THE PREVALENCE AND ASSOCIATION OF METABOLIC SYNDROME WITH BENIGN PROSTATIC ENLARGEMENT AMONG MEN TREATED AT KENYATTA NATIONAL HOSPITAL

THE UNIVERSITY OF NAIROBI

This Dissertation is presented as Part of Fulfillment for the Award of the Degree of Masters of Medicine in Urology at the University of Nairobi

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H58/87231/2016

DECLARATION

I declare that this dissertation is my original work and has not been presented for the award of any degree at any other institution or university.

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LIST OF ABBREVIATIONS

BPE	Benign prostatic enlargement
BPH	Benign prostatic hyperplasia
KNH	Kenyatta National Hospital
LUTS	Lower urinary tract symptoms
MetS	Metabolic syndrome

OPERATIONAL DEFINITIONS

Benign Prostate Enlargement (BPE)-is defined as a non-malignant increase in size of the prostate gland due to hyperplasia of prostatic stromal and epithelial cells in the transitional zone.

Benign Prostate Hyperplasia (BPH) - term reserved for the histological pattern seen as increase in number of prostatic stromal and epithelial cells in the transitional zone.

Lower urinary tract symptoms (LUTS) can be classified as voiding or obstructive symptoms such as hesitancy, poor and/or intermittent stream, straining, prolonged micturition, feeling of incomplete bladder emptying and dribbling while storage or irritative symptoms are frequency, urgency, urge incontinence, and nocturia.

Metabolic syndrome (MetS) is a cluster of metabolic abnormalities, including central obesity, dyslipidemia, hypertension, insulin resistance with compensatory hyperinsulinemia, and glucose intolerance

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ABSTRACT

Background: Metabolic syndrome, a conglomeration of metabolic derangements associated with central adiposity and insulin resistance, is thought to result in development of Benign Prostate Enlargement (BPE). We sought to establish the prevalence of metabolic syndrome in BPE and its association with BPE in order to elaborate on the cause of BPE among African populations.

Methodology: Using a cross sectional study design, 97 men seeking treatment for BPE at a Kenyan hospital were recruited through consecutive sampling approach. Exposure variables included age, lower urinary tract symptoms (LUTS), PSA levels and prostate ultrasound findings. The international prostate symptoms score (IPSS) provided a standard assessment of the severity of LUTS associated with BPE and were categorized into moderate and severe. The outcome, occurrence of metabolic syndrome, was diagnosed using any three of the following features: - waist circumference, blood pressure reading, fasting blood sugar and lipid profile above the normal laboratory ranges. Chi square test was used for hypothesis testing.

Results: The mean age of study participants was 69.5 years. Proportion of patients with moderate LUTS was 22.7% compared to severe in 77.3%. Mean PSA level was 5.44ng/ml with 38.1% of men having elevated PSA. Mean prostate size was 74.3gms. Mean fasting blood sugar was 8.21mmols/l. Mean waist circumference was 39.1 inches with high waist circumference occurring in 36.1% of participants. The mean of HDL was 57mg/dl with 30.9% having low HDL. The mean triglyceride level was 104.7mg/dl with elevated levels found in 7.2%. Hypertension was prevalent in 50.5%. The prevalence of metabolic syndrome was 33% (CI 24 - 42). Men with severe LUTs had high odds of having metabolic syndrome (OR 4 (CI 1 – 22.6), p value=.038) compared to those with moderate LUTS.

Conclusion: The prevalence of metabolic syndrome among African populations is increasing. From our findings, there is a correlation of metabolic Syndrome and BPE. With paucity of data on association between metabolic syndrome and BPE in the African continent, this study provides a new insight which will greatly help to improve management protocols of care in patients with BPE.

CHAPTER ONE: INTRODUCTION

1.0 Background

Non-communicable diseases (NCD) in recent times have emerged to be the main cause of mortality and morbidity in both underdeveloped and developed countries. Among these, Mets has had the highest global scourge NCD (1).

The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) in 2002 defined Mets as the occurrence of three or more of the following five criteria:

- Waist circumference above 40 inches in male or 35 inches in women
- Blood pressure measurement above 130/85 mmHg
- Fasting triglyceride (TG) level above 150 mg/dl
- Fasting high-density lipoprotein (HDL) level of cholesterol below 50 mg/dl in women
  Or 40 mg/dl in men
- Fasting blood sugar above 5.5mmol/l.

Each component carries the same magnitude, and none is compulsory for a diagnosis of MetS to be made (2).

BPH is a histologic diagnosis that refers to glandular epithelial tissue, connective tissue, and smooth muscle proliferation in the prostatic transitional zone, thus the name "stromo-glandular hyperplasia." BPH is probably the outcome of a multipronged process, of which precise etiology is unknown. Nonetheless, it is certain that male androgenic steroid hormones testosterone and dihydrotestosterone (DHT) assume at least a permissive role as pre-pubertal hormone deprivation prohibits BPH development (3).

BPH in ageing men is ubiquitous with global autopsy proven histological prevalence increases beginning at 40-45 years of age attaining 60% at 60 years and 80% at 80 years. The Olmsted County Study done in USA had outcomes indicating progressive rise in moderate-to-severe LUTS incidence secondary to BPE, to almost 50% by the 8th life decade (3)

Treating BPH in itself is unnecessary therefore it fails to be a target for therapeutic intervention. BPH does, however, in many men lead to an enlargement of the prostate called benign prostatic enlargement (BPE) which inadvertently leads to LUTS. Parallel to these functional and anatomical processes, LUTS increase in frequency and severity with age.

An enlarged prostate has been proposed to contribute to the male LUTS complex via at least two routes:

1. The static component due to direct BOO/BPO from enlarged tissue.
2. The dynamic component from increased smooth muscle tone and resistance within the enlarged gland.

LUTS in men is commonly associated with and/or caused by BPE, therefore a compromise terminology is often used referring to "LUTS most likely associated with BPE/BPO and BPH" or "LUTS secondary to BPE" (3).

Albeit not a life-threatening condition, the impact of LUTS/BPE on QoL can be significant and should not be underestimated accentuating the need to further understand this intrinsic relationship (3).

Mounting evidence suggests that Mets is related to BPE. Globally metabolic syndrome has been associated with BPE in 26.5% - 55.6% of the cases. A study by Dibello et al, 2016 found a 26.5% prevalence of Metabolic syndrome in men with BPH (4).

Another study by Kupellian V et al, 2009, assessing association of LUTS with metabolic syndrome in a community in Boston, found that the prevalence of metabolic syndrome was increased by up to 40% in patients with mild LUTS. Severity of LUTS associated with BPE was not correlated with increasing incidence of metabolic syndrome (5).

Numerous cohort and case control studies have assessed the risk factors for surgical treatment of BPE as a way to establish compounding BPE risk factors. These studies have assessed conventional risk factors such as alcohol intake, age, tobacco smoking and race. Given that components of MetS are modifiable risk factors and can be improved with diet and exercise, it suggests that development of BPE can be avoided or slowed down via metabolic pathways modification. As non –communicable diseases such as obesity, hypertension and diabetes reach epidemic proportions globally, understanding the potential causal relationship of Mets with BPE could produce significant improvements for the health of men (5).

CHAPTER TWO: LITERATURE REVIEW

2.1 BPH, BPE and LUTS

Benign prostatic hyperplasia (BPH) is a common disease in ageing men leading to lower urinary tract symptoms (LUTS) secondary to clinical benign prostatic enlargement. The relation between clinical BPH and LUTS is complex, because not all men with BPH develop LUTS and not all men with LUTS have BPH. To date the etiology of BPH is largely unknown and much interest has been focused on the aberrations of steroid hormones –testosterone and estrogen (3).

Histopathologically, an increase in epithelial–stromal cells number in the peri-urethral transitional zone of the prostate is characteristic of BPH. This may be due to impaired apoptosis or epithelial stromal proliferation leading to cellular accumulation. Hormones such as androgens, estrogens, growth factors and neurotransmitters may play a role either singly or in combination (3)

BPE is a progressive condition that, if left untreated, can result in far-reaching long-term complications, such as acute urinary retention, recurrent urinary tract infections, obstructive nephropathy and surgeries impacting a patient's quality of life negatively (6).

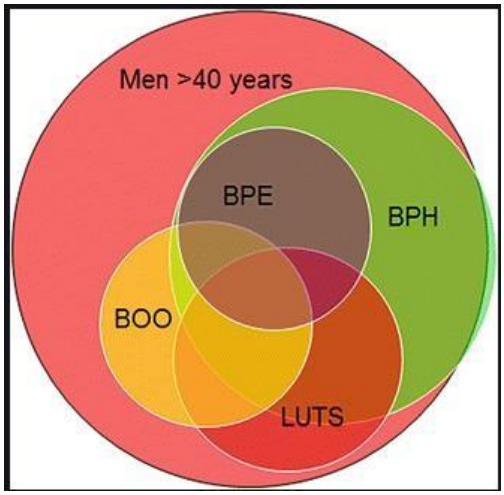


Figure 1: Relationship between BPH, BPE and LUTS

The prevalence of BPE markedly rises with increase in age. Autopsy studies have observed a prevalence of 8% in the 40 year olds, 50% in 60 year olds, and 80% in the 90 year olds(6).

With a changing demographic profile in almost all societies, it is inevitable that this disorder wascome even more prevalent and a major challenge for all health care systems in the future. An increasing body of evidence points to an association between clinical

BPE and metabolic syndrome, or individual components of the syndrome. The presence of metabolic syndrome correlates with the severity of LUTS associated with BPE, the rate of prostatic growth and seems to be a predictor of the clinical progression of BPE. The number of individual components of metabolic syndrome an individual has is also positively associated with risk of BPE, the more they are the higher one's chances of developing BPE are (7).

Undoubtedly, the constellation of cellular pathologies that give rise to the symptoms of LUTS is far more intricate than we realize and only by unraveling these complexities will we be able to design alternative strategies to prevent the adverse impact of BPE on lower urinary tract function and successfully treat it (8).

2.2 Metabolic Syndrome

Metabolic syndrome is a complex disorder defined by a constellation of closely related cardiovascular risk factors whose cause remains obscure.

These factors increase the risk of diabetes mellitus type II and atherosclerotic diseases. Currently, different definitions of MetS exist, causing substantial confusion as to whether they represent a surrogate of risk factors or one compounded disease. Besides the growing worldwide interest in the numerous clinical implications of MetS, there is still no universally accepted pathogenic mechanism or clearly defined diagnostic criteria. The first description of patients with clustering of various metabolic derangements was in early as 1923 but it was in 1988, more than five decades later, that Reaven coined the term 'syndrome X' for this entity (9). Several expert groups in the last two decades have brought forth a number of evolving definitions and criteria to identify this condition.

In 1998 the WHO, proposed that MetS may be defined by the presence of insulin resistance (IR) or its surrogates, impaired glucose tolerance (IGT) or DMT2, as essential components of the syndrome, along with at least two of the following parameters: raised BP, hypertriglyceridemia and/or low HDL-cholesterol, obesity (as measured by waist/hip ratio or body mass index (BMI)), and microalbuminuria.

Within the same year, the European Group for the Study of Insulin Resistance (EGIR) excluded microalbuminuria as an integral component of the syndrome, while it required hyperinsulinemia to be present (10).

The US National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP III) devised the newer definition on MetS in 2005 which was used in this study. Men having any three or more of the five components -central obesity,

hypertriglyceridaemia, reduced high density lipoprotein cholesterol (HDL-C), raised blood pressure and raised fasting plasma glucose was regarded as having MetS.

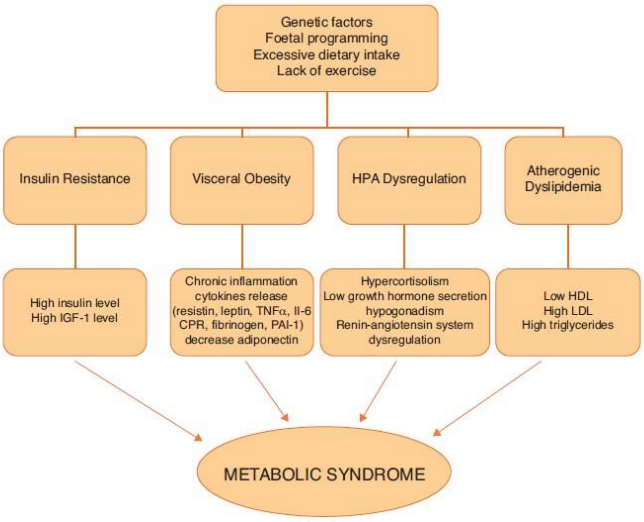
Each component carries equal importance, and no mandatory component has to be present for establishing the diagnosis of MetS(2).

In 2005 the American Heart Association and the National Heart Lung and Blood Institute updated this definition, with major modification in reducing the threshold for impaired fasting glucose (IFG).

In the same year the International Diabetes Federation (IDF) developed a new set of practical worldwide criteria introducing abdominal obesity as a prerequisite of the diagnosis of MetS to better define its nature as well as for epidemiological and clinical uses. This definition took into consideration the ethnic differences in waist circumference and reduction of the hyperglycemic threshold (10, 11).

2.3 Pathophysiology of Metabolic Syndrome

Figure 2: Pathophysiology



2.4 Etiology of BPH

To date the etiology of BPH is largely unknown and much attention has been drawn on the aberrations of steroid hormones –testosterone and estrogen.

Histopathologically, an increase in number of stromal-epithelial cells in the transitional zone of the prostate is classic characteristic of BPH. This can be as a result of failed apoptosis or proliferation of stromal epithelium leading to accumulation of cells (6).

Estrogen, androgens and growth hormone can contribute substantially either in combination or singly. Indisputably, the cellular pathologies resulting in BPE is much more complicated than it is conceptualized at the moment and devising alternative means for successful treatment can be realized exclusively through extrication of such complexities. This will avert the adverse effects of BPH on renal function (12).

2.5 Pathophysiology of BPE and MetS

2.5.1 Three-hit mechanism

Vignozzi et al. suggested a 3-hit hypothesis in the pathogenesis of BPH (12). The first hit is prostatic cellular inflammation, bolstered by metabolic variations (second hit) and compounded by sex steroid abnormalities (third hit). The collective actions of 2 or 3 hits can cause overexpression of Toll-like receptors, transformation of prostatic cells into antigen-presenting cells, activation of resident human prostate-related lymphoid tissue and excessive production of growth factors, leading to prostatic remodeling (12).

2.5.1.1 First hit- Prostatic inflammation

MetS is associated with chronic small grade inflammation, raised inflammatory markers levels like CRP and pro-inflammatory cytokines like tumor necrosis factor α (TNF-α), interleukin (IL)-8, IL-6, and IL-1p. T-cell activity causes trans-differentiation of resident stromal and epithelial cells leading to proliferation continued by an autoimmune mechanism (13).

Tissue impairment and the following chronic process of wound healing brought about by chronic inflammation can cause BPH micronodule development.

2.5.1.2 Second hit –Metabolic alterations

Insulin resistance

Insulin is a recognized mitogen and growth factor for prostatic epithelial cells (14). Either exogenous or endogenous hyperinsulinemia in the background of insulin resistance helps phosphorylation and farnesyltransferase activation, an abundant enzyme that farnesylates Ras protein. The high accessibility of farnesylated Ras at the plasma membrane increases mitogenic receptiveness of cells to several factors of growth, hence substantially playing a role in the progression of atherosclerosis and cancer. This effect is specific to insulin. Hyperinsulinaemia either directly or indirectly increase

transcription of genes taking part in sex hormone metabolism through obesity and its changed hormone metabolism. The reduced dihydrotestosterone (DHT) levels in the zone of transition of the prostate helps in smooth muscle hyperplasia. It is as well related to low sex hormone-binding globulin, hence elevates the estrogen amount and androgen getting into prostatic cells, thus elevating the risks of BPH (14).

The Insulin-like Growth Factors (IGF) are peptide hormones that have an essential role in essential cellular processes including migration, differentiation and proliferation. The IGF axis entails two receptors (type I IGFR-IR and IGF-II/M6P-R), two ligands (IGFI and IGFII), and six binding proteins (numbered IGFBP-1 to -6), the six-binding protein modulate IGF bioavailability (14).

IGF-1 increases prostate epithelial growth as evidenced in two epidemiological studies. Insulin receptors have homology with IGF receptor that can bind to IGF receptor and activate the IGF signaling pathway to help in the growth of prostatic. Additionally, insulin reduces with IGF binding protein 1 (IGFBP-1) and thus elevates IGF-1 bioavailability (15).

Hyperglycaemia activates the sympathetic nervous system by increasing unbound calcium in smooth muscle cells and neural tissues, resulting in elevated prostrate smooth muscle tone prostate ultimately worsening LUTS secondary to BPE. Additionally, hyperinsulinemia can impose a trophic influence on growth of prostate cell through plasma tissue catecholamines elevation.

2.5.2 Increased visceral adiposity

Of great interest is the association between BPE , obesity, body mass index (BMI) and the metabolic syndrome . Aromatization of testosterone to estrogen mainly occurs in adipose tissue and all men with low BMIs have high levels of serum testosterone. Higher estradiol production hinders gonadotropin production and the secretion of testosterone. This hypogonadal obesity cycle progressively leads to a higher estrogen to androgen ratio, leading to hypogonadal state.

In addition, bioactive substances named adipocytokines induces insulin resistance and associated proinflammatory and proatherogenic effects (15).

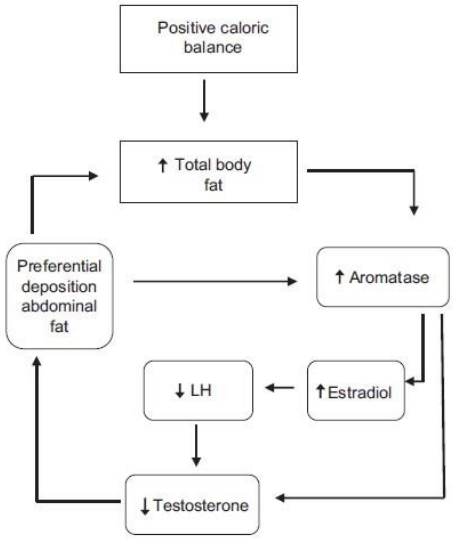


Figure 3: The hypogonadol obesity cycle

2.5.3 Dyslipidaemia

Large prospective studies have shown that dyslipidemia is a primary, widely established independent and modifiable major risk factor for cardiovascular disease and successfully controlling lipid levels can decrease the risks of ischemic cardiovascular disease.

Nandeesha et al (11)reported that in patients with symptomatic BPE, the level of HDL-C was lower, whereas level of low density lipoprotein cholesterol (LDL-C) and total cholesterol were higher as compared to those in controls. Therefore, closely monitoring and controlling high risk factors of dyslipidemia is noteable in slowing down progression to clinically significant BPE.

2.5.4 Hypertension

The sympathetic nervous system carries out an important role through alpha adrenergic fibers and receptors in both the etiology of hypertension and the BPE symptoms. Hammerstein assessed 250 patients with LUTS secondary to BPE and found non-insulin dependent diabetes mellitus (NIDDM), hypertension, height, obesity, high insulin, and low HDL levels of cholesterol as risk factors for BPE development. A link was observed between the development of BPE, hyperinsulinemia and increased sympathetic nerve activity in males (12). However, because both LUTS/BPE and hypertension increase with increasing age, it is difficult to prove a causal relationship existing in the two states and additional studies are required for proper understanding of the common underlying pathophysiologic mechanisms and a potential cause-and-effect relationship.

In the EpiLUTS survey that was established by epidemiologists and clinicians, both heart disease and hypertension and heart disease were related to severe LUTS/BPE symptom constellation. (13)

2.6 Epidemiological associations between BPE and Metabolic Syndrome.

Metabolic syndrome has been estimated to occur in 26.7% - 55.4% of men with LUTS in several studies conducted in Asian populations (5).

The results of the Third National Health and Nutrition Examination Survey (NHANES III) examining 2372 men aged above 60 years showed that a history of diabetes and hypertension were positively associated with occurrence of LUTS. Glycated hemoglobin increases were associated with increasing odds of occurrence of LUTS. Increasing odds of occurrence of LUTS were predicted by having three or more metabolic syndrome components (14).

A study by DiBello et al, 2016, in the Boston Community, UK showed that metabolic syndrome was associated with BPE. As many as 26.5% of men with BPE had metabolic syndrome compared to 20.9% of men without BPE (p value <0.001). This study further showed that the more the components of metabolic syndrome, the greater the odds of having BPH (4)

2.7 Research gaps on Metabolic syndrome and BPE in African populations.

The prevalence of metabolic syndrome among African populations is increasing according to various studies conducted (15–19). Limitations in availability of data on metabolic syndrome and BPE in the African continent are rife and have thus resulted to lack of information on the occurrence and associations in these conditions. Establishing these associations would help to improve management protocols of care in patients with BPE.

2.8 Problem Statement

Many patients miss out on getting comprehensive healthcare services by solely focusing on their urological symptoms yet they have non communicable diseases such as dyslipidemia, hypertension, obesity and diabetes which have been hypothesized to result to BPE.

Inadequate knowledge on the association of metabolic syndrome with BPE hinders optimal care of patients with BPE. Preliminary studies have suggested an association between the two. However, the evidence remains inconclusive.

It would be necessary to address the cardio-metabolic derangements that exist which would further improve the overall quality of life of such patients.

The Kenyatta National Hospital is a world class patient centered specialized healthcare facility, and the Urology surgical outpatient clinic can act as a catchment area to filter out patients requiring medical attention referring them to the medical outpatient care. This kind of holistic management will improve men's health by identifying modifiable risk factors.

2.9 Conceptual framework for the study

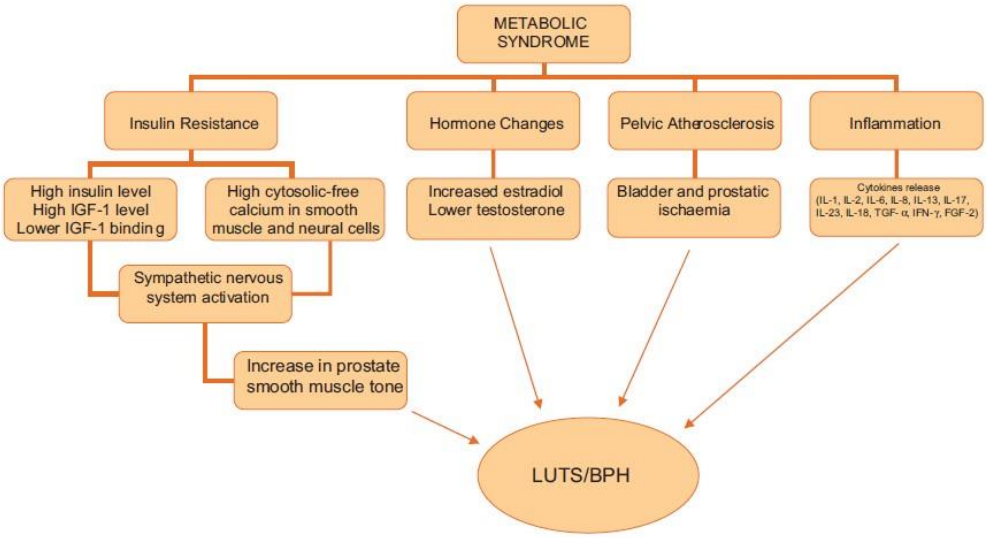
2.9.1 Narrative

Recent data has drawn focus to a relationship between BPE and the incidence of MetS with potential pathophysiologic links suggested to elucidate the relationship between the two. Incidence of MetS is noted to increase with age which is also a risk factor for BPE. Other related pathophysiological factors include being overweight, hypertension, dyslipidemia and impaired glucose metabolism with insulin resistance as the main hypothesized underlying pathogenic mechanism.

Reduced physical activity and inappropriate diet causes insulin resistance leading to increased plasma insulin levels. This in turn increases growth hormone receptors density in the liver and IGF-1 production.

2.9.2 Figurative Presentation of the Conceptual Framework

Figure 4: Conceptual framework



2.10 Study Justification

This study generates a hypothesis of the relationship between metabolic syndrome and BPE development. In the clinical setting, the outcomes suppose that, in any patient having BPE, the likely presence of hypertension, NIDDM, obesity, low levels of HDL cholesterol and high insulin need to be taken to consideration. Equally, in patients presenting with such conditions, the likelihood of a clinical BPE needs to be considered. Significant number of men older than 50yrs have lower urinary tract symptoms and these significantly contributes to a diminished quality of life. Metabolic syndrome has been hypothesized to be associated with occurrence of BPE with as many as one third of men with BPE having metabolic syndrome. However, inadequate knowledge about the causal association has led to failure to make informed decision on whether to advise men with BPE on the need to undertake lifestyle modifications that would result to improved quality of life due to improvement in urinary function. Limited data in the African set up has resulted in lack of understanding on the influence of metabolic syndrome on the occurrence of LUTS. This would hinder optimal patient care. Therefore, establishing a causal association between BPE and metabolic syndrome is necessary in developing prevention strategies for BPE thus reducing morbidity among affected groups of men.

2.11 Research Question

1. What is the prevalence of metabolic syndrome in patients with clinical benign prostatic enlargement seen at the Kenyatta National Hospital?

2. Is there an association between metabolic syndrome and clinical benign prostate enlargement?

2.12 Null hypothesis

There is no relationship between MetS and clinical BPE among patients treated at the Kenyatta National Hospital?

2.13 Study Objectives

2.13.1 Broad Objectives

To establish the prevalence of metabolic syndrome in benign prostatic enlargement and define its association with severity of LUTS amongst men seen at the Kenyatta National Hospital.

2.13.2 Specific Objectives

Among adult male patients seeking treatment for clinical benign prostatic enlargement at the Kenyatta National Hospital:

1. To determine the proportion of patients with metabolic syndrome in patients with BPE on treatment at Kenyatta National Hospital.
2. To determine the proportion of individual components of metabolic syndrome in patients with benign prostate enlargement.
3. To establish the association between the severity of LUTS associated with BPE and metabolic syndrome

CHAPTER THREE: METHODOLOGY

3.1 Study Design

This study was cross-sectional in design. The study design was suitable for the objectives as the exposure and outcome variables were measured at the same time, hence establishing the prevalence of metabolic syndrome between patients with benign prostatic enlargement.

3.2 Study Site

The study was carried out at the urology clinics within the Kenyatta National Hospital. The hospital offers comprehensive specialty services including surgical departments for urology. In addition, it has a private wing for both inpatient and outpatient services (the Doctors Plaza). The study was carried out at KNH surgical outpatient urology clinics where three clinics are run weekly by three different teams on Monday afternoon, Tuesday morning and Wednesday afternoon. On average, 400 patients with different urological conditions are reviewed and approximately 200 are BPE cases. The clinic is operated by the Consultants from both KNH and university of Nairobi (UoN) and the senior house officers from the UoN.

Follow up of patients entails running diagnostic tests (both laboratory and imaging). Routine laboratory tests include PSA levels, full hemogram, UECs while routine imaging tests include performing kidney, ureter, bladder and prostate (KUB-P) ultrasound and TRU Cut biopsy. Lipid profile and fasting blood sugar costs were covered by the principle investigator.

3.3 Study Population

The study recruited patients seeking treatment for BPE at the Kenyatta National Hospital Urology Clinics located in Clinic 24 of the main hospital. KNH being a national referral hospital and offering specialized urology services as well as reviews of patients from across the country are handled in the facility. On average 400 patients are reviewed at the urology outpatient clinic annually.

3.4 Sample Size Determination

Sample size calculation for the records to be reviewed was done using the formula of proportions for finite population as follows:

$$\text{Finite population: } n' = \frac{n}{1+\frac{z^2 \times \hat{p}(1-\hat{p})}{\varepsilon^2 N}}$$

The assumptions for this study was derived from a similar study by Cosimo De Nunzio titled 'The Correlation Between Metabolic Syndrome and Prostatic Diseases' in Morocco (3) where 16.3% of patients with benign prostatic enlargement had metabolic syndrome as follows:

- n= size of the sample

- Z= difference in statistical level = 1.96

- P = prevalence of metabolic syndrome among patients with benign prostatic enlargement (16.3%)
- E = desired precision, taken as 0.05

Substituting this in the formula gives a sample size of **97** as shown below:

$$n = n / 1 + \frac{1.96^2 \text{ x } 0.163 (1-0.163)}{0.05 \text{ x } 0.05 * N}$$

$$= \mathbf{97}$$

3.5 Selection of Study Participants/ Sampling Procedure

3.5.1 Selection of Study Participants

3.5.1.1 Inclusion Criteria

Patients presenting with LUTS secondary to BPE and

1. IPSS of 8 and above (moderate to severe)
2. An enlarged prostate greater than 30cc
3. PSA less than 10ng/ml.

3.5.1.2 Exclusion Criteria

1. Patients who declined to take part in the study

2. Patients with suspected cancer of the prostate from DRE findings and PSA levels.

3. Patients who presented to the clinic with severe acute urine retention

3.5.2 Sampling Procedure

Systematic sampling of patients with BPE was conducted where patients meeting the inclusion criteria during the study period were recruited into the study.

On average, 5 patients with BPE are reviewed in the general outpatient urology clinic 24 daily. Therefore, for the 3 months during which the study was conducted (5 patients*3 clinic days in a week *12 weeks) an average of 180 patients were expected to be reviewed during the study period. Taking the sampling frame for the 3 months, divided by the sample size of 97 to give 1.9. Rounding this up gave 2. Thus in order to achieve the desired sample size therefore, every 2^{nd} or alternate clinic visitor with BPE was recruited.

To select the first participant, a simple random sampling method was used where a coin was tossed between the first and the second visitor. From there every 2^{nd} person was recruited. In case of a patient failing to meet the inclusion criteria, the next eligible study participant was recruited.

3.6 Consenting and Study Enrollment

Upon meeting the inclusion criteria and accepting to participate in the study following health talks by the study participants and research assistants all potential study participants were escorted to a private room within the clinics for consenting and administration of the structured interview form. This was done immediately after the patient had completed their routine clinic visit.

3.7 Study Flow

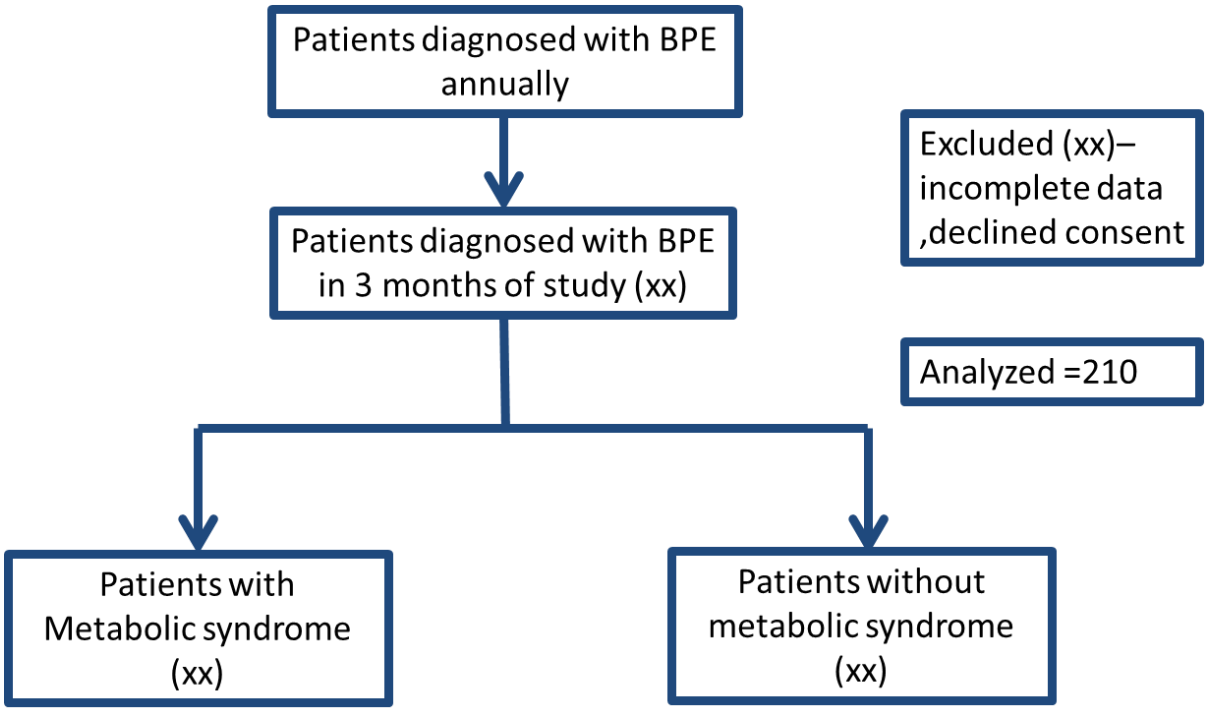


Figure 5: Study Flow showing the process of enrolment, data collection and analysis

3.8 Data variables

Table 1: Data Variables

Variable	Definition
Benign Prostatic Enlargement (Prostatic Volume, IPSS)	Independent Variable
Metabolic Syndrome	Depended Variable
Age	Independent Variable

3.9 Data Collection and Management

3.9.1 Data collection procedure

Upon successful enrolment a questionnaire was administered to the study participants by the interviewer. Clinical information including age, disease stage, procedures and tests done was collected and collaborated from the medical records. The principle investigator and the research assistants worked closely with the data management teams

at the hospital and abode by the laid down standard operating procedures for data handling and security. The files were retrieved from the filing area, and using a private room, separate from the patient flow, the information extracted before returning them to the records department.

Data from the participants was collected after clinical review to avoid interruption of services. The collected data was identified by assigning study specific unique identifiers to the study participants. In case of missing records, permission was sought from the study participants to seek clarification. All electronic data was stored in an external hard drive and password protected after encryption. The collected data was verified by the principle investigator on a daily basis before uploading it to the excel sheet for cleaning and coding. All data sets were secured by a password, only known and accessible by the principle investigator and the data manager. The participants were then asked to have an early morning fasting blood sample taken at the KNH laboratory.

3.9.2 Materials used

For the study to be carried out, a calibrated blood pressure machine, tape measure for waist circumference was needed. These were both routinely available at the urology clinics.

3.9.3 Training Procedures

The study team members (2 research assistants, data manager) underwent training on how to conduct the study, including data collection and processing. The research assistants, consultants, senior house officers and nurses in the urology clinics were also oriented about the study in a CME held at the department

3.9.4 Data Quality Assurance

The questionnaires were pre- tested, analyzed and reviewed by the supervisors and independently by 3 colleagues before a final draft was administered to the study participants. The research assistants were trained on appropriate interview techniques and filling the questionnaire. Clinical findings were input after thorough scrutiny. Unique identifiers were given to all the participants in the study. Where double entries are observed, one of the questionnaires was withdrawn, cast-off and the serialization rectified. Filled information on the questionnaire was checked for any errors and corrected on a daily basis.

3.10 Data Analysis

The analysis of data was done using the SPSS software version 26. Descriptive statistics were run using means, modes, medians and proportions, to describe clinical and demographic characteristics of the study participants including age, IPSS score distribution.

For hypothesis testing, Chi square test of independence and Fisher's exact test were used to assess the associations between occurrence of metabolic syndrome and severity of LUTS associated with BPE. A P value of less than 0.05 was considered statistically significant.

Data was presented using frequency tables, pie charts, bar graphs and written reports.

Metabolic syndrome was defined as having any three of the following symptoms, elevated fasting blood sugar of greater than 5.5 mmols/l, abnormal waist circumference of greater than 40 inches, low High density lipoprotein outside the normal laboratory reference range, or elevated high triglyceride level outside the normal laboratory reference range.

3.11 Ethical Considerations

Permission was sought from the KNH/UON Ethics Research Committee (ERC) to carry out this study as part of the UON thesis dissertation. Permission was also sought from the management of KNH. Posters explaining the study procedure were placed at strategic places in the clinics and information leaflets about the relationship between BPE and MetS shared with the patients. A continuous medical education (CME) session about the study was held the urology clinic to enlighten the health care providers.

All the study participants were subjected to an-opt out consenting procedure, and only enrolled upon voluntarily signing the consent form.

How BPE was established.

- ✓ Pertinent history documented in the file
- ✓ Clinical examination by digital rectal examination
- ✓ Baseline laboratory investigations which patient seen at the urology clinic routinely have: PSA

- ✓ A kidney, ureter, bladder and prostate ultrasound which determined prostate size. This augmented DRE findings.

The diagnosis of Metabolic syndrome was done using the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) 2002 by the presence of any three or more of the five criteria below:

- ✓ Blood pressure above 130/85 mmHg (done at triage using the clinic's calibrated digital BP machine)
- ✓ Waist circumference above 40 inches for men (taken using the tape measure available at the urology clinic)
- ✓ Fasting triglyceride (TG) level above 150 mg/dl (KNH laboratory)
- ✓ Fasting high-density lipoprotein (HDL) cholesterol below 40 mg/dl (KNH laboratory)
- ✓ Fasting blood sugar above 5.5mmol/l. (KNH laboratory)

The procedure for establishing central obesity, hypertension and other parameters were followed and explained to the study participants by the Principal Investigator or research assistant.

The participant's personal details were de-identified by use of assigned unique identifiers, only applicable to the study. This coded information was uploaded to the excel sheet and password protected. Backed up data was kept in a password encrypted external hard drive, only known to the PI. Once the results were established, they were communicated to the clinical team managing the patients for communication to the participants and referral to a physician and or diabetologist for follow up. The patient incurred the costs of treatment routinely done for patients with BPE when seen at the urology clinics which included and is not limited to PSA, KUB-P ultrasound, UEC, FHG and urinalysis. Cost of lipid profile and FBS were covered by the principle investigator.

3.12 Study Results Dissemination Plan

The results of this study are to be presented at professional meetings. The presentations are in the form of either poster or oral (platform) presentations. This will be organized at both the UON and KNH surgical departments.

A copy of the dissertation will be made available at the University of Nairobi library and the KNH research and programs department.

The principle investigator aims to be published in a peer reviewed journals and in annual urology conferences worldwide.

3.13 Study Limitations and How to Minimize Them

Confounding factors like age which influenced both metabolic syndrome and benign prostate enlargement were controlled for during multivariable data analysis

Financial implications of doing a FBS and lipid profile (ksh.2100) were borne by the principle investigator. However, funding from KNH was applied for to ease this as the study has policy implications.

3.14 Study Closure Plan and Procedure

The study was conducted in three phases: phase one entailed recruitment and data collection.

The researcher and research assistants made a diagnosis of BPE by virtue of symptomatology as deduced from the clinical history, DRE, PSA and kidney ureter bladder-prostate US. The inclusion criteria included: IPSS greater than 7, enlarged prostate >30cc, PSA less than <10ng/ml. Patient with abnormal DRE findings and elevated PSA levels suggestive of prostate cancer were investigated further with a multi-parametric MRI of the prostate and histology of prostate biopsy tissue.

The diagnosis of Metabolic syndrome was done using the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) 2002 by the presence of any three or more of the five criteria below:

- Blood pressure above 130/85 mmHg
- Waist circumference above 40 inches or 35 inches for men and women respectively,
- Fasting triglyceride (TG) level above 150 mg/dl,
- Fasting high-density lipoprotein (HDL) cholesterol below 40 mg/dl or 50 mg/dl for men and women respectively,
- Fasting blood sugar above 5.5mmol/l.

Each component carries the same significance, and no component is compulsorily present for the diagnosis of MetS.

The laboratory tests and imaging studies was done at the KNH labs and radiology department.

Phase two was data analysis and presentation to the department of surgery, UON for review.

The third phase was giving feedback to relevant stakeholders and the recommendations was incorporated in the final report prior to publishing.

3.15 Study Timelines

Table 2: Study timelines

	Aug 2020	Sep 2020	Oct 2020	Nov 2020	Dec 2020	Jan 2021	Feb 2021	Mar 2021	Apr 2021	May 2021	Jun 2021
Proposal development											
Ethics consideration											
Data collection											
Data analysis											
Dissertation submission											

STUDY BUDGET

Table 3: Study budget

ITEM	COST (KShs)	Budget justification
Research Fees	2,000	Statutory fees paid
Laboratory tests	203,700	For running samples for 97 patients
Stationery	1,000	For data collection
Statistician	40,000	To analyze data
Printing and Binding	10,000	For submission to university
Contingencies (10% total)	36,170	
TOTAL	**282,370**	

Budget Justification

The itemized budget is done accordance to the current market rates.

1. Submission of a single paper for Ethical review at UON-KNH ERC costs Ksh. 2000
2. Laboratory test for HDL, and Triglycerides costs Ksh. 2058 per lipid profile test.
3. Printing study materials will cost 10 shillings, hence 97 forms * ksh 10 = Ksh. 1000
4. Payment of a statistician to advise on data analysis will cost Ksh. 40,000 as per the market rates.
5. Printing and binding of manuscripts for submission to the university will cost Ksh. 1000 per manuscript amount to Ksh. 10000 for ten manuscripts.
6. A contingency fee of 10% has been added to cater for unforeseen costs amounting to Ksh. 36,170.

CHAPTER FOUR

4.0 Results

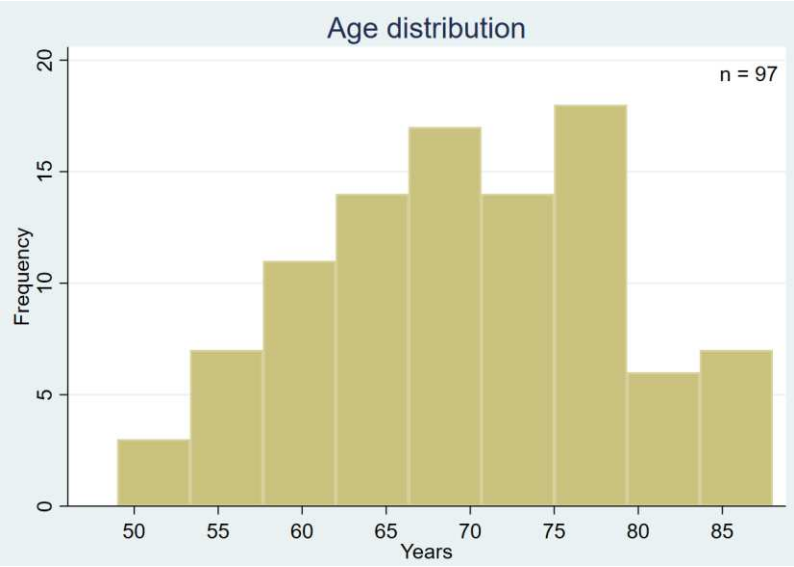
There were one hundred and seven patients who were sampled, six patients failed to meet the inclusion criteria with 4 patients having missing data. Therefore, data was analysed for 97 patients.

4.1 Clinical characteristics of men presenting with BPH

4.1.1 Age

The mean age of study participants was 69.5 years, SD 9.06, Median 70, Range 49 – 88 (Figure 6)

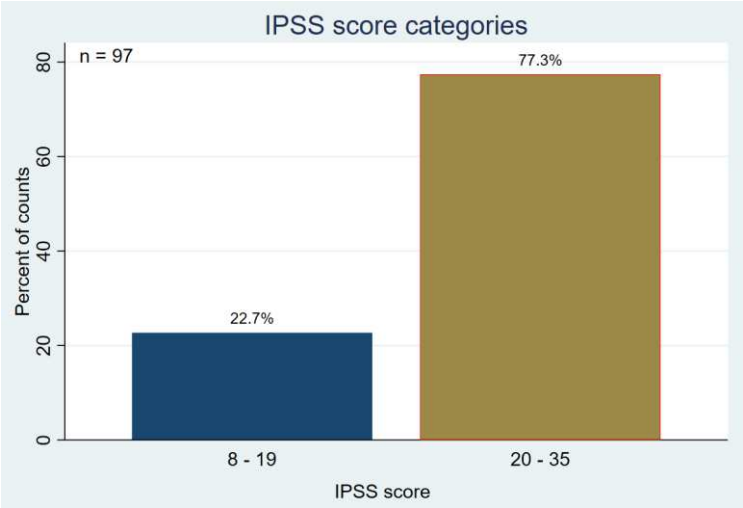
Figure 6: Showing histogram of Age distribution of men with BPH



4.1.2 IPSS score

There were two categories of IPSS in this study, from 8 – 19 which was represented 22 (22.7%) participants while 20 – 35 category was represented by 75 (77.3%) participants (Figure 7).

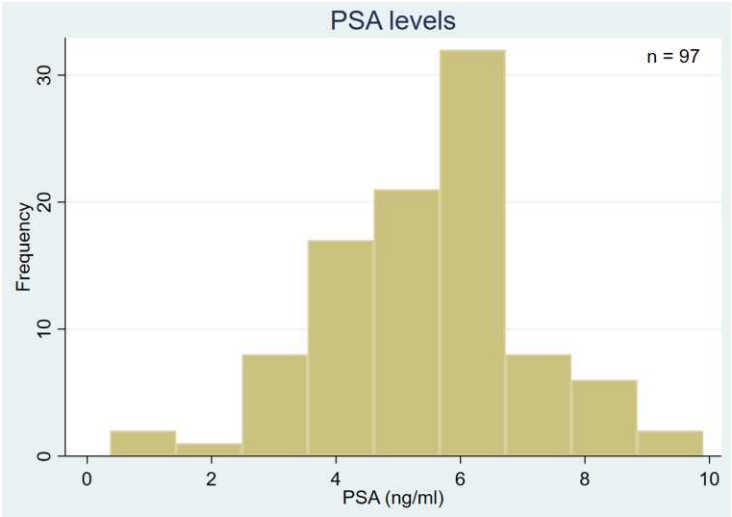
Figure 7: Categories of IPSS score



4.1.3 PSA levels

Mean PSA level was 5.44, SD 1.62, Range 0.37 – 9.9, Median 5.5 (Figure 8)

Figure 8: Histogram of PSA levels



4.1.3.1 Age specific PSA levels

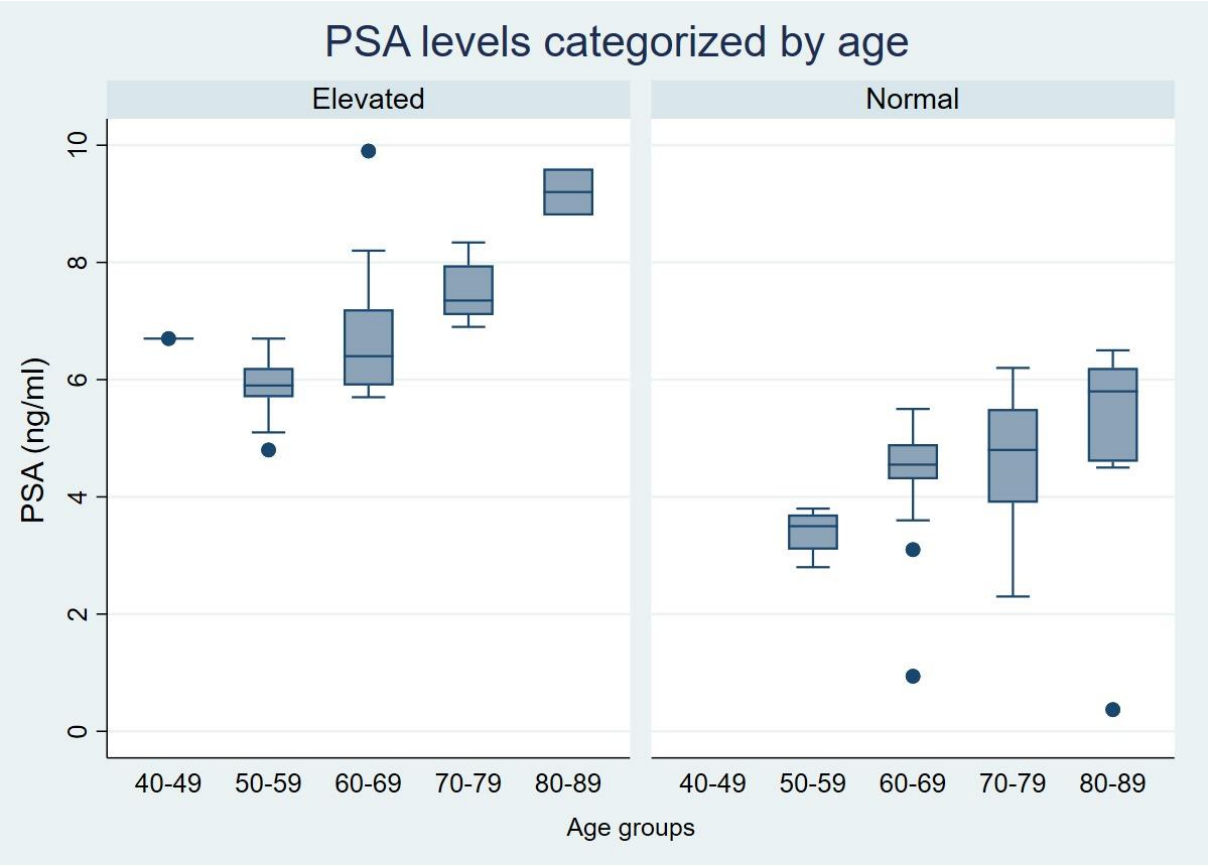
Overall, 37 (38.1%) of men had elevated PSA whereas 60 (61.9%) men had normal PSA levels. Ages specific differences in elevation of PSA are shown in Table 3 and Figure 9

Table 3: PSA levels based on Age category

Age category	PSA levels		Total
	Normal	Elevated	
40 – 49	0	1 (100)	1
50 – 59	4 (28.6)	10 (71.4)	14
60 – 69	16 (50)	16 (50)	32
70 - max	40 (80)	10 (20)	50
Total	60	37	97

Normal was defined as 0 – 2.4 in 40 – 49 years, 0 – 4.2 in 50 – 59 years, 0 – 5.5 in 60 – 69 years, 0 – 6.6 in 70 – 79 years as adopted from Morgan et al, 1996, DeAntoni et al, 1998

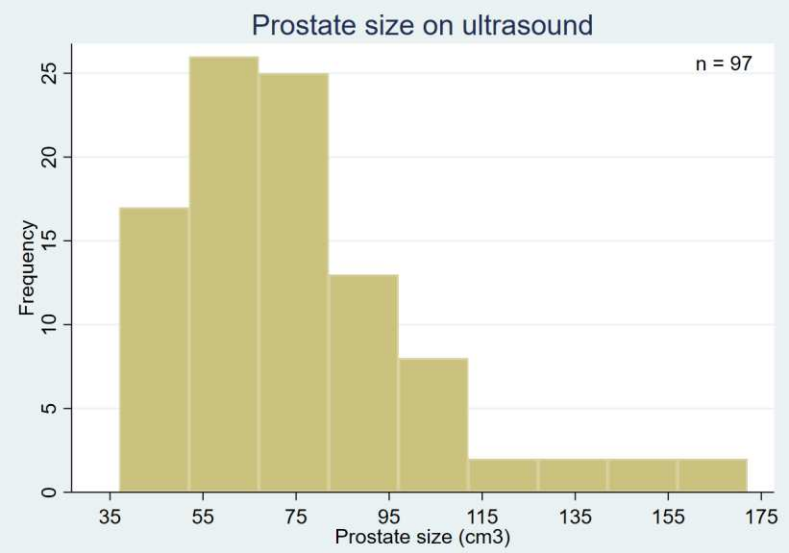
Figure 9: Age specific PSA grouped by levels



4.1.4 Prostate size on Ultrasound

Mean prostate size was 74.3gms, SD 27.6, Median 69, Range 37 – 172 (Figure 10)

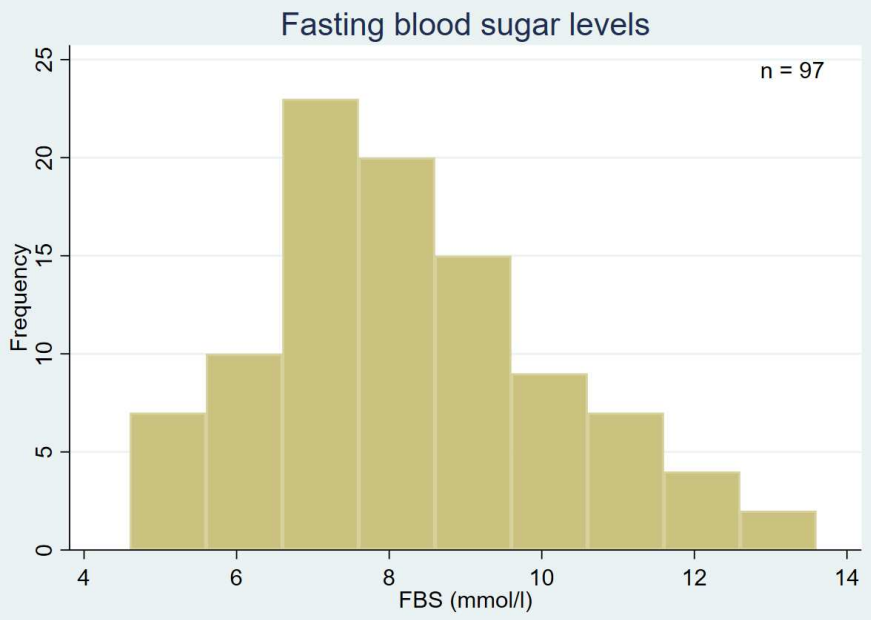
Figure 10: Histogram on Prostate size



4.1.5 Fasting blood sugar

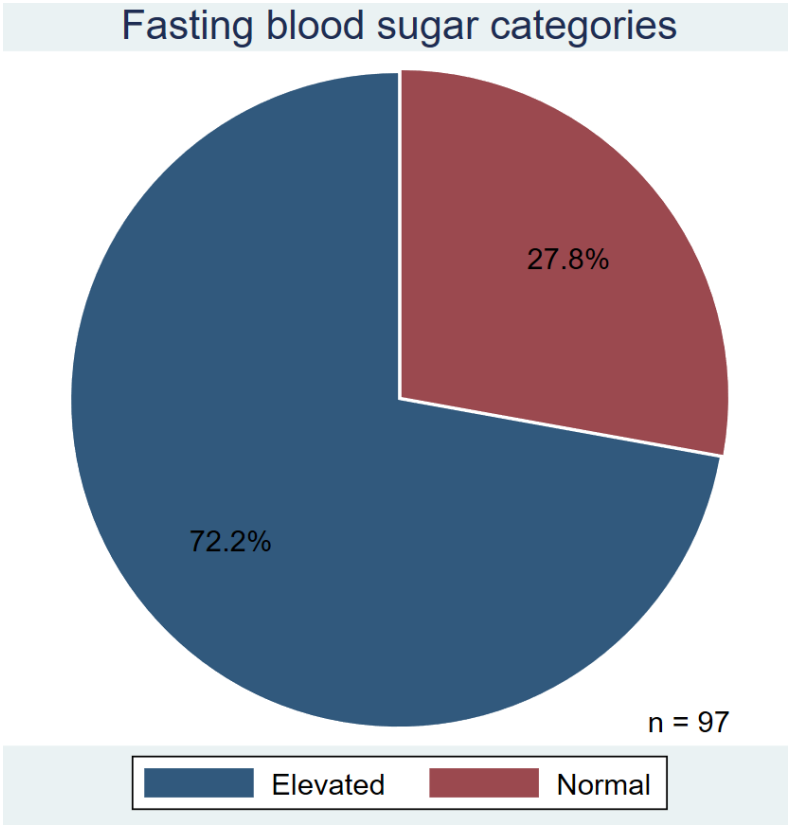
Mean fasting blood sugar was 8.21 mmols/l, SD 1.91, Median 7.9, Range 4.6 – 13.6 (Figure 11)

Figure 11: Histogram of fasting blood sugar



Amongst all the patients, high FBS >7mmols/l occurred in 70 (72.2%) of participants compared to 27 (27.8%) of participants who had normal FBS. Comparatively, 37 (38.1%) of patients reported to be diabetic. Thus as many as 34.1% patients were not on treatment for diabetes despite having high FBS (Figure 12).

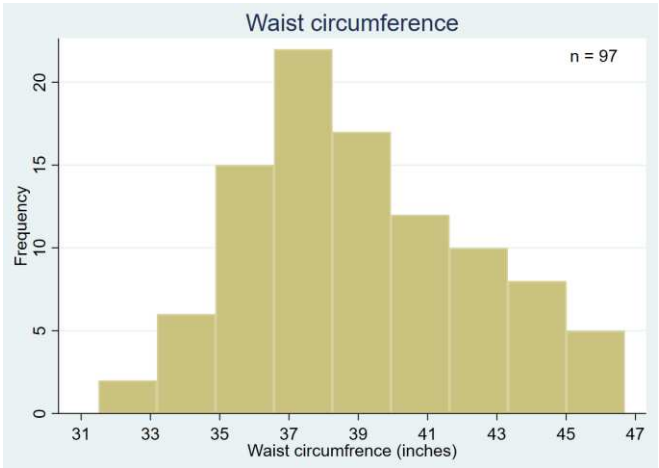
Figure 12: Categories of fasting blood sugar among BPH patients



4.1.6 Waist circumference

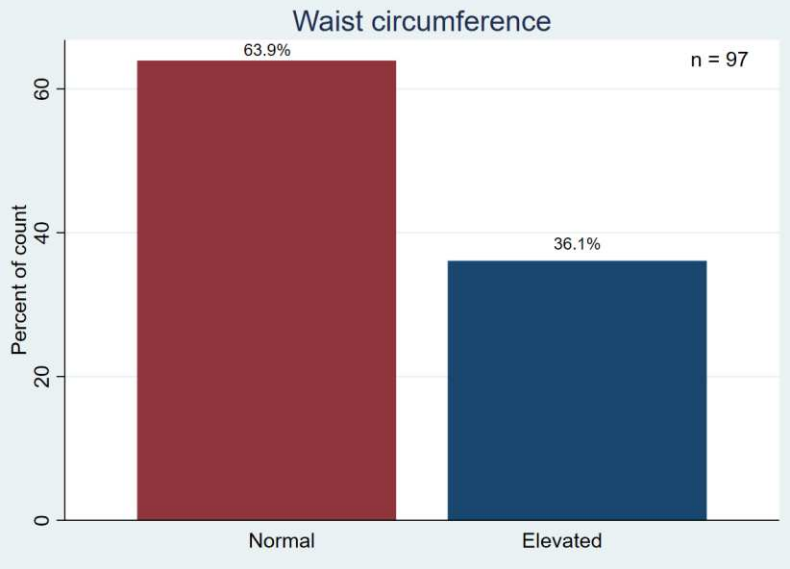
Out of 97 study participants, the mean waist circumference was 39.1 inches, SD 3.32, Median 38.4, Range 31.5 – 46.7 (Figure 13).

Figure 13: Histogram of waist circumference



Amongst all patients with BPE, high waist circumference exceeding the normal occurred in 35 (36.1%) participants compared to 62 (63.9%) who had normal waist circumference (Figure 14).

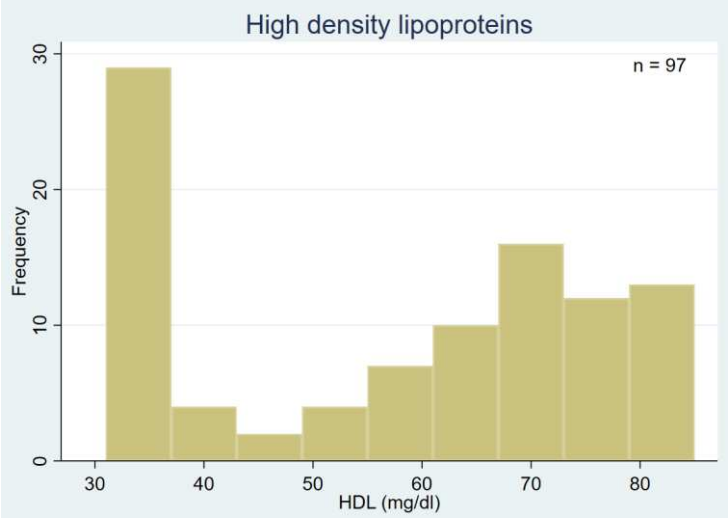
Figure 14: Pie chart showing distribution of waist circumference



4.1.7 High density lipoproteins

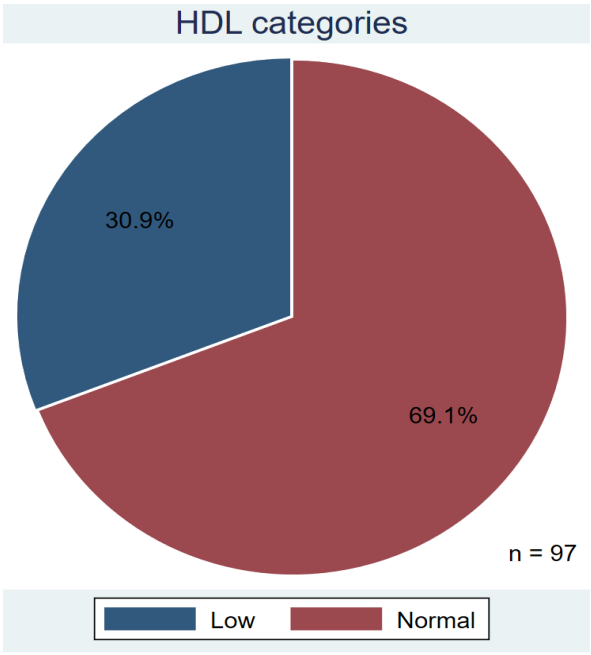
The mean of HDL was 57.1, SD 18.4, Range 31 – 85, Median 61 (Figure 15).

Figure 15: Distribution of HDL cholesterol



Amongst the study subjects, 30 (30.9%) had low hdl, while 67 (69.1%) had normal hdl (Figure 16).

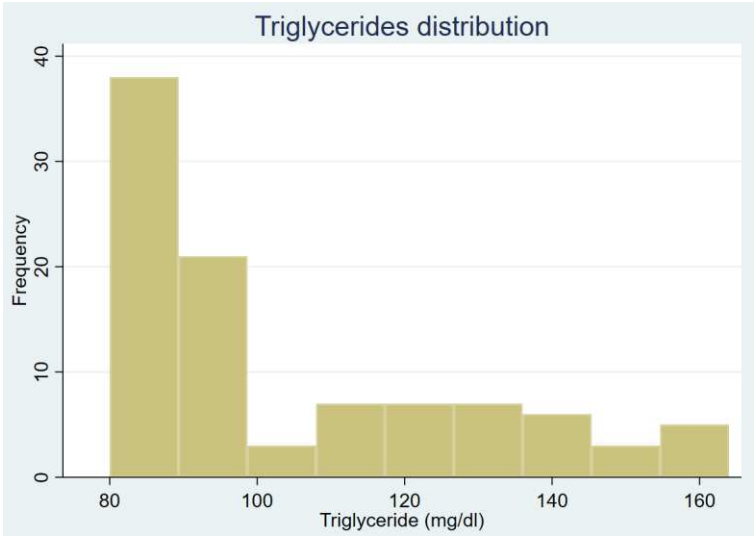
Figure 16: Pie chart of hdl distribution among patients with BPH



4.1.8 Triglyceride level

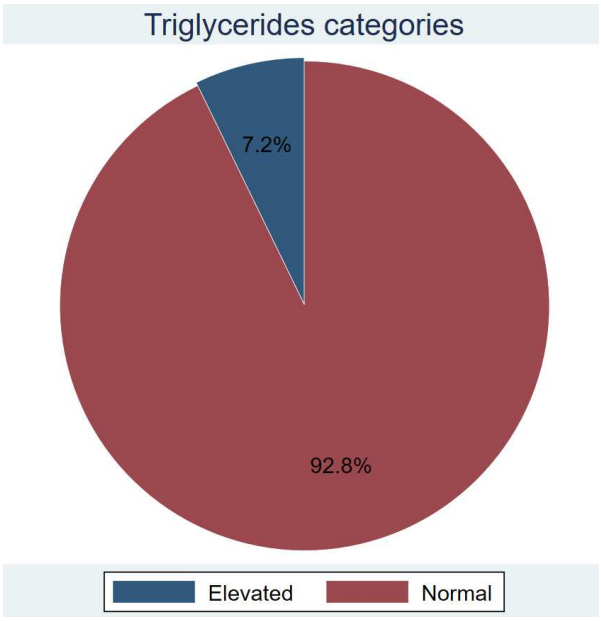
Out of 97 study subjects, the mean triglyceride level was 104.7, SD 24.5, Range 80 - 164, Median 93 (Figure17).

Figure 17: Histogram of triglyceride level



Amongst the 97 patients with BPE, elevated triglycerides were found in 7 (7.2%) compared to 90 (92.8%) who had normal levels (Figure 18).

Figure 18: Pie chart showing triglycerides categories



4.1.9 Hypertension

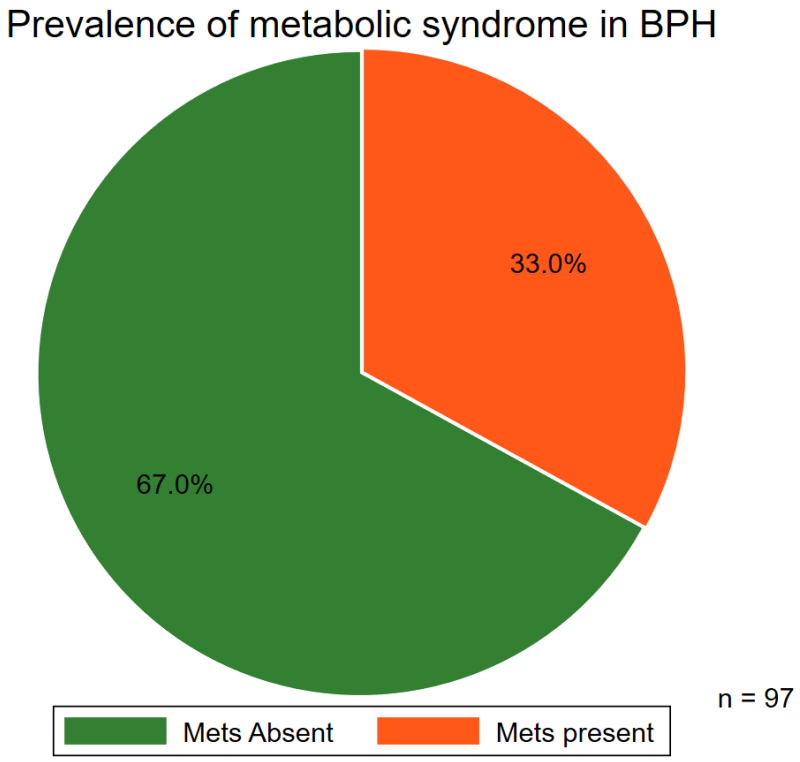
Out of the 97 patients with BPE, 49 (50.5%) had hypertension compared to 48 (49.8%) who did not. Thus the prevalence of hypertension among the study group was 50.5% (CI 40.2 – 60.8).

However there was no significant statistical association between hypertension and metabolic syndrome, p value 0.350. However, a systolic BP above 140 was associated with occurrence of metabolic syndrome at 10% significance level, with a p value of 0.071

4.2 Prevalence of metabolic syndrome

Out of 97 men 32 (33%) had metabolic syndrome compared to 65 (67%) who did not have. Therefore, the overall prevalence of metabolic syndrome was 33% (CI 24 - 42) (Figure 19).

Figure 19: Prevalence of Metabolic syndrome in BPH



4.3 Association of Metabolic Syndrome and BPE

Having metabolic syndrome resulted higher Odds of high IPSS scores with an odds ratio of 4 (CI 1.0 – 22.6) compared to not having metabolic syndrome. Thus metabolic syndrome is significantly associated with higher IPSS scores, p value 0.038

Table 4: Association between BPE and metabolic syndrome

IPSS score Category	Metabolic syndrome		Total
	Met syndrome	No met syndrome	
9 – 19	19	3	22
20 – 35	46	29	75
Total	65	33	97
	P value = 0.038, Odds ratio 4.0 (1.0 – 22.6)		

Table 5: Number of metabolic components encountered in study

Number of components	Frequency	Percent
1	10	10.3
2	51	52.6
3	11	11.3
4	20	20.6
5	5	5.2
Total	**97**	**100.0**

Table 6 : Comparison of number of metabolic syndrome components and grouped IPSS

No. of Metabolic components	IPSS score		P value
	8-19 (moderate)	20-35 (severe)	
3	2	9	0.601
4	2	18	
3	2	9	0.458
5	0	5	
4	2	18	0.633
5	0	5	

Thus there was no statistical significance when comparing categories of IPSS score and the number of components of metabolic syndrome in this study.

To assess individual components of metabolic syndrome and their association with IPSS categories, abnormal HDL and waist circumference were significantly associated with higher IPSS scores as shown in the table below.

Table 7: Individual components of metabolic syndrome and IPSS score categories

		IPSS score			
Metabolic components	**Categories**	**8-19**	**20-35**	**P value**	**Odds ratio**
HDL	Low Normal	3 19	27 48	0.037	3. 6 (1.02 – 12.2)
Waist circumference	Elevated Normal	3 19	32 43	0.013	4.7 (1.2 – 26.6)
FBS	Elevated Normal	20 2	70 5	0.655	1.4 (0.25 – 7.77)
TGL	Elevated Normal	1 21	6 69	0.499	1.8 (0.2 – 16.0)
Systolic BP	Elevated Normal	20 2	68 7	0.668	0.9 (0.2 – 5.1)

CHAPTER FIVE

5.0 DISCUSSION

Clinical benign prostatic enlargement (BPE) is one of the most common diseases in ageing men, and the most common cause of lower urinary tract symptoms (LUTS) (3). Metabolic syndrome (MetS) a conglomeration of metabolic derangements associated with central adiposity and insulin resistance has been implicated to result in the development of benign prostatic hyperplasia (BPH) which causes benign prostatic enlargement (BPE) in men (12). This study aimed to establish the prevalence of metabolic syndrome in benign prostatic enlargement and define its association with severity of LUTS amongst men seen at the Kenyatta national hospital. Knowledge on the association of metabolic syndrome with BPE would be necessary to address the cardio-metabolic derangements that exist and further improve the overall quality of life of such patients.

To achieve the objectives, this study included 97 patients presenting with LUTS secondary to BPE and IPSS of more than 10, an enlarged prostate greater than 30cc and PSA less than 10ng/ml. The study indicated a mean age of our study participants was 69.5 years, SD 9.06, Median 70, with a range of 49 – 88. Advanced age increased the risk of developing BPE. Similarly, autopsy studies done on epidemiology of clinical benign prostatic hyperplasia have observed a prevalence of 8% in the 40 year olds, 50% in 60 year olds, and 80% in the 90 year olds (6). Comparable study also show BPH is present in ageing men with global autopsy proven histological prevalence increases beginning at 40-45 years of age attaining 60% at 60 years and 80% at 80 years (3).

Benign prostatic enlargement (BPE) often leads to LUTS which increases in frequency and severity with age (3). The results of our study indicates that majority of

the patients 75 (77.3%) had severe lower urinary tract symptoms with an IPSS score of 20 – 35. This could be attributed to the fact that many of the participants included were above sixty years which is the age where moderate and severe symptoms of the condition would be observed (6). The results were consistent with a study done in USA on treatment for benign prostatic enlargement among community dwelling men, which had outcomes indicating progressive rise in moderate-to-severe LUTS incidence secondary to BPE, to almost 50% by the 8th life decade (3).

From our study, it was observed that mean PSA level was 5.44 with 37 (38.1%) of men with elevated PSA whereas 60 (61.9%) men had normal PSA levels. Mounting evidence suggests that Mets is related to benign prostatic enlargement and study by Dibello et al, 2016 found a 26.5% prevalence of metabolic syndrome in men with benign prostate enlargement (4). However, the influence of metabolic syndrome on prostate-specific antigen (PSA) level remains unclear. In our study, no significant association was found between PSA level and occurrence of metabolic syndrome (p=0.927). Conversely, a study by Jeong et al, 2010 demonstrated that metabolic syndrome was not associated with PSA level (20).

Findings from the study showed high FBS >7mmols/l occurred in 70 (72.2%) of participants. Comparatively, 37 (38.1%) of the patients were reported to be diabetic. Thus as many as 34.1% patients were not on treatment for diabetes despite having high FBS. This correlates with similar studies done worldwide showing an association of BPE and diabetes characterized by increased insulin resistance. Our study also observed the prevalence of hypertension among the study group was 50.5% (CI 40.2 – 60.8). There was no significant statistical association between hypertension and metabolic syndrome, p value 0.350. However, a systolic BP above 140 was significantly associated with occurrence of metabolic syndrome at 10% significance level, with a p value of 0.071. Studies have indicated existing evidence

of found non-insulin dependent diabetes mellitus (NIDDM) and hypertension as risk factors for BPE development (12). This data suggests that frequent testing of FBS and BP in high risk groups not only reduces the cost of treatment significantly, but is more convenient and satisfying for the patient, with no added risk of BPE.

Majority of the patients with benign prostate enlargement 62 (63.9%) had a normal waist circumference. Our study also demonstrated that majority of the participants had normal lipid profile parameters as 67 (69.1%), had normal high density lipoproteins, while 90 (92.8%) had normal triglyceride levels. This is probably a reflection of the African population who have normal lipid profile and normal waist circumferences due to dietary and socio-economic factors.(20) The US National Cholesterol Education Program Adult Treatment Panel identified that persons with central obesity, hypertriglyceridemia, reduced high density lipoprotein cholesterol (HDL-C) to be regarded as having MetS (20). Similarly, a study by Nandeesha et al (11) reported that in patients with symptomatic BPE, the level of HDL-C was lower, whereas level of low density lipoprotein cholesterol (LDL-C) and total cholesterol were higher as compared to those in controls (11). Hence, closely monitoring and controlling high risk factors of dyslipidemia can be carried out hence BPE can be avoided or slowed down via metabolic pathways modification (5)

Major finding from our study established prevalence of metabolic syndrome in patients with clinical benign prostatic enlargement was 33% (CI 24 - 42). This study demonstrated a correlation of severity Metabolic Syndrome and BPE. Having metabolic syndrome resulted in higher likelihood of high IPSS scores with an odds of 4 compared to not having metabolic syndrome. Contrary to our hypothesis, metabolic syndrome was significantly associated with higher IPSS scores with a p-value of 0.038. This result builds on existing evidence that associate metabolic syndrome to BPE. Metabolic syndrome has been estimated to occur in 26.7% - 55.4% of men with

LUTS in several studies conducted in Asian populations (5). Similarly, study by DiBello et al, 2016, in the Boston Community, UK showed that metabolic syndrome was associated with BPE with as many men as 26.5% having BPE compared to 20.9% of men without BPE (p value <0.001). The study thus showed that the more the components of metabolic syndrome, the greater the odds of having severe BPE (4).

It is worthwhile to note that the interpretation of these study findings was limited in that the study was cross-sectional in design which cannot establish a causal association between an exposure and outcome variable. A prospective study design and data collection would minimize any bias and provide us with sufficient statistical power to identify any causal association between MetS and the risk of BPH.

However the study provides insight that will not only inform policy making on the comprehensive management of patients while looking out for metabolic syndrome components .

5.1 CONCLUSION

The prevalence of metabolic syndrome among African populations is increasing according to various studies conducted (15–19). It is inevitable that this disorder will become even more prevalent and a major challenge for all health care systems in the future. From our findings, the results indicate a correlation between metabolic syndrome and BPE more so severity as shown by the IPSS. With limitations in availability of data on metabolic syndrome and BPE in the African continent, this study provides a new insight and establishing the associations will greatly help to improve management protocols of care in patients with BPE.

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ANNEXES

Annex 1: Informed Consent Form

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KENYATTA NATIONAL HOSPITAL (KNH)
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Fax: 725272
Telegrams: MEDSUP, Nairobi

PARTICIPANT INFORMATION AND CONSENT FORM FOR ENROLLMENT IN THE STUDY

This Informed Consent form is for patients attending Urology Outpatient Clinics at KNH. It was administered to eligible patients. We are requesting you to participate in this research project whose title is "**METABOLIC SYNDROME AMONG MEN WITH BENIGN PROSTATIC ENLARGEMENT AT KENYATTA NATIONAL HOSPITAL**"

I. Information Sheet (informs you in a brief overview about the research with you).

II. Certificate of Consent (for you to sign if you agree to take part).

III. Statement by the researcher/person taking consent.

A copy of the informed consent form was provided.

PART I: Information Sheet

Introduction

My name is Dr. Yvonne Wanjiru Karimi, a postgraduate student in urology at the University of Nairobi. I am carrying out research to determine the association between benign prostatic enlargement and metabolic syndrome which is a cluster of conditions

that include elevated blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol or triglyceride levels in patients seeking treatment at the Kenyatta national hospital.

Purpose of the research

I will provide information and invite you to be a participant in this research. There may be some words that you don't comprehend. Please ask me to explain as we go through the information and I will explain. After receiving the information concerning the study, you are encouraged to seek clarification in case of any doubt. This study will elucidate the prevalence and association of metabolic syndrome among men with benign prostatic enlargement. The study will also aim to justify the establishment of appropriate management protocols on cardiovascular risk factors optimization in men with MetS gearing towards holistic treatment not only limited to the relief of urological symptoms.

Type of Research Intervention

This research will involve use of questionnaires and medical records with your doctor's permission [or their representative], imaging and laboratory investigation results.
You was consenting to have your blood pressure and waist circumference measured and recorded on your initial visit at the urology clinic. This is at no extra cost and forms part of triage.
Laboratory investigations requested may include fasting lipid profile and fasting blood sugar .Both was done at the Kenyatta National hospital laboratory by taking blood samples from you early morning before eating anything. This was done by an experienced phlebotomist.

Voluntary participation/right to refuse or withdraw

It is your decision to participate or not. Whether you choose to participate or not, all the services you receive at this hospital will continue and nothing will change. If you decide against participating, you was offered the treatment that is routinely provided in this hospital for your condition. You have a choice to refuse or withdraw your participation in this study at any point.

PART II: Certificate of Consent

I have read and understood the above information/the above information has been read out to me. I have had the opportunity to ask questions and the questions that I have asked have been answered satisfactorily. I voluntarily agree and consent to participate in this research.

Print Name of Participant _____

Signature of Participant _____

Date _____

If Non -literate:

I have witnessed the reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I can confirm that the individual has given consent voluntarily.

Print Name of witness_____ Thumb print of participant

Signature of witness _____

Date _____

PART III: Statement by the researcher

I have read out the information sheet to the participant, and made sure that the participant understands that the following was done:

A decision to refuse to participate or withdrawal from the study will not in any way compromise the care of treatment.

All information given was handled with confidentiality.

The results of this study might be published to facilitate research and improved clinical guidelines. I can confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered

correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the approval has been given voluntarily.

A copy of the Informed Consent Form has been provided to the participant.

Name of researcher/person taking consent _____

Signature of researcher/person taking consent_____

Date_____

Fomu Ya Makubaliano Ya Kujiunga Na Utafiti

Fomu ya makubaliano

Nimeelezewa utafiti huu kwa kina. NakubaIi kushiriki utafiti huu kwa hiari yangu. Nimepata wakati wa kuuliza maswali na nimeelewa kuwa iwapo nina maswali zaidi, ninaweza kumwuliza mtafiti mkuu au watafiti waliotajwa hapa juu.

Jina la
Mshiriki_____

Sahihi ya mshiriki

_____ _

Tarehe_____
____

Kwa wasioweza kusoma na kuandika:

Nimeshuhudia usomaji na maelezo ya utafiti huu kwa mshiriki. Mshiriki amepewa nafasi ya kuuliza maswali. Nathibitisha kuwa mshiriki alipeana ruhusa ya kushiriki bila ya kulazimishwa.

Jina la
shahidi_____ Alama ya kidole cha mshiriki

Sahihi la shahidi_____

Tarehe _____

Ujumbe kutoka kwa mtafiti

Nimemsomea mshiriki ujumbe kiwango ninavyoweza na kuhakikisha kuwa mshiriki amefahamu yafuatayo:

Kutoshiriki au kujitoa kwenye utafiti huu hautadhuru kupata kwake kwa matibabu. Ujumbe kuhusu majibu yake yatahifadhiwa kwa siri.

Matokeo ya utafiti huu yanaweza chapishwa ili kuwezesha kuzuia na kutibu matatizo yanayosababishwa na prostate biopsy.

Ninathibitisha kuwa mshiriki alipewa nafasi ya kuuliza maswali na yote yakajibiwa vilivyo.

Ninahakikisha kuwa mshiriki alitoa ruhusa bila ya kulazimishwa.

Mshiriki amepewa nakala ya hii fomu ya makubaliano.

Jina la mtafiti _____

Sahihi ya Mtafiti _____
Tarehe_____

Annex 2: Study Questionnaire

Demographic data:

1.Study number.....

2.Patient file number……

3. Age (years).....

4.Contact number …….

5. Are you on treatment for either diabetes mellitus or hypertension?

NO ☐ DIABETES ☐ HYPERTENSION ☐

(To be filled by researcher)

6. Prostate size on KUB-P ultrasound……...

7. PSA LEVEL……ng/ml

8. BP …….mmhg

9. Waist circumference……inches

10. FBS……..mmol/l

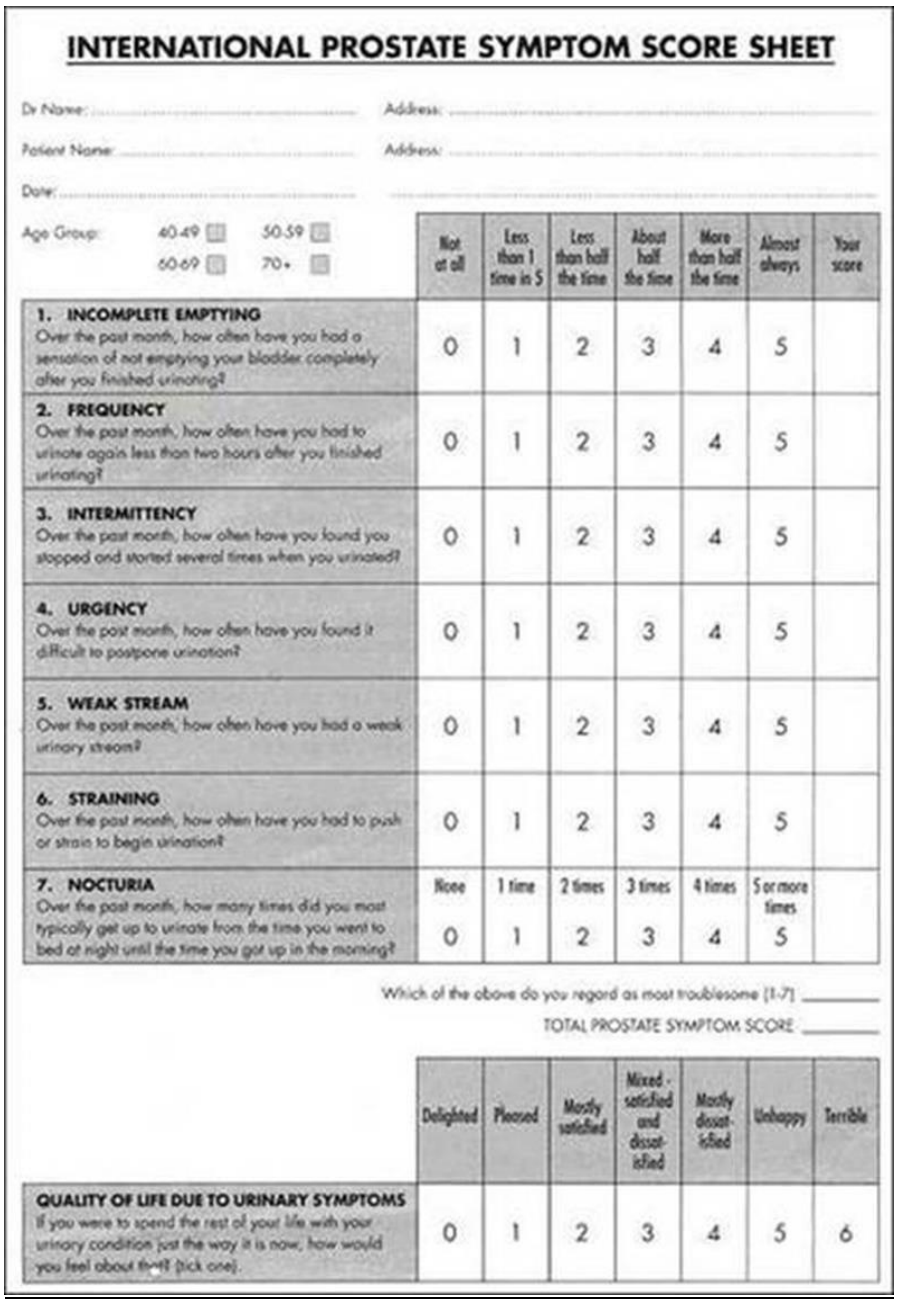
11. Triglyceride level……..mg/dl

12. High density lipid (HDL) levels…….mg/dl

13. Initial IPPS……

Mild (0-7) ☐ Moderate (8-19) ☐ Severe (20-35 ☐

Annex 3: International prostate symptom score



INTERNATIONAL PROSTATE SYMPTOM SCORE SHEET

Dr Name: ..... Address: .....

Patient Name: ..... Address: .....

Date: .....

Age Group: 40-49 ☐ 50-59 ☐ 60-69 ☐ 70+ ☐

	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your score
1. INCOMPLETE EMPTYING Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5	
2. FREQUENCY Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
3. INTERMITTENCY Over the past month, how often have you found you stopped and started several times when you urinated?	0	1	2	3	4	5	
4. URGENCY Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. WEAK STREAM Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
6. STRAINING Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
7. NOCTURIA Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	None 0	1 time 1	2 times 2	3 times 3	4 times 4	5 or more times 5	

Which of the above do you regard as most troublesome (1-7) _____

TOTAL PROSTATE SYMPTOM SCORE _____

	Delighted	Pleased	Mostly satisfied	Mixed - satisfied and dissat-isfied	Mostly dissat-isfied	Unhappy	Terrible
QUALITY OF LIFE DUE TO URINARY SYMPTOMS If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that? (tick one)	0	1	2	3	4	5	6

METABOLIC SYNDROME AMONG MEN WITH BENIGN PROSTATIC ENLARGEMENT AS SEEN AT KENYATTA NATIONAL HOSPITAL

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