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Modifiable Factors Associated with Urinary Tract Infections in Patients with Benign Prostate Hyperplasia and Prostate Cancer at Tertiary Hospital, Dar es Salaam, Tanzania

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ABSTRACT

Objectives: To determine the magnitude of urinary tract infection (UTI) and associated factors in patients with benign prostate hyperplasia and prostate cancer.

Design: Hospital-based cross-sectional study.

Settings: Urology clinic and ward at Muhimbili National Hospital, the main tertiary in Tanzania's largest city.

Participants: Patients with benign prostate hyperplasia and prostate cancer presenting with genitourinary symptoms.

Main outcome measure: The primary outcome was the prevalence of UTI and factors associated with UTI among patients with benign prostate hyperplasia and prostate cancer.

Results: The proportion of UTI was 46.5% (95% CI 41.56-51.53%). UTI was significant among in-patients, patients with indwelling urinary catheters, patients with prostate size >80 cc, and residual urine volume of > 100mLs. Age >60 (aOR = 2.0, 95% CI 1.13-3.55, p=0.018), patient with incomplete bladder emptying (aOR=2.57, 95% CI 1.44-4.59, p=0.001) and with increased duration of catheter (aOR=1.24, 95% CI 1.11-1.38, p=0.005) were significantly associated with UTI.

Conclusion: Almost half of the patients with enlarged prostate and genitourinary symptoms had laboratory-confirmed UTI. The risk of UTI increases with age, incomplete bladder emptying, and increased duration of catheterization. A one-day increase in the duration of catheterization increased the risk of UTI by 24%.

Keywords: Urinary tract infection, Benign prostate hyperplasia, Incomplete bladder emptying, indwelling urinary catheterization, Prostate cancer.

Strengths and limitations of this study

1. Using the Analytical Profile Index as an addition identification test increased the accuracy of identifying Gram-negative rods.
2. We conducted a receiver-operation curve analysis to predict the duration of the catheter in days at risk of getting UTI for men with BPH and Prostate cancer, which was not done in similar studies.

3. We enrolled patients with enlarged prostate and genitourinary symptoms without establishing if the genital symptoms were due to obstruction caused by an enlarged prostate alone without microbial infection, consequently affecting the UTI detection rate.

INTRODUCTION

In adult men, urinary tract infection (UTI) is often complicated and caused by structural or functional abnormality of the genitourinary tract. The abnormalities may be due to benign prostate hyperplasia (BPH), prostate cancer, renal stone, and catheterization (1). UTI related to an enlarged prostate develops due to inadequate bladder emptying in which static urine provides a suitable growth condition for pathogens (2). The risk for UTI increases with an increased prostate size, leading to large post-void residual (PVR) urine volume (3)

Urinary catheterization is usually employed to relieve retained urine in the urinary bladder obstructed by the enlarged prostate gland (4). A major risk for UTI is prolonged use of urinary catheters (5). However, the exact duration for urinary catheters to cause UTI is unknown (5,6). A study at Bugando, Mwanza, reported that patients who had stayed with urinary catheters beyond the recommended time accounted for 39%, and their risk for UTI increased with increased duration of the catheter (5).

Several factors associated with UTI in patients with BPH and prostate cancer have been reported with marked variations across study settings and populations (7,8). We hypothesized that understanding the predisposing factors for developing UTIs and appropriate action is critical in designing interventional strategies that are best suited to preventing UTI in this population. Therefore, we conducted the current study to understand the magnitude of UTI and determine the associated modifiable factors. In addition, we determine the appropriate duration of indwelling urinary catheter stay with a low risk of UTI.

MATERIALS AND METHODS

Study design and setting

The study was a hospital-based cross-sectional design performed at Muhimbili National Hospital (MNH) in Dar es Salaam. MNH, a referral and teaching hospital, has a 1500-bed capacity and is the largest tertiary hospital in Tanzania, with more than 1000 outpatients a week. It serves about seven million people living in the Dar es Salaam region.

Enrollment and sample size estimation

The study involved male patients with BPH and prostate cancer clinically diagnosed through digital rectal examination. We enrolled only patients presenting with genitourinary symptoms within a month who were mentally competent and could consent. Patients with a urine catheter for more than one month and those with other causes of bladder outlet obstruction, including urethral stricture, urolithiasis, bladder cancer, and neurogenic causes, were excluded from the study.

The minimum sample size was 380, calculated using the Kish and Leslie formula (1965), considering the prevalence of 44.7% in Niger, 2016 (9). Participants were enrolled consecutively from August 2021 to January 2022 until a pre-determined sample size was achieved.

Data collection

We used a structured questionnaire to collect data for socio-demographic, clinical information, and genitourinary symptoms by interviewing each patient. Briefly, these questions included the age and residence of participants, recent instrumentation and duration of the catheter in days, recent urological surgery, and recent antibiotic use. Radiological and histopathology results were obtained from the patient's files.

Urine collection

Mid-stream urine (MSU) was collected for culture from non-catheterized patients. For catheterized patients, a clump was placed above the port to allow urine to collect in the bladder, followed by disinfection of the port with 70% alcohol and iodine solution and clump release to collect urine into a sterile urine container. Ten mLs of urine were collected and sent to the microbiology laboratory at MNH for processing immediately.

Bacterial Isolation and Identification

Urine was inoculated onto cysteine lactose electrolyte deficient agar (CLED) and blood agar (BA) plates using a 1 µL loop and incubated aerobically at 37^0C for 18-24 hours. Identification from culture plates with significant bacteria growth of $\geq 10^5$ (CFU/ml) based on Gram stain characteristics, colony morphology, and biochemical tests as described by Mahon et al. (10). Gram-positive bacteria were identified by catalase, coagulase, and DNase (Remel Europe td, Dartford, UK), while Gram-negative bacteria were identified by oxidase, Kligler iron agar (KIA), urease, citrate, and Sulphur, Indole, and Motility (SIM) (Oxoid Ltd, Hampshire, UK).

Analytical Profile Index (API-20E) (Biomerieux, France) was used to identify Gram-negative rods further. *S. aureus* ATCC 25923, *E. coli* ATCC 25922, and *P. aeruginosa* ATCC 27853 were used for quality control of culture media and biochemical tests.

Statistical Analysis

Data analysis was conducted using Statistical Package for the Social Sciences (SPSS) version 27 (Armonk, NY: IBM Corp). Frequencies and percentages were used for categorical variables and median (interquartile range (IQR)) for continuous variables. The chi-square test was used to test the difference in categorical variables. A receiver operating characteristics (ROC) curve day was used to determine the appropriate duration of a urinary catheter stay to avoid UTI. A univariate regression model was used to determine the factors associated with UTI, and factors with a p-value ≤ 0.2 in a univariate model were considered for the multivariate logistic regression analysis. A p-value of < 0.05 was considered statistically significant.

Reporting Guideline

This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional studies, which provide a checklist for reporting observational studies. The checklist comprises key components that should be included in the report, including study design, sampling procedure, data collection and statistical analysis. The authors have attentively reviewed the checklist to make sure that suitable items have been included. The authors used a structured data collection tool to collect information from all study participants and used suitable statistical methods to analyze data and formulate conclusions.

Patient and Public Involvement

Patients and public were not involved in this research design, conduct, reporting or dissemination plans.

RESULTS

Description of study participants

A total of 402 participants were enrolled in the study. The median age was 68, and the IQR was 61 to 75 years. BPH was the most predominant prostatic disease, accounting for 70.4% of all participants. The median prostate size on ultrasonography was 43, and IQR was 24.0 to 74.8 cc. Most participants (46.5%) had a prostate volume of 40 ccs, whereas 19.1% of participants had a PVR urine volume of ≥100 mLs. Forty percent of the participants (161/402) had undergone invasive urological instrumentation, where the urinary catheter was the most invasive instrument employed 155/161 (96.3%).

The proportion of UTI among study participants

The overall proportion of laboratory-confirmed UTI was 46.5% (95% CI 41.56-51.53). UTI was found more in in-patients 103(58.3%) than in out-patients 85(37.4%), $p < 0.001$. UTI was significantly more among catheterized patients 85(70.2%) than non-catheterized patients 102(36.3%), $p < 0.001$. Patients who had prostate size more than 80 ccs had a significantly higher proportion of UTI 55(65.5%) than those with prostate size less than 40 cc 66 (35.5%) $p = 0.001$. Those with a PVR urine volume of more than 100 mLs had a higher proportion of UTI 25(47.2%) than those with a urine volume of less than 100 mLs 74 (32.9%) $p=0.051$. Patients who had undergone instrumentation had a significantly higher proportion of UTI 104(65.4%) than those who did not undergo invasive urological instrumentation 82(33.9%) $p = 0.001$. In comparison, there was no significant difference in UTI among patients with BPH 127(44.9%) and Prostate cancer 60(50.4%) $p = 0.309$ and among patients who had undergone recent urological surgery 53(52.5%) compared to those who did not undergo any urological surgery 134(44.5%) $p = 0.165$. (Table 1).

Factors associated with UTI

In univariate analysis, patients aged > 60 years had twice the odds of having UTI compared to those aged <60 years (cOR = 2.17, 95% CI 1.50-3.37, $p < 0.001$). In-patients had two times the odds of having UTI compared to out-patients (cOR=2.33, 95% CI 1.56-3.49, $p < 0.001$). Patients with incomplete bladder emptying (cOR=2.13, 95% CI 1.43-3.17, p<0.001), recent hospitalization (cOR=2.18, 95% CI 1.40-3.42, $p < 0.001$) had increased two times odds of having UTI. Patients who had prostate size > 80 cc (cOR=3.45, 95% CI 2.12-5.96, $p < 0.001$)

and those who had invasive urological instrumentation (cOR=3.65, 95% CI 2.39-5.55, $p < 0.001$) had increased three times odds of having UTI.

In multivariate analysis, patients aged > 60 years had twice the odds of having UTI compared to those aged <60 years (aOR = 2.0, 95% CI 1.13 - 3.55, $p = 0.018$). Patients with incomplete bladder emptying had two times the odds of having UTI compared to those with complete bladder emptying (aOR=2.57, 95% CI 1.44 - 4.59, $p = 0.001$), and UTI increased by 24% one day increase duration of the catheter (aOR=1.24, 95% CI 1.11- 1.38, $p = 0.005$) (Table 2).

Risk for UTI in indwelling catheter

ROC for developing UTI according to the duration of the urinary catheter is presented in Figure 1. The area under the curve (AUC) was 0.709 (95% CI, 0.67-0.79, $p < 0.001$), and the optimal cut-off value was 7 days. Table 3 shows data on the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for UTI at different cut-off values of catheter days. The sensitivity, specificity, PPV, and NPV for the optimal cut-off value (7 days) were 71.15%, 54.5%, 74.5%, and 50%, respectively.

DISCUSSION

The current study found forty-six out of a hundred patients with enlarged prostate and genital urinary symptoms had laboratory-confirmed UTI. Patients aged more than 60 years old and patients with incomplete bladder emptying were at high risk of developing UTI. Increasing the duration of the urinary catheter increased the risk of having UTI by 24%. Incomplete bladder emptying provides a medium for bacterial growth, increasing the chance of UTI. Corrective measures such as surgery may be indicated for these patients. While catheterization alleviates the problem of incomplete bladder emptying, the findings indicate that it should not be prolonged as the risk of UTI increases with increased duration of catheterization.

Our study's finding of the proportion of UTI in patients with an enlarged prostate is comparable with a report by Agbugui et al., where the proportion of UTI was 44.7% (3,9) However, Ghana reported a higher proportion of UTI (76.6%) among male patients with BPH having urethral catheters (11) Other studies in Austria, Saudi Arabia, and Spain reported lower UTI proportions at 13.6%, 15%, and 20.6%, respectively (12–14). The difference in proportions of UTI may be due to differences in geographical location, climatic conditions, study designs, and population

studied. A high proportion of UTI we found in the current study may be attributed to instrumentation procedures, which are a risk factor for UTI. Similarly, as the prostate enlarges due to physiological changes, it obstructs urine outflow from the bladder through the urethra, which creates an environment for bacteria to grow, which causes infected urine, leading to UTI. Some studies have shown that frequent hospital admissions expose these patients to colonization and infection with multi-drug resistant bacteria that may cause difficulty in treating UTIs in these patients (4,15,16).

As observed in this study, there was a significant association between UTIs and patients' age. Patients aged > 60 years had increased odds of infection as compared to those 60 years and below. Other studies have reported similar findings with increased risk for UTI with advanced age (1,13). Oshodi et al. reported an increase in the proportion of UTI with age in their study, with the highest proportion of 70.6% among patients aged ≥ 80 years (17). The increase in UTI with age may be due to immunosuppression and comorbidities with advanced age. Moreover, in advanced age, there is a decrease in prostatic zinc concentration caused by impaired zinc uptake by body cells (18). Zinc has been shown to play a role as an antibacterial factor, thus preventing infections related to the prostate gland and UTIs among men (19)

Incomplete urinary bladder emptying, which causes urine retention due to obstruction among these participants, has shown a significant association with UTI in this study. This is comparable to findings reported by Hyens et al. that urine stasis is a risk factor for developing UTI (20) Urine retention among these patients may be aggravated by factors such as advanced age that may lead to degeneration of the brain and hence affecting the bladder innervation, which in turn affects bladder emptying and causes incomplete bladder emptying, BPH, cancers metastasizing to the prostate gland and urethral stricture as a result of urethral trauma due to instrumentation (4). Incomplete bladder emptying also results in PVR urine volume, which harbors bacteria that may predispose to UTI (20). In this study, PVR did not show a significant association with UTI. Contrary to findings in other studies that reported that UTI was prevalent in patients with significantly high mean PVR, no cutoff value was determined to predict positive urine culture (3,21). Another study reported similar findings: asymptomatic men with a PVR of 180 ml were at high risk for UTI (3).

Several studies have shown a correlation between PVR and prostate size, with large PVR as prostate size increases, which causes a potential risk for UTI (12,22,23). However, in our study,

prostate size was not associated with UTI. Similar findings have been reported in other studies on UTI among patients with BPH and prostate cancer, whereby prostate size was not an independent predictor of UTI (7,9). The difference may be attributed to study settings and practices like antimicrobial prophylaxis, which were given to our patients to prevent UTIs.

Catheterization is usually done to drain urine due to retention among patients with enlarged prostate and bladder irrigation following surgery (4). However, the current study has shown that prolonged catheterization beyond seven days increases the risk of developing UTI. Several studies have also reported that the risk of UTI increases when the catheter stays long (5,24). The World Health Organization guideline recommends seven to ten days of urinary catheterization for post-operative catheterization following urinary surgical repair in short-term catheterization (25). The Health Infection Control Practices Advisory Committee guideline by the Centre for Disease Control does not recommend changing indwelling catheters or drainage bags as routines or fixed intervals for catheter change (26,27). However, since the medical practices and patient characteristics have changed with time, findings from our study suggest a duration of 7-10 days of urinary catheterization among patients with BPH and prostate cancer to prevent UTI. Multicenter studies should be conducted in larger populations so as to provide more findings, which will aid in providing evidence-based guidelines that will guide the duration of catheterization among this population.

One of the strengths of our study is that it reports the duration of the catheter in days at risk of getting UTI for men with BPH and prostate cancer, which was not done in similar studies. However, during enrollment of patients with BPH and prostate cancer having genitourinary symptoms, we could not establish if the genitourinary symptoms were due to obstruction caused by an enlarged prostate alone without microbial infection, consequently affecting the UTI detection rate.

Conclusion

Modifiable risk factors, incomplete bladder emptying, and catheterization were independently associated with UTI among patients with prostate enlargement. The risk of UTI increases with increasing the duration of the urinary catheter. Interventions such as surgery may be required to correct prostate size, whilst good IPC practices are fundamental during catheterization to prevent CAUTI.

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Authors' contributions

EMN, MM & AJ contributed to conceptualization and data collection. EMN, MM & AS performed the formal analysis. EMN, MM, JM, FM, MIM, AS, AM, ON, EFL, and AJ participated in the writing and thorough perusal of the manuscript and the approved final version. EMN is the guarantor of the study. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Competing interests

None declared.

Patient and public involvement

Patients and/or the public were not involved in this research's design, conduct, reporting, or dissemination plans.

Patient consent for publication

Not applicable.

Ethical Approval

The ethical approval was obtained from Muhimbili University of Health and Allied Sciences (MUHAS), Senate Research and Publications Committee. The reference number DA.282/298/01.C/. Participants were requested to sign informed consent before enrolment in the study.

Provenance and peer review

Not commissioned; externally peer-reviewed.

Data Availability Statement

Data are available on reasonable request. All relevant generated data from this study are available from the corresponding author upon reasonable request.

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Table 1: Proportion of UTI among men with BPH and Prostate Cancer at Muhimbili National Hospital

Variable	Culture results		*P – value*
	N (%)	Positive n (%)	
Age			
40-60	125	42 (33.6)	< 0.001
> 60	277	145 (52.3)	
Service unit			
IPD	175	103 (58.9)	< 0.001
OPD	227	85(37.4)	
Diagnosis (Histology)			
BPH	283	127 (44.9)	0.309
Prostate cancer	119	60 (50.4)	
Urine type			
Mid-stream urine	281	102 (36.3)	< 0.001
Catheterized urine (indwelling catheter)	121	85 (70.2)	
Prostate size (cc)			
<40	172	61 (35.5)	< 0.001
40 – 80	77	32 (41.6)	
>80	153	94 (61.4)	
Post-void residual urine volume (mLs) (N=278)			
<100	225	74 (32.9)	0.051
>100	53	25 (47.2)	
Incomplete bladder emptying			
Yes	204	113 (55.4)	< 0.001
No	198	73 (36.9)	
Invasive urological instrumentation			
Yes	159	105 (66.0)	< 0.001
No	243	82 (33.7)	
Recent urological surgery*			
Yes	101	53 (52.5)	0.165
No	301	134 (44.5)	
Surgical prophylaxis			
Yes	60	30 (50.0)	0.559
No	342	157 (45.9)	
Recent hospitalization*			
Yes	107	65 (60.7)	< 0.001
No	295	121 (41.0)	

* Duration for recent urological surgery and recent hospitalization were within 30 days

Table 2: Factors associated with UTI among patients with BPH and Prostate Cancer at Muhimbili National Hospital

Variable	Univariable analysis			Multivariable analysis		
	cOR	95% CI	*P-value*	aOR	95% CI	*P-value*
Age						
>60	2.17	1.50-3.37	0.001	2.0	1.13-3.55	0.018
40-60	Ref			Ref		
Service unit						
IPD	2.33	1.56-3.49	<0.001	1.10	0.60-2.01	0.761
OPD	Ref			Ref		
Prostate size						
>80	3.45	2.12-5.96	<0.001	1.23	0.65-2.27	0.511
40-80	1.87	1.19-2.96	0.007	1.06	0.47-2.36	0.891
<40	Ref			Ref		
Post void residual urine volume						
>100	1.90	1.03-3.50	0.039	1.32	0.67-2.59	0.001
< 100	Ref			Ref		
Incomplete bladder emptying						
Yes	2.13	1.43-3.17	<0.001	2.57	1.44-4.59	0.001
No	Ref			Ref		
Invasive urological instrumentation						
Yes	3.65	2.39-5.55	<0.001	1.06	0.46-2.44	0.901
No	Ref			Ref		
Duration of indwelling catheter	1.22	1.11-1.35	<0.001	1.24	1.11-1.38	0.005
Recent hospitalization*						
Yes	2.18	1.40-3.42	0.001	0.623	0.29-1.32	0.217
No	Ref			Ref		

cOR: crude Odds Ratio, aOR: adjusted Odds Ratio, Ref: Reference category

* Duration for recent hospitalization was within 30 days

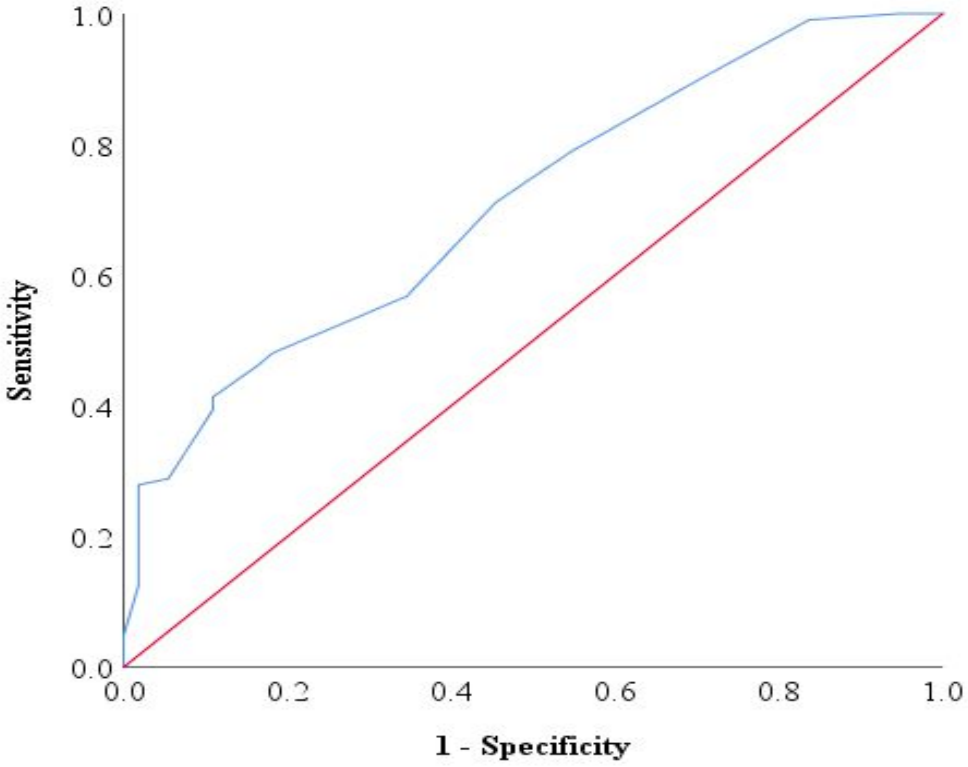

Figure 1: Receiver-operating characteristics curve for inserted urinary catheter-associated urinary tract infection based on the number of catheter days for men with BPH and Prostate cancer at Muhimbili National Hospital

Table 3: Sensitivity, specificity, positive predictive value, and negative predictive value for Catheter associated urinary tract infection at different cut-off values of catheter days.

Cut-off values of catheter days	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Youden's index	AUC	Metric Score
2	100	0	65.41	-	0.00000	0.709	1.00
3	100	5.45	66.67	100	0.05455	0.709	1.05
4	99.04	16.36	69.13	90	0.15402	0.709	1.15
5	90.38	29.09	70.68	61.54	0.19476	0.709	1.19
6	78.85	45.45	73.21	53.19	0.24301	0.709	1.24
7	71.15	54.55	74.75	50	0.25699	0.709	1.26
8	56.73	65.45	75.64	44.44	0.22185	0.709	1.22
9	48.08	81.82	83.33	45.45	0.29895	0.709	1.30
10	46.15	83.64	84.21	45.1	0.29790	0.709	1.30
11	41.35	89.09	87.76	44.55	0.30437	0.709	1.30
12	39.42	89.09	87.23	43.75	0.28514	0.709	1.29
14	28.85	94.55	90.91	41.27	0.23392	0.709	1.23
15	27.88	98.18	96.67	41.86	0.26066	0.709	1.26
16	22.12	98.18	95.83	40	0.20297	0.709	1.20
17	16.35	98.18	94.44	38.3	0.14528	0.709	1.15
18	12.5	98.18	92.86	37.24	0.10682	0.709	1.11
20	4.81	100	100	35.71	0.04808	0.709	1.05
21	3.85	100	100	35.48	0.03846	0.709	1.04
22	0.96	100	100		0.00962	0.709	1.01

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Urinary Tract Infections and associated factors among patients with an enlarged prostate at a Tertiary Hospital, Dar es Salaam, Tanzania: a hospital-based-cross sectional study

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Urinary Tract Infections and associated factors among patients with an enlarged prostate at a Tertiary Hospital, Dar es Salaam, Tanzania: a hospital-based-cross sectional study

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ABSTRACT

Objectives: To determine the prevalence of urinary tract infection (UTI) and associated factors among patients diagnosed with benign prostatic hyperplasia and prostate cancer.

Design: Hospital-based cross-sectional study.

Settings: Urology clinic and urology ward at Muhimbili National Hospital, which is the main tertiary hospital in Tanzania's largest city.

Participants: Patients with benign prostate hyperplasia and prostate cancer presenting with genitourinary symptoms.

Main outcome measure: The primary outcome was the occurrence of UTI and factors associated with UTI in patients with benign prostatic hyperplasia and prostate cancer.

Results: Four hundred and two participants were enrolled, with a median age of 68 and IQR of 61-75 years. The proportion of UTI was 46.5% (95% CI 41.56-51.53%). UTI was more prevalent among in-patients, patients with indwelling urinary catheters, patients with prostate size >80 cc, and those with residual urine volume of > 100mLs. In multivariate analysis, age >60 (aOR = 2.0, 95% CI 1.13-3.55, p=0.018), post-void residual urine volume >100 mLs (aOR=1.32, 95% CI 1.44-2.59 p=0.001), patient with incomplete bladder emptying (aOR=2.57, 95% CI 1.44-4.59, p=0.001) and prolonged catheter duration (aOR=1.24, 95% CI 1.11-1.38, p=0.005) were significantly associated with UTI.

Conclusion: Almost half of the patients with an enlarged prostate and genitourinary symptoms had a laboratory-confirmed UTI. The risk of UTI increases with age, incomplete bladder emptying, and increased duration of catheterization. A one-day increase in the duration of catheterization increased the risk of UTI by 24%.

Keywords: Urinary tract infection, Benign prostate hyperplasia, Incomplete bladder emptying, indwelling urinary catheterization, Prostate cancer.

Strengths and limitations of this study

1. Using the Analytical Profile Index as an addition identification test increased the accuracy of identifying Gram-negative rods.
2. We conducted a receiver-operation curve analysis to predict the duration of the catheter in days at risk of getting UTI for men with BPH and Prostate cancer, which was not done in similar studies.

3. We enrolled patients with enlarged prostate and genitourinary symptoms without establishing if the genital symptoms were due to obstruction caused by an enlarged prostate alone without microbial infection, consequently affecting the UTI detection rate.

INTRODUCTION

Urinary tract infection (UTI) in adult men is often complicated and caused by structural or functional abnormalities of the genitourinary tract. The abnormalities may be due to benign prostate hyperplasia (BPH), prostate cancer, bladder stones, or catheterization (1). UTI related to an enlarged prostate occurs because the bladder does not empty completely, allowing urine to stagnate and creating a suitable environment for pathogens to grow (2). The risk for UTI increases with a larger prostate size, leading to a higher post-void residual (PVR) urine volume (3).

Urinary catheterization is commonly used to relieve retained urine in the urinary bladder obstructed by an enlarged prostate gland (4). Prolonged use of urinary catheters poses a major risk for UTI. (5). However, the exact duration for urinary catheters to cause UTI is unknown (5,6). A study conducted at Bugando Medical Centre in Mwanza reported that 39% of patients had retained urinary catheters beyond the recommended time, leading to an increased risk for UTI with the duration of catheter use (5).

The occurrence of UTI in patients with BPH and prostate cancer varies across different studies and populations (7,8). Isolated bacteria causing UTI have been reported to show a high level of resistance to prescribed antimicrobials thus complicating the management of UTI in this population (9). Identifying the factors that make patients more prone to UTI and taking appropriate measures is crucial in developing effective strategies to prevent UTI in this group and therefore improving patient lifestyle and outcomes. Therefore, our current study aims to assess the magnitude of UTI and identify the factors associated with them as well as to determine the optimal duration for indwelling urinary catheter use with a low risk of UTI.

MATERIALS AND METHODS

Study design and setting

The study was a hospital-based cross-sectional design conducted at Muhimbili National Hospital (MNH) in Dar es Salaam. MNH, which is a referral and teaching hospital, has a 1500-

bed capacity and is the largest tertiary hospital in Tanzania. It sees over 1000 outpatients per week and serves approximately seven million people in the Dar es Salaam region.

Enrolment and sample size estimation

The study involved male patients who had been clinically diagnosed with BPH or prostate cancer through digital rectal examination. We only included patients who had genitourinary symptoms within the past month and were mentally competent to give consent. Patients with a urinary catheter for more than one month and those with other causes of bladder outlet obstruction, such as urethral stricture, urolithiasis, bladder cancer, and neurogenic causes, were excluded from the study.

The minimum sample size was 380, calculated using the Kish and Leslie formula (1965), considering the prevalence of 44.7% in Niger, in 2016. Participants were enrolled consecutively from August 2021 to January 2022 until the predetermined sample size was reached

Data collection

We used a structured questionnaire to gather information about the participants' socio-demographic and clinical details, as well as genitourinary symptoms. The questionnaire included inquiries about the participants' age and place of residence of participants, recent instrumentation (within 30 days of data collection) and duration of catheter use in days, recent urological surgeries (within 30 days of data collection), and recent use of antibiotics (within 30 days of data collection). We also obtained radiological and histopathological results from the patient's records.

Urine collection

Mid-stream urine (MSU) was collected for culture from non-catheterized patients. For catheterised patients, a clump was placed above the port to allow urine to collect in the bladder, followed by disinfection of the port with 70% alcohol and iodine solution and clump release to collect urine into a sterile urine container. Ten mLs of urine were collected and sent to the microbiology laboratory at MNH for processing immediately.

Bacterial Isolation and Identification

Urine was inoculated onto cysteine lactose electrolyte deficient agar (CLED) and blood agar (BA) plates using a 1 µL loop and incubated aerobically at 37^0C for 18-24 hours. Identification

from culture plates with significant bacteria growth of $\geq 10^5$ (CFU/ml) based on Gram stain characteristics, colony morphology, and biochemical tests as described by Mahon et al. (10). Gram-positive bacteria were identified by catalase, coagulase, and DNase (Remel Europe td, Dartford, UK), while Gram-negative bacteria were identified by oxidase, Kligler iron agar (KIA), urease, citrate, and Sulphur, Indole, and Motility (SIM) (Oxoid Ltd, Hampshire, UK). Analytical Profile Index (API-20E) (Biomerieux, France) was used to identify Gram-negative rods further. *S. aureus* ATCC 25923, *E. coli* ATCC 25922, and *P. aeruginosa* ATCC 27853 were used for quality control of culture media and biochemical tests.

Statistical Analysis

Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 27 (Armonk, NY: IBM Corp). We used frequencies and percentages for categorical variables and median (interquartile range (IQR)) for continuous variables. The chi-square test was used to assess the difference in categorical variables. We used a receiver operating characteristics (ROC) to determine the appropriate duration of urinary catheter stay to prevent UTI. A univariate regression model was used to identify the factors associated with UTI and factors with a p-value ≤ 0.2 in a univariate model were considered for the multivariate logistic regression analysis. A p-value of < 0.05 was considered to be statistically significant.

Reporting Guideline

This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional studies, which provide a checklist for reporting observational studies. The checklist comprises key components that should be included in the report, including study design, sampling procedure, data collection and statistical analysis. The authors have attentively reviewed the checklist to make sure that suitable items have been included. The authors used a structured data collection tool to collect information from all study participants and used suitable statistical methods to analyse data and formulate conclusions.

Patient and Public Involvement

Patients and the public were not involved in this research design, conduct, reporting or dissemination plans.

RESULTS

Description of study participants

In this study, a total of 402 participants were enrolled. The median age of the participants was 68, and the IQR was 61 and 75 years. The majority of the participants were from the outpatient (227/402, 56.2%). BPH was the most common prostatic disease, affecting 70.4% of the participants. The median prostate size measured using ultrasonography was 43, and IQR was 24.0 - 74.8 cc. Most participants (46.5%) had a prostate volume of 40 ccs, while 19.1% had a PVR urine volume of ≥100 mLs. Among the participants, 40% (161/402) had undergone invasive urological instrumentation, and the urinary catheter was the most invasive instrument used 155/161 (96.3%) while cystoscopy accounted for 3.7%.

The proportion of UTI among study participants

The overall proportion of laboratory-confirmed UTI was 46.5% (95% CI 41.56-51.53). UTI was found more in in-patients 103(58.3%) than in out-patients 85(37.4%), $p < 0.001$. UTI was significantly higher among catheterized patients 85(70.2%) than non-catheterized patients 102(36.3%), $p < 0.001$. Patients who had prostate size more than 80 cc had a significantly higher proportion of UTI 55(65.5%) than those with prostate size less than 40 cc 66 (35.5%) $p = 0.001$. Those with a PVR urine volume of more than 100 mLs had a higher proportion of UTI 25(47.2%) than those with a urine volume of less than 100 mLs 74 (32.9%) $p=0.051$. Patients who had undergone instrumentation had a significantly higher proportion of UTI 104(65.4%) than those who did not undergo invasive urological instrumentation 82(33.9%) $p = 0.001$. In comparison, there was no significant difference in UTI among patients with BPH 127(44.9%) and Prostate cancer 60(50.4%) $p = 0.309$ and among patients who had undergone recent urological surgery 53(52.5%) compared to those who did not undergo any urological surgery 134(44.5%) $p = 0.165$ (Table 1).

Table 1: Proportion of UTI among men with BPH and Prostate Cancer at Muhimbili National Hospital

Variable	Culture results		*P – value*
	N (%)	Positive n (%)	
Age			
40-60	125	42 (33.6)	< 0.001
> 60	277	145 (52.3)	
Service unit			
IPD	175	103 (58.9)	< 0.001
OPD	227	85(37.4)	
Diagnosis (Histology)			
BPH	283	127 (44.9)	0.309
Prostate cancer	119	60 (50.4)	
Urine type			
Mid-stream urine	281	102 (36.3)	< 0.001
Catheterized urine (indwelling catheter)	121	85 (70.2)	
Prostate size (cc)			
<40	172	61 (35.5)	< 0.001
40 – 80	77	32 (41.6)	
>80	153	94 (61.4)	
Post-void residual urine volume (mLs) (N=278)			
<100	225	74 (32.9)	0.051
>100	53	25 (47.2)	
Incomplete bladder emptying			
Yes	204	113 (55.4)	< 0.001
No	198	73 (36.9)	
Invasive urological instrumentation			
Yes	159	105 (66.0)	< 0.001
No	243	82 (33.7)	
Recent urological surgery*			
Yes	101	53 (52.5)	0.165
No	301	134 (44.5)	
Surgical prophylaxis			
Yes	60	30 (50.0)	0.559
No	342	157 (45.9)	
Recent hospitalization*			
Yes	107	65 (60.7)	< 0.001
No	295	121 (41.0)	

* Duration for recent urological surgery and recent hospitalization were within 30 days

Factors associated with UTI

In univariate analysis, patients aged > 60 years had twice the odds of having UTI compared to those aged <60 years (cOR = 2.17, 95% CI 1.50-3.37, $p < 0.001$). In-patients were observed to have twice the odds of having UTI compared to out-patients (cOR=2.33, 95% CI 1.56-3.49, $p < 0.001$). Patients with incomplete bladder emptying (cOR=2.13, 95% CI 1.43-3.17, p<0.001), and those with recent hospitalization (cOR=2.18, 95% CI 1.40-3.42, $p < 0.001$) were also found to have approximately two times the odds of having UTI. Moreover, patients with a prostate size > 80 cc (cOR=3.45, 95% CI 2.12-5.96, $p < 0.001$) and those who had undergone invasive urological instrumentation (cOR=3.65, 95% CI 2.39-5.55, $p < 0.001$) were observed to have approximately three times the odds of having a UTI.

In multivariate analysis, patients aged > 60 years had twice the odds of having a UTI compared to those aged <60 years (aOR = 2.0, 95% CI 1.13 - 3.55, $p = 0.018$). Patients with PVR urine volume of more than 100 mLs had a higher risk of having UTI than those with PVR urine volume of <100 mLs (aOR = 1.32, 95% CI 0.67-2.59, $p = 0.001$)Patients with incomplete bladder emptying had two times the odds of having a UTI compared to those with complete bladder emptying (aOR=2.57, 95% CI 1.44 - 4.59, $p = 0.001$). Additionally, the odds of UTI increased by 24% for each one-day increase in the duration of catheter use (aOR=1.24, 95% CI 1.11- 1.38, $p = 0.005$) (Table 2).

Table 2: Factors associated with UTI among patients with BPH and Prostate Cancer at Muhimbili National Hospital

Variable	Univariable analysis			Multivariable analysis		
	cOR	95% CI	*P-value*	aOR	95% CI	*P-value*
Age						
>60	2.17	1.50-3.37	0.001	2.0	1.13-3.55	0.018
40-60	Ref			Ref		
Service unit						
IPD	2.33	1.56-3.49	<0.001	1.10	0.60-2.01	0.761
OPD	Ref			Ref		
Prostate size						
>80	3.45	2.12-5.96	<0.001	1.23	0.65-2.27	0.511
40-80	1.87	1.19-2.96	0.007	1.06	0.47-2.36	0.891
<40	Ref			Ref		
Post void residual urine volume						
>100	1.90	1.03-3.50	0.039	1.32	0.67-2.59	0.001
< 100	Ref			Ref		
Incomplete bladder emptying						
Yes	2.13	1.43-3.17	<0.001	2.57	1.44-4.59	0.001
No	Ref			Ref		
Invasive urological instrumentation						
Yes	3.65	2.39-5.55	<0.001	1.06	0.46-2.44	0.901
No	Ref			Ref		
Duration of indwelling catheter	1.22	1.11-1.35	<0.001	1.24	1.11-1.38	0.005
Recent hospitalization*						
Yes	2.18	1.40-3.42	0.001	0.623	0.29-1.32	0.217
No	Ref			Ref		

cOR: crude Odds Ratio, aOR: adjusted Odds Ratio, Ref: Reference category

* Duration for recent hospitalization was within 30 days

Risk for UTI in indwelling catheter

A Receiver Operating Characteristic (ROC) curve illustrating the development of urinary tract infections (UTI) based on the duration of a urinary catheter is depicted in Figure 1. The area under the curve (AUC) was 0.709 (95% CI, 0.67-0.79, $p < 0.001$), with the optimal cut-off value being 7 days. Table 3 shows data on the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for UTI at various cut-off values. At the optimal cut-off value of 7 days, the sensitivity, specificity, PPV, and NPV were 71.15%, 54.5%, 74.5%, and 50%, respectively (Table 3).

Table 3: Sensitivity, specificity, positive predictive value, and negative predictive value for Catheter associated urinary tract infection at different cut-off values of catheter days.

Cut-off values of catheter days	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Youden's index	AUC	Metric Score
2	100	0	65.41	-	0.00000	0.709	1.00
3	100	5.45	66.67	100	0.05455	0.709	1.05
4	99.04	16.36	69.13	90	0.15402	0.709	1.15
5	90.38	29.09	70.68	61.54	0.19476	0.709	1.19
6	78.85	45.45	73.21	53.19	0.24301	0.709	1.24
7	71.15	54.55	74.75	50	0.25699	0.709	1.26
8	56.73	65.45	75.64	44.44	0.22185	0.709	1.22
9	48.08	81.82	83.33	45.45	0.29895	0.709	1.30
10	46.15	83.64	84.21	45.1	0.29790	0.709	1.30
11	41.35	89.09	87.76	44.55	0.30437	0.709	1.30
12	39.42	89.09	87.23	43.75	0.28514	0.709	1.29
14	28.85	94.55	90.91	41.27	0.23392	0.709	1.23
15	27.88	98.18	96.67	41.86	0.26066	0.709	1.26
16	22.12	98.18	95.83	40	0.20297	0.709	1.20
17	16.35	98.18	94.44	38.3	0.14528	0.709	1.15
18	12.5	98.18	92.86	37.24	0.10682	0.709	1.11
20	4.81	100	100	35.71	0.04808	0.709	1.05
21	3.85	100	100	35.48	0.03846	0.709	1.04
22	0.96	100	100		0.00962	0.709	1.01

DISCUSSION

This study found out of a hundred patients with an enlarged prostate and urinary symptoms, forty-six were found to have a laboratory-confirmed UTI. Patients over 60 years old and those with incomplete bladder emptying were found to be at a higher risk of developing UTI. This study also found that the longer the urinary catheter was in place, the greater the risk of developing a UTI, with a 24% increase in risk for each day the catheter was used. Incomplete bladder emptying can lead to bacterial growth, increasing the likelihood of developing a UTI. For these patients, corrective measures such as surgery may be surgery may be necessary. While catheterization can help with incomplete bladder emptying, the findings suggest that it should not be prolonged as the risk of UTI increases with longer catheter use.

The proportion of UTI in patients with an enlarged prostate was consistent with a report by Agbugui et al., which found a 44.7% UTI proportion (3,9). However, Ghana reported a higher proportion of UTI (76.6%) among male patients with BPH having urethral catheters (11). Other studies in Austria, Saudi Arabia, and Spain reported lower UTI proportions at 13.6%, 15%, and 20.6%, respectively (12–14). The differences in proportions of UTI may be due to differences in geographical location, climatic conditions, study designs, and the population studied. The high proportion of UTI in our study may be attributed to instrumentation procedures, which are a risk factor for UTI. As the prostate enlarges due to physiological changes, it obstructs urine outflow from the bladder through the urethra, creating an environment for bacteria to grow and cause infected urine, leading to UTI. Frequent hospital admissions expose these patients to colonization and infection with multi-drug resistant bacteria, which may cause difficulty in treating UTIs in these patients (4,15,16).

According to this study, there was a significant association between UTIs and the age of patients. Patients over 60 years had a higher likelihood of infection as compared to those who were 60 years or younger. Other studies have shown similar results, linking the risk of UTI with advanced age (1,13). Oshodi et al. reported an increase in the proportion of UTIs with age in their study, with the highest proportion being 70.6% among patients aged 80 years and older (17). The increase in UTI with age may be due to weakened immune systems and the presence of comorbidities in older patients. Additionally, in advanced age, there is a decrease in the concentration of zinc in the prostate due to impaired zinc uptake by body cells (18). Zinc has been found to have antibacterial properties, which can help prevent infections related to the prostate gland and UTIs among men (19).

Incomplete emptying of the urinary bladder, leading to urine retention due to obstruction, has been significantly associated with UTI in this study. This is consistent with previous findings reported by Hyens et al. that urine stasis is a risk factor for developing UTI (20). Urine retention in these patients may be worsened by factors such as enlargement of the prostate gland, cancers metastasising to the prostate gland and urethral stricture as a result of urethral trauma due to instrumentation, and advanced age, which may lead to degeneration of the brain, affecting bladder innervation, and consequently, bladder emptying (4).

In our study, a PVR > 100mls was significantly associated with UTI among these patients. Incomplete bladder emptying also results in PVR urine volume, which can harbour bacteria

and predispose to UTI (20). Additionally, other studies reported that UTI was prevalent in patients with significantly high mean PVR, however, no specific cut-off value was determined to predict positive urine culture (3,21). Another study reported similar findings: where men without symptoms but with a PVR of 180 ml were at high risk for UTI (3).

Several studies have shown that as the prostate size increases, there is a correlation with a larger PVR, which can potentially lead to an increased risk of UTI (12,22,23). A recent study by Righetto *et al*. showed that patients with renal transplants and moderate lower urinary tract symptoms benefit from urodynamic evaluation and early transurethral resection of the prostate, whereby early surgical resolution of the prostate obstruction can lead to a reduced rate of UTI (24). However, in our study, we found that prostate size was not associated with UTI. Similar findings have been reported in other studies on UTI among patients with BPH and prostate cancer, whereby prostate size was not an independent predictor of UTI (7,9). These findings may be attributed to factors such as settings and practices including the use of antimicrobial prophylaxis in our patients to prevent UTIs.

Catheterization is usually performed to drain urine due to retention in patients with enlarged prostates, and bladder irrigation following surgery (4). However, our current study has shown that prolonged catheterization beyond seven days increases the risk of developing UTI. Several studies have also reported that the risk of UTI increases with longer catheterization periods (5,25). The World Health Organization guideline recommends seven to ten days of urinary catheterization after urinary surgical repair in short-term catheterization (26). The Health Infection Control Practices Advisory Committee guideline by the Centre for Disease Control does not recommend routine changing of indwelling catheters or drainage bags at fixed intervals for catheter change (27,28). Nevertheless, since the medical practices and patient characteristics have evolved, our study suggests 7-10 days of urinary catheterization among patients with BPH and prostate cancer to prevent UTI. It is important to note that multicentre studies involving larger populations should be conducted to provide more comprehensive findings. This will be crucial in establishing evidence-based guidelines to determine the appropriate duration of catheterization among this patient population. A recent study showed that in kidney-transplanted patients with lower urinary tract symptoms, early removal of the bladder catheter can lead to a reduced rate of infection and possible impairment of the transplanted kidney (24).

One of the strengths of our study is that it includes the duration of the catheterization in days at risk of UTI for men with BPH and prostate cancer, which was not addressed in previous studies. However, we faced challenges in determining whether genitourinary symptoms in patients with BPH and prostate cancer were solely due to an enlarged prostate causing obstruction, without any microbial infection, and this may have impacted the detection rate of UTIs.

Conclusion

Our study shows, at the multivariate analysis, a positive correlation between advanced patients' age, PVR >100 mLs, incomplete bladder emptying, days of catheterization higher than 7 days and UTI among patients with prostate enlargement and genitourinary symptoms. Intervention to resolve urinary obstruction, such as prostate surgery should not be delayed in these patients, to achieve prompt catheter removal and prevention of clinically significant urinary tract infections.

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Authors' contributions

EMN, MM & AJ contributed to conceptualization and data collection. EMN, MM, PK and AS performed the formal analysis. EMN, MM, ON, JM, AS, AM, PK, EFL, and AJ participated in the writing and thorough perusal of the manuscript and the approved final version. EMN is the guarantor of the study. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. The lead author

(the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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Competing interests

None declared.

Patient and public involvement

Patients and/or the public were not involved in this research's design, conduct, reporting, or dissemination plans.

Patient consent for publication

Not applicable.

Ethical Approval

The ethical approval was obtained from Muhimbili University of Health and Allied Sciences (MUHAS), Senate Research and Publications Committee. The reference number DA.282/298/01.C/. Participants were requested to sign informed consent before enrolment in the study.

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Data Availability Statement

Data are available on reasonable request. All relevant generated data from this study are available from the corresponding author upon reasonable request.

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