DEMOGRAPHIC FACTORS AND CLINICAL DETERMINANTS OF STAGE OF PRESENTATION OF PROSTATE CANCER IN PATIENTS SEEN AT THE KENYATTA NATIONAL HOSPITAL

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DECEMBER 2023

STUDENT DECLARATION:

I declare that this study is my original work and has not been presented for the award of any degree at any other institution or university. Where I have used another person's work, I have acknowledged and referenced.

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DEPARTMENTAL APPROVAL

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ACRONYMS AND ABBREVIATIONS

AJCC – American Joint Committee on Cancer

KNH – Kenyatta National Hospital

TNM – Tumor, Nodes and Metastasis

PSA – Prostate Specific Antigen

USA – United States of America

LUTS – Lower Urinary Tract Symptoms

WHO – World Health Organization

ISUP – International Society of Urologic Pathologists

DEFINITION OF TERMS

Prostate cancer – Cancer affecting the prostate gland.

Stage of Prostate Cancer presentation – the extent to which the prostate cancer has spread throughout the patients' body at the time of presentation to the hospital as defined by the American joint committee on cancer (AJCC) staging system or the Tumour, Nodes and Metastases (TNM) staging system.

Demographics factors – the factors that affect access of a patient to medical treatment e.g.. Age, ethnicity, occupation.

Clinical factors – the factors that patients present with measurable by either clinical exam and laboratory testing e.g. PSA levels

First Degree Relative – family member who shares more than half of their genetic information with a specific other individual in their family e.g. parent, brother, son.

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ABSTRACT

Study background: Low-and-middle income countries with poor socioeconomic factors and poor healthcare structures, report lower incidence rates of prostate cancer but high morbidity at late diagnostic stage than when compared to high income countries with better socioeconomic and healthcare systems. This disparity in incidence rate and stage of diagnosis may be explained by demographic factors of health encompassing health seeking behavior that influences screening patterns and the stage of diagnosis of prostate cancer. It remains unknown the stages in which patients in Kenya present with prostate cancer and the role of screening programs in reducing morbidity and mortality from prostate cancer.

Broad objective: The aim is to explore the demographic characteristics and clinical factors influencing the stage at which prostate cancer is diagnosed in patients at Kenyatta National Hospital (KNH).

Study design: Retrospective study

Study site: Kenyatta National Hospital

Participants and methods: Seventy-Eight patients seen with prostate cancer from January 2018 – December 2022 were recruited and their file records interrogated for the relevant data. Outcome variable was stage of presentation with exposure variables being clinical and demographic factors.

Results: The average age of the patients was 69.3 years, with 84% employed in the informal sector. Kikuyu ethnicity was the most represented at 38%, followed by Kamba at 15.4%. Lower urinary tract symptoms (LUTS) and back pain were the most frequently

reported symptoms, occurring in 67.5% and 65% of cases, respectively. A family history of prostate cancer was noted in only 17% of the patients. The average Prostate Specific Antigen (PSA) level at the time of diagnosis was 406.6 ng/ml. Histopathological analysis showed that 41.1% of the cases were classified as International Society of Urologic Pathologists (ISUP) grade group 5, with 28% falling into ISUP grade 4. In terms of disease stage, 61.8% of patients were diagnosed with metastatic disease.

Conclusion: Prostate cancer is a disease of older men with a mean age of presentation of 69 years. Demographic patterns indicate that ethnicity and occupation could influence the patterns of presentation. Most patients continue to present with advanced disease. Screening and early diagnosis are recommended to promote detection of early disease.

CHAPTER ONE

1.0 INTRODUCTION

Prostate cancer is the second most common cancer among men and ranks as the fifth leading cause of cancer-related deaths worldwide. In 2020, 1.4 million new cases were reported globally, accounting for 3.8% of all cancer deaths. By 2022, developed countries observed a 14% increase in new prostate cancer cases, with an estimated 3.25 million men living with the disease [1].

Men of African descent, particularly African American men, have a higher prevalence of prostate cancer, with mortality rates double that of White men. Approximately 13% of men will be diagnosed with prostate cancer during their lifetime [1]. In Kenya, prostate cancer is the most common cancer among men, comprising 17.3% of all male cancer cases [2]. Most patients seek treatment at advanced stages. According to World Health Organization (WHO) data published in 2020, prostate cancer accounted for 0.49% of total deaths in Kenya, with an age-adjusted death rate of 24.17 per 100,000, ranking Kenya 51st globally [3].

Due to the staggering rates of prostate cancer and the associated mortality in LMICs, the stage of presentation of prostate cancer and associated factors is crucial to understanding treatment outcomes. This presentation stage is highly variant and depends on numerous factors ranging from demographic and socioeconomic factors to health access [4].

Men living in areas associated with low socio-economic standards may have poorer screening practices. As a result, they are less likely to report incidence of prostate

cancer, to show more spread of disease during diagnosis, and have poorer survival rates, but higher mortality rates [4].

In the US, 77% had localized stage at presentation, 11% had a regional stage, 5% had a distant stage according to a population database review of 3.1 million new prostate cancer cases diagnosed between 2001-2017 [5]. On the contrary, in Kenya, a case series by Wasike and Magoha in 2007 among 65 patients presenting with prostate cancer, majority, 85.7% presented with late advanced stages III(C) and IV(D). [6]

Similarly, differences in prostate cancer incidence and mortality rates have been observed among men of African, Asian, Indian, American, and European ancestry, suggesting that genetic factors and geographic variations may play a role [7]. Understanding the stage at which prostate cancer is diagnosed, along with associated factors, is crucial for improving health outcomes. This study aims to describe the stage at which prostate cancer is presented and the factors associated with it in patients at Kenyatta National Hospital (KNH).

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Epidemiology of Prostate Cancer - Global, African and Kenyan Statistics

In 2020, prostate cancer accounted for approximately 1.4 million cases worldwide, resulting in 375,304 deaths, which represents 3.8% of all cancer deaths in men [1, 8-10]. According to GLOBOCAN's 2018 reports, the prevalence of prostate cancer is higher in developed countries. In the United States, an estimated 268,490 cases were reported in 2022, with around 3.25 million men living with the disease. Prostate cancer represents about 14% of all new cancer cases, causing an estimated 34,500 deaths, or 5.7% of all cancer deaths, in the same year [11].

The incidence rate of prostate cancer in the US is 112.7 per 100,000 men per year, with a death rate of 18.8 per 100,000 men per year, based on data from 2015-2019 and 2016-2020, respectively [11]. It is projected that around 12.6% of men will be diagnosed with prostate cancer during their lifetime, based on data from 2017-2019 [11]. Additionally, African-American men have higher incidence and mortality rates from prostate cancer compared to White men, with mortality rates being approximately twice as high.

When it comes to the African continent, prostate cancer incidence rates have been on the rise in low-middle-income countries [13,14]. An incidence rate of 22.0 per 100,000 was reported as of 2016 and is estimated to be on a steady ascent [15]. Newly reported cases of prostate cancer in Africa have increased from 15% as of 1970 to 56% new reported cases in 2008, and are projected to reach about 70% of newly reported cases

by 2030 [13]. This increase has been observed at a rate of 23.2 per 100,000. Incidence rates are reported to be 64.1 per 100,000 in Southern Africa, 35.9 per 100,000 in Northern Africa, 31.9 per 100,000 in Western Africa, and 23.9 per 100,000 in Eastern Africa [8]. Among all African regions, Seychelles reported the highest increase of 10.3% during 2005–2018,followed by Kenya at 8.1%, with Mali reporting a steady increase of 6.7%,while Malawi reported 4.4% [17].

In Kenya, prostate cancer is the most common cancer among men, accounting for 17.3% of all male cancer cases, with most patients seeking treatment at advanced stages [2]. According to the latest WHO data published in 2020, prostate cancer deaths in Kenya made up 0.49% of total deaths, with an age-adjusted death rate of 24.17 per 100,000, ranking Kenya 51st globally [3].

Disparities in the above mentioned incidence rates may be explained by genetic differences, lifestyle and westernization, as well as differences in screening patterns in different countries across the globe [18,19]. A common factor worldwide is the correlation between the incidence and mortality rates of prostate cancer and advanced age, with the average age of diagnosis being 66 years[12].

2.2 Presentation of Prostate Cancer

Prostate cancer can often be asymptomatic in its early stages and may progress slowly, warranting only active surveillance through methods like rectal examinations or monitoring elevated serum prostate-specific antigen (PSA) levels. About 70% to 80% of prostate cancers originate in the peripheral glands, making them detectable as irregular hard nodules during digital rectal examinations.

These cancers are less likely than benign prostatic hypertrophy (BPH) to cause urethral obstruction in the initial stages. Small, non-palpable, and asymptomatic prostate cancers are often discovered through needle biopsies conducted to investigate elevated PSA levels. Occasionally, prostate carcinomas are unexpectedly identified during histologic examination of prostate tissue removed during transurethral resection for BPH[20].

Screening for prostate cancer in asymptomatic men remains a debated topic[22,23]. The European Randomized Study of Screening for Prostate Cancer indicated a significant reduction in prostate cancer mortality over 11 years, contrasting with the US-based Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, which found no mortality reduction over 10 years[24,25]. The US study's results were affected by issues with PSA testing in the control group[25]. Despite this, concerns persist about the benefits of widespread screening, particularly regarding over-diagnosis and over-treatment.

Prostate cancer typically becomes symptomatic and clinically evident as it progresses. Symptoms vary depending on the disease stage. Localized prostate cancer may present with lower urinary tract symptoms such as a weak urinary stream, increased frequency, and urgency[20,26]. More advanced localized disease can cause hematuria, dysuria, incontinence, hematospermia, suprapubic pain, loin pain, and rectal tenesmus26. When the cancer metastasizes, symptoms may include bone pain, lethargy, anorexia, and unexplained weight loss[27]. Prostate cancer generally spreads locally first, invading the prostatic capsule, periprostatic tissue, seminal vesicles, and the base of the urinary bladder, and less frequently, the rectum[28]. Lymphatic spread

typically involves the obturator nodes first, followed by the iliac and para-aortic nodes. Lung metastasis often results from lymphatic spread through the thoracic duct and prostatic venous plexus to the inferior vena cava. Hematogenous spread frequently targets bones of the axial skeleton, such as the lumbar spine, potentially leading to spinal cord compression, as well as the pelvis, thoracic spine, and ribs. Vertebral metastases often present as back pain and are detectable through skeletal surveys or radionuclide bone scanning, which is almost diagnostic of prostate cancer[27,28].

Unusual presentations of prostate cancer include supraclavicular lymphadenopathy, hydroureteronephrosis, constipation, and cases where digital rectal examinations (DRE) and PSA levels are normal. In such cases, PSA immunohistochemical staining is recommended[29]. A DRE is crucial if prostate cancer is suspected, as it helps detect asymmetry, nodularity, or a fixed irregular mass[20]. Tumors may also be incidentally discovered during a DRE performed for other reasons. Imaging studies have limited utility in diagnosing early prostate cancer due to their poor sensitivity and specificity[31]. The PSA assay is considered the most important test for screening prostate cancer, as PSA, a product of prostatic epithelium, is normally secreted into the semen. Thus, PSA screening can detect prostate cancers early in their development[20,32].

2.3 Staging of prostate cancer

Prostate cancer grading and staging can be performed clinically or pathologically, providing crucial prognostic information. Clinical staging relies on digital rectal examination (DRE), PSA testing, and the Gleason score[20]. The Gleason grading system is the most widely used for assessing adenocarcinoma of the prostate. It

evaluates glandular architectural differentiation and the tumor's growth pattern relative to the stroma[28].

This system categorizes tumors into two architectural patterns: primary, which is the most prevalent pattern in the tumor, and secondary. Both patterns are graded on a scale from 1 to 5, with 1 indicating the most differentiated and 5 indicating undifferentiated. Grade 1 tumors are well-differentiated, featuring uniform and round neoplastic glands forming well-circumscribed nodules, while grade 5 tumors consist of cords, sheets, and nests of cells infiltrating the stroma without glandular differentiation[28,33].

Intermediate grades fall between these extremes. If a tumor exhibits only one histological pattern, the primary and secondary patterns receive the same grade. The combined Gleason grades result in the Gleason score, ranging from 2 (1 + 1 = 2), indicating tumors entirely composed of Gleason pattern 1 cells, to 10 (5 + 5 = 10), indicating completely undifferentiated tumors[28].

A Gleason score below 6 indicates well-differentiated tumors, a score of 7 indicates moderately differentiated tumors, and scores of 8, 9, or 10 indicate poorly differentiated or undifferentiated tumors. These results, combined with findings from bone scans, CT scans, or MRI, help formulate a treatment plan[34].

Pathologic staging involves information obtained during surgery, including the examination of prostate tissue removed during the procedure[35]. This process typically involves the removal of the entire prostate and some lymph nodes, with the examination of the lymph nodes providing additional staging information[35]. The

Tumor, Node, Metastasis (TNM) system is also used to determine the tumor's location and spread[36].

In Stage I, the cancer is usually slow-growing, not detectable by DRE, and PSA levels are low, with cancer cells resembling healthy cells. Stage II cancer is confined to the prostate, with medium or low PSA levels. In Stage III, PSA levels are high, the tumor is growing, or the cancer is high-grade, indicating a locally advanced cancer likely to spread. Stage IV cancer has spread beyond the prostate to regional lymph nodes, distant lymph nodes, other body parts, or bones. These stages are critical for prognosis prediction and for selecting appropriate therapy[20].

2.4 Presentation Stage in Prostate Cancer - Early Vs Late and Geographical Variations

According to Siegel et al., 2020, assessing the stage of presentation of prostate cancer from 2001 to 2017 in the USA, unknown stage of presentation occurred in 7%, localized stage was 77%, regional was 11% and distant stage was 5% [5].

Geographical differences in prostate cancer incidence, staging, and mortality are influenced by various factors, including risk factors, health behaviors, the quality of healthcare, and access to medical services, including specialist availability[40,41]. Differences in treatment access and availability, clinician practices, patient preferences, comorbidities, and decision-making processes also contribute to these disparities[42–45]. Inequalities in diagnostic and treatment services, shaped by socioeconomic factors, healthcare policies, and proximity to medical facilities, significantly impact these outcomes. For rural residents, prostate cancer diagnosis can

bring challenges such as limited local healthcare services and long travel distances, which impose financial, psychosocial, and logistical hurdles[46,47]. Additionally, high-volume specialists and hospitals, which are often linked to rapid adoption of new treatments and technologies, multidisciplinary care, and improved clinical outcomes, are generally located in urban areas[48–50]. This urban-rural divide, highlighted in studies from countries like Australia and the USA, exacerbates access-related challenges[42,44].

There are also observed differences in prostate cancer incidence and mortality rates among men from various ethnic backgrounds, including those of African, Asian, Indian, American, and European descent, suggesting a genetic component to these geographic variations[7]. Moreover, disparities in diagnostic and screening services, treatment availability, technological advancements, and recommendations for prostate cancer testing further complicate these patterns. While the highest incidence rates are reported in developed countries, mortality rates tend to be higher in developing regions[7].

2.5 Determinants of Stage of Presentation

The stage of presentation of prostate cancer is determinant on health implications and the patients' general health seeking behavior [4]. Socio-demographic factors, financial and economic factors, physical accessibility and health service factors all play a major role. Socio-demographic factors include age, family size and structure, education and occupation.

Older age significantly influences healthcare-seeking behavior, with individuals aged 50 and above more likely to seek medical care compared to younger individuals[51].

Education also plays a critical role in early prostate cancer diagnosis, as men with higher educational attainment are more likely to be diagnosed early than those with lower education levels. Education correlates with other social determinants of health, such as income and work conditions[52]. Additionally, higher education increases awareness and understanding of health issues, making individuals more proactive in managing their health[53]. As a result, men with more education tend to undergo screening and receive earlier diagnoses of prostate cancer than those with less education.

Economic factors, including occupation, employment status, income, and spending, also affect when prostate cancer is diagnosed. Employment offers financial security, a sense of identity, and structure in daily life[54]. In contrast, unemployment can lead to material deprivation, social isolation, mental stress, and increased risk of depression, which can deter individuals from seeking healthcare. The nature of one's work, including job security, work environment, pace, hours, and opportunities for professional growth, also affects health-seeking behavior[55]. Stable jobs with secure incomes and favorable working conditions encourage regular health checkups and early medical intervention.

Aside from socio-demographic and economic factors, stage of presentation is highly influenced by the health service factors including the attitude of health providers, treatment satisfaction and access to laboratory and diagnostic facilities [55]. Having a universal health care system that ensures ease of access to health care and affordability, safeguards peoples' health and facilitates screening and early diagnosis of prostate cancer regardless of their socioeconomic status [55].

Low and middle income countries with poor socioeconomic factors and poor healthcare structures report lower incidence rates of prostate cancer but high morbidity at late diagnostic stage than when compared to high income countries with better socioeconomic and healthcare systems. This disparity in incidence rate and stage of diagnosis may be explained by social determinants of health encompassing health seeking behavior that influences screening patterns and the stage of diagnosis of prostate cancer [18,19].

2.6 Statement of the problem

Studies indicate that cancer patients in developing countries have a tendency to present with late-stage disease. However, the disparities in presentation could be explained by cultural, socio-economic and health system factors across the globe [4].

It remains undocumented the stage of presentation in Kenya and the contributing factors.

2.7 Justification

Understanding the stage of presentation in prostate cancer is important to promote screening programs where necessary. This would help create guidelines advocating for population cancer screening and prevention.

Furthermore, morbidity and mortality from cancer is increasing and policy direction has moved towards prevention and treatment of non-communicable diseases. The findings of this study will influence local screening guidelines and care for patients with prostate cancer.

2.8 Research question

1. What is the stage of presentation of prostate cancer in patients seen at KNH?

2. What are the demographic and clinical factors contributing to late stage presentation?

2.9 Objectives of the study

2.9.1 Main Objective

To determine the demographic factors and clinical determinants of the stage of presentation of prostate cancer in patients seen at the KNH.

2.9.2 Specific Objectives

i. To investigate the stages of presentation of prostate cancer in patients seen at the KNH.

ii. To determine the clinical factors at presentation in prostate cancer among patients seen at the KNH.

iii. To establish the demographic factors at presentation of prostate cancer among patients seen at the KNH.

2.10 Conceptual framework

The exposure variables such as clinical and demographic factors influence the occurrence of the outcome ie the stage of presentation. However, other unmeasured confounders may still influence the stage of presentation (figure 1).

Figure 1. Conceptual Framework

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Study Design

The research design was a retrospective study of patients who presented with prostate cancer from January 2018 – December 2022.

3.2 Study site

The study was done at KNH, a level 6 national referral hospital in Kenya. It has a bed capacity of 1800 and receives patients from all over Kenya and neighbouring countries. The study shall be carried out at the KNH records department and Clinic 19.

Kenyatta National Hospital being a national referral hospital has resources (urology, pathology and oncology specialists) to manage prostate cancer cases. Prostate cancer patients are routinely seen either in clinic 24 Urology clinics or Center for Cancer treatment at Clinic 36. File records of clinic 24 are kept in Health Records and Information Office, Clinic 19, while whose of CCC are kept in the records unit within the Center.

Approximately 1 new patient is seen in clinic 24 every week. Thus, in a month 4 new patients will be diagnosed with prostate cancer. In a year, total is 48 patients. In 5 years an estimated 240 new patients were seen in KNH.

3.3 Study Population

All patients who presented with prostate cancer during the study period at the KNH took part in the study.

3.3.1 Inclusion Criteria

All patients who presented with prostate cancer at the KNH.

3.3.2 Exclusion Criteria

i. All patients with incomplete records on prostate cancer staging.

ii. Those who fail to consent.

3.4 Sample Size determination

Sample size estimation was calculated using statistical Cochrane formula

The Formula: $N = \frac{Z^2 [P(P-l)]}{D^2}$

Where:

Z^2 = Standard error associated with chosen significance level (1.96)

D^2 = sampling error margin (0.05)

P = Expected proportion of patients; the expected P is 16% patients presenting with advanced prostate cancer - according to Siegel et al., 2020 [5].

N= Sample size

$N = \frac{1.96 \times 1.96 [0.16 (1 – 0.16)]}{(0.05)2}$

= 207

3.5 Sampling technique

Consecutive sampling technique was used.

3.6 Data collection

Records of patients who were managed for prostate cancer were retrieved from clinic 19, the records department of KNH and the oncology unit of the KNH.

To assess the stage of cancer, imaging reports of CT scans or MRIs that were undertaken during staging assessment were used.

To assess histological grade, the histological reports of prostate biopsy or prostatectomy specimens was used.

Patients records were interrogated to capture the relevant data for the study which was entered in standard questionnaire for eventual transfer to excel computer data sheet.

A research assistant (a 5^{th} medical student) was recruited, trained on data collection and briefed on the study topic and protocol.

3.6.1 Quality assurance

The principal investigator reviewed the collected data daily to ensure accuracy before entering it into an Excel sheet for cleaning and coding. The data sets were password-protected, accessible only to the principal investigator and the data manager. The standard questionnaire had patient initials and reference number but no name or direct patient identity. They were stored in lockable cupboard where only researcher had access and destroyed through shredding and incineration upon completion of study.

3.7 Variables

Independent variables

Age, clinical signs and symptoms, geographical location of study participant, occupation

Dependent variables

Stage of presentation

3.8 Data Management and Statistical analysis

Stata Version 16 was used for data analysis. Means and standard deviations described the characteristics of study participants for continuous variables, while proportions were used for categorical variables. The Chi-square test of independence assessed associations for categorical variables, and the Student's T-test was applied to continuous variables. The data were presented in frequency tables, pie charts, and bar charts.

3.9 Bias/Limitations

Missing information – unrecorded data may have impacted the findings of the study. However, multiple sources and meticulous retrieval of information was carried out to minimize the missing information bias.

3.10 Ethical considerations

The study was carried out following written approval from both the University of Nairobi and the KNH Scientific and Ethical Review Committee. As this was a retrospective study utilizing patient records, no consent was needed from the participants. Personal details of the participants were anonymized using unique identifiers specific to the study. This coded data was entered into a password-protected Excel sheet, and backup copies were stored on a password-encrypted external hard drive accessible only to the principal investigator.

CHAPTER FOUR

4.0 RESULTS

4.1 Background

The purpose of this study was to identify the socio-demographic and clinical factors influencing the stage at which prostate cancer presents in patients at Kenyatta National Hospital. The study specifically aimed to: i) examine the socio-demographic factors associated with the presentation of prostate cancer in these patients, ii) investigate the clinical factors at the time of presentation, and iii) determine the stages at which prostate cancer is presented. A total of seventy-eight patients were selected based on their file records.

4.2 Objective 1: Demographic characteristics in patients with prostate cancer

4.2.1 Age distribution

The average age was 69.3 years, Standard Deviation 9.9, Median 69, Range (29 - 90) (Figure 2).

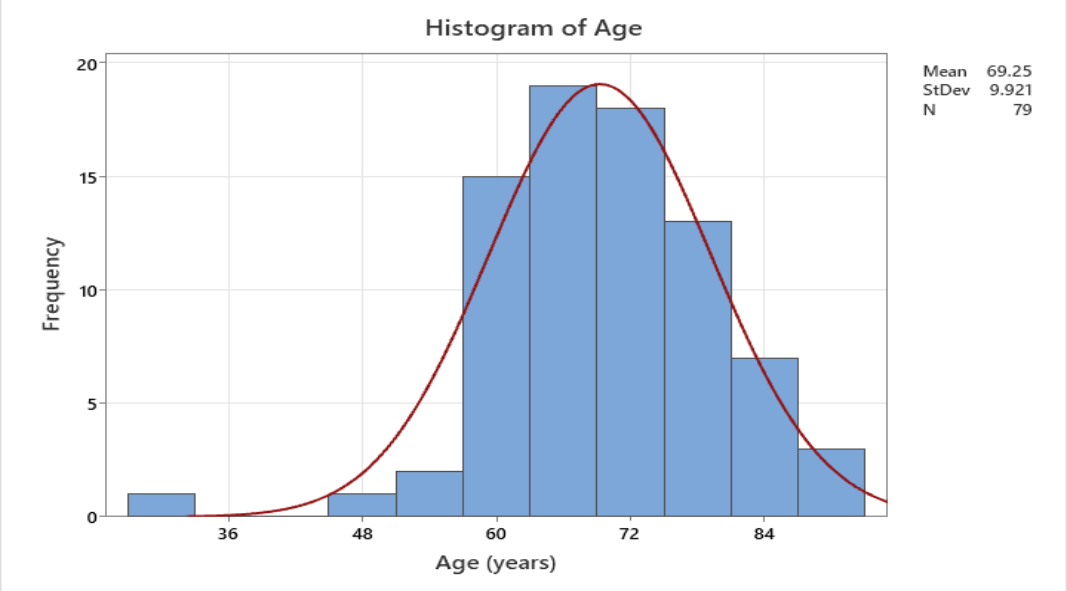

Figure 2: Age distribution

4.2.2 Occupation

Majority of the patients, 84%(n=67) had informal occupations while minority of them, 16%(n=13) had formal occupations (Figure 3).

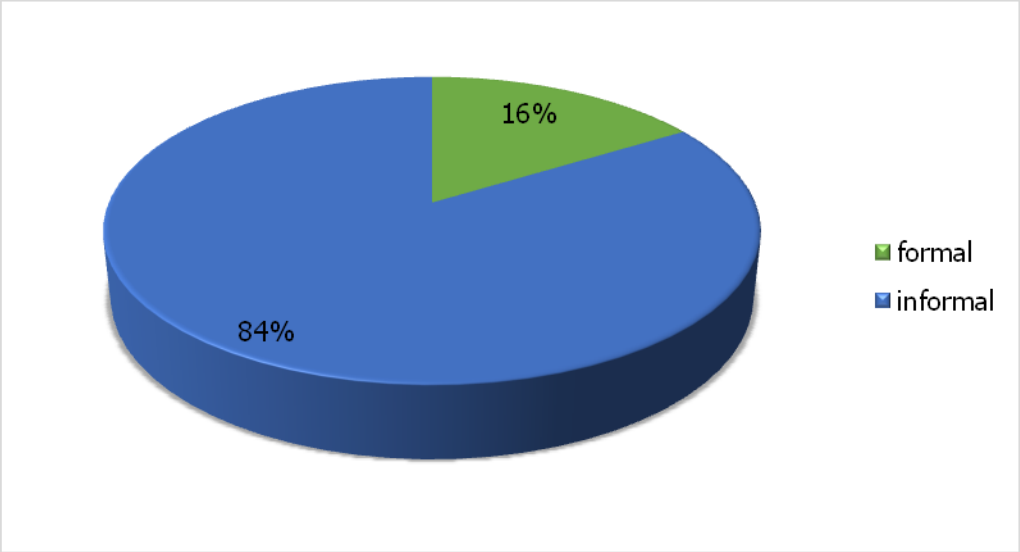

Figure 3: Occupation

4.2.3 Ethnicity

Table 1: Distribution of Ethnicity in prostate cancer patients

Ethnicity	Frequency (%)	Ethnicity	Frequency (%)
Kikuyu	30 (38.5)	Kisii	2 (2.6)
Kamba	12 (15.4)	Kamba	2 (2.6)
Meru	5 (6.4)	Ameru	1 (1.3)
Embu	4 (5.1)	Arab	1 (1.3)
Luo	4 (5.4)	Borana	1 (1.3)
Maasai	4 (5.4)	Kalenjin	1 (1.3)
Luhya	3 (3.8)	Mijikenda	1 (1.3)
Somali	3 (3.8)	Swahili	1 (1.3)
Giriama	2 (2.6)	Teso	1 (1.3)

4.3 Objective 2: Clinical characteristics in prostate cancer

4.3.1 Symptoms at presentation

Lower Urinary Tract symptoms were the most common at presentation in over two-thirds of the patients (Table 2).

Table 2: Symptoms at presentation

Symptoms		Frequency	Percentage
LUTS (weak stream, incontinence, straining, hesitancy, frequency, urgency, nocturia))	Present	54	67.5%
Back pain	Present	52	65.0%
Bone pain	Present	21	26.3%
AUR	Present	11	13.8%
Hematuria	Present	10	12.5%
Others	Present	23	28.7%
Total No. of patients		78	100%

Among the 54 patients with LUTs, 28 (51.9%) had mild (0 -7), 17 (31.5%) had moderate (8 - 19) and 9 (16.7%) had severe (20-35) LUTs (Figure 4).

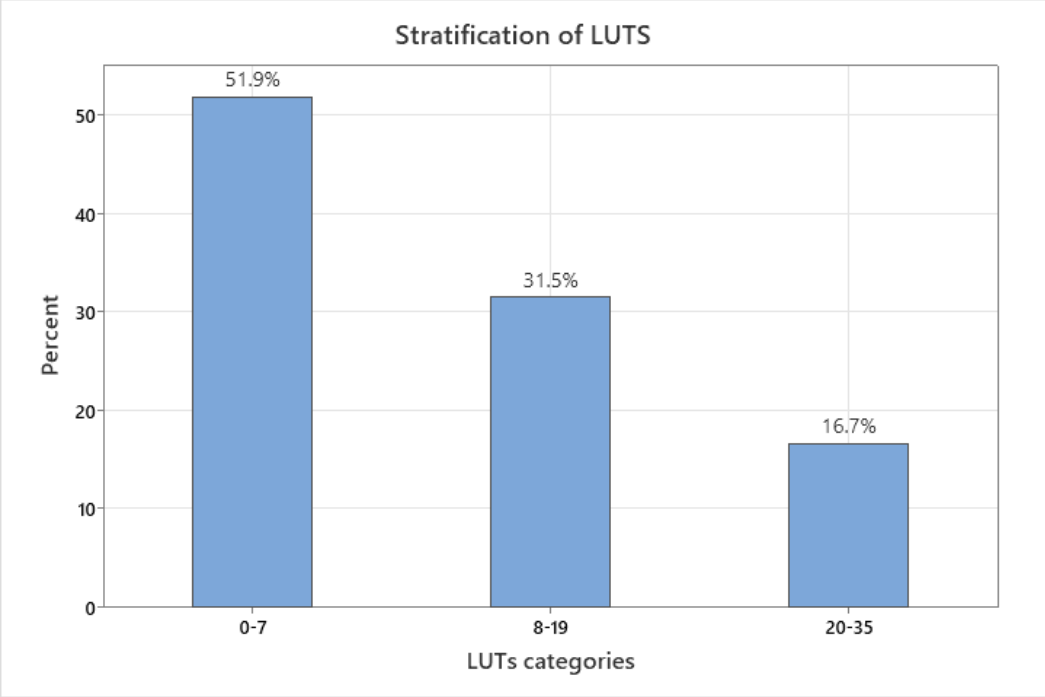

Figure 4: Stratification of LUTS

4.3.2 Family history of prostate cancer

Over two thirds of the patients (71% n=55) did not have any history of prostate cancer, 17%(n=13) had a history of prostate cancer and 12% (n=9 was not recorded (Figure 5).

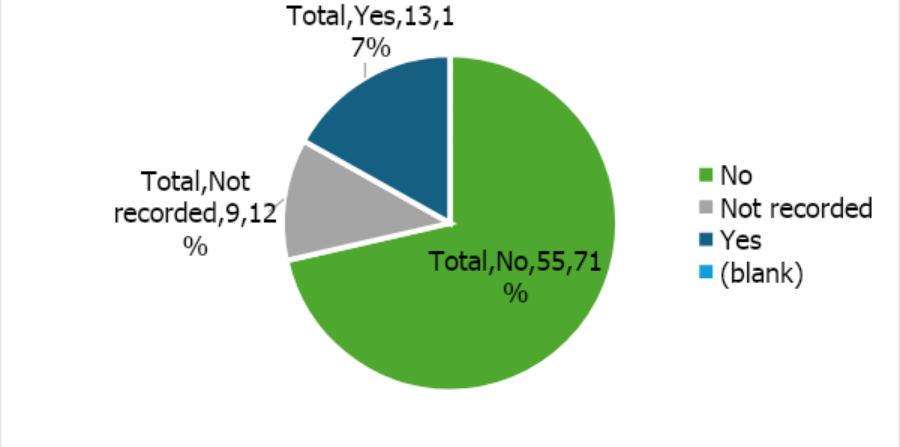

Figure 5: Family history of prostate cancer

Among the patients, only 23%(n=3) had a history emanating from a first degree relative whilst 77% (n=10) was from other relatives (Figure 6).

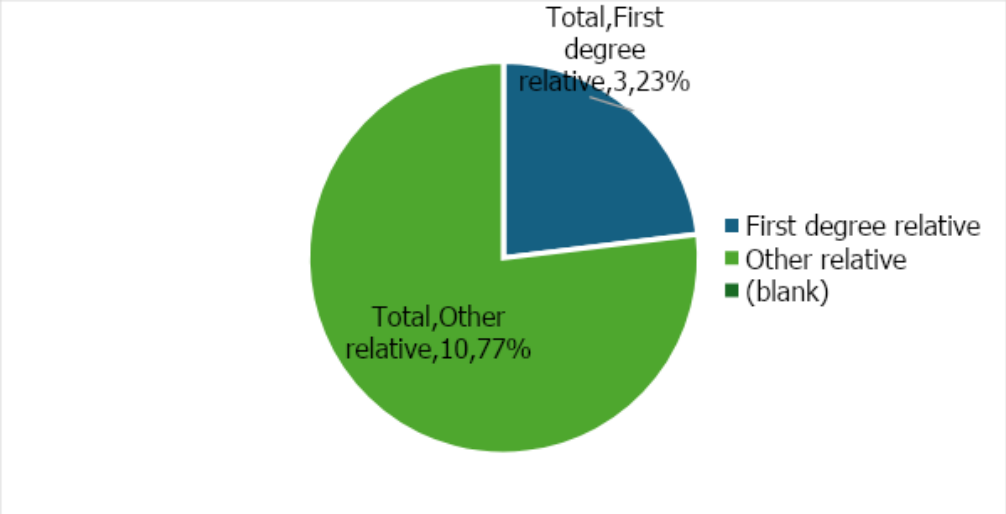

Figure 6: Showing degree of relationship.

4.3.3 PSA Levels at presentation

The mean PSA level at presentation 406.6, SD 639.4, Median 200, Range (0.025 - 3257) (Figure 7).

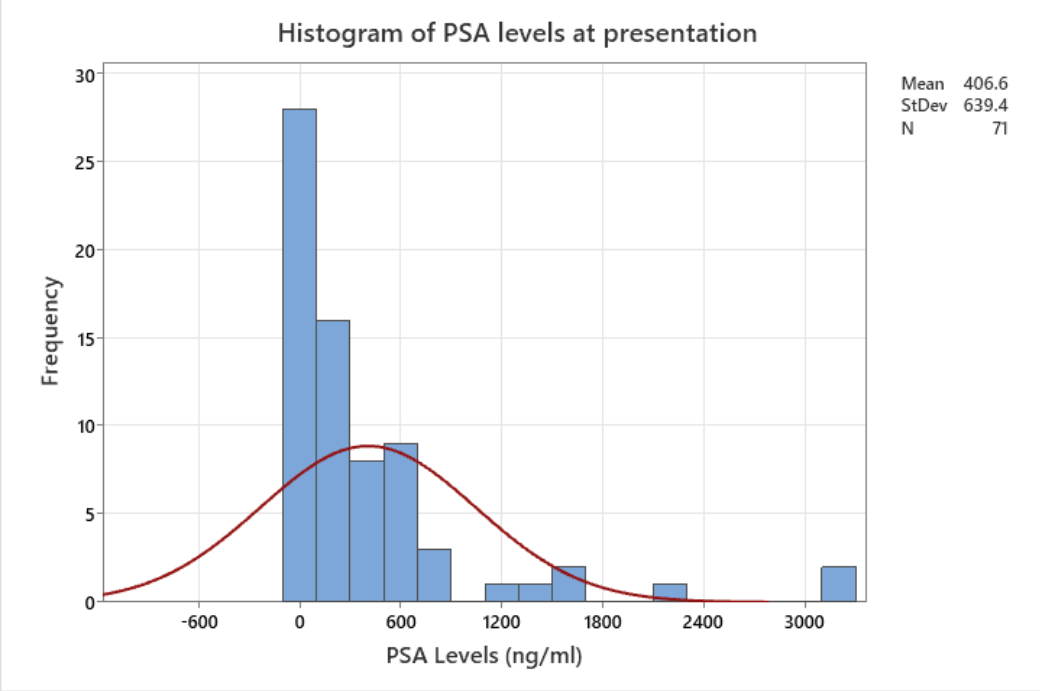

Figure 7: Histogram of PSA levels at presentation

In terms of PSA categories, majority 41 (56.9%) had PSA of over 100 ng/ml, 15 (20.8%) patients had PSA of 50 – 100 ng/ml, 4 (5.6%) patients had PSA of 20 – 50 ng/ml while 12 (16.7%) had PSA of less than 20 ng/ml.

4.3.4 Gleason grading

Advanced lesions of Gleason score were evidently more common (Table 3)

Table 3: Gleason grading in prostate cancer

ISUP Grading	Gleason Score	Frequency	Percent
1	3+3	0	0
2	3+4	17	21.3%
3	4+3	1	1.3%
4	4+4	23	28.8%
5	4+5	23	28.8%
	5+4	6	7.5%
	5+5	3	3.8%
Not indicated		7	8.8%
	Total	80	100.0

4.4 Objective 3: Stage of presentation of Prostate cancer

Advanced and metastatic prostate cancer is the most common stage of presentation (Table 4).

Table 4: Stage of presentation in prostate cancer

Risk stratification		Frequency	Percentage (%)
Risk group pathological features	Very low	3	3.8%
	Low	6	7.5%
	Favorable intermediate	3	3.8%
	Unfavorable intermediate	3	3.8%

	high	65	81.3%
Very low(n=3)	PSA <10 ng/mL	2	75%
	Fewer than three prostate biopsy fragments or cores tested positive, with cancer present in 50% or less of each fragment or core.	1	25%
Low(n=6)	PSA <10 ng/mL	6	100%
Favorable intermediate (n=3)	PSA 10 - 20 ng/mL	3	100%
Unfavorable intermediate (n=3	PSA 10-20 ng/mL	2	75%
	≥50% of positive biopsy cores	1	25%
High (n=65)	PSA >20 ng/mL	48	73.85%
	Very high	4	6.15%
	T3b to T4	3	4.6%
	Two or three high-risk features	3	4.6%
	Grade group 4 or 5	2	3.1%
	Primary Gleason pattern 5	1	1.54%

Staging	**M stage**	**44**	**55%**
	N stage	25	31.3%
	T stage	9	11.3%
	Not indicated	2	2.5%
T-staging	T0 (0 primary tumor)	2	22.2%
	T1 (Not detectable)	2	22.2%
	T3 (Present outside prostate)	2	22.2%
	T3a (Present outside of prostate capsule)	1	11.1%
	T3b (Evidence of spread to seminal vesicles)	1	11.1%
	T4 (Has spread to local structures)	1	11.1%
N-staging	N0 (0 evidence of spread to nodes)	22	88%
	N1 (Has spread to the pelvic nodes)	2	8%
	Not indicated	1	4%
M-staging	M0 (No evidence of spread outside the pelvis)	14	31.8%
	M1a (Spread to distant lymph nodes e.g., para-aortic)	3	6.8%
	M1b (Spread to bone)	21	47.7%
	M1c (Visceral spread +/- e.g. liver, lungs)	3	6.8%
	Not indicated	3	6.8%

4.5 Association between stage of presentation and demographic and clinical factors.

The Student's T-test, Chi-square test of independence, and Fisher's exact test were utilized to evaluate the factors associated with the stage of presentation. The findings are indicated in Table 5.

Table 5: Determinants of stage of presentation

Variable / Categories	Stage of presentation			P value
	Localized	Locally Advanced	Advanced	
Age (N = 78)				
Mean	69	68.8	70	0.882
SD	4	8.5	12.8	
Occupation				
Formal	0 (0)	8 (61.5)	5 (38.5)	0.898
Informal	5 (7.5)	39 (58.2)	23 (34.3)	
Family History				
Yes	1 (7.7)	7 (53.9)	5 (38.5)	0.836
No	4 (7.3)	32 (58.2)	19 (34.6)	
Unknown	0 (0)	6 (66.7)	3 (3.3)	
PSA categories				
0-20	2 (16.7)	7 (58.3)	3 (25)	0.706
20-50	0 (0)	2 (50)	2 (50)	
50-100	0 (0)	9 (60)	6 (40)	
>100	2 (4.9)	23 (56.9)	16 (39)	

Thus, there were no factors that were significantly associated with stage of presentation. This could be due to a low sample size of our study.

CHAPTER FIVE

5.0 DISCUSSION

5.1 Demographic characteristics.

In this study, the average age of patients with prostate cancer was 69.3 years. In comparison, the National Institutes of Health (NIH) in the USA reports that the average age at diagnosis is 66 years[56]. The mean age at diagnosis of prostate cancer across Africa has been listed. In Benin it is 69.5 years, Cote d'Ivoire 68 years, Ethiopia 67.7, Eldoret and Nairobi Kenya 74.2 and 67.4 respectively, Namibia 66.5 years, Mauritius 71.5 years, Seychelles 70.8, South Africa 72, Kampala Uganda 69.5, Harare, Zimbabwe 71.4 among blacks and 73.1 among whites [57].

Prostate cancer prevalence varies across different ethnical and racial groups. In the United States, the highest incidence has been noted among African-American groups at 157.6/100,000 compared to Whites 93.9, Natives and Asian-Pacific Islanders 52.4. Among American Indians / Alaska the incidence is 46.9 years [58]. According to the findings of this study, The Kikuyu ethnic group in Kenya had the highest prevalence at 38.5% followed by Kamba at 15.4%. This could be due to the fact that the two ethnic groups come from the central and eastern provinces of Kenya which are in close proximity to Nairobi county where KNH is located. Several factors have been postulated to contribute to the racial and ethnical differences in prostate cancer epidemiology. These include social-economic factors which determine accessibility to quality healthcare hence screening programs, biological factors and genetical factors. African-Americans in the USA have been found to have more chromosomal variations at 8q24 which increase the risk of prostate cancer [58].

5.2 Clinical factors

The most common symptoms at presentation in this study were Lower Urinary Tract Symptoms (LUTS) which occurred in 67.5% of the study participants. Others included back pains in 65% and bone pains in 26.3%. In a study by Hamilton et al., 2006, urine retention occurred in 3.1%, impotence 3.0%, LUTs in 1 – 3% [59]. Over 60% of patients with advanced prostate cancer eventually have invasion to the bone. Thus bone pain is a common occurrence in prostate cancer [60]. According to Zhuo et al., 2019 investigating bone invasion prevalence in prostate cancer among 1672 men noted that 44.1% of patients will have bone metastasis at presentation yet of these 27% of patients will also have bone pains [61]. Hematuria has been observed in 36.4% of men with prostate cancer according to findings from a study investigating prevalence of prostate cancer in patients with hematuria [62]. According to this study, 12.5% had hematuria.

In prostate cancer, the family history has been associated with up to 68% increased chance of developing the condition and 72% increased risk of developing lethal disease [63]. In this study, only 17% of men reported family history of prostate cancer. Younger men (<60 years) are more likely to have a familial form of prostate cancer. A registry based study in Southern Australia involving 9459 men demonstrated that a family history of prostate cancer was associated with an increased likelihood of having elevated PSA by 68% compared to 52% in those without a positive family history. Further, positive family history resulted in lower Gleason score levels (<7) in 50% compared to 39% in those without a positive family history.

Majority of patients in this study had elevated PSA as signified by a mean of 406. Notable, the uptake for screening of prostate cancer in this region is very low which

could contribute to higher levels of PSA at presentation. Out of 5716 men with prostate cancer in Australia, elevations in PSA >100 were noted in 241 (4.2%) of patients [64]. On the contrary, our study indicates that 61.1% of patients present with PSA levels greater than 100 ng/ml, PSA levels of 20 – 99.9 occurred in 22.2% of patients, 10 – 20 in 2.8% of patients and <10 ng/ml in 13.9% of the patients.

According to the Gleason scoring / ISUP groups, majority of patients in our study present with higher ISUP groups of 4 & 5. The overall survival in prostate cancer has been strongly associated with the ISUP groups as well as the PSA levels at presentation and age of presentation [64].

5.3 Stage of presentation

Notable from previous studies, the presentation of prostate cancer in this environment is usually at advanced stages and unlikely to be amenable to curative therapies. Magoha et al., 2007, [6], noted that 85.7% of patients presented with advanced late disease. However, in this study, 61.1% of patients presented with metastatic disease. Patients presenting with T stage >3, were 55.5%, thus, minimal improvements in stage of presentation are noted over a 15 year period. A study in the United States involving data from registry and comprising of 54,212 males found with prostate cancer in the 1990's indicated that 83.3% of patients had Stage I or II lesions. This emphasizes that environmental and regional differences could impact the health seeking behavior.

5.4 Conclusion and Limitation

Prostate cancer is common in older men with a mean age of presentation of 69 years. Demographic patterns indicate that ethnicity and occupation could influence the presentation. Most patients continue to present with advanced disease with time despite

tangible improvements in demographic factors in Kenya. However, the findings of this study could have been limited by a smaller sample size and the retrospective nature of the study.

5.5 Recommendations

Owing to the findings of this study, creating public awareness on prostate cancer, the need for screening is advocated for. This would aid in reduce late stage presentation. Further, conducting trainings among healthcare workers on the need to accurately diagnose and manage early prostate cancer is paramount to reducing the late stage presentation.

The role of education is an important determinant in the advanced stage at prostate cancer presentation. Furthermore, population based studies may help assess the health seeking behaviour among older men in Kenya as well as accessibility to quality healthcare in regard to diagnosis and treatment of prostate cancer. Thus further studies are recommended to elaborate on the reasons for late stage presentation.

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LIST OF APPENDICES

APPENDIX 1: DATA COLLECTION TOOL.

Form number _____

PATIENT BIODATA.

1. IP No. _____
2. Age: _____
3. Stage of presentation by T stage: ……
4. Stage of presentation by M stage:
5. Stage of presentation by N stage:
6. Stage of presentation by AJCC staging: I / II / III / IV
7. Gleason grade group:
8. LUTs at presentation (circle)
    i. Frequency
    ii. Urgency
    iii. Nocturia
    iv. Weak stream
    v. Intermittency
    vi. Straining
    vii. Incomplete emptying
    viii. Dribbling
    ix. Hesitancy
9. Obstructive uropathy (circle)
    i. Acute urine retention
    ii. Hydronephrosis
10. Duration of symptoms in months ……
11. Method of discovery of prostate cancer: Screening / Symptoms presentation
12. PSA levels at presentation: …….. ng/ml
13. Geographical residence: …… county
14. Occupation: ……