THE PREVALENCE OF PROSTATE CANCER IN MEN UNDERGOING FINGER GUIDED PROSTATE BIOPSY AT THE UNIVERSITY TEACHING HOSPITAL IN LUSAKA, ZAMBIA

By

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DECLARATION

I hereby declare that this dissertation represents my own work and that it has not previously been submitted for a degree, diploma or other qualification at this or another University. I further declare that all sources I have quoted have been indicated and acknowledged by means of complete references. It has been prepared in accordance with the prescribed guidelines for the post graduate studies Dissertations of the University of Zambia.

Researcher's Signature …… Date ……..

Supervisor' Signature…… Date……

This dissertation of Dr Chilando Brian has been approved as fulfilling the partial requirements for the Award of Master of Medicine in Urology by the University of Zambia.

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Supervisor	**Signature**	**Date**

ABSTRACT

Prostate cancer is the most common malignancy in men other than Skin cancer worldwide. In Zambia a review of histological reports showed that prostate cancer is the most common urological malignancy. Recent studies have shown that there is a high prevalence of this cancer in Africa where the population is predominantly black. From literature a lot of studies have reported a range of 30% to 60% prostate cancer detection rate in men undergoing finger guided prostate biopsies around the world. This study was undertaken to determine the prevalence and Characteristics of prostate cancer in men undergoing prostate biopsy at the University Teaching Hospital in Lusaka Zambia.

A prospective Cross Sectional Study was done at the UTH from April, 2014 to December, 2014 after getting ethical approval from UNZABREC. Patients undergoing prostate biopsy were recruited. A researcher administered Questionnaire was used to collect data on demographic details, Clinical presentation, Indication for biopsy and Prostate specific Antigen (PSA) test result. Then a finger guided, 6 core transrectal prostate biopsies were performed by experienced Urologists. The histological samples were analysed by pathologists at the UTH and other private laboratories. The obtained Data was analyzed using SPSS

A total of 146 men undergoing prostate biopsy were recruited in the study. The age range was 49 to 92 years and the Mean age was 71.57. The most common symptoms were Lower Urinary tract symptoms at 89% in all patients and only 4.3% of men came asymptomatic.56% of the patients had a suspicious DRE finding. The PSA values ranged from 2.69 to 5480ng/ml. Most patients had serum PSA more than 20ng/ml. Prostate cancer (Adenocarcinoma) was found in 61 % (89/146) and Benign prostatic hyperplasia was found in 31.4%. Chronic prostatitis was found in 5.8%. The low risk cancer with Gleason score of 2 to 6 was found in 11.9%. The intermediate risk cancer with Gleason score 7 was found in 44% while the high risk cancer was also 44%.

The prevalence of prostate cancer in men undergoing prostate biopsy at UTH was 61% and 44% of men had high risk cancers which are more aggressive with an unfavorable prognosis.

Key words: Prostate cancer, finger guided prostate biopsy, Adenocarcinoma, Benign Prostatic hyperplasia, Chronic prostatitis, Gleason score,

DEDICATION

I dedicate this work to my late brother Charles Chishala Chilando for the encouragement and support he gave to me throughout my medical training.

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ACRONYMS

DRE	-	Digital Rectal Examination
PSA	-	Prostate Specific Antigen
TRUS	-	Transrectal Ultrasound
TURP	-	Transurethral Resection of the Prostate
NCCP	-	National Cancer Control Programme
UTH	-	University Teaching Hospital
WHO	-	World Health Organisation

CHAPTER ONE

Introduction

Prostate Cancer is the commonest malignancy among males worldwide other than skin cancer. This is the most frequently diagnosed cancer among urology patients according to a review of histopathological reports at the UTH in Lusaka Zambia[1].

Zambia is a sub-Saharan country in southern Africa with a population of about 16.212 million. Its population is predominately black Africans. A lot of studies done around the world have shown that men of Sub-Sahara African descent around the world suffer disproportionately from Prostate cancer.[2]Although the prevalence is increasing in the developed world, it still under-diagnosed in the developing countries like Zambia and therefore often presents late with unfavorable outcomes [3]. The poorly developed cancer registry system has contributed to the under reporting and therefore relatively little is known about the epidemiology of Prostate cancer in men in Sub-Saharan Africa including Zambia.

This cancer has been identified as a public health problem in most of the African countries. The International agency for research on cancer (IARC) estimates that Prostate cancer is the leading cancer in terms of incidence and mortality in Africa and that Prostate cancer a is a growing problem in Africa: Approximately 57.048 African men will die of Prostate Cancer by 2030.[4]

This malignancy arises from the cells of prostate gland. The prostate gland is divided into 3 zones: peripheral, central, and transition. The peripheral zone is the largest of the zones, encompassing approximately 75% of the total prostate glandular tissue in men without BPH. Most prostate cancers originate in this peripheral zone. It is located posteriorly and extends laterally on either side of the urethra.

Cancer of the prostate patients may present with an organ confined disease or locally advanced malignancy. Men with organ-confined prostate cancer often are completely asymptomatic. In locally advanced cancer Bladder outlet obstruction is the most common sign. A few men with locally advanced disease present with haematuria, urinary tract infections and irritative voiding symptoms secondary to bladder outflow obstruction. Physical examination including a DRE is needed for the diagnosis of prostate cancer. Indurations, if detected, must alert possibility of

cancer and the need for further evaluation (PSA, TRUS, and biopsy). Locally advanced disease with bulky regional lymphadenopathy may lead to lymphedema of the lower extremities.

Diagnosis of prostate cancer is made from a transrectal biopsy done during suspicion of the malignancy. Several indications for prostate biopsy exist, including primary biopsy at the time of suspicion of cancer with high PSA test or abnormal Digital rectal examination or Both[5];

A typical transrectal prostate biopsy involves samples from the parasagittal plane on the right and left sides of the base, midzone, and apex, with each site arbitrarily assigned by the operator[5]. Several investigators demonstrated that sampling more cores improved Cancer Detection Rate without increasing morbidity.[6] As a result, today's biopsy protocols typically involve extracting 12 cores per biopsy, often from the standard sextant and other areas of the peripheral, transition, or anterior zones.[7] Despite these observations, controversy exists about the optimal strategy for prostate biopsy with regard to core number, location, labeling, and pathologic processing.[8]

Adenocarcinomas make up the 90% of prostate carcinomas on histological diagnosis. A total of 70% of prostate adenocarcinomas occur in the peripheral zone, 20% in the transitional zone and approximately 10% in the central zone. Other tumor types are relatively rare and include ductal adenocarcinoma, which occurs in the major ducts and often projects into the urethra; and mucinous adenocarcinoma, which secretes abundant mucin and does not arise from the major ducts. Transitional carcinoma of the prostate occurs within the ducts and, to a lesser extent, in the prostatic acini. Typically, primary transitional carcinomas are aggressive cancers that have a poor prognosis. Similarly, neuroendocrine (small-cell) tumors are rare and aggressive, have a poor prognosis, and typically require aggressive surgical and medical management.

The grading system developed by Gleason from data accumulated by the Veterans Administration Cooperative Urologic Research Group appears to provide the best prognostic information in addition to clinical stage and is the predominant grading system in widespread use.

Gleason score of 2 to 6 implies Low Risk cancer

Gleason score of 7 is intermediate Risk

Gleason score of 8 and above is high risk cancer

Diagnosed cancer has a heterogenous course if not treated. Some patients diagnosed with cancer of prostate will not die of the disease but, die from other co morbid conditions. Patients with low risk Grading are less likely to die from the cancer and the high risk counterparts have a higher chance of dying from the prostate cancer and its direct complications. In the United States only one in six American patients will eventually die from it.[9] Mortality rates are still high in western countries than in low risk Asian countries. A study done in 1998 showed that the world's highest mortality (30.3 to 47 per 100,000 person years) rates were seen in Caribbean countries where large part of their population is of African Descent.[9]

In Zambia, it is thought that a more aggressive form of cancer of the prostate is seen hence making it the leading cause of mortality among urology patients in the university Teaching hospital according to mortality audit reports.[10]

Statement of the Problem

Prostate cancer prevalence was previously perceived to be low in Africa. Recent studies have shown that Africa has a high prevalence up to 300 per 100,000. This is close to that found among African Americans who have the highest incidence of prostate cancer in the world. In many African countries, prostate cancer is the leading cause of cancer among men.

Prostate cancer unlike other cancers that have a homogeneous cause of progression and causing death, its disease process takes a heterogeneous course in which some patients have a very aggressive type that directly kills them while others have a less aggressive form and die from co-morbid illness in the presence of the cancer. However, in the UTH urology section, mortality audit reports showed that for the year 2013, cancer of the prostate accounted for about 60% of all mortality cases in urology patients.[10] This scenario therefore suggests that the prevalence of prostate cancer may be higher than reported.

In addition to the above reason, other reports shows that cancers in the black population are of higher grade and very aggressive to cause death. Zambia has predominantly a black population.

Despite most of our patients being at high risk of having a very aggressive and high grade malignancy that contributes to the high mortality rate, Our center has no evidence based information on the indications for prostate biopsy and histological characteristics of the cancers seen at the UTH.

In our setting finger guided prostate biopsies are still being used as the main stay method for the diagnosis of prostate cancer. This method has been reported as a least accurate in the detection of cancer and so most of the negative biopsies are thought of being false negatives. Therefore, this study should help to improve on prostate cancer diagnosis rate in men undergoing finger guided prostate biopsies.

Our study was undertaken to describe the prevalence of cancer of prostate in men undergoing finger guided prostate biopsy at UTH in Lusaka and describe the Characteristics of both patients as well as cancer type.

Research Question

What is the prevalence and Characteristics of Prostate Cancer in men undergoing prostate biopsy at the University Teaching Hospital in Lusaka?

Study Justification

A retrospective study done by Bowa and colleagues in 2004 reviewed histological reports for a period of ten years at university teaching hospital in Lusaka, showed that prostate cancer is the commonest urological malignancy diagnosed at UTH .[1] And information obtained from urology mortality audits in the department of surgery shows that prostate cancer is the leading cause of urology mortalities at UTH.[10] Also data published by GLOBOCAN in 2008 shows that Zambia has the second highest mortality rates as a result of prostate cancer in Africa at 24.7 per 100,000.[11] In view of the large burden contributed by prostate cancer in terms of morbidity and mortalities among urology patients there is need to do epidemiological and interventional studies on this important disease.

Studies done in different parts of Africa give general feeling that the prevalence of this cancer is being underestimated. The poorly developed National cancer registry system in most African countries including Zambia has contributed to this underestimation. Not all the cancers seen in the hospitals are reported because this is done on voluntary basis.

In Zambia no study has been done on the prevalence of prostate cancer in men undergoing finger guided prostate biopsy and therefore a little information is known about this cancer despite being the leading cause of mortalities among urology patients in this country. Therefore, No baseline information is available that is needed for future research in innovations that will improve both clinical management and public heath interventions in this common cancer in Zambia. This study will investigate the prevalence of cancer in men undergoing biopsy at the university teaching hospital in Lusaka, Zambia and come up with the baseline information needed for future use by medical practitioners at the UTH in the diagnosis of prostate cancer.

Aim of the study

To determine the prevalence of prostate cancer in patients undergoing prostate biopsy at UTH.

Specific objectives

1. To describe the demographic and clinical Characteristics of patients undergoing prostate biopsy
2. To describe the indications for prostate biopsy in men undergoing prostate biopsy at UTH
3. To determine the histological characteristics of prostate biopsies

CHAPTER TWO

Literature Review

Prostate cancer is the most common malignancy in men other than superficial skin cancer and the second leading cause of cancer death in Americans.[12] Worldwide incidence rates increased dramatically through the early 1990s. A study to review the prevalence rates of cancers showed that prostate cancer is the fifth common malignancy worldwide and it makes up 11.7% of new cancer cases overall, 19% in developed countries and 5.3% in developing countries.[13] Worldwide the incidence varies between countries and ethnic populations. Ries and collegues in 1997 found that the highest incidence rates occur in North America (250 per 100,000) and Scandinavia, and lowest in Asian (10 per 100,000) countries.[14]

Prostate cancer has been the most common non-cuteneous malignancy in the U.S since 1984, now accounting for one quarter of all such cancers[14]. The age-specific incidence rates increased gradually from the early 1970s up to the late 1980s in the USA. The sharp increase in prevalence rates was caused by the increased use of PSA tests in North America. This cancer is more prevalent in the black population than whites. Currently the incidence of prostate cancer among White American men is 156.7 per 100,000 population compared with 248.5 per 100 000 for Black Americans. This is the highest rates of prostate cancer in the world.[14]

The World Health Organization has estimated that the prevalence of prostate cancer in developing countries is 4%[15]. It is not among the top five causes of cancer in the developing countries according to WHO.[16] However, there is a feeling that the incidence has been underestimated particularly in Africa.

A review of literature by Chu and colleges in 2007 found that hospital based reports from African countries showed that the highest prevalence rates were reported from East and Central Africa. In Eldorent, Kenya between 1998 and 2000 a hospital incidence of 16.8 per 100,000 was reported. The same report also showed that in Blantyre, Malawi a hospital prevalence of 10.7 per 100,000 was reported between 2000 and 2001.This review also showed an increasing tread in the incidence of prostate cancer in Zimbabwe with 28.3 per 100,000 reported between1990 to 1992, 30.7 per 100,000 from 1993 to 1997 and 38.1 per 100,000 for the period 1998 to 2002.. In

kyadondo, Uganda an incidence of 37.8 per 100,000 was reported between the periods 1998 to 2002.[17]

A retrospective study of histological reports at UTH in Zambia in the period January 1990 to December 2005 showed that of all the cancers diagnosed at UTH, urological cancers represented 8.5%. The most common urological cancer was prostate cancer which was at 56% of the urological malignancies. This was followed by bladder cancer at 21.1% of all the urological cancers[1].However there is a feeling that the prevalence of prostate cancer in African countries including Zambia is mostly underestimated due to weakness in the national cancer registry and also other clinical related factors such as inadequate trained urologists and the use of less sensitive methods of diagnosis of this disease.

Studies on Prostate Biopsy Methods

Biopsies of the prostate have been used to diagnose prostate cancer since the beginning of the last century.[18] The field of prostate diagnostics, especially biopsy techniques develops rapidly.[19]Traditionary finger guided transrectal biopsies were being done to diagnose worldwide but over the last two decades, TRUS has become the gold standard in performing prostate biopsies. [20,21]Transrectal ultrasonography (TRUS) guided prostate biopsy, which is performed with a core biopsy needle passing through the rectum, was first applied for the biopsy of prostate in 1968.[22]Since the introduction of the systematic 12-core transrectal prostate biopsy guided by TRUS, it has become widely accepted, routinely performed technique for prostate cancer detection.[23] The transperineal prostate biopsy, which is performed with the core biopsy needle passing through the skin of the perineum, is far less common compared with transrectal biopsy[24].Several studies have demonstrated that the transrectal technique either figure guided or TURS guided is a faster and convenient approach for prostate biopsy.

A study done at Stanford University demonstrated that TRUS biopsies diagnosed cancer in 23 of 43 patients who had previous negative finger biopsies while confirming previously digitally diagnosed cancer in 94%.[5] In a further publication in the same journal, they showed that the yield of prostate cancer was better with six systematic random biopsies than FG biopsies of abnormal areas in the prostate.[5] The benefits of ultrasound in guiding biopsy needles became more apparent as the understanding of prostate anatomy and distribution of carcinoma improved, assisted by McNeal's description of the different zones.[25] Since then much work has been done

to determine the optimal sites and numbers of prostate biopsies to maximize cancer detection of what remains a test with a significant sampling error.

Although novel biopsy tools and methods have been approved quickly, the optimal number of cores and distribution for conducting prostate biopsies remain controversial. Numerous studies proposed that the Prostate cancer detection rate increases as the number of biopsy cores increases. Elabbady *et al* reported that the 12-core biopsy increased the Prostate cancer detection rate from 25.8% to 36.4% during a comparison with 6-core biopsy.[26] similarly, the prevalence of prostate cancer was improved from 7.7% to 13.8% in the studies of Kojima *et al* and Matsumoto *et al*.[27, 28] Certain studies showed different conclusions. In a randomized trial conducted by Naughton *et al* no significant difference in detection rate between 6-core and 12-core biopsies was found. [29] However, in the study by Kim *et al* , the prostate cancer detection rate of 12-core biopsy was identified to be lower than that of the 6-core biopsy (14.4% vs. 17.2%).[30]The consensus today for initial biopsies is to use a minimum of 10–12 laterally directed biopsies from the peripheral zones with the use of TRUS. [31,32]

Our institution (UTH) in Zambia has no transrectal ultrasound probe to enable us to perform TRUS guided biopsies.The hospital relies on sextant finger guided transrectal biopsies for the diagnosis of prostate cancer and therefore thought this may contribute to a lower prostate cancer detection rate as some biopsies may come out as false negatives.

A study done by Gohji et al entitled predicting extent of prostate cancer using systemic prostate biopsy and serum PSA levels in Japanese men found that of the 296 patients biopsied using a finger guided spring loaded biopsy gun, 52 were pathologically confirmed to have prostate cancer and staged clinically as Stage T2N0M0 and of these 32 underwent radical prostatectomy. The mean age of these patients was 63+ or – 9.And in this study,well differentiated adenocarcinoma (Gleason 2-4) was found in 21patients, moderately differentiated (Gleason 5-7) in four patients and poorly differentiated adenocarcinoma (Gleason 8-10) was found in seven. This study found also that a combination of systemic biopsy and serum PSA may be useful in predicting extraprostatic cancer.[33]

A study done in south Africa by Jehle et al, found that of the 296patients that underwent finger guided prostate biopsy 118 (45.6%) had malignancy on histology and 141(54.4) had benign

result. The mean age of the patients was 68.4+ or – 8.48. The PSA range from 8.80ng/ml to 52.8ng/ml and 109/194(56.2%) had abnormal DRE at presentation. The cancers found showed that Gleason score of 6 and below was found in 31.3%, Gleason score of 7 was found in 23.6% and those with Gleason score 8 to 10 was in 45.3% patients. The study also compared the results with ultrasound guided biopsies and concluded that while TRUS guided biopsy remains the gold standard, in centers were TRUS is not available, a systemic finger guided biopsies with a minimum of 6 cores, is a suitable alternative in patients who present with abnormal feeling on DRE. It should also considered If there is raised PSA, especially a PSA level of more than 10ng/ml.[34]

A study done by Yongshen et al in china reported that from 1999 to 2015 a total 3762 underwent systemic 6,8 and 13 core prostate biopsy, guided by finger or transrectal ultrasound at their center. In their study 1103 patients underwent sextant finger guided biopsy and found a cancer detection rate of30.8 %(340/1103). The extended finger guided 8-core biopsy was done on 401 patients and they found a prevalence of 36.7% (147/401) higher than that of the sextant(X^2=4.570, p=0.033).The prostate cancer detection in patients with abnormal DRE was 57.6%(951/1652) and this was higher than patients with only raised serum PSA(4 to 160ng/ml) at 37.8%(1283/3398).They also found that patients with high risk Gleason score were more in the patients with abnormal DRE than in patients with only elevated serum PSA (37.1% vs 25.4%,p=0.001). In this study they also found association between higher cancer detection rate and total serum PSA level, Old age, small prostate volume and lower F/t PSA ratio. During the study the mean age of patients with cancer decreased from 73.4years to 70.8years.[35]

Similar results were reported by Gong and collegues in china were they conducted 2707 prostate biopsies and found a prevalence of prostate cancer at 36.2%. They also reported that the cancer detection rate was higher in TRUS guided biopsies at 41.7% (458/1104) than in finger guided biopsies 32.5%(521/1603).They also found a mean age of patients with prostate cancer at 71.1+ or -7.12years and those with Benign findings was 68.3+ or – 8.13 years. The study also found that out 725 patients with abnormal DRE, 72% (522/725) had adenocarcinoma. They also found a strong association between DRE findings and the histology results.[36]

Another study done by Yarney et al entitled clinicopathologic features and determinants of Gleason score of prostate cancer in Ghanaian men, investigated 170 patients using TRUS guided biopsies and found a mean age of 65.4 years. Majority of their patients (73.7%) presented with a serum PSA more than 20ng/ml while 14% had PSA less than 10. Gleason score of more or equal to 7 was found in 95(56%) of the patients. Asymptomatic patients constituted 24%, urinary symptoms were present in 50.4%, and patients who presented with bone pain were 22.6% and 3% had neurological symptoms. This study also found that there was a statistically significant relationship between age and Gleason score ($p = 0.049$), PSA and Gleason score ($P = 0.0001$ and between extent of disease and Gleason score ($P = 0.0002$). The study also suggested the high fat diet, low intake of fruits and vegetables are probable risk factors for Cancer of the prostate.[37]

A study by Ezanwa et al to determine the prevalence of prostate cancer among patients with Intermediate total PSA values seen in Lagos University Teaching Hospital (LUTH), a tertiary hospital located in Nigeria. A total number of 105 patients aged 50years and above with total PSA values within the intermediate PSA range (4-10ng/ml) and normal findings of the prostate on digital examination seen from January 2010 to December 2010 were recruited for the study. These patients had no features suggestive of metastasis on clinical examination. All the patients subsequently had free PSA assay and trans-rectal guided six core biopsy of the prostate. The mean age of the patients studied was 64.4years (SD=1.6) with mean total PSA value of 6.6ng/ml (SD=1.7). One hundred patients (95.1%) presented with lower urinary tract symptoms. The prostate cancer rate following analysis of biopsy specimen was 13.3 % (14 patients) with most patients (78.6%) within 61-70 year old bracket. The histology was adenocarcinoma in all the patients; Gleason scores 5-7 predominating. They therefore concluded that the prevalence of prostate cancer among Nigerian males with intermediate total PSA and palpably benign prostate gland from this study was 13.3%[38]

CHAPTER THREE

Material and Methods

Study Design:

This study was a cross section (observational) study of patients undergoing prostate biopsy with indications for biopsy.

Study Site

The study was conducted in the department of surgery, Urology Section at the University Teaching hospital in Lusaka Zambia

Study Duration

Participants were recruited into this study from April 2014 to December 2014 in the urology section at University Teaching Hospital. Follow up and collection of histology reports were done up to August, 2015.

Target Population

The population under this study was all patients with suspected cancer of the prostate undergoing finger guided prostate at the university Teaching hospital in Lusaka, Zambia.

Inclusion criteria

All patients with indications for prostate biopsy undergoing finger guided prostate biopsy and consented to study to participate in the study

Exclusion criteria

Patients with indications but refused to consent for prostate biopsy and those who refused to participate our the study

Sample size

Sample size was calculated using prevalence formula.

$N = Z^2 x\ P\ (1-P)/d^2$

Taking the available point prevalence of prostate cancer in developing countries at 4.0% as estimated by WHO , confidence interval of 95% with standard value of 1.96 and acceptable error at 5% (0.05)

$N= 1.96^2 \times 0.04(1-0.04)/0.05^2$

N= 147, A sample size of 147 of men undergoing prostate biopsy was targeted.

Variables

Table 1 Univariate and Multivariate Variables

NO.	Variable	Definition	Scales
1	Age	Number of years from birthday	Continuous
2	Indication for biopsy	Reason for biopsy as abnormal DRE and/ or raised PSA above 4ug/ml	Categorical
3	Histological result	Microscopy result of the specimen	Categorical
4	Gleason Score	The sum of the primary predominant cell type grade and secondary cell type grade	Continuous

Data Collection and Procedures

Recruitment

All patients coming to the urology unit for suspected prostate cancer were approached and the study was explained to them. Patients willing to participate signed consents forms that were made available for them. Patients with indication for biopsy such as suspicious DRE or raised serum PSA or both were recruited. No TRUS was done because of non-availability of a TRUS probe in the hospital. Only abdominal ultrasound was done for estimation on the size of the prostate. An interviewer administered questionnaire was used to collect demographic information and serum PSA result. Then appropriate finger guided prostate biopsies were collected by multiple experienced urologists at the university teaching hospital in Lusaka.

Operation Procedure

Patient was placed in lithotomy position on the table and patient was cleaned with savlon in the perineum and anal area. Manual evacuation and cleaning of the rectum with savlon was done Local analgesia of 2% lignocaine gel was applied to rectum through the anus.

Then with the guide of the figure, six cores of the prostate gland were collected on the right and left lobes avoiding the midline. The cores were placed in a sample bottle and fixed with Formalin.

Patient was assessed for rectal hemorrhage and a rectal pack was applied to ensure haemostasis was achieved. The pack was removed after about 30minutes and reassessed.

If no bleeding was present .The patient was cleaned and removed from the table.
After the procedure antibiotics were given for five days as prophylaxis. Patients were also provided with oral analgesics for three days.

Patients were told to come back for a review after three days and in-patients were reviewed on the wards. All the early complications were investigated and treated. On the third day review patients were told to come for the next review after two weeks. The results were followed up and collected.
Patients were reviewed after two weeks and all the results were communicated to them and their chosen relatives. It should be emphasized that this is part of routine medical practice and was done at no extra cost to the patient. Effort was taken to make sure that the results of all the patients were acted upon fully and that a high standard of available care was subsequently delivered to these patients.

Laboratory Processing and Reporting

The specimens collected were fixed into formalin and were routinely processed in paraffin blocks from which the slides were cut and stained in hematoxylin and eosin. These slides were reviewed by one pathology registrar and a consultant pathologist at the University Teaching Hospital Laboratory and also at other accredited private laboratories.

Data Analysis

Data coding, checking, and cleaning were done before entry into EpiData file. Two histology reports from private laboratory had no Gleason score indicated but showed adenocarcinomas and were included as prostate cancer. Other reports that showed insignificant sample were not included in the study. Data analysis was done with SPSS 21.0.The P value of 0.05 was used to determine significance of findings. Pearson Chi-square was used to compare binary variables. The data and findings presented were obtained from 146 patients undergoing prostate biopsy at the UTH in Lusaka. Demographic Data was collected from April 2014 to December, 2014.Follow up of results was done up to August 2015.All the patients underwent a six core finger guided prostate biopsy.

Study Limitations

The population targeted was only the participants with indication for biopsy in a hospital setting therefore these findings cannot be generalized as the prevalence at community level.

The histopathology specimen was done at the University teaching hospital and other accredited private laboratories. This was done because a long waiting period at the UTH for the releasing of result. Therefore some patients decided to have their histology examination done in private facilities for prompt release of results and two reports did not include the grade of the cancer. It was not possible to trace the specimen for the purpose of grading.

The study did not exclude patients who were on Fenestride before biopsy, so this may have had a small impact on the serum PSA levels

Ethical Issues

Permission to carry out the study was granted by the Research Ethics Committee of the University of Zambia. The study subjects were required to give informed consent to participate in this study and they had the right to withdraw from the study at any given time without any compromise to the level of care. None of the patients underwent prostate biopsy purely for the purposes of the study and all patients were given counseling before and after the procedure. Patient's information was treated with the highest confidentiality and the information obtained was solely for the purposes of the study. All recruited cases and those not recruited for any reason, were offered the highest standard of care available at UTH

CHAPTER FOUR

Results

Socio-Demographic Characteristics of Participants

The socio-demographic features that were evaluated were age, Clinical presentation and PSA result.

Age

Figure 1: shows the age distribution of the participants. The age range showed a normal distribution. The age range of patients recruited was from 49 to 92 and the mean age was 71.57 years old (Std. Dev = 9.521).The peak of patients that underwent biopsy was in the age range of the seventies.

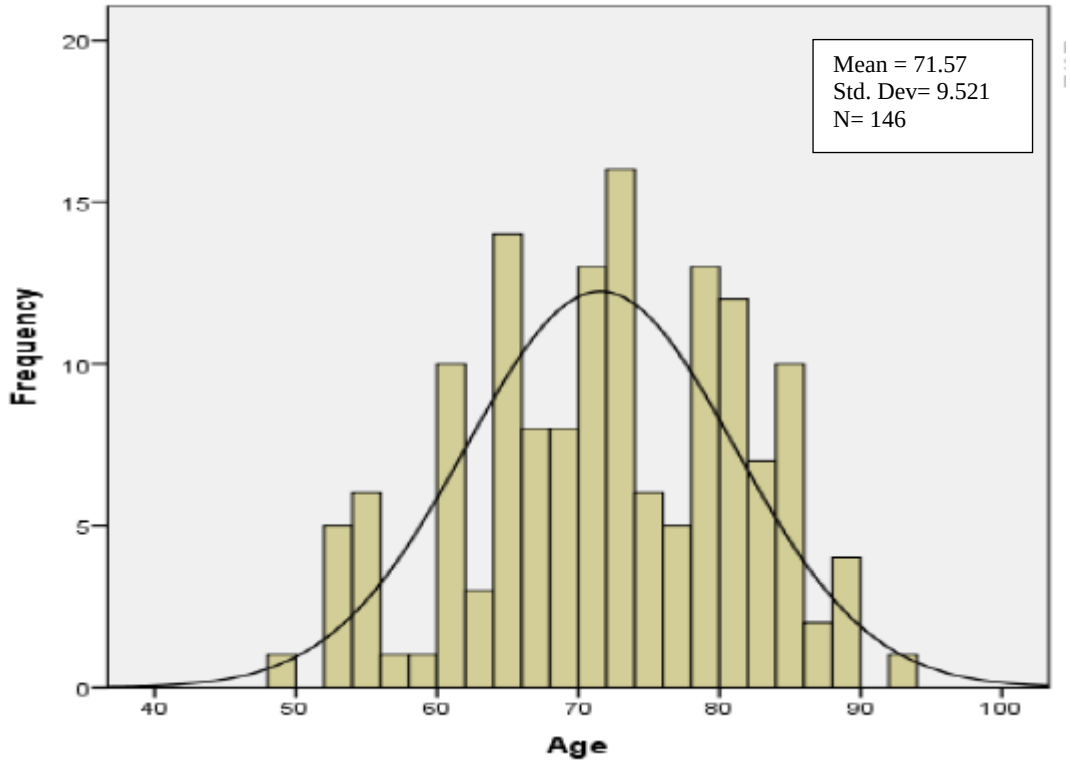

Figure 1: Age Distribution of the Participants

Table 2 shows the age categories of the patients. The table illustrates that most 80 (54.8%) were in the age range between 56 and 75 year old, 54(37%) were aged above 75years and 12(8.2%) were below 55 years old.

Table 2: Age categories of Patients

Age Range	Number of patients	Percentage %
45 years to 55years	12	8.2%
56 years to 74years	80	54.8%
75years and above	54	37%

Clinical presentation

Table 3 shows that only 6(4.1%) of the patients had no symptoms of prostate cancer and therefore came with the purpose of being screened or Medical Checkup. Majority of the participants 131(89.7%) had Lower urinary tract symptoms .11 (7.5%) participants came with advanced disease symptoms such as severe backache and paraplegia. 38(26%) had other symptoms such as haematuria, lower abdominal pains and haematospermia.

Table 3: Symptoms at First Presentation

SYMPTOMS	Frequencies, N/ of 146	Percentage of patients
Asymptomatic	6	4.1%
Lower Urinary tract symptoms	131	89.7%
Metastatic disease symptoms	11	7.5%
Other symptoms	38	26%

Physical Findings on digital rectal examination showed that most 82(56.2%) of the patients presented with suspicious feeling of the prostate of the patient .The table 3 below and Figure2 below illustrates these Physical Findings.

Table 4: Digital Rectal Examination

DRE Findings	Number of patients	Percentage
Suspicious	82	56.2
Non suspicious (Firm)	64	43.8%

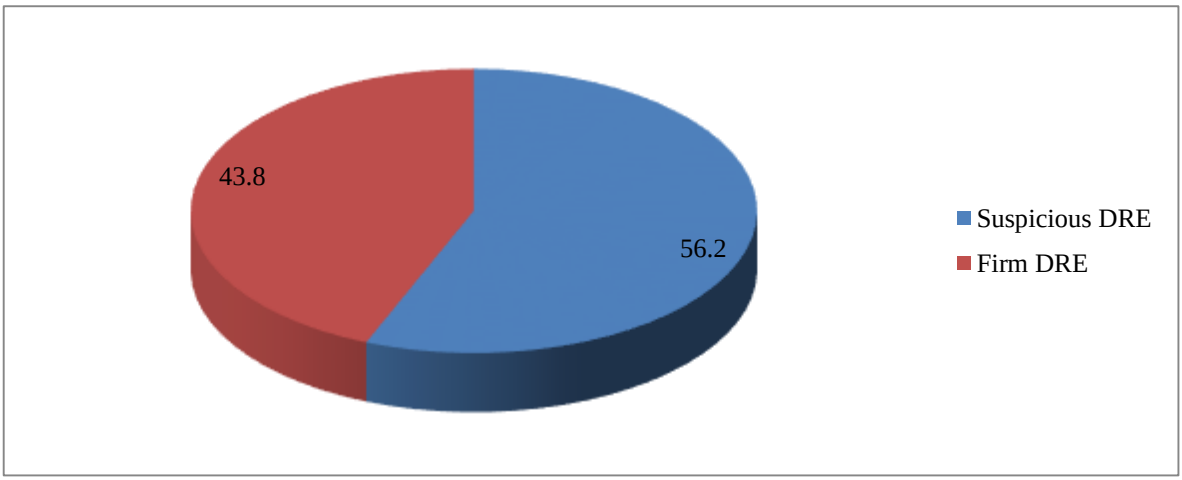

Figure 2: Digital Rectal Examination

Table 5 shows the categorization of PSA values according to the risk of prostate cancer. The minimum PSA value was 2.13 and the maximum was 5480.Most of the participants 111 (84.8%) were in the high risk PSA category. Only 5(3.8%) patients were in the low risk category.

Table 5: PSA categorization in Terms of Risk of Prostate Cancer

PSA value	Frequency, N	Percentage %
Low risk (N<10)	5	3.8
Intermediate risk (10< N<20)	15	11.4
High risk (20 < N)	112	84.8

Indication for prostate biopsy

Table 6 illustrates the indications for the prostate biopsies done on the participants. 16 (11%) had an abnormal Digital rectal examination as the only indication. PSA was the indication in 64(43.8% of the patients. Both Prostate Specific Antigen and Digital rectal examination were indications in 64(45.2%) of the patients.

Table 6: Indications for Biopsy

Indication	**Number of patients**	**Percentage**
Suspicious DRE	16	11%
Suspicious DRE and raised PSA	64	43.8%
Raised PSA	66	45.2%

Histological Pattern

Table 7 shows that 89(61%) of the patients had adenocarcinoma, 48(33.3%) had Benign Prostatic Hyperplasia. Chronic prostatitis and Normal prostate were 8(5.5%) and 1(0.7%) respectively. The prevalence of patients undergoing prostate biopsy was found to be 61%.

Table 7: Histopathology Results of Patients

Histology Result	**Number of patients**	**Percentage**
Adenocarcinoma	89	61%
BPH	48	33.3%
Prostatitis	8	5.5%
Normal	1	0.7%

Gleason Grading at Histology

Table 8 shows the grading of the cancer found in the participants according to Gleason Grades. Most of the participants 39 (26.7%) had a Gleason score of 7 and followed by Gleason score of 9 at 15.8%. The most common Gleason score was (3+4) at 15.1% and followed by (4+3) at 11.6%. The most common primary cell type was 3 and 4 was the most common secondary cell type.

Table 8: Gleason Grading at Histology

Grade (P+S)	Number of patients	Percentage
2+1	1	0.7%
2+3	1	0.7%
3+2	1	0.7%
3+3	9	6.2%
3+4	22	15.1%
4+3	17	11.6%
3+5	2	1.4%
4+4	8	5.5%
4+5	15	10.3%
5+3	4	2,7%
5+4	9	6.2%

Figure 3 Shows the pattern of the Gleason scores reported from the biopsies that were conducted and this chart shows that majority of our patients had Gleason score of 7 and above.

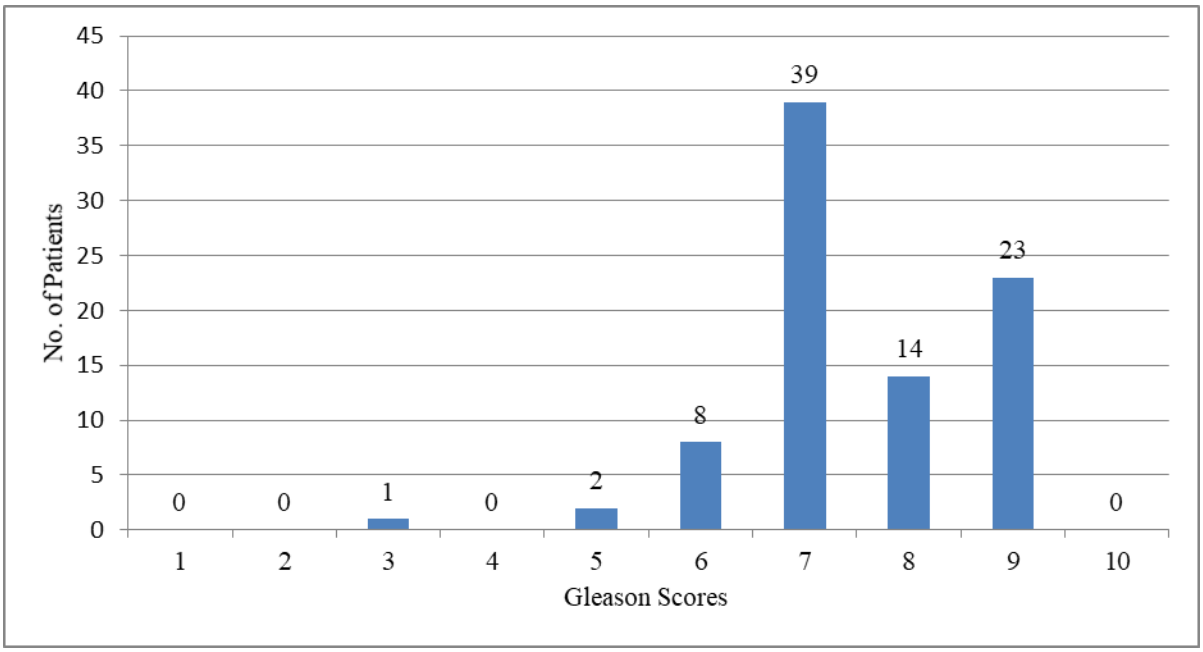

Figure 3: Gleason Score of the Cancers

Table 9 illustrates the Gleason Score Categorization. Most patients 39(57.5%) had intermediate risk with a score of 7 and 37(42.5%) patients had High risk cancers with a score of 8 and above. Only 11(12.6%) had low risk cancers with score 6 and below.

Table 9: Gleason Score according to Risk

Risk Category	**Number of patients**	**Percentage**
Low risk (Gleason score 2-6)	11	12.6%
Intermediate (Gleason 7)	39	57.5%
High risk (8 to 10)	37	42.5%
	87	100

Mean Age of patients according to histology results

Table 10 below shows that the mean age for patients diagnosed with prostate cancer is 72.25 and higher than patients with Benign Prostatic Hyperplasia which was 69.08. The minimum age of patient diagnosed with prostate cancer was 52 years.

Table 10: Mean Age of patients according to histology results

Histology Report	Number	Minimum Age	Maximum Age	Mean Age
Adenocarcinoma	89	52	92	72.25
BPH	48	49	85	69.08
Chronic Prostatitis	8	58	84	73.38
Normal	1	71	71	71

Association between age and Grade of the cancer found in the patients

Table 11 Illustrates that the age range of 49 to 55 had more high risk cancers 3(8.1%) and the group of 56 to 75 years old had 48(55.2%) in the high risk . Patients above 75 years old had most 15(38.5%) in intermediate risk and high risk was 14(37.8%).The P value was 0.883 and hence the finding was not statistically significant. There was no association between age at diagnosis and Gleason categorization.

Table 11: Age against Gleason score risk category

Age category (years)	Low risk cancer	Intermediate	High risk cancer
49 to 55	0 (0.0%)	2 (5.1%)	3 (8.1%)
56 to 75	6 (54.5%)	22 (56.4%)	48(55.2%)
Above 75	5 (45.5%)	15(38.5%)	14(37.8%)

Chi-Square = 1.170, P value=0.883

Association between the indications and histology results in patients

Table 12 shows that most 53(60.1%) of the patients with prostate cancer had both Digital rectal examination and PSA as the indications. Out of 16 patients with DRE as the only indication 12 had adenocarcinoma. Most patients 35(74.8%) with BPH had PSA as the only indication and the other 24(27%) had Adenocarcinoma. The P-value was 0.001 and therefore the finding was statistically significant. There was association between the indications and the histological result obtained after biopsy.

Table 12: Association between the indications and histology results

Indication	Adenocarcinoma	BPH	Prostatitis	Normal
Suspicious DRE	12 (13.7%)	3 (6.3%)	1 (12.4%)	0 (0%)
Suspicious DRE and raised PSA	53(60.1%)	10 (20.8%)	1 (12.4%)	0 (0%)
Raised PSA	24 (27.0%)	35 (74.8%)	6 (75%)	1 (1%)
	89 (100%)	48(100%)	8(100%)	1(100%)

Chi-Square=35.92, P-value=0.000

Association between DRE findings and histological reports

Table 13 shows that 67(75%) out of 82 patients with abnormal DRE had Prostate cancer. This gives a positive predictive (PPV) value by digital rectal examination of 75%.The finding was statistically significant (P-value= 0.001, df =1).There is an association between Digital rectal examination feeling and the histological results. This illustrates that patients with abnormal DRE are most likely to be found with prostate cancer on histology.

Table 13: Physical Examination (DRE) vs Histological Report

DRE Findings	Adenocarcinoma	Benign Finding
Suspicious DRE	67 (75.3%)	15 (26.3%)
Non-suspicious DRE	22 (24.7%)	42 (73.7%)
Total	89 (100%)	57 (100%)

Chi-Square=33.873, P-value=0.001, Positive Predictive Value (PPV) = 67/ 67+15= 0.75 by 100%= 75%

Table 14 shows that most75 (97.4%) of the patients with high risk PSA category had Prostate cancer. The intermediate risk category had patients13 (28%) with BPH. The P-value is 0.001 and hence the finding was statistically significant.

Table 14: PSA risk Category vs Histological Findings

PSA risk category	**Adenocarcinoma**	**BPH**	**Prostatitis**	**Normal**
Normal (0 to 4ng/ml)	0 (0%)	1 (2.2%)	1 (12.5%)	0 (0%)
Low risk (4 to 10ng/ml)	1 (1.3%)	2 (4.3%)	0 (0%)	0 (0%)
Intermediate risk (10 to 20ng/ml)	1 (1.3%)	13 (28.3%)	1 (12.5%)	0 (0.0%)
High Risk ((> 20ng/ml)	75 (97.4%)	30 (65.2%)	6 (75%)	1 (100%)
Total	77 (100%)	46 (100%)	8 (100%)	1(100%)

Chi-Square 31.592, P value =0.001

CHAPTER FIVE

Discussion

The general objective of the study was to determine the prevalence of prostate cancer in patients undergoing finger guided prostate biopsy at UTH. The specific objectives were 1) to describe the demographic and clinical Characteristics of patients undergoing prostate biopsy, 2) to describe the indications for prostate biopsy in men undergoing prostate biopsy at UTH and 3) to determine the histological characteristics of prostate biopsies

Demographic Characteristics of the patients

A lot of studies done around the world have shown that this cancer is a disease of the elderly. The age range of the patients that underwent finger guided Prostate biopsy at University teaching hospital in our study ranged from the 49 to 92years old. The mean age at presentation was 71.57 years (Std. Dev.= 9.517) this finding agrees with a study done in south Africa that reported the mean age for patients undergoing finger guided biopsy as 68.8(Std.Dev=8.38) and the peak age of diagnosis as the seventh decade.[34]Our study also agrees with studies from China.[35,36]However another study from Nigeria also reported a younger mean age of patients (64.4) undergoing prostate biopsy.[37]The reason may be that there is better access to cancer diagnosis services in west Africa than in Zambia where these services are centralized only to the capital city and also that clinicians in this part of Africa have a high index of suspicion leading to early diagnosis of prostate cancer in this younger age group of patients. The mean age for patients who had adenocarcinoma in our study was 72.25 and the youngest was 52 years old. This correlates well with other studies done in Africa that suggest that prostate cancer in Africa presents in the seventh decade that is a decade earlier than reports from Europe and the USA.[34,37,38,39] All studies reviewed agreed with our study that Prostate cancer is a disease of the elderly population.

Presentation of patients.

A review of literature has shown that most black men in Africa still present with locally advanced cancer (from 41% to 96% of patients) or metastatic disease (up to 59% of cases) and are usually diagnosed because of longstanding symptom or complications due to advanced cancer.[38, 39]

Most (89.7%) of the patients in this study presented with Lower urinary tract symptoms and some with history of urinary retention .This finding correlates well with another study done in South Africa that showed that patients present mostly when they start experiencing urinary symptoms and by this time the cancer is either locally advanced or in the metastatic stage.[34] One important finding was that a higher percentage (7.5%) of patients presented with symptoms of advanced disease such as paraplegia or paraparesis than what has been reported from South Africa at only 1%.[34] This shows that a lot more of our patients present to health facilities late because of either lack of knowledge about the disease as a result of poorly sensitized communities and also challenges of access to cancer diagnosis and treatment services especially in the rural parts of our country. The other contributing factor could be that all our patients were black Africans with most of them having high risk cancers that are more aggressive and advance to metastatic disease quicker than those reported in South Africa where they have a considerable large population of Caucasian counterparts.

Most of researchers in Africa have found that the low social-economic status, poor educational status and unequal access health services has largely contributed to a very poor cancer screening culture.[34]Our study showed that only about 1% of our patients presented asymptomatic. These are the patients who were captured from the little screening services that are being provided around the country. Therefore, our study agrees with other reports from other sub-Saharan countries. The poor knowledge and difficulties in the access to cancer screening services are mostly the reasons attributed to this poor screening culture in our country.

Physical Findings of patients.

Physical examinations revealed that 56% of the patients undergoing biopsy have an abnormal DRE. This finding agrees with other studies that reported a 50% of abnormal DRE among the patients undergoing finger guided prostate biopsy.[34]This finding shows that slightly more than half of our patients present with tumors of T stage above stage T1.This agrees with other hospital based reports from Senegal, Ghana and South Africa.[11] This can be attributed to the fact that there is little or no provision of early diagnostic tests such as PSA in most hospitals in Zambia like most of other African countries.

In our study we found a statistical significance between the Digital Rectal Examination findings and the histological result after prostate biopsy. This showed a strong association between DRE findings and Prostate cancer detection at the University Teaching Hospital in Lusaka. The positive predictive value of DRE in these patients who had raised PSA values (Majority with more than 4) was 75%. This finding correlates well with other studies that have reported a range of 30% to 80%.[35, 36,41,42,43.]

Indications for biopsy

Most 66 (45.2%) of the patients in our study had PSA as a lone indication then followed by those who had both abnormal DRE with raised PSA at 64(43.8%). The biopsy results obtained showed that 53(59.6%) out of 64 patients who had both abnormal DRE and raised PSA value, had adenocarcinoma on histopathology. Only Twenty four out of 66 patients who had only raised PSA as the indication had Prostate cancer. Therefore the study showed that when PSA and DRE are used as complimentary indications the Positive Predictive value is increased. This agrees with other studies done in other parts of the world.[44, 45]This can be explained by the fact that PSA is organ specific and not specific to cancer and but, increased chance of finding cancer in patients who had an abnormal DRE with a raised PSA. For patients who had PSA as a lone indication the chances of finding cancer were lower because other conditions such as BPH and transurethral procedure can result in the increase of serum PSA levels. Though we had a lower proportion of patients that had prostate cancer in the group with only raised PSA, it is important to observe that this test led to the early diagnosis of organ confined cancers that were not palpable on examination.

Most of the studies that have been done in Africa and North America have shown that Black Africans have higher serum PSA values than Caucasians after correcting tumor size and stage. In this study we found that the total serum PSA values ranged from 2.96ng/ml to 5680ng/ml. This finding collates well with another study done by Amayo and Obara who were evaluating PSA levels in East African men with prostate cancer and reported a range of 1.78ng/ml to 4339ng/ml.[46]This high PSA values in Zambian and other African men is attributed to probably high tumor size and late stage at presentation. This study also found a statistical association (P-value = 0.001) between PSA risk categories and the number of patients who had Prostate cancer. The high risk patients with PSA of more than 20 had the highest percentage of patients with

prostate cancer on histopathology. This finding agrees with other observational and randomized trials which have shown that both the future risk of prostate cancer and the chance of finding cancer on Prostate biopsy increase with the increase in serum PSA level.[35, 44, 45].

Histological pattern.

All the cancers found on histopathology in this study were adenocarcinoma. The study found that most 89(61%) of patients had adenocarcinoma. Benign prostatic hyperplasia was found in 48(32.9%) and Chronic prostatitis was found in 8(5.5%). There was no report which showed premalignant categories. This histological pattern finding agreed with the study done by Jehle et al in South Africa.[34] However, the reported percentage of prostate cancer found was higher in our study.The prevalence of prostate cancer in men undergoing finger prostate biopsy was found to be 61% which is higher than what has been reported from South African, China and Japan.[34, 35, 36]This can be attributed to the fact that most of our patients presented with advanced cancer with elevated serum PSA above 20ng/ml compared to those investigated in the other studies.

Studies have shown that the use of finger guided prostate biopsy gives a large number of false negatives and so some of the negative biopsies may be false.[5]To improve on the diagnosis and to avoid repeating of the biopsy procedure, image guided(e.g TRUS, MRI-guided) should be used to improve on the detection rate. However,in our resource limited setting were image guided biopsy methods are not available, the high prevalence found in this study shows that finger guided prostate biopsy can still be used to diagnose prostate cancer especially in patients presenting with an abnormal DRE.

Cancer grading at diagnosis

Our study found that most of the patients with prostate cancer have Gleason grading of 7 and above. The cancers diagnosed were mostly high risk and intermediate risk with Gleason grading of 7 to 10. This finding agrees with the other studies done in west and south Africa.[11, 34, 37, 38, 39] However, does not agree with another report from Senegal that showed that most of their patients had low risk cancers with majority having a Gleason score of 6.[11] The cancers found in our patients were poorly differentiated (Gleason score 8 to 10) and moderately poor differentiated (Gleason 7) which are very aggressive and have an unfavorable outcome without proper treatment. The predominant primary cell type in the scores was grade 3 and the commonest

secondary cell type was 4.Only about 3% of the reports had well differentiated cell types(Grade 1 or 2).This agrees with another study done by Okolo and collegues in a study entitled Correlation of PSA and Gleason score in Nigerian men with prostate cancer.[47]This finding can be attributed to the fact that all our patients were black men in the sub-Saharan region who are genetically predisposed to developing high grade and more aggressive cancers as reported in literature by other studies done around the world.[11,39] The finding can also be attributed to the fact that the population investigated was mostly patients with cancer that had progressed to clinical disease and not patients with indolent prostate cancer which is usually low risk and less aggressive and hence the need to do a broad study at community level to prove this finding. The other reason is that most of our patients had high risk total serum PSA (more than 20ng/ml) who are likely to have high Gleason scores(8 to 10) as described in literature.[35]

In our study there was no statistical association between Gleason grading of prostate cancer and the age at which the patients presented. This agreed with another study done in Nigeria.[47]The patients that presented young (49 to 55years old) presented with similar grades of cancer as the elderly patients. Therefore there is need to increase the index of suspicion by medical personnel in order to improve on early diagnosis and provide curative interventions in these young patients.

CHAPTER SIX

Conclusion and Recommendations

Conclusion

From this study the following conclusions were drown:

1. The age range of Patients undergoing finger guided prostate biopsy at the University teaching hospital was from 52 to 92 and Mean age was 71.57years. The mean age for patients with prostate cancer at UTH is 72.25.
2. Most of the patients present with locally advanced prostate cancer as most patients come when they have Lower urinary tract symptoms
3. 56% of the patients undergoing biopsy have an abnormal DRE which shows that they have cancer above Stage T1
4. Most of patients with prostate cancer had bothabnormal DRE and Raised PSA
5. Most of the patients had Gleason score of 7 and above. The predominant primary cell type had a Gleason grade 3. The cancers found were mostly poorly differentiated and moderately poorly differentiated and these cancers are very aggressive
6. The prevalence of prostate cancer in men undergoing finger prostate biopsy is 61%

Recommendations

The study has established that sixty one percent of the patients undergoing finger guided biopsy have prostate cancer. This cancer detection is compared to most of the reports. Therefore we recommend that:

1. All patients aged 45 and above presenting to UTH urology with LUTS should have a DRE done
2. Patients presenting with abnormal DRE should have prostate biopsy done
3. There is need to do more research to compare these results with the prevalence in patients undergoing imaging guided biopsies such as TRUS,TRUS- contrast enhanced colour Doppler ultrasound and Magnetic Resonance Imaging guided(MRI)

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APPENDIX ONE

Data Collection Sheet

A: Demographic Characteristics Study Number:……

1: Age [ ]

2: Marital Status
- Single [ ]
- Married [ ]
- Widower [ ]
- Divorced [ ]

3: Provincial residence ……

4: Educational Background
- None [ ]
- Primary [ ]
- Secondary [ ]
- Tertiary [ ]

B: Clinical Presenting Features of patients undergoing biopsy

i Asymptomatic [ ]
ii Lower urinary tract symptoms [ ]
iii Urinary retention [ ]
iv Advanced (Metastatic) disease [ ]
v Others [ ]

C: Digital rectal examination

i Non Suspicious feeling [ ]
ii Suspicious feeling [ ]

D: Laboratory test (Total serum PSA)

i PSA availability Yes [ ] No [ ]

ii If Yes, PSA value …….

E: Indication for Biopsy	Abnormal DRE	[ ]	Raised Total PSA [ ]
F: Histological Findings	Adenocacinoma	[ ]	
	BPH	[ ]	
	Prostatitis	[ ]	
	Normal	[ ]	
	Others	……..	

If Adenocarcinoma, Gleason Score ……+……=……...

APPENDIX TWO

Participant Information Sheet

My name is Dr. Brian Chilando, a resident doctor in urology, department of surgery at the University Teaching Hospital. I am conducting a study on the prevalence of cancer of the prostate in patients undergoing routine biopsy. The purpose of the study is to determine the prevalence and characteristics of prostate cancer at UTH.

I am requesting you to participate in the study on voluntary basis. Prostate biopsy will be done by a qualified medical practitioner.

During the prostate biopsy, you may experience some discomfort or pain at the site of collection. To minimize this, trained personnel will collect the biopsy using the smallest needle which is sterile, under local anesthesia and aseptic technique will be employed.

Although you may not directly benefit from participating in the study, you will make major contribution to the information known about cancer of the prostate. In the future others will benefit because doctors and scientist will know the prevalence of this cancer.

The study will not delay your treatment nor prolong your stay in the hospital. The researcher will keep the records and results of your biopsy locked in the cabinet and the keys will be kept by the researcher and the results will not be disclosed to other people neither will other people be told of you participation in the study.

If you feel that you have been injured or inconvenienced as a direct participation in the study, you are at liberty to withdraw from the study at any time without any penalty or loss of benefits.

In any case of any questions or seek clarifications please contact me Dr. Brian Chilando on 0969760282, department of surgery, university Teaching Hospital , P/B
RW1X, Lusaka.

You may also contact the chairman of the University of Zambia Biomedical and
Research Ethics Committee. Ridgeway campus, P.O Box 50110, Lusaka, Zambia

Telephone 0211-256067.

APPENDIX THREE

Certificate of Consent

You are signing of this form means that you understand the information presented and that you want to participate in the study. You understand that participation is voluntary and you may withdraw from the study at any time. If you agree to participate in the study, kindly sign the consent form that follows.

I ……of address……..

On this day of ……month of ……. Of the year…….. Do understand the importance and the risks of participating in this study have been explained to me

I have read the foregoing information, or it has been read to me. I have had an opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research and agree to the terms of the study as laid by the researcher.

Signature or print of participant …….

Name of the participant ……..

Date…… (Day / month / year)

Statement by a witness

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

Name of witness: …….

Signature of the witness……Date…….