THE EFFECT OF MULTIPLE PREGNANCIES AND LACTATION ON BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN

POSTMENAPOZAL KADINLARDA GEBELİK SAYISI VE LAKTASYONUN KEMİK MINERAL DANSİTESİ ÜZERİNE ETKİLERI

Serap DEMİR, M.D., Mustafa CESUR*, M.D., Müjde AKTÜRK*, M.D., Selma KARAAHMETOĞLU*, M.D.

Afyon Kocatepe University, Medical Faculty, Department of Internal Medicine, Afyon-Turkey
Ankara Numune Hospital, Endocrinology and Metabolism Clinic, Ankara-Turkey
Gazi Medical Journal 2003; 14: 109-114

ABSTRACT

Purpose: Pregnancy and lactation are the two stages of life that cause changes in the calcium and bone metabolism. This study was designed to evaluate the effect of multiple pregnancies and lactation on the bone mineral density (BMD) of postmenopausal women. Methods: Ninety-nine normal weight, non-smoking postmenopausal women without a history of immobilization and drugs affecting BMD were included in the study. The subjects were grouped according to the number of pregnancies (group 1 included 1-4 pregnancies, group 2 included 5-9 and group 3 included ≥10) and total duration of lactation (≤ 20 months as group 1, 20-60 months as group 2 and ≥60 months as group 3). Total duration of menstrual cycles was calculated for each subject. Bone density of the lumbar vertebrae 1-4, (L1-4), femoral neck, Ward's triangle and trochanter regions were measured with dual energy X-ray absorptiometry. Results: An increased number of pregnancies caused lower BMD in the spine, but the duration of lactation has no effect on the BMD of any site and the total duration of menstruation also had no effect on BMD in the postmenopausal period. Conclusion: Subsequent pregnancies without a sufficient interval in between may cause insufficient mineral replacement in maternal tissues and predispose the woman to osteoporosis.


INTRODUCTION

Pregnancy and lactation are the two stages in a woman’s life that are characterized by hormonal changes. These changes raise the question as to whether these stages have any effect on bone mineral density (BMD). Due to bone mineralization in the fetus and as the neonate needs calcium, a 3-10% drop and regain of bone density in the woman can be seen during these periods (1). During pregnancy, the increased calcium need of the fetus can be met mainly by increased maternal intestinal calcium absorption and decreased renal calcium losses and to a lesser extent by increased calcium
Table- 1: Clinical characteristics of the subjects grouped according to the number of pregnancies.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>25.2 ± 2.3</td>
<td>25.8 ± 2.7</td>
<td>26 ± 2.1</td>
<td>-0.05</td>
</tr>
<tr>
<td>Age</td>
<td>55.7 ± 6.3</td>
<td>58.8 ± 6.6</td>
<td>60.6 ± 4.5</td>
<td>-0.05</td>
</tr>
<tr>
<td>Duration of menstrual period</td>
<td>30.3 ± 5.5</td>
<td>32.8 ± 7</td>
<td>32.9 ± 5.5</td>
<td>-0.05</td>
</tr>
<tr>
<td>Duration of lactation</td>
<td>26.1 ± 28.9</td>
<td>53.9 ± 34.3</td>
<td>108.7 ± 63.9</td>
<td>-0.01</td>
</tr>
</tbody>
</table>

Values are given as the mean ± standard deviation.

Table- 2: Clinical characteristics of the subjects grouped according to the duration of lactation.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>57.8 ± 6.1</td>
<td>57.7 ± 7.1</td>
<td>60.5 ± 4.7</td>
<td>-0.05</td>
</tr>
<tr>
<td>BMI</td>
<td>24.8 ± 2.3</td>
<td>25.7 ± 2.5</td>
<td>26.3 ± 2.2</td>
<td>-0.05</td>
</tr>
<tr>
<td>Parity</td>
<td>3.4 ± 2.0</td>
<td>5.9 ± 3.9</td>
<td>7.8 ± 3.6</td>
<td>-0.01</td>
</tr>
<tr>
<td>Duration of menstrual period</td>
<td>30.2 ± 5.9</td>
<td>31.7 ± 6.4</td>
<td>33.7 ± 5.9</td>
<td>-0.05</td>
</tr>
</tbody>
</table>

Values are given as the mean ± standard deviation.

Table- 3: Results of DEXA (BMD) in the subjects grouped according to the number of pregnancies.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1+ (g/cm²)</td>
<td>0.797±0.10</td>
<td>0.754±0.10</td>
<td>0.705±0.10</td>
<td>0.044</td>
</tr>
<tr>
<td>Femoral neck (g/cm²)</td>
<td>0.794±0.99</td>
<td>0.640±0.09</td>
<td>0.636±0.10</td>
<td>0.561</td>
</tr>
<tr>
<td>Trochanteric region (g/cm²)</td>
<td>0.513±0.08</td>
<td>0.521±0.08</td>
<td>0.485±0.06</td>
<td>0.429</td>
</tr>
<tr>
<td>Ward's triangle (g/cm²)</td>
<td>0.513±0.10</td>
<td>0.488±0.09</td>
<td>0.480±0.10</td>
<td>0.522</td>
</tr>
</tbody>
</table>

Values are given as the mean ± standard deviation.

Table- 4: Results of DEXA (BMD) in the subjects grouped according to the duration of lactation.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1+ (g/cm²)</td>
<td>0.784±0.10</td>
<td>0.770±0.10</td>
<td>0.745±0.10</td>
<td>0.470</td>
</tr>
<tr>
<td>Femoral neck (g/cm²)</td>
<td>0.623±0.10</td>
<td>0.655±0.09</td>
<td>0.925±1.30</td>
<td>0.212</td>
</tr>
<tr>
<td>Trochanteric region (g/cm²)</td>
<td>0.498±0.07</td>
<td>0.535±0.08</td>
<td>0.505±0.08</td>
<td>0.139</td>
</tr>
<tr>
<td>Ward's triangle (g/cm²)</td>
<td>0.489±0.10</td>
<td>0.522±0.10</td>
<td>0.481±0.10</td>
<td>0.347</td>
</tr>
</tbody>
</table>

Values are given as the mean ± standard deviation.

resorption from the maternal skeleton (1,2). However, during lactation, the maternal skeleton is the main source for the calcium need of the neonate (3-5). The purpose of this study is to determine whether the BMD of postmenopausal women is affected by the number of pregnancies and the total duration of lactation.

MATERIALS AND METHODS

Among the women admitted to the osteoporosis clinic, 187 healthy postmenopausal women completed a questionnaire covering medical and reproductive histories. Women who were smoking, obese (body mass index ≥30) or underweight (body mass index <18.5), over 65 years of age and who had a history of immobilization history or of drugs affecting BMD such as glucocorticoids were excluded. The remaining 99 postmenopausal women who fulfilled the criteria were included in the study. The subjects were grouped according to the number of completed pregnancies (1-4 pregnancies in group 1, 5-9 pregnancies in group 2, ≥10 pregnancies in group 3) and the total duration of lactation (<20 months in group 1, 20-60 months in group 2, >60 months in group 3). The total duration of menses was also calculated for each patient. The BMDs of lumbar vertebrae 1-4 (L1-4), femoral neck, Ward's triangle and trochanter regions were measured with dual energy X-ray absorptiometry (DEXA).

The statistical analysis of data was performed by one-way ANOVA and correlation tests.
Results are given as mean ± standard deviation.

RESULTS

Mean age in the groups 1, 2 and 3 according to the number of pregnancies was 55.7 ± 6.3 years (range: 44-65 years), 58.8 ± 6.6 years (range: 44-65 years) and 60.6 ± 4.5 years (range: 50-65 years), respectively. The patients grouped according to the total duration of lactation had a mean age of 57.8 ± 6.1 years (range: 44-65 years), 57.7 ± 7.1 years (range: 44-65 years) and 60.5 ± 4.7 years (range: 49-65) in groups 1, 2 and 3, respectively. The clinical characteristics of the groups are shown in detail in Tables 1 and 2. We found that an increased number of pregnancies was associated with decreased BMD in the lumbar region but no effect of pregnancy was seen at other sites. There was no association between BMD and the total duration of lactation or menses. The BMD measurements at various sites according to the number of pregnancies and duration of lactation are shown in Tables 3 and 4, respectively.

DISCUSSION

Skeletal adaptation is a complex event affected by nutritional, environmental and physiological factors. Pregnancy and lactation, which are the two main reproductive cycles, are also suspected to affect BMD.

In the literature, there are conflicting results related to the effect of pregnancy and lactation on BMD. We found that an increased number of pregnancies is associated with lower BMD at the lumbar spine, but the duration of lactation does not have a clinically important effect on BMD during postmenopausal life and the total duration of menstruation is not a predictor of BMD status.

There are other studies supporting our finding that pregnancy causes an approximately 2% decrease in BMD, especially at the lumbar spine (6-10). Black et al reported a mean reduction in spinal BMD of 3.5% in the 9 months from prepregnancy to the immediate postpartum period (8). Drinkwater and Chesnut showed that lumbar BMD decreased 3.3% during pregnancy but returned to prepregnancy values during lactation, while bone loss at the femoral neck continued during lactation (11). Some follow-up studies show that pregnancy causes mineral loss, but during or after a certain duration of lactation and resumption of menses it recovers (9,10). Lactation may have a protective role or the cessation of lactation may be a trigger for a bony replacement process. It is known that during lactation the basal concentration of prolactin is high and estradiol level is low (12), which can lead to osteoporosis. The cessation of lactation restores these hormones to normal levels and may start recovery.

In contrast to our results, Grainge et al found that pregnancy causes an increase in BMD at the femoral neck and total radius (13). However, they could not show a positive effect on the spine, trochanter or total body and they also reported, in parallel to our findings, that no association was present between the total duration of breastfeeding and BMD at any site. In a study including perimenopausal women aged between 40 and 54, those with a lactation history were found to have a higher lumbar BMD compared to those without such a history, but no significant increase was detected at the mid- or distal radius (14). Lamke et al showed that pregnant women exhibit a loss in trabecular bone but not in cortical bone (15). They also found that while lactation shorter than 3 months causes mineral loss during the first 3 months, nursing for longer than 3 months does not cause mineral loss and suggested that nursing for a longer period may play a protective role. A positive relationship between parity and bone mass was reported by Murphy et al (16). Fox et al found that a 1.4% increase in distal radius bone density was observed with each additional birth, but they did not investigate the spine or hip (17). Sowers et al demonstrated that fetal demand for calcium has a minimal effect on BMD at parturition (18).

Besides these conflicting results, Koetting and Wardlaw could not find a relation between a history of long-term lactation and bone density (19). Hadji et al (20) and Karlsson et al (21) suggested that neither parity nor breast feeding could be used as risk factors for osteoporosis. It was also reported that the negative effect of pregnancy and lactation on the maternal bone mass was spontaneously compensated for after weaning (10). In another study, conducted in a group of women who were pregnant or lactating during most of their adult reproductive lives due to their religious beliefs, it was shown that multiple pregnancies followed by lactation
without a recovery interval are not associated with lowered BMD (22). In the literature there are some reports of fractures during puerperium due to pregnancy-associated osteoporosis (23-27). The actual incidence is unknown and although it seems to be idiosyncratic (28) its pathogenesis is still obscure. Even in these cases, the recovery of BMD after pregnancy and especially following the cessation of lactation was reported.

Grainge et al pointed out the importance of the total duration of menses (13). They reported that years of menstruation is a good predictor of BMD. Fox et al showed that women with earlier menarche, longer menstruation and longer total duration of menses had greater distal radius bone density (17). However, we could not find either a negative or positive association between total duration of menses and BMD.

The bony changes during pregnancy and lactation and the causative factors for these changes are still under investigation. Parathyroid hormone-related peptide (PTHrP) is one of these factors. It originates from the placenta and is suggested to contribute to the maintenance of the fetal-maternal calcium gradient (29,30). It is found that PTHrP may induce uncoupled bone turnover with decreased cortical bone formation (31). It is also elevated during the postgestational period, but its effect on the calcium metabolism during lactation has been found to be weak and temporary. Therefore, it is suggested that PTHrP does not seem to participate significantly in the regulation of bone turnover during lactation (32). Its role seems greater, however, because different parathyroid hormone (PTH) receptors are identified and cloned, and the almost ubiquitous distribution of PTHrP and PTH/PTHrP receptor (33) suggests the existence of other PTH-related receptors in the body and a much greater complexity of the bone and mineral metabolism. Factors such as pre-pregnancy BMI, weight gain, dietary calcium intake, physical activity, diabetes mellitus and hypertension during pregnancy and correlation with baby weight and height were also investigated. Although pre-pregnancy BMI and weight gain during pregnancy could not be linked with changes in BMD, the women with greater bone density and nulliparous women were demonstrated to have a greater extent of loss postpartum (34,35). Sowers et al showed that pregnancy during adolescence causes bone loss more than that during adult life (35). Pregravid weight, gynecological age, age at menarche, greater dietary intake, less physical activity, and pregnancy hypertension and preclampsia were found to be not related to bone change (35). A previous study using the single photon absorptiometry method for radial bone mineral content assessment reported low bone mass in infants of diabetic mothers compared to control subjects (36). However, it is shown by using dual X-ray absorptiometry, which is accepted as an accurate and precise noninvasive technique for assessing bone mineralization, that bone mineralization and fat mass are increased at birth in infants of diabetic mothers compared to reference curves (37). Infants of diabetic mothers are hyperinsulinemic and hyperinsulinemia causes a marked stimulation of bone matrix synthesis and cartilage formation (37). Insulin also increases insulin-like growth factor production by the liver, which enhances bone collagen and matrix synthesis and stimulates the replication of cells of the osteoblast lineage (37). It is suggested that there is an increase in bone formation in pregnant women with type 1 diabetes that may be related to the increased amount of insulin administered and the improvement in diabetic control associated with pregnancy (38). Postpartum bone mineral density showed a significant, positive correlation with baby weight and height (34).

Although preclampsia is reported not to be associated with bone changes, calcium supplementation was associated with an approximately 50% decrease in the risk of all types of pregnancy-induced hypertension (39,40). Calcium supplementation during the third trimester of pregnancy and vitamin D supplementation during the 27th and 32nd amenorrhea weeks in winter are also reported to reduce bone resorption and prevent hypocalcemia respectively (41,42). Breast-milk calcium concentration and hence the calcium intake of the breast-fed infant may be influenced by maternal calcium intake during the preceding pregnancy, but there are also studies suggesting that the changes in the calcium and bone metabolism of the mother and infant that accompany lactation are independent of the current calcium intake (43). It is thought that there must be hormonal mechanisms other than PTH/PTHrP, calcitonin
and 1,25 dihydroxyvitamin D, as yet unidentified, involved in regulating the homeostatic changes in the calcium and bone metabolism associated with pregnancy and lactation (43).

Subsequent pregnancies without a sufficient interval in between may cause insufficient mineral replacement in maternal tissues and predispose the woman to osteoporosis. The difference between the results of our study and some of the other studies in the literature may be due to the different ethnic groups, eating habits and attitudes during parturition of the study populations. The exact effect of pregnancy and lactation can be determined by a study performed in larger populations including different ethnic groups and in populations with different dietary habits and lifestyle. An understanding of the recovery mechanism after the cessation of lactation and the underlying causes leading to different results in these studies may be very important when considering the future therapy of osteoporosis.

Correspondence to: Serap DEMİR, M.D.
Dumlupınar Mh. Tuzbap Agah Cad. 41/10 Tekay Apt.
03200 AYFON - TÜRKİYE
Phone: 272 - 213 78 58
272 - 217 17 53
Fax: 272 - 217 20 29
e-mail: serapbas@yahoo.com

REFERENCES


