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Original Article

Association of Menopause, Reproductive Years, and Bone Mineral Density in Postmenopausal Women with Natural Menopause

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Abstract

Introduction: The age at menopause has been found to be associated positively with bone mineral density (BMD), and the age at menarche has been found to be associated negatively with BMD. The association is due to the amount or duration of estrogen exposure.

Materials and Methods: Initial study population consisted of postmenopausal women of 40-70 years reporting to the Integral Institute of Medical Sciences and Research, Dasauli, Kursi Road, Lucknow, as outpatient department patients. The final study group included only postmenopausal women with natural menopause. Duration of study was of 2 years from April 2014 to April 2016. The association of reproductive years and timing of menopause, BMD, age of menarche, and age of menopause were compared in the study. The continuous and categorical variables were compared by analysis of *t*-tests and Chi-square analysis, respectively.

Results: Out of 1022 postmenopausal women studied, 389 women had low BMD, and 633 women had high BMD. Out of 389 women, 49 (12.6%) women were <30 reproductive years, 302 (77.6%) women were between 30 and 39 years, and 38 (9.7%) were more than 40 reproductive years. Out of 633 women, 79 (12.5%) women, 490 (77.4%) women, and 63 (9.9%) were of <30, 30-39, and >40 reproductive years, respectively. Out of 389 women with low BMD, 88 (22.6%) and 301 (77.3%) were women with early menopause <49 years and late menopause >49 years, respectively. Out of 633 women with high BMD, 138 (21.8%) and 495 (78%) were women with early menopause <49 years and late menopause >49 years, respectively. The study showed the comparison in mean age, BMD, age of menarche, and age of menopause between Group 1 (early menopause <49 years) and Group 2 (late menopause >49 years). The mean age of Group 1 and Group 2 was 43.50 years (standard deviation [SD] 7.39) and 54.2 years (SD 4.8), respectively. $P < 0.0001$, extremely statistically significant. *t*-test = 25.91, df = 1020, 95% confidence interval −11.5112–−9.8888.

Conclusion: Longer the reproductive years, late the menopause, and earlier the menarche, there was positive association with bone density.

Key words: Bone mineral density, Menopause, Osteoporosis

INTRODUCTION

According to some studies, age at menopause has been found to be associated positively with bone mineral density (BMD),[1,2] and the age at menarche has been found to be associated negatively with BMD.[3] The association is due to the amount or duration of estrogen exposure.[4] The estrogen levels at a given point of time are influenced by underlying physiological and environmental factors.[5] Some studies show age of menarche or menopause seems to be limited or of no importance for osteoporosis when subjects are of age 75 or older.[6,7]

Although dual-energy X-ray absorptiometry (DEXA) is the golden standard for diagnosis of osteoporosis, quantitative ultrasound (QUS) of calcaneum is a less expensive, portable, screening tool of sensitivity 67.6% as against DEXA 76.6%.[6-8] Some studies show QUS calcaneum

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sensitivity 39.25%, specificity 91.71%, positive prediction 72.41%, and negative prediction of 73.14%.[9,10]

This study sought to examine the relationship of the timing of menopause and reproductive years with BMD.

Aim

To study the association of menopause, reproductive years, and BMD in postmenopausal women with natural menopause.

Objective

To study the relationship of timing of menopause, length of reproductive years (calculated by age of menopause-age of menarche) with BMD in postmenopausal women with natural menopause.

MATERIALS AND METHODS

Study design: Cross-sectional study.

The initial study population will consist of postmenopausal women of 40-70 years reporting to the Integral Institute of Medical Sciences and Research, Dasauli, Kursi Road, Lucknow, Uttar Pradesh, India, as outpatient department patients.

Final study group will include only postmenopausal women with natural menopause.

Duration of study: 2 years from April 2014 to April 2016.

Sample size: Complete enumeration.

Inclusion Criteria

Subjects are women of 40-70 year old, who reported suspension of menstruation for at least 1 year before the study, without any medical or surgical reason.

Exclusion Criteria

a. Medical conditions such as renal disease, insulin-dependent diabetes mellitus, liver disease, rheumatoid arthritis, malignancy, chronic disease that affect skeleton, abnormalities of parathyroid, thyroid, and adrenal glands
b. Surgical conditions such as partial/total gastrectomy, hysterectomy with/without oophorectomy
c. Drugs-prior use of estrogen replacement therapy, corticosteroids, diuretics, cytotoxic drugs, anabolic steroids, bisphosphonates, calcitonin, or Vitamin D.

Data Collection

All of the women will be counseled, and information sheet in patients own language will be given and written informed consent will be obtained from the subjects participating in the study.

The self-administered questionnaire will be used to collect information about lifestyle, past and present health condition, previous and current physical activities, dietary calcium intake, reproductive history, and breastfeeding practices were taken. To further reduce the influence of variables, menopausal women, who are non-smokers, parous, breastfed women with moderate physical activity and with no contraceptive history, were included in the selection criteria.

Investigation BMD analysis by calcaneal QUS.

RESULTS

The mean age of 1022 postmenopausal women was 48.85 years (standard deviation [SD] 6.14). The mean age of menopause and mean age at menarche for all women was 48.20 (SD3.61) and 14.76 years (SD2.24). The reproductive years is calculated as (age of menopause age of menarche). The reproductive period ranged from 12 to 52 years, with mean 32.0 years (SD4.53). The reproductive years were further grouped into <30 years, 30-39 years, and ≤40 years. The BMD results were categorized into osteopenia/higher BMD (T score −1.0-−2.5) and low BMD/osteoporosis (T score −2.5 and below).

The *t*-tests were used for continuous variables. The ANOVA test was used for more than two groups. The *P* value was calculated. Out of 1022 postmenopausal women studied, Table 1 shows that 389 women had low BMD, and 633 women had high BMD. Out of 389 women, 49 (12.6%) women were <30 years reproductive years, 302 (77.6%) women were between 30 and 39 years, and 38 (9.7%) were more than 40 reproductive years. Out of 633 women, 79 (12.5%) women, 490 (77.4%) women, and 63 (9.9%) were of <30, 30-39, and >40 reproductive years, respectively.

Out of 389 women with low BMD, 88 (22.6%) and 301 (77.3%) were women with early menopause <49 years and late menopause >49 years, respectively. Out of 633 women with high BMD, 138 (21.8%) and 495 (78%) were women with early menopause <49 years and late menopause >49 years, respectively. Table 2 shows the covariates and BMDs by timing of menopause and length of the reproductive period, and it shows the comparison in mean age, BMD, age of menarche, and age of menopause between Group 1 (early menopause <49 years) and Group 2 (late menopause >49 years). The mean age of Group 1 and Group 2 was 43.50 years (SD 7.39) and 54.2 years (SD 4.8), respectively. $P < 0.0001$, extremely statistically significant. *t*-test = 25.91, df = 1020, 95% confidence interval −11.5112-−9.8888.

The mean age of menarche of Group 1 and Group 2 was 14.24 years (SD 2.24) and 15.28 years (SD 2.62), respectively. $P < 0.0001$, extremely statistically significant. *t*-test = 5.43, df = 1020, 95% confidence interval −1.4163-−0.6637. The mean age of menopause of Group 1 and Group 2 was 45.4 years (SD 3.61) and 51.10 years (SD 2.61), respectively. $P < 0.0001$, extremely statistically significant. *t*-test = 26.43, df = 1020, 95% confidence interval −6.1236-−5.2764. The BMD of Group 1 and Group 2 was −3.1 (SD1) and −2.3 (SD 1), respectively. $P < 0.0001$, extremely statistically significant. *t*-test = 10.61, df = 1020, 95% confidence interval −0.948-−0.652.

The women with three categories of reproductive years differed significantly by age at menarche and age at menopause. The mean age of 30, 30-39, and >40 was 54.07, 57.31, and 59.20 years, respectively. The $F = 47.543$, $P = 0.000$, highly significant, MS = 827.727, df = 2, SS = 1655.454. The age of menarche of 30, 30-39, and >40 was 16.20, 14.71, and 12.31 years, respectively. The $F = 41.269$, $P = 0.000$, highly significant, df=2, SS = 863.31, MS = 431.66. The age of menopause of 30, 30-39, and >40 was 43.56, 48.7, and 54.35 years, respectively. The $F = 125.017$, $P = 0.000$, highly significant, df = 2, SS = 6598.42, MS = 3299.21. The BMD of 30, 30-39, and >40 was −3.0, −2.6, and −2.1, respectively. The $F = 22.865$, $P = 0.000$, highly significant, df = 2, SS = 45.730, MS = 22.865.

Table 1: Distribution of variables in 1022 postmenopausal women according to bone mineral density

Variables	Bone Osteoporosis low BMD (*n*=389)	Density Osteopenia higher BMD (*n*=633)	All women (*n*=1022)
Reproductive period (years)			
<30	49 (12.6)	79 (12.5)	128 (12.5)
30-39	302 (77.6)	490 (77.4)	792 (77.4)
>40	38 (9.7)	63 (9.9)	101 (9.8)
Timing of menopause (%)			
Early (age <49 years)	88 (22.6)	138 (21.8)	226 (22.1)
Late (age >49 years)	301 (77.3)	495 (78)	796 (77.9)

BMD: Bone mineral density

DISCUSSION

Francucei *et al.*[1] in 2010, Bulgakavo and Davydkin[2] (2009) and Gallagher[3] (2007) found age at menopause to be associated positively with bone mineral density.

Boonen *et al.*[4] (2005) Panichkul *et al.*[5] (2004) Juby[6] (2004) and Tomkinson *et al.*[7] (2003) found the age at menarche to be associated negatively with bone mineral density. Also Tomkinson *et al.*[7] in 2003 showed the association is due to the amount or duration of estrogen exposure. Francucei *et al.*[1] in 2007 and Gallagher[3] in 2003 found the estrogen levels at a given point of time are influenced by underlying physiological and environmental factors.

However Francucei *et al.*[1] in 2010 and Gallagher[3] in 2003 found age of menarche or menopause seems to be limited or of no importance for osteoporosis when subjects are age 75 or older.

Quantitative ultrasound (QUS) of calcaneum is a less expensive, portable, screening tool of sensitivity 67.6% as against DEXA 76.6% as shown by Juby[6] (2004), Tomkinson *et al.*[7] 2003 and Diez-Perez *et al.*[8] 2003. Some studies by Van den Berg *et al.*[9] 2001 and Langton and Langton[10] 2000, show QUS calcaneum sensitivity 39.25%, specificity 91.71%, positive prediction 72.41% and negative prediction of 73.14%.

The menopausal loss of ovarian estrogen is known to be associated with rapid decrease in bone mineral density, leading eventually to increased fracture risk.

During, pregnancy and lactation there is increased loss of calcium and inorganic phosphates from the mother's body. The increased exposure to estrogen and progesterone, enhanced the absorption of calcium in the intestine and increased the conservation of calcium in the kidneys. The women with higher age had lower bone mass. The study showed, timing of menopause was statistically extremely significant. The BMD was low in <30 years reproductive years as compared to bone density in 30-39 years and >/40 years category.

Table 2: Covariates and bone mineral densities in postmenopausal women according to timing of menopause and length of reproductive period

Covariables	Timing of menopause				Reproductive periods (years)			
	Early <49 (*n*=226)	Late >49 (*n*=796)	*t*-test	*P*	<30	30-39	>40	*F*
Mean age (years)	43.50	54.2	28.05	<0.0001	54.07	57.31	59.20	47.54
BMD	−3.1	−2.3	12.41	<0.0001	−3.0	−2.6	−2.1	41.26
Age at menarche	14.24	15.28	6.50	<0.0001	16.20	14.71	12.31	125.01
Age at menopause	45.4	51.10	29.20	<0.0001	43.56	48.7	54.35	22.86

BMD: Bone mineral density

CONCLUSION

Thus, longer the reproductive years, late the menopause, and earlier the menarche, there was positive association with bone density. However, further studies may be needed to improve statistical significance in terms of risk analysis by including continuous variables and categorical variables such as weight, height, body mass index, number of pregnancies, number of births, smoking, use of oral contraceptives, breastfeeding, and calcium intake in the study.

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