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Influence of number of deliveries and total breast-feeding time on bone mineral density in premenopausal and young postmenopausal women

Gloria Tsvetov[a,b,*], Sigal Levy[c], Carlos Benbassat[a,b], Ilana Shraga-Slutzky[a,b], Dania Hirsch[a,b]

[a] Institute of Endocrinology, Rabin Medical Center, Beilinson Hospital, Petach Tikva, Israel
[b] Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[c] Statistical Education Unit, The Academic College of Tel Aviv Yaffo, Israel

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ABSTRACT

Objectives: Pregnancy and lactation have been associated with decline in bone mineral density (BMD). It is not clear if there is a full recovery of BMD to baseline. This study sought to determine if pregnancy or breast-feeding or both have a cumulative effect on BMD in premenopausal and early postmenopausal women.
Study design: We performed single-center cohort analysis. Five hundred women aged 35–55 years underwent routine BMD screening from February to July 2011 at a tertiary medical center. Patients were questioned about number of total full-term deliveries and duration of breast-feeding and completed a background questionnaire on menarche and menopause, smoking, dairy product consumption, and weekly physical exercise. Weight and height were measured. Dual-energy X-ray absorptiometry was used to measure spinal, dual femoral neck, and total hip BMD.
Main outcome measures: Associations between background characteristics and BMD values were analyzed.
Results: Sixty percent of the women were premenopausal. Mean number of deliveries was 2.5 and mean duration of breast-feeding was 9.12 months. On univariate analysis, BMD values were negatively correlated with patient age ($p = 0.006$) and number of births ($p = 0.013$), and positively correlated with body mass index ($p < 0.001$). On multiple (adjusted) logistic regression analysis, prolonged breast-feeding duration, but not number of deliveries, was significantly correlated to a low BMD ($p = 0.008$). An effect was noted only in postmenopausal women. The spine was the most common site of BMD decrease.
Conclusions: Prolonged breast-feeding may have a deleterious long-term effect on BMD and may contribute to increased risk of osteoporosis later in life.

1. Introduction

Pregnancy and breast-feeding may place significant stress on calcium metabolism, with a consequent impact on bone metabolism and bone mineral density (BMD). During pregnancy, 2–3% of the maternal total-body calcium content is transferred to the fetus. Although endocrine changes induce a compensatory mechanism to conserve calcium, prospective studies suggest that pregnancy is nevertheless associated with a loss of 2.1–9.4% of BMD in the spine, and up to 3.9% of BMD in the hip [1–3]. There are weak data suggesting that calcium supplementation may benefit pregnant women with low calcium intake, but not those with normal or high calcium intake [4]. If pregnancy is followed by lactation, an additional 250–400 mg of daily calcium is lost in the breast milk; in some cases, the loss can reach 1000 mg [5]. Moreover, during lactation, the calcium-conserving compensatory mechanism gradually disappears, and the new homeostatic calcium mechanism favors the newborn's skeleton independent of the mother's calcium balance or intake [1]. The combined effect of parathyroid hormone-related protein secretion and estrogen deficiency increase the mother's skeletal resorption. Thus, by 6 months of lactation, approximately 3–7% of the maternal BMD may be lost [1,4,6,7]. Every so often, cases of pregnancy- and lactation-related osteoporosis and even fracture appear in the literature [8].

* Corresponding author at: Institute of Endocrinology, Rabin Medical Center, Campus Beilinson, Petah Tikva 49100, Israel. Tel.: +972 3 9377182; fax: +972 3 9211403.
E-mail addresses: Gloria.tsvetov@gmail.com, gloriats@clalit.org.il (G. Tsvetov).

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Despite the large body of research and case studies on changes in BMD during pregnancy and breast-feeding, the recovery process of BMD to baseline level and the predominant effect of pregnancy and/or lactation on this process are still controversial. Studies focusing on the impact of lactation on BMD values showed a mostly reversible effect, especially in women who breast fed for 3–6 months or less [9–11]. However, in studies analyzing the long-term relationships among parity, lactation and osteoporosis, the findings are less clear. A large cross-sectional study from Japan reported an inverse correlation between total lactation period and BMD, but only in women 40–44 years old. In older postmenopausal women, the correlation disappeared after adjusting for age [12]. Single-center cohort studies noted an association of number of deliveries and breast-feeding duration with a decrease in BMD later in life [13–15]. However, some epidemiological studies showed that the number of deliveries and lactation time exerted a protective effect on bone mineralization, or even increased it [16,17] and others reported no significant findings [18,19].

Overall, the majority of these studies included postmenopausal women or study groups with a wide age range (40–89 years), making interpretation of the results difficult. Together, these findings raise the question of a cumulative effect of pregnancies and total breast-feeding time on bone density later in life. We hypothesized that if bone loss is not completely restored postpartum, subsequent pregnancies and lactation may ultimately increase the risk of osteoporosis. Thus, the aim of the present study was to evaluate the effect of number of deliveries and total breast-feeding time on BMD values in a homogenous group of healthy premenopausal and early postmenopausal women.

2. Patients and method

A cross sectional study performed at the Bone Density Unit of the Endocrine Institute, Rabin Medical Center, Israel. The study protocol was approved by the institutional Ethics Committee.

2.1. Subjects

The study group consisted of 500 women aged 35–55 years that were referred to our center to perform bone densitometry as part of a routine screening plan on an annual basis. It is a common practice in Israel for employers to include a health screening program as an added benefit in their employee contracts. It is given equally to all employees, regardless of age, gender, or job assignment. The program covers a routine physical exam, laboratory tests, chest X-ray, ECG, eye exam, and bone densitometry. None of these women had a chronic disease that could affect bone density, such as hyperparathyroidism, thyrotoxicosis, malabsorption, and anorexia. Women who were previously or currently treated for osteoporosis or who were receiving medication known to affect bone density were excluded. It is known that the recovery from bone density loss during pregnancy and lactation may take several months after termination of lactation. We sought to analyze the data of women in a steady state and therefore did not include women who had delivered a child during the last 2 years.

2.2. Clinical parameters

Prior to the BMD test, the women were questioned about the number of full-term deliveries and duration of breast-feeding after each delivery and completed a standard background questionnaire on age at menarche and menopause, duration of menopause, smoking, dairy-product consumption, vitamin supplementation, and weekly physical exercise. Data were also obtained on past fractures, but because the sample was small, this parameter was not included in the statistical analysis. Height and weight were then measured, and body mass index (BMI) was calculated. Before starting the BMD test, the technician confirmed the information on number of deliveries and lactation. Dual-energy X-ray absorptiometry (DEXA; Lunar iDXA ME+200181, GE Healthcare, USA, coefficient of variation 1.1%) was used to measure spinal, dual femoral neck, and total hip density. Results were standardized by *T* score as provided by the manufacturer.

Women were classified according to their menopausal status: premenopausal if they had regular menstrual periods or any menstrual bleeding at last year before BMD measurement, postmenopausal if no menstrual bleeding was noted during the last year.

2.3. Statistical analysis

Associations between clinical characteristics and BMD were determined using Pearson correlation coefficient. To test the effect of the target variable (overall breast-feeding duration), we combined the DXA results in the 3 sites into a single measure by dichotomizing the *T* score for each location as >-2.0 or ≤ -2.0. Overall risk was defined as an abnormal (low) *T* score in at least one site. Fifty-eight women (11.6%) met this criterion. The variables found to be associated with BMD T-score on univariate analysis, namely, age (years), BMI (kg/m^2), and number of births, and the variable of interest, overall breast-feeding duration (months), were then fitted to a logistic regression model to predict the odds of a woman being at risk.

Clinical parameters associated with osteoporosis risk were identified by multiple logistic regression analysis. This model is suitable for predicting dichotomous outcomes and made it possible to test the effect of each variable while taking the effect of the remaining variables in the model into account. Two regression methods were applied: forced entry and stepwise (forward-Wald). Stepwise regression is commonly used when the regression model includes variables that may be correlated with each other. This method selects variables into the model such that insignificant variables or variables that are inter-correlated with each other are eliminated from the final model. The regression analysis was repeated in different methods to provide a more comprehensive picture of the inter-correlations between the various study variables. Comparing the results that the two models yield helps understand the confounding between the number of births and breast-feeding duration and its effect on the results. Similarly, running the analysis for pre- and post-menopausal women separately was done in order to avoid the obvious confounding between age and menopausal status, and to accurately determine the stage at which the study parameters start affecting the outcome measures.

3. Results

3.1. Clinical characteristics of the study group

Five hundred women fulfilled the inclusion criteria and completed the background questionnaire. Three women were excluded from analysis because of incomplete data, and one woman was excluded because of an extreme breast-feeding period. Data from the remaining 496 women were analyzed (Table 1).

Average age of the sample was 47 years (30–55 years). Sixty percent of the women were premenopausal. The postmenopausal women were within 5 years of the last menstrual cycle. Fifty-nine women (11.8%) were current smokers. Most of the women (84%) consumed dairy products regularly. Only 15% and 18.6% used calcium and vitamin D supplementation, respectively. Two hundred eighty two women (56.4%) exercised habitually.