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Effect of First Pregnancy Age/Teenager Pregnancy or No Pregnancy On Bone Mineral Density in Peri-Menopausal Women

Ali Ovayolu[1*], Aylin Turan[2], Selver Güler[3], Ayla Yava[4]

[1]*Department of Obstetrics and Gynecology, Medical School of Istinye University, Istanbul, Turkey*
[2]*Department of Obstetrics and Gynecology, Cengiz Gokcek Women's and Children's Hospital, Gaziantep, Turkey*
[3]*Department of Nursing, Faculty of Health Sciences, Kilis 7 Aralik University, Kilis, Turkey*
[4]*Surgical Nursing Department, Faculty of Health Sciences, Hasan Kalyoncu University, Sahinbey, Gaziantep, Turkey*

ABSTRACT

This study compares bone mineral density (BMD) scores in peri-menopausal women with and without a history of teenage pregnancy (TP) or pregnancies (TPs), for the femoral neck and lumbar spine. Obstetric history, history of menstruation, education, exercise, sex, marital status, residency, income level, and tobacco/alcohol use were assessed. After a DEXA scan, both groups were compared for variables. A total of 485 patients were included in the study. Most of the analyzed demographic characteristics showed no significant difference between the research groups. The childless group had a higher incidence of femoral bone osteopenia than the group without a history of teenage pregnancy (non-TP) ($p<0.05$). However, there was no difference in the lumbar spine results between the TP(s), non-TP, and no pregnancy groups. The BMD, T, and Z scores of women's femoral neck/lumbar spine did not alter according to whether they had had one or more TPs. Despite numerous studies, modifiable variables that impact peri-menopausal women's bone health, such as TPs, have not yet been sufficiently identified. Further studies are still needed to find the causes of bone loss in peri-menopause and develop preventive measures/treatments.

Keywords: Adolescent pregnancy; body mass index; bone loss; determinants; primary osteoporosis; risk factors

Introduction

Teenage pregnancies (TPs), also known as adolescent pregnancies, are defined as younger than 20 years of age. TPs are still a global problem and are related to poverty and ignorance. TPs have short-term effects (maternal/fetal effects), as well as long-term effects (psychological/women's health effects) (1, 2). The estimated global TPs ratio in the world has decreased over time to 11.6% (3). Recently, parallel to this global decline, the adolescent-specific fertility rate also decreased from 4.9% in 2001 to 1.3% in 2021 in Turkey (4). The rates of TPs in our hospital also decreased from 21% in 2014 to 12% in 2018 (5).

In females, an increase in bone mass begins in the teenage (~40%) years and peaks in the late twenties (about 27 years old) (6). Teenage females reach a peak bone mass (PBM), and this PBM constitutes the most important determinant of osteoporosis in menopause. PBM is affected by genetic factors, and also hormonal factors which are modifiable. Researchers showed that TPs might have undesirable effects on PBM. It is well known that the maternal body's demand for calcium rises during gestation/lactation, which is recompensed with enough intake. There is continuing debate about the harmful effects of TPs on PBM (7). However, the impact of gravidity on bone mass is debatable. Hellmeyer et al. (8) suggested that a 2-9% loss might occur during pregnancy, whereas Yumusakhuylu et al. (9) considered that pregnancy-related bone mineral density (BMD) loss was insignificant. It was also shown that pregnancy-associated changes in bone mass might be reversible (10, 11). According to a Royal College of Obstetricians and Gynaecologists assessment, bone mass levels return to normal after delivery/breastfeeding, and there is no increased long-term fracture risk among females with high parity (12). In the published literature, some studies compared women with a history of TP and those without, and Ward et al. (13) found

***Corresponding Author:** Ali Ovayolu, Department of Obstetrics and Gynecology, Liv Hospital, 27080 Gaziantep, Turkey
E-Mail: drovayolu@yahoo.com, Tel.: +90 342 360 08 88, Fax: +90 342 360 02 90
ORCID ID: Ali Ovayolu: 0000-0003-0234-3026, **Aylin Turan:** 0000-0002-8367-0063, **Selver Güler:** 0000-0003-2984-4306, **Ayla Yava:** 0000-0003-3468-6779
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a lower bone mass at the radial diaphysis in women with TP, and Lloyd et al. (14) also found a lower femoral bone mass in women with a history of TP.

Years before the last menstrual period, physical and mental changes occur. This transition period is known as peri-menopause, and it can last anywhere from four to eight years. It begins with alterations in the interval between periods and concludes one year following the last menstrual cycle. In light of the current literature, the effect of TP/TPs on bone mass in peri-menopausal women remains controversial. A study on Korean women demonstrated the adverse effects of TP history on bone mass at different phases of menopause (15). The risk factors for lower postmenopausal BMD have been extensively established, and there is also considerable evidence that bone loss occurs before menopause. Risk factors for decreased premenopausal BMD and higher premenopausal/peri-menopausal bone loss, on the other hand, are poorly known (16). Alterations in hormone-related BMD are reported to happen before the onset of menopause (17). For this reason, we performed this research on premenopausal women, not (post)menopausal women.

The purpose of this study was to provide new evidence to help clarify this topic. Thus, we conducted a large cohort study to assess the effect of selected BMI, gestational, exercise, smoking, and medical history characteristics on BMD in women going through menopause, as assessed at the lumbar spine and femoral neck.

Materials and Methods

Study Population: This study was conducted between November 2017 and January 2021 in the Obstetrics and Gynecology Department of our hospital. In our outpatient clinic, women who presented with gynecologic problems (e.g. menstrual irregularity, urinary symptoms, vaginal discharge, well-being control) were invited to enroll in the study by first author. Healthy peri-menopausal women aged between 40 and 57 years were asked to take part (Figure 1). All women signed a written informed consent form before admittance. The data was then collected through face-to-face interviews. The interview time with the women lasted approximately 15 minutes. The Ethics Committee of Hasan Kalyoncu University approved the study (Reference number: 2017/11). The study protocol was created in accordance with the Helsinki Declaration.

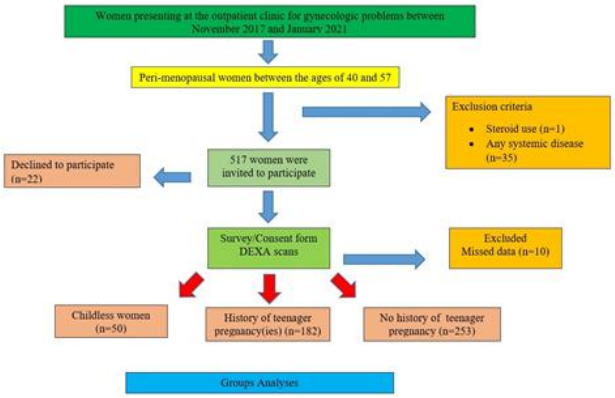

Fig. 1. Diagram of Patient Enrolment and Analysis

The peri-menopausal state was defined as either continuing oligomenorrhea or ongoing amenorrhea lasting less than a year. At inclusion, each woman's age, height, weight, body mass index (BMI), age of menarche, obstetric history, history of smoking, consumption of alcohol, history of regular exercise, history of regular sex, residence, education level, income status, current/past medical conditions, and current/past medication were all recorded. For parity and live births, we only looked at full-term pregnancies (18).

The exclusion criteria were as follows: history of fracture, family history of osteoporosis, use of glucocorticoids, autoimmune diseases such as rheumatoid arthritis, collagen vascular disease, diabetes mellitus, and inflammatory bowel disease, surgical menopause, and those who had any anti-osteoporosis treatment or hormone replacement therapy at the time of BMD measurement or within the past 6 months.

The women were categorized based on their TP history: none, one, and two or more. The women were divided into three categories based on their smoking history: none, former smoker, and active smoker. The women were also classified into three groups based on how often they consumed alcohol: never, socially, and frequently. Having regular sex and a history of regular exercise were divided into two categories: none and present. The education levels were categorized as follows: illiterate, elementary education, high school, and university. The women's accommodation was divided into two categories: rural and urban. The three income levels were classified as follows: low (living on minimum wage), medium, and high (>50,000 Turkish Lira per month). Unmarried, married, and widowed/divorced/separated were the three marital status categories. Dual X-ray absorptiometry (DEXA) remains the "gold

standard" method of BMD assessment worldwide (19). One qualified technician scanned the DEXA measurements. At admission, BMD (in grams per square centimeter) was measured at the lumbar spine (L2-4) and the femoral neck using DEXA (Hologic QDR Discovery, Bedford, Massachusetts, USA). According to the lowest T score of BMD values at the lumbar vertebra (L1-L4) and right femur, the patients were classified into three groups: normal, osteopenic, and osteoporotic. Osteoporosis was classified as a T score ≤ -2.5, osteopenia as a T score ranging from -1.1 to -2.4, and normal as a T score ≥ -1.0 (20). All women were categorized as underweight (BMI <20 kg/m^2), normal (20-24.9 kg/m^2), overweight (25-29.9 kg/m^2), obese (30-39.9 kg/m^2), and severely obese (>40 kg/m^2). The BMD, T, and Z scores of women in different BMI groups were then compared. All women were also categorized according to their ages at admission to the study as 40-44 years, 45-49 years, and over 49 years. Then, the T scores of the women in these different age groups were also compared. All women were categorized regarding their duration of fertility (years of menstruation) at admission to the study as ≤33 and >33 years, and the T scores of these women in these different groups were also compared.

Statistical Analyses: The minimum number required in each group was determined as 194 with the expectation that there would be a small effect size (d=0.28) between the TP group and the non-TP group femoral neck variable being statistically significant (α=0.05; 1-β=0.80). To balance the TP and non-TP groups, it was decided to include the same number of non-TP groups (7). Power analysis was performed using the G*Power 3.9.1 software. Descriptive statistics of the data obtained from the study are given using mean, standard deviation for numerical variables, and frequency and percentage analysis for categorical variables. The normality of the distribution of the variables was examined using the Shapiro-Wilk test. In the comparison of these variables according to categorical variables, the independent samples t-test/Mann-Whitney U test was used for categorical variables containing two groups, and the analysis of variance/Kruskal-Wallis test was used for categorical variables containing three or more groups. In addition, the differences between categorical variables were tested using Chi-square analysis. Analyses were performed using the SPSS 22.0 program. The significance level was chosen as $p<0.05$.

Results

The research included 50 (10.3%) childless women, 182 (37.5%) women with a history of TP, and 253 (52.2%) women without a history of TP, as shown in Table 1. There were 115 (63.2%) women with one TP history, 54 (29.7%) women with two TP histories, 12 (6.6%) women with three TP experiences, and one (0.5%) woman with four TP histories in the TP group. Statistics for early TPs were not estimated because there were only seven early TPs (age <15 years) in the study (5). The findings of the BMD scans of the femoral neck and lumbar spine showed no changes between the three groups, as shown in Table 2. T and Z scores of the femoral neck and lumbar spine also showed no changes between the three groups. The BMD, T, and Z scores of women on the femoral neck and lumbar spine showed no relationship between the women with history of TP and women with history of TPs ($p>0.05$), as shown in Table 3. The BMD, T, and Z scores of women on the femoral neck and lumbar spine showed no relationship between the underweight (n=6; 1.2%), normal (n=63; 13%), overweight (n=173; 35.7%), obese (n=230; 47.4%), and severely obese (n=13; 2.7%) groups.

The BMD and T scores of women in the femoral neck and lumbar spine showed no relationship between the three different age groups (40-44, 45-49, and over 49 years), as shown in Table 4. When the mean ages of peri-menopause at admission were compared between the TP group and TPs group, no statistical difference was detected (46.14 ± 4.14 vs. 45.36 ± 3.23 years, respectively; p=0.187). Additionally, there was no correlation between the T scores of women in the femoral neck and lumbar spine of those who gave birth before the age of 28 years (n=391; 89.9%) and after the age of 27 years (n=44; 10.1%).

The BMD, T, and Z scores of women in the femoral neck and lumbar spine showed no correlation with premenopause age, weight, BMI, age at menarche, parity, live-born, smoking history, and regular exercise. There was no correlation between women with older menarche ages (>14 years) (n=76; 15.7%) and those without (n=409; 84.3%), according to the T scores of women in the femoral neck and lumbar spine.

Table 1: The Sociodemographic Variables and Baseline Characteristics of Women with History of Teenage Pregnancy, Women Without History of Teenage Pregnancy, and Childless Women During the Peri-Menopausal Period

Variables	Childless women group (n=50) (Mean±SD) (median (Q1-Q3))	TP group (n=182) (Mean±SD) (median (Q1-Q3))	Non-TP group (n=253) (Mean±SD) (median (Q1-Q3))	p
Age (years)	45.74±3.42 45.00 (44.00-48.00)	45.85±3.84 46.00 (43.00-48.00)	46.14±3.62 46.00 (43.00-48.00)	0.632[a]
Weight (kilograms)	74.22±13.34 72.50 (64.00-82.00)	75.93±12.19 75.50 (66.00-85.00)	75.62±11.98 75.00 (66.00-84.00)	0.679[a]
BMI (kg/m2)	30.08±5.44 28.87 (25.65-33.30)	30.22±4.70 30.41 (26.67-33.22)	30.11±4.91 29.64 (26.56-33.49)	0.968[a]
Gravity (n)	None	4.83±2.10 4.00 (3.00-6.00)	4.08±2.02 4.00 (3.00-5.00)	0.001*.[b]
Parity (n)	None	4.27±1.66 4.00 (3.00-5.00)	3.44±1.68 3.00 (2.00-4.00)	0.001*.[b]
Live born (n)	None	4.09±1.56 4.00 (3.00-5.00)	3.29±1.61 3.00 (2.00-4.00)	0.001*.[b]
Age at first delivery (years)	None	17.54±1.32 18.00 (17.00-19.00)	24.42±4.34 23.00 (21.00-26.00)	0.001*.[b]
TP (n)	None	1.45±0.64 1.00 (1.00-2.00)	None	0.001*.[b]
Age at first period (years)	13.42±1.54 13.00 (12.00-14.00)	13.07±1.35 13.00 (12.00-14.00)	13.20±1.46 13.00 (12.00-14.00)	0.284[a]
Fertility duration (years)	32.32±3.75 32.00 (30.00-35.00)	32.78±3.99 32.00 (30.00-35.00)	32.94±3.85 33.00 (30.00-35.00)	0.581[a]
Marital status				
Married, n (%)	41 (82.00)	167 (91.76)	240 (94.86)	0.001*.[a]
Single, n (%)	7 (14.00)	3 (1.65)	3 (1.19)	
Divorced/widowed, n (%)	2 (4.00)	12 (6.59)	10 (3.95)	
Education				
Illiterate, n (%)	22 (44.00)	76 (41.76)	84 (33.20)	0.002*.[a]
Elementary, n (%)	18 (36.00)	94 (51.65)	121 (47.83)	
High School, n (%)	4 (8)	10 (5.49)	20 (7.91)	
University, n (%)	6 (12)	2 (1.10)	28 (11.07)	
Residence				
Urban, n (%)	46 (92.00)	170 (93.41)	241 (95.26)	0.556[a]
Rural, n (%)	4 (8.00)	12 (6.59)	12 (4.74)	
Tobacco use				
Never, n (%)	39 (78.00)	115 (63.19)	174 (68.77)	0.318[a]
Past, n (%)	2 (4)	19 (10.44)	20 (7.91)	
Current, n (%)	9 (18.00)	48 (26.37)	59 (23.32)	
Alcohol				
Never, n (%)	46 (92.00)	176 (96.70)	247 (97.63)	0.088[a]
Social, n (%)	4 (8.00)	6 (3.30)	4 (1.58)	
Regular, n (%)	0 (0)	0 (0)	2 (0.79)	
Exercise				

Regularly, n (%)	2 (4.00)	12 (6.59)	21 (8.30)	0.516[a]
Irregularly, n (%)	48 (96.00)	170 (93.41)	232 (91.70)	
Sex				
Regularly, n (%)	33 (66.00)	144 (79.12)	200 (79.05)	0.109[a]
Irregularly, n (%)	17 (34.00)	38 (20.88)	53 (20.95)	
Household income				
Low, n (%)	43 (86.00)	154 (84.62)	211 (83.40)	
Medium, n (%)	7 (14.00)	28 (15.38)	42 (16.60)	0.876[a]
High, n (%)	0 (0)	0 (0)	0 (0)	

TP: teenager pregnancy(ies).
[a]Chi-Square tests. [b]Independent sample t-tests.
*Significant at 0.05 level.

Table 2: DEXA Scan Results of Women with History of Teenage Pregnancy, Women Without History of Teenage Pregnancy, and Childless Women During Peri-Menopausal Period

	Childless (n=50) (Mean±SD) (median (Q1-Q3))	TP (n=182) (Mean±SD) (median (Q1-Q3))	Non-TP (n=253) (Mean±SD) (median (Q1-Q3))	p
Femoral neck (g/cm²), Std	0.91±0.12 0.91 (0.82-0.98)	0.94±0.14 0.94 (0.84-1.02)	0.94±0.12 0.93 (0.86-1.01)	0.764[a]
Lumbar spine (g/cm²), Std	0.98±0.12 0.97 (0.90-1.08)	0.97±0.12 0.97 (0.89-1.04)	0.99±0.13 0.98 (0.91-1.06)	0.096[a]
Femoral neck (Z score)	0.13±0.96 0.05 (-0.60-0.70)	0.34±1.00 0.30 (-0.40-1.00)	0.31±0.97 0.20 (-0.30-1.00)	0.392[b]
Lumbar spine (Z score)	-0.03±1.15 -0.20 (-0.80-0.80)	-0.14±1.15 -0.20 (-1.00-0.60)	0.00±1.03 0.00 (-0.70-0.70)	0.424[b]
Femoral neck (T score)	-0.26±0.97 -0.25 (-1.10-0.40)	-0.03±1.01 -0.05 (-0.80-0.60)	-0.04±0.95 -0.10 (-0.70-0.60)	0.303[b]
Lumbar spine (T score)	-0.62±1.12 -0.70 (-1.30-0.30)	-0.71±1.17 -0.70 (-1.60-0.00)	-0.52±1.06 -0.60 (-1.30-0.10)	0.190[b]
Femoral DEXA scan results				
Normal range (T score above -1), n (%)	34 (68.00)	145 (79.67)	213 (84.19)	
Osteopenia (T score between -1 and -2.4), n (%)	16 (32.00)	37 (20.33)	40 (15.81)	0.026*.[c]
Osteoporosis (T score below -2.5), n (%)	None	None	None	
Lumbar DEXA scan results				
Normal range (T score above -1), n (%)	30 (60.00)	106 (58.24)	164 (64.82)	
Osteopenia (T score between -1 and −2.4), n (%)	18 (36.00)	63 (34.60)	83 (32.80)	0.163[c]
Osteoporosis (T score below -2.5), n (%)	2 (4.00)	13 (7.10)	6 (2.40)	

TP: teenage pregnancy(ies).
[a]Kruskal-Wallis tests, [b]ANOVA tests, [c]Chi-square tests.
*Significant at 0.05 level.

Table 3: DEXA Scan Results of Women with History of Teenage Pregnancy and Women with History of Teenage Pregnancies During Peri-Menopausal Period

	TP (n=115) (Mean±SD) (median (Q1-Q3))	TPs ≥2 (n=67) (Mean±SD) (median (Q1-Q3))	p
Femoral neck (g/cm2), Std	0.929±0.147 0.944 (0.832-1.011)	0.959±0.123 0.934 (0.876-1.068)	0.268[a]
Lumbar spine (g/cm2), Std	0.964±0.126 0.960 (0.870-1.043)	0.973±0.118 0.971 (0.900-1.042)	0.660[b]
Femoral neck (Z score)	0.278±0.997 0.400 (-0.500-0.900)	0.458±1.011 0.300 (-0.300-1.300)	0.244[b]
Lumbar spine (Z score)	-0.163±1.164 -0.200 (-1.000-0.600)	-0.091±1.140 -0.100 (-0.600-0.600)	0.684[b]
Femoral neck (T score)	-0.112±1.012 0.000 (-0.900-0.500)	0.118±0.984 -0.100 (0.500-1.000)	0.137[b]
Lumbar spine (T score)	-0.754±1.196 -0.800 (-1.600-0.000)	-0.643±1.138 -0.600 (-1.500-0.100)	0.541[b]
Femoral DEXA scan results			
Normal range (T score above -1), n (%)	89 (77.4)	56 (83.6)	
Osteopenia (T score between -1 and -2.4), n (%)	26 (22.6)	11 (16.4)	0.317[c]
Osteoporosis (T score below -2.5), n (%)	None	None	
Lumbar DEXA scan results			
Normal range (T score above -1), n (%)	62 (53.9)	44 (65.7)	
Osteopenia (T score between -1 and -2.4), n (%)	45 (39.1)	18 (26.9)	0.239[c]
Osteoporosis (T score below -2.5), n (%)	8 (7.0)	5 (7.5)	

TP: teenage pregnancy; TPs: teenage pregnancies ≥2.
[a]Mann-Whitney U test. [b]Independent sample t-tests. [c]Chi-square tests.
*Significant at 0.05 level.

Table 4: DEXA Results According to Age Categorization of Women During the Peri-Menopausal Period Included in The Study

	40-44 years (n=170) (Mean±SD) (median (Q1-Q3))	45-49 years (n=182) (Mean±SD) (median (Q1-Q3))	≥50 years (n=253) (Mean±SD) (median (Q1-Q3))	p
Femoral neck (g/cm2), Std	0.94±0.13 0.94 (0.85-1.02)	0.94±0.12 0.93 (0.84-1.02)	0.93±0.12 0.92 (0.83-1.01)	0.392[a]
Lumbar spine (g/cm2), Std	0.98±0.11 0.98 (0.90-1.05)	0.98±0.12 0.97 (0.89-1.07)	0.99±0.17 0.97 (0.91-1.05)	0.974[a]
Femoral neck (T score)	-0.016±0.969 -0.1 (-0.7-0.6)	-0.065±0.99 -0.1 (-0.80-0.60)	-0.134±0.91 -0.20 (-0.80-0.40)	0.548[b]
Lumbar spine (T score)	-0.65±1.0 -0.60 (-1.40-0.00)	-0.56±1.15 -0.70 (-1.40-0.20)	-0.63±1.2 -0.70 (-1.30-0.10)	0.915[b]
Femoral DEXA scan results				
Normal range (T score above -1), n (%)	142 (83.5)	181 (78.7)	69 (81.2)	
Osteopenia (T score between -1 and -2.4), n (%)	28 (16.5)	49 (21.3)	16 (18.8)	0.477[c]
Osteoporosis (T score below -2.5), n (%)	None	None	None	
Lumbar DEXA scan results				
Normal range (T score above -1), n (%)	105 (61.8)	140 (60.9)	55 (64.7)	
Osteopenia (T score between -1 and -2.4), n (%)	58 (34.1)	81 (35.2)	25 (29.4)	0.852[c]
Osteoporosis (T score below -2.5), n (%)	7 (4.1)	9 (3.9)	5 (5.9)	

[a]Kruskal-Wallis tests, [b]ANOVA tests, [c]Chi-square tests.
*Significant at 0.05 level.

The T scores of women in the femoral neck and lumbar spine showed no relationship between the duration of the fertility of the ≤33 years' group (n=281; 57.9%) and >33 years' group (n=204; 42.1%). There was no correlation between women who lived in urban areas (n=457; 94.2%) and women who lived in rural areas (n=28; 5.8%) according to the T scores of women in the lumbar spine and femoral neck (p=0.333 and p=0.933, respectively). There was a weak positive and statistically significant relationship between the T scores of women in the femoral neck and live-born numbers (r=0.100; p=0.027). There was also a weak positive and statistically significant relationship between the T scores of women in the femoral neck and parity (r=0.098; p=0.030). No statistically significant correlation was detected between the T scores of women in the lumbar spine and parity/live-born numbers.

The childless group had more femoral bone osteopenia than the non-TP group (p<0.05), as shown in Table 2. There was a significant difference in first pregnancy age in women with (n=93, 19%) and without femoral neck osteopenia (17.7±9.2 vs 19.7±7.6 years, p=0.026, respectively). There was no difference in first pregnancy age in women with and without normal lumbar spine T scores (19.5±7.9 vs 19.1±8.1 years, p=0.656, respectively).

Discussion

The impact of TP(s) on bone mass is still debatable, with contradicting findings suggesting either a wide range of negative effects or no detectable effects (7). In this study, we investigated the effects of some reproductive characteristics (e.g. age at menarche, age at first

pregnancy), exercise, and smoking on BMD in peri-menopausal Turkish women.

Menopause is a hereditary condition that has mostly unforeseeable effects on bone mass. When we consider the prevalence and consequences, bone loss in peri-menopause is a real concern for both personal and population health. Teenage and peri-menopausal periods, the two ends of reproductive years, are very important times for bone health. Some earlier studies showed that bone loss started before premenopause and accelerated during the period of menopausal transition (21). It is difficult to pinpoint an optimal time frame for assessing bone mass because it is hard to check for these confounding variables. Accordingly, in the present study, menopausal women were excluded to prevent the expected fluctuation in bone mass amongst women of a similar age. Screening for osteoporotic fracture risk in large populations for primary osteoporosis is unlikely to be cost-effective. The inability to reach desired PBM, prior bone loss, or current bone loss may all be contributing factors to low bone density in the peri-menopausal period (19). Therefore, it makes sense to clarify whether pregnancy/TP(s) poses a risk of BMD in peri-menopausal women.

Researchers also showed that additional body weight was the most important protective factor for higher BMD over time at the lumbar spine and femoral neck. High school sports, in the teenage period, were also demonstrated to be protective factors for increased BMD. In contrast, current physical activity was not related to BMD or bone loss. It is unknown if all forms and durations of physical exercise impact BMD accumulation. As a result, teenage physical activity may have a substantial impact on PBM development, and higher BMD premenopause. In this malnourished and largely inactive community, daily physical exercise, number of deliveries, and lactation were not related to BMD status. At each skeletal location, neither age nor smoking status exhibited a significant relationship with BMD t scores. Smoking also had no influence on BMD or bone deterioration in premenopausal heavier women, according to the studies (16, 22). Due to their rarity in our patients, women who habitually drank alcohol could not be analysed for this study. There was also no effect of current regular physical exercise identified. The fact that the women in this research were largely overweight or obese may explain the BMI/weight effect on BMD not being different.

Among the peri-menopausal women, those with a history of at least one pregnancy did not vary compared with women without a history of pregnancies/nulliparous in terms of BMD (23). In contrast, we found that the childless group had more femoral bone osteopenia than the non-TP group. This discrepancy may be due to the small number of women in the childless group.

Although calcium is transferred to the fetus from the maternal body during pregnancy/breastfeeding, women have a compensatory mechanism(s) for their own calcium/bone metabolism. Regarding the impact of parity on BMD, there are still contradictory findings in the literature (24). According to some research, higher parity, which may result in estrogen sensitivity, increases bone density and a decreased risk of fractures (25, 26). Although we found that there was a weak relationship between the T scores of women in the femoral neck and parity/live born in our study. With the assessment of several confounding factors (e.g. live born, the period between the deliveries, breastfeeding duration, dairy-product consumption, malnutrition), these results may not be accused directly in terms of bone health. However, we did not include breastfeeding duration in this study due to likely memory errors by patients. On the other hand, women with three or more children had a 48% to 56% lower risk of significant fragility fracture than nulliparous women, regardless of BMD. Tre'mollieres et al. discovered this in early postmenopausal women; however, our observation of peri-menopausal women agrees with this earlier study (26).

There is still some disagreement over how TP(s) histories relate to BMD in later life. The findings of previous studies ranged from negative to positive consequences. It was shown that TP raised the risk of postmenopausal osteoporosis by 2.2 times (15). In contrast to that, among peri-menopausal women, other researchers found that the femur neck BMD of women who had TP was higher than in those of the non-TP group, although the lumbar region BMD of these women did not change (7). Having more than one child in the teenage period was observed to decrease BMD in the postmenopausal period according to Kaya et al., even though they only had a limited number of patients in their study. They also showed the risk of osteoporosis was 6.8 times greater in patients who had two TPs (6). By contrast, we found that TP and TPs have no detrimental effects on BMD in the peri-menopausal period,

despite the limited number of instances in our research.

Although there is no agreement in the literature, a statistically significant preventive effect against osteoporosis was shown for the duration of fertility of above 33 years by Cavkaytar et al. They also showed that first pregnancy age was not effective on BMD scores in postmenopausal women (20). The findings from our cohort indicate that no significant associations of the duration of fertility over 33 years with BMD scores were identified. But in our study, none of the study's subjects was postmenopausal. In line with Cavkaytar et al.'s research, we find that first delivery age did not affect BMD scores in peri-menopausal women. On the other hand, more studies on this topic could be needed, according to our finding that women with femoral neck osteopenia have lower first delivery age.

There is no consistent relationship between menarche age and BMD or long-term bone alteration (16). A later menarcheal age (>14 years) was indicated to have a lower BMD and a faster peri-menopausal bone loss rate (11). Decreased BMD in peri-menopausal women can be caused by a failure to accumulate enough PBM, a loss of BMD following PBM acquisition, or both (16). Contradictory data have been found in the literature about the effect of the first delivery following PBM on BMD (20). The results from our cohort show that there are no connections between BMD scores and menarche age/peri-menopausal age/first delivery age/older first delivery age (beyond 27 years).

Generally, TP/TPs have different sociodemographic features such as educational level, poverty, and malnutrition (15). According to Durrani et al., high socioeconomic status may be susceptible to osteoporosis, and bone deterioration might also be strongly linked to urbanization (27). In contrast, other researchers showed that geographic location and BMD levels were not correlated (28). In the current study, in line with the previous study, no relationship was found between the residence location and peri-menopausal BMD scores.

Follicle-stimulating hormone (FSH) is used for premenopause diagnosis but is limited by its high inter- or intra-cycle variability (29). Therefore, we did not compare FSH and BMD scores because we thought that FSH levels showed too much fluctuation in the peri-menopausal period. Studies can be planned with anti-Müllerian hormone or antral follicle counts.

A strength of our study is that our analyses excluded women with any systemic condition (e.g. chronic hypertension and thyroid diseases) and those who used any type of medication/supplement intake. A limitation of the study was that it was conducted on women with similar socioeconomic status and demographic backgrounds. The major limitation of our study is that we could not reach the number of cases for each group determined in the power analysis. Although this study investigated TPs and premenopausal BMD, the methodology was observational and cannot ascribe causality without additional evidence.

There is a need for studies to determine the rate of bone loss in premenopause and/or early peri-menopause with objective markers or tests. Advanced/comprehensive studies are needed that recognize the influence of teenage births on premenopausal BMD. Due to the complexity of the relationship between bone health and peri-menopausal women's low BMD, multimodal prevention interventions and multicenter studies are required such that physicians may decide on the necessity for the implementation of suitable treatments in younger women.

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