

Effects of multiparity and duration of breast-feeding on maternal bone mineral density in post-menopausal Kurdish women: A retrospective study

Siamak Derakhshan¹, Mozaffar Mahmoudi², Sirous Shahsawari³

¹Department of Radiology and Nuclear Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran

²Department of Radiology, Paramedical Faculty, Kurdistan University of Medical Sciences, Sanandaj, Iran

³Department of Environmental Health, Health Faculty, Kurdistan University of Medical Sciences, Sanandaj, Iran

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ABSTRACT

Introduction: There is considerable amount of controversy about the long term effects of multiparity and duration of breast-feeding on maternal bone mineral density after menopause. This study was conducted to determine whether multiple pregnancy and prolonged duration of breast-feeding are independent predictors of low bone mass in post-menopausal Kurdish women.

Methods: In a retrospective study, we evaluated 991 post-menopausal women with mean age of 58.9 years screened for osteoporosis by dual energy X-ray absorptiometry (DXA). According to the parity (1-2, 3-4, 5-7, >7 children) and total duration of breast-feeding (1-24, 25-60, 61-96, >96 months) they were classified. Bone mineral density (BMD) results for femoral neck and lumbar spine were classified into three groups (normal, osteopenia, and osteoporosis) according to the WHO criteria. Binary logistic regression was used to assess the independent associations of low femur or spine BMD with parity and total duration of breast-feeding.

Results: We found that women with 5 or more children and having more than 60 months history of total breast-feeding, were older ($p<0.001$) with higher prevalence of osteoporosis ($p<0.001$). However, after adjusting for age only parity was independent predictor for osteopenia (OR: 1.336; 95% CI 1.29-1.735) while total duration of breast-feeding was not an independent predictor of low bone mass.

Conclusion: Multiparity has a detrimental effect on maternal BMD. History of multiple pregnancy is a risk factor for low bone mass in post-menopausal women. However, prolonged duration of breast-feeding has no long-term adverse effect on maternal BMD in post-menopausal age.

Key words: Multiparity; Breast-feeding; Bone density; Menopause; Osteoporosis

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Corresponding author: Siamak Derakhshan, Department of Radiology and Nuclear Medicine, Kurdistan University of Medical Sciences, Sanandaj, Iran. E-mail: siamakderakhshan@yahoo.com

INTRODUCTION

Osteoporosis is one of the most important health problem in post-menopausal women. Optimum management of modifiable risk factors is essential for prevention of osteoporosis as the most common reason for fracture and reducing the health costs related to this disease [1].

It is reported that women lose 2-9% of their BMD at the end of a pregnancy despite compensatory mechanisms such as increased intestinal absorption and decreased renal excretion of calcium during pregnancy [2]. Lactation also has profound effect on bone resorption. It negatively affects calcium and phosphate metabolism due to physiologic hyperprolactinemia and secondary hypoestrogenemia so it is not surprising that BMD is averagely 4-6% decreased after 6 months of lactation [3]. Some studies have shown BMD gain of 5% six months after weaning; however, it is not clear whether this recovery is completely occurred in women with high parity and prolonged total duration of breast-feeding [4]. There is also significant controversy about the effect of lactation on BMD after menopause [5, 6]. While some studies have reported decreased BMD in post-menopausal women with history of multiparity or prolonged breast-feeding [7, 8] many others have shown no change [9, 10] or even increased BMD in the post-menopausal women [11-14]. Differences in population sample might be the major cause of the contradictory results. For example in developing counties where number of children and total duration of breast-feeding is usually more than developed countries while calcium and vitamin D intake is poor [2]. So, we aimed to evaluate the effects of multiparity and prolonged breast-feeding on BMD in a large sample of post-menopausal women in Kordestan, Iran.

METHODS

Study sample

This study was based on a retrospective analysis of 1750 post-menopausal women referred for measuring BMD in Kurdistan nuclear medicine center – Kordestan province, Iran- by DXA method between 2012 and 2015. A total of 991 post-menopausal women (with mean age of 58.95 ± 8.6 years) were included in the study. The exclusion criteria were nulliparity, no breast-feeding, premature ovarian failure (menopause < 40 years of old), smoking, history of inflammatory arthritis, type I diabetes mellitus, chronic gastrointestinal or liver disease, chronic renal disease, cancer, hematological disorders, endocrine disorders and taking alcohol or drugs known to affect bone mass (estrogen, thyroxin, corticosteroids, anticoagulants and phenytoin). Menopausal state was determined by absent of period

for at least 6 months. Body mass index (BMI) was calculated by dividing weight on height squared (kg/m^2). Demographic data, medical history, daily dairy product intake, weekly exercise, number of live births, duration of breast feeding for each child and age at menopause were obtained from a detailed questionnaire being filled by interviewing each women. A dairy unit had been defined as daily intake of one glass of milk/yogurt or 30 grams of cheese. The studied sample was divided into two groups of inadequate dairy intake (less than one dairy unit) and adequate dairy intake (>1 dairy unit). Adequate exercise had been defined as at least 30 minutes of regular exercise (eg. jogging, swimming,) three times a week. Accordingly, the studied population was divided into two groups of with and without adequate weekly exercise.

Bone mineral density (BMD)

BMD (g/cm^2) was measured at anterior-posterior projection of the lumbar spine (L2-L4) and non-dominant (left) proximal femur (femoral neck) using a Norland XR46 densitometer machine (Norland Corp., Ford Atkinson, WI, USA) by DXA method. T-score (peak bone mass percentage in normal subjects) was measured depending on the software and database used in the devise. According to the WHO criteria, BMD of the femoral neck and the lumbar vertebrae were classified as normal (T-score > -1.0 SD), osteopenia (T-score -1.0 to -2.5 SD) and osteoporosis (T-score < -2.5).

Statistical analysis

In women with more than one child, total period of breast-feeding was calculated by summing up the months of breast-feeding for each child. The women were divided into groups according to the parity (1-2 children, 3-4 children, 5-7 children and more than 7 children). Then they were divided into other groups according to total period of breast-feeding (1-24 months, 25-60 months, 61-96 months and more than 96 months). Finally, mean period of breast-feeding for each child was calculated by dividing total duration of breast feeding to total number of children and the women were divided into different groups according to these variables (1-6 months, 7-12 months, 13-18 months, 19-24 months and >24 months). Binary logistic regression was used to assess the independent associations of low femur or spine BMD with parity and total duration of breast-feeding. The same method was also used for BMD groups (osteopenia and osteoporosis according to the WHO criteria). The data was statistically analyzed using SPSS for windows (version 21), Chi-square and T test were used and p value < 0.05 was considered significant.

RESULTS

Nine hundred ninety one post-menopausal women ranged from 44 – 90 years old, with a mean age of 58.95 ± 8.6 years and mean age of menopause of 48.4 ± 4.7 years were analyzed. The women had mean parity of 5.5 ± 3.1 (minimum 1 and maximum 15) and mean duration of breast-feeding of 94.5 ± 68.7 months. Only 12% of the subjects ($n=120$) had normal BMD. Prevalence of osteoporosis and osteopenia were 33% ($n= 326$) and 55% ($n=545$), respectively.

Prevalence of osteopenia (p -value = 0.88) and osteoporosis (p -value = 0.17) was not significantly different between the groups with inadequate and adequate daily dairy intake in the studied population (Table 1).

There was also no significant difference in prevalence of osteopenia between two groups of with and without adequate exercise (p -value=0.38). Osteoporosis was significantly higher (p -value=0.0001) in the group without adequate weekly exercise (Table 2); however, the subjects in this group were also significantly older than the group with adequate exercise (Table 3). Age has profoundly

a detrimental effect on bone mineral density so it seems that the higher prevalence of osteoporosis in the first group was most likely due to older age rather inadequate exercise.

The basic characteristics and BMD of the women according to the parity was seen in Table 4. There were no differences in BMI, weight and age of menopause between the groups of women with different parity. Women with more than 5 children were older than others and they had a longer duration since menopause. The BMD both in lumbar spine and femoral neck were lower in women with more than 5 children.

The basic characteristic and BMD of the women according to total duration of breast-feeding was shown in Table 5. The women with total duration of breast-feeding more than 96 months were older and they have longer duration since menopause. No difference was seen in age at menopause, BMI and weight between the groups. Lumbar BMD was lower in women with more than 96 months of breast-feeding while femoral BMD was lower in the two latest groups (women with total duration of breast-feeding of 61-96 months and > 96 months).

Table 1: Prevalence of osteopenia and osteoporosis according to daily dairy intake.

Daily dairy intake	Osteopenia			p-value	Osteoporosis			p-value
	No	Yes	Total		No	Yes	Total	
Inadequate	112(17.7%)	519(82.3%)	631(100%)	0.88	112(26.3%)	314(73.7%)	426(100%)	0.17
Adequate	8(18.6%)	35(81.4%)	43(100%)		8(40.0%)	12(60.0%)	20(100%)	
Total	120(17.8%)	554(82.2%)	674(100%)		120(26.9%)	326(73.1%)	446(100%)	

Table 2: Prevalence of osteopenia and osteoporosis according to weekly exercise.

Weekly exercise	Osteopenia			p-value	Osteoporosis			p-value
	No	Yes	Total		No	Yes	Total	
Inadequate	44(16.2%)	227(83.8%)	271(100%)	0.38	44(19.0%)	187(81.0%)	231(100%)	0.0001
Adequate	76(18.9%)	327(81.1%)	403(100%)		76(35.3%)	139(64.7%)	215(100%)	
Total	120(17.8%)	554(82.2%)	674(100%)		120(26.9%)	326(73.1%)	446(100%)	

Table 3: Mean age of two groups of with and without adequate weekly exercise.

	Number	Mean age (y)	p-value
Without adequate exercise	458	62	0.0001
With adequate exercise	542	56	

Table 4: Basic characteristics and bone mineral density (BMD) in the postmenopausal women, grouped according to number of children born.

All women (n=991)	Number of children born				
	1-2 (n=143)	3-4(n=306)	5-7(n=298)	>7 (n=244)	
Normal	120(12.0%)	34(23.9%)	51(16.7%)	26(8.7%)	8(3.3%)
Osteopenia	545(55.0%)	80 (56.0%)	206(67.3%)	158(53.0%)	105(43.0%)
Osteoporosis	326(33.0%)	29(20.1%)	49(16.0%)	114(38.3%)	131(53.7%)
Age (year)	58.9(58.4-56.2)	54.4(53.2-55.6)	55.4(54.7-56.2)	60.0(59.1-60.9)	64.9(63.9-65.9)
BMI	28.3(28.02-28.6)	27.7(27.1-28.4)	28.1(27.6-28.6)	28.5(28.0-29.1)	28.6(28.0-28.6)
Weight (Kg)	68.0(67.3-68.7)	66.8(65.0-68.7)	67.3(66.1-68.6)	69.2(67.8-70.6)	68.1(66.6-69.6)
Age of menopause (year)	48.4(48.1-48.7)	47.7(47-48.4)	48.4(47.9-48.9)	48.4(47.8-49.0)	48.8(48.1-49.4)
Duration since menopause (year)	10.3(9.8-10.9)	6.5(5.3-7.7)	7(6.3-7.8)	11.4(10.4-12.4)	15.8(14.6-16.9)
Total duration of breast-feeding (month)	94.2(90.3-98.8)	28.6(25.8-31.4)	55.5(52.3-58.7)	107.9(102.6-113.3)	168.2(159-177.3)
L ₂ -L ₄ vertebrae BMD (g/cm ²)	0.826 (0.816-0.837)	0.877 (0.850-0.903)	0.880(0.862-0.897)	0.812(0.793-0.830)	0.744(0.726-0.763)
Femoral neck BMD (g/cm ²)	0.759 (0.750-0.767)	0.802(0.779-0.825)	0.808(0.794-0.822)	0.743(0.728-0.758)	0.690(0.674-0.706)

Table 5: Basic characteristics and bone mineral density (BMD) in the postmenopausal women, grouped according to total duration of breast-feeding.

All women (n=991)	Total duration of breast-feeding			
	1-24(n=143)	25-60(n=258)	61-96(n=186)	>96(n=404)
Age(year)	56.4(55.3-57.6)	55.9(55.0-56.8)	57.6(56.4-58.7)	62.5(61.6-63.3)
Age of menopause	48.5(47.8-49.2)	48.1(47.5-48.6)	48.2(47.5-48.8)	48.6(48.1-49.2)
Duration since menopause (year)	8.0(6.8-9.2)	7.8(6.9-8.7)	9.0(7.8-10.2)	13.5(12.6-14.4)
BMI	27.9(27.3-28.6)	28.1(27.6-28.7)	28.5(27.8-29.2)	28.5(28.0-28.9)
Weight (Kg)	67.4(65.7-69.1)	67.2(65.7-68.7)	68.2(66.3-70.8)	68.6(67.5-69.7)
L ₂ -L ₄ vertebrae BMD (g/cm ²)	0.856(0.830-0.882)	0.816(0.842-0.880)	0.851(0.828-0.887)	0.780(0.765-0.797)
Femoral neck BMD (g/cm ²)	0.770(0.749-0.792)	0.798(0.782-0.814)	0.778(0.759-0.793)	0.721(0.708-0.735)

The basic characteristic and BMI of women according to mean duration of breast-feeding for each child was seen in Table 6. There were no differences in age, age of menopause, BMI, weight and duration since menopause between the groups. In all of the groups, women with longer mean duration of breast-feeding for each child also had no significant difference in lumbar BMD and femoral BMD compared to women with shorter duration of breast-feeding for each child.

Binary logistic regression analysis showed that only age and parity were independent risk factors for osteopenia in the femur or spine while total duration of breastfeeding was not found to be an independent risk factor (Table 7).

It also showed that age was independent risk factor for osteoporosis in the femur or spine (Table 8). Neither parity nor total duration of breast-feeding was not independent risk factor for osteoporosis.

Table 6: Basic characteristics and bone mineral density (BMD) in the postmenopausal women, grouped according to total duration of breast-feeding by children.

	Duration of breast-feeding by children(month)				
	1-6 (n=119)	7-12 (n=166)	13-18 (n=248)	19-24 (n=391)	>24(n=67)
All women (n=991)					
Age (years)	58.7(57.4-60.0)	58.3(57.1-59.6)	58.9(57.7-60.0)	59.2(58.4-60.2)	58.3(56.1-60.5)
Age of menopause	48.7(47.8-49.6)	48.6(47.9-49.3)	48.4(47.4-48.7)	48.4(48.0-48.9)	48.5(47.2-49.8)
Duration since menopause (year)	9.9(8.5-11.4)	9.8(8.5-11.1)	10.4(9.3-11.6)	10.5(9.6-11.4)	9.2(7.0-11.5)
BMI (Kg/m ²)	27.9(27.2-28.5)	28.5(27.8-29.3)	28.1(27.7-29.3)	28.5(28.0-28.9)	28.2(28.0-28.6)
Weight (Kg)	66.8(64.9-68.6)	68.5(66.5-70.4)	66.7(65.3-68.2)	68.7(67.5-69.8)	68.6(65.8-71.4)
Children (n)	4.95(4.41-5.51)	5.41(4.89-5.93)	5.62(5.22-6.02)	5.77(5.48-6.06)	5.26(4.56-5.97)
L ₂ -L ₄ vertebrae BMD (g/cm ²)	0.814(0.787-0.840)	0.800(0.797-0.850)	0.843(0.827-0.864)	0.824(0.807-0.842)	0.836(0.793-0.878)
Femoral neck BMD (g/cm ²)	0.741(0.720-0.762)	0.758(0.736-0.780)	0.774(0.756-0.792)	0.756(0.742-0.771)	0.778(0.741-0.814)

Table 7: Independent predictors of osteopenia.

Predictor	Sig	OR	95% Confidence interval	
			Lower	Upper
Age	0.002	1.062	1.023	1.102
Weight	0.842	0.996	0.958	1.036
BMI	0.939	1.004	0.906	1.112
Duration of menopause	0.222	1.036	0.979	1.098
Parity	0.030	1.336	1.029	1.735
Total duration of breast-feeding	0.250	0.992	0.979	1.006

Table 8: Independent predictors of osteoporosis.

Predictor	p-value	OR	95% Confidence interval	
			Lower	Upper
Age	0.0001	1.205	1.148	1.265
Weight	0.104	1.045	0.991	1.102
BMI	0.521	0.956	0.834	1.097
Duration of menopause	0.665	0.983	0.908	1.063
Parity	0.078	1.303	0.970	1.751
Total duration of breast-feeding	0.750	0.997	0.982	1.013

DISCUSSION

In our study, we evaluated the effects of parity and duration of breast-feeding on bone mineral density in post-menopausal Iranian Kurdish women. The results showed that subjects with more than 4 children and subjects with total duration of breast-feeding more than 60 months had lower BMD both in femur and spine. Osteoporosis was also more prevalent in these two groups. However, they were also older and have longer duration of menopause than subjects with less than 5 children and less than 60 months of breast feeding. In the binary logistic regression analysis, age and multiparity were shown to be independent variables for osteopenia in the femur or spine. So, it seems that in subjects with longer duration of breast-feeding it is the effect of age not duration of breast-feeding on lowering BMD. Binary logistic regression analysis also showed that only age was the independent predictor for osteoporosis. Neither multiparity nor total duration of breast feeding was not independent predictor for osteoporosis.

Calcium homeostasis and bone metabolism are changed significantly during pregnancy and breast-feeding. Calcium absorption in the gut and renal tubular reabsorption of calcium are increased during pregnancy [15, 16]. However, high maternal parathyroid hormone (PTH) and increased urinary excretion of calcium due to high glomerular filtration rate during pregnancy are the major causes of decreasing maternal BMD [17, 18]. Parathormone-related peptide and low estrogen levels during period of lactational amenorrhea are suggested to be the major contributing factors for bone loss during breast-feeding [17]. It is estimated that maternal BMD is decreased (average 4-6%) at the end of pregnancy and breast-feeding [19]. However, it is shown that women usually return to normal BMD without treatment 6 -12 months after weaning [4, 10, 20]. It is not clear whether these changes in maternal

BMD have any long term effect on women BMD after menopause [21].

Similar to our study, Heidari et al showed that osteoporosis was more prevalent among post-menopausal women with more than 7 parity in north of Iran [22]. Similarly, a study was performed by Steieglitz et al on 130 Tsimane women demonstrating that higher parity was associated with reduced BMD after adjusting for potential confounders [23]. In a study performed by Alam et al on 75 post-menopausal women with parity 1-13, it showed that a significant negative correlation was present between parity and T-score of the lumbar spine and femur so mean T-score of BMD were more negative as number of parity increases [24].

Unlike our study, a population-base study conducted on 210 Sri Lankan women by Lenora et al showed that multiparity had no detrimental effect on maternal BMD in post-menopausal age [25]. In contrast with our study, Schnatz et al reported that history of pregnancy and breastfeeding protected against development of postmenopausal osteoporosis [14]. A study by Specker et al on 168 Hutterite women aged 40-80 years also showed that high parity was associated with increased bone size and strength [13]. However, an observational study performed by Streeten et al on 424 women with homogenous lifestyle and high parity showed that the beneficial effect of high parity on BMD was lost after menopausal transition and, therefore, high parity had neither a detrimental nor beneficial effect on long-term bone health [26]. Similarly, Lekamwasam et al studied 713 healthy, community dwelling post-menopausal women in Sri Lanka. They showed that in an adjusted analysis, differences in phalangeal BMD and BMC among multiparous and nulliparous women were partially explained by the differences of age and body weight between the groups and the unique effect of parity was difficult to determine [27].

Long-term effect of breast-feeding on the maternal BMD has been evaluated in many studies. Similar to our study, Lenora et al showed that prolonged breast-feeding had no detrimental effects on maternal BMD in post-menopausal women [25]. Sawo et al showed successive periods of long lactation were not associated with progressive skeletal depletion [9]. A study performed by Kayani et al on 200 women with mean age of $50 + 0.78$ years it was revealed that lactation during reproductive years of life did not put women on increased risk of developing low bone mineral density after menopause [28]. Kalkwarf et al also showed that lactation was not associated with an increased risk of osteoporotic fractures [10]. In a study on post-menopausal Turkish women, Yazici et al also showed that breast-feeding duration was not a risk factor for low bone mass in later life [29]. Hosseinpanah et al studied 245 healthy postmenopausal women aged 40 to 80 in Tehran. Unlike our study, they showed that femoral and lumbar spine BMD were inversely associated with the total duration of breastfeeding [21]. In a study by Kim HJ et al, they showed that among 1694 postmenopausal Korean women total breastfeeding duration was associated with postmenopausal low BMD [30]. Another Korean study by Hwang et al also showed that prolonged breastfeeding was associated with low BMD in the lumbar spine and higher prevalence of osteoporosis [31]. Tsetov et al also showed that prolonged breast-feeding may have a deleterious long-term effect on BMD and may contribute to increased risk of osteoporotic later in life [7]. Bolzetta et al studied 752 women with a mean age of $64.5 + 9.3$ which 23% of them reported vertebral osteoporotic fracture. Women with vertebral fracture had breastfed for longer periods. So they concluded that duration of breastfeeding was a risk factor for vertebral fractures [8].

The reason for these conflicting results might be in part due to different patient selections (sample size, age, and ethnicity). Compared to other studies, the major difference of our study are larger population, higher number of children and much longer total duration of breast feeding. Unlike some other studies, we exclude patients with co-morbidities and other confounding factors such as HRT that affecting bone mass. Another limitation of these studies –including ours- is the lack of measurement of vitamin D levels. It should be mentioned that many studies have been carried out in developed countries where maternal nutrition is usually adequate opposed to studies been performed in developing countries with lower socio-economic background [32].

One of weaknesses of our study was the requirement for the subjects to recall total duration of breast feeding for each child. Recall bias may have occurred during data collection. The wide range (from 44 to 90 years) of age might also be a limiting factor. Despite

adjusting for age, other age-related factors such as limited physical activity may have influenced the results.

CONCLUSION

Our study shows that in this group of women, multiple pregnancies are an independent risk factor for low bone mass after menopause. Post-menopausal women with longer total duration of breast-feeding have lower BMD; however, total duration of breast-feeding is not an independent predictor of low bone mass. This may result from interaction with other factors particularly age as a strong predictor of osteopenia and osteoporosis in post-menopausal state.

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