

Evaluation of Uropathogens in Bladder Outlet Obstruction Secondary to Benign Prostatic Hyperplasia

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Abstract

Objectives: Although less than 3% of patients with Catheter Associated Asymptomatic Bacteria (CA-ASB) develop bacteremia with urinary pathogen; risk is 36 times increased with indwelling catheter. This study aimed at evaluating the uropathogens and the antimicrobial susceptibility test results were examined using automated identification and antimicrobial susceptibility testing system.

Methods: Urine cultures from 78 men with urinary retention secondary to BPH were evaluated. Distribution of the bacteria causing catheter associated bacteremia and their antimicrobial susceptibility test results were examined using automated identification and antimicrobial susceptibility testing system.

Results: A large proportion of patients with CA-ASB were older (≥ 60 years; $P=0.02$). The prevalence of infection was significantly higher in patients on urethral catheters than those on suprapubic catheters. ($P=0.011$) There was a high prevalence of micro-haematuria and proteinuria (60.5% and 37.2% respectively). *Escherichia coli* was the commonest organism found in all age groups. There was increased resistance of organism to the four commonly used urinary tract antibiotics (ampicillin, pefloxacin, levofloxacin and erythromycin). The prevalence of multi-resistance was 10.8%.

Conclusion: In a total of 78 samples, 83.3% showed significant growth of pathogens. A slightly more cases of CA-ASB were recorded among elderly patients (≥ 65 years; 52.3 %). Nitrofurantoin is recommended as the first drug of choice in this country if not contraindicated.

Introduction

Catheter Associated Asymptomatic Bacteria [CA-ASB] in patients with indwelling urethral catheter, suprapubic catheter, or intermittent catheterization has been defined as the presence of $\geq 10^5$ cfu/mL or ≥ 1 bacterial species in a single catheter urine specimen in a patient without symptoms compatible with UTI [1]. Urinary catheterization is very prevalent in hospitals especially in the initial management of patients with Benign Prostatic Obstruction [BPO] [2].

The duration of catheterization varies from patient to patient and has been reported to be the most important factor for the development of CA-ASB in the developed world [1]. Other notable risk factors include the lack of systemic antimicrobial therapy after catheterization, microbial colonization of drainage bag, blood transfusion, place of catheter insertion and older age among others [3].

There are significant consequences of CA-ASB which are usually associated with an inflammatory response in both short- term and long- term catheterized patients [4].

Although less than 3% of subjects with CA-ASB develop bacteremia with the urinary isolate [4], the risk of bacteremia in men with indwelling catheters in some centers has been reported to increase from 3 to 36 times compared to that of men without an indwelling catheter [5]. In addition, infectious complications that may arise in patients with CA-ASB include urinary catheter blockade, bladder calculus formation, urethritis, abscesses and prostatitis [6]. Non-infectious complications include nonbacterial urethral inflammation, urethral strictures, mechanical trauma, and mobility impairment [7,8].

Considering these sequelae, CA-ASB in a patient with BPO can lead to a major health calamity due to its recurrence nature. Screening for and treatment of CA-ASB are recommended to reduce this infection in catheterized patients which may develop secondary to mucosal bleeding during catheter placement [1]. Identifying patients at high risk for bacteremia would enable clinicians to target those patients for interventions such as giving antimicrobial agents, early catheter removal or surgery. Therefore, research directed at evaluating the uropathogens in men with BPO should lead to new and improved diagnosis, prevention, and treatment options.

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It is with this background that this study was carried out to evaluate the uropathogens in men with BPO receiving care from Ekiti State University Teaching Hospital, Ado-Ekiti, South western Nigeria.

Materials and Methods

Patients

The study was a cross sectional study conducted at Ekiti State University Teaching Hospital, Ado-Ekiti, Nigeria. The study lasted a period of 12 months; from March 2016 to February 2017.

Inclusion criteria

All male patients with a diagnosis of BPO on catheter for more than 48 hours who were willing to participate in the study by signing the consent form were included in the study.

Exclusion criteria

All patients who were chronically bed ridden and those with obvious psychiatric illness, patients on antibiotic therapy and those who were symptomatic for UTI were excluded from the study.

Sample collection and processing

Clean-catch, catheter urine samples from the patients were obtained and processed within 2 hours of collection. Each well mixed specimen was inoculated using a standard wire loop into blood and MacConkey agar or using only Cysteine Lactose Electrolyte Deficient [CLED] agar and incubated aerobically at 37°C for 24 hours.

Urine was examined macroscopically for colour and turbidity. Microscopic examination of centrifuged urine sediments was done by examination under x 40 objective for pus cells, red blood cells, casts, crystals and parasites. Urinalysis was done on all samples.

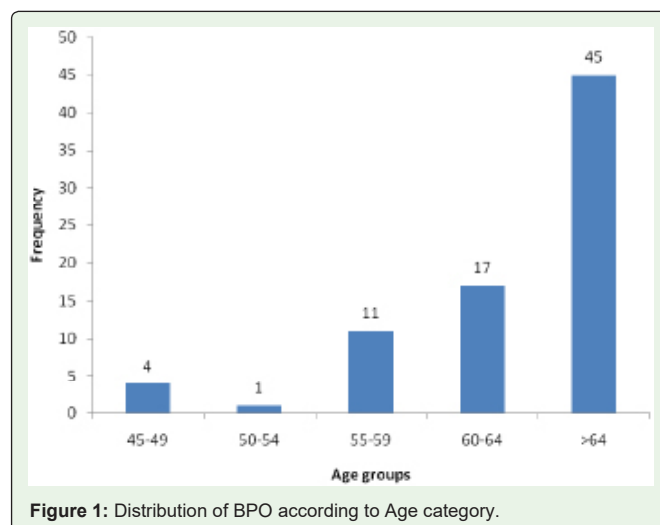
Culture was examined for significant growth after incubating for 24 hours. Bacteriuria of 103/μL and above was considered as significant growth. Colonies were characterized using a combination of colonial morphology, Gram staining, standard biochemical and serological tests where appropriate.

Antibiotic sensitivity testing was performed using the modified Kirby Bauer disc Diffusion method. [9] Pure colonies of isolated organism were suspended in sterile normal saline inside bijou bottles and the turbidity of the suspension adjusted to 0.5 McFarland's standard. A sterile cotton swab was dipped into the suspension and squeezed against the side of the bottle. The swab was then used to inoculate already dried Mueller Hinton agar before the application of single antibiotic discs and subsequently incubated at 37°C aerobically for 18-24 hours.

Zone diameters of inhibition around each disc were measured using a calibrated ruler and interpreted according to National Committee for Clinical Laboratory Standard (NCCLS). *Escherichia coli* (ATCC 25922), *Staphylococcus aureus* (ATCC (25923) and

Table 1: Urine growth of pathogen according to age group.

Age category in years	45-49	50-54	55-59	60-64	≥65	χ ²	p-value
Culture positive	4	0	10	17	34	11.615	0.02
No growth	0	1	1	0	11		



Pseudomonas aeruginosa (ATCC 2785) were used as control for gram negative, gram positive and pseudomonas isolates respectively.

The antibiotics discs used included Ofloxacin (5μg), Augmentin (10μg), Levofloxacin (5μg), Cefuroxime (30μg), Cefotaxime (30μg), Ceftriaxone (30μg), Nitrofurantoin (300μg), Gentamycin (30μg), Erythromycin (5μg), Perfloracin (5μg) and Ampicillin (10μg).

Ethical Approval

Ethical approval was given by Ekiti State University Teaching Hospital ethical committee.

The study was conducted in accordance with Helsinki Declaration, 1989 Revision. All participants had written informed consent before participation in the study.

Statistical analysis

Data was analyzed using Statistical package for Social Sciences version 20; qualitative variables were reported as percentages in frequency tables. Cases of CA-ASB, isolated organisms and their sensitivity patterns were reported in proportion of the total no of cases. Level of significance was set at $p < 0.05$.

Results

A total of 78 patients were recruited into the study. The age range was 45-86 years. Mean age was 67.6±10.07. The prevalence of CA-ASB was 83.3%.

Figure 1 shows that BPO was commonest at 65 years and above.

Table 1 shows that growth of pathogens was significantly higher in the age group 65 years and above.

Table 2 shows that the most prevalent clinical presentation of BPO was urinary retention followed by dysuria.

Table 2: Demographic and clinical characteristics of study population.

Parameters	Frequency
Mean age (SD)	67.6(10.07)
Mean weight (SD)	59.4 (8.7)
Mean height (SD)	1.6 (0.08)
Currently married (%)	71(91.0)
Not currently married (%)	7(9.0)
No/primary education (%)	20(25.6)
Secondary education (%)	14(17.9)
Tertiary education (%)	44(56.4)
Currently employed (%)	26(33.3)
Not currently employed (%)	52(66.7)
Haematuria (%)	8(10.3)
Dysuria (%)	45(57.7)
Frequency (%)	3(3.8)
Hesitancy (%)	30(38.5)
Urinary retention (%)	55(70.5)
Past history of retention (%)	40(51.3)
Past history of UTI (%)	30(38.5)
Duration of catheterization (%)	
1. <30 days	50(64.1)
2. ≥30 days	28(35.9)
P=0.248	
Type of catheterization (%)	
1. Urethral	51(65.4)
2. Suprapubic	27(34.6)
P=0.011	
Where catheter was passed (%)	
1. Private hospital	37(47.4)
2. Emergency unit of teaching hospital	34(43.6)
3. Outpatient clinic	7(9.0)
P=0.611	

Table 3 shows that the commonest urinalysis finding in BPO was haematuria followed by proteinuria. Commonest microscopic finding was pyuria and commonest pathogen was E.coli.

Besides, nitrofurantoin was the most sensitive drug in BPO and the quinones have the highest resistant pattern.

Discussion

Benign Prostatic Hyperplasia (BPH) has been reported as the most common cause of urinary retention in older men [10]. The mean age of men with urinary retention secondary to BPH in this study was 67.6%±10.07 years. This is similar to the report of Yenli and colleagues who also reported the mean age of 62.8±16.8 years among Ghanaian men with urinary obstruction secondary to BPH [11]. The prevalence of 83.3% was recorded in this study. This is a very high prevalence compared to 33% recorded by Oshodi and

Table 3: Microbiological and biochemical evaluation of the study population.

Parameters	Frequency (%)
Urinalysis	
Micro-haematuria	48(61.5)
Protein	29(37.2)
Leucocytes	3(3.8)
Glucose	2(2.6)
Nitrite	2(2.6)
MICROSCOPY	
RBC	39(50.0)
WBC(>5)	34(43.6)
WBC(<5)	44(56.4)
Bacteria	14(17.9)
Cast	4(5.1)
Culture positive	65(83.3)
Isolated Organism (N=65)	
E.coli	31(47.7)
Kebsiella	15(23.1)
Staph.aureus	10(15.4)
Proteus mirabilis*	7(10.8)
Pseudomonas aeruginosa*	5(7.7)
Sensitivity Pattern (N=65)	
Nitrofurantoin	39(60.0)
Cefuroxime	21(32.3)
Ceftazidime	17(26.2)
Gentamicin	12(18.5)
Ofloxacin	9(13.9)
Ciprofloxacin	3(4.6)
Augmentin	2(3.1)
Ampicillin	0(0.0)
Perfloxacin	0(0.0)
Erythromycin	0(0.0)
Levofloxacin	0(0.0)
Multi-resitant	7(10.8)**

*2 samples had more than one organism; **Organism resistant to all tested drugs.

colleagues in their study of UTI among patients with BPH [12]. This is in agreement with the fact that indwelling catheter is associated with increased frequency of CA-ASB [1].

The tendency to develop CA-ASB increases with advance age. In our study, we discovered that older men developed CA-ASB with men aged 65 years and above having significantly higher bacteria colonization than younger men (P=0.002). This finding may be due to the fact that increasing age is associated with decreased resistance to bacterial colonization, altered bladder emptying, poor perianal hygiene and urinary incontinence capable of enhancing the likelihood of developing infection/contamination [10].

The commonest presentation was complete cessation of urine (70.5%). This is majorly due to the fact that men in this country

do not usually seek medical care until their medical condition has deteriorated. Thirty-four (43.6%) patients presented at the emergency department for the first time. This may be attributable to many factors *visa-viz* out-of-pocket payment for medical services, hospital protocols leading to prolonged waiting during consultations, ignorance and believe in traditional or alternative therapies. All these usually lead to delay in seeking early medical intervention. There is the need to urgently address the issue of medical insurance in this country as it is done in developed world.

In this study, about half of the patients (47.4%) presented to the private hospitals not necessarily because of cheaper services but due to prompt attention they get during the acute emergency of urinary obstruction. At times proximity of their residential place to the private hospitals may be responsible for the higher number of patients there rather than the tertiary care centre. Nonetheless, there was no significant difference in the development of CA-ASB ($P=0.611$).

The prevalence of infection was significantly higher in patients on urethral catheters than those on suprapubic catheters. ($P=0.011$) This is in agreement with Saint and colleagues study [8] that the use of suprapubic catheters is associated with a lower risk of UTI than the use of urethral catheters.

However, shorter duration of catheterization [<30 days] appear not to influence the outcome of CA-ASB in this study. There was no clear reason for this finding. Further studies into these trends are necessary.

Furthermore, evaluation of the urinalysis in our study indicated that the most prevalent abnormality was micro-haematuria (61.5%). This may be due to recurrent mucosal bleeding as a result of catheter placement at the initial management of the urinary obstruction or subsequent catheter replacement. This is similar to the argument of Hooton and colleagues [1] that it is necessary to screen for and treat CA-ASB in order to reduce this infection in catheterized patients which may develop secondary to mucosal bleeding during catheter placement [1]. There was also high prevalence of proteinuria (37.7%) which may be a pointer to a degree of disturbances in both the glomerular filtration and tubular reabsorption of proteins. This is indicative of a slight glomerular dysfunction and a permanent defect in the proximal tubule to reabsorb proteins probably due to a delay in the management of the obstruction [13]. This is even worse in our environment where 51.3% had previous history of urinary retention. It is important to educate people in this country on the need for early referral to a specialist when any lower urinary tract symptom is noted.

Moreover, the commonest uropathogens in this study were *E.coli*, *Klebsiella*, *Proteus*, and *Pseudomonas* species with a prevalence of 47.7%, 15.4% and 7.7% respectively. This is not too different from the finding of Oshodi and colleagues who reported a high prevalence with *Proteus* spp, *Pseudomonas* spp and *E.coli* in northern Nigeria [12]. But while *E.coli* was the commonest in our study, Oshodi and colleagues found the commonest organism to be *Proteus* spp. No reason could be immediately adduced for this difference but may be related to slight socio-cultural differences between the people from the western part of Nigeria and those from the northern part [14].

The isolated uropathogens were mostly sensitive to nitrofurantoin, followed by cefuroxime and ceftazidime. High resistance to pefloxacin, ampicillin, levofloxacin, and erythromycin in this study

is similar to the finding of Oshodi and colleagues [12]. This implies that the resistant strains may have undergone directional selection where a single phenotype is favored, causing the trait frequency to continuously shift in one direction. The favored trait will then increase in frequency independent of its relative dominance over others [12].

The increased resistance to fluoroquinolones is in agreement with Zhang et al, Osterlund et al and Goettsch et al [15-18]. This is in support of our earlier reasons. However, a recent meeting organized by the National Institute of Allergy and Infectious Diseases (NIAID) in the USA seemed to promote the use of fluoroquinolones as the first empirical treatment for all complicated UTIs, including CAUTIs [19,20]. Whilst this policy might be practical, it may be difficult to extrapolate this to our community because of the high tendencies to abuse drugs.

The prevalence of multi-resistance (10.8%) recorded in this study requires further evaluation beyond the scope of this study.

Conclusion

There is high prevalence of CA-ASB in Nigeria and the commonest uropathogen is *E.coli*. Nitrofurantoin is the most common sensitive antibiotic but there are high multi-resistant strains. Quinones and penicillin are not first line medications in the management of CAUTIs in this country.

Limitations

This study has some limitations. The fact that only eleven discs were tested has ruled out other antibiotic discs that may show sensitivity. Besides, only 78 urine samples were tested which is rather too few to be generalized to the entire population. Also, being a hospital based study; a community based research may yield better results.

Since no urine sample was collected prior to catheter placements, some of the patients may have harbored infection that was only manifesting after catheter has been passed. Thus giving rise to a false CA-ASB.

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