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Original Paper

Urinary Pathogens and Their Antimicrobial Susceptibility in Patients with Indwelling Urinary Catheter

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ABSTRACT
The indwelling urinary catheter (IUC) is the most significant risk factor for developing nosocomial urinary tract infections (UTIs). In order to determine the spectrum of bacterial etiology and antibiotic resistance pattern of uropathogens causing catheter associated UTI, a convenient sample size of ninety-two (92) patients on urethral catheter was investigated. Ethical approval for the study was obtained from the OAUTHC research and ethical committee. Catheter stream urine samples were obtained from all patients and cultured on appropriate culture media. Suspected isolates were identified by a combination of standard tests and using MICROBACT GNA12A/B/E. Susceptibility of the isolates against thirteen (13) antibiotics was performed by the disc diffusion method. Significant bacteriuria was observed in 60.9% (56) catheter specimen urine (CSU) received, while 39.1% (36) were culture negative. Of the 56 positive culture, the predominant organisms were *Klebsiella oxytoca*, 28.6 %(16), *Proteus vulgaris,* 23.2% *(13)* and *Staphylococcus aureus,* 12.5% (7). Overall, the antimicrobial susceptibility results showed that all the isolates were highly resistant to the antibiotics tested. Over 50% resistance was recorded for trimethoprim/sulfamethoxazole, gentamicin and amoxicillin/clavulanic acid. More than 25% of the isolates were resistant to nitrofurantoin. This study indicates that catheter stream UTI caused by multiply resistant bacteria are common in our hospital. There is a need to establish standard guidelines on the care of catheter for all units in the hospital with a view to preventing nosocomial infections associated with the use of the catheter in patients. We also advocated prudent use of antibiotics.

Key words: Antibiotic resistance, Urinary catheter, Uropathogens, Urinary tract infection

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INTRODUCTION

Urinary tract infections (UTIs) are the most common infections found in the hospital as well as long-term care setting. The indwelling urinary catheter (IUC) is the most significant risk factor for developing catheter-associated urinary tract infections (CAUTIs). The risk of acquiring a urinary tract infection depends on the method and duration of catheterisation, the quality of catheter care, and host susceptibility among others. Several studies have indicated that between 75 and 80% of all healthcare associated UTIs follow the insertion of a urinary catheter (Bryan and Reynolds 1984; Bonadio *et al*., 2001). Although usually benign, CAUTI causes bacteremia in 2-4% of patients and have been associated with a case fatality rate three times as high as non-bacteriuric patients (Barkham *et al*., 1996; Tal *et al*., 2005).

Catheter-associated urinary tract infections are associated with increased morbidity, mortality, and costs resulting from additional diagnostic testing, change of treatment regimes and increased length of stay in the hospital (Bryan and Reynolds, 1984; Askarian *et al*., 2003).

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Although not all CAUTIs can be prevented, it is believed that the incidence can be reduced through active surveillance and by the proper management of the indwelling catheter (Apisarnthanarak *et al*., 2007). Therefore, this study was designed to determine the spectrum of bacterial etiology and antibiotic resistance pattern of uropathogens in catheter associated UTI and to provide local epidemiological data on CAUTI in our hospital in support of the activities of the Infection Control Unit.

MATERIALS AND METHODS

Study Setting and Design

The study was conducted at Obafemi Awolowo University Teaching Hospital, Ile-Ife, Southwestern, Nigeria between October 2007 and March 2008. A convenient sample size of ninety-two (92) patients on urethral catheter was included in the study. Ethical approval for the study was obtained from the OAUTHC Research and Ethical Committee. A specially designed surveillance form which required the primary physician attending to the patient to fill in the details was employed for the study. Where it was not possible, information on the patient was extracted from the case notes. The surveillance form was approximately used to determine the number of days for the onset of bacteriuria based on the following information: date of hospital admission, date of catheter insertion, reason, infection onset and specimen collection. In accordance with the study protocol, patients were monitored from the day the urinary catheter was inserted until a CAUTI was diagnosed, the patient was discharged, transferred or died, or until the 30 day surveillance period ends. Admission data (number of admissions and number of patient days) for each ward was also noted. A worksheet was designed for recording the results of all laboratory tests. Results of the microscopy and all positive cultures for any pathogens were reported immediately to the attending physician and or the Infection Control Unit.

Microbiological Tests

There was no serial catheter urine culture but catheter stream urine was collected from all patients suspected with CAUTI and on closed catheter drainage. Detailed specimen collection, procedure and transportation were based WHO guidelines (Lau *et al*., 2007; Long and Vince, 2007). Using, the calibrated loop (1µl) technique for semi-quantitative urine culture, the samples were cultured using CLED agar (Oxoid, UK). Plates were incubated aerobically overnight at 37°C. Those with significant growth were identified by standard bacteriological methods including colony morphology, Gram stain, catalase, coagulase test and the use of MICROBACT 12E (MB1130 – OXOID, UK) for Gram negative bacilli. Antibiotic sensitivity pattern of the bacterial isolates were determined by agar diffusion method and interpreted according to published guidelines (Rosenblatt, 1983; Chaitram *et al*., 2003).

Data Analysis

Analysis of all clinical and laboratory data was carried out using the SPSS. Parameters were compared using univariate and multivariate logistic regression and chi-square tests. Student t-test was used to compare the outcome of UTI due to catheterization. Categorical data was expressed as mean ± SD and a p-value of <0.05 was accepted as being statistically significant.

RESULTS

A total of ninety-two (92) patients on urinary catheter were surveyed in this study. There were 52 (56.5%) females with a culture positive rate of 70.6% (36) and 40 (43.5%) males with a culture positive rate of 78%. The mean age was 40.8 years (SD 19.6years). The distribution of the catheterized patients according to wards is as follows: post natal ward: 22(23.9%), gynaecological ward: 4(4.3%) and female medical ward: 14(15.2%) and male medical ward: 14(15.2%). In the adult surgical wards, there were 12 (13%) females and 14 (15.2) males, while pediatrics surgery was 6(6.5%) males. The sub-specialty wards like the Intensive Care Unit (ICU), Orthopedics, and Renal wards had 2 (2.2%) males each. The primary unit where catheter was inserted could not ascertained for fifty-two patients {52 (56.5%)}. In 40 patients for whom the point of insertion of catheter could be ascertained 33.7 % (Operating Theater 12 (13%) and wards 19(20.7%)) had catheter insertion between the theater and the wards while Accident and Emergency unit was 9(9.8%).

The average number of days for the onset of bacteriuria after catherisation was 12.2 days (range day 2- 60 days) in twenty-one (21) patients. It was difficult to determine exactly the onset of bacteriuria for seventy-one

(71) and duration of catheter placement in forty-one (41) patients, which on the average was 7days (range 1-90days ± 17) could not be determined since the data were missing from their record. Significant bacteriuria (10^5 colony forming unit/ml) was observed in 60.9% (56) of catheter specimen urine (CSU) received while 39.1% 36 did not have a significant growth.

Table 1: Distribution of Bacterial isolates from Culture Positive Specimens

Bacterial Organisms	Frequency (%) of Isolation
Acinetobacter iwoffi	2 (3.6.)
Citrobacter freundi	2 (3.6)
Escherichia coli	3 (5.4)
Enterobacter agglomerans	3 (5.4)
Klebsiella oxytoca	16 (28.6)
Klebsiella pneumoniae	4 (7.1)
Proteus vulgaris	13(23.2)
Providencial spp	1(1.8)
Pseudomonas aeruginosa	2 (3.6)
Serratia marcescens	2 (3.6)
Staphylococcus aureus	7 (12.5)
Yersinia enterocolitica	1(1.8)

Of the 56 specimens with significant growths, 87.5% (49) was due to a variety of gram-negative organisms while 12.5% (7) was attributed to *Staphylococcus aureus* alone. Amongst the gram-negative organisms, isolates from the genera, *Klebsiella*, 35.7% (20) and *Proteus*, 23.2% (13) were predominant, followed by *Escherichia* and *Enterobacter* that were 5.4% (3) each. Other genera such as *Acinetobacter*, *Citrobacter*, *Serratia* and *Pseudomonas* were 3.6% (2) each. *Providencia and Yersinia* had the least isolation rate (Table 2).

Taking an overall view of the antimicrobial susceptibility results of the isolates, they were highly resistant to the tested antibiotics. The resistance rate ranges from 50-100% for trimethoprim/sulfamethoxazole, nalidixic acid and amoxicillin/clavulanic acid. Over 75% of the isolates were resistant to gentamicin and more than 25% to nitrofurantoin. *Proteus vulgaris* had low resistance to ceftriaxone (15.4%) whereas E*. coli* was resistant across the different classes of antibiotics. Table 3 shows the specific susceptibility profile of each isolate to the antimicrobial tested.

DISCUSSION

Hospital-acquired catheter-associated urinary tract infection (CAUTI) is one of the major conditions of nosocomial infections in the health care setting. Our findings indicate that this can be a major problem also in our health care setting considering that 60% of patients on catheter had significant bacteriuria. The high percentage of significant bacteriuria recorded is consistent with similar observations elsewhere (Bonadio *et al*., 2001; Bonadio *et al*., 2005). Although, in this study, the culture positive rate reported is higher than 51% reported from South Africa (Habte *et al*., 2009), 43.3% from Ethiopia (Teshager *et al*., 2008), 30% from Nicaragua (Matute *et al*., 2004) and 39% from India (Kothari and Sagar, 2008), it was lower than the 88.5% culture positive rate reported in a study carried out within the same geographic environment as our hospital (Taiwo and Aderounmu, 2006). This can be explained by the differences in the population studied such as mean age, pre-morbid state and the reasons for admission.

However, evidence-based guidelines indicate that asymptomatic bacteriuria is not a clinically significant condition that warrant treatment intervention (Cope *et al*., 2009). This is particularly of significant interest in developing country where hospital acquired infection programs need optimum strengthening to reduce the incidence of catheter-associated UTI (Onipede *et al*., 2004) and to avoid unwarranted treatment of asymptomatic bacteriuria. In support of this point of view, this study observed that several key information that are essential to infection control activities were not documented. Information such as point and date of insertion of catheter, as well as the duration of catheter insertion which are important to determine the evolution (i.e. where and onset) of bacteriuria were missing in the hospital records of most of the patients.

Nevertheless, there was strong indication of symptomatic bacteriuria which warranted specimen collection except in a few. For cases that were not obviously symptomatic, additional information would have justified the need to commence antibiotics together with other interventions such as catheter change. This is contrary to Cope and colleagues' recommendation that better recognition of asymptomatic bacteriuria from symptomatic CAUTI, which are consistent with evidence-based guidelines, may play an important role in reducing unneeded antibiotic usage in hospitalized patients (Cope *et al.*, 2009).

Furthermore, the institution of a CAUTI prevention program which include staff education, ongoing monitoring of CAUTI incidence, monitoring catheter insertion and ensuring prompt removal, and careful attention to techniques for catheterization and catheter care has been advocated for developing countries (Willson *et al*., 2009). Therefore, the need to review of the existing policy and guidelines on the insertion and care of urinary catheter in our health care settings is indispensable.

The pattern of uropathogens cultured in this study is consistent with similar findings elsewhere in patients with CAUTI in South Africa (Habte *et al*., 2009), Kuwait (Al-sweih *et al*., 2005), Nigeria (Iregbu *et al*., 2002) and Iran (Askarian *et al*., 2003), in which Gram-negative bacilli, especially members of the family enterobacteriacae were the predominant isolates. However, in this study, members of the genus *Klebsiella* 35.7% were more commonly identified compared to *E. coli* 5.4%, an observation that has been documented in CAUTI elsewhere (Habte *et al*., 2009). Other researchers have also concluded that the frequency of isolation of *E. coli* as a causative agent of UTI is slowly declining and it is being replaced by other members of the enterobacteriaceae and enterococci (Ko *et al*., 2008; Teshager *et al*., 2008).

Overall, the antimicrobial susceptibility results showed that all the isolates were multiply resistant to the tested antibiotics. This high-level resistance to commonly used antimicrobial drugs by uropathogens has been documented (Anandkumar *et al*., 2003) and it is consistent with our findings. There are many factors that may be responsible for the high level of resistance such as the frequent use of antibiotics for therapy and prophylaxis, the ease of procurement of antibiotics in developing country and other socio-economic factors as documented by Okeke *et al*. (1999). Although extended spectrum beta-lactamase (ESBL) in uropathogens has been documented (Kothari and Sagar, 2008), in this study, there was no deliberate attempts to test for extended spectrum beta lactamase (ESBL) in the isolates and this is a limitation but one can safely assume that they are present judging by the high level of resistance across different classes of antibiotics. More research is clearly necessary to ascertain this form of resistance among uropathogens in this setting.

In conclusion, this study indicates that catheter stream UTI caused by multiply resistant Gram-negative bacteria is common in our hospital. Regular surveillance of the bacterial spectrum and their susceptibility patterns to various antimicrobial agents are therefore essential for a rational use of antimicrobial drugs. Also, there is a need to establish standard guidelines on the care of catheter for all units in the hospital with a view to preventing nosocomial infections associated with the device in patients.

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Table 2: Antimicrobial Resistant Pattern of Isolates

Organism (n)	STX (%)	NIT (%)	GEN (%)	NAL (%)	AXO (%)	OFL (%)	AUG (%)	CHL (%)	TET (%)	AMX (%)	CIP (%)	COL (%)	STR (%)
A. iwoffi (2)	1(50)	1(50)	2 (100)	2 (100)	NT	1(50)	1(50)	NT	NT	1(50)	NT	NT	NT
C. freundi (2)	2(100)	1(50)	2(100)	1(50)	NT	1(50)	NT	NT	NT	NT	NT	1 (50)	1 (50)
E. coli (3)	3 (100)	3 (100)	3 (100)	3 (100)	NT	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	NT	NT	NT
E. agglomerans (3)	3(100)	2(66)	3(100)	3(100)	NT	3 (100)	3 (100)	NT	NT	3 (100)	NT	NT	NT
K. oxytoca (16)	15 (94)	7(44)	14(88)	14(88)		10 (71)	11 (79)		NT	13 (81)	NT	NT	NT
K. pneumoniae (4)	4(100)	1(25)	3(75)	4(100)	2(50)	4 (100)	3(75)	NT	NT	2(50)	NT	2 (50)	2 (50)
P. vulgaris (13)	11(85)	8(61)	12 (92)	8(61)	2(15)	9 (69)	11 (85)	1(8)	NT	11 (85)	NT	NT	NT
Providencia spp (1)	1(100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	NT	NT	1 (100)	NT	NT	NT
P. aeruginosa (2)	2(100)	NT	2 (100)	1(50)	NT	1(50)	2(100)	2(100)	2(100)	2 (100)	2 (100)	NT	NT
S. marcescens (2)	2 (100)	NT	2 (100)	2 (100)	NT	2 (100)	1(50)	NT	NT	2(100)	NT	NT	NT
S. aureus (7)	7(100)	NT	6(86)	NT	5(71)	3(43)	7 (100)	3(43)	3(43)	7 (100)	3(43)	NT	NT
Y. enterocolitica (1)	1(100)	NT	1(100)	1 (100)	NT	1 (100)	1 (100)	NT	NT	1 (100)	NT	NT	NT

Legend: *Figures in parenthesis show number of isolates tested. NT=Not tested. STX= Trimethoprim/Sulfamethoxazole, NIT= Nitrofurantoin, GEN = Gentamicin , NAL= nalidixic Acid, AXO= Ceftriaxone OFX = Ofloxacin, AUG= Amoxicillin/Clavulanic acid, CHL = Chloramphenicol , TET = Tetracycline, AMX=Amoxicillin, ERY = Erythromycin, CIP= Ciprofloxacin , COL=Colistin, STR= Streptomycin, AMP= Ampicillin

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