Original Investigation / Orijinal Araştırma

DOI: 10.4274/tod.00719

Effects of Reproductive Factors on Bone Mineral Densitometry

Reproduktif Faktörlerin Kemik Mineral Dansitometresi Üzerine Etkileri

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Summary

Aim: To determine the effects of reproductive factors on bone mineral density (BMD) in postmenopausal women.
Materials and Methods: A total of 1196 postmenopausal women with BMD (g/cm^2) measurements at lumbar vertebra (LS) and femur neck (FN) were enrolled. Demographic, reproductive characteristics and Body Mass Index (BMI) of patients were defined. In order to define BMD related factors, multiple regression analysis was employed.
Results: Main results were as follows: mean age= 59.97±8.56 yrs; weight= 73.49±13.06 kg; BMI= 29.25±5.22kg/m^2, age of menarche= 14.00±1.64 yrs; number of deliveries 4.22±2.09; total breastfeeding duration= 60.77±38.80 months; number of breastfeeding per day= 8.23±3.91; menopausal age= 47.12±4.22 yrs; duration of menopause= 12.80±9.10 yrs; LS BMD= 0.993±0.171 gr/cm2; FN BMD 0.844±0.14 gr/cm2. There were negative correlations between LS BMD and FN BMD values and age, menopause duration, total breastfeeding duration, and number of breastfeeding per day. There were positive correlations between LS and FN BMD values, and weight and BMI scores. Additionally, there were negative correlations between LS and FN BMD values, and age of menarche and number of deliveries. In linear stage regression analysis, weight, number of breastfeeding per day, postmenopausal duration, duration of total breastfeeding and age of menarche were defined as the most significant predictors for LS BMD, whereas weight, postmenopausal duration and number of breastfeeding per day were defined as the most significant predictors for FN BMD.
Conclusion: LS and FN BMD in postmenopausal women are related to reproductive factors, so reproductive factors should also be considered in the evaluation of risk factors in postmenopausal women. (Turkish Journal of Osteoporosis 2012;18:8-12)
Key words: Menopause, bone mineral density, reproductive factors, osteoporosis

Özet

Amaç: Postmenopozal kadınlarda reprodüktif faktörlerin kemik mineral yoğunluğu (BMD) üzerine etkilerini tespit etmek amaçlandı.
Gereç ve Yöntemler: Çalışmaya lomber vertebra (L1-4) (LS) ve femur boyun (FN) düzeyinde BMD (gr/cm^2) ölçümleri yapılmış olan 1196 postmenopazal kadın dahil edildi. Hastaların demografik, reprodüktif özellikleri ve vücut kütle indeksi (BMI) (kg/m^2) belirlendi. BMD ile ilişkili faktörleri belirlemede çoklu regresyon analizi kullanıldı.
Bulgular: Hastalarda ortalama yaş 59,97±8,56, ağırlık 73,49±13,06 kg, VKİ 29,25±5,22 kg/m^2, adet yaşı 14,00±1,64, doğum sayısı 4,22±2,09, toplam emzirme süresi 60,77±38,80 ay, günlük emzirme sayısı 8,23±3,91, menapoz yaşı 47,12±4,22, menopoz süresi 12,80±9,10 yıl, LS BMD 0,993±0,171 gr/cm^2, FN BMD 0,844±0,14 gr/cm^2 idi. Hastalarda LS BMD ve FN BMD değerleri ile yaş, menopoz süresi, toplam emzirme süresi, günlük emzirme sayısı arasında negatif korelasyon saptandı. LS ve FN BMD değerleri ile, ağırlık ve BMI skorları arasında pozitif korelasyon saptandı Yine LS ve FN BMD değerleri ile adet yaşı ve doğum sayısı arasında negatif korelasyon saptandı. Lineer basamak regresyon analizlerinde, ağırlık (p<0,001), günlük emzirme sayısı (p<0,001), menapoz sonrası geçen süre (p<0,001), toplam emzirme süresi (p<0,012), ilk adet yaşı (p<0,007) LS BMD için, ağırlık (p<0,001), menapoz sonrası geçen süre (p<0,001) ve günlük emzirme sayısı (p<0,001) FN BMD için en önemli belirleyiciler olarak bulundu.
Sonuç: Postmenopozal dönemdeki kadınlarda LS ve FN BMD, reprodüktif faktörler ile ilişkili gözükmektedir. Bu nedenle postmenopozal kadınlarda osteoporoz risk faktörleri değerlendirirken reproduktif faktörlerde dikkate alınmalıdır. (Türk Osteoporoz Dergisi 2012;18:8-12)
Anahtar kelimeler: Menopoz, kemik mineral yoğunluğu, reprodüktif faktörler, osteoporoz

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Introduction

Osteoporosis is a metabolic bone disease, characterized by low bone mass and micro-architectural deterioration of bone structure, leading to compromised bone strength and increased risk of fragility fractures (1,2). Commonly encountered in postmenopausal women, osteoporosis not only causes increased mortality and morbidity, but also affects quality of life negatively (3). BMD is a marker for osteoporotic bone fractures and also affected by factors, such as genetics, nutrition, physical exercise, diseases and drugs (4,5). Peak bone mass is the mainstay of BMD and generally acquired in the early thirties, when pregnancy and lactation occur (4). In light of literature, however, inconsistent data are present, related to the effects of reproductive history on BMD. The number of studies investigating the effects of reproductive factors on osteoporosis is considered to be insufficient in Turkey, a developing country.
In the study, it was aimed to determine the relationship between reproductive factors and BMD in postmenopausal women.

Materials and Methods

Patients

Applying to the Department of Physical Therapy and Rehabilitation, Konya Education and Research Hospital between October 2010 and January 2012, a total of 1196 out-patients in postmenopausal period, whose BMD (g/cm^2) measurements were performed at LS and FN levels at anterior-posterior projection by dual energy X-ray absorptiometry (DEXA), were enrolled into the study. Approval from the local ethics committee was obtained, and informed consents of participants were provided. Age, age of menarche, number of deliveries, age of menopause, duration of postmenopause, duration of total breastfeeding and number of breastfeeding per day were defined in the evaluation form. Weights and heights of participants were recorded, and BMI (kg/m^2) values were calculated. Patients with history of menopause earlier than 40, surgical menopause, secondary amenorrhea longer than 6 months, consuming alcohol and smoking, severe systemic diseases, experienced fractures, and conditions affecting bone density at present or in the past like hypercortisolism, thyrotoxicosis, DM, malabsorption, celiac disease, anorexia nervosa, hyperparathyroidism and rheumatologic disease, on hormone replacement therapy (HRT), taking drugs affecting bone metabolism including calcium and vitamin D, other drugs causing osteoporosis (antiepileptics, streoids, thyroid hormone therapy), receiving thiazide group of diuretics, exercising regularly and diagnosed with any vertebral fracture in T4-L5 interspaces, constituted the exclusion criteria of the study. In order to exclude osteomalacia and hyperparathyroidism, parathormone (PTH), calcium, phosphorus, alkaline phosphatase (ALP) measurements were performed via blood test, as well as routine laboratory tests.

Statistical Analysis

SPSS package program was used for statistical analysis. Descriptive statistical results (mean-standard deviation) were given as mean ± SD. Pearson's correlation analysis was employed to calculate correlations between independent variables, and LS and FN BMD scores. Multiple regression analysis was performed in order to define the effect level of variables with statistically significant correlations on LS and FN BMD scores. The rates of statistical significance and confidence interval were accepted as $p<0.05$ and 95%. Among correlation coefficients, the score between 0-0.25 was evaluated as no correlation, between 0.25-0.50 as small, between 0.50-0.75 as medium, and between 0.75-1.00 as strong.

Results

Characteristics of patient were presented in Table 1. Negative correlations were found to be between LS BMD and FN BMD and age (r:-0.336 $p<0.001$; r:-0,462 $p<0.001$), duration of menopause (r:-0.395 $p<0.001$; r:-0.513 $p<0.001$), duration of total breastfeeding (r:-0.332 $p<0.001$; r:-0.285 $p<0.001$), and number of breastfeeding per day (r:-0.336 $p<0.001$; r:-0.287 p<0,001). Negative correlations were also observed between LS and FN BMD values and number of deliveries (r:-0,189 $p<0.001$; r:-0.160 $p<0.001$) and age of menarche (r:-0.196 $p<0.001$; r:-0.186 $p<0.001$). However, positive correlations were found between LS and FN BMD values and weight (r:-0.432 $p<0.001$; r:-0.411 $p<0.001$) and BMI (r:-0.405 $p<0.001$; r:-0.380 $p<0.001$) (Table 2). Linear regression analyses were performed separately for dependent variables of LS and FN BMD. Postmenopausal duration (R2=0.134; $p<0.001$), weight (R2=-0.267; $p<0.001$), number of breastfeeding per day (R2=0.208; $p<0.001$), duration of total breastfeeding (R2=0.80; $p<0.018$) and age of menarche (R2=0.79; $p=0.010$) were defined as the most significant determinants for LS BMD. Postmenopausal duration (R2=0.251; $p<0.001$), weight (R2=-0.180, $p<0.001$) and number of breastfeeding per day (R2=0.124; $p<0.001$) were the most significant determinants for FN BMD.

Table 1. Reproductive Characteristics and BMI Values of Participants

	Participants (n:1196)
Age (year)	59.97±8.56
Weight (kg)	73.49±13,06
BMI (kg/m^2)	29.25±5.22
Parity (number of deliveries)	4.23±2.09
Age of Menarche (years)	14.00±1.64
Lactation (total months)	60.77±38.80
Daily Number of Breastfeeding	8.23±3.91
Age of Menopause (years)	47.12±4.22
Years since Menopause (years)	12.80±9.10
Vertebral BMD	0.993±0.17
Femur Neck BMD	0.844±0.14

BMD, Bone Mineral Density; BMI, Body Mass Index.

Table 2. Correlation Coefficients between Reproductive Factors and BMD

	FN BMD	LS BMD	Daily number of breastfeeding	Lactation (total months)	Years menopause	Parity	Age of menarche	Weight	BMI	Age
Age	-.462**	-.336**	.191*	.377**	.870**	.358**	.141*	-.229*	-.192*	1
BMI	.380**	.405**	-.153*	-.136*	-.210*	-.054	-.160*	.875**	1	
Weight	.411**	.432**	-.191**	-.162**	-.259**	-.091**	-.152**	1		
Age of menarche	-.201*	-.196**	.116*0	.114**	.169**	.116**	1			
Parity	-.160*	-.189*	.248**	.629**	.326**	1				
Years menopause	-.513**	-.395**	.224**	.378**	1					
Lactation (total months)	-.285**	-.332**	.364**	1						
Daily number of breastfeeding	-.287**	-.336**	1							
LS BMD	1									
FN BMD	1									

BMD, Bone Mineral Density; BMI, Body Mass Index; LS, Lumbar Spine; FN, Femur Neck
* Correlation is significant at p<0.05
** Correlation is significant at p<0.001

Discussion

In the study, where we investigated the effects of reproductive factors on BMD in postmenopausal women, a statistically significant negative correlation was found between age, and LS BMD and FN BMD. These results were consistent with the results of studies, reporting negative correlation between age and LS and FN BMD (6,7), age and FN BMD (8) and age and LS BMD (9). In another study, Mizuno et al. and Ryan et al. reported no relationship between age and LS BMD, and age and LS and FN BMD, respectively (10,11).

Typically, osteoblastic and osteoclastic functions are at equilibrium in middle aged women (12). Age-related bone loss commences at 45-50 years of age, the equilibrium related to remodeling of bone structure is disrupted, and bone resorption exceeds bone formation (12). Bone resorption is increased more in menopausal period (9). With advanced age, the production of growth hormone stimulating renal production of 1,25(OH)2D3 is decreased (13). Therefore, the plasma level of 1,25(OH)2D3 indicating a positive effect on osteoclast differentiation and osteoblast proliferation decreases. In addition, the decrease in physical activity, amount of calcium taken via diet and calcium absorption in conjunction with old age also contributes to bone loss (14).

Overweight leads to pressure on bone tissue and causes an increase in bone density (15). Also, estrogens accumulating in adipose tissue have positive effects on bone density (14,15). In a study by Waugh et al., low body weights in women between 40 and 60 were reported to be risk factors for low BMD (16). In our study, a significantly positive correlation was determined between weight and BMI, and FN and LS BMD values. In a study performed by Aksakal et al. in Turkey and another performed by Mizuno et al. on Japanese women, positive correlations were found to be between weight and LS BMD (11,17). In addition to such findings, Ryan, Kroger, Ho and Berenson also reported positive correlations between weight and LS and FN BMD (6,7,10,18).

While premenopausal bone loss is 0.25-1% per annum, the loss is accelerated up to 2-5% in peri- and postmenopausal periods (19). Encountered in women during menopause, the most important reason of decreased bone density is caused by estrogen deficiency (10). During and after menopause, productions of sex hormones like estrogen, progesterone and testosterone are markedly decreased. Since osteoblasts are stimulated by sex hormones, activity of osteoblasts is decreased during menopause. Bone loss is accelerated due to uncontrolled osteoclastic activity (20). In several studies investigating the association between BMD and duration of menopause, a negative correlation was determined (7,10,11,15,21). Additionally, in a recent review, strong evidence was suggested, indicating postmenopausal status is a risk factor for low BMD (16). In our study, a marked negative correlation was determined between postmenopausal period, and LS and FN BMD values, and our findings were consistent with the ones found in those studies. Our findings also indicated that an increase is present between postmenopausal period and risk of osteoporosis, and postmenopausal period is a determinant of low BMD values.

Upon scanning the literature, contraversial results were detected to be reported in studies investigating the relationship between BMD and age of menarche. In various studies, it was reported that age of menarche had no significant effect on total hip and LS BMD (22), and LS and FN BMD (10,11) in postmenopausal women. It was reported in some other studies that age of menarche is disproportioned to BMD (22-25).

In our study, it was observed that the higher age of menarche is, the lower the BMD values are. The likeliness of the relationship between age of menarche and bone mineral density can be

explained by long reproductive period (23). Height and age of menarche are important indicators of health status and nutrition within the periods of childhood and adolescent (7,26). Early age of menarche seems to have positive effects on BMD due to longer reproductive period and its relationship with peak bone mass.

The relationship between parity and BMD are contraversial in literature. Several studies are present, both reporting no relationship (11,16,27) and relationship (28-30) between parity and bone mass. It is reported that increased parity protects women in postmenopausal period from osteoporosis (28). Alali and Gur et al. demonstrated a negative correlation between parity and BMD (31,32). In our study, however, there was a weak negative correlation between number of deliveries, and LS and FN BMD values. During pregnancy, approximately 30 g of calcium is transferred from maternal resources for fetal skeletal mineralization. Maternal bone loss becomes more prominent within the last months of gestation, when fetal skeleton is rapidly mineralized (33-35). The findings indicate that BMD values may be altered during and after pregnancy (33), and pregnancy may increase the risk of osteoporosis in later stages of maternal life (35). It is considered that the high rate of parity affected BMD values negatively in our participants.

In studies performed, it is reported that temporary loss of bone mass occurs at the rate of 3-7% in women breastfeeding at least for 6 months (35-37), but bone-mineral loss is restored on a large scale in 6-12 month-period after the discontinuation of breastfeeding (5,36,38). The condition may be due to a decrease in lactation demand, because infants are fed with solid food after month 6 despite the continuation of lactation. The duration and rate of regaining of lost bone mass depend on the duration of breastfeeding and amenorrhea in postpartum period and affected region of skeleton. Nonetheless, there is a conflict over the effects of lactation on BMD at the later stages of life. While various studies indicate that long term lactation has positive effects on BMD of women in postmenopausal period (39), others report no effects (17,27,40,41). In our study, long term lactation was demonstrated to have negative effects on BMD of women in postmenopausal period, which is consistent with the study performed by Gur et al. and Dursun et al. (42,43). Lactation may not be considered as an important risk factor for osteoporosis in western countries, where people have no children more than two. However, prolonged duration of lactation should still be considered as an important risk factor in countries with high parity, like Turkey.

Despite high number of patients enrolled into the study, some limitations affecting our results are present. First, the participants were questioned about the duration of total breastfeeding and the number of breastfeeding per day for each child. No attitutes related to breastfeeding could be detected, although World Health Organisation (WHO) has defined attitutes related to breastfeeding as "exclusive" or "predominant". When infants are breastfed for at least 6 months, 4 times a day without any food or drinks including water, it is called exclusive breastfeeding. However, in predominant breastfeeding, infants are predominantly breastfed, but the infants also receive water, water-based drinks and fruit juices. By standardizing the status of breastfeeding, WHO aims to decrease the uncertainty of lactation results in further studies. Unfortunately, another limitation in our study is that serum levels of vitamin D and daily calcium intakes from the diet can be undetected. Finally, LS BMD measurements were performed only in antero-posterior projection. The accuracy of BMD measurements of spine in antero-posterior projection can be affected by soft tissue calcifications, such as osteophyte and especially aortic calcification (2).

Consequently, the findings in the study indicate that advanced age, low BMI, advanced age of menarche, long duration of menopause, high rate of parity, long term lactation and high number of breastfeeding per day may have negative effects on BMD in women in postmenopausal period. In the evaluation of women in postmenopausal period as to the risk of osteoporosis, the effects of reproductive factors on BMD should also be taken into consideration.

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