leading cause of nosocomial infections with significant morbidity, mortality, and additional healthcare related costs. 80% of UTIs in a hospital setting in the US are estimated to be due to a catheter, leading to a longer length of hospital stay. About 13,000 deaths (mortality rate 2.3%) are attributed to urinary tract infections (UTI) in the US[3].

Other risk factors associated with catheter-associated bacteriuria include a variety of states including female sex, catheter insertion outside the operating room, catheter care violations, rapidly fatal underlying illness, older age, diabetes mellitus, elevated serum creatinine at the time of

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catheterisation and poor general physical conditions as assessed by different scales like SAPS II score (Simplified Acute Physiological Score)[4].

Approximately 15% cases of nosocomial bacteraemia are attributed to the urinary tract, and bacteriuria is the most common source of Gram-negative bacteraemia among hospitalised patients.

Complications of long-term catheterisation (> 30 days), in addition to almost universal bacteriuria, include lower and upper urinary tract Infection, bacteraemia, frequent febrile episodes, catheter obstruction, renal and bladder stone formation associated with urease producing uropathogens, local genitourinary infections, fistula formation, incontinence, and even bladder cancer[5].

Bacteriuria in patients with short-term catheters is usually caused by a single organism[6]. *Escherichia coli* is the most frequent species isolated, although it comprises fewer than one-third of isolates[7]. Other Enterobacteriaceae, such as, Klebsiella species, Serratia species, Citrobacters species, non fermenters such as *Pseudomonas aeruginosa*, and Gram-positive cocci, including coagulase-negative Staphylococci and Enterococcus species, were also isolated.

In contrast to patients with short-term catheterisation, urinary tract infections in patients with long-term catheterisation are usually polymicrobial[8].

Funguria, mostly candiduria, is reported in 3% - 32% of patients catheterised for short periods of time. The recovery of Candida species from urine samples presents the clinician with a dilemma, because the presence of Candida can signify either simple colonisation of lower urinary tract and the catheter which may not need treatment or an upper UTI including both ascending pyelonephritis and renal candidiasis, which requires aggressive treatment[9].

Catheter-associated bacteriuria comprises a large reservoir of antimicrobial-resistant organisms, particularly in critical care units, and can be the source of cross-infection. It is reported that 15% of episodes of hospital-acquired bacteriuria occur in clusters, and these often involve highly antimicrobial-resistant organisms. Widespread use of third-generation Cephalosporins and Fluoroquinolones has created selective advantage for the spread of multiple drug resistant extended-spectrum beta-lactamase producing *E. coli*, *Klebsiella*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and Methicillin-resistant *Staphylococcus aureus* among the Intensive care units across the globe[10,11]. There have been reports of Imipenem resistant isolates of *Pseudomonas aeruginosa* isolated from urine samples of catheterised patients of a tertiary care referral and teaching hospital of New Delhi, India[12]. The genotypic presence of an extended-spectrum beta-lactamase (ESBLs) producing and/or metallo-beta-lactamase (MBL) producing organism in severe infections can result in treatment failure even in cases in which the minimal inhibitory concentration (MIC) of the cephalosporin or carbapenem chosen for treatment is in the susceptible range[13,14]. This gives an alert to the Clinical Microbiology Laboratory as there are considerable number of multi-drug resistant Gram-negative isolates, which are not usually screened for ESBL or MBL as a routine.

Various studies done worldwide have shown changing patterns in the aetiology of UTIs[15]. However, studies on CAUTI in India are few[16]. The objective of this prospective cohort study was to record the clinical profile of adults who develop CAUTI in the Intensive Care Unit of a tertiary care hospital, along with the determination of the causative bacteria, and their respective antimicrobial sensitivity and, resistance patterns, which would help in better understanding of the current trends at tertiary care hospitals and assisting in formulation of guidelines for empirical treatment of CAUTI while awaiting the culture sensitivity.

Material and Method

This was a cross-sectional, hospital based, observational study done at tertiary care hospital in New Delhi. The study was approved by the ethical committee of the hospital and was performed after taking written informed bilingual consent from the subjects for the study.

The primary objective was to study the clinico-microbiological profile of catheterised adult patients with catheter-associated Urinary tract infections (CAUTI) and to determine the significant predictors or risk factors associated with catheter-associated urinary tract infections (CAUTI) in the above group of patients.

Previous studies performed for assessing catheter-associated urinary tract infections showed an incidence between 2.45% to 24.7%. Thus an assumption of 14% as the incidence of CAUTI was made and, with an error margin of 5%, a minimum required sample size at 5% level of significance is 180 patients. However, we collected a sample data of 200 patients over a period of 18 months from critical care area of the hospital that includes various intensive care units (ICUs), operation theater (OT) complex, and post-anaesthesia care unit (pre-op). All patients were catheterised by trained staff (Senior resident doctors, Consultants, or Nursing staff trained for the procedure) under aseptic precautions as per the standard operating procedures of Infectious disease control department of the hospital. Infection control guidelines are in strict adherence to IDSA guidelines. All patients having an indication for catheterisation with Foley's catheter over 18 yrs were included. Patients already diagnosed as case of UTI before

catheterisation, baseline urine routine and microscopy examination revealing significant pyuria, condom catheters, suprapubic catheters and percutaneous nephrostomy tubes, Foley's catheter having been removed within 48 hours of catheterisation after procedure, catheterised outside our hospital prior to admission, history of recurrent UTI, anatomical abnormality causing urethral obstruction/ urethral stricture, etc., and not giving consent were excluded from the study.

Data was collected by direct observation, interviewing the treating physicians, and from the patient's medical records. It was recorded for each patient using a structured proforma, which included the following parameters: age, sex, diagnosis at admission, functional status, mental status, indication for catheterisation, place of catheterisation (emergency/ICU), duration of catheterisation, analysis of urine R/M and urine C/S reports. Functional status was classified as either ambulatory or non-ambulatory (subjective assessment of the observer) and mental status classified as alert or impaired (confused, drowsy, stuporous, and comatose). The indications for catheterisation were documented.

Urine specimens were collected from the indwelling catheter by observing all aseptic precautions and transferred and subsequently transported in a sterile, leak-proof container, secured with a lid and sent immediately to the microbiology lab or if in the rare case that immediate transport to the laboratory was not possible, the sample was refrigerated at 2 - 8°C and sent within the next 24 hours.

Specimen after catheter removal from patient (after 48 hours of removal of catheter or after 7 days of catheterisation – whichever is earlier) was a midstream clean catch urine sample.

The following samples were collected under all aseptic conditions using universal precautions and were sent for urine routine and microscopy (R/M):-

1. A baseline sample at the time of catheterisation in order to exclude those with a pre-existing urinary tract infection,
2. Second sample at 48 hrs, and
3. A third sample after 7 days of catheterisation or 48 hrs of catheter removal (whichever was earlier).

Sample for urine culture and sensitivity (C/S) was sent immediately following a positive 2nd or 3rd urine routine/ microscopy report showing significant pyuria (≥ 10 leucocytes/HPF).

Urine routine and microscopy (R/M) examinations were performed using auto-analyser-COBAS A urine culture was performed after inoculating each sample on a CLED agar plate and density of isolates (colony count) was established by counting the number of colonies and expressing the same in terms of Colony Forming Units per ml (CFU/ml) after multiplying with 100. All isolates were identified by their colony characteristics and Gram-stained appearance, and then processed in the VITEK 2 COMPACT automated system (BIOMERIEUX) for identification and antibiotic susceptibility.

Case definition

CAUTI was defined in patients with indwelling urethral catheterisation for a period of at least 48 hours along with presence of symptoms or signs (new onset or worsening of fever, rigors, altered mental status, malaise, or lethargy with no other identified cause; flank pain; costovertebral angle tenderness; acute haematuria; pelvic discomfort; or in those whose catheters have been removed, dysuria, urgent or frequent urination, or suprapubic pain or tenderness) compatible with UTI, with no other identified source of infection along with e"10^3 colony forming units (CFU)/ml of e"1 bacterial species in a single catheter urine specimen or in a midstream voided urine specimen from a patient whose urethral catheter has been removed within the previous 48 hours[17].

Catheter-associated asymptomatic bacteriuria (CAASB) was defined in patients with indwelling urethral catheterisation by the presence of e"10^5 CFU/ml of e"1 bacterial species in a single catheter urine specimen in a patient without symptoms compatible with UTI.

Statistical analysis

The data was analysed, for various categorical variables and was expressed as frequencies and percentages. The various risk factors for catheter-associated UTI (variables) have been compared using Chi-square/Fisher's exact test. Also, Odds ratio has been computed for every such comparison. A p-value < 0.05 is considered statistically significant. Statistical Package for Social Sciences (SPSS) version 15.0 software has been used for data analysis.

Results

A total of 200 patients formed the study population, and amongst them 139 were males and 61 were females. The average age was 57.3 ± SD 17.92 years with range of 19 - 93 years. Most of the patients included in the study were elderly with age more than 60 years (45.5%). The highest numbers of male patients as well as female patients were > 60 years of age (64 patients and 27 patients respectively).

A total of 25 (12.5%) patients in our study developed an episode of catheter-associated urinary tract infection within

7 days of catheterisation. Most of the patients with CAUTI were from the Medical ICU (18 out of 25, i.e., 72.00%). After categorising all the patients, irrespective of their gender, it was seen that the age group of > 60 years contributed the largest share to the burden of CAUTI cases (64.00% of all CAUTI cases) followed by patients in the sixth decade of life (20.00%). Male patients over the age of 60 years contributed to maximum number of CAUTI cases (13 patients, 52%) of the total CAUTI cases in our study. This age group also had the highest rate of CAUTI among all the male catheterised patients of different age groups.

In the females second decade patients had highest rate of CAUTI (50.00%, 1 of the total 2 female patients), followed by females in the sixth decade (16.67%). On an aggregate, males contributed to the maximum burden of CAUTI cases (18 out of 25, i.e., 72.00%), while females contributed to a lesser extent (7 out of 25, i.e., 28.00%). The most common indication for catheterisation in our study was for critically ill patients, (i.e., 127 out of 200). This group also contributed to the maximum burden of CAUTI cases (19 out of 25). While as a preoperative preparation only 4 out of 55 (rate of 07.27%) patients developed CAUTI.

Table I: Indication for catheterisation and occurrence of CAUTI.

Indication for catheterisation	CAUTI Absent		CAUTI Present	
	No. of patients (n)	%	No. of patients (n)	%
Critically ill patients requiring accurate measure of urinary output	108	61.71	19	76.00
Need to measure urine output accurately in an uncooperative patient	4	2.29	0	0.00
Preoperative catheter insertion	51	29.14	4	16.00
Trauma	11	6.29	2	8.00
Patients with neurogenic bladder or retention	1	0.57	0	0.00
TOTAL	175	100	25	100

Association of risk factors in CAUTI

Various risk factors were hypothesised from the review of literature, and were tested for significance in our study. The statistical analyses to test for significance, of the most important risk factors are stated below.

Age: Association of age of the patient as a risk factor for the development of CAUTI within 7 days of catheterisation was evaluated and it was found that 16.67% of catheterised patients e" 60 years of age developed CAUTI within 7 days of catheterisation, compared to 8.65% of patients aged less than 60 tears. Age e" 60 years significantly affects the development of CAUTI (p-value = 0.043) and it was observed that patients 60 years of age or older were 2.1 times more likely to develop CAUTI than those aged less than 60 years.

Gender: It was seen that 18 out of 139 male patients (12.95%) developed CAUTI within 7 days of catheterisation, compared to 11.48% female patients, although the rate of occurrence of CAUTI among both genders was similar, our study did not show female gender as a statistically significant risk factor for the development of CAUTI (p-value = 0.386). It was possibly due to lesser number of female patients in the study.

Duration: Duration of catheterisation was an important risk factor for the development of CAUTI. It was seen that 18 out of 110 patients (16.36%) with duration of catheterisation of 4-7 days developed CAUTI, compared to only 7.78% of patients who were catheterised for only 2 - 3 days. The duration of catheterisation significantly affects the development of CAUTI (p-value = 0.034). Patients with duration of catheterisation of more than 3 days, were 2.3 times more likely to develop CAUTI, than were the patients who were catheterised for less than 3 days.

Diabetes: It was observed that 19.23% of patients with diabetes mellitus as a primary or secondary diagnosis, developed CAUTI within 7 days of catheterisation, compared to 10.14% of patients without diabetes mellitus. "Diabetes mellitus" as a primary or secondary diagnosis significantly affects the development of CAUTI (p- value = 0.044). Patients with documented diabetes mellitus are 2.1 times more likely to develop CAUTI than non-diabetic patients with indwelling urethral catheters.

Creatinine: High serum creatinine level was an independent risk factor for the development of CAUTI within 7 days of the catheterisation. 18.31% of patients with high levels of serum creatinine (e" 1.2 mg/dl) developed CAUTI within 7 days of catheterisation, compared to 09.30% of patients with lower or normal values. The "serum creatinine level" significantly affects the development of CAUTI (p-value = 0.033). Patients with documented high creatinine levels are 2.1 times more likely to develop CAUTI than patients with indwelling urethral catheters having normal creatinine levels.

Mental status: Level of consciousness of patients who were catheterised revealed that 16.84% patients with impaired level of consciousness developed CAUTI within 7 days of catheterisation as compared to 08.57% of alert patients. The "level of consciousness" significantly affects the development of CAUTI (p-value = 0.039). Patients with impaired consciousness are 2.2 times more likely to develop CAUTI than alert patients with indwelling urethral catheter.

Ambulation: As functional status showed that 15.97% of

non-ambulatory patients developed CAUTI within 7 days of catheterisation, compared to 07.41% of ambulatory patients. The "functional status" significantly affects the development of CAUTI (p-value = 0.036) and it showed that non-ambulatory patients were 2.4 times more likely to develop CAUTI than ambulatory patients with indwelling urethral catheters.

Bacterial isolates obtained in CAUTI

A maximum of three urine routine and microscopy samples were collected from each patient, the first one at time of catheterisation, the second one at 48 hours of catheterisation and the third one after a week of catheterisation. Urine culture was sent following report of significant pyuria seen in second or third samples. Many patients were unavailable for the third sample due to catheter withdrawal, death or discharge from the hospital.

After computation of all the bacterial isolates of different CAUTI patients, it was observed that *E. coli* was the most commonly grown isolate (13 out of 25; 52.00%). *Enterococcus spp.* were the second highest contributing organisms (20.00%) followed by *Pseudomonas spp.* (04 out of 25; 16.00%). *Klebsiella pneumoniae* was isolated from 03 cases (12.00%). High levels of resistance to various broad spectrum antimicrobials were seen in case of the Gram-negative and Gram-positive isolates. Overall, between 23 to 39% of the *Escherichia coli* isolates, 67 to 100% of the *Klebsiella pneumoniae* isolates, and 75% of the *Pseudomonas* isolates were resistant to one or more carbapenems tested for susceptibility. The consequence of high rate of fluoroquinolone prescription in the wards and ICUs was reflected in all islolates of *E. coli, Klebsiella,* and *Pseudomonas* (100% each) showing resistance to Ciprofloxacin.The most effective drug against the Gram-negative isolates was Colistin. All the isolates of *E. coli*, *Klebsiella*, and 03 out of 04 isolates of *Pseudomonas* were susceptible to those two drugs. Two out of five strains (40.00%) of *Enterococcus spp.* were resistant to Vancomycin and Teicoplanin. All the strains were susceptible to Linezolid.

Discussion

Catheter-associated urinary tract infection (CAUTI) remains a leading cause of nosocomial infections with significant morbidity, mortality, and additional healthcare related costs. The increasing drug resistance among nosocomial pathogens, particularly the Gram-negative bacilli, has raised a serious cause of concern in dealing with CAUTI. Holistic approach of good catheter care, hand hygiene of care givers, proper maintenance of perineal hygiene of the patients, adherence to strict antimicrobial prescription policies and proper antimicrobial stewardship by infection control units have become extremely necessary for controlling the emergence of nosocomial outbreaks of CAUTI with multi-drug resistant isolates.

In the Indian context, few studies appear to have been conducted on detailed clinical and microbiological profile of CAUTI. Various studies from India have given information on the resistance patterns of the responsible bacterial isolates[18].

A total of 200 patients with indwelling urethral catheter were included in our study and catheters were placed in intensive care units (ICUs) or the post-anaesthesia care unit (also called the pre-op) under supervised expert care. Paraplegia, cerebrovascular disease and female sex were found to statistically increase the chances of a CAUTI[19]. In our study lesser number of female patients were catherised thus explains lower number of CAUTI in females.

The age of the patients included in the study varied between 18 to 93 years. Most of the patients included in the study were elderly aged $\geq$ 60 years of age (45.5%). Wide range of variation in observations was evident on reviewing the literature. It was that the incidence was as low as 8.5% to 73.3%, which has been published worldwide for CAUTI, among patients with an indwelling catheter's. Some of the studies have expressed their rates of infection against a denominator of 1000 catheter days. Thus, due to the discrepancy of denominators, it was not possible to compare the rate of CAUTI from all the studies reviewed with our own study.

The wide variation in the observations from various studies could be due to:-

1. Results being collected from various studies reported from developed countries, which exclusively included the patients from the ICUs, the private hospitals and nursing homes, had lower rates than the studies reported from public hospitals of developing countries, including patients from general medical and surgical wards.
2. The different definitions of CAUTI and HAUTI (hospital acquired urinary tract infection) that the various studies have adapted in labeling their cases, also varied to a great extent.
3. Various terms and acronyms like "asymptomatic bacteriuria","catheter associated urinary tract infection (CAUTI)","symptomatic catheter associated urinary tract infection (SUTI)", "acute bacteremic catheter-associated urinary tract infection (ABUTI)","complicated urinary tract infection" etc are used extensively in the literature. Thus studies often failed to clarify them objectively.

Table II: Risk factors: Various risk factors were found in different studies.

Study	Age > 60 yrs	Female sex	Non ambulatory	Impaired mental status	Diabetes mellitus	Ser. creatinine > 1.5 mg/dl
Kamat *et al*[13]	Significant p < 0.05	insignificant	–	insignificant	–	–
Bhatia *et al*[20]	Significant p < 0.05	insignificant	Significant p < 0.05	insignificant	–	–
Puri *et al*[21]	Significant p < 0.05	Significant p < 0.05	–	–	–	–
Danchaivijitir *et al*[22]	–	Significant p < 0.05	–	–	–	–
Zacharias *et al*[23]	insignificant	insignificant	Significant p < 0.05	Significant p < 0.05	insignificant	–
Present study	Significant p < 0.05	insignificant	Significant p < 0.05	Significant p < 0.05	Significant p < 0.05	Significant p < 0.05

Almost all the studies, excluding ours experienced a significantly higher rate of CAUTI among female catheterised patients. Kamat *et al* have stated that the incidence of CAUTI was more among the catheterised females patients when compared with their male counterparts[13]. In our study it was not statistically significant (P = 0.652) and we documented higher number of male patients than the female patients (139 versus 61).

All the risk factors hypothesized to affect infection rate in urinary catheterised patients were not uniformly studied in all the reports. Neither could we take into account all the possible risk factors, but there were some statistically significant findings in our study. Patients 60 years of age or older were 2.1 times more likely (p-value = 0.043) to develop CAUTI than those aged less than 60 years.

Duration of catheterisation was an important risk factor and patients with catheterisation of more than 3 days were found to have 2.3 times more incidence of CAUTI (p-value = 0.034) when compared with patients who were catheterised for less than 3 days. Diabetic were 2.1 times more likely (p-value = 0.044) to develop CAUTI than non-diabetic patients with indwelling urethral catheters. Similarly individuals with impaired consciousness had 2.2 times more likelihood (p-value = 0.039) of developing CAUTI. A similar observation was made with non-ambulatory patients who had 2.4 times incidence of CAUTI (p-value = 0.036) in comparison with ambulatory patients. We also observed in our study that patients who had documented high creatinine levels, had higher incidence (up to 2.1 times) of CAUTI (p- value = 0.033). Though, we could not ascertain in our study the exact cause of this it is most likely that these patients already had an element of pyelonephritis or renal compromise secondary to occult lower Urinary tract infection or minimal outflow obstruction. In order to reduce the risk of CAUTI, duration of catheterisation, antibacterial coated catheter and strict infection control measures during catheterisation have been recommended[24]. CAUTI are seenmore frequently in patients where insertions have been done under poor aseptic techniques, improper maintenance and socio adaptive factors. Cultural and behavioural changes in hospitals policies go along way in preventing catheter-associated UTI. It was documented that such policies reduced both unadjusted and adjusted analysis of catheter-associated UTI rates per 1000 catheter-days[25]. Provider based studies have shown poor knowledge about ideal aseptic technique based catheterisation. A study showed that the knowledge of doctors was statistically significantly better (P < 0.05) than nurses in identifying the indications for catheterisation in critically ill patients. Similarly in same study only 57% out of all the respondents could identify preventive measures for the development of CAUTI[26].

Conclusion

A universally accepted definition of CAUTI needs to be adhered to while defining a case of CAUTI. The existing criteria emphasizes too much on the presence of symptoms, but with a decree of "no other recognised cause". This approach creates practical confusion in the field level, particularly for two groups of patients especially the ones who are critically ill and unconscious, hence proper elicitation of pain and tenderness becomes impractical and those that may have other non-UTI causes of fever, supra-pubic tenderness or flank pain. Hospitals need to have more stringent catheter insertion and catheter care policies. Stringent policies need to be formulated for insertion of indwelling catheters in health care facilities and they need to be adhered to when treating these patients.

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