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ELEVATED SERUM OSTEOCALCIN LEVELS AS A SURROGATE MARKER OF PRIMARY OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN
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ABSTRACT

Background: **Primary osteoporosis is increasingly becoming a major public health concern in African populations. Complications arising from this condition can be catastrophic; ranging from hip fractures to lumbar spinal injuries. Early diagnosis and prevention are useful in mitigating its effects. The Dual Energy X-ray Absorptiometry (DXA) scan is not a widely affordable and accessible diagnostic tool to many in our setting. There is need for an alternative, affordable and accessible marker for early screening of osteoporosis.**

Objective: **To correlate serum osteocalcin level with DXA findings in the diagnosis of osteoporosis in postmenopausal women.**

Design: **This was an analytical cross-sectional study.**

Setting: **Orthopaedic outpatient clinic of the Kenyatta national Hospital.**

Participants: **61 postmenopausal women aged 50 years and above were assessed for both neck of femur and lumbar vertebrae DXA bone mineral density and serum osteocalcin levels.**

Results: **Twenty-eight (46%), 11 (18%) and 22 (36%) women had normal, osteoporotic and osteopenic bone mineral density levels respectively. Serum Osteocalcin levels for normal, osteopenic and osteoporotic groups was 12.51±2.5 ng/ml, 22.14±5ng/ml and 31.46±8ng/ml respectively (p=0.00). There was a negative correlation between osteocalcin levels and DXA femoral neck bone mineral density (Coefficient – 0.68, P = 0.00). Women with Osteoporosis (T-score ≤ -2.5 SD) consistently had osteocalcin levels of ≥ 25.1 ng/ml.**

Conclusion: **Serum Osteocalcin levels are predictive of DXA findings and elevated levels can be considered as a surrogate marker of primary osteoporosis in postmenopausal women.**

INTRODUCTION

Osteoporosis poses a major public health challenge worldwide with Africa being no exception. Fragility fractures are increasingly becoming a burden in African countries [1, 2]. In Kenya alone, there were 245/100,000 hip fractures attributable to osteoporosis [1]. Currently, there is paucity of data on osteoporosis in Africa. There is no existing screening method for osteoporosis due to limited accessibility and affordability of diagnostic equipment.

DXA densitometer is a radiological device that utilizes two X-ray beams with very low radiation of about a tenth of that of a standard chest X-ray on the patient's body to determine BMD [3, 4]. It targets specific aspects 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 lumbar vertebrae. Peripheral DXA Device targets forearm and is rarely used. Bone mineral density is classified as normal, osteopenia and osteoporosis where T score are less than -1 SD, -1 to -2.5 SD, and -score ≤ -2.5 SD respectively.

Osteocalcin is the most reliable bone turnover marker because of its tissue specificity, wide availability, and relatively low variations [5]. Its serum level rises in rapid bone turnover. Therefore, it is currently used to monitor efficacy of anti-resorptive drug in the management of osteoporosis [6]. Several authors have further sought to establish its role in the diagnosis and screening of osteoporosis [7, 8]. Findings of these studies have largely been inconclusive, with mixed results. The aim of this study is to correlate the serum levels of osteocalcin with bone mineral density, in view to elucidate the predictive value of osteocalcin in primary osteoporosis.

MATERIALS AND METHODS

Sixty-one consenting post-menopausal women were randomly recruited from the orthopaedic outpatient clinic of the Kenyatta National hospital from January 2018 to March 2018 into this study after institutional ethical approval. Women with metabolic bone diseases, fractures, tumors, with any existing medical condition, history of tuberculosis and renal disorders were excluded. After collecting their biodata, a 5 ml Blood sample was taken from each participant by the principal investigator, centrifuged and stored at -20^{0}C. These blood samples were coded and subsequently analyzed using ELISA, marked by monoclonal antibodies targeting human osteocalcin antigens by a certified laboratory technician. The amount of substrate turnover was determined colorimetrically by measuring the absorbance which was proportional to the human osteocalcin concentration. The detection range of the kit was 4 - 64ng/ml, with a sensitivity level of 0.31. Simultaneously each patient underwent bilateral femur neck and lumbar vertebrae DXA scans using Lunar Prodigy pro GE™ bone scanners. The patient's biodata, serum osteocalcin and bone mineral density were collated, decoded and entered into SPSS® version 25 and analyzed using one-way ANOVA and Pearson's correlation test. A p value of ≤ 0.05 was considered significant.

RESULTS

The age range of the participants was 50 to 84 years with a mean of 61±8 years. Participants BMD 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 difference in the ages of the women in the different age groups was not significant (p = 0.193). Serum Osteocalcin levels for normal, osteopenic and osteoporotic groups was 12.51±2.5 ng/ml, 22.14±5ng/ml and 31.46±8ng/ml respectively (p=0.00).

Table 1

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

Status		BMD		T Scores		BMI	Age
		Femur	Spine	Femur	Spine		
Normal n=28	Mean	1.09	1.22	0.729	0.53	30.90	59
	SD	0.104	0.14	0.82	1.31	5.95	8
Osteopenia n=22	Mean	0.88	1.00	-1.082	-1.45	29.18	63
	SD	0.112	0.09	0.92	0.68	5.41	22
Osteoporosis n=11	Mean	0.75	73.29	-2.88	-3.08	24.92	62
	SD	0.11	240.35	2.8227	1.07	4.89	11

There was a negative correlation between the serum level of osteocalcin and femoral bone mineral density (Coefficient – 0.68, P = 0.00) [Figure 1]. Serum level of osteocalcin levels correlate negatively with spine bone mineral density T scores (Coefficient -0.7, P = 0.00) [Figure 2].

Figure 1: A scatter plot showing the correlation between femoral neck BMD and osteocalcin levels

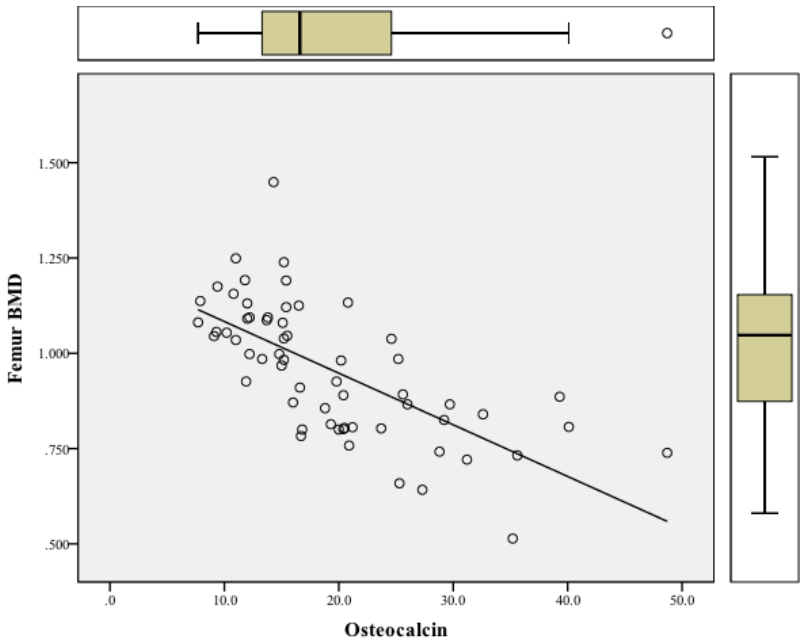
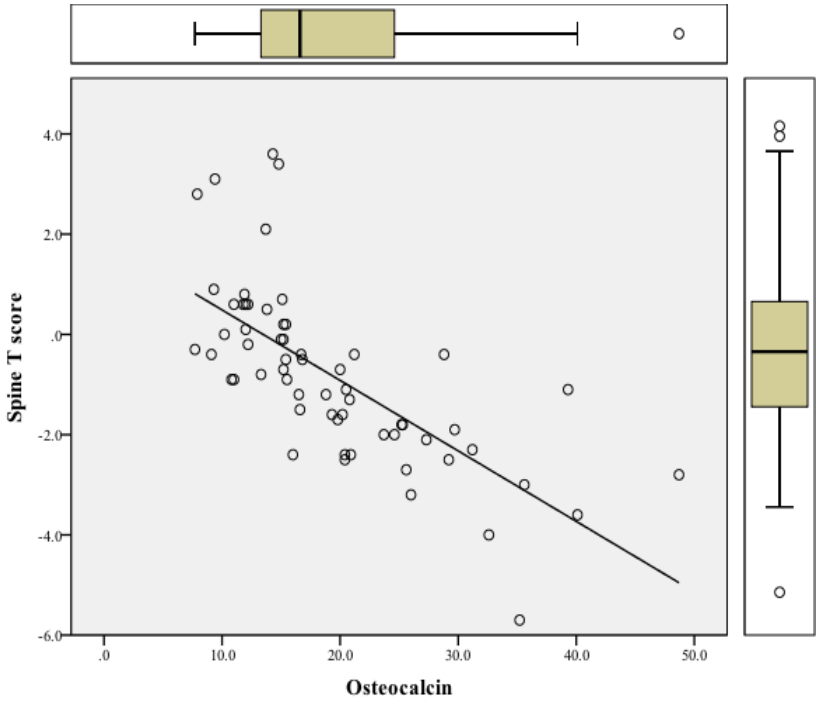


Figure 2: A scatter plot showing the correlation between spine T scores and osteocalcin levels



Osteocalcin levels were recoded 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 2). The overall mean positive predictive value of bone mineral density is therefore 92%.

Table 2

Predictive values of osteocalcin in osteoporosis

		Bone Mineral Density			Total
		Normal	**Osteopenia**	**Osteoporosis**	
Osteocalcin (ng/ml)	≤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**

DISCUSSION

In this study, there was a negative correlation between the serum osteocalcin levels and bone mineral density. In as much as the readings were within the normal laboratory reference levels, these levels were high in postmenopausal women with osteopenia and higher in those with osteoporosis. Similar observations were made by other authors [7, 8]. In our study the serum level of osteocalcin in the osteoporotic group was ≥25.1ng/ml. This level was higher than the 16.1 ng/ml

described in the study by Kalaeselvi et al (2013) and 22.2 ng/ml described by Singh et al (2015). These two Indian studies were case control studies which focused on two main groups, osteoporotic and non-osteoporotic women groups. In the current study, all participants were postmenopausal, with the bone mineral density and osteocalcin levels determined separately as part of the study. Because the bone mineral density is a known gold standard determinant of osteoporosis, it was compared to osteocalcin to ascertain the correlation. Additionally, this study also demonstrated that the serum osteocalcin levels of ≥ 25.1 ng/ml are predictive of osteoporosis in postmenopausal women, with an overall predictive value of 92%.

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. It is clearly shown that only women with osteopenia and osteoporosis had high and higher serum osteocalcin level. This is remarkable and therefore buttresses the previous suggestion by Singh et al (2015) for the use of serum osteocalcin as a screening tool [7]. This can be beneficial in low resourced countries where accessibility and affordability for DXA scans still remain a hurdle in the screening of postmenopausal women for osteoporosis.

It is interesting to note that all postmenopausal women in this study had normal laboratory values of serum osteocalcin. Despite these 'normal' values, postmenopausal women with increasing levels ≥ 15.5 ng/ml were found to be osteopenic and osteoporotic with distinct predictive values which correlated with DXA findings. There is therefore need to recalibrate the reference levels of osteocalcin in different physiologic states. However, because of the small sample size due to financial constraints, 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 resourced settings. Large multicenter studies need to be carried out including both males and females. In conclusion, there is a negative correlation between serum osteocalcin levels and femoral BMD and T scores. Hence, serum osteocalcin value is predictive in osteoporosis.

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