April 30, 2020

PharmacologyOnLine

Archives • 2020 • vol.1 • 92-104

PREVALENCE OF URINARY TRACT INFECTION AND ANTIBIOTIC RESISTANCE PATTERN OF ISOLATES IN BENIGN PROSTATIC HYPERPLASIA PATIENTS WITH URINARY CATHETER SEEN AT A TERTIARY HOSPITAL IN ENUGU STATE, NIGERIA

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Abstract

Benign Prostatic Hyperplasia (BPH) is a serious ailment seen in men over the age of 50 in Nigeria. This condition can lead to bladder outlet obstruction. Insertion of urethral catheter in BPH patients enables free urination but this poses risk of urinary tract infection (UTI) and its complications. This study aimed at investigating BPH patients with urethral catheter for UTI and antibiotic resistance pattern of the isolates. In this cross-sectional study, 100 BPH patients aged 31-100 years with indwelling urethral catheter between one month and one year attending urology clinics at University of Nigeria Teaching Hospital (UNTH) Ituku-Ozalla, Enugu State Nigeria, were investigated. Ethical approval, informed consents, biodata/socio-demographic variables of the patients were obtained. The study was conducted between April and October 2017. Mid-Stream urine sample of each patient was obtained from the catheter immediately before change of catheter. Culture, urinalysis, standard biochemical tests and antibiotic susceptibility tests were performed using standard microbiological methods. Ninety-three (93%) samples were positive for UTI. *Escherichia coli* was the most frequent isolate 38 (39.6%) followed by *Proteus* spp 15 (15.5%), *Enterobacter* spp 11 (11.5%), *Klebsiella* spp 8 (8.3%), *Staphylococcus aureus*, Coagulase negative *Staphylococcus* (CoNS) and *Pseudomonas* spp 7 (7.3%) each, *Bacillus* spp 2 (2.1%) and *Neisseria gonorrhoea* 1 (1.0%). Age groups 31-40 years and 91-100 years ranked highest in prevalence for UTI (100%) each. Gram positive and Gram negative isolates both showed multi-drug resistance. Gram positive isolates showed highest resistance to ciprofloxacin 71.4% followed by erythromycin, ampicillin, cloxacillin, levofloxacin, ofloxacin, clindamycin (64.3%) each and least to gentamycin 28.6%. Gram negative isolates also showed highest resistance to cefuroxime and amoxicillin (86.3%) each followed by nitrofurantoin 85% and least to gentamycin 45%. Periodic screening for UTI, antibiotic susceptibility tests with other drugs and proper management of these patients are recommended.

Keywords: *Benign Prostatic Hyperplasia, Prevalence of Urinary Tract Infection, Urethral catheterized patients, Antibiotic Resistance Pattern*

Introduction

Benign prostatic hyperplasia (BPH) is an age related ailment commonly seen in men older than 50 years. Benign prostatic hyperplasia also called the prostate enlargement is a non-cancerous increase in size of the prostate [1]. As the lumen of the prostatic urethra becomes compromised by fibroadenomatous growth in the peri-urethral region of the prostate, urine outflow is obstructed progressively resulting in incomplete bladder emptying causing stasis and may predispose patients to infection [2].

Symptoms of BPH may include frequent urination, difficulty initiating urination, weak stream, inability to urinate or loss of bladder control [1]. BPH is the most common cause of lower urinary tract symptoms (LUTS) [3]. BPH can cause bladder outlet obstruction (BOO) [4] which symptoms include abdominal pain, a continuous feeling of a full bladder, frequent urination, acute urinary retention (inability to urinate), pain during urination (dysuria), problems starting urination (Urinary hesitancy), slow urine flow, starting and stopping (urinary intermittency) and nocturia. If left untreated, BPH can be progressive and incomplete voiding results in residual urine or urinary stasis which can lead to increased risk of urinary tract infection [5]. Complications of BPH include urinary tract infection (UTI), bladder stones and chronic kidney problems [6].

It is estimated that about 105 million people are affected globally with BPH [7]. BPH typically begins after the age of 40 [1]. Half of males age 50 and over are affected [6] and after the age 80, about 90% of males are affected [1].

Urinary tract infections refer to the presence of microbial pathogens within the urinary tract. UTI is usually classified by the site: bladder (cystitis), kidney (pyelonephritis) or urine (bacteriuria) and also can be asymptomatic or symptomatic [8].

A host of pathogenic organisms can cause UTI but bacteria are the most implicated. Others include viruses, fungi and parasites. Majority of UTI are caused by enteric bacteria that make up the normal gastro intestinal flora [2]. Many studies have shown *Escherichia coli* as the most common isolate from urinary tract infections [9,10,11,12,13] while others have shown *Staphylococcus* species to be the most frequent isolates in their UTI studies [14,15].

Different prevalence rates for UTI have been obtained from previous studies: in Maiduguri Nigeria 62.0% [10], in Northern Iran 14.96% [12], in Ndjamena Chad 32.7% [13], in Enugu State Nigeria 37.5% [15]. Manifestations of UTI's vary from mild cystitis to pyelonephritis and septicaemia [16]. Significant morbidity and or mortality may arise from improperly treated UTI [17]. Previous studies have reported various prevalence rates for UTI in BPH patients: in Ilorin Nigeria 33% [2], in Benin Nigeria 44.7% [18], in Thandalam Chennai India 45.1% [19].

Bladder outlet obstruction in BPH patients can lead to urethral catheterization. Long term urethral catheterization is a risk factor for urinary tract infection [20]. Urinary tract infection is the most common complication of intermittent catheterization [21]. Catheters provide microorganisms with direct access to the normally sterile urinary tract, there by predisposing to bacteriuria and funguria [22]. Different prevalence rates have been recorded for UTI in BPH patients with indwelling urethral catheter: 62.5% in Bida, North Central Nigeria Akobi *et al* [23], 70% in 1994 – 1996, 72% in 2004 – 2006 and 69% in 2011 – 2015 in Warsaw Dybowski *et al* [24].

Recurrent UTI in urethral catheterized BPH patients, frequent administration of antibiotic to them empirically or abuse of antibiotics by "over the counter purchase" without prescription by these patients could result to antibiotic resistance. Antibiotic resistance of uropathogens is a growing concern globally and its consequence include very limited drugs for treatment of patients, increase in length of stay by the BPH patients awaiting surgery, complications of UTI such as pyelonephritis, urosepsis, shock, death or post-surgery infection on these BPH patients. A previous study on UTI in BPH patients with urethral catheter Akobi *et al* [25] have shown an overall mean high multi-drug resistance pattern of uro-pathogens isolated to 11 drugs they tested with highest resistance shown to augmentin 94 %, followed by ampicillin 93.4 %, gentamycin 90 %, cefuroxine 86.4 %, nalidixic acid 81.0 %, ciprofloxacin and ceftazidine 75.8 % each, Ofloxacin 72.8%, ceftriazone 68.6%, levofloxacin 56.2% with least resistance to nitrofurantoin 36.3%. The present study therefore investigated the prevalence of UTI in BPH patients with urinary catheters awaiting surgery at the University of Nigeria Teaching

Hospital (UNTH) Ituku-Ozalla Enugu State Nigeria, determined the profile of organisms causing UTI in the BPH patients, frequency of the isolates and antibiotic resistance pattern of the isolates to commonly used antibiotics in the study area Enugu state Nigeria.

Methods

Study design

The present study was a cross-sectional study.

Study area

This study was conducted in Enugu state, South East Nigeria, West Africa.

The study population

The study population consisted of 100 patients who had been diagnosed of benign prostatic hyperplasia at the urology clinics of University of Nigeria Teaching Hospital (UNTH) Ituku – Ozalla, Enugu State Nigeria, who were on urethral catheter and awaiting surgery. The patients visited the urology clinics of the hospital for change of urethral catheter periodically (every three weeks) and for management and had been on the urethral catheter between one month and one year. Some have had urinary tract infections either once or more and had previously taken antibiotic once or more than once for UTI. Confirmed BPH patients with urethral catheter attending the urology clinics of UNTH Ituku-Ozalla during the period of study, who gave their informed consents and who had not been on any antibiotics two weeks before and during sample collection were included in the study.

Sampling Methods

A total of 100 BPH patients with urethral catheter who had come to change their catheters at the urology clinic of UNTH Ituku-Ozalla, Enugu state Nigeria and who gave their informed consent for inclusion in the study, were investigated for UTI after Ethical clearance (approval) was obtained from the Health Research and Ethics Committee of the UNTH Ituku-Ozalla. The patients had been on urethral catheter due to bladder outlet obstruction (BOO) and were aged 30-100 years. The patients were randomly selected using convenience random sampling technique. The study was conducted between April and October, 2017. Demographic and clinical history of the patients were obtained before sample collection using structured questionnaires. Those on antibiotic therapy two weeks before or during sample collection were excluded.

Sample collection

Urine sample of each patient was collected from the catheter into a sterile urine bottle containing boric acid by the help of a doctor on duty at the urology clinic during change of urethral catheter of the patients.

Sample processing (Analysis)

This was according to modified method of Cheesbrough [26].

Urine culture

Each urine sample was cultured onto blood agar plate, Cysteine Lactose Electrolyte Deficiency (CLED) agar plate and Sabauraud dextrose agar tube slant using a sterile calibrated wire-loop that holds 0.002ml of urine. The plates were incubated at 37^{o} c for 24 hours for possible isolation of bacterial colonies while the tubes were incubated at 37^{o} c for 48 hours for possible isolation of *Candida* species.

Urinalysis

Macroscopic examination of the urine samples was performed by checking for their colour and turbidity. Urine chemistry was carried out on each urine sample using the dipstick method with combi 9^{TM} test strip. Each urine sample was poured into a clean test tube and one test strip of the combi 9 ^{TM} was dipped into the urine and examined for any colour change depicting the presence of some vital parameters such as glucose, protein, nitrate, bilirubin, blood, leucocyte esterase, ascorbic acid, ketones etcetera. The urine samples were centrifuged and microscopic examination was done on the urine deposits noting the presence of abnormal constituents such as WBC's, RBC's, casts, yeast cells, etcetera. Pyuria was regarded as significant when pus cells were >10WBC's/HPF [26].

Macroscopic examination of plate and tube cultures

Colonies of growth observed on each culture plate was examined macroscopically for its morphological characteristics such as size, shape, color, edge, elevation, haemolysis on blood agar, fermentation, number of colonies, for evidence of significant bacteriuria. Growths observed on tube slants were also examined macroscopically.

Microscopic examination of colonies

Colonies of growths with significant bacteriuria ($\geq 10^{5}$CFU/ml of urine) on plates with pure cultures, were subjected to Gram staining technique and were examined microscopically. These pure colonies

were subbed onto nutrient agar slants and incubated overnight at 37°C for further identification tests.

Biochemical tests

Subcultures of growths with significant bacteriuria were subjected according to their Gram reaction, to catalase test, coagulase test, oxidase test, Indole, methyl-red, voges-proskauer and citrate utilization tests (IMViC test) for further identification of the colonies.

Antibiotic susceptibility tests

Antibiotic susceptibility tests were performed on confirmed bacterial isolates using Kirby-Bauer disc diffusion technique [27]. Gram positive drug discs used were erythromycin 10mcg, ceftriaxone 30mcg, ampicillin 30mcg, cloxacillin 10mcg, levofloxacin 5mcg, cephalexin 30mcg, ciprofloxacin 5mcg, gentamycin 10mcg, ofloxacin 10mcg, clindamycin 10mcg. Gram negative drug discs used were nitrofurantoin 100mcg, gentamycin 10mcg, ciprofloxacin 10mcg, chloramphenicol 10mcg, ofloxacin 10mcg, cefuroxime 10mcg, peflacin 10mcg, ceftriaxone 30mcg, amoxicillin 30mcg, streptomycin 30mcg.

Statistical analysis

Data's generated from this study were analyzed using one-way analysis of variance (ANOVA) and Fisher's Exact test for contingency.

Results

Out of the 100 urine samples from BPH patients with urethral catheter examined for UTI in the present study, 93 were positive with a prevalence of 93%. The age groups 31-40 years and 91-100 years had the highest prevalence for UTI (100%). However, age group difference in the number of positive cases for UTI was not statistically significant ($p > 0.05$, p value = 0.6063) using Fisher's exact test (Table 1).

Out of 93 positive cases for UTI obtained from this study, 96 bacterial isolates were obtained. *Escherichia coli* was the most frequent isolate 38 (39.6%) followed by *Proteus* spp 15 (15.5%), *Enterobacter* spp 11 (11.5%), *Klebsiella* spp 8 (8.3%), *Staphylococcus aureus*, coagulase negative *Staphylococcus* (CoNS) and *Pseudomonas* spp 7 (7.3%) each, *Bacillus spp* 2 (2.1%) and *Neisseria gonorrhea* 1 (1.0%). Difference in the number of different organisms isolated was not statistically significant ($p > 0.05$, p value = 0.7699) using one way analysis of variance (ANOVA) (Table 2).

Result of antibiotic susceptibility tests for Gram positive organisms (Table 3) revealed that *S. aureus* isolates showed multi-drug resistance to nine out of the 10 drugs tested on them with highest resistance to clindamycin 85.7% followed by erythromycin, ampicillin, cloxacillin, levofloxacin, cephalexine, ciprofloxacin, ofloxacin (71.4%) each, ceftriaxone 57.1% with least resistance to gentamycin 42.9%. CoNS showed highest resistance to ciprofloxacin 71.4% followed by erythromycin, ampicillin, cloxacillin, levofloxacin, ofloxacin (57.1%) each with least resistance to gentamycin 14.3%. Overall, the Gram positive isolates showed high level multi-drug resistance with highest mean resistance to ciprofloxacin 71.4% followed by erythromycin, ampicillin, cloxacillin, levofloxacin, ofloxacin, clindamycin (64.3%) each with mean least resistance to gentamycin 28.6% (equivalent to 71.4% mean susceptibility) (Table 3).

Antibiotic susceptibility tests for Gram negative organism ((Table 4) showed that *E. coli* had the highest resistance to nitrofurantoin, cefuroxime and amoxicillin (84.2%) each followed by chloramphenicol, ofloxacin and peflacin (78.9%) each with least resistance to gentamycin 36.8%.

Proteus spp showed highest resistance to peflacin 86.7 followed by nitrofurantoin, cefuroxime and amoxicillin (80.0%) each and least resistant to streptomycin 46.7%.

Enterobacter spp showed highest resistance to cefuroxime, peflacin and amoxicillin (100%) each followed by nitrofurantoin, streptomycin (90.9%) each with least resistance to ceftriaxone 27.3%.

Klebsiella spp showed highest resistance to nitrofurantoin, cefuroxime, peflacin and amoxicillin (100%) each followed by ciprofloxacin, chloramphenicol and ceftriaxone (87.5%) each with least resistance to streptomycin 25.0%.

Pseudomonas spp showed highest resistance to nitrofurantoin, cefuroxime, ceftriaxone and amoxicillin (85.7%) each followed by ciprofloxacin, ofloxacin and peflacin (71.4%) each with least resistance to gentamycin 14.3%.

The lone *Neisseria gonorrhea* showed 0% resistance (100% susceptibility) to all the drugs tested.

Overall, the Gram negative isolates showed high level of multi-drug resistance to the drugs tested with mean highest resistance to cefuroxime and amoxicillin (86.3%) each followed by nitrofurantoin

85% with mean least resistance to gentamycin 45.0% (55% susceptibility) (Table 4).

Discussion

Benign prostatic hyperplasia (BPH) is a condition that is currently affecting many men over the age of 50 years in Nigeria. Drugs and surgery are the most popular treatments for this ailment in Nigeria presently and the surgery is expensive which most BPH patients cannot easily afford. Most men affected are usually from 60 years upwards and those above 70 years are most often frail for the surgery to be performed on. This necessitates the insertion of urethral catheter in these patients to enable them void urine while getting ready both physically and financially for the surgery. This carriage of urethral catheter in most men gets prolonged with intermittent changes of the catheter every three weeks which predisposes these patients to UTI and its complications, hence the need for this study.

In this study, out of 100 urine samples from urethral catheterized BPH patients examined for UTI, 93 were positive with a prevalence of 93% (Table 1). This prevalence obtained in the present study is higher than 62.5% prevalence of UTI obtained by Akobi *et al* [23] at Bida, North Central Nigeria and that obtained by Dybowski *et al* [24] at Warsaw in their retrospective study for three periods 1994 – 1996 (70%), 2004 – 2006 (72%) and 2011 – 2015 (69%). Generally, the prevalence of UTI obtained in the study of Akobi *et al* [23], the study of Dybowski *et al* [24] and the present study, are similar since they all obtained high prevalence for UTI in the BPH patients with urethral catheter that each studied. Oshodi *et al* [2] obtained a lower prevalence of 33% for UTI in BPH patients without urethral catheter and this rate is lower than the prevalence of UTI obtained in the works of [23] and [24] which were on BPH patients with urethral catheter. This further confirmed the statement that despite best care and precautions, long term catheterization is linked to an almost 100% risk of bacteriuria [28]. The disparity in the prevalence obtained between the present study and the other studies could be attributed to different ways of handling these patients during the insertion and change of the urinary catheter in the different hospitals they were attending. The aseptic precautions that these doctors may be taking in the different hospitals to ensure that the catheters were not contaminated before insertion may differ. How skilled the person inserting the urinary catheter is, matters since the technique of insertion of the catheter can push normal flora on the skin surrounding the urethral opening into the urethra which may result to UTI. Urinary tract infection may occur through catheter related infection by the following: (1) contamination of the operators' hand when the hands are not washed with soap and water before wearing gloves (2) the part of the catheter entering the bladder may be contaminated causing urinary tract infection when the water lubricant applied to the tip of the catheter is contaminated from the outside. (3) when there is ineffective cleaning of the meatus which may lead to the introduction of organism from the patient skin and this may occur when the urinary meatus is not wiped with disinfectant [29]. The longer the time the indwelling urethral catheter stays, the more the likely the chances of organisms being introduced hence leading to UTI. Long term urethral catheterization is a risk factor for urinary tract infection [20]. Again, the period for change of these catheters every two or three weeks according to different hospitals could predispose to UTI. Urinary tract infection is the most common complication of intermittent catheterization [21]. Catheters provide microorganisms with direct access to the normally sterile urinary tract, there by predisposing to both bacteriuria and funguria [22].

Age group 31-40 years and 91-100 years recorded the highest prevalence of 100% for UTI amongst the BPH patients studied followed by age group 61-70 years 94.7%, 71-80 years 94.1%, 81-90 years 87.5%, 51-60 years 84.6% while age group 41-50 years had no patients sampled (Table 1). This result showed no definite pattern for UTI either prevalence increasing with increase in age or decreasing with increase in age. Age group difference in the number of positive cases was not statistically significant ($p > 0.05$, p value = 0.6063). This result is similar to that of Akobi *et al* [23] in which the age group 90-100 years ranked highest in prevalence (100%) for UTI followed by age groups 46-50 years and 81-85 years 76.9% each, 71-75 years 76.1%, 56-60 years 64.1%, 76-80years 61.7% while age group 51-55 years was least 42.1%, with no definite pattern for prevalence of UTI with regards to age group. The findings of the present study and the study of Akobi *et al* [23] is in disagreement with

the work of Hussein *et al* [30] which showed that the prevalence of UTI in males increases with increase in age and the result of Oshodi *et al* [2] which showed that there was steady increase in the prevalence of urinary tract infection with age among the BPH patients they studied with highest prevalence of 70.6% at ages 80 years and above.

Out of the 93 positive cases for UTI encountered in this study, 96 bacterial isolates were obtained with three samples containing double isolates. *Escherichia coli* was the most frequent isolates 38 (39.6%). This result agrees with the results of Akobi *et al* [23] and Dybowski *et al* [24] in which *Escherichia coli* was the most prevalent isolates they encountered in their retrospective studies on UTI and bacteriuria respectively. Other studies on UTI, in BPH patients with UTI and in catheter associated UTI's, have isolated *E. coli* as the most common bacterial isolates [10,11,12,29,30,31]. The study of [23], [24] and the present study each isolated *Escherichia coli*, *Proteus* spp, *Klebsiella* spp, *Staphylococcus aureus*, *Pseudomonas* spp and CoNS (*Staphylococcus* albus) from their studies on UTI in BPH patients with urethral catheter, showing that these organisms are common amongst BPH patients.

Antibiotic susceptibility tests performed in the present study revealed that *Staphylococcus aureus* showed highest resistance to clindamycin 85.7% followed by erythromycin, ampicillin, cloxacillin, levofloxacin, ciprofloxacin, ofloxacin, cephalexin (71.4%) each, ceftriaxone 57.1% with least resistance to gentamycin (42.9%). This result differs from the result of Akobi *et al* [25] on UTI in patients with indwelling urinary catheter at Bida, Niger State, Nigeria in which resistance of *Staphylococcus aureus* isolates they obtained was lower than that of the present study for ciprofloxacin 67.6%, levofloxacin 47.1%, ofloxacin 41.2% but higher for ceftriaxone 64.7%, gentamycin 91.2%, ampicillin 97.1%. The work of Anejo-Okopi *et al* [10] on antibiotic resistant pattern of UTI's in symptomatic patients at Maiduguri, Nigeria revealed that *S. aureus* isolates from their study showed very low percentage resistance to ciprofloxacin 8.3%, ofloxacin 25.0%, gentamycin 8.3% compared to the result of the *S. aureus* isolates in the present study which recorded much higher percentage resistance to these drugs – ciprofloxacin and ofloxacin (71.4%) each, gentamycin 42.9%. However, their result showed high resistance of *S. aureus* isolates to ampicillin 66.7% though this is still lower than 71.4% resistance of *S. aureus* isolates to ampicillin in the present study. The lower percentage resistance of *S. aureus* isolates obtained in the study of Anejo-Okopi *et al* [10] for the same drugs tested in the present study and that of Akobi *et al* [25] could be because the study of Anejo-Okopi *et al* [10] was on patients with UTI while that of the present study and the work of Akobi *et al* [25] were on BPH patients with urethral catheter for a period of one month to one year. Long term urethral catheterization is a risk factor for urinary tract infection [20]. Treatment of UTI with antibiotics empirically in these BPH patients by many clinicians in the present study area before laboratory results are out and indiscriminate purchase of antibiotics "over the counter" without prescription by these BPH patients in the study area may have contributed to the high level of antibiotic resistance by the isolates in this study. Treatment of UTI is often started empirically and therapy is based on information determined from the antimicrobial resistance pattern of the urinary pathogens [32]. The prevalence of antimicrobial resistance among urinary pathogens has been increasing worldwide due to aberrant use of antibiotics in practice [33, 34].

The CoNS isolates in the present study also demonstrated multi-drug resistance with highest resistance shown to ciprofloxacin 71.4% followed by erythromycin, ampicillin, cloxacillin, levofloxacin and ofloxacin (57.1%) each, ceftriaxone, cephalexine and clindamycin (42.9%) each with least resistance to gentamycin 14.3%. This result is in disagreement with the result of Akobi *et al* [25] who obtained much higher percentage resistance of 100% for ampicillin, gentamycin and ceftriaxone by *Staphylococcus* albus isolates. The *Staphylococcus* albus isolates in the work of Akobi *et al* [25] showed 0% resistance (100% susceptibility) to ciprofloxacin, ofloxacin and levoloxacin which does not also agree with the result of the present study in which the CoNS isolates showed high resistance to these drugs. Overall, the Gram positive isolates in this study showed high multi-drug resistance pattern to the drugs tested on them with highest mean resistance to ciprofloxacin 71.4 followed by erythromycin, ampicillin, cloxacillin, levofloxacin, ofloxacin and

clindamycin (64.3%) each, cephalexin 57.1%, ceftriaxone 50%, with least mean resistance to gentamycin 28.6%.

In this study, amongst the Gram negative isolates, *Escherichia coli* isolates showed highest resistance to nitrofurantoin, amoxicillin and cefuroxime 32 (84.2%) each followed by chloramphenicol, ofloxacin and peflacin 30 (78.9%) each, ceftriazone 27 (71.1%), ciprofloxacin 25 (65.8%), streptomycin 23 (60.5%) with least resistance to gentamycin 14 (36.8%). This result has some similarities with the work of Akobi *et al* [25] in which their *E. coli* isolates were resistant to ofloxacin 76.5%, ceftriaxone 70.0% and differed in their resistance to gentamycin 87.9% which was higher than 36.8% obtained in the present study while resistance of *E. coli* to nitrofurantoin in their study was 38.1% compared to 84.2% obtained in the present study. Also resistance of *E. coli* isolates to ciprofloxacin (77.3%) and cefuroxime (92.7%) in the work of Akobi *et al* [25] were much higher than that obtained for the same organism for same drugs in the present study. The result of the present study does not agree with the work of Mihankhah *et al* [12] on patients with clinical symptoms of UTI in Northern Iran which recorded very low resistance rates for *E. coli* to ciprofloxacin 14%, 14%, 26% in years 2013, 2014,2015 respectively, ceftriaxone 24%, 4%, 30% in years 2013, 2014, 2015 respectively, nitrofurantoin 17%, 12%, 7% in years 2013, 2014, 2015 respectively, gentamycin 38%, 35%, 39% in years 2013, 2014, 2015 respectively. The present study was on BPH patients with urethral catheter and long term urethral catheterization is a risk factor for urinary tract infection [20]. UTI treatment with antibiotics is carried out usually before receiving microbiology test results. This therapy, without rational drug prescription occasionally leads to antibiotic resistance and treatment failure is its result [35]. This empirical treatment which may have been practiced by some clinicians in the present study area and over the counter purchase of antibiotics by the BPH patients without prescription, may have contribute to high antibiotics resistance encountered in this study.

Proteus spp showed highest resistance to peflacin 86.7% in this study followed by nitrofurantoin, cefuroxime and amoxicillin (80%) each, ciprofloxacin 73.3%, gentamycin, chloramphenicol, ofloxacin (66.7%) each, ceftriaxone 60% while the least was streptomycin 46.7%. This result has some similarities with the result of [25] since their work also showed high percentage resistance of *Proteus* species to gentamycin 80%, cefuroxime 90%, ofloxacin 70%, ciprofloxacin and nitrofurantoin 60% each, ceftriaxone 50%, though resistance rate for antibiotics in their work was higher for cefuroxime, gentamycin and ofloxacin compared to rates obtained for same drugs in the present study. The work of Anejo-Okopi *et al* [10] recorded much lower resistance rate of *Proteus* to the drugs they tested: ciprofloxacin and chloramphenicol 16.7% each, ofloxacin and gentamycin 33% each.

In this study, *Enterobacter* spp showed highest resistance to cefuroxime, peflacin and amoxicillin (100%) each, followed by nitrofurantoin and streptomycin (90.9%) each, ofloxacin 81.8%, ciprofloxacin and chloramphenicol (72.7%) each, gentamycin 45.5% while ceftriaxone recorded 27.3%. The results of this study has some similarities and differences with the study of Mihankhah *et al* [12] in which the *Enterobacter* isolates from their study on UTI for three years showed lower resistance to ciprofloxacin 20%, 25% and 0% for years 2013, 2014 and 2015 respectively and lower resistance for nitrofurantoin 20%, 0% and 17% for year 2013, 2014 and 2015 respectively compared to the resistance rates shown by *Enterobacter* to same drugs in the present study. The Enterobacter isolates showed very high resistance to gentamycin for years 2013 and 2014 (100%) each and lower rate of 33% in year 2015.

Klebsiella spp isolates in the present study showed very high resistance to almost all the drugs tested in this study: nitrofurantoin, cefuroxime, peflacin and amoxicillin (100%) each followed by ciprofloxacin, chloramphenicol and ceftriaxone (87.5%) each, gentamycin and ofloxacin (75%) each while the least was streptomycin 25%. The 100% resistance shown by *Klebsiella* to cefuroxime in the present study tallies with the 100% resistance by *Klebsiell*a spp isolates to same drug in the work of Akobi *et al* [25]. Their study also showed high level resistance by *Klebsiella* spp isolates to gentamycin, ciprofloxacin, ofloxacin, nitrofurantoin and ceftriaxone (50%-90%) which is similar to 75-100% resistance shown by *Klebsiella* spp to same drugs in the present study. Anejo-Okopi *et al* [10] recorded lower resistance rates for *klebsiella* spp isolates to ciprofloxacin

31.6%, ofloxacin 15.8%, chloramphenicol 20% than the resistant rates shown by *klebsiella* spp for same drugs in the present study. However, gentamycin recorded higher resistance of 84.2% in their work for *klebsiella* spp than the rate obtained in the present study.

Pseudomonas spp isolates in the present study showed high resistance to most of the drugs tested with highest resistance shown to nitrofurantoin, cefuroxime, ceftriaxone and amoxicillin (85.7%) each followed by ciprofloxacin, ofloxacin and peflacin (71.4%) each, chloramphenicol 57.1% with very low resistance to streptomycin 28.6% and gentamycin 14.3%. Similar high rates of resistance by *Pseudomonas* were obtained in the study of [25] with cefuroxime 93.1%, ofloxacin 89.7% and ciprofloxacin 82.8% although these rates are slightly higher than those obtained in the present study. Gentamycin showed very high resistance in their work 89.7% compared to the 14.3% obtained in the present study.

The very high resistance pattern of urinary isolates to most drugs tested in the works of Akobi *et al* [25] and the present study, could be as a result of the fact that patients investigated in both studies had BPH with urinary catheters which they have carried between one month to one year while waiting for surgery, with episodes of UTI in these patients most of the time being treated empirically with antibiotics by clinicians before laboratory results were out. Again, some of the patients purchase these antibiotics indiscriminately to treat themselves without doctor's prescription, and these result to abuse of antibiotics and subsequent resistance of these uropathogens to antibiotics. The work of Anejo-Okopi *et al* [10] and Mihankhah *et al* [12] were mainly on patients with urinary tract infections and not on BPH patients with urinary catheter hence the lower rates of resistance of their isolates to most drugs they tested. However, the lone *Neisseria* spp isolates showed 0% resistance to all the drugs tested in this study. The antimicrobial resistance pattern of bacterial isolates from urinary tracts differs among bacteria and antibiotics, geographic regions and institutions [36, 37].

In conclusion, the present study has shown very high prevalence of 93% for UTI in the BPH patients studied. *Escherichia coli* was the most frequent isolate encountered 39.6%. Age group difference for prevalence of UTI in these patients showed no statistically significant difference ($p > 0.05$). Antibiotic susceptibility test results revealed that both Gram positive and Gram negative isolates showed multi-drug resistance to the drugs tested with mean least resistance shown by both to gentamycin 28.6% and 45% respectively, therefore making gentamycin the drug of choice for treatment of UTI in these patients. Periodic screening of BPH patients with urinary catheter for UTI followed by antibiotic susceptibility tests with new drugs on isolates from positive cases and proper management of these patients are recommended.

Acknowlegements

The authors wish to thank the management of UNTH Ituku-Ozalla, Enugu State, Nigeria and their Health Research and Ethics Committee, for granting us ethical approval which enabled us use their patients for this study. Thanks to the doctors and nurses working in the urology clinic of UNTH during the period of this study for assisting us in sample collection. We wish to thank the Head of the Department of Medical Laboratory Sciences of the University of Nigeria Enugu Campus and the Director of Christ Centre Medical Laboratory, Enugu, Enugu State, Nigeria Mr Chris Ireoba, for allowing us use their Microbiology laboratories for this study.

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Table 1: Distribution of positive cases for urinary tract infection in the BPH patients with urethral catheter sampled according to age group

n = 100

Age group(years)	Number sampled	Number positive for UTI	Percentage (%) Prevalence
31-40	5	5	100
41-50	0	0	0
51-60	13	11	84.6
61-70	38	36	94.7
71-80	34	32	94.1
81-90	8	7	87.5
91-100	2	2	100.0
Total	100	93	93

Table 2: Frequency distribution of bacterial isolates from urine samples of BPH patients with urethral catheter examined

n = 96

Bacterial organisms isolated	Number isolated	Percentage (%)
Escherichia coli	38	39.6
Proteus species	15	15.6
Enterobacter species	11	11.5
Klebsiella species	8	8.3
Staphylococcus aureus	7	7.3
CoNS	7	7.3
Pseudomonas species	7	7.3
Bacillus species	2	2.1
Neisseria gonorhoea	1	1.0
Total	96	100

Table 3: Antibiotic resistance pattern of Gram positive bacteria isolated from UTI in BPH patients with urinary catheter (Percentages in bracket)

Orgs isolated	No isolated	Antibiotics Tested									
		E	CT	AM	CL	LV	CX	CIP	GN	OF	CD
S. aureus	7	5 (71.4)	4 (57.1)	5 (71.4)	5 (71.4)	5 (71.4)	5 (71.4)	5 (71.4)	3 (42.9)	5 (71.4)	6 (85.7)
CoNS	7	4 (57.1)	3 (42.9)	4 (57.1)	4 (57.1)	4 (57.1)	3 (42.9)	5 (71.4)	1 (14.3)	4 (57.1)	3 (42.9)
Total	14	9 (64.3)	7 (50)	9 (64.3)	9 (64.3)	9 (64.3)	8 (57.1)	10 (71.4)	4 (28.6)	9 (64.3)	9 (64.3)

Key: E = Erythromycin, CT = Ceftriaxone, AM = Ampicillin, CL = Cloxacillin, LV = Levofloxacin CX = Cephalexin, CIP = Ciprofloxacin, GN = Gentamycin, OF = Ofloxacin, CD = Clindamycin, CoNS = Coagulase Negative *Staphylococcus*

Table 4: Antibiotic resistance pattern of Gram negative bacteria isolated from UTI in the BPH patients with urinary catheter studied (Percentages in bracket)

Orgs isolated	No iso	Antibiotics Tested									
		N	GN	CIP	C	OF	CF	PF	CT	AX	ST
E. coli	38	32 (84.2)	14 (36.8)	25 (65.8)	30 (78.9)	30 (78.9)	32 (84.2)	30 (78.9)	27 (71.1)	32 (84.2)	23 (60.5)
Proteus spp	15	12 (80.0)	10 (66.7)	11 (73.3)	10 (66.7)	10 (66.7)	12 (80.0)	13 (86.7)	9 (60.0)	12 (80.0)	7 (46.7)
Entero spp	11	10 (90.9)	5 (45.5)	8 (72.7)	8 (72.7)	9 (81.8)	11 (100)	11 (100)	3 (27.3)	11 (100)	10 (90.9)
Kleb spp	8	8 (100)	6 (75.0)	7 (87.5)	7 (87.5)	6 (75.0)	8 (100)	8 (100)	7 (87.5)	8 (100)	2 (25.0)
Pseud spp	7	6 (85.7)	1 (14.3)	5 (71.4)	4 (57.1)	5 (71.4)	6 (85.7)	5 (71.4)	6 (85.7)	6 (85.7)	2 (28.6)
Neisse gonorrh	1	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total	80	68 (85.0)	36 (45.0)	56 (70.0)	59 (73.8)	60 (75.0)	69 (86.3)	67 (83.8)	52 (65.0)	69 (86.3)	44 (55.0)

Key: N = Nitrofurantoin, GN = Gentamycin, CIP = Ciprofloxacin, C = Chloramphenicol, OF = Ofloxacin, CF = Cefuroxime, PF = Peflacin, CT = Ceftriaxone, AX = Amoxicillin, ST = Streptomycin, Orgs = Organisms, iso = isolated, spp = species, Entero = *Enterobacter,* Kleb = *Klebsiella,* Pseud = *Pseudomonas*, Neisse = *Neisseria*, gonorrh = *gonorrhoea*