Effects of Lactation and Age of First Pregnancy on Postmenopausal Osteoporosis

Postmenopozal Osteoporozda Laktasyon ve İlk Gestasyonel Yaşın Etkisi

Nilgun Senol Guler[1], Gultekin Adanas Aydın[2], Ismihan Gurgen[2]

[1] Balıkesir University Faculty of Medicine, Balıkesir, Turkey

[2] Bursa Çekirge State Hospital, Bursa, Turkey

Abstract

Aim: Several factors have been suggested in the etiology of postmenopausal osteoporosis (OP). In this study, we aimed to investigate the possible effects of lactation, number of pregnancies, and age of first pregnancy on postmenopausal OP.

Materials and Methods: Four hundred and twenty-seven postmenopausal patients aged between 45 and 70 years were screened for OP between April 2015 and December 2015. A questionnaire was administered to all of the patients in order to obtain data about their age, height, weight, age of menopause and menarche, chronic illnesses, concomitant drug use, family history, postmenopausal hormone therapy history, number of pregnancies, childbearing age, and lactation period at each pregnancy. The bone mineral density (BMD) was measured by using dual-energy X-ray absorptiometry; measurements of the femoral neck, total femur and the lumbar vertebrae L1–L4 and L2–L4 were recorded. The patients were divided into two groups as those with OP (n=73) and those without OP (n=354).

Results: The number of pregnancies was statistically higher in the OP group in comparison to the non-OP group (p=0.037). No significant difference was found between the groups in terms of nulliparity, primiparity, and multiparity.

Discussion and Conclusion: The results of our study suggest that lactation and age of first pregnancy have no effect on developing postmenopausal OP.

Keywords: postmenopausal osteoporosis; lactation; gestational age

Öz

Amaç: Postmenopozal osteoporozun (OP) etiyolojisinde çeşitli faktörler öne sürülmüştür. Bu çalışmada gebelik sayısı, emzirme ve ilk gebelik yaşının postmenopozal OP üzerindeki olası etkilerini araştırmak amaçlanmıştır.

Gereç ve Yöntemler: Nisan 2015—Aralık 2015 döneminde 45–70 yaşlarındaki toplam 427 postmenopozal hasta OP taramasına alındı. Yaş, boy, kilo, menopoz ve menarş yaşı, kronik hastalık, eş zamanlı kullanılan ilaç, aile öyküsü, postmenopozal hormon tedavisi geçmişi, gebelik sayısı, doğum(lar) sırasındaki yaş ve (her) gebelikteki laktasyon dönemi bilgilerini edinmek amacıyla, tüm hastalara bir anket uygulandı. Kemik mineral yoğunluğu (KMY), dual enerjili X-ray absorbsiyometri kullanılarak ölçüldü; femur boyun, femur total, L1–L4 ve L2–L4 değerleri kaydedildi. Hastalar OP (n=73) ve OP olmayan grup (n=354) olarak ikiye ayrıldı.

Bulgular: Gebelik sayısı OP grubunda OP olmayan gruba göre istatistiksel olarak daha yüksekti (p=0,037). Gruplar arasında nulliparite, primiparite ve multipariteye göre anlamlı fark yoktu.

Tartışma ve Sonuç: Çalışmamızda elde edilen sonuçlar laktasyonun ve ilk gebelik yaşının postmenopozal OP gelişimine bir etkisi olmadığını göstermektedir.

Anahtar Sözcükler: postmenopozal osteoporoz; emzirme; gebelik yaşı

Geliş Tarihi /*Received* : 01.11.2017
Kabul Tarihi /*Accepted*: 20.12.2017

DOI: 10.21673/anadoluklin.348820

Sorumlu Yazar/*Corresponding Author*
Nilgun Senol Guler
Balıkesir University Faculty of Medicine, Physical Medicine and Rehabilitation, Balıkesir-Uşak Road, Çağış Campus, 10145 Balıkesir/Turkey
E-mail: senolnilgun@yahoo.com

INTRODUCTION

Osteoporosis (OP) is a condition characterized by low bone mass with microarchitectural deterioration in bone tissues, leading to increased bone fragility and susceptibility to fractures (1). Given the high morbidity and mortality rates attributable to OP, clarification of the risk factors at younger ages prior to fractures is of utmost importance (1). The fracture risk depends on the amount of bone loss in old age and the peak bone mass (PBM).

The bone tissue is affected by the changes that occur during the female reproductive period (2). Pregnancy and lactation are the two stages of life that induce significant changes in both hormonal and calcium metabolisms in women. In several studies, the bone mineral density (BMD) is reported to decrease by 4 to 6% during the first six months of lactation and to recover by about 5% during the six months following breastfeeding (3).

However, the effects of pregnancy and lactation on postmenopausal OP are controversial. There have been previous studies investigating the relationship between lactation and OP and reporting that BMD values were found to decrease, or that the values remained unchanged (4–7). Furthermore, some authors have demonstrated a positive effect on BMD (8,9). However, the long-term effects of pregnancy and lactation on OP have yet not been elucidated fully.

In the present study, we aimed to investigate the possible effects of lactation, number of pregnancies, and age of first pregnancy on postmenopausal OP.

MATERIALS AND METHODS

The study protocol was approved by the ethics committee of the associated training and research hospital. Written informed consent was obtained from each participant. The study was conducted in accordance with the Declaration of Helsinki principles. Four hundred and twenty-seven postmenopausal patients aged between 45 and 70 years who were screened for OP at Department of Physical Therapy and Rehabilitation between April 2015 and December 2015 were included. Menopause was defined as the absence of menstrual cycle for at least one year.

Patients who were diagnosed with rheumatoid arthritis, inflammatory bowel disease, hyperthyroidism, Cushing syndrome, hyperparathyroidism, and those who were on medication with drugs known to increase the risk of developing OP (such as oral corticosteroids, bisphosphonates, and thyroxine) were excluded from the study.

A questionnaire was administered to all of the patients in order to obtain data about their age, height, weight, age of menopause and menarche, chronic illnesses, concomitant drug use, family history, postmenopausal hormone therapy history, number of pregnancies, childbearing age, and lactation period at each pregnancy. The bone mineral density (BMD) was measured by using dual-energy X-ray absorptiometry (DEXA); measurements of the femoral neck, total femur, and the lumbar vertebrae L1–L4 and L2–L4 were recorded. The patients were divided into two groups as those with OP (n=73) and those without OP (n=354). A T-score of -2,5 was used as the cut-off value in accordance with the World Health Organization criteria.

Statistical Analysis

Statistical analysis was performed by using the Number Cruncher Statistical System (NCSS, ver. 2007) software (NCSS LLC., Kaysville, UT, USA). The descriptive data were expressed in mean and standard deviation (SD). The independent t-test was used to compare the binary groups of variables with normal distribution and the Mann-Whitney U test to compare the binary groups of variables with abnormal distribution. The chi-square test was performed to compare the qualitative data and the Tukey's multiple comparison test to compare the subgroups. One-way analysis of variance (ANOVA) was carried out to compare the multiple groups. Logistic regression analysis was performed to identify the factors affecting the presence of OP. $p<0.05$ was considered statistically significant.

RESULTS

The demographic and clinical characteristics of the patients are shown in Table 1. Compared to the non-OP group, age was higher (p=0.0001) and the BMI values were statistically significantly lower (p=0.004) in the OP group.The data concerning the number of births and age of first pregnancy are presented in Table 2. The

Table 1. Demographic and clinical characteristics of the patients

		Non-OP group (n=354)		OP group (n=73)		p
Age		58.73±7.77		63.1±7.26		**0.0001**
Height (cm)		158.84±5.94		157.51±6.53		0.087
Weight (kg)		74.38±12.97		68.48±13.35		**0.0001**
BMI		29.45±4.8		27.65±4.73		**0.004**
Chronic disease		97	27.40%	27	36.99%	0.101
Any drugs used continuously?		218	61.58%	48	65.75%	0.503
Smoking		44	12.43%	9	12.33%	0.981
Cigarettes smoked a day		13.23±11.28		9.33±6.91		0.325
Alcohol consumption		2	0.57%	0	0.00%	0.519
Cal-D vitamin use		66	18.64%	26	35.62%	**0.001**
Cal-D vitamin duration (month)		16.86±16.11		19.5±22.4		0.632
Menopausal age		46.32±5.29		45.88±5.79		0.523
Menarche age		13.75±1.61		13.74±1.37		0.965
Type of menopause	**Natural**	307	86.72%	64	87.67%	0.827
	Surgery	47	13.28%	9	12.33%	
Postmenopausal hormone therapy	**No**	326	92.09%	68	93.15%	0.757
	Yes	28	7.91%	5	6.85%	
Any bone fracture experienced?		70	19.77%	16	21.92%	0.678
Familial OP		37	10.45%	5	6.85%	0.347

BMI: body mass index; OP: osteoporosis

number of pregnancies was statistically higher in the OP group, compared to the non-OP group (p=0.037). However, there was no significant difference between the groups in terms of number of births (nullipara, p=0.882; primipara, p=0.852; multipara, p=0.974). Furthermore, the mean age of first pregnancy in the OP group was 20.86±3.52 years while 21.69± years in the non-OP group, which again indicated no significant difference between the two groups (p=0.111).

The breastfeeding data are summarized in Table 3. Of the 427 patients, 388 had a history of breastfeeding, and there was no significant difference between the groups in terms of breastfeeding history. In addition, 83.2% of the 333 patients who got pregnant for the first time under the age of 25 had a history of breastfeeding, although no significant difference in terms of mean breastfeeding duration was observed between the patients whose first pregnancy occurred under and over the age of 25. In the OP group, however, the mean breastfeeding duration and the mean breastfeeding duration for each child were found to be significantly higher (p=0.015 and p=0.023, respectively).

Multiple logistic regression analysis showed that age was significantly higher (p=0.001) and BMI values were significantly lower (p=0.004) in the OP group, compared to the non-OP group (Table 4).

DISCUSSION

Postmenopausal OP is considered a major health problem worldwide. Osteoporotic fractures are the main causes of mortality and morbidity in elderly patients (10).

Several factors including age, BMI, sex, family history, level of exercise, and smoking history have been suggested in the etiology of OP (1). In addition to these, reproductive factors such as menarche age, menopausal age, number of pregnancies, age of first pregnancy, and menopausal duration have certain effects on BMD (11).

In the literature, there are various studies investigating the effects of parity on BMD. In studies conducted in the United States and Japan, multiparity did not appear to have long-term positive effects on BMD

Table 2. Number of births and age of first pregnancy

		Non-OP group (n=354)		OP group (n=73)		p
Number of births		2.59±1.18		2.88±1.25		**0.037**
Groups by number of births	**Nullipara**	24	6.78%	4	5.48%	0.882
	Primipara	24	6.78%	6	8.22%	0.852
	Multipara	306	86.44%	63	86.30%	0.974
Age of first pregnancy (year)		21.69±4		20.86±3.52		0.111
First pregnancy under age 25	**Yes**	272	82.42%	61	88.41%	0.224
	No	58	17.58%	8	11.59%	

OP: osteoporosis

Table 3. Breastfeeding characteristics of the patients with and without OP

		Non-OP group (n=354)		OP group (n=73)		p
BF history	**Breastfeeding (-)**	33	9.32%	6	8.22%	0.766
	Breastfeeding (+)	321	90.68%	67	91.78%	
Mean BF duration (months)		11.31±6.13		13.43±7.34		**0.015**
Mean BF duration per child (months)		11.17±6.19		13.16±7.87		**0.023**
Mean BF duration	**< 1 year**	151	47.00%	26	38.81%	0.218
	≥ 1 year	170	53.00%	41	61.19%	
History of BF under age 25	**Breastfeeding (-)**	8	2.94%	2	3.28%	0.889
	Breastfeeding (+)	264	97.06%	59	96.72%	
Mean BF duration under age 25 (months)		11.42±5.98		13.85±8.09		**0.009**
Mean BF duration under age 25	**< 1 year**	122	46.21%	23	38.98%	0.313
	≥ 1 year	142	53.79%	36	61.02%	
Mean BF duration per child under age 25 (months)		11.23±6.04		13.53±8.08		**0.014**
Mean BF duration per child under age 27	**< 1 year**	131	49.62%	28	49.23%	0.764
	≥ 1 year	133	50.38%	31	50.77%	

BF: breastfeeding; OP: osteoporosis

(12,13). In two studies conducted in Turkey, however, increase in the number of deliveries was found to be a risk factor for developing OP, despite the fact that it was found to have a protective effect against OP in another study (14,15,5). In the present study, the number of pregnancies was not found to be an independent indicator for developing postmenopausal OP, consistent with previous findings (6,16).

Recently a growing number of studies have investigated the effects of age of first pregnancy on BMD. About 90% of BMD is reached around the age of 17 while 99% of PBM is reached around the age of 27 (17). Factors reducing bone formation during this period affect PBM, thus leading to postmenopausal OP development. The rate of bone mass acquisition varies with age: Bone tissue is accumulated rapidly in adolescence, and bone mass reaches its peak level in the late 20s and early 30s (18,19). With respect to bone mass acquisition rate, it takes time for bone tissue to recover in case of bone loss during the rapid acquisition period whereas bone tissue acquisition is interrupted in case of bone loss during the slow acquisition period (20).

A study by Yun et al. included three groups according to age of first pregnancy as those aged under 23, between 24 and 29, and over 30 years, and the rate of OP was found to be higher in the group aged between 24 and 29 (20). In another study by Schnatz et al., an age of first pregnancy greater than 27 years was found to have a protective effect against BMD (21). In a study by Okyay et al.(5), breastfeeding over one year was found to increase the OP risk by 7.1 times in women under the age of 27. Cavkaytar et al., however, found no relationship between age of first pregnancy and low BMD (22). In contrast with the aforementioned study,

Table 4. Pregnancy and lactation characteristics and risk of OP development according to multiple logistic regression analysis

	p	OR	95.0% CI for OR	
			Lower	Upper
Age	**0.001**	1.08	1.03	1.12
BMI	**0.005**	0.92	0.86	0.98
Number of births	0.903	0.98	0.70	1.37
Mean BF duration per child (months)	0.245	0.98	1.05	1.34
Mean BF duration per child under age 25 (months)	0.327	0.90	0.81	1.15

BMI: body mass index; BF: breastfeeding.

Ozdemir et al. showed that advanced maternal age at first pregnancy increased the risk of developing OP (14).

In the present study, we found no statistically significant difference between the OP and non-OP groups in terms of age of first pregnancy, which was 21.69±4 years in the OP group and 20.86±3.52 years in the non-OP group. Therefore, we conclude that changes during pregnancy can be tolerated, since about 90% of PBM is formed during this age range with rapid bone formation.

Likewise, the effects of lactation on OP development are still under investigation. In a study by Sowers et al., a decrease of 5 to 6% was observed in the BMD values of women who had breastfed for at least six months (23). In another study by Sowers et al. where intermittent bone turnover markers and BMD values were followed from the early postpartum period, BMD values of the femoral neck and spine were found to return to baseline values at 18 months and at 12 months, respectively (24). The authors also reported that breastfeeding and return of menstrual cycle were the main factors associated with the altered bone turnover markers during a 6- to 18-month follow-up period. In these patients, bone recovery was achieved when breastfeeding was discontinued and menstruation cycle returned (23).

Although breastfeeding has negative effects on bone mass, studies investigating the long-term effects of breastfeeding have yielded controversial results. In several studies lactation was found to have a protective effect against OP, although other authors reported that lactation increased the OP risk or that there was no relationship (5–9,24).

In our study, we divided the patients into two groups as those with OP and without OP. Although there was significant difference between the two groups in terms of mean breastfeeding duration, mean breastfeeding duration for each child, mean breastfeeding duration under the age of 25, and mean breastfeeding duration for each child under the age of 25, these were not found to be independent indicators for OP in the multivariate logistic regression analysis.

Finally, this study has several limitations. It was a cross-sectional study and the data were obtained through a questionnaire answered by the patients. The data concerning pregnancy and breastfeeding were also collected retrospectively. In addition, diets, physical activity levels, and vitamin D levels of the patients as elements affecting OP development were not studied. Although the questionnaire included inquiry on breastfeeding duration, frequency of breastfeeding was not addressed.

In conclusion, our study results suggest that lactation and age of first pregnancy have no effect on developing postmenopausal OP. However, further prospective and large-scale studies are needed to confirm our findings.

REFERENCES

1. Raisz LG. Screening for osteoporosis. N Engl J Med. 2005;353(2):164–71.
2. Tuppurainen M, Kroger H, Saarikoski S, Honkanen R, Alhava E. The effect of gynecological risk factors on lumbar and femoral bone mineral density in peri- and postmenopausal women. Maturitas. 1995;21(2):137–45.
3. Kalkwarf HJ, Specker BL. Bone mineral loss during lactation and recovery after weaning. Obstet Gynecol. 1995;86(1):26–32.
4. Dursun N, Akin S, Dursun E, Sade I, Korkusuz F. Influence of duration of total breast-feeding on bone mineral density in a Turkish population: does the priority of risk factors differ from society to society? Osteoporos Int. 2006;17(5):651–5.

5. Okyay DO, Okyay E, Dogan E, Kurtulmus S, Acet F, Taner CE. Prolonged breast-feeding is an independent risk factor for postmenopausal osteoporosis. Maturitas. 2013;74(3):270–5.
6. Lenora J, Lekamwasam S, Karlsson MK. Effects of multiparity and prolonged breast-feeding on maternal bone mineral density: a community-based cross-sectional study. BMC Women's Health. 2009;9:19.
7. Henderson PH, Sowers M, Kutzko KE, Jannausch ML. Bone mineral density in grand multiparous women with extended lactation. Am J Obstet Gynecol. 2000;182(6):1371–7.
8. Wiklund PK, Xu L, Wang Q, Mikkola T, Lyytikainen A, Volgyi E, et al. Lactation is associated with greater maternal bone size and bone strength later in life. Osteoporos Int. 2012;23(7):1939–45.
9. Huo D, Lauderdale DS, Li L. Influence of reproductive factors on hip fracture risk in Chinese women. Osteoporos Int. 2003;14(8):694–700.
10. Johnell O, Kanis J. Epidemiology of osteoporotic fractures. Osteoporos Int. 2005;16(Suppl. 2):S3–7.
11. Bolzetta F, Veronese N, De Rui M, Berton L, Carraro S, Pizzato S, et al. Duration of breastfeeding as a risk factor for vertebral fractures. Bone. 2014;68:41–5.
12. Streeten EA, Ryan KA, McBride DJ, Pollin TI, Shuldiner AR, Mitchell BD. The relationship between parity and bone mineral density in women characterized by a homogeneous lifestyle and high parity. J Clin Endocrinol Metab. 2005;90(8):4536–41.
13. Kritz-Silverstein D, Barrett-Connor E, Hollenbach KA. Pregnancy and lactation as determinants of bone mineral density in postmenopausal women. Am J Epidemiol. 1992;136(9):1052–9.
14. Ozdemir F, Demirbag D, Rodoplu M. Reproductive factors affecting the bone mineral density in postmenopausal women. Tohoku J Exp Med. 2005;205(3):277–85.
15. Demir B, Haberal A, Geyik P, Baskan B, Ozturkoglu E, Karacay O, et al. Identification of the risk factors for osteoporosis among postmenopausal women. Maturitas. 2008;60(3):253–6.
16. Hwang I, Choi Y, Lee W, Kim J, Lee I, Kim S, et al. Association between prolonged breastfeeding and bone mineral density and osteoporosis in postmenopausal women: KNHANES 2010–2011. Osteoporos Int. 2016;27(1):257–65.
17. Abrams SA. Normal acquisition and loss of bone mass. Horm Res. 2003;60(Suppl. 3):71–6.
18. Bonjour JP, Theintz G, Buchs B, Slosman D, Rizzoli R. Critical years and stages of puberty for spinal and femoral bone mass accumulation during adolescence. J Clin Endocrinol Metab. 1991;73(3):555–63.
19. Recker RR, Davies KM, Hinders SM, Heaney RP, Stegman MR, Kimmel DB. Bone gain in young adult women. JAMA. 1992;268(17):2403–8.
20. Yun BH, Choi YR, Choi YS, Cho S, Lee BS, Seo SK. Age at first delivery and osteoporosis risk in Korean postmenopausal women: the 2008–2011 Korea National Health and Nutrition Examination Survey (KNHANES). PLoS ONE 2015;10(5):1–10.
21. Schnatz PF, Barker KG, Marakovits KA, O'sullivan DM. Effects of age at first pregnancy and breast-feeding on the development of postmenopausal osteoporosis. Menopause. 2010;17(6):1161–6.
22. Cavkaytar S, Seval MM, Atak Z, Findik RB, Ture S, Kokanali D. Effect of reproductive history, lactation, first pregnancy age and dietary habits on bone mineral density in natural postmenopausal women. Aging Clin Exp Res. 2015;27(5):689–94.
23. Sowers MF, Hollis BW, Shapiro B, Randolph J, Janney CA, Zhang D, et al. Elevated parathyroid hormone-related peptide associated with lactation and bone density loss. JAMA. 1996;276(7):549–54.
24. Sowers M, Eyre D, Hollis BW, Randolph JF, Shapiro B, Jannausch ML, et al. Biochemical markers of bone turnover in lactating and nonlactating postpartum women. J Clin Endocrinol Metab. 1995;80(7):2210–6.