FACTORS ASSOCIATED WITH URINARY TRACT INFECTIONS IN PATIENTS UNDERGOING TRANSRECTAL PROSTATE BIOPSY AT ADULT HOSPITAL OF THE UNIVERSITY TEACHING HOSPITALS, LUSAKA, ZAMBIA

By

NKAMBO MALEMUNA

A Dissertation Submitted to The University of Zambia School of Medicine in Partial Fulfilment of the requirements for the award of Master of Medicine in Urology

University of Zambia

LUSAKA

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DECLARATION

I, **Dr Nkambo Malemuna**, declare that this **dissertation** is my own original work and that it has not been presented to any other university for a similar or any other degree award.

Signature …….. Date …….

SUPERVISOR

This dissertation has been submitted for examination with my approval.

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ABSTRACT

Background: Transrectal prostate biopsy is currently the standard technique for obtaining tissue to make a histological diagnosis of prostate cancer. Infectious complications after the procedure can occur despite patients being on antibiotic prophylaxis. These complications range from being mild to severe and life-threatening. Growing evidence attributes this to the increasing resistance to the commonly used antimicrobial agents. The study therefore aimed at evaluating the risk factors of urinary tract infections following prostate biopsy, establishing the pathogens involved and their resistance patterns.

Methodology: This was a prospective cross-sectional study of a consecutive cohort of patients who underwent transrectal prostate biopsy at the adult Hospital of the University Teaching Hospitals between September 2019 and February 2020. All patients meeting the inclusion criteria were enrolled, demographic and clinical details were obtained using a questionnaire. Rectal swabs and urine for culture were collected before the procedure. A second urine sample for culture was collected one week after the procedure. Data analysis was conducted using STATA version 13 and results with p-value less than 0.05 were considered significant.

Results: Of the 139 patients who participated in the study, 18 (12.9%) had a urinary tract infection after prostate biopsy. HIV seropositive status was a significant predictor for development of UTI after prostate biopsy. *Escherichia coli* was the most common pathogen isolated in the rectal swab (63%). In post biopsy urine, *Escherichia coli* was isolated in 67% (12/18) of patients with UTI. Its resistance to the routinely used antibiotic (Ciprofloxacin) was 83% (10/12) and sensitivity to Fosfomycin and Nitrofurantoin was 100 % and 75% respectively.

Conclusion: The prevalence of UTIs after transrectal prostate biopsy was 12.9% and *E coli* was the main causative organism. HIV seropositive status, history of having been in acute urinary retention and paraplegia were independent predictors of UTI after prostate biopsy.

Keywords: pre-biopsy antibiotic prophylaxis, transrectal prostate biopsy, rectal swab, urinary tract infection.

DEDICATION

I dedicate this research work to my wife Sharon, my wonderful children Ackim and Amira and my parents, Chief Mushala and Netter Malemuna. Thank you for your unconditional support, patience and understanding during the period of formulating this document.

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ABBREVIATIONS

AUR	Acute Urinary Retention
BMI	Body Mass Index
CFU	Colony forming units
HIV	Human Immunodeficiency Virus
LUTS	Lower Urinary Tract Symptoms
PSA	Prostate Specific Antigen
STATA	Statistics and data
TRUS	Transrectal Ultrasound
UTH	University Teaching Hospitals
UNZABREC	University of Zambia biomedical research and ethics committee

CHAPTER ONE: INTRODUCTION

1.1 Background

Prostate biopsy is the most common procedure performed in the outpatient urological clinic at the adult hospital of the University Teaching Hospitals, urology section (UTH audit, 2018). It is usually performed when cancer of the prostate is suspected, based on digital rectal examination and/or prostate specific antigen (PSA) levels. A transrectal prostate biopsy is the primary modality used to diagnose prostate cancer. It is a well-tolerated procedure hence is commonly performed on an outpatient basis (Williamson et al, 2013).

Most complications of transrectal prostate biopsies are minor, such as pain, haematuria, hematospermia, and rectal bleeding, and are self-limiting and therefore seldom require intervention. However, major complications such as febrile urinary tract infections (UTIs) or Urosepsis frequently require hospital admission for supportive care and parenteral antibiotic administration (Pinkhasov et al, 2012). Despite being a well-tolerated procedure, prostate biopsy complications are reported in up to 50% of cases. Of the major complications, infectious complications are potentially life-threatening ones (Young et al, 2009).

It is theorized that bacterial flora harboured in the rectum are introduced into the genitourinary system or systemically into the bloodstream following perforation of the rectal mucosa with the transrectal biopsy needle (Batura et al, 2010). The prevalence of urinary tract infections ranges from 2% to 6% and that of sepsis from 0.2% to 2%. One recent study reported that among post-prostate biopsy patients hospitalized with *E coli* bacteraemia, 25% had severe sepsis requiring intensive care unit (ICU) admission (Williamson et al, 2013).

Patients with long-term urethral catheters are significantly more likely to develop an infectious complication after prostate biopsy compared to patients without catheters (Samsir et al, 2010). Several recent reports suggest that the incidence of infectious complications after transrectal prostate biopsy is increasing. The reasons for these

reported increases in prostate biopsy infections are unclear but suggested contributory factors include rising rates of antimicrobial resistance to recommended antibiotic prophylaxis that is routinely given to patients undergoing prostate biopsy (Loeb et al, 2012). Therefore, the successful management of urinary tract infection complicating transrectal prostate biopsy depends on the recognition of its unique features, the pathogens involved and their antimicrobial susceptibility (Tal et al. 2013).

Antibiotic prophylaxis is one of the methods used in the prevention of infectious complications. Fluoroquinolones are recommended as first-line prophylactic agents before transrectal biopsy in current guidelines (AUA guidelines, 2012). They are particularly useful in antimicrobial prophylaxis due to their broad spectrum of activity against intestinal flora and high prostatic tissue levels obtained after oral administration (Drusano et al, 2010). Despite routine antibiotic prophylaxis, infectious complications are a continued threat following transrectal prostate biopsies and *Escherichia coli* is the primary organism worldwide causing infection in patients receiving a transrectal prostate biopsy (Young et al, 2009).

Although only reported from smaller cohorts to date, evidence supports the existence of a link between post-biopsy infection with an antibiotic-resistant *E coli* and receipt of an antimicrobial agent in the months preceding biopsy (Young et al, 2009). Moreover, the link between prior antibiotic exposure, colonization with an antibiotic-resistant *E coli*, and subsequent post-biopsy infection with the antibiotic-resistant *E coli* has also been demonstrated (Steensels et al, 2012).

Given increasing rates of antibiotic resistance in *E coli* in many countries and the frequent isolation of such organisms in cases of post-biopsy sepsis, a key question is whether universal use of prophylactic antibiotics will remain an appropriate recommendation. Rather than a “one size fits all” model, recent data suggest that a tailored approach to prophylaxis may be more clinically useful and cost-effective (Steensels et al, 2012). This requires knowledge of the local sensitivity patterns of the organisms. The role of prebiopsy screening for resistant pathogens, followed by culture-directed antimicrobial prophylaxis has been assessed in several studies (Taylor et al, 2012).

Since most post transrectal biopsy infections are caused by rectal flora, rectal swab culture-directed antibiotic prophylaxis may be the most reasonable approach in reducing infections. In particular, it is suggested that screening for antibiotic-resistant *E coli* may allow identification of those men harbouring such organisms in their endogenous gastrointestinal flora prebiopsy, and for whom antibiotic prophylaxis may not be appropriate (Liss et al, 2011).

Zambia has adopted the guidelines for antimicrobial prophylaxis in the prevention of infectious complications related to prostate biopsy from other continents. The local sensitivity patterns of the rectal flora among men undergoing prostate biopsy are not well established to support the antimicrobial choice possibly resulting in the high prevalence of urinary tract infections. Therefore, a study of the factors associated with urinary tract infections in men undergoing prostate biopsy is of paramount importance.

1.2 Statement of the problem

The use of antibiotic prophylaxis before urologic surgical procedures is a recognized strategy to prevent postoperative infections (Saase et al, 1998; Bonkat et al, 2017). However, despite these measures being put in place, we do get cases of Urinary tract infections, Urosepsis, and other infection-related complications post prostate biopsy (UTH audit, 2018).

The acceptable prevalence of UTIs after prostate biopsy is less than 10% (Lange et al, 2009). It is less because recommended antibiotic prophylaxis is given to patients undergoing prostate biopsy prior to the procedure. However, in our practice, we are seeing a high prevalence of UTIs as much as 30% (UTH Urology clinic registry, 2018) and this is depicted in the high number of cases of non-elective hospital admissions following biopsy. This is despite patients receiving antibiotic prophylactic treatment before biopsies.

It, therefore, remains to be known the factors that are associated with Urinary tract infections in patients undergoing prostate biopsy.

1.3 Significance

If bacterial growth on a rectal swab culture proves to be a significant predictor of clinical infection, then knowing the local profiles may have important implications in the evaluation of the suitability of prophylactic regimes. The antimicrobial profile of the rectal swabs may also be useful in aiding the empirical treatment of patients presenting to the hospital with infectious complications after prostate biopsy and in guiding targeted antibiotic prophylaxis.

By reducing the chances of infection after transrectal prostate biopsy and its subsequent treatment and by reducing the development of multidrug-resistant strains as compared to the augmented approach, a targeted approach reduces overall health care costs (Taylor et al, 2012).

Infections cause morbidity to the patient and therefore prostate biopsy is proving to be a relatively unsafe procedure. There is a need to make the procedure safe by targeted prophylaxis according to the local sensitivity patterns. This reduces the cost to the patient in accessing healthcare post-biopsy and reduces the loss of productivity due to illness. There is also a reduction in the cost to the healthcare system in terms of human resources, hospital stay, and drugs used in treating infectious complications. Infection is costly to the institution (Batura et al, 2010) and the patient.

1.4 Research Question

This study sought to answer the following research question: What are the factors associated with urinary tract infections in patients undergoing transrectal prostate biopsy?

1.5 Objectives

1.5.1 Main Objective

To find out factors associated with urinary tract infections in patients undergoing transrectal prostate biopsy.

1.5.2 Specific Objectives

1. To determine the prevalence of urinary tract infections in patients undergoing transrectal prostate biopsy at UTH.
2. To establish the microbiological profile of rectal flora and urine in patients with UTI after prostate biopsy.
3. To determine whether the demographic and clinical characteristics of patients undergoing prostate biopsy had an effect on them developing urinary tract infections.

CHAPTER TWO: LITERATURE REVIEW

Numerous studies have been carried out world over to look at the factors that could explain the occurrence of infectious complications after prostate biopsy. In China, Wu et al, 2018, did a study to ascertain the risk factors associated with infectious complications after trans-rectal ultrasound guided prostate biopsy. They found that history of diabetes, BMI >28.196 kg/m² and preoperative catheterization were independent risk factors for infection after prostate biopsy. The study showed that the prevalence of UTIs after biopsy was 4.99% and *E coli* was the most frequent pathogen with significant resistance to fluoroquinolones.

According to a study done by Eruz et al, 2017, in Turkey whose aim was to identify the risk factors associated with the development of infectious complications after prostate biopsy and to investigate the role of intestinal colonisation of bacteria that are resistant to prophylactic antibiotics, it was found that the prevalence of UTIs after prostate biopsy was 10.1%. The study demonstrated that recent antibiotic usage, the presence of a permanent urinary catheter at the time of biopsy, history of urolithiasis, a recent history of hospitalisation and intestinal colonisation by ciprofloxacin-resistant bacteria significantly increased the risk of UTI after transrectal prostate biopsy.

Sultan et al did a study in Saudi Arabia in 2016 which aimed at determining the prevalence of urinary tract infections (UTIs) secondary to trans-rectal biopsy of the prostate, the pathogens involved and patterns of antibiotic resistance in a cohort of patients. In this study, a total of 139 patients were recruited. Twenty-nine (29) patients were worked up for symptoms suggestive of UTI, out of which 4 had uncomplicated UTI. The prevalence of UTI was determined to be 2.8% and the most common pathogens were *Escherichia coli* (90.1%) and *Klebsiella pneumoniae* (9.1%). Resistance to the routinely used prophylaxis (ciprofloxacin) was observed in 10 of these patients (90.9%).

Otrock et al did a similar study in 2004 at a tertiary institution in Lebanon to determine the incidence of urinary tract infections (UTIs) following transrectal guided needle biopsy of the prostate and the bacteriology of these infections. Two hundred and seven (207) patients underwent transrectal prostate biopsy. Thirteen patients (13) were

admitted with UTI. All had rigors and fever on admission. Symptoms appeared at a mean of 2.7 days. Age and hypertension were found to be significant independent predictors of infectious complications after prostate biopsy. The UTI prevalence in this study was found to be 3.86%. All positive cultures grew *Escherichia coli* resistant to ciprofloxacin, with 5 isolates producing extended-spectrum beta-lactamases.

In South Korea, Choi et al carried out a study in 2014 whose aim was to determine the incidence of infectious complications after prostate biopsy and identify the associated risk factors. They analysed 1,195 patients who underwent a prostate needle biopsy at their hospital between January 2007 and December 2012. Patients who experienced post-biopsy febrile UTI that occurred within 7 days were investigated. The study determined the prevalence of UTIs to be 3.00%. It was also found that biopsy core number $\geq$ 12 and body mass index (BMI) >25 kg/m² were independent predictors of infectious complication after prostate biopsy. *E coli* was the most frequent pathogen (80%), followed by *Enterococcus faecalis* (8%) and *Pseudomonas aeruginosa*, *Proteus mirabilis*, and *Burkholderia cepacia* (1%). Resistance patterns were most commonly seen with ampicillin (85.7%), piperacillin (75%), fluoroquinolone (70%), cephalothin (57.1%), and amoxicillin/clavulanic acid (33.3%). However, 90% or greater susceptibility was demonstrated for amikacin, imipenem, piperacillin/tazobactam, cefazolin, tigecycline, and aztreonam.

In New Zealand, Sanders et al did a study in 2012 to assess the local incidence and causative organisms of hospital admissions with infectious complications after transrectal prostate biopsy. The prevalence of UTIs was found to be 1.83%. The most common isolated pathogen was *Escherichia coli* (88.5%), followed by *Klebsiella* (7.7%) and *Proteus mirabilis (3.8%).* The majority of the *E coli* was resistant to amoxicillin (78%), and over half had intermediate or complete resistance to fluoroquinolones (57%). Significant resistance was also seen with trimethoprim (52%). A combination of gentamicin and ceftriaxone provided an effective regime against all *E coli* cultured. Factors that were identified as possible contributors to increasing hospital admission rates after transrectal prostate biopsy included diabetes, recent quinolone use and the number of cores performed.

A North American study by Zaytoun et al in 2010 looked at the sensitivity and resistance of *Escherichia coli* in patients with infectious complications after prostate biopsy. The sensitivity and resistance of *E coli* were attained through the analysis of urine cultures of patients with suspected infection. The prevalence of UTIs in this study was determined to be 1.18%. *E coli* was isolated in 50% of the patients with a positive culture. They therefore concluded that fluoroquinolone-resistant *E coli* was a significant risk factor in patients with febrile urinary tract infection after prostate biopsy.

In Canada, *Lange* et al did a retrospective study in 2009 to determine the incidence of infectious complications (urosepsis) following transrectal prostate biopsy. Urine samples were analysed for resistance and sensitivity patterns. The prevalence of UTIs was found to be 0.25%. *E coli* was isolated in 45% of patients with a positive urine culture. Resistance patterns were most commonly seen with ciprofloxacin (92%), ampicillin (92%), piperacillin (58%), sulphamethoxazole (58%), and tetracycline (58%). These organisms were most sensitive to nitrofurantoin (92%), gentamicin (67%), tobramycin (67%), and cefazolin (83%).

In another study carried out in Lebanon, it was found that the prevalence of urosepsis following transrectal prostate biopsy was 9.4%. *E coli* resistance to the recommended antibiotics was 72.2%. The study also established that age and hypertension comorbidity were the independent predictors of urosepsis after prostate biopsy (Shahait M et al, 2014).

According to my search, no study has been done in Zambia or Africa in general to determine the prevalence of urinary tract infections post transrectal prostate biopsy and its associated factors. It is clear from the studies reviewed that the prevalence of UTI following transrectal prostate biopsy is low. Why we are seeing many UTIs remains to be determined and proved.

CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Research Methods

In this part of the dissertation, detailed descriptions of the methods used in the study are presented. Cardinal aspects include data collection techniques, study type, sampling methods and procedures, data collection and analysis, ethical considerations.

3.2 Study Design

The study was a prospective cross-sectional study conducted on patients undergoing transrectal prostate biopsy.

3.2.1 Study site

The study was conducted in the Department of Surgery; Urology section at the University Teaching Hospitals, Adult hospital, Lusaka, Zambia.

3.2.2 Target Population

All men scheduled for prostate biopsy

3.2.3 Study Population

Patients undergoing prostate biopsy at UTH, not on antibiotic treatment for other medical conditions.

3.3 Criteria

3.3.1 Inclusion criteria

Patients scheduled for prostate biopsy according to guidelines.

3.3.2 Exclusion criteria

- Patients on antibiotic treatment for other medical conditions.
- Patients who refuse to consent

3.4 Sample size

The sample size was determined using the Open Source Epidemiologic Statistics (OpenEpi) software version 3.01 for a cross-sectional study. Using hypothesized percentage frequency of UTI of 10% and a confidence level of 95%, the sample size was found to be 139.

3.5 Sampling

Systematic random sampling method was used.

3.6 Procedure

Patients scheduled for prostate biopsy were enrolled in the study and informed consent was obtained. Demographic and clinical data were collected using a data collection tool. Rectal swabs were collected using cotton-tipped culture swabs in a standard collection system without enrichment immediately before prostate biopsy. Midstream Urine (MSU) for culture and sensitivity was also collected in a sterile container before the procedure. At this point, the patient was handed over to the attending doctor to proceed with the biopsy. The researcher had no influence on who did the biopsy in terms of experience or how many cores of prostate tissue were obtained.

Prostate biopsy (finger-guided or transrectal ultrasound-guided) was performed as per standard procedure using an 18mm biopsy needle and patients received the standard 5-day antibiotic prophylaxis of oral Ciprofloxacin (Ciprofloxacin is empirically given as antibiotic prophylaxis to patients who have shown up for biopsy).

The collected urine and rectal swab samples were transferred to the microbiology laboratory within 2 hours of collection. Patients were educated on the possible complications of the procedure, their symptoms and instructed to report back early to the hospital if they developed any of them; otherwise, they were followed up according to routine practice at 1 week after biopsy at which point a second urine sample was collected by the researcher for culture and sensitivity.

Samples were inoculated on blood agar and CLED/MacConkey agar and incubated for 24-48hrs. Significant growth was when pure colonies of organisms met a threshold of 10^5 cfu/ml. Antimicrobial sensitivity testing was carried out by the Kirky-Bauer disc diffusion technique (Clinical and Laboratory Standards Institute, 2017). Research assistants who were part of the protocol development were involved in the study.

3.7 Study limitations

The researcher had no influence on the number of cores/punctures that were done in the procedure as this was at the discretion of the attending doctor. The researcher also had no influence on the experience of the attending doctor performing the biopsy.

3.8 Variables

3.8.1 Independent variables

1. Age
2. Level of education
3. Home residence
4. Clinical features
    a. Diabetes
    b. Hypertension
    c. HIV status
    d. Lower urinary tract symptoms
    e. History of acute urinary retention
    f. Paraplegia
5. Duration of symptoms
6. History of having a urethral catheter inserted before.
7. Prostate specific antigen (PSA)
8. Prostate volume
9. Rectal swab microbiology
10. Type of biopsy
    a. Finger-guided
    b. Transrectal ultrasound (TRUS) guided
11. Number of biopsy cores obtained

3.8.2 Dependent Variables

Urinary tract infection after prostate biopsy

3.9 Data Collection

Data was collected using data collection sheets through interviews and file reviews. Data was then entered into a Microsoft Excel spreadsheet.

3.10 Data Analysis

Data was collected using a structured questionnaire and entered into an excel spreadsheet and exported to STATA version 13.1 for analysis. All continuous variables were tested for normality using the shapiron-wilk test.

To describe continuous variables such as age and duration of symptoms, mean and standard deviation was used if data was normally distributed. If not normally distributed, the median and interquartile range was used.

To compare continuous variables such as duration of symptoms with a categorical variable such as the presence of a urinary tract infection, Unpaired T-test was used if data was normally distributed and Mann-Whitney test if data was not normally distributed.

To determine an association between categorical variables such as the history of catheter use and urine culture, Chi-square or Fishers exact (if numbers in any of the cell was less than 5) was used.

To determine the correlation between duration of symptoms and PSA result, Pearson's correlation was used if data normally distributed and Spearman's correlation if data not normally distributed.

To determine factors associated with urinary tract infections in patients undergoing transrectal prostate biopsy, Multivariate multiple logistic regression was used.

All statistical tests were done at a 95% confidence interval level and statistical significance was carried out at a p-value < 0.05.

3.11 Ethical Consideration

Benefits: There were no direct benefits for the participants. The participants did not receive any special treatment and did not receive any financial benefits for participating in the study. All procedures, investigations and follow up were as per standard routine management.

Risks: There was no direct risk to participants as the study was not interventional.

Confidentiality: A high level of confidentiality was maintained at all times. Participant's names were not used instead, numbers were used for identification. The data collection sheets were kept under lock and key and only the researcher had access to the key. Once the information was entered into a computer, which was password protected and the password was only known to the researcher.

Voluntarism: Participation in this study was completely voluntary, no coercion was used. Patients were free to withdraw from the study at any time without having to give a reason and this did not have any implications on their management.

Written Consent: A written informed consent was obtained from each patient before their enrolment into the study.

CHAPTER FOUR: RESULTS

This chapter presents the findings of the study. The main objective was to find out factors associated with urinary tract infections in patients undergoing transrectal prostate biopsy. The specific objectives were to determine the prevalence of urinary tract infections in patients undergoing transrectal prostate biopsy at UTH, to establish the microbiological profile of rectal flora and urine in patients undergoing transrectal prostate biopsy and to determine whether the demographic and clinical characteristics of patients undergoing prostate biopsy had an effect on them developing urinary tract infections.

4.1 Demographic Characteristics of study participants

There were a total of 139 participants in this study. The mean age of the study participants was 67.9 (± 9.3) years. The majority of the participants, 76 (54.7%) had tertiary education and 6 (4.3%) only had primary education. Eighty-one (58.3%) of the participants resided in medium density areas while 9 (6.5%) resided in low-density areas as shown in Table 4.1.

Table 4. 1: Baseline demographic characteristics of the study participants

Variable		
Age*	67.9 (SD, ±9.3)	
	Category	Proportion (%)
Education level	Primary	6 (4.3)
	Secondary	57 (41.0)
	Tertiary	76 (54.7)
Residence	Low density	9 (6.5)
	Medium-density	81 (58.3)
	High density	49 (35.3)

*mean and standard deviation reported; SD= standard deviation

4.2 Clinical Characteristics of study participants

In this study, the mean PSA, prostate volume, number of prostate biopsy cores and duration of symptoms was 87.5 ng/ml, 78.6 ml, 7.0 cores and 3.4 months respectively. Twenty-four (17.3%) of the patients were diabetic, 63 (45.3%) were hypertensive and 12 (8.6%) were HIV positive. The majority of the participants 110 (79.1%) experienced LUTS, 45 (32.4%) reported having an episode of AUR. Four (2.9%) of the participants were paraplegic, 38 (27.3%) gave a history of urethral catheter use. Seventy-two (51.80%) of the participants underwent finger-guided prostate biopsy while 67 (48.20%) underwent transrectal ultrasound-guided prostate biopsy as shown in Table 4.2.

Table 4.2: Baseline clinical characteristics of the study participants

Variable	Value	
Duration of symptoms*	3.4 (SD, ±2.7)	
PSA*	87.5 (SD, ±91.5)	
Prostate volume*	78.6 (SD, ±33.0)	
Number of biopsy cores*	7.0 (SD, ±1.0)	
	Category	Proportion (%)
Diabetes	Yes	24 (17.3)
	No	76 (54.7)
Hypertension	Yes	63 (45.3)
	No	76 (54.7)
HIV status	Positive	12 (8.6)
	Negative	127 (91.4)
LUTS	Yes	110 (79.1)
	No	29 (20.9)

Table 4.2 continued

AUR	Yes	45 (32.4)
	No	94 (67.6)
Paraplegia	Yes	4 (2.9)
	No	135 (97.1)
History of catheter use	Yes	38 (27.3)
	No	101 (72.7)
Biopsy type	Finger guided	72 (51.80)
	TRUS guided	67 (48.20)

*mean and standard deviation reported; SD= standard deviation; LUTS=lower urinary tract symptoms; AUR=acute urinary retention; HIV= human immunodeficiency virus; TRUS=transrectal ultrasound

4.3 Comparison of age between participants who had culture positive urine and negative urine culture post prostate biopsy.

When the age was compared between participants who had culture-positive urine to those who had culture-negative urine post prostate biopsy, the mean age was 70.8 years for participants with culture-positive urine and 67.5 years for participants with culture-negative urine. However, this was not statistically significant ($p = 0.157$) as shown in Figure 4.1 below.

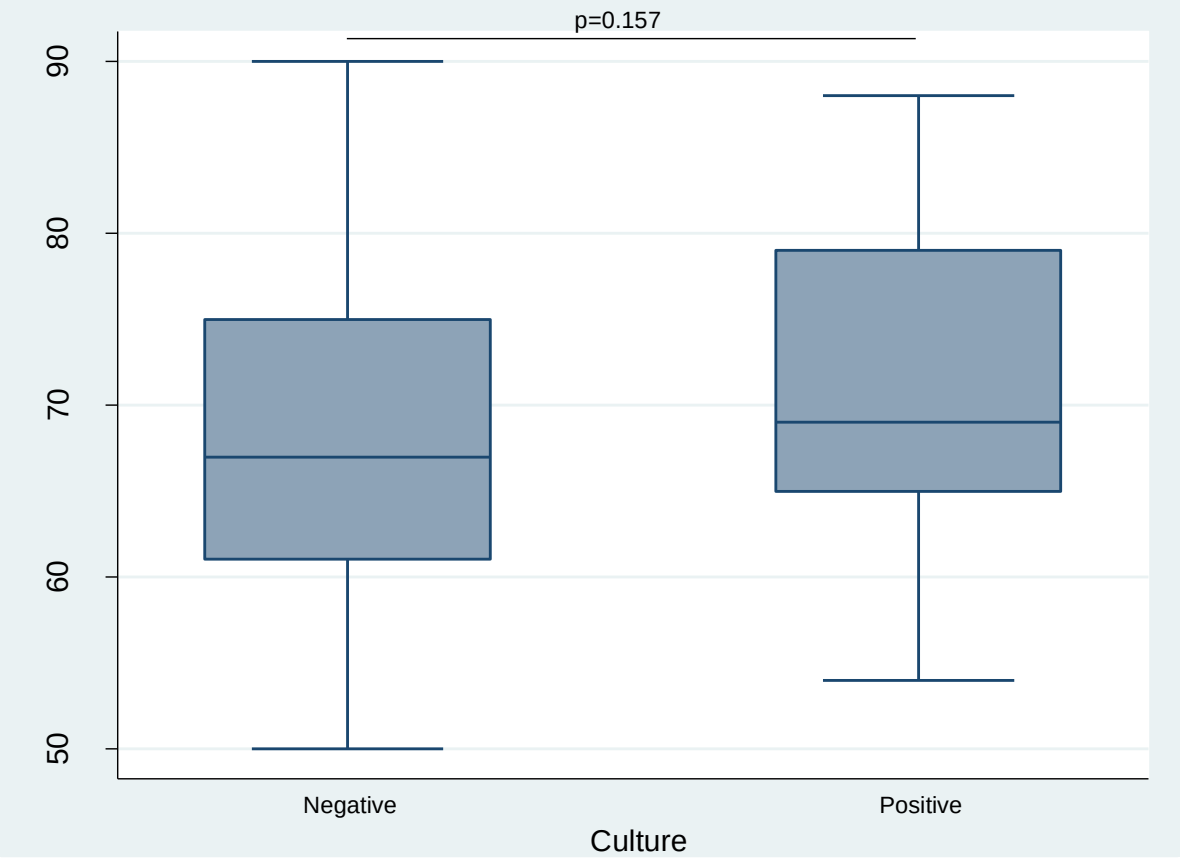

Figure 4.1: Comparison of age between participants who had culture-positive urine and negative urine culture post prostate biopsy.

4.4 Association between demographic characteristics and urine culture

The results showed that 9 (15.8 %) of those who had secondary education and 9 (11.9 %) of those with tertiary education had a positive urine culture after prostate biopsy. In terms of residence, 2 (22 %) of patients from low density, 7 (8.6 %) from medium density and 9 (18.4 %) from high-density residential areas developed a positive urine culture after prostate biopsy. However, none of these variables were statistically significant as shown in Table 4.3 below.

Table 4. 3: Association between demographic characteristics and urine culture

Variable		Urine Culture		
		Positive	**Negative**	**p-value**
Education level	Primary	0 (0.0)	6 (100)	0.501
	Secondary	9 (15.8)	48 (84.2)	
	Tertiary	9 (11.9)	67 (88.1)	
Residence	Low density	2 (22.2)	7 (77.8)	0.192
	Medium density	7 (8.6)	74 (91.4)	
	High density	9 (18.4)	40 (81.6)	

4.5 Association between clinical characteristics and urine culture

Table 4.4 below shows that there was a statistically significant association between HIV seropositivity, AUR, paraplegia, history of catheter use and positive urine culture.

Table 4.4: Association between clinical characteristics and urine culture

Variable		Urine Culture		
		Positive	**Negative**	**p-value**
Diabetes*	Yes	4 (16.7)	20 (83.3)	0.551
	No	14 (12.2)	101 (87.3)	
Hypertension	Yes	10 (15.9)	53 (84.1)	0.350
	No	8 (10.5)	68 (89.5)	
HIV status*	Positive	4 (33.3)	8 (66.7)	0.028
	Negative	14 (11.0)	113 (90.0)	
LUTS*	Yes	14 (12.7)	96 (87.3)	0.879

	No	4 (13.8)	25 (86.1)	
AUR	Yes	10 (22.2)	35 (77.8)	0.024
	No	8 (8.5)	86 (91.5)	
Paraplegia*	Yes	3 (75.0)	1 (25.0)	0.0001
	No	15 (11.1)	120 (88.9)	
Catheter use	Yes	8 (21.1)	30 (78.9)	0.081
	No	10 (9.9)	91 (90.1)	
Biopsy type	Finger-guided	8 (11.1)	64 (88.9)	0.503
	TRUS guided	10 (14.9)	57 (85.07)	

* Fishers exact; otherwise, chi-square

4.6 Comparison between participants' comorbidities and urine culture

There was no statistically significant difference between participants' comorbidities with urine culture (p=0.513): in terms of distribution, positive cultures were more common among patients with diabetes (DM) with HIV co-infection (17%) followed by those with diabetes and hypertension at 16.7%. (**Figure 4.2**)

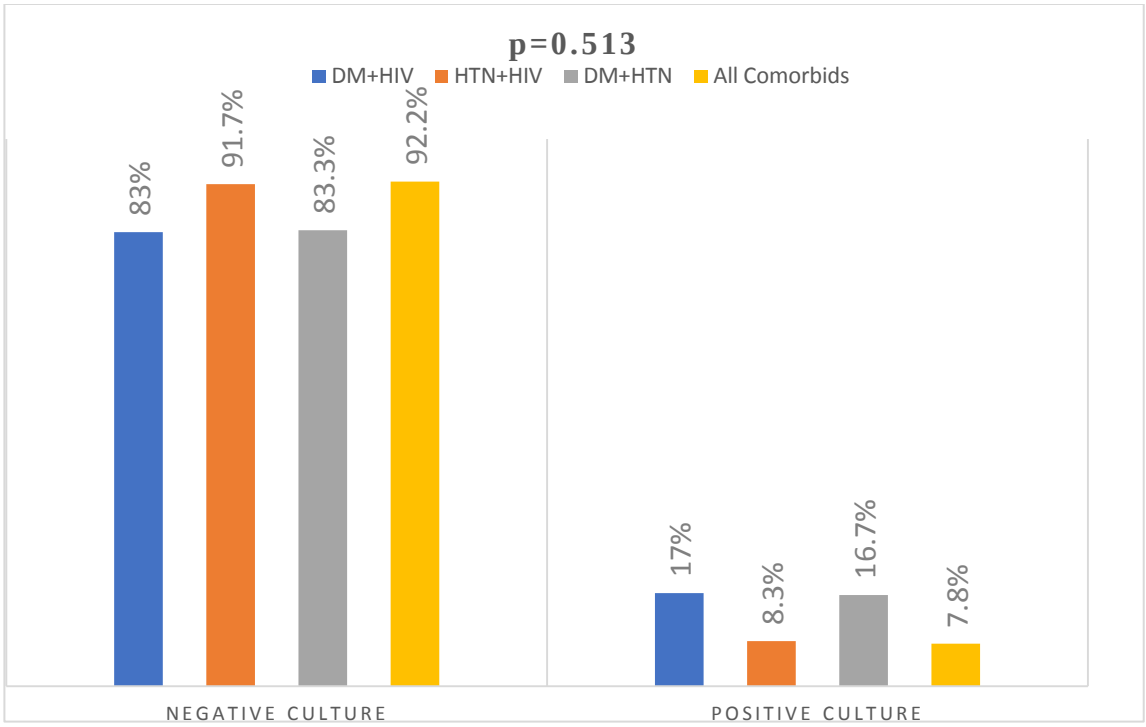

Figure 4.2: Comparison between participants' comorbidities and urine culture

4.7 Comparison between PSA and urine culture

When the PSA was compared between participants who had culture-positive urine to those who had culture-negative urine post prostate biopsy, the mean PSA was 100ng/ml for participants with culture-positive urine and 58.25ng/ml for participants with culture-negative urine. This was statistically significant (p = 0.032) as shown in Figure 4.3 below.

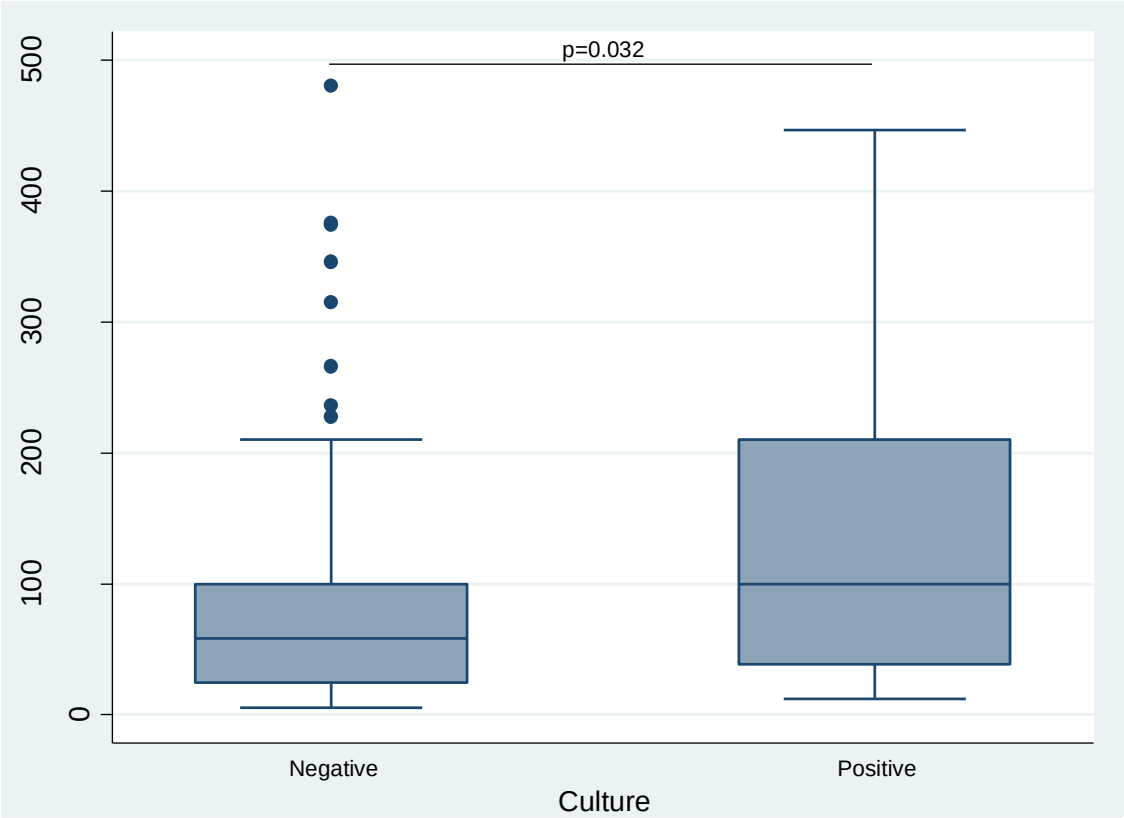

Figure 4.3: Comparison between PSA and urine culture

4.8 Comparison between Prostate volume and Urine culture

When the prostate volume was compared between participants who had culture-positive urine to those who had culture-negative urine post prostate biopsy, the mean prostate volume was 78.6 ml for participants with culture-positive urine and 70 ml for participants with culture-negative urine. This was statistically not significant (p = 0.314) as shown in Figure 4.4 below.

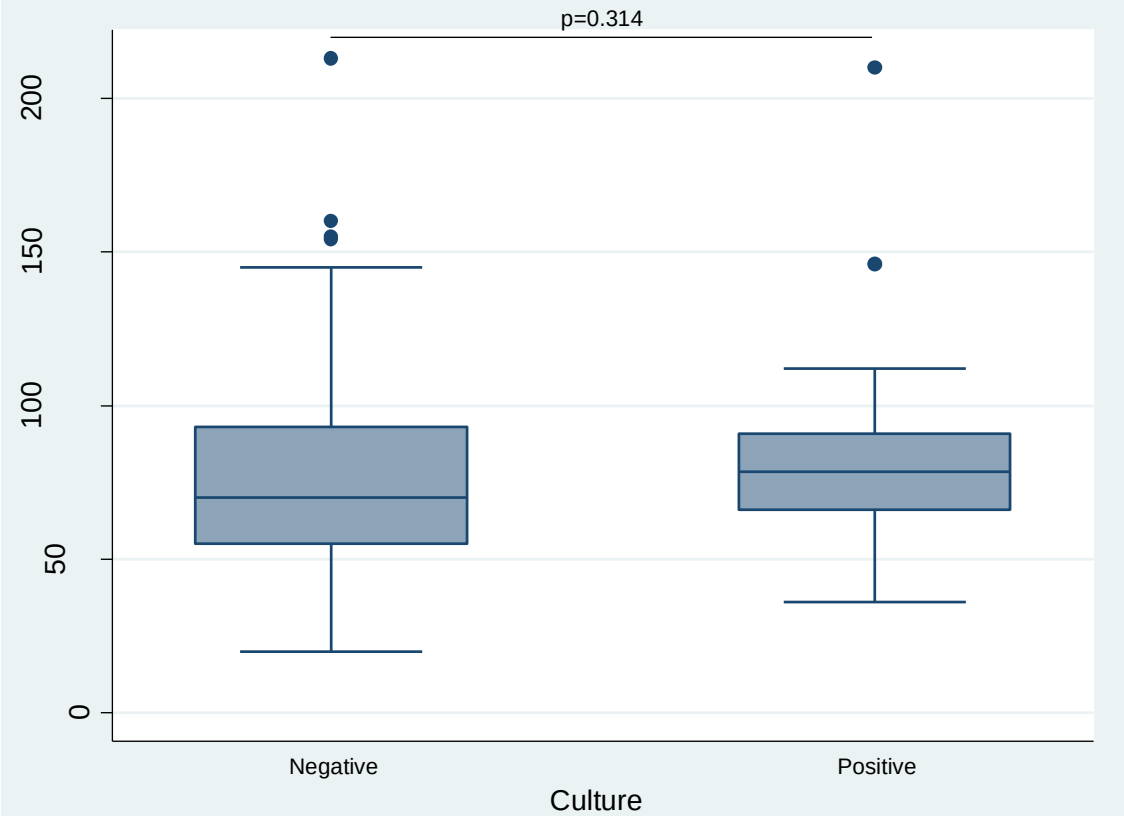

Figure 4.4: Comparison between prostate volume and urine culture

4.9 Comparison between number of biopsy cores and urine culture

According to figure 4.5, 16.2% (11/69) of the participants who had 8 number of cores used on them had a positive urine culture compared to 10.1% (7/69) of the participants who had 6 biopsy cores. The single participant who had 5 cores has a negative urine culture. However, there was no statistically significant association between the number of cores used and urine culture (p=0.516).

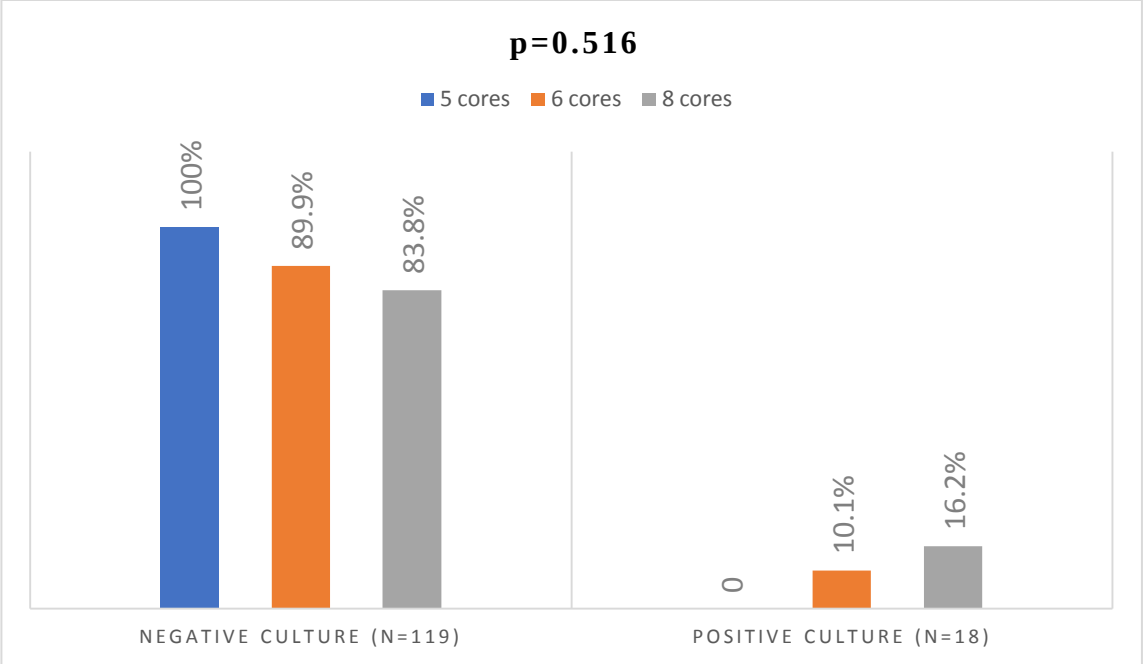

Figure 4.5: Comparison between number of cores and urine culture

4.10 Rectal swab microbiology of participants with a positive urine culture after prostate biopsy

The results show that *Escherichia coli* was the predominant rectal organism (63%) followed by *Klebsiella* (22.2%), *Enterobacter sp* (11.1 %) and *Pseudomonas* (3.7 %). *E coli* showed 93 % resistance to Gentamycin and 82 % resistance to Ciprofloxacin. On the other hand, *E coli* was 100 % sensitive to Nitrofurantoin and Fosfomycin. *Klebsiella* was 67 % resistant to Gentamycin and 100 % sensitive to Nitrofurantoin and Fosfomycin. *Enterococcus sp* was 100% resistant to Ciprofloxacin and 100 % sensitive to Nitrofurantoin and Fosfomycin. *Pseudomonas* was 100 % resistant to Gentamycin and ciprofloxacin and 100 % sensitive to Nitrofurantoin as shown below in Table 4.5

Table 4.5: Rectal swab microbiology of participants with a positive urine culture post prostate biopsy

Organism/ Antibiotic	**Sensitive (%)**	**Resistant (%)**	**Organism/ antibiotic**	**Sensitive (%)**	**Resistant (%)**
Escherichia coli (n=17)			***Enterococcus sp (n=3)***		
Gentamycin	1 (7)	13 (93)	Gentamycin	-	-
Fosfomycin	12 (100)	0 (0)	Fosfomycin	2 (100)	0 (0)
Ciprofloxacin	2 (18)	9 (82)	Ciprofloxacin	0 (0)	1 (100)
Nitrofurantoin	6 (100)	0 (0)	Nitrofurantoin	1 (100)	0 (0)
Klebsiella Pneumoniae (n=6)			***Pseudomonas aeruginosa (n=1)***		
Gentamycin	1(33)	2 (67)	Gentamycin	0 (0)	1 (100)
Fosfomycin	2 (100)	0 (0)	Fosfomycin	-	-
Ciprofloxacin	2 (100)	0 (0)	Ciprofloxacin	0 (0)	1 (100)
Nitrofurantoin	-	-	Nitrofurantoin	1 (100)	0 (0)

4.11 Urine culture after prostate biopsy

Of the 139 participants that were included, 18 (12.9%) had culture-positive urine after the prostate biopsy. *E coli* was the most commonly isolated organism, n=12 (66.7%) followed by *Klebsiella* n=3 (16.7%), *Staphylococcus aureus* n=2 (11.1%) and *Pseudomonas aeruginosa* n=1 (5.5%). *E coli* was 100 % resistant to ampicillin, co-amoxiclav, gentamycin, nalidixic acid and 83 % resistant to ciprofloxacin. It was 100% sensitive to Fosfomycin and 75 % sensitive to nitrofurantoin.

Klebsiella showed 100% resistance to ampicillin, co-amoxiclav, cefazolin, nitrofurantoin, 83% resistance to gentamycin and fosfomycin, 75 % resistance to nalidixic acid. It showed 100% sensitivity to ciprofloxacin and 75% sensitivity to nalidixic acid. *Staphylococcus aureus* showed 100% resistance to ampicillin, co-amoxiclav, fosfomycin, cefazolin, nitrofurantoin and 100% sensitivity to gentamycin and ciprofloxacin. *Pseudomonas* showed 100% resistance to co-amoxiclav, gentamycin, cefazolin and 100% sensitivity to ampicillin, fosfomycin, ciprofloxacin and nitrofurantoin as shown below in Table 4.6

Table 4. 6: Organism-based sensitivity and resistance profile of urine for participants with positive urine culture post prostate biopsy

Organism/ Antibiotic	**Sensitive (%)**	**Resistant (%)**	**Organism/ antibiotic**	**Sensitive (%)**	**Resistant (%)**
Escherichia coli (12)			***Staph aureus (2)***		
Ampicillin	0 (0)	12 (100)	Ampicillin	0 (0)	2 (100)
Co-amoxiclav	0 (0)	12 (100)	Co-amoxiclav	0 (0)	2 (100)
Gentamycin	0 (0)	12 (100)	Gentamycin	2 (100)	0 (0)
Fosfomycin	12 (100)	0 (0)	Fosfomycin	0 (0)	2 (100)
Cefazolin	0 (0)	12 (100)	Cefazolin	0 (0)	2 (100)
Ciprofloxacin	2 (17)	10 (83)	Ciprofloxacin	2 (100)	0 (0)
Nitrofurantoin	9 (75)	3 (25)	Nitrofurantoin	0 (0)	2 (100)
Nalidixic acid	0 (0)	10 (100)	Nalidixic acid		

Klebsiella Pneumoniae (3)			***Pseudomonas aeruginosa (1)***		
Ampicillin	0 (0)	3 (100)	Ampicillin	1 (100)	0 (0)
Co-amoxiclav	0 (0)	3 (100)	Co-amoxiclav	0 (0)	1 (100)
Gentamycin	1 (33)	2 (67)	Gentamycin	0 (0)	1 (100)
Fosfomycin	1 (33)	2 (67)	Fosfomycin	1 (100)	0 (0)
Cefazolin	0 (0)	3 (100)	Cefazolin	0 (0)	1 (100)
Ciprofloxacin	3 (100)	0 (0)	Ciprofloxacin	1 (100)	0(0)
Nitrofurantoin	0 (0)	3 (100)	Nitrofurantoin	1 (100)	0 (0)
Nalidixic acid	1 (33)	2 (67)	Nalidixic acid		

4.12 Univariate Ordinal Logistic Regression of baseline demographic characteristics

According to Table 4.7 below, there was statistically significant relationship between the patients' demographic characteristics (age, place of residence) and having a Urinary tract infection after transrectal prostate biopsy.

Table 4. 7: Univariate Ordinal Logistic Regression of baseline demographic characteristics

Variable		OR	95% CI	p-value
Age		1.04	0.98-1.10	0.16
Residential area	Low density	Ref		
	Medium	0.33	0.06-1.91	0.22
	High density	0.79	0.14-4.44	0.79

Participants 4.13 Univariate Ordinal Logistic Regression of potential clinical risk factors for infection after prostate biopsy

On Univariate regression, it was found that participants who were HIV seropositive were 0.25 times more likely to develop urinary tract infections than those who were negative (COR= 0.25, 95% CI: 0.07-0.93, p-value = 0.04). Participants with a history of having been in acute urinary retention were more likely to develop urinary tract infections than those without that history (COR= 0.33, 95% CI: 0.12-0.89, p-value = 0.03). The results also show that those who were paraplegic were more likely to develop urinary tract infections than those who were not (COR= 0.04, 95% CI: 0.004-0.43, p-value = 0.007). There was no statistically significant relationship between diabetes, hypertension, LUTS, duration of symptoms, history of being catheterised, psa, number of biopsy cores and biopsy type with development of urinary tract infection after prostate biopsy as shown in Table 4.8 below.

Table 4. 8: Univariate Ordinal Logistic Regression of potential risk factors for infection after prostate biopsy

Variable		**OR**	**95%CI**	**P-value**
Diabetes	Yes	Ref		
	No	0.69	0.21-2.32	0.55
Hypertension	Yes	Ref		
	No	0.62	0.23-1.69	0.35
HIV status	Positive	Ref		
	Negative	0.25	0.07-0.93	0.04
LUTS	Yes	Ref		
	No	1.10	0.33-3.62	0.88
AUR	Yes	Ref		
	No	0.33	0.12-0.89	0.03

Paraplegia	Yes	Ref		
	No	0.04	0.004-0.43	0.01
Duration of symptoms		1.11	0.94-1.30	1.22
Catheter use	No	Ref		
	Yes	2.43	0.88-6.71	0.09
PSA		1.01	1.00-1.01	0.08
Prostate volume		1.01	0.99-1.02	0.25
Number of cores		1.3	0.79-2.17	1.06
Biopsy type	Finger guided	Ref		
	TRUS guided	1.4	0.52-3.80	0.51

4.14 Multivariate multiple logistic regression of potential risk factors for infection after prostate biopsy

According to multivariate analysis, HIV positive participants were 0.15 times more likely to have an infection after prostate biopsy than HIV negative participants (AOR=.0.15, 95% CI= 0.03-0.74, p= 0.02). Those with a catheter were at a 1.42-fold increased risk of infection after prostate biopsy than those without a catheter but it was not statistically significant (AOR=2.43, 95% CI: 0.42-4.79, p=0.57). There was no significant relationship between the other clinical factors and development of UTI after prostate biopsy as shown in Table 4.9 below.

Table 4. 9: Multivariate multiple logistic regression of risk factors for infection after prostate biopsy

Variable		OR	95% CI	P-value
Age		1.02	0.95-1.10	0.52
HIV status	Positive	Ref		

	Negative	0.15	0.03-0.74	0.02
Catheter use	No	Ref		
	Yes	1.42	0.42-4.79	0.57
Paraplegia	Yes	Ref		
	No	0.16	0.01-4.23	0.27
PSA		1.00	1.00-1.01	0.13
AUR	Yes	Ref		
	No	0.34	0.06-1.84	0.21

AUR= acute urinary retention; PSA= prostate specific antigen

CHAPTER FIVE: DISCUSSION

5.1 Socio-demographic data

In this study, all the patients recruited were of African origin. The average age of the participants at presentation was 67.9±9.3 years (Table 1). This correlated well with an American Surveillance, Epidemiology and End Result (SEER) report 2006-2010 which reported an average age of 66 years for the diagnosis of prostate cancer. In another study done in Egypt by Abd el Halima et al, 2009, the average age for prostate cancer detection was found to be 66.2 years and it correlated with our findings. Our study found that for every one-unit increase in age, the study participant was 4% likely to have a positive urine culture post prostate biopsy (COR= 1.04, 95% CI: 0.98-1.10). However, this finding was not significant (p = 0.16).

In terms of residence, the study found that most of the participants lived in medium density areas (58.3%), followed by high and low-density areas (35.3% and 6.6% respectively). Residential status was assessed to establish if there was a correlation between the participant's residence and the development of an infection. There was no correlation between where one resided and the risk of them having an infectious complication after prostate biopsy (COR= 0.79, 95% CI: 0.14-4.44, p=0.79).

5.2 Association between clinical characteristics and urinary tract infection after prostate biopsy

Diabetes has been known to increase the risk of infectious complications following transrectal prostate biopsy. Carignan et al reported a case-controlled study from a Canadian tertiary-care center that showed that diabetes was an independent risk factor for infectious complications following prostate biopsy. Similar findings were demonstrated by Loeb et al in a European randomized trial. Contrary to these findings, our study demonstrated that diabetes did not increase the risk of infectious complications after transrectal prostate biopsy. Our findings were similar with those of Wu et al who reported on a 10-year single-centre study in south china that revealed that diabetes was not an independent predictor of infection after prostate biopsy.

We also found a correlation between the patients' HIV status and the risk of them developing an infection after prostate biopsy. HIV positive patients were 0.25 times likely to develop an infection after prostate biopsy (adjusted OR= 0.15, 95% CI: 0.03-0.74, p-value = 0.02). Untreated HIV leads to a decline in CD4 counts which may lead to an increase in the incidence of infection after surgery. Savioz et al, 1998, found that CD4 cell count had an influence on the complication rate after surgery.

Univariate analysis showed that patients with an indwelling urethral catheter were at a 2.43-fold increased risk of infection after prostate biopsy than those without a catheter (OR=2.43, CI: 0.88-6.71). This was similar to a study by Aus et al, 1996, which revealed that patients with preoperative catheterization were at a 2.3-fold increased risk of infection after prostate biopsy than those without preoperative catheterization. According to de Jesus et al, 2006, a catheter in the urinary tract may be treated as a foreign object that facilitates the proliferation of pathogenic microorganisms. Our findings were close to significant (p=0.09), which may have been caused by relatively small sample size.

Paraplegia also stood out as a predictor for the development of infectious complications after prostate biopsy on Univariate analysis (COR=0.04, 95% CI: 0.004-0.43, p-value=0.01). This could have been because most of the paraplegic patients had an indwelling urethral catheter which could have predisposed them to develop urinary tract infections after prostate biopsy. Another reason could be because most paraplegics have full rectums during biopsy which could predispose them to infection after the procedure. This finding however was not significant on Multivariate analysis.

5.3 Rectal swab microbiology and its relation to urinary tract infection after prostate biopsy.

Escherichia. coli was the predominant rectal organism (63%), followed by *Klebsiella* (22.2%), *Enterobacter sp* (11.1 %) and *Pseudomonas* (3.7 %). *E coli* showed a 93 % resistance to Gentamycin and 82 % resistance to Ciprofloxacin. On the other hand, *E coli* showed 100 % sensitivity to Nitrofurantoin and Fosfomycin. In a similar study by Singh et al, 2017, *E coli* was the main isolated organism on rectal swab cultures (99.5%) and of these cultures, 41.7% harboured fluoroquinolone-resistant *E coli*.

To demonstrate the importance of rectal flora and its relation to urinary tract infection after prostate biopsy, Batura et al assessed prebiopsy rectal swab cultures and found that several patients harboured fluoroquinolone-resistant organisms. The study showed that post-biopsy urinary tract infections were caused by fluoroquinolone-resistant *E coli*, which suggests a strong correlation between rectal swab isolates and organisms causing infectious complications. These findings are consistent with those of our study in which the predominant organism *E coli* was isolated in both rectal swab and urine culture and showed high resistance to the commonly used drugs for prophylaxis (ciprofloxacin and gentamycin). This therefore underpins the need to do pre-procedural rectal cultures and offer culture directed antimicrobial prophylaxis in order to prevent UTIs caused by resistant organisms.

The same conclusion was made by Duplessis et al, 2012 and Taylor et al, 2012 who proposed that pre-procedural rectal cultures be obtained before TRUS-guided biopsy to identify antibiotic-resistant flora and thus facilitate targeted antibiotic prophylaxis based on the sensitivity profiles. The main drawback of a targeted approach in a developing country is that it is resource-intensive and requires rectal swab cultures of all patients with the associated cost. On the other hand, in a cost-effectiveness analysis, the cost of implementing the targeted strategy is way much lower because the cost associated with hospitalizations is reduced.

5.4 Urine culture and sensitivity after prostate biopsy

Our study showed that the prevalence of urinary tract infections after transrectal prostate biopsy in our setting was 12.9 %. This was significantly high when compared to studies done in other regions. Sultan et al, 2017 demonstrated that the prevalence of UTIs after prostate biopsy was 2.8%. Similar studies by Otrock et al in Lebanon, Choi et al in South Korea and Sanders et al in New Zealand also demonstrated low UTI prevalence of 3.86%, 3.00% and 1.83% respectively. One of the reasons why we are having a higher UTI prevalence could be due to poor catheter care in most of our patients.

The study found that *E coli* was the most common pathogen causing urinary tract infections after transrectal prostate biopsy (67%), followed by Klebsiella (17%), Staphylococcus aureus (11%) and Pseudomonas aeruginosa (5.5%). Sultan et al found that the most common pathogens were Escherichia coli (90.1%) and Klebsiella pneumoniae (9.1%). *E coli* showed 100% resistance to ampicillin, co-amoxiclav, gentamycin, cefazolin and 91% resistance to ciprofloxacin. Ciprofloxacin and gentamycin are the routinely used antibiotics for prophylaxis as recommended by the EAU guidelines. This finding is not unique to our study. Overwhelming evidence through published literature is demonstrating a continuous increase in resistance to the routinely used prophylactic antibiotic ciprofloxacin. Choi et al reported on the incidence rate of infectious complications, and their data suggested that quinolone resistance has been increasing in recent years. Steensels et al also showed that quinolone-resistant infections after TRUS are on the rise. The likely explanation for the observed increase in quinolone resistance could be increased use of the drugs for other medical conditions. Ciprofloxacin has been the antibiotic of choice for the treatment of UTIs, mostly because of its potent activity against a large spectrum of clinically relevant pathogens (Chao et al, 2019). The other possible explanation is that patients harbour quinolone-resistant *E coli* in their rectal flora which is introduced into the urinary system after prostate biopsy (Steensels et al). This explanation is supported by our study which found the presence of quinolone-resistant *E coli* in the rectal flora of patients undergoing prostate biopsy.

The *E coli* showed 100% sensitivity to fosfomycin and 75% sensitivity to Nitrofurantoin. Fosfomycin is a recommended first-line drug when available because of preserved pathogen susceptibility (Longo et al). Therefore, alternative prophylactic agents should be preoperatively determined by rectal swab cultures to reduce the rate of infections after prostate biopsy.

There was a single case where Pseudomonas aeruginosa n=1 (4.8%) was isolated in urine. It showed 100% resistance to co-amoxiclav, gentamycin, cefazolin and 100% sensitivity to ampicillin, fosfomycin, ciprofloxacin and nitrofurantoin. One possible explanation is the contamination of prostate biopsy equipment that had not been

adequately cleaned. Gillespie et al, 2006 did a report that looked at cases of pseudomonas aeruginosa infection after TRUS-guided prostate biopsies in which contamination of the equipment was the likely source. According to the study, the practice of rinsing the needle-guide with tap water after reprocessing might have contributed to its contamination. Pseudomonas is well known to colonize tap water and can form biofilms on medical devices that are difficult to remove. The isolation of Pseudomonas in urine after prostate biopsy underscored the importance of adherence to recommendations for the cleaning and disinfection of prostate biopsy equipment prior to the procedure.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

The prevalence of UTI in patients undergoing transrectal prostate biopsy was 12.9% and *E. coli* was the most common isolated organism.

Factors to be statistically significantly associated with developing urinary tract infections after transrectal prostate biopsy are being HIV seropositive, history of acute urinary retention and those presenting with paraplegia. HIV is an independent predictor of developing UTIs after prostate biopsy when other factors are controlled for.

6.2 Recommendations

1. HIV positive patients, those with history of acute urinary retention and those presenting with paraplegia should be given targeted prophylactic antibiotics.

2. The recommended prophylactic antibiotics in this studied population in Zambia are Nitrofurantoin or Fosfomycin.

3. Pre-biopsy rectal swabs to be considered (especially in patients with risk factors such as HIV seropositivity and paraplegia) followed by culture directed antibiotic prophylaxis before prostate biopsy.

3. A study to determine whether the number of cores/punctures made and/or the experience of the doctor performing the procedure has an effect on the patient developing a UTI after the procedure be carried out.

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APPENDICES

Appendix A: PARTICIPANTS INFORMATION SHEET

My name is Dr Nkambo Malemuna, a medical doctor pursuing a masters degree in urology in the Department of Surgery at the University Teaching Hospital. As part of my academic qualification, I am conducting a study to establish the factors that are associated with urinary tract infections in patients undergoing transrectal prostate biopsy.

Prostate biopsy is a surgical procedure that involves getting a piece of tissue from the prostate gland using a special kind of needle for analysis in the laboratory. The prostate is accessed through the rectal route. It is generally a safe and well-tolerated procedure. However, sometimes pain, bleeding and infection can occur as a complication of transrectal prostate biopsy. This is usually avoided by giving pain killers and antibiotics before and after the procedure.

The purpose of this study is to help us establish some of the causes of urinary tract infections in patients undergoing prostate biopsy and hence help us in the prevention of these infections. During this study, your participation will require a detailed history of symptoms after which a rectal swab and urine specimen will be taken just before the prostate biopsy is done. A second urine sample will be collected 1 week later. The specimen will be taken to the laboratory for processing.

Your identity and all information collected from you during this study will be kept confidential under lock and key, to which only the researcher will have access to. The study will not affect your treatment in any way nor will it have any added benefit outside the standard management of your condition.

Your participation will be voluntary and written consent will be obtained from you indicating that you understand the procedure and are willing to go through with it. If at any time during the study you feel injured, inconvenienced or for whatever reason you feel the need to withdraw from the study, you shall be permitted and treatment will not be withheld.

Any queries or clarifications can be directed to me, Dr Nkambo Malemuna, 0972992920, department of Surgery, P/bag RW1X, UTH, Lusaka. You may also contact the University of Zambia Biomedical and research ethics committee (UNZABREC), Ridgeway campus, P.O. BOX 50110, Lusaka.

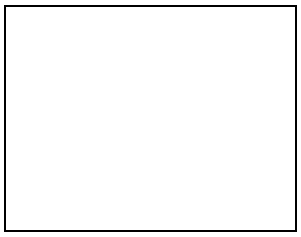
Appendix B: CONSENT FORM

I_____ have read the foregoing information, or it had been read to me. I have had the opportunity to ask questions concerning the study and these have been answered to my satisfaction. I consent voluntarily to participate in this study and understand that I have the right to withdraw from the study at any time.

Signature of participant

_____Date_____

Participant thumb print



Signature of researcher _____Date

_____

STATEMENT BY RESEARCHER

I have accurately read out the information sheet to the participant and to the best of my ability made sure that the participant understands that the following will be done

I confirm that the participant was allowed to ask questions about the study and all the questions asked have been answered correctly and to the best of my ability. I confirm that the participant has not been coerced into giving consent and that it has been given freely and voluntarily.

Name of researcher _____

Signature of researcher _____Date

_____

WITNESS FORM

I have witnessed the accurate reading of the consent form to the participant and the individual had the opportunity to ask questions. I confirm that the participant has given consent freely.

Name of witness _____

Signature of Witness _____ Date

_____

Appendix C: DATA COLLECTION SHEET

Patient code _____

No.	Question	Coding category
PART A: Socio-demographic information		
A1	Age	<50----------0 50 -59 ------1 60 -69------2 70-79-------3 >80---------4
A2	Education level	Nil----------1 Primary --- 2 Secondary--3 Tertiary-----4
A3	Home residence (indicate place) ……..	1. low density 2. medium density 3. high density
PART B: Clinical Presentation		
B1	Diabetes	Yes ----- 0 No ------ 1
B2	Hypertension	Yes ----- 0 No ------ 1
B3	HIV status	Positive ------ 0 Negative ----- 1

B3	Lower Urinary Tract Symptoms	Yes ----- 0 No ------ 1
B4	Acute urinary retention	Yes ------ 0 No ------ 1
B5	Paraplegia	Yes ------0 No ------ 1
B6	Duration of symptoms	<1month------0 1-3month-----1 4-6month-----2
B7	History of catheter use	Yes-----0 No------1
PART C: Clinical Investigations		
C1	Prostate specific antigen	Not done---------0 0-3.9ng----------1 4.0-9.9----------2 10.0-19.9---------4 >20 ng----------5
C2	Prostate volume	Not measured…0 <24cm3----------1 25-29cm3--------2 30-39cm3--------3 40-49cm3--------4 >50cm3----------5
C3	Type of biopsy	Finger-guided------ 1

		TRUS-guided------ 2
C4	Number of biopsy cores obtained	
C5	Rectal swab	Culture ……. Sensitivity ……. …….
C6	Urine culture (Pre-biopsy)	Culture ……. Sensitivity ……. …….
PART D: FOLLOW UP		
D1	Urine culture (post-biopsy)	Culture ……. Sensitivity ……. …….

Appendix D: UNZABREC ETHICAL APPROVAL FORM

UNIVERSITY OF ZAMBIA
BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067
Telegrams: UNZA, LUSAKA
Telex: UNZALU ZA 44370
Fax: + 260-1-250753
Federal Assurance No. FWA00000338

Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia
E-mail: unzarec@unza.zm
IRB00001131 of IORG0000774

29th August 2019.

REF. No. 193-2019

Dr. Nkambo Malemuna,
University Teaching Hospitals,
Department of Surgery,
P/Bag RW
1X,
Lusaka.

Dear Dr. Malemuna,

RE: "FACTORS ASSOCIATED WITH URINARY TRACT INFECTIONS IN PATIENTS UNDERGOING TRANSRECTAL PROSTATE BIOPSY AT THE ADULT HOSPITAL OF THE UNIVERSITY TEACHING HOSPITALS, LUSAKA, ZAMBIA" (Ref. No. 193-2019)

The above-mentioned research proposal was presented to the Biomedical Research Ethics Committee Meeting on 27th August, 2019. The proposal is **approved**. The approval is based on the following documents that were submitted for review:

a) Study proposal
b) Questionnaires
c) Participant Consent Form

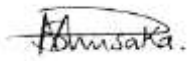
APPROVAL NUMBER : REF. 078-2019

This number should be used on all correspondence, consent forms and documents as appropriate.

- **APPROVAL DATE : 28th August 2019**
- **TYPE OF APPROVAL : Standard**
- **EXPIRATION DATE OF APPROVAL : 27th August 2020**
  After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the UNZABREC Offices should be submitted one month before the expiration date for continuing review.
- **SERIOUS ADVERSE EVENT REPORTING**: All SAEs and any other serious challenges/problems having to do with participant welfare, participant safety, and study integrity must be reported to UNZABREC within 3 working days using standard forms obtainable from UNZABREC.
- **MODIFICATIONS**: Prior UNZABREC approval using standard forms obtainable from the UNZABREC Offices is required before implementing any changes in the Protocol (including changes in the consent documents).
- **TERMINATION OF STUDY**: On termination of a study, a report must be submitted to the UNZABREC using standard forms obtainable from the UNZABREC Offices.
- **NHRA:** Where appropriate, apply in writing to the National Health Research Authority for permission before you embark on the study.
- **QUESTIONS**: Please contact the UNZABREC on Telephone No.256067 or by e-mail on unzarec@unza.zm.
- **OTHER**: Please be reminded to send in copies of your research findings/results for our records. You're also required to submit electronic copies of your publications in peer-reviewed journals that may

  emanate from this study. Use the online portal: unza.rhinno.net for further submissions.

Yours sincerely,



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