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Bone Mineral Changes During Pregnancy and Lactation

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Significant calcium transfer from the mother to the fetus and infant occurs during pregnancy and lactation, theoretically placing the mother at an increased risk for osteoporosis later in life. During pregnancy, intestinal calcium absorption increases to meet much of the fetal calcium needs. Maternal bone loss also may occur in the last months of pregnancy, a time when the fetal skeleton is rapidly mineralizing. The calcium needed for breast milk production is met through renal calcium conservation and, to a greater extent, by mobilization of calcium from the maternal skeleton. Women experience a transient loss of approx 3–7% of their bone density during lactation, which is rapidly regained after weaning. The rate and extent of recovery are influenced by the duration of lactation and postpartum amenorrhea and differ by skeletal site. Additional calcium intake does not prevent bone loss during lactation or enhance the recovery after weaning. The recovery of bone is complete for most women and occurs even with shortly spaced pregnancies. Epidemiologic studies have found that pregnancy and lactation are not associated with an increased risk of osteoporotic fractures.

Key Words: Bone mass; osteoporosis; lactation; pregnancy; postpartum amenorrhea; ovarian function.

Introduction

Significant changes in maternal calcium and bone metabolism occur during pregnancy and lactation to meet the calcium needs for fetal bone mineralization and breast milk production. The large transfer of calcium to the fetus and infant could reduce maternal bone mass if there were no adaptations to conserve calcium during reproduction. A woman's reproductive period (ages 20–40 yr) occurs around the time of peak bone mass and density. The peak bone mass an individual attains is currently believed to be a significant predictor of osteoporotic fracture later in life *(1)*. If pregnancy and/or lactation result in a sustained reduction in bone mass or density, they could theoretically increase future risk of osteoporotic fracture.

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Pregnancy

Calcium Transfer

A term infant contains approx 25–30 g of calcium, the majority of which is transferred to the fetus during the last trimester of pregnancy *(2)*. The average daily transfer of calcium in the first trimester is 2 to 3 mg/d whereas the rate at 35 to 36 wk of gestation is estimated to be 250 mg/d. Maternal diet has little effect on the amount of mineral transferred. Calcium supplementation in mothers during pregnancy affects bone fetal mineral accretion measured at birth only when dietary calcium intake is <600 mg/d *(3)*.

Adaptations in Calcium Metabolism During Pregnancy

There are three possible sources of calcium to support fetal bone accretion: increased intestinal calcium absorption, renal calcium conservation, and mobilization of calcium from the maternal skeleton. Increased intestinal calcium absorption appears to be an important compensatory mechanism for securing additional calcium during pregnancy. The fractional absorption of calcium increases by 60–70% during pregnancy—from approx 33–36% in the nonpregnant state to 50–56% in the second trimester and to 54–62% in the third trimester *(4,5)*. For women with calcium intakes of 1 g/d, this would correspond to an increased absorption of 185 mg/d in the second trimester and 235 mg/d in the third trimester, amounts close to fetal needs. The increased absorption of calcium occurs in parallel with an increase in serum 1,25-dihydroxyvitamin D concentrations *(4,5)*. The mechanism responsible for the increase in serum 1,25-dihydroxyvitamin D concentrations is uncertain. The increase occurs early in gestation, prior to an increase in maternal parathyroid hormone (PTH) concentrations, and it has been speculated that the 1,25-dihydroxyvitamin D may be of placental origin *(6)*. Despite the increased need for calcium, renal calcium excretion increases by 46% (approx 76 mg/d) over the course of pregnancy among women with calcium intakes of approx1200 mg/d *(4)*. This increase is owing to the increase in glomerular filtration rate that occurs during pregnancy *(7,8)* and increased absorptive load *(9,10)*. A decrease in renal calcium excretion in the third trimester has been found in women with very low dietary calcium intakes (≤400 mg/d) *(7)*.

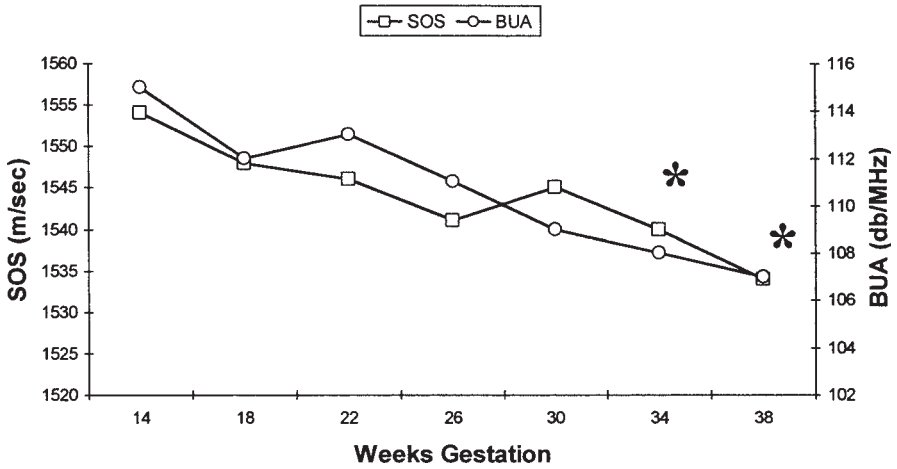

Fig. 1. Longitudinal ultrasound measurements of the os calcis during pregnancy. SOS and BUA measurements were significantly lower ($p < 0.05$) at 34 and 38 wk of gestation compared to baseline (*). (Data from ref. *24.*)

Bone Changes Observed During Pregnancy

There are case reports of pregnancy-associated osteoporosis, and it has been suggested that this pathologic condition either is a transient failure of the usual calcitropic hormonal changes that usually occur during pregnancy, or occurs in women with preexisting osteopenia *(11,12)*. Investigation of typical changes in bone density during pregnancy has been hampered by concern regarding exposure of the fetus to radiation associated with dual X-ray absorptiometry measurement. To circumvent this, investigators either have limited bone density measurements to peripheral skeletal sites during pregnancy so that the fetus is not exposed to additional radiation, or have obtained baseline measurements before pregnancy and follow-up measurements shortly after delivery. Several longitudinal studies have found loss of bone density during pregnancy. Reported losses range from 2 to 2.6% at the ultradistal radius *(13,14)*, 2 to 4% at the spine *(8,15,16)*, and 2.4 to 3.6% at the hip *(8,17)*. Other studies have not found bone density changes during pregnancy, possibly because of small samples sizes or long intervals between baseline measurement and pregnancy *(4,5,18,19)*. One study found that bone density at trabecular-rich sites (pelvis and spine) decreased by 3 to 4% during pregnancy, whereas bone density at cortical sites (arms and legs) increased by 2% *(16)*.

Some studies have used quantitative ultrasound, which does not involve radiation, to estimate bone density at peripheral skeletal sites during pregnancy. Ultrasound measures of speed of sound (SOS), broadband ultrasound attenuation (BUA), and other indices utilizing these measures are correlated with bone density measurements *(20)*. However, other investigators have found poor correlations and speculated that ultrasound measures properties of bone other than density *(21,22)*. Studies that obtained ultrasound measurements of the os calcis or phalanges throughout pregnancy found decreases in ultrasound measures, particularly in the last trimester when the transfer of calcium to the fetus is the greatest (Fig. 1) *(23–26)*. The magnitude of decrease varied among studies, depending on the follow-up interval and type of measure, ranging from 1.2 to 10.8%. Aguado et al. *(26)*, in a study of 40 women, found that the decrease was greater for women whose calcium intake was <1 g/d, whereas no relationship between bone changes and calcium intake was found in a larger longitudinal study of 230 women *(27)*. Sowers et al. *(27)* found that nulliparous women and adolescents who were still growing during pregnancy had the largest decreases in ultrasound indices. Growth and increases in body weight during pregnancy, and how the resultant increase in bone loading may modify bone changes have not been described.

Bone lost during pregnancy appears to be regained over the 12–24 mo postpartum. The magnitude of bone gain postpartum is comparable with that lost during pregnancy. Among women who do not breast feed their infants, reported increases in bone density by 6 mo postpartum range from 0.9 to 2.0% at the distal radius *(18,28)* and 0.4 to 1.4% at the lumbar spine *(28,29)*. At 12 mo postpartum, increases of 1.1% at the distal radius *(28)*, 2.0–2.1% at the lumbar spine *(28,29)*, 1.8% of total body, and 2.9% at the trochanter *(30)* have been found. Hopkinson et al. *(31)* found continued bone mineral accretion in the second year postpartum so that by 24 mo postpartum, lumbar spine bone mineral density (BMD) was 2.8% higher and total body bone mineral content was 2.3% higher than at 2 wk postpartum. Since there were no nonpostpartum control subjects, it is not clear what portion of this gain was the result of a normal age-related bone increase. Laskey et al. *(30)* measured bone mass over a 12-mo period in 11 nonlactating postpartum women and 22 women of reproductive age who had not been pregnant. They found an increase in total body and trochanteric bone mass among postpartum women, but no significant change in bone mass among nonpostpartum

women. These findings provide evidence that the bone changes observed postpartum are in response to pregnancy and not normal age-related increases in bone mass or density.

Biochemical markers that are thought to reflect bone formation and bone resorption have been used to gain a better understanding of the dynamics of bone turnover throughout pregnancy. Concentrations of osteocalcin, alkaline phosphatase, and P1CP are reduced or unchanged in the first half of pregnancy and increase in the last trimester to concentrations one to three times that of nonpregnant women *(8,25,32)*. Markers of collagen breakdown, such as pyridinoline, deoxypyridinoline, and NTx, increase throughout pregnancy *(4,8,25,32)*. Interpretation of changes in bone turnover markers during pregnancy is difficult. It is not known whether during pregnancy there is altered marker metabolism; whether there is increased marker clearance owing to increased renal filtration; to what extent the biochemical markers originate in the fetus, placenta, or uterus; and whether concentrations may be affected by the hemodilution that occurs with pregnancy *(16)*. Collectively, however, the data are consistent with an increasing rate of bone turnover throughout pregnancy.

Lactation

Calcium Transfer

Lactating women lose an average of 250 mg of calcium/d in breast milk *(30)*. Calcium concentrations of human milk are regulated within a relatively narrow range but change slightly over the course of lactation. Calcium concentrations increase during the first month postpartum and then slowly decrease after approx 4 mo of lactation, returning to levels similar to that observed at 1 mo postpartum *(33)*. Dietary calcium does not affect calcium concentrations of milk *(34,35)*, and provision of additional calcium to lactating women with habitually low calcium intakes (<300 mg/d) does not increase calcium concentrations of milk *(36)*. Lower calcium concentrations of milk have been observed in women who were vitamin D deficient and had a low calcium intake *(37)*.

Adaptations in Calcium Homeostasis During Lactation

Despite the significant daily transfer of calcium into milk, maternal serum calcium concentrations are unchanged *(4,38)* or slightly elevated *(39,40)*. Unlike during pregnancy, intestinal calcium absorption does not increase during lactation *(4,41–43)*, and serum concentrations of 1,25-dihydroxyvitamin D in lactating women are similar to those of nonlactating postpartum women *(38)*. One study found a slight increase (from 31 to 37%) in fractional calcium absorption after weaning, which was accompanied by a similar increase in 1,25-dihydroxyvitamin D concentrations *(41)*, but this was not found by other investigators *(4)*. The primary mechanism of calcium conservation during lactation is increased renal tubular reabsorption of calcium and decreased urinary calcium loss *(36,39,44–46)*. However, decreased urinary calcium excretion has not been found in all studies *(38,47,48)*. The hormonal signal for renal calcium conservation is unclear. Serum concentrations of PTH, a major hormonal modulator of renal calcium reabsorption, are lower in lactating women compared with nonlactating women *(38)*. One possible hormonal signal for increased renal calcium reabsorption during lactation is PTH-related peptide (PTHrP). Circulating concentrations of PTHrP are increased during lactation, particularly in early lactation *(49–52)*, and are inversely related to PTH concentrations *(50)*. PTHrP binds to the PTH receptor and stimulates renal calcium reabsorption similar to that of PTH *(53)*.

Bone Changes During Lactation

Significant amounts of calcium needed to maintain maternal serum calcium concentrations and milk production come from mobilization of calcium stored in bone. Several studies have found significant losses of bone mineral during lactation, with the amount of bone loss varying by skeletal site. There are reported losses of 3–9% at the spine and hip *(4,28–30,47,48,54,55)*, 1 to 2% of the total body *(29–31)*, and 0–5% at the forearm *(28–30,36,47)*. Bone loss occurs rapidly within the first 3–6 mo of lactation and remains lower with continued lactation. The rate of bone loss at the spine and hip in lactating women is noteworthy because it greatly exceeds the typical rate of bone loss in postmenopausal women (1 to 2%/yr).

The amount of bone loss is related to the length of lactation and breast milk volume *(30)* and is independent of exercise *(56)* and dietary calcium intake *(30,54)*. Bone loss during lactation occurs in women with a wide variety of calcium intakes, and calcium supplementation has little effect *(28,29,36)* on bone loss during lactation (Fig. 2). An important determinant of bone loss during lactation is the length of postpartum amenorrhea irrespective of the length of lactation *(57)*. Changes in PTH and 1,25-dihydroxyvitamin D are not associated with the degree of bone loss *(38)*. Serum concentrations of PTHrP, estradiol, and prolactin (PRL) are reported to be associated with lactation-induced bone loss *(49)*.

The bone loss that occurs during lactation is transient, and several longitudinal studies have now shown that there is a rapid increase in bone density after weaning. The gain in bone after weaning is of similar magnitude to that lost during lactation. Recovery of bone density at the spine occurs within 3–6 mo postweaning *(30)*, whereas some studies have found that recovery at the femoral neck takes longer *(31,50)*. Polatti et al. *(28)* studied 274 women who breast fed for 6 mo and then weaned by the seventh mo. They found that women who resumed menses prior to 5 mo postpartum had a smaller bone deficit at 6 mo than women who had not resumed menses. However, there were no differences in the net bone density changes at 12 or 18 mo postpartum between those who resumed menses within 5 mo

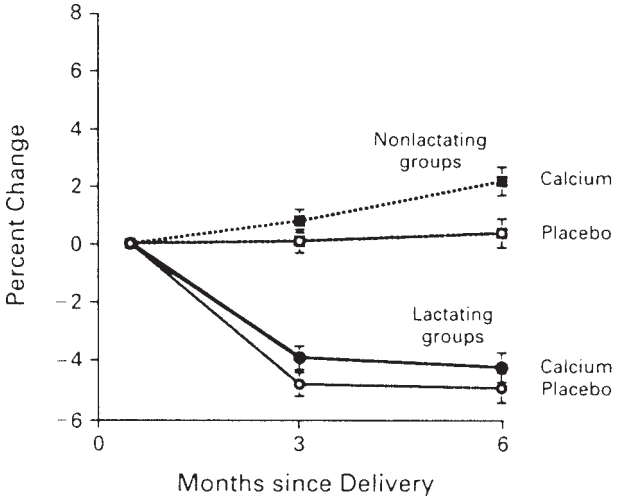

Fig. 2. Effect of calcium supplementation and lactation on mean (± SE) percentage change in BMD of lumbar spine during first 6 mo postpartum. Values are adjusted for baseline BMD, height, weight, change in weight, dietary intake of calcium, and level of physical activity. $p = 0.01$ for the effect of calcium; $p < 0.001$ for the effect of lactation; and $p = 0.23$ for the interaction between calcium supplementation and lactation. (Reprinted from ref. *29.*)

postpartum and those who had not. The duration of lactation and postpartum amenorrhea vary widely among women, thereby leading to large individual differences in the amount and rate of bone loss and recovery.

Whether there are factors other than the restoration of ovarian hormones and reduction of PRL and PTHrP concentrations to within the normal range that stimulate bone gain after lactation is not known. Recovery of bone density following resumption of menses occurs in women across a wide range of calcium intakes, is not enhanced with calcium supplementation *(28,29)*, and appears to be complete for most women by 18–24 mo postpartum. Because the bone lost during lactation is regained, there is no need to treat or prevent the lactation-induced bone loss.

Bone Density, Fracture Risk, and History of Lactation

Overall, lactation is not associated with bone density later in life or with increased fracture risk. Several studies have reported no association between bone density and lactation history *(58–60)*, although others have reported either an increased *(61–65)* or a decreased *(66,67)* BMD with lactation history. Henderson et al. *(60)* recently found similar bone density in 30 grand multiparous women, who had borne at least six children and had breast fed each child for greater than 6 mo, compared with nulliparous women, indicating no detrimental effect of shortly spaced pregnancies on bone density. A recent, large case-control study of 1328 incident patients with hip fracture and 3312 randomly selected control subjects found that parity was modestly associated with a reduced risk of hip fracture (risk was reduced by 10% per child with a 95% confidence interval of 5–14%), and that there was no association between fracture risk and duration of lactation *(68)*. A longitudinal study of 9000 women over age 65 found no association between hip fracture and the number of children breast fed *(69)*. These findings indicate that there is no relationship between fracture risk and high parity or history of breast feeding.

Although the majority of studies have not found an association between either bone density or fracture risk and lactation history, few investigations have been made among adolescents who are still growing, or among women who breast feed multiple infants. It is not known whether the additional mineral demands placed on the skeleton during growth or while nursing more than one infant has any long-term implications for the mother's bone health.

Conclusion

In summary, the available evidence suggests that increased intestinal calcium absorption during pregnancy meets much of the fetal calcium needs, although maternal bone loss also may occur in the last months of pregnancy, a time when the fetal skeleton is rapidly mineralizing. The calcium needed for breast milk production is met through renal calcium conservation and by mobilization of calcium from the maternal skeleton. Women experience a transient loss of bone density during lactation that is rapidly regained after weaning. The rate and extent of recovery is influenced by the duration of lactation and postpartum amenorrhea and differs by skeletal site. Additional calcium intake does not prevent bone loss during lactation or enhance the recovery after weaning. The recovery of bone is complete for most women and occurs even with shortly spaced pregnancies. Epidemiologic studies have found that pregnancy and lactation are not associated with an increased risk of fracture.

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