**Per Urethral Catheterisation: Microbial Growth Incidence and its Management**

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**ABSTRACT**

The urinary tract is the most common site of nosocomial infections accounting for more than 40% of the total number reported by acute care hospitals and affecting approximately 600,000 patients per year. Catheter Associated Urinary Tract Infection (CAUTI) defines in terms of “bacteriuria” and “urinary tract infection” frequently. Bacteriuria or funguria levels >10\(^3\) colony-forming units (CFU) have been shown to be highly predictive of CAUTI, given that these levels increase to 10\(^5\) CFU within 24 to 48 hours. In Indian population, catheter-associated urinary tract infection (CAUTI) is an important cause of morbidity and mortality, affecting all age groups. Biofilm is the predominant mode of growth in aquatic ecosystems and, as such, plays a central role in the pathogenesis of Catheter Associated Urinary Tract Infections (CAUTI). The present review focuses to evaluate the incidence and pattern of microbes in catheter-associated urinary tract infection and provides information about the etiology of CAUTI. Most of the studies concluded that gram negative pathogen *E.coli* showed the highest incidence rate and other pathogens like *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, and *staphylococcus* species also having the incidence rate in the patient having CAUTI. The antibiotic resistance pattern showed the variation in resistance and sensitivity of antibiotics against the pathogens. The present study focuses on the incidence of the microbial growth in patient having catheterization and also elucidates the antibiotic sensitivity pattern. It is necessary to determine the antibiotic resistance and sensitivity status during and after the catheterization.

**Introduction**

The urinary tract is the most common site of nosocomial infections accounting for more than 40% of the total number reported by acute care hospitals and affecting approximately 600,000 patients per year. Sixty six percent to 86% of these infections usually follow instrumentation of urinary tract, mainly catheterization. The risk of acquiring a urinary tract infection (UTI) depends on method and duration of catheterization, the quality of catheter care and host susceptibility. [1]

Catheter Associated Urinary Tract Infection (CAUTI) defines in terms of “bacteriuria” and “urinary tract infection” frequently. [2] Bacteriuria or funguria levels >10\(^3\) colony-forming units (CFU) have been shown to be highly predictive of CAUTI, given that these levels increase to 10\(^5\) CFU within 24 to 48 hours. [3] The 2009 Infectious Diseases Society of America (IDSA) guidelines define CA-UTI as “the presence of symptoms or signs compatible with UTI with no other identified source of infection along with [≥1 bacterial species]” from a catheterized or previously catheterized (≤48 hours) urine sample.[4]

Signs and symptoms associated with CAUTI such as fever, disuria, urgency, flank pain and leukocytosis have also been shown to have a low positive predictive value for CAUTI.
diagnosis since 90% of them are asymptomatic. A catheter in the urethra also prevents continuous urethral exposure to large numbers of organisms in the infected urine, averting urethritis, and consequently, urgency and disuria. [5] Millions Of urinary tract catheterizations are carried out worldwide for purposes of control, repair, diagnosis and treatment. The risk of infection per procedure is from 1 to 2%. This risk increases to 3 to 7% per catheterization day in such a way that nearly all patients will present with bacteriuria after 30 days of urethral catheterization. [6]

Catheter Associated Urinary Tract Infections, the most common type of nosocomial infection, account for over 1 million cases annually also elucidated from the recent study. [7] Some other studies focuses that the daily incidence of bacteriuria is 3-10%, after catheterization. Between 10% and 30% of patients who undergo short-term catheterization (ie, 2-4 days) develop bacteriuria and are asymptomatic. Between 90% and 100% of patients who undergo long-term catheterization develop bacteriuria. About 80% of nosocomial UTIs are related to urethral catheterization; only 5-10% related to genitourinary manipulation. [8]

In Indian population, catheter-associated urinary tract infection (CAUTI) is an important cause of morbidity and mortality, affecting all age groups. [9] Bacteriuria or candiduria is almost inevitable in nearly half of the patients who require an indwelling urinary catheter for more than 5 days. [2][10] Asymptomatic bacteriuria constitutes a major pool of the antibiotic-resistant strains of pathogens with critical care units. [11] CAUTI is also a major cause of hospital-acquired bacteraemia, [12] that may be associated with enhanced in-hospital mortality rates.

CAUTI is usually deemed present if there are at least 10^3 colony-forming units (cfu)/mL of 1 or 2 micro-organisms identified by urine culture. [13] While 'significant' bacteriuria is defined as >10^5 cfu/mL, once micro-organisms are detected in the urine, in the absence of anti-microbials, it is almost inevitable to reach the 10^5 cfu/mL level quite rapidly. An ICU-acquired UTI refers to those patients who develop a positive urine culture first identified on ICU Day 3 (48 h) or later. [14] Patients developing positive urine cultures within 48 h of being discharged from an ICU could also be defined as having ICU-acquired UTI.

The Centers for Disease Control and Prevention (CDC) defines CAUTI for those patients who have an indwelling catheter in place for 48 h or more. [15] For diagnosing UTI, the CDC requires that the patient should be manifesting symptoms such as fever or chills, new onset of burning pain, urgency or frequency if not catheterized at that point of time, change in urine character, flank or suprapubic pain or tenderness or change or decrease in mental or functional status in patients.

**Pathogenesis**

To understand the pathogenesis of infection of the catheter associated, it is necessary to understand the formation of biofilm on the surface of catheter. The formation of bacterial biofilms on surfaces appears to be a universal bacterial strategy for survival in both nature and disease. [16] Recent evidence indicates that bacterial biofilms might also be involved in biomaterial-related bacterial infections. A biofilm is not a static, filmy slime layer but rather is a living organism composed of multiple species of bacteria and their secreted polysaccharide slime layer matrix and components deposited from bodily fluids. [17]

Catheter are a good medium of bacterial growth because once they gain entry in the urinary tract, bacteria produce various adhesions that allow them to attached with the catheter wall and that leads to formation of biofilms. Biofilm is the predominant mode of growth in aquatic ecosystems and, as such, plays a central role in the pathogenesis of Catheter Associated Urinary Tract Infections (CAUTI). Most aspects of the diagnosis, treatment, and prevention of CAUTI are influenced by the tenacity of biofilm-associated uropathogens. The biofilm mode of living is a highly advantageous response of the micro-organisms to the environmental stresses of the urinary tract environment. [18]

The first step in formation of catheter-associated biofilm is deposition of a conditioning film on the surface of the device. It is generally accepted that bacteria gain entrance to the bladder from retrograde intra luminal ascent of organisms from contaminated open collection vessels in the early days, [19] from the collecting bag or disconnected catheter drainage tube junction since the introduction of the closed urinary drainage system, [20] and extra luminally from a colonized urethral meatus if strict sterile closed drainage is maintained. [21][22] The biofilm protects the organism from the antimicrobials and the host immune response. [23]

Observations in animal models of the closed catheter drainage system have disclosed that bacteria form thick coherent biofilms adherent to experimentally contaminated drainage spouts extending proximally into the drainage bag and subsequently into the catheter. [24][25] Employing a bacteriologically stressed animal model of short term catheterization (fewer than seven days), contamination of the drainage spout or accidental disconnection of the drainage tube resulted in bacteriuria within a short time (32 to 48 h). If a strict sterile closed drainage system was maintained and the urethral meatus-catheter junction was inoculated, the extraluminal route would assume greater importance in the development of bacteriuria; however, this pathway was considerably slower (72 to 168 h). These findings regarding the relative importance of the intraluminal and extraluminal periurethral routes were confirmed in further animal model studies employing a microbicidal hurdle or barrier in the outlet tube of the drainage bag. [26][27]
In in-vitro system, it could be demonstrated that the bacteria were ascending the surface of the catheter in a coherent biofilm containing bacterial cells in their secretory products or glycocalyx.

In the absence of antibiotics it appeared that the ascending bacterial biofilm was moving by two mechanisms:

1. Rapidly dividing bacterial cells spreading along the catheter surface within the glycocalyx material of the biofilm.
2. Planktonic or floating bacterial cells within the urine column leapfrogging just ahead of the adherent biofilm, perhaps assisted by the turbulence caused when the urine flow meets the biofilm front.

The movement of ‘saltatory’ bacteria may allow some bacteria to establish adherent microcolonies ahead of the ascending biofilm, which expand with the main bacterial aggregate into the ascending coherent biofilm. [28]

Planktonic bacteria being released from the biofilm adherent to the Foley catheter can be easily demonstrated in aspirated urine cultures: however, at this point the bacteria are colonizing only the catheter surface. The intravesical segment of the Foley catheter eventually becomes covered with a much thicker colonizing adherent bacterial aggregate enclosed within the bacterial slime matrix. This macroscopic bacterial biofilm can create flow kinetic problems by partially blocking catheter islets and reducing the tubular diameter of the catheter lumen. This biofilm-induced disruption of effective urine flow may increase the volume and perhaps pressure of the residual urine that is always present in catheterized bladders. [29]

A thin blanket of mucus or glycosaminoglycan coats the bladder mucosal surface and appears to inhibit bacterial adherence to the uroepithelium. The indwelling Foley catheter appears to disrupt this bladder mucus or glycosaminoglycan layer and causes mechanical irritation and even erosion of the bladder mucosa, exposing surfaces that allow bacterial adherence. [30] Once the organisms gain access to the bladder mucosa, exposing surfaces that allow bacterial invasion into host cells. [34]

These adhesins also contribute to the direct triggering of host and bacterial signaling pathways, assisting in the delivery of antimicrobial resistance. [31]

Microbial growth incidence

The pattern of microbial growth in catheter associated urinary tract infection patients approximately very common, there may be gram positive or gram negative activity that causes the biofilm formation leads to infection.

Enteric pathogens (eg, Escherichia coli) are most commonly responsible, but Pseudomonas species, Enterococcus species, Staphylococcus aureus, coagulase-negative staphylococci, Enterobacter species, and yeast also are known to cause infection. Proteus and Pseudomonas species are the organisms most commonly associated with biofilm growth on catheters. [8]

Uropathogenic Escherichia coli (UPEC), the primary cause of community-acquired urinary tract infections (UTIs), account for 50% of nosocomial UTIs, including CAUTIs. [32] After urinary catheterization, the pathogenesis E.coli results in disruption of the normal mechanical and antimicrobial defenses of the bladder. [33] UPEC strains and other uropathogens must attach to uroepithelial cells and the catheter surface to colonize and initiate CAUTI and may express a variety of adhesins to assist in this initial attachment. These adhesins also contribute to the direct triggering of host and bacterial signaling pathways, assisting in the delivery of bacterial products to host tissues, and promoting bacterial invasion into host cells. [34]

Proteus species are the causative organism for the catheter associated urinary tract infection. Colonization of the intestinal tract allows Proteus to establish reservoirs for transmission into the urinary tract by intermittent colonization of the periurethral region. This intermittent colonization can lead to the subsequent contamination of the catheter, thus allowing nosocomial infections to develop. [35] The three species of Proteus associated with UTIs are Proteus mirabilis, Proteus vulgaris, and Proteus penneri. Proteus mirabilis is the third most common cause of complicated UTI (12%) and Proteus vulgaris is the second most common cause of catheter-associated bacteriuria in patients catheterized long term (15%). [36]

Other most frequent causative agents of catheter associated urinary tract infection include Klebsiella pneumoniae, pseudomonas aeruginosa, Enterococci species and staphylococci species. Klebsiella pneumoniae is a gram negative bacteria mainly involved in Enterococci species. Recent studies found the causative uropathogens responsible for the infection in which, E.coli was found to be the most frequently isolated uropathogen in 70%, followed by Klebsiella pneumoniae 16%, Pseudomonas aeruginosa 4%, Acinetobacter spp 2%, coagulase negative Staphylococci 6% and Enterococci Spp 2%. [18]
Study at Nigeria showed that early onset of UTI had developed for 4 days at the ICU and late onset developed for 5 days after at the ICU admission and microorganism responsible for urinary catheter related infection, were the following, E. coli (16%), Pseudomonas aeruginosa (7%), Morganella morgani (4 %), Klebsiella (4 %), Citrobacter (4%), Proteus mirabilis (3%), Enterococcus fæcalis and coagulase negative Staphylococcus (7%),, Candida (12%) and other fungi, stating that most Urinary Catheter Related Infection had a late onset of the infection which was caused by only certain organism and were mainly due to E.coli and C. Albicans. [37]

**Prevention of CAUTI**

According to CDC guidelines the catheter associated urinary tract infection preventive measures categorised in two main categories i.e. Category I (Strongly recommended), Category II (Moderately recommended). [38] Both the categories emphasis on the prevention of CAUTI.

**Category I:**
- Catheterize only when necessary.
- Educate personnel in correct techniques of catheter insertion and care.
- Emphasize hand washing.
- Insert catheter using aseptic technique and sterile equipment.
- Secure catheter properly.
- Maintain closed sterile drainage.
- Obtain urine specimens aseptically.
- Maintain unobstructed urine flow.

**Category II:**
- Periodically re-educate personnel in catheter care.
- Use smallest suitable catheter bore.
- Avoid irrigation unless needed to prevent or relieve obstruction.
- Refrain from daily meatal care.
- Do not change catheters at arbitrary intervals.

In term of delaying the bacteriuria, the preventive strategies categories as effective, possibly effective, effective only for short-term catheterization, ineffective, and novel approaches. Effective strategies include closed drainage and catheter removal. Closed drainage, in which the collection tube is fused to the drainage bag, reduces the incidence of bacteriuria. In possible effective strategies, a system maintained to remind the physician who among their patients has urinary catheters might shorten the duration of catheterization and, thus, decrease the incidence of CAUTI. The strategies changing catheter materials to render the catheter surface inhospitable to biofilm formation is a clever idea, this approach is effective for prevention of UTI only in the setting of short-term catheterization. Use of antimicrobial agents, either systemically or inserted directly into bladder are the strategies that have proven ineffective for prevention of CAUTI. The novel approach strategies include Disrupt quorum sensing, Iron scavenging catheters, Bacterial interference showed the effectiveness towards the catheter associated urinary tract infection. [39]

For the prevention of catheter associated urinary tract infection, it is necessary to shorten the duration of catheter and examine the regular culture for the detection of incidence of microbial growth and also elucidate the antibiotic sensitivity pattern. The specific antibiotic used according to sensitivity report. Catheter associated urinary tract infection preventive strategies effective for the welfare of patient health.

**Antibiotic sensitivity**

The availability of antibiotic is remarkable and new agents are frequently added. But now a day’s bacteria develops resistance, including methods that may decrease the intracellular concentrations of the antibiotic, deactivate the antibiotic, change the binding sites for the antibiotic, and develop adaptations that bypass the need for the binding site targeted by the antibiotic. [40]

From the previous study it was clearly showed that bacterial uropathogen isolates from patients with UTIs revealed the presence of high levels of single and multiple antimicrobial resistances against commonly prescribed drugs. E. coli which is the predominant cause of UTI, showed high percentage of resistance to ampicillin and amoxicillin (100%), and low resistance to ciprofloxacin (14.3%). Klebsiella spp which is the second most prevalent pathogen of UTI displayed a similar resistance pattern as of E.coli and showed hundred percent resistant to ampicillin and amoxicillin; however, all isolates were susceptible to ciprofloxacin and all others gram negative isolates were similarly resistant to ampicillin and amoxicillin as to that of E. coli and K. Pneumonia.[41]

Another study from India also showed that 80% resistance to nalidixic acid, ampicillin, cephotaxime and Cotrimoxazole. The study also elucidates that there is a correlation between biofilm production and resistance to multiple antibiotics, Therapy against UTI should be guided by antimicrobial susceptibilities as increasing numbers of urinary isolates are developing resistance to commonly used antibiotics. The therapy used for the catheter associated urinary tract infection used after the antibiotic sensitivity test performed that helps in knowing the resistance and sensitivity of antibiotic against the microorganisms. [18]

Study at Nigeria elucidates that the gram negative organisms such as E.Coli etc showed high resistance to commonly used antibiotics such as ampicillin (100%), gentamicin (90.9%), tetracycline (89.1%), cotrimoxazole (87.3%), cefuroxime (81.1%), nalidixic acid (87.3%), nitrofurantoin (67.3%), colistin (63.7%), perfoxacin (65.5%) and ciprofloxacin (56.4%). Staphylococcus aureus isolates were also resistant to penicillin (100%), gentamicin (100%), cotrimoxazole (100%), chloramphenicol (100%), cloxacillin (83.3%), tetracycline (83.3%), erythromycin (66.7%) and cefuroxime (66.7%). Only
So it is necessary to check out the patient reports for the environmental factors etc. shows variations that differ due to genetic differences, catheterization. The sensitivity pattern against pathogens due to poorly prescribed antibiotic during and after particular pathogen. shows the existence and which antibiotic sensitive against that pathogen. Cotrimoxazole and other 1st line drugs. Pseudomonas aeruginosa, which is most common cause of hospital-acquired UTI, was less sensitive to quinolones and cephalosporin than aminoglycosides. Klebsiella spp and Enterobacter were the 2nd most common isolate organisms from this study found to be resistant to common antibiotics like amoxicillin and quinolones, cephalosporins. These were sensitive to fosfomycin and aminoglycosides. From the study it was clearly examine that susceptibility for quinolones was 51% (Ciprofloxacin, Norflaxacin, Nalidixic acid). Among cephalosporhins, Cefazidime and Ceftriaxone showed high susceptibility (75%) while cepalexin showed least susceptibility (43%).

Previous study at Nepal predicts that E.coli was the principal pathogens showed higher susceptibility to common antibiotics Ampicillin, Cotrimoxazole and norflaxacin. The study also explains that all the other previous studies reported that a high prevalence of resistance to Norflaxcin, Ampicillin and Ciprofloxacin but this study showed the different study that showed ciprofloxacin was sensitive towards Klebsiella pathogens. Pseudomonas aeruginosa, which is a common cause of hospital-acquired UTI, was less sensitive to the common antibiotics but highly sensitive to amikacin, piperacillin, ciprofloxacin and gentamicin. The cephalosporins, cepalexin showed low mean susceptibility (49.7%) but ceftazidime showed high mean susceptibility. The study finally concluded that antibiotic showed the variation in resistance and sensitivity towards the pathogens. Another study at Nigeria determines that Ofloxacin, Gentamicin, Augmentin showed the sensitivity towards the micro organisms but Nitrofurantoin and Cetizidine have the least sensitivity. Cotrimoxazole and Amoxygen demonstrated resistances. The study finally concluded that gram negative bacteria E.coli has the highly incidence value among all other organisms causing CAUTI and antibiotic sensitivity pattern test predicts that Ofloxacin and Gentamycin are the most effective drugs against the micro organisms. From the results of these studies finally concluded that pathogens show the resistance to mostly of 1st line antibiotic due to poorly prescribed antibiotic during and after catheterization. The sensitivity pattern against pathogens shows variations that differ due to genetic difference, environmental factors etc.

So it is necessary to check out the patient reports for the antibiotic sensitivity pattern during and after the catheterization that helps in determining which pathogen shows the existence and which antibiotic sensitive against that particular pathogen.

Management

The management of CAUTI is probably the topic of greatest interest for the clinicians. Most of the study concluded that antibiotic resistance occurs due to the poorly prescribed antibiotics during and after the catheterization or many other factors like inappropriate sterilisation of catheter and microbial contamination during insertion. For the management of CAUTI, Centers for Disease Control and Prevention (CDC) guideline includes:

[1] Aseptic insertion of urinary catheters by properly trained personnel, using aseptic technique and sterile equipment (with an exception being that clean technique is appropriate for chronic intermittent catheterisation)


For the management long term catheter changing supports by most of the evidence. The previous study in 2000 by Raz et al reported that changing the long term catheter led to improved clinical and microbiological outcomes. Bacteriuria disappeared among most of the subjects by changing technique. Their hypothesis for the improved clinical outcomes with catheter change was that removal of the “bioburden” of the catheter-associated biofilm helped decrease the severity of inflammation and the probability of recurrence.

Another clinical question for the management of CAUTI is the duration of antibiotics necessary to treat CAUTI. The previous studies concluded that the appropriate duration of therapy for CAUTI lies between 3 and 14 days, and the duration of catheterization is likely to be an important variable in determining the optimal duration of therapy.

The management of patient is necessary to prevent the risk associated CAUTI and from the complications during and after the catheterization. The antibiotic sensitivity pattern test very much helpful in determining the pathogen and sensitive antibiotic against that pathogen. It is also necessary to determine the resistance of antibiotics in the patient that can prevent the irrational prescribing pattern of antibiotic.

Future directions

It is hoped that medical technology will allow the advancement in catheterization procedures, need and duration for catheterization and provide advance improvements in the design of drainage system of urinary catheter. Biomaterial research is an exploding new science, and research must continue with these new materials in respect to mucosal biocompatibility and effectiveness in reducing bacterial biofilm attachment. It is anticipated that new biomaterials will eventually reduce bacterial adherence and biofilm formation and subsequently decrease the rate of catheter-associated infection. New antibiotics being developed may be able to penetrate the bacterial biofilm and may be more effective in this and other prosthesis-related infections. Further studies are required to rationalize the use of antibiotics both to prevent and treat catheter-associated infection. For now the most
effective way to reduce the incidence of catheter-associated infection is to avoid indwelling Foley catheterization if at all possible, or at least to reduce the length of time the catheter remains in the bladder.

Conflict of interest statement
We declare that we have no conflict of interest.

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