

Research Article





# Antibiotic sensitivity patterns of uropathogens isolated from catheterized patients in a tertiary care hospital in Dhaka, Bangladesh

#### **Abstract**

Among nosocomial infections catheter associated urinary tract infection (CAUTI) is one of the most common infection. The antibiotic resistance amongst the uropathogens isolated from CAUTI are multi-drug resistant and a growing public health problem in the world including Bangladesh. The study objective was to determine the aetiology of uropathogens in catheter associated urinary tract infection and find out their anti-microbial sensitivity pattern among the isolates. A cross sectional study was done from July 2016 to June 2017 in Dhaka Medical College, Bangladesh. Urine samples were collected from 400 patients with suspected CAUTI which were processed microbiologically and antimicrobial sensitivity was performed. Out of 400 patients Escherichia coli (38.93%) was the most common isolated organism followed by Pseudomonas spp, (15.98%), Klebsiella spp,  $(8.61\%), \textit{Proteus} \ \text{spp.} \ (7.38\%) \ \textit{Enterobacter} \ \text{spp,} \ (6.56\%) \ \text{and} \ \textit{Acinitobacter} \ \text{spp.} \ (1.22\%).$ Among the Gram positive isolates Staphylococcus aureus (1.64%) and Coagulase negative Staphylococeus (6.97%%) were isolated. Enterobacteriaceae showed high resistant to commonly used antimicrobials Amoxiclav, Gentamycin, Ceftriaxone, azithromycin ciprofloxacin, cortimoxazole and were sensitive to colistin ,nitrofurantoin ,imepenem, Meropenem. Many isolates showed multi- drug resistance pattern hence strict aseptic precaution has to be taken prior to catheter insertion and after to prevent infection.

Keywords: CAUTI, nosocomial, uropathogens, antimicrobial resistance

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## Introduction

Urinary tract infection (UTI) is defined as a condition in which bacteria are established and multiplying within the urinary tract.1 In UTI the presence of growth of more than 105 colony forming unit (CFU) of bacteria per ml of urine for asymptomatic individual and 10<sup>3</sup> for symptomatic individual.<sup>2</sup> 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. 66% 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.3

An indwelling urinary catheter is a drainage tube that is inserted into the urinary bladder through the urethra, is left in place, and is connected to a closed collection system. A catheter-associated urinary tract infection (CAUTI) occurs when germs (usually bacteria) enter the urinary tract through the urinary catheter and cause infection. As CAUTI constitute 40%-50% of all hospital infections,<sup>4</sup> there is increase in the hospital stay of the patient along with increase in the use of higher antibiotics. The overall cost of health care also increases. A catheter-associated urinary tract infection (CAUTI) increased morbidity and mortality.5

The presence of potentially pathogenic bacteria and an indwelling catheter predisposes to the development of a nosocomial UTI. The bacteria may gain entry into the bladder during insertion of the catheter, during manipulation of the catheter or drainage system, around the catheter, and after removal.6 Risk factors for bacteriuria in patients who are catheterized include longer duration of catheterization, colonization of the drainage bag, diarrhea, diabetes, absence of antibiotics, female gender, renal insufficiency, errors in catheter care, catheterization late in the hospital course, and immunocompromised or debilitated states.7

Indiscriminate use of antimicrobial agents is a common practice in underdeveloped and many developing countries that often leads to emergence of resistant microorganisms. This raises alarms to implement a nationwide antimicrobial surveillance and in-vitro susceptibility testing with strict adherence to antibiotic policy to inhibit the spread of drug resistant microbes in the country. As a common practice, empirical antimicrobial treatment is initiated before the laboratory results of urine culture are available which may lead to emergence and spread of antimicrobial resistant strains.8

## Materials & methods

A cross sectional study was done from July 2016 to June 2017. Total 400 urine samples of clinically suspected CAUTI patients were collected from Urology department, Gynae and Obstetrics department, Pediatric department, ICU, and HDU of burn unit of Dhaka Medical College, Dhaka, according to CDC guidelines using sterile needle from tubing of catheter under aseptic precautions. All patients were catheterized after admission in the hospital.

All urine samples were first evaluated for presence of significant pus cell ( $\geq$  5/HPF) by microscopic examination after centrifugation. Two hundred and forty- four (61%) samples with significant pus cells were found which were inoculated on blood agar and MacConkey agar media. Urine culture was done by standard loop method.9 A





standard calibrated (4 mm diameter) wire loop was used to take a fixed known volume (0.01ml) of urine. The inoculated culture plates were aerobically incubated at 37°C for 24 hours. Incubated plates were observed for the presence of any bacterial growth after 24 hours. If growth occurred, colony count was done to calculate the number of colony forming unit per ml of urine.

A single colony represents one organism. If an incolumn of 0.01 ml produces 20 colonies, the number of organisms represents in 0.01 ml of urine is 20. So one ml of urine contains 2 X  $10^3$  organisms. A count of 1 X  $10^5$  or more bacteria per ml of urine was considered as clinically significant.  $^{10}$ 

All the organisms will be identified by colony morphology, hemolytic criteria, staining character, pigment production and biochemical tests as per standard techniques.

All bacteria isolates were tested for antimicrobial susceptibility by Kirby-Bauer modified disc-diffusion technique.<sup>11</sup> The antimicrobial discs were used according to the standard antibiotic panel for isolated organisms. Antibiotic discs were obtained from commercial source (Oxoid Ltd, UK).

## Media for antibiotic susceptibility test

Mueller-Hinton agar media was used for antimicrobial susceptibility test.

#### **Control strain**

Esch. coli ATCC 25922 was used as control strain to assess the performance of the method.

## **Results & discussion**

A total of 400 urine samples from suspected catheterized UTI patients were included in this study. Out of 400 samples, 270 samples were positive for significant pus cell ( $\geq$  5/HPF), which were selected for culture. Out of 270 samples, 244 (90.37%) were culture positive and 26 (9.63%) were culture negative (Figure 1).

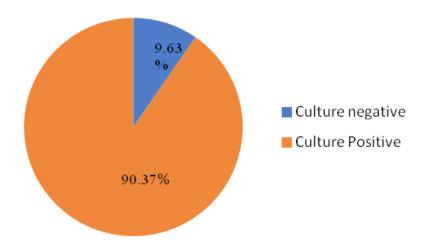


Figure I Culture results of urine samples having significant pus cell (n=270).

Table 1 shows that microscopical findings of pus cell in relation to urine culture. Out of 85 cases having pus cell count 5-9/HPF (few) in urine, 73 (85.88%) were culture positive. Out of 123 cases having pus cell count 10-20/HPF (moderate) in urine, 111 (90.24%) were culture positive. Out of 62 cases having pus cell count >20/HPF (plenty) in urine 60 (96.77%) were culture positive.

The distribution of the patients having positive urine culture by age and sex are shown in Table 2. Out of 244 culture positive cases, 163 were male and 81 were female. The ratio between male and female was 2:1. Frequency of CAUTI in case of male was highest (31.28%) in age group of 31–45 years followed by (25.77%) in age group 46 – 60 years. In case of female, the peak of CAUTI was highest (35.81%) in age group of 31-45 years.

Table I Comparison of urine culture with pus cell in population with significant pus cell (N=270)

Pus Cell/HPF           Urine culture         05-Sep         Oct-20         >20           Positive         73         111         60           -85.88%         -90.24%         -96.775           Negative         12         12         2				
Positive 73 III 60 -85.88% -90.24% -96.775	Pus Cell/HPF			
-85.88% -90.24% -96.77%	Urine culture	05-Sep	Oct-20	>20
	Positive	73	111	60
Negative 12 12 2		-85.88%	-90.24%	-96.77%
	Negative	12	12	2
-14.12% -9.76% -3.23%		-14.12%	-9.76%	-3.23%
Total 85 123 62	Total	85	123	62
-100 -100 -100		-100	-100	-100

**Table 2** Distribution of the patients having positive urine culture by age and sex (N = 244)

Age group in years n (%)						
Sex	≤ 15	16-30	31-45	46-60	> 60	Total n (%)
Male	8 (4.91)	34 (20.86)	51(31.28)	42 (25.77)	28 (17.18)	163(100.00)
Female	4 (4.94)	18 (22.22)	29 (35.81)	14 (17.28)	16 (19.75)	81(100.00)
Total	12 (4.92)	52 (21.31)	80 (32.79)	56 (22.95)	44 (18.03)	244(100.00)

Table 3 shows that the distribution of the isolated organisms among urine culture positive cases. Among the 244 culture positive cases, gram positive bacilli were isolated from 192 (78.69%) cases,

gram negative cocci were isolated from 21 (8.61%) cases and Candida spp. were isolated from 31 (12.70%) cases.

Table 3 Distribution of the isolated organisms among culture positive cases (N=244)

Isolated organism	Positive n (%)
Gram negative bacilli	192 (78.69)
(Esch.coli, Pseudomonas spp., Klebsiella spp., Proteus s	pp., Enterobacter spp., Acinitobacter spp.)
Gram positive cocci	21(8.61)
(Staphylococcus aureus, CONS)	
Candida spp.	31 (12.70)
	244 (100.00)

#### CONS= Coagulase negative staphylococeus

Figure 2 shows the distribution of organisms isolated from urine samples. Out of 244 culture positive cases, 95 (38.93%) were *Esch. coli*, 39 (15.98%) were *Pseudomonas* spp, 21 (8.61%) were *Klebsiella* spp, 18 (7.38%) were *Proteus* spp., 16 (6.56%) were *Enterobacter* spp.,

3 (1.22%) were *Acinitobacter* spp., 4 (1.64%) were *Staphylococeus aureus*, 17 (6.97%) were *coagulase negative Staphylococeus* and 31 (12.79%) were *Candida* spp.

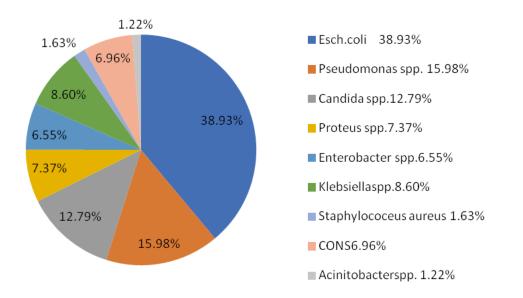


Figure 2 Isolated bacteria in urine samples from catheterized patients (N=244).

Antimicrobial resistance pattern of the isolated gram-negative bacteria are shown in Table 4. Almost all the isolated bacteria of the present study were sensitive to colistin except *Proteus* spp. Among the isolated *Esch.coli*, 14% were resistant to carbapenems, 96.48% to amoxiclay, 75.78% to azithromycin, ceftriaxone and Cefotaxime, 77.89% to ceftazidime 91.57% to cotrimoxazole, 57.89% to

gentamicin, 36.84% to nitrofurantoin. Among the isolated *psedumonas* spp., 12.82% were resistant to carbapenems, 92.30% resistant to amoxiclav, 82.05% to azithromycin, 76.92% to ceftriaxone, 71.79% to ceftazidime and cefotaxime, 74.35% to ciprofloxacin 89.74% to cotrimoxazole, 56.41% to gentamicin, 30.76% to nitrofurantoin.

Table 4 Antibiotic resistance pattern of isolated gram-negative bacteria (N= 192)

Antimicrobial drugs	Esch.coli (N=95) n (%)	Pseudomonas spp. (N=39) n (%)	Klebsiella spp. (N=21) n (%)	Proteus spp. (N=18) n (%)	Enterobacter spp. (N=16) n (%)	Acinitobacter spp (N=3) n (%)
Amoxiclav	92 (96.48)	36 (92.30)	17 (80.95)	13 (72.22)	11 (68.75)	3 (100.00)
Azithromycin	72 (75.78)	32 (82.05)	16 (76.19)	11 (61.11)	12 (75.00)	
Ceftriaxone	72 (75.78)	30 (76.92)	15 (71.42)	12 (66.66)	13 (81.25)	2 (66.66)
Ceftazidime	74 (77.89)	28 (71.79)	14 (66.66)	11 (61.11)	12 (75.00)	I (33.33)
Cefotaxime	72 (75.78)	28 (71.79)	14 (66.66)	10 (55.55)	12 (75.00)	I (33.33)
Ciprofloxacin	80 (84.21)	29 (74.35)	16 (76.19)	12 (66.66)	12 (75.00)	2 (66.66)
Colistin	0 (0.00)	0 (0.00)	0 (0.00)	10 (55.55)	0 (0.00)	0 (0.00)
Cotrimoxazole	87 (91.57)	35 (89.74)	19 (90.47)	15 (83.33)	14 (87.5)	3 (100.00)
Gentamicin	55 (57.89)	22 (56.41)	12 (57.14)	11 (61.11)	5 (31.25)	I (33.33)
Imipenem	14 (14.73)	5 (12.82)	4 (19.04)	I (5.55)	I (6.25)	0 (0.00)
Meropenem	14 (14.73)	5 (12.82)	4 (19.04)	I (5.55)	I (6.25)	0 (0.00)
Nitrofurantoin	35 (36.84)	12 (30.76)	5 (23.80)	6 (33.33)	3 (18.75)	0 (0.00)

N = Total number

n = Number of resistant bacteria

Among the isolated klebsiella spp. 19.04% were resistant to carbapenems, 80.95% resistant to amoxiclay, 76.19% to azithromycin and ciprofloxacin 71.42% to ceftriaxone, 66.66% to ceftazidime and cefotaxime, 90.47% to cotrimoxazole, 57.14% to gentamicin, 23.80% to nitrofurantoin. Among the isolated proteus spp. 5.55% were resistant to carbapenems, 72.22% to amoxiclay, 61.11% to azithromycin, ceftazidime and gentamicin, 66.66% to ceftriaxone and ciprofloxacin, 55.55% to cefotaxime and colistin, 83.33% to cotrimoxazole, 33.33% to nitrofurantoin. Among the isolated enterobacter spp. 6.25% were resistant to carbapenems, 68.75% to amoxiclav, 75.00% to azithromycin, ceftazidime, cefotaxime and ciprofloxacin, 81.25% to ceftriaxone, 87.50% to cotrimoxazole, 33.25% to gentamicin, 18.75%

to nitrofurantoin. Among the isolated acinitobacter spp. 100% were resistant to amoxiclav and cotrimoxazole, 66.66% to ceftriaxone and ciprofloxacin, 33.33% to ceftazidime, cefotaxime and gentamicin.

Table 5 shows the incidence of MDR, XDR and PDR strains isolated from gram negative bacilli. Isolated Esch. coli were predominant, which were 60.87% and 11.96% as MDR and XDR strains, followed by 58.97% and 10.25% of *Pseudomonas* spp.as MDR and XDR strains, 52.38% and 14.29% of Klebsiella spp. as MDR and XDR strains, 50% and 5.56% of Proteus spp. as MDR and XDR strains, 43.75% and 6.25% of Enterobacter spp. as MDR and XDR strains, respectively and 66.67% Acinitobacter spp.as MDR strains. There were no detected PDR strains.

Table 5 Frequency of MDR, XDR and PDR among the isolated gram negative bacteria (N = 192)

Isolated organism	MDR (%)	XDR n (%)	PDR n (%)
Esch.coli (N=95)	56 (60.87%)	11 (11.96%)	-
Pseudomonas spp. (N=39)	23 (58.97%)	4 (10.25%)	-
Klebsiella spp. (N=21)	11 (52.38%)	3 (14.24%)	-
Proteus spp. (N=18)	9 (50.00%)	I (5.56%)	-
Enterobacter spp. (N=16)	7 (43.75%)	I (6.25%)	-
Acinitobacter (N=3)	2 (66.67%)	X	-
Total	108 (56.25%)	20 (10.42%)	-

Antibiotic resistance pattern of isolated Staphylococcus aureus and CONS are shown in Table 6. Among the isolated Staphylococcus aureus 100% were resistant to ceftriaxone and gentamicin, 75% to amoxiclav, azithromycin and ciprofloxacin, 50% to amikacin. Among the isolated coagulase negative Staphylooccus, 70.58% were

resistant to azithromycin and ciprofloxacin, 58.82% to amoxiclav and gentamicin, 88.23% to ceftriaxone, 47% to amikacin, 17.64% to levofloxacin and oxacillin and none was resistant to cefoxitin, linezolid and vancomycin.

Table 6 Antibiotic resistance pattern of isolated Staphylococcus (N=21)

Antimicrobial drugs	Staphylococcus aureus (N=4) n (%)	CONS (N=17) n (%)
Amikacin	2 (50.00)	8 (47.00)
Amoxiclav	3 (75.00)	10 (58.82)
Azithromycin	3 (75.00)	12 (70.58)
Cefoxitin	0 (0.00)	0 (0.00)
Ceftriaxone	4(100.00)	15 (88.23)
Ciprofloxacin	3 (75.00)	12 (70.58)
Gentamicin	4 (100.00)	10 (58.82)
Levofloxacin	0 (0.00)	3 (17.64)
Oxacillin	0 (0.00)	3 (17.64)
Linezolid	0 (0.00)	0 (0.00)
Vancomycin	0 (0.00)	0 (0.00)

N = Total number

n = Number of resistant bacteria

Catheter associated urinary tract infections (CAUTIs) are serious health affecting problems in hospitalized patient, a total of 400 urine samples from suspected UTI patients were tested for the presence of significant pus cell (pus cell ≥5/HPF), of them 270 samples were positive for significant pus cell, which were selected for culture. Out of 270 samples 244 (90.37%) were culture positive, of them 213 (87.30%) were bacteria and 31 (12.70%) were candida. That is, 53.25% of catheterized patient developed bacteriuria. Association for professionals in infection control and epidemiology revealed 26% of patients who have indwelling catheters will develop bacteriuria. Rahman et al.<sup>12</sup> from Bangladesh reported 24.14% growth of bacteria. The higher incidence of significant bacteriuria of the present study might be due to only urine samples with significant pus cells were inoculated after proper screening. So, it can be concluded that screening test for pyuria before culture may be helpful in increasing the sensitivity of culture result and decreasing the cost by decreasing the unnecessary use of culture.

In the present study, the incidence of CAUTI was 53.25% and the ratio between male and female was 2:1. Catheterized male patients were more than the female patients. In this study age and sex distribution of majority of the cases from whom the urine samples collected were in the age group of 31 to 45 years. Frequency of CAUTI in case of male was found highest 31.28% in age group of 31-45 years followed by 25.77% in age group 46 – 60 years. In case of female, the peak of CAUTI was found highest 35.81% in age group of 31-45 years (Table 2). Nandini et al. (2016), reported the incidence of CAUTI is 21.6%, which was similar to earlier studies by Kulkarni et al (2014), Bagchi et al.13, N Bhatia et al. (2010). Male predominance was also seen by Nandini et al. (2016) in CAUTI, male 33 (61.11%) than female 16 (38.88%) patients, similar male preponderance were reported by Jaggi et al.<sup>14</sup> Indranil et al.<sup>15</sup> found the number of CAUTI cases in males was 24.35% and in females 34.29% which does not corelate with present study.

In this study, majority, 78.69% of CAUTI were due to gram negative bacilli and 8.61% were due to gram positive cocci. Remaining 12.7% were due to candida infection (Table 3). All the isolated grampositive cocci were sensitive to cefoxitin, linezolid and vancomycin (Table 6). These findings were in agreement with the study conducted by Sarwar (2016) from DMCH where 39.40% Staph. aureus and

none of the CONS were resistant to cefoxitin. In another study from DMCH Rahman (2014) reported that 66.67% of Staph. aureus and 33.33% of CONS were resistant to cefoxitin. Nandini et al.16 reported that among the isolated gram-positive cocci, all were sensitive to linezolid and vancomycin, which were similar to the present findings. Sarwar (2016) also reported that among the isolated gram-positive cocci, all were sensitive to linezolid, 10% of Staph. epidermidis were resistance to vancomycin. It was evident that 100% of Staph. aureus and 57% to 89% of CONS were resistance to ceftriaxone and gentamicin respectively. Gentamycin 68.75% resistant found by Gezmu et al.<sup>17</sup> 75% of Staph. aureus and 69.2% of CONS were sensitive to ceftriaxone and 50% of Staph. aureus and 100% of CONS were sensitive to gentamicin were found by Mansour et al.19 which were not similar with present study. Bhani et al.20 reported that 50% of the isolated gram positive cocci were resistant to ceftriaxone and 75% were resistant to gentamicin, which corresponds with present study. The reported high resistance rates to one of the first line antibiotics may be due to the misuse and overdose of these antibiotics in DMCH as well as in the country.12

Antibiotic resistance among uropathogens has become a public health concern in Bangladesh.20 Under individual predisposing conditions, E. coli can multiply rapidly in the urinary tract of an UTI patient. In this study, 60.87% and 11.96% of isolated Esch. coli were detected as MDR and XDR strains, respectively, followed by 58.97% and 10.25% of Pseudomonas spp. as MDR and XDR strains, 52.38% and 14.29% of Klebsiella spp. as MDR and XDR strains, 50% and 5.56% of *Proteus* spp. as MDR and XDR strains, 43.75% and 6.25% of Enterobacter spp. as MDR and XDR strains, respectively and 66.67% Acinitobacter spp.as MDR strains (Table 5). The finding of the present study was supported by the results of the study done by Khanal (2006), Upadhaya et al. (2013) and Awasthi et al. (2015) noted the MDR causing UTI to be 56.09%, 48% and 42.86% respectively. Silpi et al. (2015) reported that most prevalent MDR in their study was E. coli (31.6%) followed by Klebsiella pneumoniae (30%) and the commonest XDR strains were detected from Pseudomonas aeruginosa (32.2%), followed by Klebsiella pneumoniae (27.8%). Increasing haphazard use of antibiotics and sales of substandard drugs are responsible for development of multi drug resistance among the bacteria.21 Due to development of drug resistance against commonly

used antibiotics among the bacteria the therapeutic options have

#### Conclusion

The frequency of UTIs associated with the use of indwelling urinary catheter. Many uropathogens isolated from CAUTI showed multi drug resistance. Hence proper care and safety measures should be emphasized for effective prevention of CAUTI. If prescribing of antimicrobials according to culture and sensitivity pattern can be practiced, inappropriate use of antimicrobials will be reduced.

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### **Conflicts of interest**

The author declares there is no conflict of interest.

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