COMPARATIVE ASSESSMENT OF THE BONE MINERAL DENSITY AND VITAMIN D LEVELS IN PREMENOPAUSAL AND POSTMENOPAUSAL FEMALES OF INDIA

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ABSTRACT

Background: In females of the South Asia region, vitamin D deficiency has been highly prevalent. This can be due to non-access to sunlight, sunblock, home-stay, and poor dietary intake, Insufficient intake of vitamin D and calcium can lead to bone loss, especially in postmenopausal females.

Aim: The present study aimed to comparatively assess the bone mineral density and vitamin D levels in premenopausal and postmenopausal females of India.

Methods: The study assessed 200 premenopausal females constituting the controls and 200 postmenopausal females constituting the test group. In all 400 subjects, vitamin D levels were assessed to note vitamin D deficiency. This was followed by scanning (DEXA scan) for bone mineral density. The data gathered was statistically assessed to get results.

Results: Moderate deficiency of Vitamin D was higher in a post-menopause group with 43% (n=86) females and had a lower incidence in the pre-menopausal control group with 15% (n=30) females with moderate deficiency of vitamin D. For the severe deficiency, it had a high incidence in post-menopausal females with 36% (n=72) females and a low incidence of severe vitamin D deficiency was seen in the pre-menopausal control group with 2% (n=4) females. In premenopausal females, low bone mineral density was seen in 34% (n=68) of study subjects and was very low in 1% (n=2) females. In the study group of post-menopausal females, the bone mineral density was low in 62% (n=124) of the study subjects and was very low in 24% (n=48)

of the study subjects. For BMD and 25 OHD levels, the difference in the two groups was statistically significant with $p<0.001$.

Conclusion: The present study shows the effect of menopause on bone mineral density and vitamin D levels. There is a significant difference in bone mineral density and levels of vitamin D in postmenopausal females and females of reproductive age.

Keywords: Bone mineral density, calcium, menopause, postmenopausal, Vitamin D

INTRODUCTION

Vitamin D is a highly prevalent disorder globally affecting subjects from both genders. However, it is more prevalent in female subjects. Vitamin D deficiency nearly affects 1 billion subjects globally. The deficiency of Vitamin D is more common in postmenopausal females. Among many sources of Vitamin D in humans, the majority of the Vitamin D is taken from direct sunlight which is an easily available source.[1] Other available sources of Vitamin D are dietary sources rich in multivitamin supplements, vitamin D, and/or fish oil. In South Asia regions such as India, deficiency of Vitamin D is highly attributed to being the gender-based affecting majority of the females. The gender specification can be due to limited sunlight exposure, veil practice in rural areas, homestay during sunlight hours, and poor dietary intake. Inadequate intake of vitamin D and calcium causing deficiency in postmenopausal females can further lead to increased bone loss in the post-menopause phase.[2] The deficiency of Vitamin d in post-menopausal females is common globally. However, a decrease and high prevalence are reported in South Asia regions including India owing to the lack of dietary intake with vitamin D where a focus needs to be placed on increased vitamin D intake in the diet.[3]

Vitamin D is a vital mineral essential for the normal functioning of the human body. It plays a vital role in the prevention of fractures, bone strengthening, and bone development. Various countries, including Saudi Arabia, have made fortification of food with Vitamin D to make the majority of females who stays at home or follow the veiling practice get vitamin D required.[4] Deficiency of Vitamin D can lead to various diseases including increased fracture risk, osteopenia secondary to bone loss, osteoarthritis, and/or osteoporosis. Vitamin D also works as a hormone and is needed for bone mineralization and calcium absorption which directly affects the BMD (bone mineral density). A reduction in vitamin D can lead to a reduced BMD which can increase the fractured impact and cause bone loss.[5]

BMD is an assessment of the number of inorganic minerals in the bones. The bone area having minerals is vital to maintaining bone strength in fracture cases, and prevention of diseases like osteoporosis and osteopenia. Various factors affecting BMD are low vitamin D levels, BMI ((body mass Index), sedentary lifestyle, alcohol consumption, diseases involving bone loss, genetics, age, and gender.[6] BMD is also affected by various comorbidities like hypertension and diabetes mellitus. After a subject attains the peak bone mass by the age of 18-20 years and the completion of the skeletal maturation, the levels of BMD start to decrease. Low skeletal mass and osteoporosis are less common entities compared to their female counterparts in the postmenopausal as well as premenopausal era causing a lower BMD in females near menopause and a higher BMD in male subjects.[7]

Also, previous literature data have reported a direct correlation between BMD and low levels of vitamin D. BMD is a reliable assessment tool for diseases like osteoporosis and osteopenia. In adult subjects, increased vitamin D levels can lead to low bone mass with the help of Vitamin D supplements, food fortification with Vitamin D, and/or increased dietary intake of Vitamin D to get adequate BMD. Other factors that may affect BMD and vitamin D levels are assessed in the present study.[8] The literature data is scarce focusing on the poor BMD and vitamin D levels in females of India. Hence, the present study aimed to comparatively assess the bone mineral density and vitamin D levels in premenopausal and postmenopausal females of India.

MATERIALS AND METHODS

The present cross-sectional clinical study was done to comparatively assess the bone mineral density and vitamin D levels in premenopausal and postmenopausal females of India. The study population comprised the subjects from the Outpatient Departments of the Institute. After explaining the study protocol, informed consent, in both written and verbal format was taken from the study participants.

The inclusion criteria for the study were females presenting with complaints of mood change, muscle cramps, muscle weakness, bone pain, and/or fatigue. The study sample was constituted of 400 female subjects. The study assessed 200 premenopausal females who were in the age range of 35 years to 45 years and were taken as the controls. Another study group was constituted of 200 females from postmenopausal females in the age range of 45-75 years. The exclusion criteria were subjects not willing to participate and having systemic disorders or comorbidities.

After the final inclusion of females in the study, detailed clinical history was recorded for all the participants followed by the reproductive history. All history and data were noted on the preformed structured proforma. Other data gathered were laboratory investigations, hemoglobin levels, levels of vitamin D (25-OHD), and sociodemographic data. The subjects were also asked about their previous bone fractures, parathyroid disorders, osteopenia, osteoporosis, hypertension, and/or diabetes.

For all the participants, levels of vitamin D were assessed in subjects with suspected deficiency of vitamin D. Blood samples were collected under strict aseptic and sterile conditions from the cubital vein by collecting 5ml blood. After centrifugation, serum was separated from the blood within two hours of collection and was kept at 20^{o}C. Electrochemiluminescence was used to assess the levels of serum vitamin D.A level of >20 ng/mL or 50nmol/L was considered as a normal serum level of 25-OHD or vitamin D. Vitamin D insufficiency and vitamin D deficiency was defined by the levels of 12-20ng/ml and <12ng/ml respectively. Based on the serum vitamin D levels, all subjects were categorized.

Bone mineral density was assessed for all the subjects using the dual-energy X-ray absorptiometry scan after removing any metallic object from their body and making them lie on the soft table. On the hip and lower spine of each subject, the scanner was moved. T-scores and Z-scores were used to assess bone density and to interpret the results. T-scores assess the density of bone and a comparison was done with the bone density in 30 years old adults. Normal bone density was defined by a T-score of -1 or more, -1 to -2.5 depicted osteopenia or low bone

density, and -2.5 or low showed osteoporosis. The subjects were categorized into normal density, osteopenia/low density, and osteoporosis/low density. The Z-scores depict the comparison of the bone density of a subject to the average person of the same gender and age.

The data gathered were analyzed statistically using SPSS software version 26.0 (IBM, Chicago, IL). The data were expressed in means and standard deviation and percentages and frequency for categorical data as BMD categories, vitamin D, and age groups. The Association of BMD and vitamin D levels with menopause status in females was assessed using the chi-square test. The significance level was considered at $p<0.05$.

RESULTS

The present cross-sectional clinical study was done to comparatively assess the bone mineral density and vitamin D levels in premenopausal and postmenopausal females of India. The study assessed 200 premenopausal females who were in the age range of 35 years to 45 years and were taken as the controls. Another study group was constituted of 200 females from postmenopausal females in the age range of 45-75 years. The demographic data of the study subjects are described in Table 1. The mean age of the study subjects from the post-menopause group was 53.72±8.1 years and 28.43±7.3 years for the control group (premenopausal females). The age range for post-menopause and pre-menopause females was 45-75 years and 35-45 years respectively. Based on the BMI of the study participants, from the post-menopause group, 20% (n=40), 23% (n=46), 38% (n=76), and 19% (n=38) subjects were obese, overweight, normal weight, and underweight respectively. In the pre-menopause groups, obese, overweight, normal weight, and underweight subjects were 26% (n=52), 20% (n=40), 36% (n=72), and 18% (n=36) subjects respectively. No morbidity was seen in 10% (n=20) subjects from post-menopause and 70% (n=140) subjects from the pre-menopause group respectively. Diabetes mellitus was seen in 45% (n=90) subjects from the post-menopause and 25% (n=50) subjects from the pre-menopause group. Hypertension was reported in 64% (n=128) subjects and 16% (n=32) subjects from the post-menopause and pre-menopause groups respectively as shown in Table 1.

On assessing the bone mineral density in the two groups of study subjects, it was seen that for the control group comprising 200 premenopausal females, the BMD (bone mineral density) was normal in 65% (n=130) study subjects followed by low bone mineral density in 34% (n=68) study subjects, and was very low in 1% (n=2) females from the control group. In the study group of post-menopausal females, the bone mineral density was low in 62% (n=124) of the study subjects and was very low in 24% (n=48) of the study subjects. The bone mineral density was normal in 14% (n=28) of study females in the post-menopausal phase of their life. The bone mineral density was low and very low in females of the post-menopause group compared to the pre-menopause group. This difference was statistically significant with $p<0.001$ as depicted in Table 2.

Concerning the assessment of the levels of 25-OHD in the two groups of study females, normal levels were not seen in any female from the post-menopause group (study group) and were seen in 34% (n=68) females from the control group (post-menopause group). Mild deficiency of vitamin D was seen in 21% (n=42) subjects from the post-menopause group and in 49% (n=98)

subjects from the pre-menopause group. Moderate deficiency of Vitamin D was higher in a post-menopause group with 43% (n=86) females and had a lower incidence in the pre-menopausal control group with 15% (n=30) females with moderate deficiency of vitamin D. For the severe deficiency, it had high incidence in post-menopausal females with 36% (n=72) females and a low incidence of severe vitamin D deficiency was seen in the pre-menopausal control group with 2% (n=4) females (Table 2).

DISCUSSION

The present study assessed 200 premenopausal females who were in the age range of 35 years to 45 years and were taken as the controls. Another study group was constituted of 200 females from postmenopausal females in the age range of 45-75 years. The mean age of the study subjects from the post-menopause group was 53.72±8.1 years and 28.43±7.3 years for the control group (premenopausal females). The age range for post-menopause and pre-menopause females was 45-75 years and 35-45 years respectively. The age distribution in the study participants was similar to the studies of Hashemipour S et al[9] in 2006 and Jackson RT et al[10] in 2018 where authors assessed subjects with similar age distribution as in the present study.

Based on the BMI of the study participants, from the post-menopause group, 20% (n=40), 23% (n=46), 38% (n=76), and 19% (n=38) subjects were obese, overweight, normal weight, and underweight respectively. In the pre-menopause groups, obese, overweight, normal weight, and underweight subjects were 26% (n=52), 20% (n=40), 36% (n=72), and 18% (n=36) subjects respectively. No morbidity was seen in 10% (n=20) subjects from post-menopause and 70% (n=140) subjects from the pre-menopause group respectively. Diabetes mellitus was seen in 45% (n=90) subjects from the post-menopause and 25% (n=50) subjects from the pre-menopause group. Hypertension was reported in 64% (n=128) subjects and 16% (n=32) subjects from the post-menopause and pre-menopause groups respectively. These results were consistent with the previous studies of Roy DK et al[11] in 2007 and Mezquita-Raya P et al[12] in 2001 where a significant increase in weight and BMI was seen in the post-menopausal females compared to females in the premenopausal age group.

The study results showed that on assessing the bone mineral density in the two groups of study subjects, it was seen that for the control group comprising 200 premenopausal females, the BMD (bone mineral density) was normal in 65% (n=130) study subjects followed by low bone mineral density in 34% (n=68) study subjects, and was very low in 1% (n=2) females from the control group. In the study group of post-menopausal females, the bone mineral density was low in 62% (n=124) of the study subjects and was very low in 24% (n=48) of the study subjects. The bone mineral density was normal in 14% (n=28) of study females in the post-menopausal phase of their life. The bone mineral density was low and very low in females of the post-menopause group compared to the pre-menopause group. This difference was statistically significant with $p<0.001$. These findings were in agreement with the findings of Tereszkowski CM et al[13] in 2012 and Warming L et al[14] in 2002 where authors reported a significant decrease in bone mineral density in postmenopausal females.

For the assessment of the levels of 25-OHD in the two groups of study females, normal levels were not seen in any female from the post-menopause group (study group) and were seen in 34% (n=68) females from the control group (post-menopause group). Mild deficiency of vitamin D was seen in 21% (n=42) subjects from the post-menopause group and in 49% (n=98) subjects from the pre-menopause group. Moderate deficiency of Vitamin D was higher in a post-menopause group with 43% (n=86) females and had a lower incidence in the pre-menopausal control group with 15% (n=30) females with moderate deficiency of vitamin D. For the severe deficiency, it had high incidence in post-menopausal females with 36% (n=72) females and a low incidence of severe vitamin D deficiency was seen in the pre-menopausal control group with 2% (n=4) females. These vitamin D level comparisons were in line with Kharroubi A et al[15] in 2017 and Harinarayan CV et al[16] in 2011 where a severe and very severe deficiency of vitamin D was seen in the post-menopausal females.

CONCLUSION

The present study shows the effect of menopause on bone mineral density and vitamin D levels. There is a significant difference in bone mineral density and levels of vitamin D in postmenopausal females and females of reproductive age. A significant association was seen between vitamin D deficiency and decreased bone mineral density to the age of females. Dense BMD was higher vitamin D levels seen in the females of reproductive age compared to post-menopausal females. Hence, the study recommends the use of diet modifications, daily sunlight exposure, and calcium and vitamin D supplements in the females of the post-menopause phase.

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TABLES

Characteristics	**Study group (post-menopause)**		**Control group (pre-menopause)**	
	Number (n=200)	**Percentage (%)**	**Number (n=200)**	**Percentage (%)**
Mean age (years)	53.72±8.1		28.43±7.3	
Age range (years)	45-75		35-45	
BMI (kg/m2)				
Obese	40	20	52	26
Overweight	46	23	40	20
Normal weight	76	38	72	36
Underweight	38	19	36	18
Associated comorbidity				
No morbidity	20	10	140	70
Diabetes mellitus	90	45	50	25
Hypertension	128	64	32	16

Table 1: Demographic data of study participants

Parameter	**Study group (post-menopause)**		**Control group (pre-menopause)**		**p-value**
	Number (n=200)	**Percentage (%)**	**Number (n=200)**	**Percentage (%)**	
BMD (bone mineral density)					
Normal	28	14	130	65	**<0.001**
Low	124	62	68	34	
Very Low	48	24	2	1	
25-OH D levels					
Normal	0		68	34	**<0.001**
Mild deficiency	42	21	98	49	
Moderate deficiency	86	43	30	15	
Severe deficiency	72	36	4	2	

Table 2: Vitamin D and BMD levels in the study subjects