PREDICTIVE VALUES OF OSTEOCALCIN IN OSTEOPOROSIS AT THE KENYATTA NATIONAL HOSPITAL

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF REQUIREMENTS FOR THE AWARD OF MASTERS OF MEDICINE (M.Med)
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DECLARATION

I hereby declare that this research is my original work and has never been presented in any form or manner for the award of a degree at any other university.

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CERTIFICATE OF AUTHENTICITY

This is to certify that this dissertation is the original work of Dr. Robert Gayflor Mulbah, a Resident pursuing Master of Medicine in the Department of Orthopaedic Surgery with registration number H58/70022/2013 of the University of Nairobi. This research was conducted at the Kenyatta National Hospital, Nairobi, Kenya. It has not been presented in any other university for an award of a degree.

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Acknowledgment

I am extremely grateful for the opportunity to conduct this study at this crucial period of my academic sojourn. Let me begin by quickly acknowledging the omnipotent God for his bountiful blessings and the numerous contributions of writers and publishers of many articles cited during the development of this study.

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DEDICATION

This research project is dedicated to my beloved brother, Mr. David Z. Mulbah, who played the role of our deceased parents throughout my academic sojourn. I also like to dedicate this aspect of my academic journey to my deceased parents, Mr. and Mrs. Wollier Mulbah, who would have loved to see this day come to fruition. You made the wisest decision to invest your meager resources in the education of your children.

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LIST OF ABBREVIATIONS

BMD	……	Bone Mineral Density
DXA	……	Dual-Energy X-Ray Absorptiometry
FRAX	……	Fracture Risk Assessment Tool
KNH	……	Kenyatta National Hospital
N-MID	……	N-terminal mid-molecule
OSCAL	……	Osteocalcin
RANK	……	Receptor Activator of Nuclear factor Kappa
RANKL	……	Receptor Activator of Nuclear Factor Kappa Ligand
SD	……	Standard Deviation
TNF	……	Tumor Necrosis Factor
UoN	……	University of Nairobi
WHO	……	World Health Organization

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1.1 OPERATIONAL DEFINITIONS

Menopause: A period of complete cessation of monthly menstrual cycle which is age-related.

Postmenopausal woman: A postmenopausal woman is a woman of ages 50 years and above with associated cessation of the menstrual cycle.

Osteopenia: A condition associated with low bone mineral density as defined by WHO to be T score of less than -1 and greater than -2.5 SD.

Osteoporosis: A condition associated with the low bone mineral density of T-score less than or equal to -2.5 SD.

Osteocalcin: A bone matrix protein produced by osteoblast and is released in circulation when bone is resorbed**.** It is thought to serve as an attachment site for hydroxyapatite.

Estrogen: A female hormone responsible for the monthly cyclic menstrual period which plays a role in the control of the osteoclastic activity. It is profoundly reduced in postmenopausal women.

ABSTRACT

Background

Osteoporosis is increasingly becoming a major health problem in the Kenyan population, especially postmenopausal women. Two previous hospital-based studies put the prevalence at 24.5%.

The disease is debilitating and affects the overall health of the population. Complications arising from this orthopaedic condition can be catastrophic; ranging from hip fractures to lumbar fragility fractures. To mitigate its effect, there is a need to identify early diagnostic modality. This allows planned intervention including pharmacological approach and lifestyle modifications aimed at preventing the progression of the disease.

Currently, the gold standard for the diagnosis of the disease is Dual Energy X-ray Absorptiometry (DXA) scan. This is not affordable and accessible to many people in the Kenyan setting according to the International Osteoporosis Society audit. Therefore, the search for an alternative, affordable and accessible marker to pick up early osteoporosis and to serve as a clinical screening and diagnostic tool is a necessity.

Objective

To correlate Osteocalcin level with DXA findings in the diagnosis of osteoporosis in the Kenyan setting, in postmenopausal women and assess fracture risk

Methodology

This is an analytical cross-sectional study done on postmenopausal women ages 50 years and above. The study period was from 1st March –31st May 2018, at the Kenyatta National Hospital in Nairobi, Kenya. Participants were recruited at the Orthopaedic Clinic of Kenyatta National Hospital. These participants were taken to Medanta AfriCare in Nairobi for the neck of both femurs and lumbar spine densitometry. Samples of blood were simultaneously taken from each patient, centrifuged and transported to Lancet Kenya at 20 degrees Celsius for determination of Osteocalcin levels.

Results

A total of 61 postmenopausal women were assessed for necks of both femur and lumbar vertebrae DXA findings and serum Osteocalcin levels. 11 women constituting 18% were found to be osteoporotic while 22 (36%) were osteopenic. BMI did not have any association with BMD levels of both femur and lumbar spines and with serum Osteocalcin levels. There was a correlation between Osteocalcin levels and DXA findings for the neck of the femur. Women with normal T-score of greater than -1 SD were found to have serum Osteocalcin levels less than or equal to 15.5 ng/ml while those with Osteopenia (T scores between -1 and -2.5 SD) had Osteocalcin levels between 15.6 – 25 ng/ml. Women with Osteoporosis (T-score $\leq$ -2.5 SD) had consistent Osteocalcin levels greater than 25.1 ng/ml).

Conclusion

Eighteen percent of postmenopausal women are osteoporotic. The study revealed that there is a strong correlation between Serum Osteocalcin levels and BMD levels in postmenopausal women. Serum Osteocalcin levels are predictive of DXA findings. Therefore Serum Osteocalcin levels should be considered as a screening tool for osteoporosis in postmenopausal women, especially in low resource communities.

CHAPTER ONE: INTRODUCTION AND LITERATURE REVIEW

1.1 Introduction

Osteoporosis is a progressive systemic disorder of the skeletal system characterized by reduced bone mineral density, micro-architectural breakdown of bone tissue and high susceptibility to fractures.[1,2] It is a debilitating condition associated with profound morbidity and complications such as hip, vertebral, lower and upper limbs fractures. It, therefore, poses a major public health challenge worldwide with Kenya being no exception. Associated fragility fractures are increasingly becoming a burden in African countries.[3,38] In Kenya, there were 245/100,000 hip fractures attributable to osteoporosis according to a report by Hilliard.[3] In 2010, it was noted that the likelihood of fragility fractures in patients with osteoporosis above 75 years within Kenya was a significant health issue.[4] It has been reported that many of these fractures are preventable because they occur in people who were previously osteopenic.

Currently, there is a paucity of data on osteoporosis in Kenya due to no existing affordable method for screening osteoporosis. Three functional DXA machines are owned and operated by private facilities at an average cost of one hundred United States Dollars ($100) or ten thousand Kenyan Shillings per scan, which is not generally affordable to the majority of the population. All major referral hospitals in the counties and the national referral and teaching hospital are without any DXA machine. This can be attributed to the high cost of procuring and installing DXA BONE DENSITOMETER in the local setting, which currently stands at twenty-five thousand United States Dollars ($25,000) or two and a half million Kenyan Shillings. Therefore, many diagnoses of osteoporosis are made following a fragility fracture with plain X-rays.

DXA Densitometer is a radiological device that utilizes two X-ray beams with low radiation of about a tenth compared to a standard chest X-ray to determine BMD.[50,51] It targets a specific

aspect of the skeletal systems based on the type used. Two types currently in use are Central DXA Device and Peripheral DXA Device. Central DXA Device is the commonest and scans the neck of femur and L2 lumbar vertebrae. Peripheral DXA Device targets forearm and is rarely used.

There are many bone markers used to assess bone turnover including alkaline phosphatase and urinary hydroxyproline. Most of these markers are not tissue specific. Osteocalcin is the most reliable because of it is tissue specific, widely available, with relatively low variations.[42] It is the most significant non-collagenous bone matrix protein produced by Osteoblasts. Its serum level rises in rapid bone turnover. Therefore, it is currently used to monitor how the efficacious an anti-resorptive drug is in the management of osteoporosis[36]. However, the serum level of Osteocalcin has been found to be useful in screening for primary osteoporosis by Singh et al in the Indian population.[15]

Early screening for osteoporosis is to identify people, who are at risk of osteoporosis and to prevent fragility fractures. Postmenopausal women are particularly at risk of getting osteoporosis because of the effect of depleted estrogen level on bone mineral density. This is a period in a woman's life associated with cessation of menstruation; usually occurring between ages 45-50 years in the black population.[15]

1.2 Review of Literature

1.2.1 The Burden of Osteoporosis

Osteoporosis is responsible for morbidity and mortality globally. Currently, it affects over two million people in the world.[5] According to the International Osteoporosis Foundation (IOF), more than 8.9 million fractures occur annually worldwide.[6] Postmenopausal women are at increased risk. 1 in every 3 women above age 50 will experience osteoporotic fractures compared to 1 in every 5 men of the same age group.[6] In Kenya, although there is a paucity of data like other parts of Africa. Odawa et al found 24.5% prevalence rate among postmenopausal women following a hospital-based study.[8, 26]

In Africa today, there is limited data on the epidemiology of Osteoporosis, especially among black Africans. However, community-based studies on the Afro-Americans point to low incidence compared to other races. In South Africa, Osteoporosis is less prevalent in the black population.[7] Odula et al in a separate study at the Aga Khan University Hospital in Nairobi compared Caucasians and Asians and black Kenyans and found higher prevalence rate among Caucasians and Asians than blacks.[8]

Osteoporosis, therefore, poses a huge socioeconomic burden on the world's population with Kenya being no exception. Treatment of osteoporosis and management of fragility fractures are associated with profound economic stress on societies. In women over the age of 45 years, the condition is significantly responsible for frequent visits for bone-related conditions such as low back pain than many other conditions including diabetes, Myocardial Infarction, and breast cancer.[9] Studies have shown that many women who sustain fragility fractures are insufficiently diagnosed and managed for probable osteoporosis amidst these numerous visits.[10,30,32]

1.2.2 The role of Estrogen depletion in the pathophysiology of osteoporosis in postmenopausal women

The relationship between low estrogen levels and bone loss has been well established. It's estimated that reduced Estrogen level is responsible for 75% of bone loss that occurs in postmenopausal women.[31,33] Immediately after menopause, bone mass turnover is directly related to increased bone loss and likelihood for fragility fracture due to reduced estrogen level.[12, 24]

The role of Estrogen is to prevent bone resorption by osteoclasts. It brings about apoptosis of osteoclasts; resulting in a reduced lifespan of these bone-resorption cells. Lifespan of an osteoclast stands at 6 weeks. The hormone facilitates the expression of Osteoprotegerin (OPG) by Osteoblast, which prevents RANK ligand from binding to RANK. Hence, the presence of Estrogen results in the inhibition of the formation, differentiation, and survival of Osteoclasts.[24] Consequently, bone resorption is minimized.

Three members of TNF and its receptor superfamily are directly linked to the regulation of bone resorption. Osteoblast produces RANKL, the potent ligand for RANK, a receptor found on the hematopoietic cell. The interaction of RANKL with RANK promotes the conversion of hematopoietic precursor cell into bone resorption cell. Estrogen impairs the activities of a number of cytokines and growth factors that exert their effects via the RANK/RANKL pathway. Moreover, it stimulates Osteoblasts directly to secrete OPG, which acts as a decoy for RANKL.

In postmenopausal women, the Estrogen level is very low. The inhibitory effect on Osteoclast is reversed. Osteoclastic activity is potentiated. Hence there is massive bone turnover resulting in osteopenia and subsequent osteoporosis. Studies have demonstrated that low Estradiol levels are associated with significant bone loss.[9, 11, 1]

Srinivasan et al noted that the single most intriguing factor in the pathophysiology of reduced bone mineral density in postmenopausal women is the profound decrease in Estrogen level. This accounts for the increment in the number of osteoclast and subsequent bone depreciation.[12]

It has also been noted that low estrogen level sensitizes bone to respond significantly to parathyroid hormone. Parathyroid hormone then facilitates the Vitamin D production, which increases the absorption of Calcium in the digestive and renal systems. It also remarkably stimulates osteoclasts indirectly; culminating in more bone resorption and weakening.[12]

1.2.3 Bone Markers in Osteoporosis

There are currently a number of bone markers used in evaluating bone turnover in osteoporosis and efficacy of drugs used in its management. They include serum levels of total Alkaline Phosphatase, bone-specific Alkaline Phosphatase, Osteocalcin, Urinary Hydroxyproline, and bone sialoprotein. Of all these markers, Osteocalcin has an advantage because it is tissue-specific and widely available with minimum variations among persons and a negligible amount in abnormal tissues such as calcified blood vessels.[42]

1.2.4 Biology of Osteocalcin

Osteocalcin is a bone gamma carboxyglutamic acid protein (BGLAP) found in the bone extracellular matrix with a molecular weight of 5800 kDa. It is composed of 49 amino acids including three residues of gamma-carboxyglutamic acid. It is secreted by Osteoblast, and incorporated in the bone extracellular matrix. Osteocalcin level is increased into circulation following bone resorption and subsequently cleared by renal and hepatic systems as a whole molecule. Its half-life is about 5 minutes. Therefore, normal serum osteocalcin level represents the fraction of the molecule that has been released in circulation under normal condition.

It is a biomarker of bone formation since it is produced by bone-forming cells, Osteoblast. However, it has been found to correlate with bone turnover in osteoporosis as reported by Delmas et al.[28,44] It is therefore employed currently to monitor the effectiveness of Bisphosphonates.[29]

1.2.5 Biosynthesis of Osteocalcin

Osteocalcin is synthesized primarily by Osteoblasts with an only small amount produced by Odontoblast. This process is facilitated by 1, 25 dihydroxy Vitamin D and is Vitamin K dependent. Carboxylation of this molecule is increased by Vitamin K.[13, 17] Intracellular synthesis begins with the detachment of pro-osteocalcin from rough Endoplasmic reticulum. Prior to its secretion from the cell, specific glutamic acid residues are carboxylated by a post-translational, Vitamin K-dependent enzymatic carboxylation to form gamma-Carboxyglutamic acid (GLA).

It has been reported that human Osteocalcin consists of three Gla residues per molecule.[45, 43] After division, a large percentage of Osteocalcin is deposited into the bone matrix and this is facilitated by Calcium-binding properties of the Gla residues. A portion of about 10-30 % directly from osteoblast is released into circulation.[43] This determines the normal serum levels. However, in patients treated with Warfarin as well as in Vitamin K deficiency, there is inhibition of Carboxylase enzyme and subsequent secretion of non-carboxylated Osteocalcin.[47,43]

Non-carboxylated Osteocalcin weakly binds to hydroxyapatite and hence released into the serum.

1.2.6 The diagnostic utility of Osteocalcin

Osteocalcin level is increased into circulation from the bone matrix during bone breakdown; hence it is considered a marker of bone turnover.[14,26] Singh et al demonstrated that serum Osteocalcin level measurement is a useful tool for picking up low bone density in primary osteoporosis as exemplified in post-menopausal women in the Indian population. Osteocalcin was found to be in correlation with BMD level.[15]

Although the function is not vividly understood, Osteocalcin has been found to be a deposition site for hydroxyapatite crystals. Osteocalcin is rapidly excreted by the renal system at a Glomerular filtration rate (GFR) of 90-120 ml/min and to a minimum extent, the liver. The half-life is 5 minutes. An abnormality of GFR tends to markedly affect serum Osteocalcin level. Hence its level is also increased in chronic debilitating renal or liver diseases.[13,16]

Osteocalcin elevated levels are primarily related to increased bone turnover. However, it is decreased in patients on anti-resorptive agents. The normal serum level in adult male ranges from 1.1-42 ng/ml while in females, it stands at 0.7-42 ng/ml with normal osteocalcin level in the averaged postmenopausal woman to be 9-42 ng/ml. A sample of testing consists of serum and is usually collected in a plastic vial with a volume of 0.5 – 1ml. It can remain stable for 14 days frozen or 72 hours at temperature 2-8^0 Celsius.[17, 27]

Measurement

Several Immunoassays have been developed including enzyme immunoassays (ELISA) and radioimmunoassay. Osteocalcin ELISA is an enzyme immunological test for determining its serum level. It relies on the usage of two highly sensitive monoclonal antibodies against human Osteocalcin.[28] Assay Kit has a sensitivity level of 0.31ng/ml and a range of 4.0-64 ng/ml.

The stability of Osteocalcin is storage- method dependent. It has been found that 50-70% after 6-24 hours is stable at ordinary room temperature and 40-80% after 2 weeks at 4 degrees Celcius.[48] Blumsohn et al further reported that the concentration was found to be unchanged for N-terminal mid Molecule (N-MID) after 3 hours at room temperature and after 24 hours at 4 degrees.[49] They also noted that mixed protease inhibitor and collection of samples on the ice have been found to improve stability.[49]Protease inhibitors are chemicals that inhibit protease activities.

Since different antibodies recognize different fragments, no standard currently exists for Osteocalcin assays. However, antibodies that pick up both the large amino-terminal mid molecule fragment and the intact molecule appear to provide more clinical information. It has been noted that both large N-terminal Mid molecule (N-MID) fragment and intact osteocalcin are found in circulation.[29]

Cleavage of Osteocalcin is frequently occurring in circulation between amino acid 43 and 44 by plasmin[52]. This explains why total osteocalcin is variable. The N-MID fragment resulting from division is reported to be the most stable by Chen et al and therefore branded as Osteocalcin-S. It is the true marker of bone turnover.[29]

1.2.7 Current concept on the diagnosis of Osteoporosis in postmenopausal women

WHO defines osteoporosis as BMD level determined by DXA scan to be less than -2.5 standard deviations (SD); that's below the mean value for young adults for same age and sex (T-score). It further classifies it as osteopenia, osteoporosis, and severe osteoporosis according to BMD grading. Osteopenia is T-score between -1 and -2.5 SD of adult BMD while osteoporosis is t-score below -2.5 SD. Severe osteoporosis is t-score less than -2.5 SD plus a fragility fracture.[39]

Currently, the detection of osteoporosis in postmenopausal women relies solely on the quantitative assessment of bone mineral density (BMD).[18] It is considered a major determinant of

bone strength with the significant clinical prediction of fracture risk in addition to other factors such as age. BMD is regarded as the standard measure for the detection of osteoporosis and the assessment of fracture risk. Majority of fragility fractures occur in patients reported having BMD in the previous osteopenic range.

Fracture risk can be evaluated using a fracture risk assessment tool (FRAX) developed by the National Institute of Health Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and therapy. It is an essential evaluation tool for the prediction of fracture considering clinical risk factors. The output gives a 10-year probability of major osteoporotic fractures (spine, hip, forearm).[19] It has also been found that fracture risk rises approximately for every standard deviation below the mean for a young adult.[20] The disadvantage of this FRAX tool is that it doesn't include all countries and it is internet dependent which is a hindrance to usage in remote communities.

BMD is currently determined by the use of DXA scans. It represents the amount of bone mass per unit volume or per unit area. A patient's BMD can be referenced to other young normal adults of the same sex using the T-score. T-score is the number of standard deviations the patients BMD is above or below the reference value for a healthy (30) thirty-year-old adult. The commonest areas scanned are femoral neck and the lumbar vertebrae. DXA is the most reliable method because it is reproducible; although other techniques include quantitative ultrasound, quantitative computed tomography.[21]

Quantitative ultrasound relies on the use of ultrasound modality to measure BMD utilizing the calcaneus. The draw-back is that it demands expertise for the interpretation of ultrasound velocity. On the other hand, Qualitative Computed Tomography measures BMD using X-ray

computed tomography scanner with a calibrated standard. It is the only image technique capable of accessing exclusively BMD of trabecular bone in Lumbar spine.[22,33]

1.3 Problem statement and Justification

Currently, the gold standard for the diagnosis and screening is Dual-Energy X-ray absorptiometry (DXA). It determines the bone mineral density (BMD) as a way of determining early osteopenia or osteoporosis. However, its availability, accessibility, and affordability are major hindrances in considering DXA as a screening tool for populations in low resource countries like Kenya. There were two DXA machines for forty million people in Kenya compared to 0.6 DXA per one million in Morocco.[25] Hence, early diagnosis and screening for osteoporosis is still a major challenge in Kenya.

It's against this backdrop that an alternative diagnostic tool for early screening of the local population is a necessity. Since Osteocalcin is embedded in the bone matrix, its serum level is expected to rise in high bone turn over and this is quantifiable. This study is focused on the determination of the diagnostic potential and utility of serum osteocalcin levels.

The result of this study will inform clinicians, especially in low resource countries on an alternative and reliable clinical tool of screening patients for osteoporosis, which will be accessible and affordable to the population.

1.4 Research Question

What is the relationship between Osteocalcin levels and DXA generated T-score?

1.5 Null Hypothesis

There is no correlation between Osteocalcin level and DXA T-scores.

1.6 Broad Objective

To correlate Osteocalcin level with DXA T-scores in postmenopausal women at the Kenyatta National Hospital in this population

1.6.1 Specific Objectives

I. To determine the proportion of women with osteoporosis in the study population.

II. To determine the predictive values of Osteocalcin using serum osteocalcin level

III. To assess fracture risk in postmenopausal women with osteoporosis at Kenyatta National Hospital using FRAX score and BMD

CHAPTER TWO: STUDY METHODOLOGY

2.1 Study Design

This was an analytical cross-sectional study. Two broad groups of postmenopausal women were studied. Group I comprised all postmenopausal women with normal DXA scan T-score above -1 SD while those with abnormal DXA scans of T-score less than -1 SD constituted group II.

2.2 Study Setting

The study was conducted in the orthopaedic outpatient clinic of the Kenyatta National Hospital, the teaching, and referral hospital. Based on clinical assessment at Kenyatta National Hospital, patients were recruited. Due to lack of DXA machine and Osteocalcin measuring equipment and reagents, patients were transported to Medanta AfriCare for DXA scanning and blood sample collection.

2.3 Study Duration

This study was conducted for a period of two consecutive months from 1st May 2018 to 30th June 2018.

2.4 Target Population

Postmenopausal women who are residents of Kenya with the ages 50 years and above and attending the Orthopaedic clinic for orthopaedic care constituted the target population of this research.

2.5 Study Population

These were consenting postmenopausal women who met the inclusion and exclusion criteria for the study.

2.5.1 Inclusion Criteria

Postmenopausal women who visited the orthopaedic outpatient clinic at the Kenyatta National Hospital during the study period (1st May- 30th June 2018) with ages 50 years and above and fulfilled the inclusion characteristics.

2.5.2 Exclusion Criteria

Postmenopausal women with the below listed criteria were excluded from the study:

1) Secondary osteoporosis
2) Bone Tuberculosis
3) Chronic renal or liver diseases
4) History of smoking and alcohol consumption
5) Medication such as corticosteroids, anticonvulsants, heparin, and bisphosphonates
6) History of radiotherapy and chronic bowel disease
7) Bone tumors, Rheumatoid Arthritis, and abnormal thyroid functions
8) Declined consent

2.6 The Sample Size

The sample size was determined by Fishers' formula for an analytical cross-sectional study to come up with a total sample of 61 postmenopausal women as shown below:

$$\textbf{\textit{Sample size (N)}} = \quad n \geq \frac{Z\alpha/2^2 \ \square^2}{d^2}$$

$\square$ = standard normal variate for power @80%= 0.4

$Z\alpha/2$ =standard normal for the level of statistical significance=1.96

d=margin of error; 10%

Hence $N=\frac{(1.96)2(0.4)2}{(0.1)2} = 61.4$ Therefore, sample size = **61 post-menopausal women**

2.6.1 Sampling Method

The systematic sampling method was used for this study. Study participants were selected following their availability at the Kenyatta National Hospital in the Orthopaedic Outpatients Clinic. A list was initially prepared with contact details. Only patients on odd numbers were sent for DXA scans and blood sample collection to determine osteocalcin levels.

2.7 Study Personnel

Study personnel were the Principal Investigator and two Research Assistants, who were fifth-year medical students. Before the study commenced, two hours of training was given to Research Assistants on the ethical guidelines and procedure of the study. This enabled the research assistants to fully understand the objectives of the study, ethical guidelines of the study, the process, and the importance of informed consent, filling up the data collection tool. proper handling of sample collection and subsequent transportation to Lancet Kenya laboratory.

2.8 Study Procedures

All Postmenopausal women, who qualified as per the inclusion and exclusion criteria, to enter the study, were sampled systematically using the following two phases:

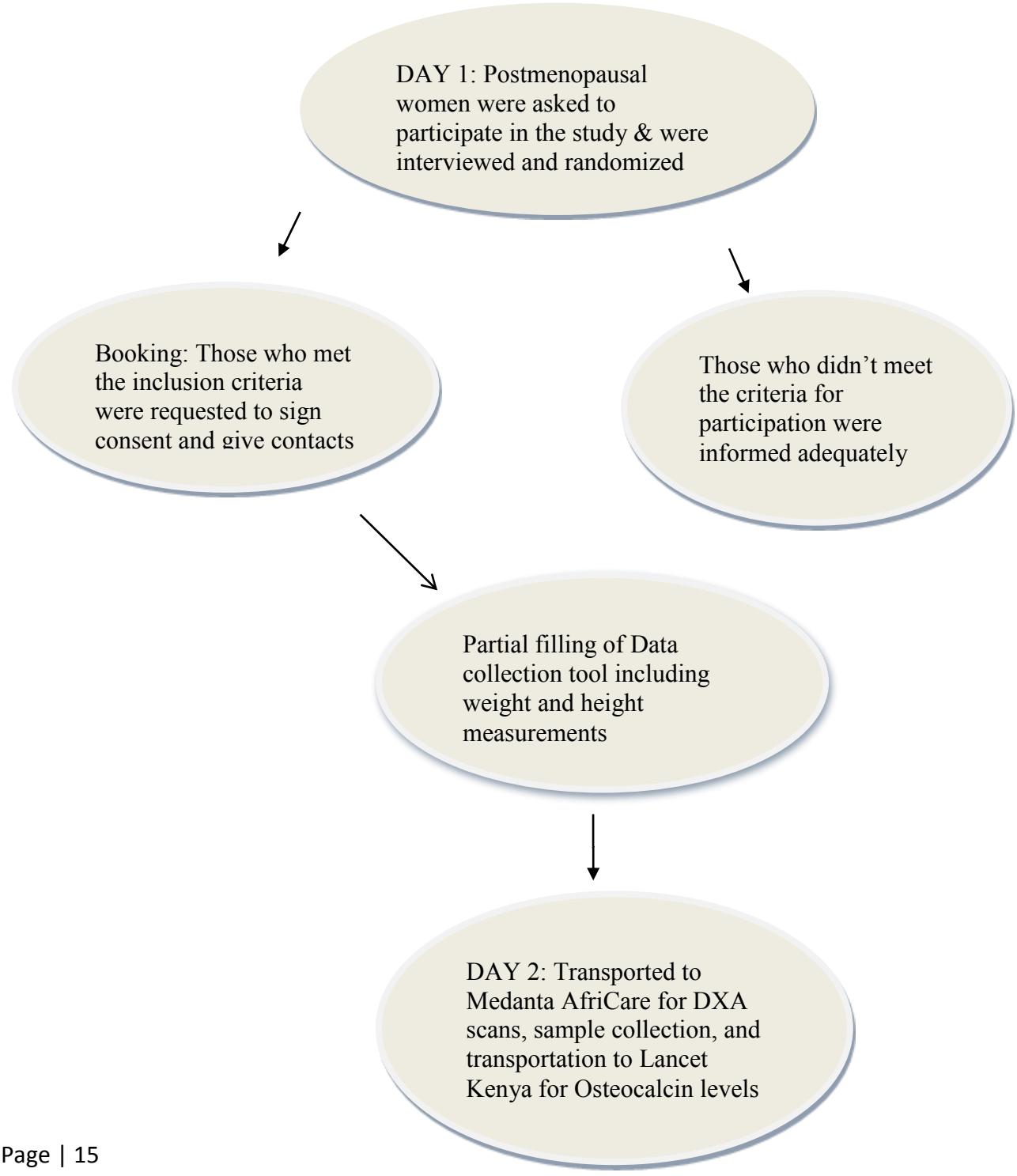
I. Days of Recruitment at Kenyatta National Hospital

II. Days of Sample collection at Medanta AfriCare: All women recruited were transported to Medanta for the below activities:

1) 5 ml Blood sample was taken from each person by the principal investigator using the median vein, centrifuged for 10 minutes at Medanta facility and subsequently transported on Ice in a cooler box at an average temperature of 4 degrees Celsius to Lancet Kenya for laboratory analysis to determine Osteocalcin level.

2) Simultaneously each patient underwent bilateral femur neck and lumbar vertebrae DXA scans using GE Lunar Prodigy Pro Bone Densitometer. Others who weren't selected were informed appropriately.

Figure 1: Study Procedure Algorithm



2.9 Data Collection and Management

Data was collected using a data collection tool which was fully completed for every participant following the availability of results of DXA scanning and Osteocalcin levels. Data were entered into a Microsoft Access database with in-built consistency and validation checks. Data were processed and kept in a protected external storage device (USB/disc) accessible only to the Principal Investigator and Statistician.

2.9.1 Data Analysis

Descriptive statistics (mean, mode, frequencies) were reported to describe the variables while inferential statistics to correlate DXA BMD levels with Osteocalcin levels. Data were scrutinized using Statistical Package for Social Sciences (SPSS) Version 25.0 and outcomes presented in the form of tables and graphs.

2.10 Ethical Considerations

The Kenyatta National Hospital Ethical and Research Committee approved the research proposal before the commencement of the study.

The study was conducted in accordance with existing guidelines of the University of Nairobi, which included seeking permission from Kenyatta National Hospital-University of Nairobi Ethical and Research Committee (KNH-UoN ERC), consent of participants and strict adherence to confidentiality.

No woman was denied care at the Orthopaedic Clinic for refusing to participate in the study. No money was offered to the study participants. All participants with osteopenia and osteoporosis were seen on specific days for the sole purpose of revealing their status and recommendations.

2.11 Study Limitations

1) Patient's fear of an invasive procedure such as taking a blood sample

2) Unavailability for DXA Scanning after recruitment

3) Timing between recruitment and taking of blood samples

4) The study largely depended on the availability of participants after recruitment for both osteocalcin levels and DXA scanning in order to complete the study. There was a total of ten patients who opted to leave the study after being recruited due to personal reasons.

CHAPTER THREE: RESULTS

A total of sixty-one postmenopausal women who came to Kenyatta National Hospital and met the eligibility criteria were enrolled and analyzed for this study. Results are presented according to objectives. The mean age of the participants was 61±8 years with age range from 50 – 84 years. The mean BMI of the participants was 29±5.9 kg/m^2 and ranged from 17.6 to 48.87 kg/m^2. The mean femoral and spine BMD for normal individuals was 1.0±0.11 g/cm^2 and 1.22±0.144 g/cm^2 respectively.

All participants were categorized into three groups (normal, osteopenia, and osteoporosis) based on DXA findings as per WHO recommendation. The mean age of the normal, osteopenic and osteoporosis groups were 59±8yrs, 63±9yrs, and 62±9yrs respectively (Table 1). The disparity in the ages of the women in the different age categories was not significant (p = 0.193).

Table 1: Mean osteocalcin in the different bone mineral density states

Status		Age (years)	BMI	Osteocalcin (ng/ml)
Normal	Mean	59.18	30.90	12.51
	Number	28	28	28
	SD	8.14	5.95	2.46
Osteopenia	Mean	63.68	29.18	22.14
	Number	22	22	22
	SD	9.19	5.41	5.76
Osteoporosis	Mean	62.00	24.92	31.46
	Number	11	11	11
	SD	9.13	4.89	8.07

The normal group consisted of women with a T score greater than -1 SD, Osteopenia between -1 to -2.5 SD, and Osteoporosis group ≤ -2.5 SD (Table 2). Serum Osteocalcin levels for normal BMD, osteopenic and osteoporotic groups were 12.51±2.5 ng/ml, 22.14±5ng/ml and

31.46±8ng/ml respectively (Table 1). Using a one-way Analysis of Variance (ANOVA), the mean difference in osteocalcin level in these three groups was significant (P = 0.01).

Correlation between osteocalcin and Bone Mineral Density

There was a negative correlation between the serum level of osteocalcin and femoral bone mineral density (Coefficient – 0.68, P = 0.01) [Figure 2]. There was a positive correlation between the serum level of osteocalcin and spine bone mineral density, although this correlation was not significant (Coefficient 0.747, P = 0.49) [Figure 3]. There was a negative correlation between the serum level of osteocalcin and femoral neck bone mineral density T scores (Coefficient -0.55, P = 0.01) [Figure 4]. There was a negative correlation between the serum level of osteocalcin and bone mineral density T scores (Coefficient -0.7, P = 0.01) [Figure 5].

Figure 2: A scatter plot showing the correlation between femoral neck BMD and osteocalcin levels

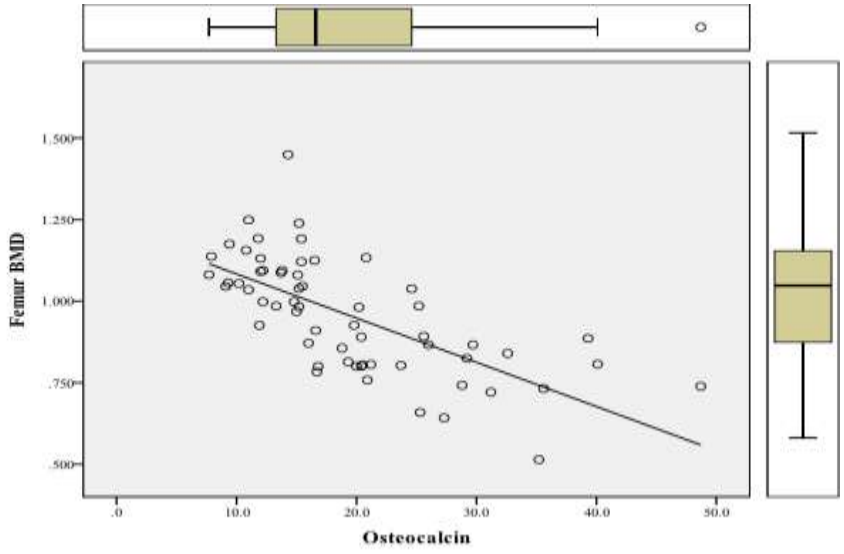


Figure 3: A scatter plot showing the correlation between lumbar spine BMD and osteocalcin levels

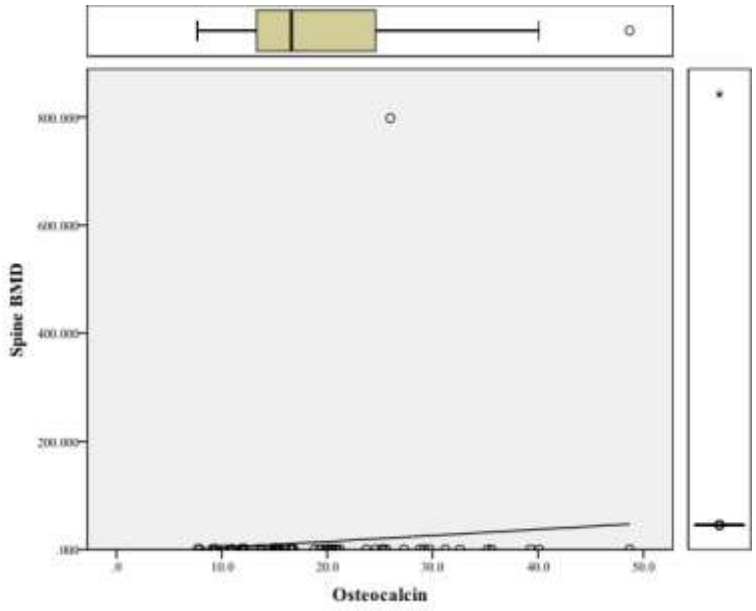


Figure 4: A scatter plot showing the correlation between femoral neck T scores and osteocalcin levels

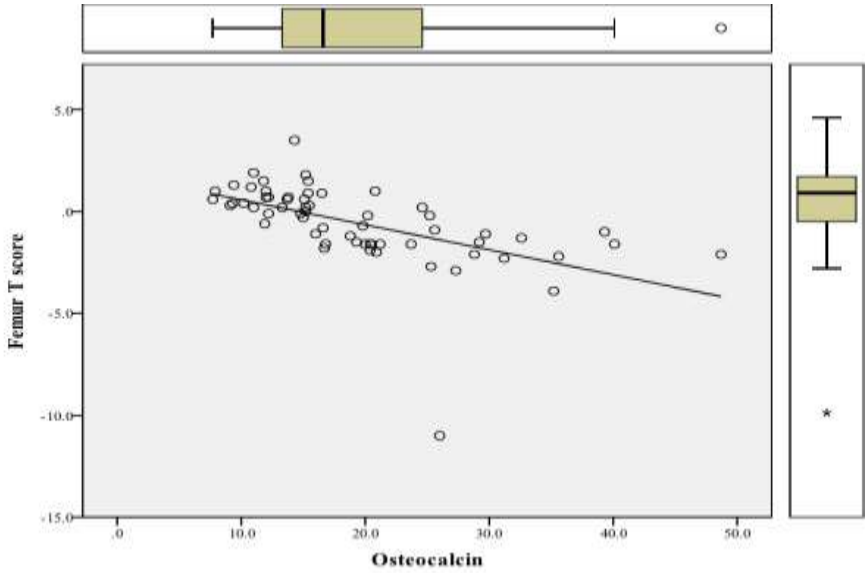
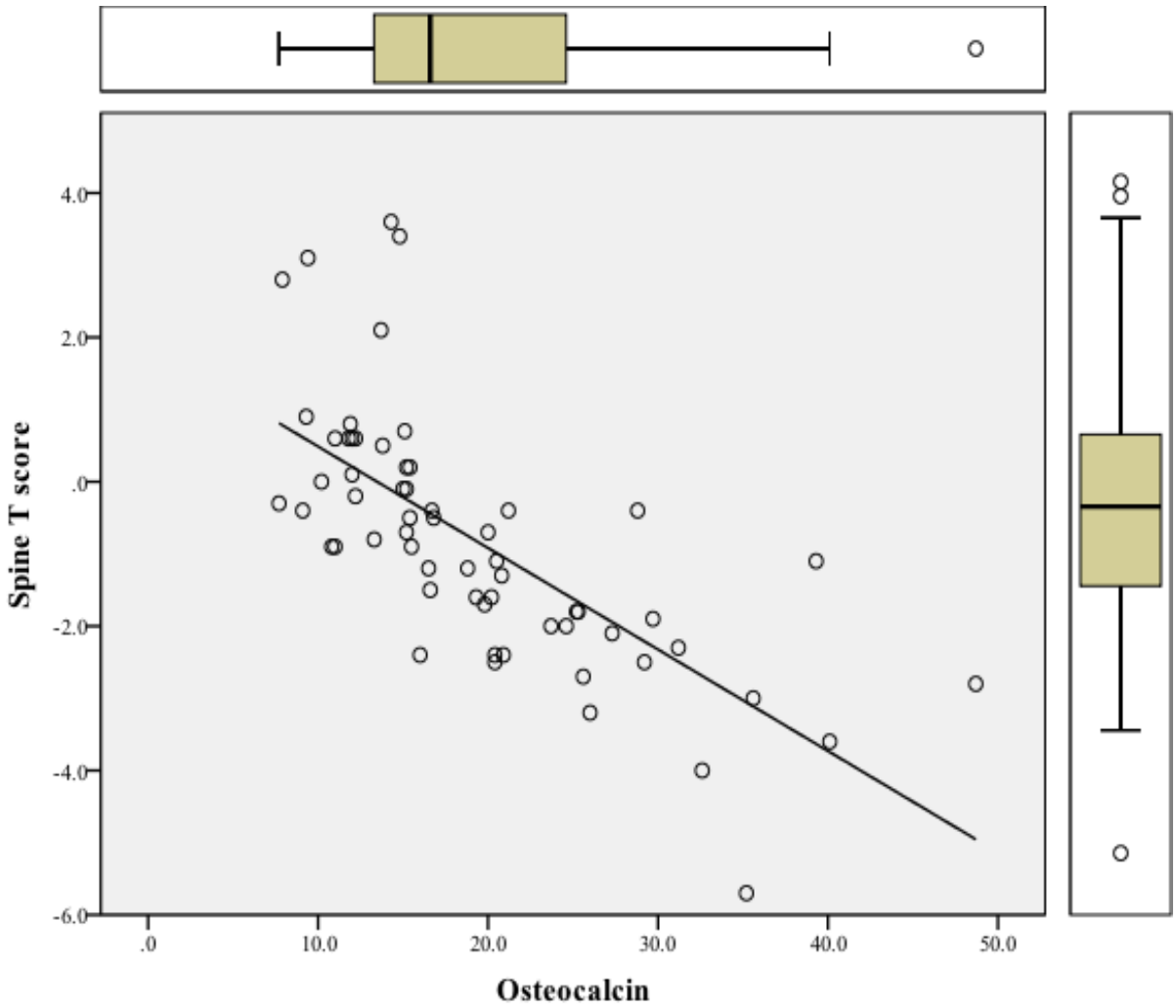


Figure 5: A scatter plot showing the correlation between spine T scores and osteocalcin levels



Osteoporosis in the sample of women

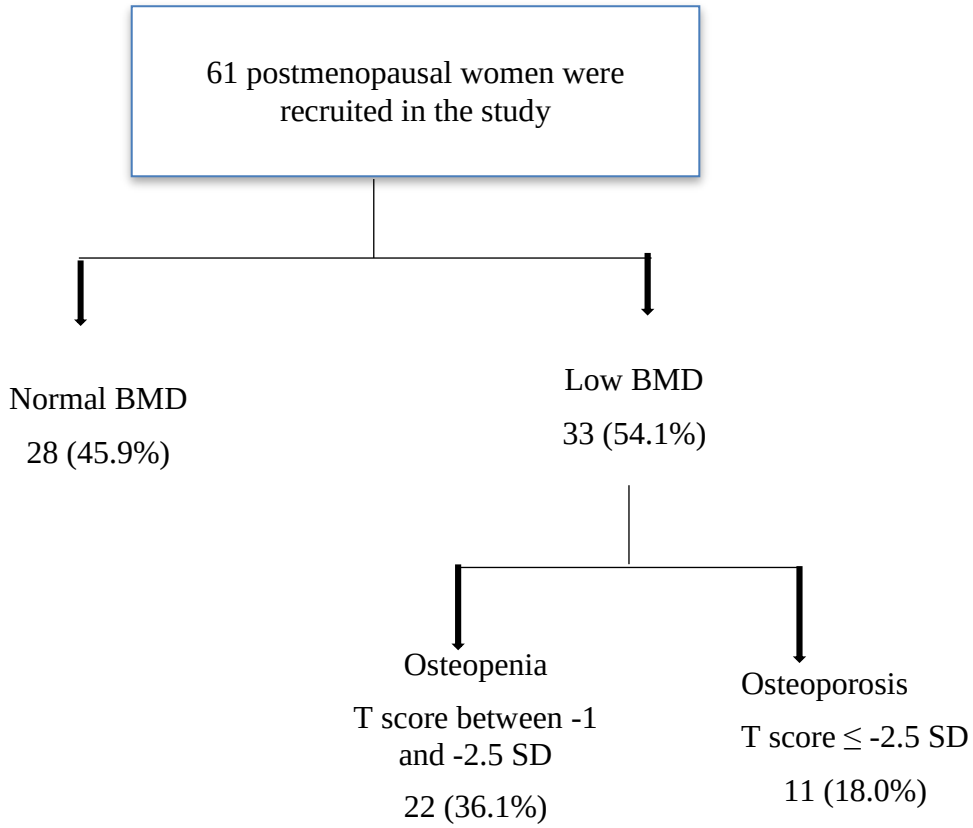
In total, Eighteen percent of the women had osteoporosis (Table 1, Figure 6). The mean age of these women was 62±9 years while their mean BMI was the lowest, that is 24±4.8. The mean difference in BMI between the osteoporotic, osteopenic and Normal women was significant (P = 0.00). Twenty-two women constituting 36.1 % were found to be osteopenic while twenty-eight (28), 45%, had the normal bone mineral density (Table 1). The mean age group for the osteopenic group was 63 ±9 years (Table 1, Figure 6). Osteocalcin levels were highest in the

osteoporotic group (Table 1).

Predictive value of Osteocalcin

Osteocalcin levels were categorized into three groups; that is ≤15.5ng/ml, 15.6 – 25ng/ml and those with ≥25ng/ml. On cross tabulation, between osteocalcin levels and the diagnosis of the women based on BMD, the levels of osteocalcin in ranges of ≤15.5ng/ml, 15.6 – 25ng/ml and those with ≥25ng/ml were positively predictive of BMD as normal, osteopenic and osteoporotic in 100%, 78% and 100% respectively (Table 4). The overall mean positive predictive value of bone mineral density is therefore 92%.

Figure 6: Proportion of women with osteoporosis among the postmenopausal in the study group



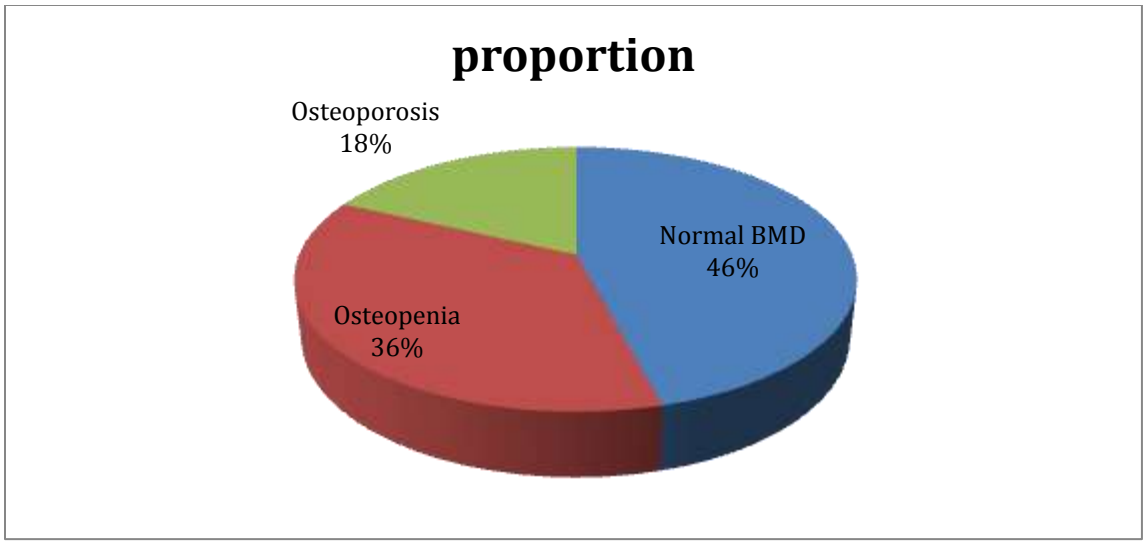


Table 2: The Mean BMD and T scores in the different bone mineral density states

Status		Femur BMD	Spine BMD	Femur T score	Spine T score
Normal	Mean	1.09	1.22	0.729	0.53
	Number	28	28	28	28
	SD	0.104	0.14	0.82	1.31
Osteopenia	Mean	0.88	1.00	-1.082	-1.45
	Number	22	22	22	22
	SD	0.112	0.09	0.92	0.68
Osteoporosis	Mean	0.75	73.29	-2.88	-3.08
	Number	11	11	11	11
	SD	0.11	240.35	2.8227	1.07

Table 3: Osteocalcin - bone density cross tabulation

		Conclusions			Total
		Normal	Osteopenia	Osteoporosis	
Osteocalcin	≤15.5	28 (100%)	0	0	28
	15.6 - 25	0	17 (78%)	0	17
	≥25.1	0	5	11 (100%)	16
Total		28	22	11	61

Table 4: Predictive values of osteocalcin in osteoporosis

		Conclusions			Total
		Normal	Osteopenia	Osteoporosis	
Recoded Osteocalcin	≤15.5	28 (100%)	0	0	28
	15.6 - 25	0	17 (78%)	0	17
	≥25.1	0	5	11 (100%)	16
Total		28	22	11	61

FRAX scores in the studied population

The result of FRAX showed that ten year's probability of hip fractures in these women ranges from 0.1 – 2.0 and increases with age. Major osteoporosis score was related to the level of BMD and T scores. Hence there is a low probability of hip fractures ages between 50-66 years compared to older women with ages 70 -73 years.

Table 5: 10 year's probability of fracture for 11 postmenopausal osteoporotic women

Age	The hip fracture probability score	Major osteoporosis score
50	0.1	1.0
51	0.1	1.1
52	0.1	1.0
58	0.4	1.9
59	0.4	2.0
59	0.4	1.6
66	0.4	2.7
70	0.7	2.8
71	1.6	4.1
73	2.0	4.5
73	2.0	5.1

CHAPTER FOUR: DISCUSSION AND CONCLUSION

4.1 Discussions

The intent of this study was to correlate Osteocalcin levels in serum with DXA findings. The outstanding objective of the research was to identify the predictive values of serum Osteocalcin levels in the diagnosis of osteoporosis in postmenopausal women at the Kenyatta National Hospital.

Osteoporosis is a debilitating skeletal disorder affecting all bones of the skeletal system. However, it is predominately seen early in trabecular bones like the proximal femur and lumbar spines than cortical diaphyseal bones. Hence, the neck of femur and lumbar spines are common areas of interest as it relates to the diagnosis of osteoporosis. These are anatomical sites that are susceptible to fragility fractures.

Numerous efforts have been made over the years in determining the BMD using the neck of femur and lumbar spine. None has been widespread and approved for use as compared to Dual Energy X-ray absorptiometry (DXA). Currently, DXA is the WHO gold standard for the diagnosis of osteoporosis. However, accessibility and affordability have been a major hindrance in using DXA as a evaluation tool for osteoporosis in many low resource settings like Kenya.

It is therefore against this backdrop that many efforts have been made recently to find the alternate marker to serve as a screening tool. Currently, none has succeeded in clearly portraying the diagnostic potential of an alternative screening tool. Most are inconsistent and unreliable with DXA findings. However, serum osteocalcin has been identified to play a dual role as a bone formation marker during treatment of osteopenia and osteoporosis and a marker of bone depreciation during osteoclastic activity. Since it is produced by osteoblast and deposited in bone matrix, during excessive bone turnover, it is released in circulation and this is quantifiable. High

osteocalcin levels have been associated with high bone turnover. This study provides the first predictive values of osteocalcin in osteoporosis. It succinctly categorizes serum osteocalcin levels in correlation with DXA findings in black postmenopausal women in Sub-Saharan Africa.

In all, the study failed to authenticate height, weight, and resulting BMI as factors that correspond with BMD levels as elucidated by other researchers. There was no remarkable disparity between normal postmenopausal women and those with low BMD. This is in consonance with what was reported by Singh et al in the Indian population.[15]

Age plays a major factor in osteoporosis. The study found significant inverse proportionality between the age of postmenopausal women and BMD levels. Higher BMD was found in younger participants while lower BMD was largely found in older women. This is similar to what was reported by other researchers.[2,8,15]

In this study, serum osteocalcin levels were increasingly high in postmenopausal women with osteopenia and higher in those with osteoporosis as per DXA findings. Hence there is also inverse proportionality. Lowest T score $\leq$ -2.5 SD was associated with the highest serum osteocalcin level $\geq$25.1 ng/ml. This clearly demonstrates that serum osteocalcin levels are predictive in osteoporosis especially in postmenopausal women.

The study tested serum osteocalcin levels for correlation with femoral BMD, Spine BMD, T score femur, and T score lumbar spine using Pearson's Correlation Coefficient. Detailed Analysis revealed a negative correlation between osteocalcin levels and femoral BMD. A negative correlation was noted between serum osteocalcin levels and T-score femur. However, there was a weak correlation between osteocalcin levels and lumbar spine T scores. Hence serum osteocalcin levels were categorized into three groups in consonance with DXA findings. Normal

femoral BMD and T scores correlated with serum osteocalcin levels ≤ 15.5 ng/ml with 100% accuracy. Osteopenia (T score from -1 to -2.5 SD) was found with serum osteocalcin level ranging from 15.6 -25 ng/ml with 78% accuracy. Osteoporosis (T score ≤-2.5 SD) was related to serum osteocalcin levels ≥25.1 ng/ml with 100% accuracy. These values are predictive and have the ability to distinguish postmenopausal women with normal BMD from women who are osteopenic and osteoporotic.

The study, therefore, suggests that these consistent predictive values of osteocalcin can be used as a screening instrument and a clinical tool in the diagnosis and screening for osteoporosis with a confidence level of 95%. It is clearly shown that only women with osteopenia and osteoporosis had high and higher serum osteocalcin level respectively. This is remarkable and therefore concurs with Singh et al in their suggestion for the use of serum osteocalcin as a screening tool.[15] This will be beneficial to low resource countries where accessibility and affordability for DXA scan still remain a hurdle in the screening of postmenopausal women for osteoporosis. It is easy to get samples of blood from remote and inaccessible areas and transport safely to laboratory settings for determination of serum osteocalcin levels. This will address many sequelae of the disease which have been found to be preventable when early diagnosis is made.

The study also found osteoporosis to be prevalent in 18% of postmenopausal women in Kenya. This is slightly lower than what was reported by Odawa et al in 2004[26]. The disparity could be due to differences in sample size, sampling and screening methods. The average 10 years probability of a hip fracture in these postmenopausal women with major osteoporosis FRAX score was 0.73 with a mean age of 62 years. This means 73% will have fragility fracture in ten years.

It is interesting to note that all postmenopausal women in this study had normal laboratory values of serum osteocalcin in medical literature. Despite these ‘normal' values, postmenopausal women with increasing levels of ≥ 15.5 ng/ml were found to be osteopenic and osteoporotic with distinct predictive values which correlated with DXA findings. It is therefore suggested that serum osteocalcin levels be adjusted to correlate with current reality in order to be utilised as an evaluation tool for osteoporosis.

However, because of the small sample size due to the limited time frame, this study agrees with previous suggestions by other researchers that more effort is needed to build the consensus for its utilization as a screening tool for osteoporosis especially in low resource settings. Large multicentre studies need to be carried out and can include a large sample size with both males and females in the population.

4.2 Conclusion

The study showed that 18% of the participants had osteoporosis and 36.1% osteopenia. This study has shown a negative correlation between serum osteocalcin levels and femoral BMD and T scores. Hence, serum osteocalcin value is predictive in osteoporosis. It also demonstrated that current normal laboratory values are associated with abnormal DXA findings. However, its increasing trend is consistent with DXA findings for normal, osteopenia, and osteoporosis. It is, therefore, appropriate to categorize serum osteocalcin levels in three different parameters to portray current realities.

4.3 Recommendations:

The following recommendations if considered will improve the screening method in low resource countries and therefore reduce the sequelae of osteoporosis such as fragility fractures by early diagnosis of the condition and institution of timely management.

1. Recoding serum osteocalcin levels as portrayed in this study to screen the population
2. DXA to be used only as a confirmation tool in people found to be osteoporotic before the initiation of treatment as suggested by previous studies. This will be beneficial to low resource communities.

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APPENDICES

Appendix 1: Consent for participation

Department of Orthopaedic Surgery

College of Health Sciences

University of Nairobi

Study Title: PREDICTIVE VALUES OF OSTEOCALCIN IN OSTEOPOROSIS AT THE KENYATTA NATIONAL HOSPITAL

Principal Investigator: DR. ROBERT GAYFLOR MULBAH

Background of the Study: Osteoporosis, a condition associated with bone weakening is becoming a serious problem in Kenya especially among the postmenopausal women, women 50 years and above. If it's not diagnosed early through screening, many people with the condition may get fractures from trivial fall or hit. Currently, the only standard means of screening people is Dual Energy X-ray Absorptiometry (DXA). It's not affordable and available for everyone in Kenya and many low resourced countries because of the cost and the quantity. Therefore, this study is aimed at finding another means of screening that will be affordable and available for our setting. It's about comparing DXA findings with the bone maker called Osteocalcin; so as to determine the predictive value of Osteocalcin in Osteoporosis

Broad Objective: To correlate Osteocalcin level with DXA scans in the diagnosis of osteoporosis in postmenopausal women as well as assess fracture risk using bone mineral density (BMD).

Informed Consent: I have been informed by Dr. Robert Gayflor Mulbah that he is conducting a study on the predictive values of osteocalcin in osteoporosis at the Kenyatta National Hospital. This study is being conducted as partial fulfillment for the award of a degree in Master of Medicine in the Department of Orthopaedic Surgery at the University of Nairobi. By this form, written consent is being sought for my participation in the study.

My rights as a research participant: This form provides adequate information to me about this study for participation. When I agree to participate, I will be asked to sign at the end of the form to prove my consent. A copy of the signed form will be given to me to keep as my record. I understand that my participation in this research is entirely voluntary. I may decide to quit the study at any time. My decision will not affect my medical care or possible participation in future research studies in any form or manner.

Purpose and method of the study: The purpose of the study is to obtain information that will be used to determine the diagnostic potential of Osteocalcin. The information will help clinicians in making early and better diagnoses of osteoporosis in low resourced countries like Kenya in the future and as such improve medical care for future patients. The study will involve clinical assessment by the investigator at the Kenyatta National Hospital. I will then be recruited and transported to Medanta AfriCare in Westlands for DXA scan at no cost to me. A blood sample will be taken from me for determination of my bone quality by the investigator.

Risks to me: I understand that there are no added risks attributable to the study besides those associated with the investigations such as minor pain during the drawing of my blood.

Potential benefits to me: I shall not be required to make any payments towards the study. I will be transported at no cost to me as well as get free investigations. I will get information about

the status of my bones and the management required to prevent complications such as broken bone. I shall not be paid for any investigations related to this study.

Right of withdrawal: I also know that I can opt out of the study at any time. This will not interfere with my right for treatment at this facility and the right to participate in future research.

Confidentiality: A study number is known to me and the study personnel will be used instead of my name on the data collection sheet and samples. Personal and medical information about me will not be released to anyone other than the following without my permission: authorized study personnel, Department of Orthopedic Surgery, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (KNH-UoN ERC).

Ethical Issues: If I have any questions or concerns regarding ethical issues during my participation in this research, I have the right to contact the Kenyatta National Hospital-University of Nairobi Research and Ethics Committee through its secretary:

Prof. M. L. Chindia,

Secretary, KNH/UoN-ERC,

Kenyatta National Hospital

P.O.Box 20723, Nairobi

Tel: (020) 2726300

If I have any questions at any time regarding the study, I also have the right to contact the Principal Investigator: Dr. Robert Gayflor Mulbah

Department of Orthopedic Surgery

Tel: +254702500967 Email: robmulbah1@gmail.com

DECLARATION OF CONSENT

I _____, hereby consent to take part in the research to be carried out by Dr. Robert Gayflor Mulbah. By this consent, I've agreed that my participation is voluntary.

Signature/thumb print: _____

Date: _____

Where applicable

Next of Kin _____

Date: _____

Appendix 2: Translated Consent form (Swahili)

IDHINI YA KUSHIRIKI

IDARA YA UPASUAJI WA ORTHOPEDIKI

CHUO CHA SAYANSI ZA AFYA

CHUO KIKUU CHA NAIROBI

Kichwa cha Utafiti: VIDOKEZO VYA MAFUNZO YA OSTEOCALCIN KATIKA OSTEOPOROSIS KATIKA HOSPITALI KENYATTA NATIONAL

Mtafiti Mkuu: DKT. ROBERT GAYFLOR MULBAH

Usuli ya Utafiti: Osteoporosis, hali inayohusishwa na kudhoofisha mfupa ni kuwa shida kubwa nchini Kenya hasa kati ya wanawake wa postmenopausal, wanawake wa miaka 50 na zaidi. Ikiwa haipatikani mapema kupitia uchunguzi, watu wengi wenye hali wanaweza kupata fractures kutoka kuanguka kidogo au kugonga. Hivi sasa, njia pekee ya kawaida ya kuchunguza watu ni Dual Energy X-ray Absorptiometry (DXA). Haina bei nafuu na inapatikana kwa kila mtu nchini Kenya na nchi nyingi za chini kwa sababu ya gharama na wingi. Kwa hiyo, utafiti huu una lengo la kutafuta njia nyingine ya uchunguzi ambayo itakuwa nafuu na inapatikana kwa kuweka yetu. Ni kuhusu kulinganisha matokeo ya DXA na mtengeneza mfupa aitwaye Osteocalcin; ili kuamua thamani ya predictive ya Osteocalcin katika Osteoporosis

Funya mfunga: Kuunganisha kiwango cha Osteocalcin na uchunguzi wa DXA katika ugonjwa wa ugonjwa wa osteoporosis katika wanawake wa postmenopausal na pia kutathmini hatari ya fracture kwa kutumia wiani wa madini ya mfupa (BMD).

Nidhamu iliyojulikana: Nimeambiwa na Dk. Robert Gayflor Mulbah kwamba anafanya utafiti juu ya maadili ya utabiri wa osteocalcin katika osteoporosis katika Hospitali ya Kenyatta ya Taifa. Utafiti huu unafanyika kama utimilifu wa sehemu kwa ajili ya tuzo ya shahada katika Mwalimu wa Dawa katika Idara ya Upasuaji wa Orthopedic katika Chuo Kikuu cha Nairobi. Kwa fomu hii, idhini iliyoandikwa inatafutwa kwa kushiriki kwangu katika utafiti.

Haki zangu kama mshiriki wa utafiti: Fomu hii inanipa habari za kutosha kuhusu utafiti huu kwa kushiriki. Ninapokubali kushiriki, nitaulizwa kuingia mwisho wa fomu ili kuthibitisha idhini yangu. Nakala ya fomu iliyosainiwa nitapewa kushika kama rekodi yangu. Ninaelewa kuwa ushiriki wangu katika utafiti huu ni kikamilifu kwa hiari. Naweza kuamua kuacha kutoka kwenye utafiti wakati wowote. Uamuzi wangu hautathiri huduma yangu ya matibabu au ushiriki iwezekanavyo katika masomo ya utafiti ujao kwa namna yoyote au namna yoyote.

Kusudi na mbinu ya utafiti: Kusudi la utafiti ni kupata taarifa ambayo itatumika kutambua uwezekano wa uchunguzi wa Osteocalcin. Taarifa itasaidia waganga kufanya maambukizi mapema na bora ya ugonjwa wa kutosha kwa ugonjwa wa osteoporosis katika nchi za chini kama Kenya katika siku zijazo na hivyo kuboresha huduma za matibabu kwa wagonjwa wa baadaye. Utafiti huo utahusisha tathmini ya kliniki na uchunguzi katika Hospitali ya Taifa ya Kenyatta. Mimi kisha kuajiriwa na kusafirishwa kwenda Medanta AfriCare katika Westlands kwa DXA Scan bila gharama kwangu. Sampuli ya damu itachukuliwa kutoka kwangu kwa uamuzi wa ubora wangu wa mfupa na uchunguzi.

Hatari kwangu: Ninaelewa kuwa hakuna hatari zilizoongeza kutokana na utafiti isipokuwa wale waliohusishwa na uchunguzi kama vile maumivu madogo wakati wa kuchora damu yangu.

Faida za uwezekano kwangu: Mimi si lazima kufanya malipo yoyote kuelekea utafiti. Nitafirishwa kwa gharama nafuu na kupata uchunguzi wa bure. Nitapata taarifa kuhusu hali ya mifupa yangu na usimamizi unaohitajika ili kuzuia matatizo kama vile mfupa uliovunjwa. Siwezi kulipwa kwa uchunguzi wowote unaohusiana na utafiti huu.

Haki ya kujiondoa: Mimi pia ninajua kwamba ninaweza kuondoka katika utafiti wakati wowote. Hii haitaingilia haki yangu ya matibabu katika kituo hiki na haki ya kushiriki katika utafiti ujao.

Usiri: Nambari ya kujifunza inayojulikana kwangu na wafanyakazi wa utafiti watatumika badala ya jina langu kwenye karatasi ya kukusanya data na sampuli. Maelezo ya kibinafsi na ya matibabu kuhusu mimi hayatatolewa kwa mtu yeyote isipokuwa yafuatayo bila ruhusa yangu: wafanyakazi wenye utafiti wenye mamlaka, Idara ya Upasuaji wa Orthopediki, Hospitali ya Taifa ya Kenyatta-Chuo Kikuu cha Nairobi na Maadili ya Utafiti (KNH-UoN ERC).

Masuala ya Kimaadili: Ikiwa nina maswali yoyote au wasiwasi kuhusu masuala ya kimaadili wakati niliposhiriki katika utafiti huu, nina haki ya kuwasiliana na Kliniki ya Taifa ya Kenyatta-Chuo Kikuu cha Utafiti na Maadili ya Nairobi kwa njia ya katibu wake:

Prof. M. L. Chindia,

Katibu, KNH / UoN-ERC,

Hospitali ya Taifa ya Kenyatta

P.O.Box 20723, Nairobi

Simu: (020) 2726300

Ikiwa nina maswali yoyote wakati wowote kuhusu utafiti, mimi pia nina haki ya kuwasiliana na Mpelelezi Mkuu:

Dkt Robert Gayflor Mulbah

Idara ya Upasuaji wa Orthopediki

Simu: +254702500967

Barua pepe: robmulbah1@gmail.com

TAMKO LA IDHINI

Mimi _____, hapa napenda kushiriki katika utafiti uliofanywa na Dkt Robert Gayflor Mulbah. Kwa idhini hii, nimekubaliana kuwa ushiriki wangu ni wa hiari.

Kuchapishwa saini / kidole: _____

Tarehe: _____

Ambapo husika

Karibu na Kin _____

Tarehe: _____

Appendix 3: Data Collection Tool

Department of Orthopaedic Surgery

College of Health Sciences

University of Nairobi

Assigned ID#: _____ Date: _____

1) Age :_____ Date of Birth _____

2) Sex:_____ Weight (KG) _____

3) Height_____ Occupation _____

4) BMI _____ phone #: _____

5) HX of previous fracture: Yes ( ) No ( )

6) HX of fractured hip among parents: Yes( ) No ( )

7) Currently smoking : Yes ( ) No ( )

8) Glucocorticoid use: Yes ( ) No ( )

9) Rheumatoid Arthritis: Yes ( ) No ( )

10) Alcohol consumption: Yes ( ) No ( )

11) Femoral Neck BMD (g/cm^3): _____

12) Serum Osteocalcin level (ng/ml): _____

*Adopted from FRAX TOOL

Appendix 4: Budget

Item	Unit cost	Number	Cost
Serum Osteocalcin	2,999	61	182,939
DXA Scan	3,000	61	183,000
Ethics Committee	2,000	1	2,000
Statistician	30,000	1	30,000
Research Assistants	10,000	2	20,000
Printing and binding	9,000	1	9,000
Transportation	28,000	1	28,000

Total = 454,939 KSH ($4,549)

Appendix 5: Implementation Time Table

Task performed	**Estimated Time**
Proposal development	October 2017-January 2018
Proposal submission to the department	February 2018
First submission to KNH-UoN ERC	February 2018
Resubmission to KNH-UoN ERC	April 2018
Approval by KNH-UoN ERC	May 2018
Pretesting and training of assistants	May 2018
Data collection	May 2018 – June 2018
Dissertation writing	June 2018 – July 2018
Dissertation presentation	July 2018