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Antibiotic Resistance Pattern of Urinary Catheter Biofilm and Urine - in Tertiary Care Hospital, Bangladesh

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Abstract

Catheter-Associated Urinary Tract Infection (CAUTI) is common worldwide health care associated problem. Antibiotic resistance in CAUTI is due to wide spread use of urinary catheter and inappropriate use of antibiotics. The present study highlights the trend of organism and their resistance patterns.

This observational prospective study was done on 100 CAUTI patients in Comilla medical college hospital, Comilla, Bangladesh. Urine culture positive patients collected by suprapubic puncture meet the criteria of CAUTI with formation of biofilm in catheter was selected.

E.coli was the most frequently isolated pathogen in both urine and biofilm (60% vs.72%) followed by *Klebsiella* and others. Biofilm strains displayed relatively high resistance against tested antibiotics. The *E.coli* in both urine and biofilm shows high resistance against ciprofloxacin and cotrimoxazole (80%& 65% vs 84% & 82% respectively), and low for imipenem and amikacin (5% and 18% vs 8% and19% respectively). Urine and catheter biofilm resistant to all tested drugs was observed for *E.coli* in 6.95% and 3.33% cases respectively.

E.coli was the most frequent isolate followed *Klebsiella* and others. E. coli in both urine and biofilm showed the high resistance to the quinolones and cotrimoxazole and low for carbapenems and amikacin.

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Introduction

In Bangladesh, antimicrobial resistance is a major issue confronting organized health care which is due to widespread use of antimicrobial drugs with inappropriate dose, duration by primary health care workers in general population. Catheter-Associated Urinary Tract Infection (CAUTI) is the most frequent healthcare associated infection in the United States also [1, 2]. Approximately one in every five patients admitted with acute illness in hospital receives an indwelling catheter [1, 3]. Due to its frequent and unnecessary use many patients are placed at risk of CAUTI which has got significant economic impact and is believed to be reasonably preventable [3 - 6]. The underlying cause of CAUTI is formation of a pathogenic biofilm on the surface of the indwelling urinary catheter which is an adherent layer of accumulated microorganisms and their extracellular products [7–9]. The biofilm protects the organism against both host defenses and antibiotic therapy. Frequently organism migrates from biofilm in to the bladder within 1 to 3 days [10]. Biofilms also contribute to an increased risk of antimicrobial resistance, as the microorganisms are able to share genetic material at a faster rate [10]. Additionally, some bacterial biofilms have the ability to alter the urine pH, facilitating the development of catheter encrustations. These encrustations obstruct urine flow and increase the risk of CAUTI. The risk of urinary tract infection is related to the length of time the catheter is in place. Long-term catheters colonized by extensive biofilms, which can have profound effects on the health of the patient.

There is clear distinction between of Catheter-Associated Asymptomatic Bacteriuria (CAASB) and CAUTI [11]. Substantial numbers of patients are being diagnosed inappropriately with CAUTI, for which they receive treatment that is not recommended. This inappropriate treatment is potentially harmful in terms of emergence of resistant pathogens, suprainfections, and unnecessary costs. Preventing CAUTI used to be relatively is low priority in acute care. Many hospitals are now facing the challenge of implementing practices to prevent healthcare-acquired CAUTI. More than 50% of hospitals did not monitor which patients had urinary catheters or the duration of catheter use [12]. Providers often fail to document the indications for or placement of urinary catheters. Many organizations have adopted the practices advocated in evidence-based guidelines but still struggle with implementation and lack of methods for efficient and reliable performance of prevention practices.

In the face of increased incidence of resistant urinary tract infection and CAUTI in this population, the present study designed to see bacteriology and antibiotic resistance patterns of biofilm and urine in patients with indwelling urinary catheter which will refocus on providing quality patient care.

Materials and Method

This was an observational prospective study done on adult patient with age above 18 years in the department of medicine and urology, Comilla Medical College Hospital, Comilla, Bangladesh during the period of 1st January, 2013 to 31st December, 2013. The patient's undergone indwelling catheterization for urinary retention or incontinence having overt visible biofilm in inner surface of collecting portion of urobag was first identified. Initially 125 patients were selected. Patients who were on antibiotic, was advised to stop the drug for 48 hours and then included in this study. Catheter was clamped for three hours and urine samples were collected in sterile container through suprapubic puncture from the patients. Only those patients shows any bacteria in urine culture was included in this study. Out of 125 initially selected patients 100 patients was found urine culture positive and were included in the study. As Catheter-Associated Asymptomatic Bacteriuria (CAASB) is a distinct condition [13] associated with a low incidence of sequelae, resolve spontaneously on removal of the catheter and treatment is unlikely to confer clinical benefit [14] were excluded from this study. Patient's clinical presentation, co morbid illness, duration of catheterization was noted in data sheet. A cross section of about 10 cm of both end clamped collecting portion of urobag tube was collected and it was longitudinally splinted to collect swab for culture of biofilm. A modified semi-quantitative technique using a standard calibrated bacteriological loop transfers the 0.001ml of sample on Blood agar and MacConkey agar media. After allowing the material to be absorbed into the agar, the plates were then inverted and incubated aerobically at 37°C for 24 hours. Anti microbial susceptibility were tested by Kirby- Bauer disc diffusion technique using Muller Hinton Agar as per recommendation of CLSI (Clinical and Laboratory Standard Institute). The colony count was done using semi quantitative method available in our center. Number of colonies obtained is multiplied by 1000 to obtain the colony forming units (cfu)/ml [15]. Identification of bacteria 10^5cfu/ml or more in biofilm considered as significant. The characteristic bacteria on the culture media were aseptically isolated. Kirby-Bauer Disk Diffusion Susceptibility test protocol was followed to determine the breakpoint of susceptibility. As per protocol, zone of inhibition was measured in mm for each antibiotic disk placed. Using the CLSI guide line the susceptibility or resistance of the organism to each drug was determined. For each drug the interpretation was done according to zone of inhibition size – Susceptible (S), Intermediate (I) or Resistant (R). The antibiotics susceptibility test was done with amoxyclav, cefotaxime, ceftriaxone, nitrofurantoin, ceftazidime, cefuroxime, ciprofloxacin, cotrimoxazole, amikacin, imipenem nalidixic acid. Calculations were performed using SPSS 11.5 for windows XP. Both the authors vouch for the completeness and accuracy of data and analyses presented.

Observation and Results

Patient's characteristics and time duration since catheterization were shown in Tables 1 and 2

Table 1: Patients characteristics (n=100)

Variables	Categories	Frequency	Percentage
Age (M±SD) in years	56.20 ± 20.67 years		
Sex	Male	61	61
	Female	39	39
Symptoms	Fever with chills and rigor	100	100
	Loin pain	55	55
	Lower abdominal pain	80	80

Table 2: Duration since catheterization

Duration	Number of patients (n=100)	Percentage (%)
Short term catheter (1-7 days)	15	15
Medium term catheter (7-28 days)	71	71
Long term catheter (over 28 days)	14	14

Table 3: Distribution of uropathogens urine and biofilm sample

Organism Isolated	Urine	Biofilm
Escherichia coli	70	72
Klebsiella pneumoniae	15	18
Pseudomonas aeruginosa	8	12
Acinetobacter	5	3
Enterococci	4	5
Proteus	3	3
Total	105	113

Table 3: shows distribution of uropathogens urine and biofilm samples. *E. coli* was most frequent isolate in both urine and

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biofilm samples followed by *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. It is also observed multibactrial isolates in 5 urine samples and 13 biofilm samples.

Table 4: Antibiotic resistance pattern of organisms isolated in urine

Organism Isolated	Resistance									Resistant to all
	Ciprofl-oxacin	Cotrim-oxazole	Ceftria-xone	Cefur-oxime	Amik-acin	Nitrofurantoin	Imipenem	Amox yclav	Ceftazidim	
Escherichia coli	48 80%	29 65%	41 68.44%	33 55%	11 18.44%	9 15%	3 5%	35 58.44%	33 55%	2 3.33%
Klebsiella pneumoniae	13 92.31%	12 84.62%	10 69.24%	11 76.93%	6 38.47%	5 30.77%	3 15.39%	12 84.62%	12 84.62%	0
Pseudomonas aeruginosa	5 71.43%	5 71.43%	6 85.72%	5 71.43%	3 42.86%	2 28.57%	1 14.28%	6 85.75%	6 85.75%	0
Acinetobacter	4 100%	3 75%	3 75%	2 50%	2 50%	2 50%	0	3 75%	3 75%	0
Enterococci	2 66.67%	2 66.67%	3 100%	3 100%	3 100%	1 33.33%	0	3 100%	1 33.33%	0
Proteus	3 100%	2 66.67%	2 66.67%	3 100%	1 33’33%	2 66.67%	0	2 66.67%	3 100%	0

Antibiotic resistance pattern of organisms isolated in urine showed in table 4. Resistance pattern of *E.coli* against ciprofloxacin, cotrimoxazole, ceftriaxone, cefuroxime, ceftazidime, nitrofurantoin, amoxyclav, amikacin and imipenem was 80%, 65%, 68%, 55%, 55%, 15%, 58%, 18% and 5% respectively.

Table 5: Antibiotic resistance pattern of organisms isolated in biofilm

Organism Isolated	**Resistance**										**Resistant to all**
	Ciprofloxacin	Cotrim-oxazole	Ceftri a-xone	Cefuroxime	Amikacin	Nitrofurantoin	Imipenem	Amoxyclav	Ceftazidim	Nalidixic acid	
Escherichia coli	61 84.73%	56 77.78 %	50 69.45 %	46 63.89%	19 26.29 %	21 29.17%	6 8.34%	53 73.62%	43 59.73%	67 93.06 %	5 6.95%
Klebsiella pneumoniae	16 88.89%	16 88.89 %	12 66.67 %	11 62.14%	6 33.33 %	5 27.78%	2 11.12%	12 66.67%	8 44.45%	17 94.45 %	1 5.55%
Pseudomonasaeruginosa	9 75%	11 91.67 %	12 66.67 %	12 66.67%	4 33.33 %	3 25%	1 8.33%	9 75%	6 50%	11 91.97 %	0
Acinetobacter	3 100%	2 66,67 %	2 66.67 %	3 100%	1 33.33 %	2 66.67%	0	3 100%	2 66.67%	3 100%	0
Enterococci	5 100%	3 60%	3 60%	4 80%	2 40%	1 20%	0	4 80%	3 60%	4 80%	0
Proteus	2 66.67%	3 100%	2 66.67 %	3 100%	1 33.33 %	1 33.33%	0	2 66.67%	2 66.67%	3 100%	0

The table- 5 shows antibiotic resistance pattern of organisms isolated in biofilm. Resistance pattern of *E.coli* against ciprofloxacin, cotrimoxazole, ceftriaxone, cefuroxime, ceftazidime, nitrofurantoin, amoxyclav, amikacin and imipenem was 85%, 78%, 69%, 64%, 60%, 30%, 73%, 26% and 8S% respectively. The table also shows resistant to all tested drugs for *E.coli* in 5 samples (6.95%) and klebsiella in 1 sample (5.55%).

Discussion

In this study all the patients were above 18 years with mean age of 56.20 ± 20.67 years, with 61% male and 39% female. All patients were febrile. Lower abdominal pain and loin pain was found in 80% and 55% respectively. Medium and long term catheterizations are most susceptible to develop CAUTI 71% and 14% respectively.

In our study *E.coli* was the most frequently isolated pathogen in both urine and biofilm (60% vs.72%) which was similar to other study [16-18]. Next to *E. coli*, *Klebsiella* and *Pseudomonas* was the frequent isolate although in some other study shows Staphylococcus as second most important isolate [19].

Higher resistance pattern for *E.coli* in urine and biofilm sample was found against ciprofloxacin and cotrimoxazole (80%& 65% vs 84% & 82% respectively). Loss of antibiotic sensitivity to commonly used antibiotics is a major clinical problem to treat CAUTI. Previous study in ICDDR, B in the year of 2007 demonstrated resistance to cotrimoxazole against *E. coli* was near 33% [20]**.** We can be concluding from this observation that cotrimoxazole is going to loss its sensitivity against uropathogens in Bangladesh and at present we should not consider this drug as an effective first line therapy in CAUTI. Similarly our study obviously shows fluoroquinolones are no more useful against uropathogens. Antibiotics shows lowest resistance pattern in both urine and biofilm were imipenem and amikacin (5% and 18% vs 8% and19% respectively). Study also shows bacterial biofilm are often associated with dramatically loss its sensitivity to antibiotics which is similar to other studies [21]. In catheter biofilm resistant to all drugs were found in case of *E.coli* in 5 samples (6.95%) and *klebsiella* in 1 sample (5.55%). Urine samples resistant against all tested antibiotics were only in case of *E.coli* in 3.33% cases. Widespread use of antimicrobial drugs with inappropriate dose, duration by primary health care workers in general population leading to development of multiple drug resistance strain

Microbial biofilm have been associated with a variety of persistent infections which respond poorly to conventional antibiotic therapy. Antibiotic therapy against device associated biofilm organisms often fails without the removal of the infected implant although they are not resistant to antibiotics per se [22]. To lower burden related to CAUTI we have to broaden our knowledge regarding safe use of indwelling urinary catheter. We also suggest inserting urinary catheters using aseptic technique and sterile equipment.

Conclusion

E.coli was the most frequent isolate followed *Klebsiella* and others. *E. coli* in both biofilm and urine showed the high resistance to the quinolones and cotrimoxazole and low for carbapenems and amikacin. Unnecessary catheterization should be avoided and early removal of urinary catheters is beneficial that are no longer necessary.

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