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Catheter Associated Urinary Tract Infection: Aetiologic Agents and Antimicrobial Susceptibility Pattern in Ladoke Akintola University Teaching Hospital, Osogbo, Nigeria

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ABSTRACT

The objective of this study was to identify microbial pathogens associated with bacteriuria and UTI in patients with indwelling urethral catheters and determine their susceptibility patterns to commonly used antimicrobial agents in our institution. Catheter urine and catheter tip specimens of all the patients were analyzed by microscopy and culture on Blood, MacConkey and CLED agar plates. Pure colonies of isolated organism were biochemically characterized and disc diffusion antibiotic susceptibility was performed on each bacterial isolate. The commonest indication for catheterization is benign prostatic hyperplasia (BPH, 62.3%). One hundred and eight patients (88.5%) were urine culture positive for microbial pathogens with 126 microbial isolates while 14 (11.5%) were bacteriologically sterile. Ninety two of those positive (85.1%) each had one organism recovered, 14 (13.0%) had two organisms recovered and 2 (1.9%) had 3 organisms recovered. Klebsiella spp were the commonest pathogen isolated with 46 (36.6%), followed by Pseudomonas spp 34 (27.0%), Escherichia coli 26 (20.6%), Staphylococcus aureus 12 (9.5%), Proteus mirabilis 4 (3.2%), Candida albicans 4 (3.2%) and coagulase negative staphylococci 2 (1.6%). The in vitro antibiotic susceptibility pattern of the Gram negative organisms 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%), perfloxacin (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 perfloxacin (66.7% sensitivity) and ciprofloxacin (83.3% sensitivity) appear effective. We conclude that catheter-associated UTI in our institution is caused by multi-resistant microbial pathogens which has occurred consequent on prophylactic antibiotic therapy administered after catheterization. Emphasis should be placed on good catheter management rather than the use of prophylaxis, to reduce the incidence of catheter associated UTI. ***(Afr. J. Biomed. Res. 9: 141 – 148)***

Keywords: *Catheter, UTI, multi-resistant, pathogen*

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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 (CDC, 1979; Meers 1988; Warren 1997). Sixty six percent to 86% of these infections usually follow instrumentation of urinary tract, mainly catheterization (Martin and Bookrajian, 1962). The risk of acquiring a urinary tract infection (UTI) depends on method and duration of catheterization, the quality of catheter care and host susceptibility.

Reported infection rates vary widely, ranging from 1% - 5% after a single brief catheterization (Turck *et al*, 1962) to virtually 100% for patients with indwelling urethral catheters draining into an open system for more than 4 days (Kass, 1956). Over 20% of patients catheterized and maintained on closed drainage on busy hospital wards may be expected to become infected (Kunin and McCormack, 1966; Garibaldi *et al*, 1974). Host factors which appear to increase the risk of acquiring catheter associated-UTI include advanced age, debilitation and the postpartum state (Brumfitt *et al*, 1961; Kunin, 1979)

Catheter-associated UTI are caused by a variety of pathogens, including *Escherichia coli, Klebsiella, Proteus*, enterococci, *Pseudomonas, Enterobacter, Serratia* and *Candida*. Many of these micro organisms are part of the patients' endogenous bowel flora but they can also be acquired by cross-contamination from other patients or hospital personnel or by exposure to contaminated solutions or non-sterile equipment (Selden *et al*, 1971; McLeod 1958).

Catheter-associated UTI in healthy patients is often asymptomatic and is likely to resolve spontaneously with the removal of the catheter. Occasionally, infection persists and leads to such complications as prostatitis, epidydymitis, cystitis, pyelonephritis and Gram-negative bacteraemia particularly in high risk patients (Kunin, 1979). The last complication is serious since it is associated with a significant mortality but fortunately occurs in less than 1% of catheterized patients (Steere *et al*, 1979; Kreger *et al*, 1980).

Although community acquired UTI has been well investigated in different groups of patients in Nigeria (Akinkugbe *et al*, 1973; Ekweozor and Onyemenem, 1996; Odutola *et al*, 1998), only few studies (Oni *et al*, 2003) have investigated and documented the aetiological agents of catheter-associated UTI or their susceptibility pattern to antimicrobial agents. In our institution, catheterization is a frequent procedure performed for patients with urinary tract obstructive lesions such as benign prostatic hyperplasia who are awaiting surgery and also as a routine in the management of unconscious patients to monitor their urine output. In this study, we identified the microbial pathogens associated with bacteriuria and UTI in catheterized patients and determined their susceptibility patterns to commonly used antimicrobial agents. This, we hope, will serve as a guide in the selection of appropriate antimicrobial agents for prophylaxis and empiric therapy of catheter associated UTI in patients on indwelling urinary catheters in our institution.

MATERIALS AND METHODS

Subjects

This study is cross sectional involving 122 patients attending the urology clinic or admitted into different wards of Ladoke Akintola University Teaching Hospital. They all had indwelling urethral catheters inserted under aseptic condition for various medical and surgical indications (Table 2). Patients with symptoms of urinary tract infections prior to catheterization were excluded. For those attending the urology clinic, catheters are usually inserted and routinely changed after 2 or more weeks or changed when there are clinical complaints of fever, dysuria, cloudy urine, blockage or other symptoms of urinary tract infections. For those on admission, catheters are removed when they are deemed no longer necessary or when there are symptoms of infections.

Specimen collection

Prior to catheter change or removal from each patient, 10 ml of urine was obtained from the distal edge of the catheter tube (after cleaning with an antiseptic) using a sterile needle and syringe into sterile universal container (Kunin and McCormack, 1966; Kunin, 1979) and transported to the medical microbiology laboratory for analysis. The tip of the catheter removed from each patient was cut with a sterile surgical blade and also sent for culture.

Microscopy and culture isolation

Urine microscopy was performed on uncentrifuged catheter urine specimen to detect the presence of leukocytes, erythrocytes and other cells. A sterile calibrated wire loop was used to deliver a loopful (0.01ml) of urine onto each of Blood, MacConkey and CLED agar plates and incubated aerobically at 37^{o}C for 24-48 hours. A sterile forcep was used to pick the catheter tip and rubbed along the agar surfaces of each of the three media types and incubated accordingly. Significant growth of ≥ 100 bacteria/ml of catheter urine (Warren, 1997) was interpreted as at least one colony of bacterial organism per plate, while all organisms recovered from the catheter tip cultures were characterized.

Pure colonies of isolated organism on the culture plates were biochemically characterized to identify the species using recommended guidelines (Barrow and Feltham, 1993). Antibiotic susceptibility was performed on pure colonies of each species to commonly used antimicrobial agents using the disc diffusion method (Bauer *et al*, 1966) on Mueller-Hinton agar. The zone diameter of inhibition for each antimicrobial agent was compared with the NCCLS interpretive table (NCCLS, 1997) to determine sensitivity or resistance. Control strains of organisms used were *Staphylococcus aureus* NCTC 6571, *Escherichia coli* NCTC 10418 and *Pseudomonas aeruginosa* NCTC 10662.

Bio-data analysis

Relevant bio-data were obtained from each patient using a prepared standard proforma that include demographic data such as hospital number, age, sex, occupation, religion and marital status. Other data obtained were underlying illness, indication for catheterization, length of catheterization, prophylactic antibiotic used and symptoms attributable to catheterization. Analysis was done using SPSS 11.0 statistical package. Association between variables was determined using Chi-square with level of significance set at $p < 0.05$.

RESULTS

A total 122 patients with indwelling urinary catheters were studied, 106 were males while 16 were females, giving a male to female ratio of 6.6 to 1. The age range is 11 - 104 years with a mean age of 66.6 years. The age group 61-70 years constitutes the largest group with 39.3% followed by the age group 71-80 (26.2%) and age group 51-60 (18.0%). Over 90% of patients are above 50 years of age (Table 1).

Table 1:
Age and sex distribution of patients on indwelling urethral catheter at Ladoke Akintola University Teaching Hospital, Osogbo

Age group (yrs)/Sex	Male (%)	Female (%)	Total (%)
< 10	0	0	0 (0)
11-20	2	0	2 (1.6)
21-30	0	4	4 (3.3)
31-40	0	2	2 (1.6)
41-50	0	2	2 (1.6)
51-60	20	2	22 (18.0)
61-70	44	4	48 (39.3)
71-80	30	2	32 (26.2)
81-90	8	0	8 (6.6)
91-100	1	0	1 (0.8)
> 100	1	0	1(0.8)
Total	**106**	**16**	**122 (100)**

All the patients had indwelling urethral catheter inserted for a period ranging from 48 hours to over 28 days before change or removal (Table 2) and all were routinely placed on prophylactic systemic antibiotic following catheterization. The commonest indication for catheterization was (i.) bladder outflow obstruction due to benign prostatic hyperplasia (BPH) in 76 (62.3%) patients, carcinoma of the prostate 8 (6.6%), urethral stricture 8 (6.6%), testicular tumour 2 (1.6%): (ii) post-operative 14 (11.5%), (iii.) cerebrovascular disease 4 (3.3%), (iv.) intestinal obstruction 2 (1.6%), and (v) others 8 (8.2%). (Table 2)

Table 2:
Indication for indwelling catheterization in relation to length of catheterization among patients at Ladoke Akintola University Teaching Hospital, Osogbo

Indication for catheterization	Length of catheterization (days)					
	2-7	8-14	15-21	22-28	> 28	Total (%)
1. BPH	-	-	21	28	27	76 (62.3)
2. Ca prostate	-	-	1	2	5	8 (6.6)
3. Urethral stricture	-	3	3	2	-	8 (6.6)
4. Testicular tumour	-	-	-	-	2	2 (1.6)
5. Post-operative	14	-	-	-	-	14 (11.5)
6. CVD	-	4	-	-	-	4 (3.3)
7. Intestinal obstruction	1	1	-	-	-	2 (1.6)
8. Not stated	-	8	-	-	-	8 (6.6)
Total	**15**	**16**	**25**	**32**	**34**	**122 (100)**

Table 3:
Length of catheterization in relation to development of significant bacteriuria and UTI among patients at Ladoke Akintola University Teaching Hospital, Osogbo

Length of catheterization (days)	Significant bacteriuria		No significant bacteriuria		Total (%))
	UTI	No UTI	UTI	No UTI	
1-7	1	2	1	11	15 (12.3)
8-14	12	2	-	2	16 (13.1)
15-21	22	3	-	-	25 (20.5)
22-28	29	3	-	-	32 (26.2)
> 28	26	8	-	-	34 (27.9)
Total	**90**	**18**	**1**	**13**	
	108		**14**		**122 (100)**

Table 4:
Microbial isolates from patients with indwelling urinary catheter in LAUTECH Teaching Hospital, Osogbo

Isolate	Number (%)
Escherichia coli	26 (20.6)
Pseudomonas aeruginosa	26 (20.6)
Pseudomonas florescens	6(4.8)
Pseudomonas pyocyanea	2 (1.6)
Klebsiella aerogenes	16 (12.7)
Klebsiella pneumoniae	4 (3.2)
Klebsiella ozaena	4 (3.2)
Klebsiella spp	22 (17.5)
Proteus mirabilis	4 (3.2)
Staphylococcus aureus	12 (9.5)
Coagulase negative staphylococci	2 (1.6)
Candida albicans	4 (3.2)
Total	**126 (100)**

Of the 122 patients, 108 (88.5%) had significant bacteriuria, 14 (11.5%) had no bacteriuria and 91 (74.6%) had UTI. Of the 108 patients with significant bacteriuria, 90 (83.3%) had symptoms of UTI and > 5 white blood cells/ml of urine while only 1 (7.1%) of the 14 patients who were bacteriologically sterile had symptoms and > 5 WBC/ml of urine. Table 3 relates the length of catheterization to development of bacteriuria and urinary tract infections. One hundred and seven patients (87.7%) had urethra catheter in place for more than 1 week while only 15 (12.3%) had it for less than a week. Of the 107 patients, 105 had significant bacteriuria out of which 89 had UTI while only 2 had no bacteria in urine. Of the 15 patients with urethra catheter in place for less than 1 week, only 3 had significant bacteriuria out of which 1 had UTI while 12 had no bacteria in the urine but 1 of this had UTI..

A total of 126 microbial isolates were recovered from the 108 patients with significant bacteriuria. In 92 (85.1%) patients, only one species of organism was recovered while in 14 (13.0%) two species were recovered and in 2 (1.9%) 3 species were recovered. *Klebsiella spp* were the commonest pathogen isolated with 46 (36.6%), followed by *Pseudomonas spp* 34 (27.0%), *Escherichia coli* 26 (20.6%), *Staphylococcus aureus* 12 (9.5%), *Proteus mirabilis* 4 (3.2%), *Candida albicans* 4 (3.2%) and coagulase negative staphylococci 2 (1.6%). (Table 4).

The catheter tip specimen culture was positive for pathogens in all the 122 patients and essentially, the pathogens cultured were the same as those isolated from the 108 subjects with positive urine culture. The sensitivity of catheter specimen for diagnosis of catheter associated UTI is 98.9% but specificity is 41.9%, and positive and negative predictive values of 83.3% and 92.6% respectively. Although the sensitivity of catheter tip specimen was 100%, the specificity and negative predictive value is 0% (Table 5).

The *in vitro* antibiotic susceptibility pattern of the Gram negative organisms 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%), perfloxacin (65.5%) and ciprofloxacin (56.4%). (Table 6).

Table 5:
Diagnostic values of catheter specimen of urine and catheter tip

Method	Catheter urine		Catheter tip	
	with UTI	without UTI	with UTI	without UTI
Culture positive	90	18	91	31
Culture negative	1	13	0	0
Total	**91**	**31**	**91**	**31**
	122		**122**	

For catheter urine, sensitivity = 98.9%, specificity = 41.9%, PPV = 83.3%, NPV = 92.9%
For catheter tip, sensitivity = 100%, Specificity = 0%, PPV = 74.6%, NPV = 0%

Table 6:
In vitro susceptibility patterns of Gram negative bacterial pathogens in catheter – associated UTI in LAUTECH Teaching Hospital, Osogbo

Antibiotic		Amp (%)	Gent	Tet	Cot	Nit	Col	Cef	Nal	Cipro	Pef
E. coli (n =26)	S	0(0)	0(0)	4(18.2)	4(18.2)	10(38.5)	12(46.2)	0(0)	0(0)	0(0)	0(0)
	R	26(100)	26(100)	22(81.8)	22(81.8)	16(61.5)	14(53.8)	26(100)	26(100)	26(100)	26(100)
Klebs spp (n= 46)	S	0(0)	8(17.4)	6(13.0)	8(17.4)	18(39.1)	24(52.2)	14(30.4)	10(21.7	20(43.5)	20(43.5
	R	46(100)	38(82.6	40(87.0)	38(82.6)	28(60.9)	22(47.8)	32(69.6)	36(78.3	26(56.5)	26(56.5
Pseudo sp (n=34)	S	0(0)	2(5.9)	2(5.9)	2(5.9)	6(17.7)	4(11.8)	6(17.7)	4(11.8)	20(58.8)	14(41.2
	R	34(100)	32(94.1	32(94.1	32(94.1	28(82.3	30(88.2)	28(94.1	30(88.2	14(41.2)	20(58.8
Proteus spp	S	0(0)	0(0)	0(0)	0(0)	2(50)	0(0)	NT	0(0)	4(100)	4(100)
(n=4	R	4(100)	4(100)	4(100)	4(100)	2(50)	4(100)	NT	4(100)	0(0)	0(0)
Overall R (%) (n= 110)		110 (100)	100 (90.1)	98 (89.1)	96 (87.3)	74 (67.3)	70 (63.7)	86 (78.2)	96 (87.3	62 (56.4)	72 (65.5

Amp = Ampicillin, Tet = Tetracycline, Gent = Gentamicin, Cot = Cotrimoxazole, Col = Colistin, Nit = Nitrofurantoin
Nal = Nalidixic acid, Cef = Cefuroxime, Cipro = Ciprofloxacin, Pef = Perfloxacin, S = Sensitive, R = Resistant

Table 7:
In vitro susceptibility pattern of *S. aureus* in catheter-associated UTI in LAUTECH Teaching Hospital, Osogbo

Antibiotic		Pen	Clox	Tet	Ery	C/col	Gent	Cot	Cef	Cipro	Pef
S. aureus											
(n=12)	S	0(0)	2(16.7)	2(16.7)	4(33.3)	0(0)	0(0)	0(0)	4(33.3)	10(83.3)	8(66.7)
	R	12(100)	10(83.3	10(83.3	8(66.7)	12(100)	12(100)	12(100)	8(66.7)	2(16.7)	4(33.3)

Pen = Penicillin, Clox = Cloxacillin, Tet = Tetracycline, Ery = Erythromycin, C/col = Chloramphenicol, Gent = Gentamicin, Cot = Cotrimoxazole, Cef = Cefuroxime, Cipro = Ciprofloxacin, Pef = Perfloxacin
S = Sensitive, R = Resistant

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 perfloxacin (66.7% sensitivity) and ciprofloxacin (83.3% sensitivity) appear effective (Table 7).

DISCUSSION

Urinary catheterization is generally indicated to relieve urinary tract obstruction, to permit urinary drainage in patients with neurogenic bladder dysfunction and urinary retention, to aid urologic surgery and to obtain accurate measurement of urinary output in clinically ill patients. An estimated 4 million patients are subjected yearly to urinary catheterization and therefore at risk for catheter-associated infection and its related sequelae. In this study, 108 (88.5%) of the 122 patients studied had significant bacteriuria, while 91 (74.6%) had UTI. The infection rate was 13.3% (2/15) if catheter had been in place for a week or less and increase to 98.9% (89/107) if catheter has been in place for more than one week. Although this rate is lower than the 100% reported by Kass (Kass, 1956) after 4 or more days catheterization draining into open system, it is by far higher than those of Kunin and colleague (Kunin and McCormack, 1966) and Garibaldi *et al* (Garibaldi *et al*, 1974) who in separate studies on indwelling urethral catheters maintained (for more than one week) on continuous closed drainage system, reported rates of less than 25%. This means more attention should be placed on catheter care and in the prevention of errors in the closed drainage system which was employed in our study. Also, use of catheter should be limited to carefully selected patients so as to reduce the size of population at risk.

One host factor that predisposes to catheter associated UTI is advanced age (Brumfitt *et al*, 1961). The mean age of patients in this study is 66 years and the age group 61-70 years constitutes the largest group (39.3%) while over 90% of the patients were above 50 years of age. This finding agrees with a previous study (Oni *et al*, 2003) in another institution located in the same geographical zone as ours. Males were also predominantly affected in our study. Although this is a reversal of what obtains in simple uncomplicated UTI where females tends to be more commonly affected, it is known that males are prone to obstructive urinary lesion especially from BPH, cancer of the prostate and stricture which occurred with advancing age.

Despite the fact that all the patients had prophylactic systemic antibiotics as a routine after catheter change, an overall infection rate of 74.6% (91/122) was recorded. This calls for reassessment of the rational for prophylactic antibiotic use after catheterization. Several other studies (Turck *et al*, 1962; Kass, 1956; Kunin and McCormack, 1966; Garibaldi *et al*, 1974; Britt *et al*, 1977; Oni *et al*, 2003) have shown antibiotic prophylaxis to be ineffective and rather lead to emergence of resistant pathogens as evidenced in this study.

Catheter specimen of urine was sensitive in detecting UTI by culture in 98.9% of patients (90/91) but was only 41.9% specific. The predictive value of a positive culture was 83.3% and of negative culture 92.6%. This implies that positive culture may not necessarily indicate a UTI, however, a negative culture most of the time excludes a UTI.

In contrasts, catheter tip, which was 100% sensitive in detecting a UTI by culture, is associated with high false positives with 0% specificity. Therefore, positive culture of a catheter tip specimen is not indicative of UTI and its use in the investigation of catheter-associated UTI should be discarded. Some researchers (Stark and Maki, 1984; Isenberg, 1998) have found Foley catheter tips to be unsuitable and unacceptable for culture as demonstrated in our study.

The commonest pathogen isolated in this study was *Klebsiella spp* followed by *Pseudomonas spp, Escherichia coli, Staphylococcus aureus, Candida albicans* and CONS in that order. This is the pattern of distribution seen in most studies (Selden *et al*, 1971; McLeod 1958; Oni *et al*, 2003). Many of these pathogens are part of the patients' endogenous bowel flora but some may have been acquired by cross-contamination from other patients or hospital personnel or by exposure to contaminated solutions or non-sterile equipment. A recent study (Taiwo *et al*, 2005) in our institution has reported the presence of some of these organisms in the hospital environment. The infection was monomicrobial in 85% of patients and more than one isolate was recovered in about 15%. Although catheter associated UTI is frequently polymicrobial (Oni *et al*, 2003; Yoshikova *et al*, 1996), this was not the case in our study.

The antimicrobial susceptibility pattern confirms that most of the urinary isolates in our environment are resistant to the commonly used antibiotics including the cephalosporin and fluoroquinolones. This high resistant pattern could have resulted from poorly guided antibiotic prophylaxis after catheterization and empiric therapy of catheter associated UTI. In particular, the high resistance of the Gram negative isolates to the fluoroquinolones is worrisome as these are reserve drugs for treating resistant infections. Some researchers (Threfall *et al*, 1997; Oni *et al*, 2001; Oni *et al*, 2003; Livermore *et al*, 2002; Daini *et al*, 2005) have however pointed the danger of abuse of these drugs with consequent development of resistance, the effect of which we are beginning to see in our environment.

Since bacteriuria is almost inevitable on long term catheterization as reported by previous researchers (Kass, 1956; Turck *et al*, 1962; Warren, 1997), and as shown in our study, we advise that patient's catheters should be changed periodically to prevent formation of concretions and obstruction that can lead to infection. Although prophylactic systemic antibiotics have been known to delay onset of bacteriuria in catheterized patients, there is no justification for routine use as this practice has been shown to be associated with emergence of resistant pathogens (Warren, 1997). Treatment of catheter-associated UTI in this institution should be guided by the result of susceptibility test of isolated organisms.

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