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Bone Loss in Black South African women: Transition from Perimenopause to Menopause

Lineo Matsela[1,*], Olakunle A. Towobola[2] , Ephraim T. Mokgokong[1]

[1] Department of Obstetrics & Gynaecology, School of Medicine, Sefako Makgatho Health Sciences University, Pretoria, South Africa

[2]Department of Internal Medicine, School of Medicine, Sefako Makgatho Health Sciences University, Pretoria, South Africa

* Corresponding author

Email: lineomatsela@yahoo.com（Lineo Matsela）

ABSTRACT

Objective: Loss of bone mineral density follows as a consequence of hormonal changes, as women transit from perimenopause to menopause. This study investigated the effect of such a transition on bone demineralisation among Black South African women.

Methods: Two groups of women stratified by their menstrual history into perimenopause (n = 28) and postmenopause (n = 32), were enrolled for the study. Each of the study participants had her Body Mass Index (BMI) determined and a sample of blood was taken and analysed for follicle stimulating hormone (FSH). Bone mineral density was assessed for the hip bone using the Dual-Energy X-ray Absorptiometry machine (DEXA; Hologic 4500).

Results: The mean age (± SD) of perimenopausal women was 44.6 years (± 3.6) compared with 63.4 years (± 7.2) for postmenopausal women. There was no statistical significant

difference in the BMI of women in the two groups ($p = 0.4671$) and the serum FSH concentration of 46 to 100 mIu/mL (mean = 78 mIu/Ml; ± 0.69) confirmed the status of postmenopause. The negative slope of the change in hip BMD amongst perimenopausal women (-0.0006) translates to BMD loss of 0.06% per annum. This compares with hip BMD loss of -0.0025 (i.e. BMD loss of 0.25%/annum) amongst the postmenopausal women. This represents a 4-fold loss of BMD in postmenopausal compared with perimenopausal women.

Conclusions: This study provides evidence that black South African women would begin to experience loss of bone mineral density of the hip in their transition from perimenopause to postmenopausal state.

Keywords: Bone Mineral Density; perimenopause; postmenopause, Dual Energy Absorptiometry

Introduction

Osteoporosis is a skeletal disorder characterised by compromised bone strength, predisposing to an increased risk of fracture [(1)]. Bone strength reflects the integration of two main features: bone density and bone quality [(1)]. Bone strength is highly correlated with its mass and mineral content [(2)]. Factors that are associated with both bone density and quality are race, age and gender, reproductive history, body build, genetic factors and dietary factors. According to Melton et al., there are three fracture sites that are particularly characteristic of osteoporosis, namely the vertebrae, femoral neck and radius, and they constitute an enormous public health problem in developed countries [(3)].

One third of all women over the age of 65 years have one or more vertebral fractures which may be associated with severe and sometimes prolonged pain, spinal deformity and loss of height [(2)]. Hip fracture, which affects one in three women who survive to extreme old age, has a mortality at 6 months of around 12 – 20% and results in increased incapacitation and/or hospitalisation in the majority of survivors [(3)]. The life-time risk of Colles fracture after the age of 50 years is no different from that of hip fracture, and although these fractures have less devastating effects on the patients, they require out-patient hospital treatment and do create considerable inconvenience [(4)]. Age is associated with an increased incidence of bone fragility fractures. There is an exponential increase in hip and vertebral fractures in Western

countries [2]. This exponential increase does not occur in other countries, examples being New Zealand, where both men and women have similar hip fracture incidence rates [5, 6], while the rates are higher among the black South African men compared to Black South African women [7]. This information on black South African women is out-dated, considering the fact that the report is over 30 years old and that it does not take into account recent developments, which include urbanisation. Reports based on the hip bone cannot be extrapolated to vertebral and other fractures[8]. The literature suggests that osteoporotic fractures are less prevalent among Afro-Americans in the US compared to Caucasians [9]. Comparison of the bone mineral density between Caucasians in South Africa and the US, as well as blacks in South Africa and the US, suggests a greater bone strength in people of black African descent in both countries when compared to Caucasians [10]. This is further strengthened by a Cape Town study which also showed that bone mineral density was higher among black women compared to Coloured women in a large sample of premenopausal women [10]. A study by Kruger and associates further suggests a high prevalence of osteoporosis among black South African women in North West Province [11]. A study by Matsela and Co-workers [12] which was published in 2017, has also highlighted the prevalence of osteoporosis among black South African women, in Odi, Soshanguve and Garankuwa districts of Pretoria. These two studies have provided unequivocal evidence of the occurrence of osteoporosis in black South African women.

During the early years of life, from birth to approximately 20 years, formation and mineralisation of bone occur. Between the ages of 20 and 39 years, optimisation and maintenance of peak bone mass occur and from ages of 39 to 59 years, the menopausal transition occurs – a shift in ovarian hormone concentration and the eventual predominance of bone resorption. From about the age of 60 to 79 years of age, a substantial number of women are at risk of osteoporosis, primarily because of bone resorption. At 80 years of age, osteoporosis becomes more evident in many postmenopausal women, with bone mineral loss, matrix deterioration, increasing fragility and the presence of co-morbid conditions [13].

Currently, there is good evidence to support the hypothesis that growth trajectory may be programmed in utero or during very early postnatal life, and that environmental factors at this stage in development, may influence peak bone mass and later bone loss and thus the increased risk of osteoporosis in later years. Programming is the term used to describe persisting changes in structure and function caused by environmental stimuli during critical periods of early development [14, 15]. Poor nutrition during intrauterine life can lead to permanent damage during rapid cell division. This is one of the mechanisms by which poor

nutrition may permanently programme the body [15]. There is evidence that weight in infancy is a determinant of bone mass in adulthood [16, 17].

Delayed menopause is associated with a positive effect on the bone. It promotes high bone mineral density and reduced risk of hip fracture in older women [18]. On the other hand, premature menopause or surgical menopause is associated with reduced bone mass and an increased risk of fracture [18].

This study was conceptualised to investigate the effect of transition from perimenopause to menopause on bone demineralisation among Black South African women and to assess the rate of bone loss during this transition.

Methodology

The study was approved by the institutional ethics committee of Sefako Makgahto Health Sciences University and each of the women signed an informed consent form to participate in the study. Before commencement of the study, each participant was re-interviewed to reinforce the following information in addition to the information given during their participation in the previous study.

1. Previous occurrence of fractures
2. Family history of fractures
3. Life style of the participants – establishing whether they smoked or drank alcohol.
4. Drug usage history to exclude corticosteroid therapy, use of highly active anti-retroviral drugs or anti-epileptic drugs.
5. Presence of chronic diseases such as diabetes mellitus or hypertension.

The participants were among women who had participated in a previous study titled "Knowledge and attitude of black South African women toward menopause: the impact of culture and traditions" [19]. The participants were transported in groups of four to the Department of Physiology at the Steve Biko Hospital in Pretoria (South Africa) where the bone mineral density were performed. Each of the women had their height measured, and were weighed on an electronic scale. Body Mass Index was calculated for each participant by dividing weight by height m^2.

The anthropometric measurement was followed by an evaluation of the bone mineral density using the Dual Energy X-ray Absorptiometry (DEXA, Hologic 4500) machine. Blood sample

was taken from each women to investigate the serum levels of follicle stimulating hormone (FSH).

The study population consisted of two groups of women - twenty-eight perimenopausal women (participants who were menstruating with episodes of amenorrhea between three months but less than twelve months and thirty-two menopausal women (participants who had not menstruated for 12 months or more. Data from the study were analysed using SPSS (Statistical Package for Social Sciences, version 21.0). Descriptive statistics were used to describe the data with frequencies, cross tabulations. A one-way ANOVA test was carried out for inferential analysis and p-value ≥0.05 was noted to be statistically significant. Linear regression was performed to reflect the relationship of ages of the participants to a changing trend in the loss of BMD of the hip.

Results

The ages of the participants ranged from 38 to 54 years (perimenopausal women) as compared with a range of 43 – 77 years for postmenopausal women with a mean (± SD) of 45.8 (± 4.0) for perimenopuasal and 58.9 (± 9.3) for postmenopausal women (Table 1). The Table also shows that

Table 1: Age and anthropometric evaluation of participants

Variables		Perimenopausal women	Postmenopausal women	p-values
Age (yrs):	Range	38 – 54	43 – 77	
	Mean	45.8	58.9	< 0.0001
	SD	4.0	9.3	
				0.0245
Weight (Kg):	Range	52 – 167	49 – 122	
	Mean	94.2	78.3	
	SD	30.2	16.9	0.0182
Height (cm):	Range	145 – 182	135 – 175	0.9833
	Mean	163.1	158.0	
	SD	7.5	8.2	

BMI:	Range	17.1 – 51.0	25 – 44.8	
	Mean	31.6	31.4	
	SD	6.9	6.7	

Key: SD = standard deviation, BMI = Body Mass Index

In Table 2, the serum concentration of FSH among perimenopausal women range from 7 – 34 mIu/mL with a mean (± standard deviation) of 20 mIu/mL (± 0.66). This compared with postmenopausal women with FSH concentration ranging from 46 – 100 mIu/Ml and a mean (± SD) of 78.0 mIu/mL (± 0.69). The increase in the FSH values between perimenopausal and postmenopausal women was statistically significant ($p < 0.0001$).

Table 2: Serum FSH levels and Bone Mineral Density of the hip bone [perimenopausal versus postmenopausal women]

Variables	Perimenopausal women [n = 28]	Posrmenopausal women [n = 32]	p-value
Serum FSH (mIu/ml)			
Range	7.0 – 34.0	46.0 – 100.0	
Mean	20.0	78.0	<0.0001
SD	0.66	0.69	
DEXA (T-scores) for BMD of the Hip: (WHO normal value: ≥ 1.0)			
Range	0.855 – 1.388	0.626 – 1.411	
Mean	1.088	0.967	0.1064
SD	0.123	0.165	
T-score < 1.0	6 (21.4%)	20 (62.5%)	0.0284

DEXA results obtained from hip bone densitometry were expressed based on the WHO recommended T-scores for the hip. In this series, although the average T-scores for perimenopausal and postmenopausal women did not yield any statistical significant difference, it was noted that women in the postmenopausal group were 3-times more likely to have T-scores below the recommended WHO normal, when compared with their perimenopausal women.

The graphic below portrays the trend of change in BMD with age for perimenopausal women. The notations in the formula; y = -0.0006X + 1.0845 for perimenopausal women only, indicate the following:

Y = is the vertical axis, that is BMD (hip) in gram/cm^2

-0.0006 indicates the negative slope of the trendline/change. In terms of BMD (hip), this change in slope indicates that the BMD (hip) in average reduces by about 0.06% each year for a woman in the subject population.

x = is the horizontal axis, that is age in years.

1.0845 – this is an intercept of the trendline/slope and the vertical axis, y (BMD - hip)

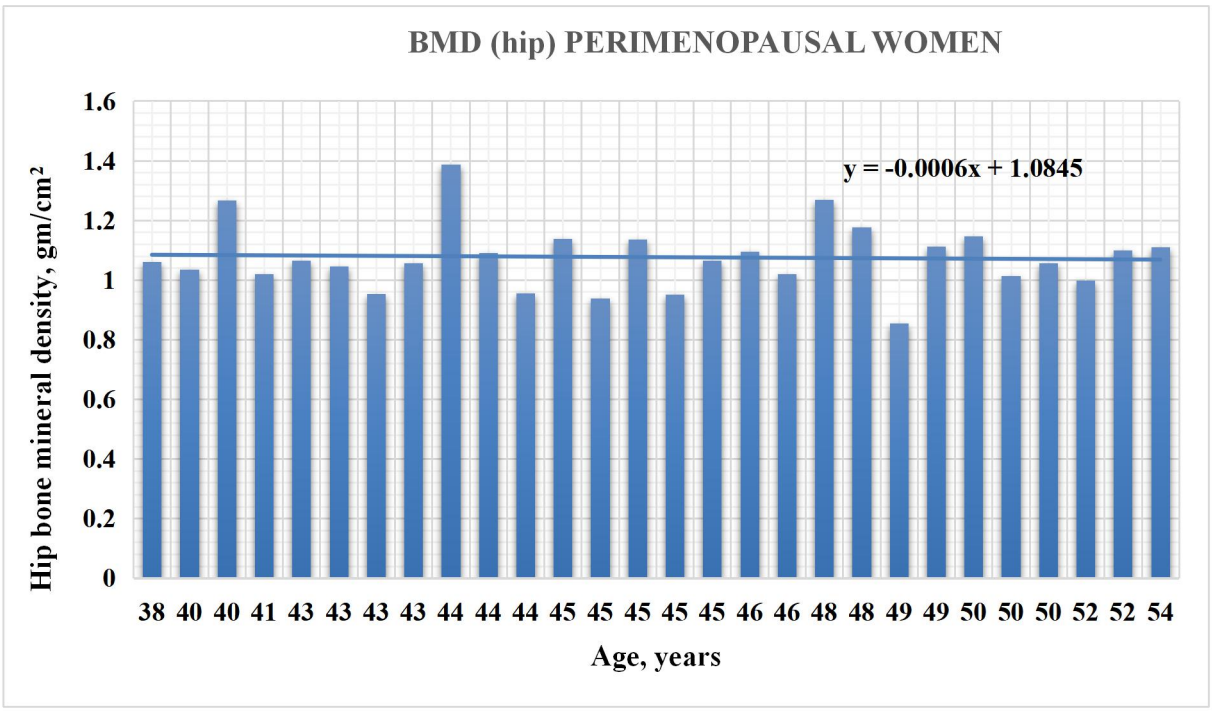

Figure 1: Graph depicting bone demineralization in perimenopausal women

Figure 2 below shows the trend of change in BMD with age for menopausal women. The notations in the formula; y = -0.0025X + 1.008 for menopausal women only, indicate the following:

y = is the vertical axis, that is BMD (hip) in gram/cm2

-0.0025 indicate the negative slope of the trendline/change. In terms of BMD (hip), the change in slope indicates that the BMD of the hip bone, in average reduces by about 0.25% each year for a woman in the menopausal group.

x = is the horizontal axis, that is age in years.

1.008 = this is an intercept of the trendline/slope and the vertical axis, y (BMD - hip)

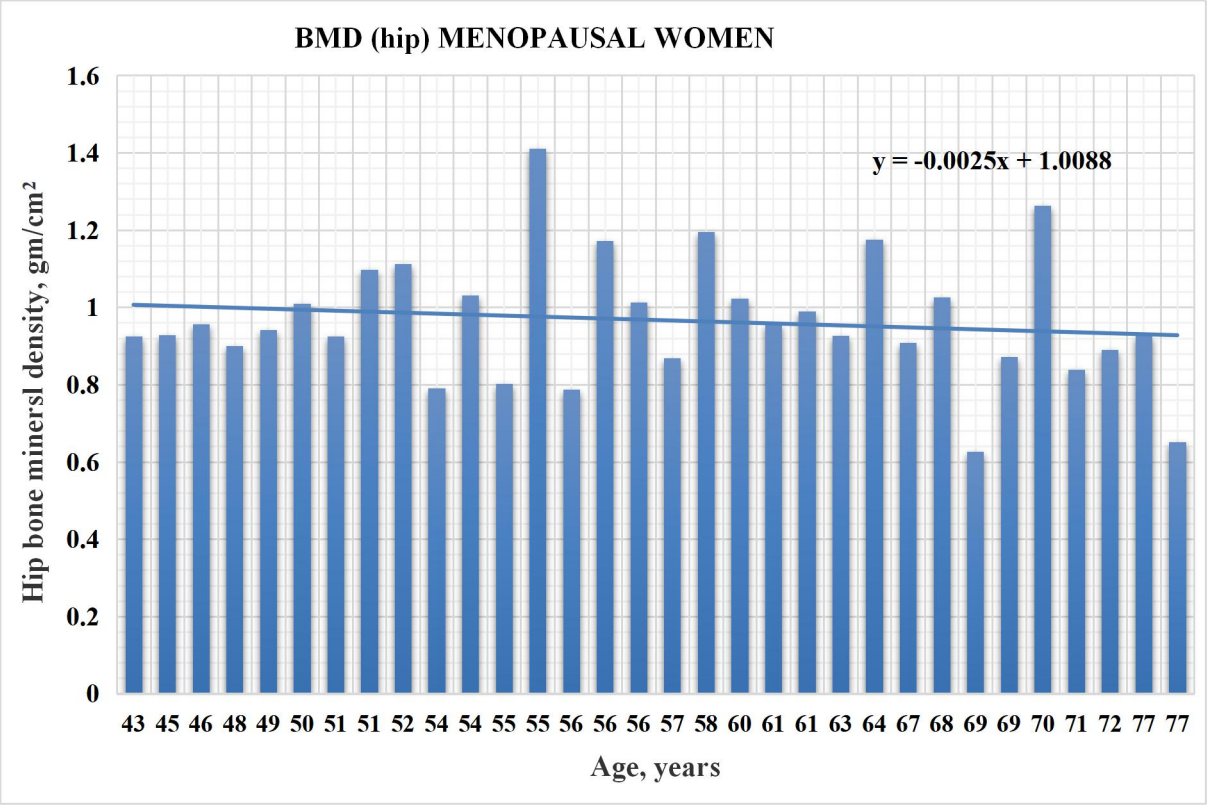

Figure 2: Graph depicting bone demineralization in menopausal women

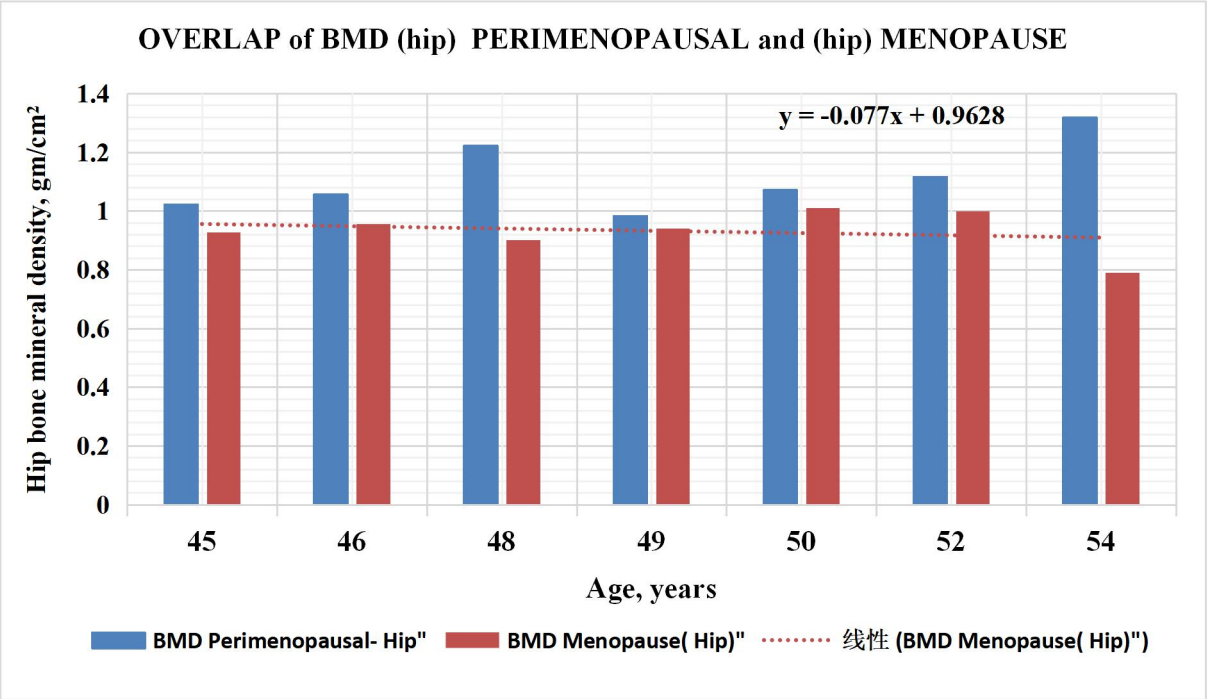

Figure 3: Graph depicting greater bone demineralization in postmenopausal than in perimenopausal women.

The graph in Figure 3 portrays the overlap between the two groups of women, namely postmenopausal and perimenopausal women. The notations in the formula; y = 0.0077X + 0.9628 for menopausal women only, indicate the following:

y = is the vertical axis, that is BMD (hip), gram/cm^2

-0.0077 indicates the negative slope of the trendline/change. In terms of BMD (hip), the change in slope indicates that the BMD (hip) in average reduces by about 0.77% each year for the subject population.

x = is the horizontal axis, that is age in years.

0.9628 = this is an intercept of the trendline/slope and the vertical axis, y (BMD - hip)

Discussion

The study shows that there were two women (7;1%) who were osteopenic. All the perimenopausal women who participated in the study were in the late perimenopausal stage according to the stages of reproductive Aging Workshop (STRAW) classification [19]. This

stage is associated with accelerated bone loss [20-22], and it continues through the early post menopause. Increased levels of follicle stimulating hormone (FSH) in the range of 34-56 IU/L in the perimenopausal stage have solidified the association of accelerated bone loss at this stage [20-22]. In this study the highest levels of FSH were 34 IU/L. Other studies have included the bone resorption markers which in conjunction with FSH still confirm that bone loss is accelerated in the late perimenopausal stage [20;21]. Bone markers have been used to monitor the response to treatment for osteoporosis [23]. Alkaline phosphates; osteocalcin and procollagen type-1 are produced by osteoblasts while N-telopeptide or serum C-telopeptide are often used to assess bone degradation. The bone resorption markers have been found to be high in premenopausal women while high in postmenopausal women. Studies are not uniform in analysing bone markers in perimenopausal women. The clear rise in these resorption markers was seen in one study which was two years before the final menstrual period and picked up at 1.3years after final menstrual period [21].

In the study of Women Across the Nation; the accelerated bone loss in the perimenopausal period was 1;8% to 2;3% annually in the lumbar spine and I;0% to 1;4% in the hip. Body weight was found to be an important predictor of the rate of bone loss independent of the differences in race or ethnicity of the population [24]. In this study; the annual bone loss in the perimenopausal period is low and this is supported by the fact that black south African women have a thicker bone mass due to their genetic predisposition [25].

There is scarcity of data that describes bone turnover from the premenopause to menopause beyond 5 years postmenopause; however, there is benefit that accrues from to analysing the information gathered, for the purpose of decision making about screening of women for osteoporosis. The gold standard in screening for osteoporosis remains DEXA scans; bone markers can be utilized to determine when screening should be repeated especially in developing countries such as South Africa where DEXA is not readily available at all health institutions [21]. Decisions on the medical treatment for osteoporosis may be managed or monitored with ease if there is adequate knowledge of rates of bone loss. Long term usage of anti-resorptive therapy and its safety concerns which confront both health workers and patients, can be adequately analysed by a combination of both bone mineral density changes and bone turn-over marker [21].

The association of bone loss and oestradiol levels has also been identified. It has been established that levels of less than (>5pg) are associated with higher fracture rates compared to those of levels that are higher [26]. The European Vertebral osteoporosis study (EVOS) has

also found the negative relationship between oestradiol and bone markers in women under the age of 65. However, it was emphasized that the findings in the study, could not be extrapolated to women in the perimenopausal transition [27].

Bone loss is also associated with an increase in the medullary bone diameter; periosteal diameter and decrease in the strength index. These factors are realised in the postmenopausal women. The fracture risk may be identified by reduction of the strength index [28]. This is information

extrapolated from bone density study of the forearm. Bone mineral density in most studies is done on the vertebrae and the hip. This study still succeeded to establish the effect of menopause on bone loss.

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