Ahead of Print

Turk J Urol 2018 • DOI: 10.5152/tud.2018.25588

TURKISH JOURNAL OF UROLOGY

GENERAL UROLOGY

Original Article

Comparison of uropathogens and antibiotic susceptibility patterns in catheterized ambulant middle-aged and elderly Nigerian patients with bladder outlet obstruction

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Cite this article as: Adegun PT, Odimayo MS, Olaogun JG, Emmanuel EE. Comparison of uropathogens and antibiotic susceptibility patterns in catheterized ambulant middle-aged and elderly Nigerian patients with bladder outlet obstruction. Turk J Urol 2018: DOI: 10.5152/tud.2018.25588.

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Submitted:
21.07.2017

Accepted:
21.02.2018

Available Online Date:
05.06.2018

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Available online at
www.turkishjournalofurology.com

ABSTRACT

Objective: Advanced age is one of the notable risk factors for catheter-associated urinary tract infections (CAUTIs), and differences between middle aged and elderly men with CAUTIs is poorly understood. This study aimed at comparing the pattern of urinary pathogens and antibiotic susceptibility in ambulant catheterized middle-aged and elderly Nigerian men.

Material and methods: One hundred and fifty-four patients catheterized for >48 hours had provided clean catch mid-stream urine samples for microscopic analysis, culture and sensitivity tests. Eighty-two men aged <65, and 72 men aged ≥65 years matched for age, level of education, occupation and marital status were compared.

Results: Prevalence of CAUTIs among middle-aged men was middle-aged men was higher than the elderly (90.2% and 80.6% respectively) but this was not statistically significant (p=0.086). CAUTIs in middle-aged men with suprapubic catheters were significantly more frequent than those with urethral catheters (p=0.000). The prevalence of CAUTIs in middle-aged men with urethral stricture was different from other causes of bladder outlet obstruction (p=0.004). Men with indwelling catheters longer than 2 weeks had higher CAUTIs (p=0.000). *Escherichia coli* was the commonest pathogen in both groups while nitrofurantoin was the most sensitive drug.

Conclusion: There are differential rates of CAUTIs in both the middle-aged men and the elderly with bladder outlet obstruction in our environment. The knowledge of the common pathogens and the antibiotic susceptibility will prevent irrational antibiotic use. Middle-aged men had higher prevalence of CAUTIs when *Proteus* spp. was the infectious agent. However, *E. coli* was the commonest pathogen of CAUTIs in all men. Also, middle- aged men with suprapubic catheters had higher rates of CAUTIs. Nitrofurantoin was the best drug in all men with CAUTIs but elderly men had higher rates of multi-resistance.

Keywords: CAUTIs; comparison; elderly men; middle aged; susceptibility; uropathogens

Introduction

The insertion of a catheter into the bladder increases the susceptibility of a patient to urinary tract infections (UTIs). Being a foreign body, it serves as the initiation site of infection by introducing opportunistic organisms into the urinary tract. The majority of these uropathogens are fecal contaminants or skin residents from the patient's own native or transitory microflora that colonize the peri-urethral or perineal area.[1-5] Bacterial entry into the bladder can occur at the time of catheter insertion, through the catheter lumen, or along the catheter-urethral/catheter-skin interface.[6]

Indwelling urinary catheters favour the colonization of uropathogens by different mechanisms. They serve as a surface for the attachment of host cell binding receptors that are recognized by bacterial adhesins, thus enhancing microbial adhesion. Besides, urinary catheters may damage the protective uroepithelial mucosa, which leads to the exposure of new

binding sites for bacterial adhesins.[7] Also, the presence of the indwelling catheter in the urinary tract disrupts normal mechanical defences of the host, resulting in an overdistension of the bladder and incomplete voiding that leaves residual urine in the bladder for microbial growth.[8] Advanced age and debilitation, among other factors, are equally important factors which tend to increase the risk of catheter-associated urinary infections (CAUTIs) in men.[9]

Catheter-associated urinary infections where a patient had an indwelling urinary catheter not less than 48 hours before onset of the event, are the most common type of nosocomial infections, accounting for over 1 million cases annually[10] or over 40% of all nosocomial infections in hospitals and nursing homes[11-13] and constitute 80% of all nosocomial UTIs.[14] Due to this high incidence, the overall cost for medical intervention of nosocomial UTIs is staggering, with an estimated $424 million to $451 million spent annually in the United States to manage these infections in the year 1996.[15] These costs will inevitably rise due to advances in preventive medicine that extend life expectancy leading to increased number of middle aged and the elderly people. The elderly (defined as age group ≥65 years) population as at 2007 accounted for approximately 12.6% of the total population of the United States[16], their health care expenses amounted to about one-third[17] of the estimated $1 trillion in U.S. health expenditures.[18] When both age groups (middle aged and elderly) are considered, cost of treatment would be a fortune to any nation.

Despite the imminent threat of infection from potent opportunistic nosocomial multi-resistant strains, most cases of catheter-associated bacteriuria or the presence of bacteria in the urine are asymptomatic. However, when an episode of CAUTI becomes symptomatic, the resulting sequelae can range from mild (fever, urethritis, and cystitis) to severe (acute pyelonephritis, renal scarring, calculus formation, and bacteremia) pathologic conditions. Left untreated, these infections can lead to urosepsis and death.[13,19] Furthermore, the extensive uses of antimicrobial agents have invariably resulted in the development of antibiotic resistance, which, in recent years, has become a major problem worldwide.[20]

Since the incidence of CAUTIs is a major health concern all over the world world, research directed at understanding the uropathogens and susceptibility patterns of CAUTIs, especially considering the middle aged and the elderly is imperative. Besides, the etiology of UTI and the antibiotic resistance of uropathogens have changed over the past years, both in the community and among the cases with nosocomial infection.[21,22] But there are few literatures that have compared the uropathogens and susceptibility patterns in the middle aged [45 to 64 years of age] and elderly (aged ≥65 years) male patients with CAUTIs. Therefore, this study has important implications for physicians in prescribing empirical treatment and appropriate management of the patients catheterized with the indication of bladder outlet obstruction (BOO). In addition, it will help authorities to formulate antibiotic prescription policies.

This study aimed at comparing the types of urinary pathogens and antibiotic susceptibility patterns in catheterized ambulant middle-aged and elderly men.

Material and methods

This is a prospective study conducted at urology outpatient clinic of Ekiti State University Teaching Hospital, Ado-Ekiti. From 1st March, 2015 to 28th February, 2016. All these patients had BOO accepted secondary to benign prostatic enlargement, prostate cancer and urethral stricture. A size 16/18 Fr Foley catheter was inserted per urethra or through the suprapubic cystostomy tract under strict asepsis for the aforementioned indications.

Inclusion criteria

Among all ambulant ≥45 year-old male patients catheterized for >48 hours only those that were willing to participate by signing the consent form were included in the study. All recruitments were within the study period of 12 months.

Exclusion criteria

Female patients, all chronically bedridden male patients with spinal cord injury, cerebrovascular accident and other neurological diseases (eg. multiple sclerosis, spinal stenosis), those with obvious psychiatric illness, diabetes mellitus, chronic alcoholism, patients currently using antibiotics or any immunosuppressive drugs were excluded from the study. Patients with abdominal stoma and perineal wounds were also excluded.

The pattients that met the inclusion criteria had their body mass indices (BMIs) calculated as weight in kilograms divided by height in square meters.

Specimen processing

About 20 mL of mid-stream urine sample form each patient draining through Foley catheter were collected by “clean catch” method into a properly labelled sterile universal bottle. All samples were transported to Microbiology Laboratory of Ekiti State University Teaching Hospital, Ado-Ekiti, Ekiti State, Nigeria within 30 mins of sample collection. At the Medical Microbiology laboratory, each throroughly mixed specimen was inoculated using a standard wire loop into blood and MacConkey agar or using only cysteine lactose electrolyte deficient (CLED) medium (Himedia, Mumbai, India) and incubated aerobically at 37°C for 24 hours.

Urine samples were examined macroscopically for colour and turbidity and and the results were documented. Centrifuged urine sediments were examined microscopically under 40 x magnification for pus cells, red blood cells, casts and crystals and parasites.

Culture media was examined for significant growth after 24 hours. Bacteriuria of $10^5/\mu L$ and above was considered as significant growth.[23] 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.[24] Pure colonies of isolated organism were suspended in sterile normal saline inside Bijou bottles and the turbidity of the suspension was 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 on already dried Mueller-Hinton agar before the application of single antibiotic disc 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) criteria. *Escherichia coli* (ATCC 25922), *Staphylococcus aureus* (ATCC 25923) and *Pseudomonas aeruginosa* (ATCC 2785) were used as control for gram negative, gram positive and pseudomonas isolates respectively. The antibiotic discs used included ofloxacin (5 μg), amoxicillin/clavulanate (10 μg), levofloxacin (5 μg), cefuroxime (30 μg), ceftazidime (30 μg), ceftriaxone (30 μg), gentamycin (30 μg), erythromycin (5 μg), perfloxacin (5 μg), ampicillin (10 μg) and nitrofurantoin (300 μg).

Ethical issues

Ethical clearance was obtained from the Ethics and Research Committee of the Ekiti State University Teaching Hospital, Ado-Ekiti, Ekiti State, Nigeria.

Statistical analysis

Data were analysed using Statistical Package for Social Sciences version 20 (IBM SPSS Statistics; Armonk, NY, USA); qualitative variables were reported as percentages in frequency tables. Cases of CAUTIs, isolated organisms and their sensitivity patterns were reported as percentage of the total number of cases in each of the two age groups. Association between CAUTIs and other variables such as age group, diagnosis, type and duration of catheter was assessed using *chi*- square test. Similarly, bivariate association between the isolated organisms and the age groups was assessed using chi-square test. Level of significance was set at $p<0.05$.

Results

A total of 154 patients participated in this study. Eighty-two men were middle-aged while 72 men were elderly. The age range for the middle- aged patients was 45-64 years (mean age, 55.94±6.8 years) while it was 65-86 years (mean age, 75.33±5.7 years) for the elderly.

The mean BMI for the middle aged was 24.15±3.66 kg/m^2 (range=18.0-32.90) while it was 22.45±2.61 kg/m^2 in the elderly (range=16.70-29.30). There was a statistical difference in the means (p=0.000). In both groups BMIs did not significant correlate with CAUTI (t=1.545, p=0.127).

The socio-demographic variables of the patients are shown in Table 1. The ratio of the middle aged men to the elderly was 1:1

Table 1. Socio-demographic characteristics of the study population

	Age group (years)				
SD characteristics n=154	**<65 (%)**	**≥65 (%)**	**X^2**	**df**	**p**
Tribe					
Yoruba	82 (53.2)	72 (46.8)			
Educational status					
Literate	31 (48.4)	33 (51.6)			
Illiterate	51 (56.7)	39 (43.3)	1.017	1	0.330
Occupational status					
Currently employed	23 (64.9)	26 (53.1)			
Currently unemployed	59 (56.2)	46 (43.8)	1.149	1	0.303
Marital status					
Currently married	65 (50.8)	63 (49.2)			
Currently unmarried	17 (65.4)	9 (34.6)	1.851	1	0.200

Table 2. Prevalence of CAUTIs according to duration and route of urine drainage in both groups

Variables n=154	CAUTI YES (%) n=132	CAUTI NO (%) n=22	X^2	df	p
Age group (years)					
<65	74 (90.2)	8 (9.8)			
65 and above	58 (80.6)	14 (19.4)	2.939	1	0.086
Route of urine drainage					
Urethral	59 (76.6)	18 (23.4)			
Suprapubic	73 (94.8)	4 (5.2)	10.394	1	0.002
Duration of catheterization					
<2 weeks	8 (40.0)	12 (60.0)			
≥2 weeks	124 (92.5)	10 (7.5)	39.228	1	0.000

Age	Route of urine drainage	CAUTI Yes	CAUTI No	Total	X^2	p
<65 yrs	Urethral	25 (75.8%)	8 (24.2%)	33 (100.0%)	13.163	0.000
	Suprapubic	49 (100.0%)	0 (0.00%)	49 (100.0%)		
≥65 yrs	Urethral	34 (77.3%)	10 (22.7%)	44 (100.0%)	0.778	0.286
	Suprapubic	24 (85.7%)	4 (14.3%)	28 (100.0%)		

Table 3. Prevalence of CAUTI according to clinical diagnosis at different age groups

Age	Route of urine drainage	CAUTI Yes	CAUTI No	Total	X^2	p
<65 yrs	BPO	31 (93.9%)	2 (6.1%)	33 (100.0%)	10.877	0.004
	PCA	8 (61.5%)	5 (38.5%)	13 (100.0%)		
	US	35 (97.2%)	1 (2.8%)	36 (100.0%)		
≥65 yrs	BPO	34 (77.3%)	10 (22.7%)	44 (100.0%)	1.120	0.5
	PCA	21 (87.5%)	3 (12.5%)	24 (100.0%)		
	US	3 (75.0%)	1 (25.0%)	4 (100.0%)		

BPO: benign prostatic obstruction; PCA: prostatic cancer; US: urethral stricture; CAUTI: catheter-associated urinary infection

and there was no significant difference between the two groups with respect to age, marital status, level of education and occupation.

Table 2 shows the route of urine drainage. In the middle-aged men, 100% of those who had suprapubic drainage developed CAUTI. This was significantly different from those who had urethral drainage (p=0.000). Whereas in the elderly, 85.7% of men on suprapubic drainage had CAUTI. There was no statistically significant difference compared to elderly men (77.3%) on urethral drainage.

The duration of catheterization was significantly associated with CAUTI (p<0.000). Majority of the middle-aged men had catheter in situ for more than 2 weeks (92.5%) whereas few (7.5%) elderly men had been catheterized for more than 2 weeks. This difference was statistically significant.

The prevalence of CAUTI vis-à-vis the clinical diagnosis is depicted in Table 3. There was a significant difference in the prevalence of CAUTI among men with urethral stricture, prostate cancer, BPO in the middle aged (p=0.004) when compared to the elderly. Also, US was seen less frequently in the elderly compared to the middle aged. The prevalence of CAUTI in BPO and US was higher in middle aged than in the elderly.

Table 4 shows that *E. coli* was the most prevalent uropathogen in both age groups. However, among the isolated uropathogens,

Table 4. Prevalence of isolated organisms among men in the two groups

Isolated organism	Age group <65 (%)	Age group ≥ 65 (%)	X^2	df	p
***Pseudomonas* spp**					
Yes	8 (9.8)	9 (12.5)			
No	74 (90.2)	63 (87.5)	0.294	1	0.588
E. coli					
Yes	32 (39.0)	23 (31.9)			
No	50 (61.0)	49 (68.1)	0.837	1	0.360
Staph.aureus					
Yes	7 (8.5)	7 (9.7)			
No	75 (91.5)	65 (90.3)	0.065	1	0.798
***Proteus* spp.**					
Yes	19 (23.2)	4 (5.6)			
No	63 (76.8)	68 (94.4)	9.364	1	0.002
***Klebsiella* spp.**					
Yes	13 (15.9)	16 (22.2)			
No	69 (84.1)	56 (77.8)	1.017	1	0.313

Table 5. Drug sensitivity and resistance patterns

Sensitivity/Age group	<65; n=82	≥65; n=72
Cefuroxime	33 (40.2%)	12 (16.5%)
Gentamycin	30 (36.6%)	14 (19.4%)
Ampicillin	2 (2.4%)	0 (0.0%)
Ciprofloxacin	6 (7.3%)	4 (5.6%)
Ofloxacin	12 (14.6%)	5 (6.9%)
Amoxicillin/sodium clavulanate	3 (3.7%)	3 (4.2%)
Nitrofurantoin	44 (53.7%)	35 (48.6)
Ceftazidime	24 (29.3%)	15 (20.8%)
Perfloxacin	0 (0.0%)	0 (0.0%)
Levofloxacin	0 (0.0%)	0 (0.0%)
Erythromycin	0 (0.0%)	0 (0.0%)
Resistance/Age group	**<65; n=82**	**≥65; n=72**
Cefuroxime	41 (50%)	44 (61.1%)
Gentamycin	44 (53.7%)	42 (58.3%)
Ampicillin	72 (87.8%)	56 (77.8%)
Ciprofloxacin	68 (82.9%)	52 (72.2%)
Ofloxacin	62 (75.6%)	51 (70.8%)
Amoxicillin/sodium clavulanate	71 (86.6%)	53 (73.6%)
Nitrofurantoin	30 (36.6%)	21 (29.2%)
Perfloxacin	73 (89.0%)	57 (79.2%)
Ceftazidime	50 (61.0%)	40 (55.6%)
Multidrug resistant	4 (4.9%)	11 (15.3%)

E. coli and *Proteus* spp. were more prevalent in the middle aged than the elderly. *Pseudomonas*, *Staph. aureus* and *Klebsiella* were more prevalent in the elderly. CAUTI caused by *Proteus* spp. was seen statistically significantly more frequent in the middle aged compared to the elderly (p=0.002).

The drug sensitivity and resistance patterns in the studied population are compared in Table 5. Nitrofurantoin was found to be the most sensitive antibiotic in both groups among the eleven tested antibiograms. The second most sensitive drug in the middle aged was cefuroxime whereas ceftazidime was the second most sensitive antibiotic in the elderly. The least sensitive antibiotics in both age groups were perfloxacin, levofloxacin and erythromycin. The most resistant antibiotic in both groups was perfloxacin. However, the prevalence of multidrug resistance was significantly higher in the elderly men (p=0.000).

Discussion

Urinary tract infections are the second most common infectious diseases in community after the respiratory tract infections. These infections account for up to 7 million visits per year in the United States with a mean yearly cost for the related antibiotic treatment estimated at more than one billion dollars.[24] UTIs account for the most frequent diseases in the nosocomial settings with the incidence of over 40% and about 80% of nosocomial UTIs is related to urinary catheterization.[14,24]

CAUTIs are the most common causes of hospital-acquired infections, especially in the elderly patients and several risk factors have been identified to be responsible for its development including advanced age, female gender, previous antibiotic usage, prolonged hospital stay before catheter insertion and immunosuppression among others.[9,25,26]

CAUTIs have been also the most common complication associated with indwelling urinary catheter use.[27] This is due to the fact that urinary catheter connects heavily colonized perineum with sterile bladder, providing a direct route for bacterial entry along both its external and internal surfaces.[28] Urine often pools in the bladder or in the catheter, and urinary stasis encourages bacterial multiplication. Obstruction of the catheter can lead to overdistension and ischemic damage of the bladder mucosa, thus increasing its susceptibility to bacterial invasion.[29]

Furthermore, Juthani-Mehta et al.[30] reported that with the advent of antiseptic techniques, vaccinations, antibiotics, and other public health measures, life expectancy has risen to 76 to 80 years in most developed nations[30] while life expectancy in less developed nations has not prolonged in similar fashion. But the mean age of 76 years recorded in the elderly in this study is a pointer to the fact that life expectancy in lesser developed nations is approaching towards that of the developed world. This may not be unconnected with the fact that the world is rapidly becoming a global village with rising technological advancement for improved health information now readily available to developing world. Therefore, hospital-acquired infection may also increase which can be contributed to the level of colonization with resistant pathogens in health care workers because of prolonged contact[30] with patients who may present with BOO.

In addition, one of the risk factors for the development of UTI globally is the age factor due to age-associated immune function, exposure to nosocomial pathogens and increasing number of comorbidities with aging.[30]

In our study, the prevalence rates of CAUTIs in the middle-aged men and the elderly were 90.2% and 80.6% respectively. This is similar to a high prevalence recorded by Sayal et al.[27] but far higher than those of Bakke et al.[31], Mohamed et al.[32] and Teshager et al.[33] who reported a prevalence of 50.6%, 43.3% and 53.33%, respectively. The prevalence rate of CAUTI among middle aged men with average age of 56 years in this study is quite dissimilar to UTI rate of 35% detected in a population of similar age who were managed with Continuous Intermittent Catheterization (CIC) for their urine drainage as reported by Bakke et al.[31] UTI. Although the underlying pathologies were different.

The high prevalence of CAUTIs in this study further supports the fact that advanced age carries high risk of CAUTIs[9] which means that both the middle aged and the elderly could be affected However, the high prevalence (80.6%) in the elderly patients could be as a result of changes in immune function with decreased resistance to bacterial colonization, poor perineal hygiene and increased number of comorbidities.[25,27,34] Though the higher prevalence of CAUTI in the middle aged than the elderly in this study could not be ascertained; psychological disability in daily activities may be also responsible for this higher prevalence rate. A prospective research on the etiologic factors for this higher prevalence might be necessary as a future project.

Besides, it was observed in this study that middle-aged men with suprapubic catheters had significantly higher CAUTI than men with urethral catheters ($p<0.05$). This is contrary to the report of Saint et al. which indicated that suprapubic catheters have a low-risk of CAUTIs compared with urethral catheters as a result of lesser colonization of abdominal skin with uropathogens.[35] Higher prevalence rate detected in patients with suprapubic catheters in our study may be due to surgical site infection that might develop from the cystostomy stoma in some of the patients with prolonged urinary drainage. In this study a higher proportion of men (55.30%) with CAUTI had suprapubic drainage, and 92.5% of them had prolonged drainage.

In our study we found that men catheterized for prolonged periods had significantly higher incidence of CAUTI than those with shorter duration of catheterization ($p<0.05$). High prevalence of CUTI associated with prolonged use of catheter drainage in this study is similar to the findings of Bello et al.[36] and Ikuerowo et al.[37]. In a cross-sectional survey at a Nigerian tertiary institution, the mean duration of catheterization as reported by Bello et al.[36] was 12 months with a range of 3 to 120 months. While another study by Ikuerowo et al.[37] reported a mean duration of 23 months. Therefore, it is not unusual in this part of the world to find people carrying indwelling urethral catheters for several months or even years. Financial constraints as a result of out-of-pocket payment health-care financing strategy and long waiting list for surgery, probably due to paucity of urologists, are some of the reasons for prolonged catheter drainage.[38-40]

Gram-negative bacteria were the predominantly isolated uropathogens in this study and the most common organism was *E. coli spp*. in both age groups with no significant intergroup difference ($p>0.05$) but the second commonest pathogen was *Proteus* spp. in the middle-aged men which was significantly different from that found (*Klebsiella* spp) in the elderly ($p<0.05$). This is in concordance with other studies that also reported *E. coli* as the most prevalent organism.[27,41] It is similar to Sayal et al.[27] who reported that predominantly gram-negative isolates are seen in patients with prolonged catherization.

Rational use of antibiotics is essential in CAUTIs to prevent untoward effects of medications and bacterial resistance. This study showed that most organisms in both age groups were sensitive to nitrofurantoin which is noted for its high effectiveness against most strains of *E. coli* and enterococci.[42] The cost of this medication is relatively cheaper when compared with other antibiotics and this might be an added advantage for the majority of patients with financial constraints in our settings. However, this drug must be administered with caution in the elderly due to its potential toxicity for renal impairment.[43] Ceftazidime offers a good alternative, being the second most sensitive drug, in the elderly and those with renal compromise.

In conclusion, the prevalence of CAUTI was slightly higher in the middle-aged men than the elderly; while suprapubic catheters were more prone to CAUTI than urethral catheters. Duration of catheterization longer than 2 weeks was significantly associated with higher prevalence of CAUTIs. *E. coli* was the commonest uropathogen in both groups and it was most sensitive to nitrofurantoin.

What is New About This Study?

1. Prevalence of CAUTI is slightly higher in the middle- aged men than the elderly.
2. Suprapubic catheter carries higher risk of CAUTI in the middle- aged men with BOO than the elderly.
3. Urethral stricture is significantly associated with higher CAUTI in the middle aged rather than elderly.
4. CAUTI caused by *Proteus mirabilis* is significantly predominant in the middle aged men compared to the elderly.
5. Nitrofurantoin had the highest sensitivity to isolated uropathogens in CAUTI in this study.
6. Elderly men have higher multidrug-resistance pattern.

Recommendations

1. Urine drainage through suprapubic catheter should be avoided as much as possible in the middle aged men with BOO where feasible.
2. When managing middle aged with CAUTI secondary to BOO, there should be a high index of suspicion for *E. coli* and *Proteus mirabilis*.
3. Nitrofurantoin or cefuroxime may be used as an empirical treatment in middle- aged men with CAUTI.
4. Definitive therapy should be performed where practicable within 2 weeks of urine drainage especially in the middle aged so as to reduce CAUTIs and enhance their quality of life.
5. When definitive therapy not feasible, catheter should be changed more frequently, not more than 2 weeks or use low friction (silicon-coated) catheters if available, to reduce bacterial colonization.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ekiti State University Teaching Hospital (Approval No: EKSUTH/ A67/2015/12/005).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – P.T.A., M.S.O.; Design – P.T.A., M.S.O.; Supervision – P.T.A., M.S.O., J.G.O.; Resources – P.T.A., E.E.E., M.S.O., J.G.O.; Materials – P.T.A., M.S.O., E.E.E., J.G.O.; Data Collection and/or Processing – P.T.A., M.S.O.; Analysis and/or Interpretation – E.E.E., P.T.A.; Literature Search – P.T.A., M.S.O., J.G.O., E.E.E.; Writing Manuscript – P.T.A., M.S.O., J.G.O.; Critical Review – P.T.A., M.S.O., J.G.O., E.E.E.; Other – P.T.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors have declared that they did not receive any financial support for this study.

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