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ORIGINAL ARTICLE

Effect of reproductive history, lactation, first pregnancy age and dietary habits on bone mineral density in natural postmenopausal women

Sabri Cavkaytar · Mehmet Murat Seval · Zeliha Atak · Rahime Bedir Findik · Sevgi Ture · Demet Kokanali

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Abstract
Aim The aim of this study was to investigate the possible risk factors related with osteoporosis in women with spontaneous menopause.
Methods Five hundred and one postmenopausal women were divided into three groups as normal, osteopenic and osteoporotic according to their bone mineral density (BMD). By face-to-face interview, parity, age at menarche, age at menopause, duration of fertility, duration of menopause, first pregnancy age, total lactation period, exercise, smoking were assessed. Women with menopause age before 40 years, surgical menopause, who had any anti-osteoporosis treatment, hormone replacement therapy at the time of BMD measurement and corticosteroid use longer than 6 months were excluded from the study.
Results Among 501 postmenopausal women, 107 women were classified as normal, 170 as osteopenic and 224 as osteoporotic. Among demographic features of patients, there was statistically significant difference between the groups in age, BMI and parity ($p < 0.001$, $p < 0.0001$ and $p = 0.002$, respectively). There were statistically significant differences between the groups in case of age at menopause, duration of fertility and duration of menopause ($p = 0.013$, $p = 0.013$ and $p < 0.0001$, respectively). In the multivariate logistic regression analysis, BMI over 32 and fertility duration over 33 years had a statistically significant protective effect against osteoporosis (OR 0.42, CI 95 % 0.27–0.66; OR 0.36, CI 95 % 0.24–0.56, respectively), but age was positively correlated with osteoporosis (OR 1.13, CI 95 % 1.01–1.17)
Conclusions Duration of fertility (years of menstruation) longer than 33 years and body mass index higher than 32 seem to protect against postmenopausal osteoporosis. Age is also an independent risk factor for postmenopausal osteoporosis.

Keywords Postmenopausal osteoporosis · Risk factors · Lactation · First pregnancy age · Duration of fertility · Body mass index

Introduction

Osteoporosis is an important health problem characterized by compromised bone strength that leads to increased fracture risk [1]. In a recent report, the economic burden of osteoporosis in 27 European Union countries was estimated at 37 billion euro and were expected to increase 25 % in 2025 [2]. So identification of risk factors to prevent postmenopausal osteoporosis (POPS) is very important.

Since etiology of POPS is multifactorial [3], it is difficult to reveal the risk factors properly. Advancing age, female sex, low body mass index (BMI), smoking, family history, lifestyle changes and medical history have been reported as risk factors for osteoporosis [3, 4].

Despite the well-known risk factors, there is conflict about the effect of reproductive characteristics (age at

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S. Cavkaytar (✉) · R. B. Findik · D. Kokanali
Department of Obstetrics and Gynecology, Ankara Dr Zekai Tahir Burak Women' Health Research and Education Hospital, Gurpinar sokak.No: 4/8, Cebeci, Ankara, Turkey
e-mail: sabri.cavkaytar@gmail.com

M. M. Seval · Z. Atak · S. Ture
Department of Obstetrics and Gynecology, Ankara Kecioren Research and Education Hospital, Ankara, Turkey

menarche, age at menopause, duration of fertility, parity, age at first pregnancy and total lactation period) on POPS in the literature.

There are also conflicting reports about the effect of paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) on bone mineral density (BMD) and fracture risk [5–8]. Eating patterns and dietary habits have been found to affect the bone mass also [9–11].

In this study, we investigated the effects of reproductive characteristics, dietary habits (black tea, vegetarian status), exercise, smoking, paracetamol, NSAID consumption on BMD in postmenopausal Turkish women.

Materials and methods

Five hundred and one postmenopausal women who were admitted to Ankara Kecioren Education and Research Hospital between January 2012 and April 2013 were included in this study. The study was approved by the Ethical Committee of Ankara Kecioren Education and Research Hospital.

Women with menopause age before 40 years, surgical menopause, who had any anti-osteoporosis treatment or hormone replacement therapy at the time of BMD measurement or within the past 6 months and corticosteroid use longer than 6 months were excluded from the study.

Informed consent was provided from all the women and the data were collected by face-to-face interview. Demographic features, reproductive history (parity, age at menarche, age at menopause, duration of fertility, duration of menopause, first pregnancy age, total lactation period), dietary habits (black tea drinking, vegetarian status) and paracetamol or NSAID consumption were recorded (Table 1).

The patients were divided into three groups as normal ($n = 107$), osteopenic ($n = 170$) and osteoporotic ($n = 224$) according to the lowest T score of BMD values at the lumbar vertebra (L1–L4) and right femur (neck, intertrochanteric and ward triangle) by dual energy X-ray absorptiometry (DEXA) method using Hologic 4500 QDR (Discovery). Osteoporosis was defined as a T score ≤ -2.5, osteopenia as T score from -1.1 to -2.4 and normal as a T score ≥ -1.0 [12].

Menopause was defined as amenorrhea lasting more than one year. Exercise was defined as walking at least 30 min per day. Low socioeconomic status was defined as "monthly income lower than 1000 Turkish Liras" according to the 2012 Turkish Statistical Institute report [13]. Any gestation lasting at least 28 weeks was defined as pregnancy. Total lactation period was mentioned as months.

As dietary habits, black tea-drinking patients were described as "drinking black tea at least 1 cup in a day" and patients preferring vegetarian diet were described as vegetarian.

Paracetamol or NSAID consumption was recognized if patients were current users or received at least three or more prescriptions in last year.

Data were stored and analyzed using the Statistical Package for the Social Sciences version 13.0 (SPSS, Chicago, IL, USA). Normality was tested by Kolmogorov–Smirnov test. Non-normally distributed metric variables were analyzed by the Kruskal–Wallis test for the comparison of the variables among the groups. Chi-square test (Fischer's exact test), student t test and Mann–Whitney U test were used for the comparison of data between the groups. For the variables that showed statistically significant differences between the groups, univariate and multivariate logistic regression models have been performed. p values less than 0.05 were considered significant.

Results

Five hundred and one postmenopausal women were classified as normal (n 107), osteopenic (n 170) and osteoporotic (n 224) according to their BMD. Demographic and reproductive characteristics of the patients are shown in Table 1. Among demographic features of patients, there was statistically significant difference between the groups in age, BMI and parity ($p < 0.001$, $p < 0.0001$ and $p = 0.002$, respectively). There was no statistically significant difference in vegetarian status, black tea drinking, smoking, exercise and low socioeconomic status between the groups. When we consider the reproductive characteristics of the patients, there were statistically significant differences between the groups in case of age at menopause, duration of fertility and duration of menopause ($p = 0.013$, $p = 0.013$ and $p < 0.0001$, respectively). There was no statistically significant difference in first pregnancy age and total lactation period between the groups.

The percentage of patients who had lactation period over 45 months was statistically significantly higher in the osteoporotic and osteopenic group than the control group ($p = 0.018$).

In the univariate logistic regression analysis of the variables, age, parity and lactation over 45 months were positively correlated with osteoporosis [odds ratio (OR) 1.1, 95 % confidence interval (CI) 1.07–1.14; OR 1.16, CI 95 % 1.04–1.30; OR 1.46, CI 95 % 1.02–2.09, respectively) (Table 2). On the other hand, BMI over 32 and fertility duration over 33 years were negatively correlated with osteoporosis (OR 0.48, CI 95 % 0.31–0.72; OR 0.58, CI 95 % 0.41–0.83, respectively). In the multivariate logistic regression analysis of variables for osteoporosis,

Table 1 Demographic, dietary characteristics and reproductive history of the patients according to BMD

	Normal (*n* 107)	Osteopenia (*n* 170)	Osteoporosis (*n* 224)	*p*
Age (years)*	53 (41–67)	54 (41–78)	57 (46–84)	<0.001
BMI (kg/m^2)*	31.2 (20.6–45.2)	29.7 (18.7–45.8)	28.9(19.4–48.7)	<0.0001
Vegetarian status, *n* (%)	22 (20.6)	38 (22.4)	36 (16.1)	NS
Black tea drinking, *n* (%)	78 (72.9)	113 (66.5)	153 (68.3)	NS
Current smoking, *n* (%)	21 (19.6)	36 (21.2)	35 (15.6)	NS
Exercise, *n* (%)	35 (32.7)	57 (33.5)	89 (39.79	NS
Low socioeconomic status, *n* (%)	14 (13.1)	30 (17.6)	48 (21.4)	NS
Literate, *n* (%)	93 (86.9)	143 (84.1)	185 (82.6)	NS
Paracetamol, *n* (%)	15 (14.0)	17 (10)	34 (15.2)	NS
NSAID, *n* (%)	25 (23.4)	41 (24.1)	45 (20.1)	NS
Diabetes mellitus, *n* (%)	24 (22.4)	21(12.4)	36 (16.1)	NS
Hypertension, *n* (%)	34 (31.8)	55 (32.4)	69 (30.9)	NS
Parity*	3 (0–6)	3 (0–11)	3 (0–15)	0.002
Age at menopause*	49 (40–58)	48 (40–57)	47 (40–56)	0.013
Duration of fertility (years)*	35 (25–46)	35 (26–44)	33 (24–44)	0.013
Duration of fertility >33 years *n* (%)	71 (66.4)	103 (60.6)	111 (49.6)	0.008
Duration of menopause (years)*	4 (1–21)	6 (1–30)	11(1–34)	<0.0001
First pregnancy age*	20 (15–41)	20 (15–37)	20 (15–40)	NS
Total period of lactation (months)*	36 (0–144)	42 (0–168)	48 (0–192)	NS
Lactation period >45 months *n* (%)	37 (34.9)	78 (46.7)	114 (51.6)	0.018

* Data are presented as median (minimum–maximum)

NS non-significant

Table 2 Logistic regression analysis for osteoporosis

	Univariate logistic regression			Multivariate logistic regression		
	OR	CI 95 %	*p*	OR	CI 95 %	*p*
Age	1.10	1.07–1.14	<0.001	1.13	1.01–1.17	<0.0001
Parity	1.16	1.04–1.30	0.008	–	–	–
BMI >32 (kg/m^2)	0.48	0.31–0.72	<0.0001	0.42	0.27–0.66	<0.0001
Fertility duration >33 years	0.58	0.41–0.83	0.003	0.36	0.24–0.56	<0.0001
Lactation >45 months	1.46	1.02–2.09	0.036	–	–	–

BMI over 32 kg/m^2 and fertility duration over 33 years had a statistically significant protective effect against osteoporosis (OR 0.42, CI 95 % 0.27–0.66; OR 0.36, CI 95 % 0.24–0.56, respectively), but age was positively correlated with osteoporosis (OR 1.13, CI 95 % 1.01–1.17) (Table 2).

Discussion

In this cross-sectional study, after the multivariate logistic regression analysis of variables for osteoporosis, BMI over 32 kg/m^2 and fertility duration over 33 years had a statistically significant protective effect against osteoporosis (OR 0.42, CI 95 % 0.27–0.66; OR 0.36, CI 95 % 0.24–0.56, respectively), but age was positively correlated with osteoporosis (OR 1.13, CI 95 % 1.01–1.17) (Table 2).

In the literature, there is good evidence that lower BMI is associated with higher osteoporosis risk [14–16]. Ho et al. [15] have found that weight was the best predictor of osteoporosis at each of six skeletal sites measured. Kroger et al. [16] reported that each kilogram increase in weight resulted in an increase in BMD at the lumbar spine 0.004 g/cm^2 and femur neck by 0.005 g/cm^2 among 1600 perimenopausal women in Finland. In our study, women with BMI >32 kg/m^2 had statistically significant protective effect against osteoporosis similar with the literature.

There is inconsistent evidence that older age is associated with lower BMD after adjustment for menopausal status [17]. Although most of the studies have reported negative association between older age and BMD [14–16], some studies found no relationship between age and BMD

[18, 19]. We have found that older age is an independent risk factor for osteoporosis.

Although some studies reported negative association between older age at menarche and BMD [14, 15], in many of the studies, age at menarche was not found to be associated with BMD similar to our study [20–23]. Also in a recent review, inconsistent evidence was found between older age at menarche and BMD [17]. This might be explained by the differences in years of menopause in these studies.

In case of menopause age, no relationship between BMD and menopausal age [22, 24], lower BMD in women with menopausal age between 40 and 44 years old [25] have been reported. In our study, age at menopause was statistically significantly lower in the osteoporotic group and duration of menopause was significantly higher in the osteoporotic group (Table 1).

In the present study, we have found that fertility duration over 33 years had a statistically significant protective effect against osteoporosis (Table 2). Similar to our study, duration of fertility was positively correlated with BMD in the literature [20, 21, 26]. Among French postmenopausal women, duration of fertility has been reported as the best predictor of spinal BMD [26] and longer duration of menstruation was associated with higher BMD in Australian postmenopausal women [27]. On the other hand, in a study from Morocco, no relationship has been reported between the duration of fertility and BMD [24]. But in this study, all the participants were not postmenopausal and nearly half of the women had low calcium intake.

In a study from Sweden consisting of 1044 postmenopausal women who were all 75 years old, it has been reported that duration of fertility did not influence BMD in old age [23]. This finding might be attributed to the very old age of the participants.

In the literature, there are conflicting results about the effect of parity on BMD. In our study in the univariate analysis of variables, parity had a negative effect on BMD, but in multivariate logistic regression model, there was no association between the parity and osteoporosis in agreement with other studies [17, 20, 28]. But in two studies from Turkey, high parity was determined as a risk factor for osteoporosis [29, 30]; however, a recent study from Turkey has found that parity has a protective effect for osteoporosis [31]. These conflicting results could be explained with the evaluation of different confounding factors (dietary calcium intake, time interval between the parities, hormone replacement therapy, anti-osteoporosis treatment, etc.) in different studies.

Effect of total lactation period on osteoporosis is another debated subject. The fetus mobilizes 30 g of maternal calcium for skeleton formation [32] which comes mostly from increased intestinal absorption and substantially mobilization from the maternal skeleton during pregnancy. But during lactation, maternal skeleton supplies most of this calcium [32]. Bone loss during lactation is transient and is reversed postpartum [33]. Recovery period depends on the length of both lactation and postpartum amenorrhea [34]. In fact, selection criteria of the patients cause this discrepancy in the literature. Schnatz et al. [35] reported that lactation decreased the incidence of POPS and Chantry et al. [36] found that lactation might be associated with greater BMD in adolescent motherhood. But both in these reports, the definition of lactation was "exclusively lactation for at least 1 month". On the other hand, most of the patients had prolonged lactation periods in the studies that reported negative association between BMD and lactation [31, 37]. The time interval between the pregnancies was not mentioned in most of the studies [31, 35, 37]. Similar to our results, many studies did not find any correlation between lactation and BMD [20, 22]. Also in a recent review, no association between parity, lactation and lower BMD has been accepted as good evidence according to the literature [17].

Since peak bone mass (PBM) is important in the development of POPS, effect of age at first pregnancy on BMD has been studied in the recent years. Schnatz et al. [35] have found that women whose first pregnancy was after PBM ($\geq$27 years) and who had a history of breastfeeding had the lowest prevalence of POPS. On the other hand, Okyay et al. have reported that osteoporosis risk in women who breast-fed >1 year per child under age 27 was increased 7.1-fold [31]. Ozdemir et al. [29] reported increased risk of osteoporosis in women who had a higher age at first pregnancy. In the present study, although age at first pregnancy over 24 seems to protect against bone loss in univariate logistic regression, in the multivariate logistic regression model we could not find any correlation between the age at first pregnancy and lower BMD.

Vegetarian diet has been found beneficial for bone health because of increased phytoestrogens and calcium intake [9, 38]. Contrastly, Ho-Pham et al. [39] reported that vegan diets were associated with lower BMD, newly reported normal BMD in vegetarians [40]. In this study, there was no relationship between the vegetarian status and BMD. Among 5379 postmenopausal women, there was no difference in mean broadband ultrasound attenuation of calcaneum between different dietary groups [10]. But vegetarian status of our patients was not determined by a food frequency questionnaire which might be a weakness of our study.

Recently, it has been reported that black tea might prevent early bone loss in a rat osteoporosis model [41]. We also investigated the effect of black tea drinking on BMD, but there was no association between the groups. Also in a study from Turkey, black tea drinking had no statistically significant effect on BMD in agreement with our study [11].

Effect of paracetamol and NSAID consumption on BMD and fracture risk is also not well understood. NSAIDs inhibit the synthesis of prostaglandins which increases bone resorption by osteoclasts. On the basis of this, higher BMD was found in NSAIDs users than the non-users [42, 43] but this was not associated with fracture risk reduction [42]. Paracetamol was shown to inhibit osteoblast activity in vitro [44] and paracetamol use was found as a risk factor for fracture [8]. Similar to our study Danish Osteoporosis Prevention Study (DOPS) reported no association between paracetamol, NSAID consumption and BMD [6], but NSAID was associated with an increased fracture risk in DOPS. We had no data of patients about fracture history.

The limitations of our study are the potential selection bias seen in cohort studies. Although the data were collected by face-to-face interview, recall bias might have occurred also. Some osteoporosis-related factors such as presence of connective tissue diseases and dietary sources of calcium and vitamin D were not mentioned which might be a weakness of our study.

We tried to select a homogenized group of patients who had natural menopause, and excluded patients who had anti-osteoporosis treatment and hormone replacement therapy. Although very difficult, we tried to control the possible confounding factors such as reproductive history, dietary habits, exercise, smoking and socioeconomic status in our study. These might be accepted as the strength of our study.

In conclusion, duration of fertility (years of menstruation) longer than 33 years and body mass index (BMI) higher than 32 seem to be protective against postmenopausal osteoporosis but advanced age is an independent risk factor for postmenopausal osteoporosis and bone loss. However, the multifactorial etiology of osteoporosis makes the prospective studies difficult in terms of standardization of the patients and determination of a sole risk factor.

Conflict of interest The authors declare that they have no conflict of interest.

Human and Animal Rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the author.

Informed consent Informed consent was obtained from all individual participants included in the study.

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