

Review

Maternity and bone mineral density

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ABSTRACT During pregnancy and lactation, changes occur in a variety of factors which have great potential to influence bone mineral density (BMD). Smoking habits, the level of alcohol consumption, the level of physical activity, body weight, soft tissue composition and hormone levels are all factors that change during the course of these conditions. Some of these factors are capable of increasing BMD, and some can reduce it. Due to these various changes, it is virtually impossible to predict the development in BMD that will occur during a pregnancy and lactation. However, longitudinal studies have suggested that both pregnancy and lactation are associated with a BMD loss of up to 5%, albeit that the BMD recovers after weaning. Cross-sectional studies have indicated that women with many children and a long total period of lactation have similar or higher BMD and similar or lower fracture risk than their peers who have not given birth. As the studies showing this trend have been observational and cross-sectional case-control studies, the conclusions can only be regarded as being suggestive, and no causality can be proven.

Metabolically, the skeleton is a highly active organ with 10–15% of the bone mineral content being changed in the course of 1 year (Parfitt et al. 1995). This is a physiological mechanism whereby the old bone, full of microfractures, is removed and replaced by new healthy bone where it is most needed. Bone mineral density (BMD), the amount of mineral within the skeleton, is one of the best predictors of bone strength and a reduction in BMD by one standard deviation (SD) or about

10%, is known to double the fracture risk (Cummings et al. 1995). If the BMD of an individual is found to be 1.0–2.5 SD below the BMD of normal young individuals of the same sex, then the condition is called osteopenia, and a more than 2.5 SD lower BMD is called osteoporosis (WHO 1994). However, osteoporosis does not cause problems until the clinically relevant endpoint for low BMD occurs, namely a fracture. Thus, studies which use fractures as the endpoint when different risk factors are being evaluated must always be regarded as stronger evidence than a similar study design using surrogate endpoints, such as BMD.

Today, a generally low BMD in an elderly population is a major problem for the community at large. Low BMD occurs as a result of an inadequate accrual of BMD during growth, leading to a reduced peak bone mass, or an increased age-dependent bone loss (Bonjour et al. 1994, Bass et al. 1998). As the accrual of BMD during puberty is more than double in magnitude compared to the loss during the rest of life (Bass et al. 1998), peak bone mass is probably of major importance for the risk of developing osteoporosis later in life. This hypothesis is supported by reports in which it has been proposed that 60% of the variance in BMD at age 65 is the result of the peak bone mass attained (Kelly et al. 1995). As in most biological variables, BMD is predominantly regulated by genetics; 60–80% of the variance in BMD has been estimated to be determined by genetic factors (Hui et al. 1990, Kelly et al. 1995). The rest of the variance is influenced by environmental factors, such as a pregnancy or a period of lactation.

There has never been, and will never be, a randomized, double-blind, placebo-controlled trial (RCT) demonstrating that pregnancy and lactation influence the BMD level or incidence of fracture. Blinded RCTs, the highest level of “evidence”, cannot be performed, as neither the investigator nor the participant can be blinded as to pregnancy and lactation. Instead, we have to draw our inferences on the basis of retrospective and prospective, observational, cohort studies and cross-sectional, observational and case-control studies. As these studies all subject to the risk of systematic bias, they can never be regarded as hypothesis-testing. They can only be hypothesis generating, and causality can never be proven. Lack of the highest level of evidence within the evidence-based hierarchy is not proof of lack of efficacy, however, and today, when we draw our inferences, we can only rely on the literature carrying the highest level of evidence.

The purpose of this review is to present the most important changes in the factors that are capable of influencing BMD during a pregnancy and lactation. Our aim has also been to present the data that actually support or oppose the hypothesis that pregnancy and lactation lead to short-term or long-term negative effects on BMD and fracture risk. We asked four specific questions: (i) do pregnancy and lactation lead to changes in environmental factors that can influence BMD, (ii) do pregnancy and lactation result in a reduction in BMD, (iii) is there an association between parity and low BMD, and (iv) is there an association between parity and increased fracture risk?

Publications were searched in Medline from 1966 onwards using the following search words: bone mineral density, bone mass, BMD, pregnancy, lactation, multiparity, multiple pregnancies, and fractures. The criterion was that the articles had to be published in English, or at least presented as an English abstract. From relevant articles, the search was continued repeatedly through the path “related manuscript” until no more relevant articles appeared. The reference list in the thesis “Maternity and Bone” (Holmberg-Marttila 2001) was also included in the search. The priority for this review was then to include and draw inferences from published articles with the highest level of evidence. We found mainly two types of study designs: (1)

prospective observational studies, controlled and uncontrolled, following BMD from before or at the start of a pregnancy or lactation to after delivery and weaning, and (2) retrospective and prospective observational and case-control studies addressing the relationship between parity and BMD or fracture incidence. In all studies cited, relative changes are presented, and all changes were statistically significant unless otherwise stated.

Methodological problems when BMD is evaluated in pregnant and lactating women

Evaluation of BMD in pregnant and lactating women has attendant problems. It is well known that both weight and soft tissue composition influence the measurement of BMD by current bone scanning techniques (Sievanen 2000, Karlsson et al. 2001). If a prospective study finds changes in the BMD, with additional changes in the soft tissue, we must always ask whether the discrepancy in BMD between the two measurements is based on actual discrepancies in the BMD, or whether a discrepancy in the soft tissue composition between the measurements could have led to the false conclusion that changes in BMD have occurred (Sievanen 2000, Fogelholm et al. 2001, Karlsson et al. 2001).

Weight, lean body mass and fat content are all factors that change during both pregnancy and lactation, and are thus confounding factors when changes in BMD are being evaluated (Pipe et al. 1979). No consensus exists on how the BMD data should be presented—unadjusted for weight or soft tissue composition (Sowers et al. 1991a), adjusted for changes in weight (Kalkwarf and Specker 2002), or adjusted for changes in fat and lean body mass separately (Karlsson et al. 2001). Furthermore, the fluid shift that occurs during and just after a pregnancy (Southgate 1987), also influences the estimation of BMD. The increase in extracellular fluid, together with the altered distribution of tissue volume resulting from the development of the fetus, and changes in the placental and mammary compartments, make measurements even more difficult to interpret (Prentice 2000b). The third problem is an ethical one, as most measuring techniques use ionising radiation, and the radiation will also reach the fetus. Such measurements should be avoided, leading to baseline measurements in prospective

studies being done before conception and after delivery—in many studies years before and years after the pregnancy in question.

Changes in factors that can influence BMD during a pregnancy

The most prominent mineral of the skeleton is calcium. There is strong evidence that calcium is vital for the skeleton during growth (Parfitt et al. 1995), young adulthood (Cummings et al. 1995) and in old age (Andon et al. 1994), and that a relationship exists between calcium intake and fracture risk in the elderly (Andon et al. 1994). Calcium functions as a threshold nutrient, i.e. calcium intake is relevant up to a threshold level only, and adding more calcium above this level will not improve BMD (Matkovic and Heaney 1992). The calcium supply comes into focus during a pregnancy, as the pregnant mother provides the fetus with calcium, approximately 50 mg/day at 20 weeks of gestation and rising to 330 mg/day at 35 weeks (Prentice 2000a). This higher calcium demand should theoretically lead to a lower BMD in the pregnant woman if her skeletal reserves of the mineral have been used, but as physiological mechanisms increase calcium absorption in the gut and the kidney, usually this leads to a calcium supply that is sufficient for both the mother and the fetus. This view is supported by studies reporting that calcium supplementation in pregnant women with normal or high calcium intake has little or no effect on their BMD (Cross et al. 1995). By contrast, there is some evidence that pregnant women with low calcium intake may benefit from calcium supplementation (Raman et al. 1978, Prentice 2000a). Other dietary components such as protein, magnesium, zinc, copper, iron, fluoride, and vitamins D, A, C and K are also required for normal bone metabolism, while some—such as, for example, a high intake of caffeine and alcohol—exert a negative influence on BMD (Anderson 1992, Ilich and Kerstetter 2000). Many women reduce both smoking and alcohol consumption during pregnancy, and theoretically, this could (if anything) lead to increased maternal BMD.

During a pregnancy, there is also an increase in maternal weight and fat content (Jaque-Fortunato et al. 1996, Karlsson et al. 2001). The increased weight results in an increased mechanical load on

the skeleton and the increased fat content leads to an increased peripheral production of estrogen, both hypothetically influencing the BMD in an anabolic way (Lindsay et al. 1992). Furthermore, the production of estrogens by the placenta, predominantly estriol but also estradiol and estron, leads to generally high levels of estrogens (Catt 1970). As estrogen is regarded as the most important regulatory hormone for the skeleton, these changes could hypothetically lead to increased BMD.

Physical activity is another important anabolic regulatory factor for BMD (Karlsson et al. 2000). As pregnant women often reduce their normal level of physical activity, at least during the latter part of the pregnancy, this could theoretically lead to reduction in BMD. Thus, due to all the changes described above that could influence BMD, is it virtually impossible to predict the final change in BMD that would occur during a pregnancy.

Are there any changes in BMD during a pregnancy?

In a cross-sectional case-control study involving 73 women, Karlsson et al. (2001) reported a 7.6% lower lumbar spine BMD and a 3.9% lower total body BMD in women who had just given birth, after adjustment for differences in soft tissue composition, compared to 55 age- and sex-matched controls. This has been the only published study to take the soft tissue discrepancies into account when evaluating the effect of a pregnancy. Several prospective, controlled and non-controlled studies have supported the data presented by Karlsson et al. (Figure 1). From a study of 6 women, Drinkwater and Chesnut (1991) reported a 2.4% reduction in femoral neck BMD and a 2.2% reduction in radial shaft BMD. Black et al. (2000), in a study of 10 women, found a 3.2% reduction in both spine and total hip BMD. In a study involving 38 women, More et al. (2001) reported a 4.9% reduction in ultra-distal forearm BMD. Holmberg-Mattila et al. (1999) found 3.0% reduction in spine BMD in 5 women, while Naylor et al. (2000) found a 3.2% reduction in pelvis BMD and a 4.6% reduction in spine BMD in 16 women. Ritchie et al. (1998) reported a 9% loss in spine BMD in 14 women. In contrast, Sowers et al. (1991a) found no loss in BMD in 32 women, which is similar to the findings of Cross et al. (1995) in 10 women. However, the

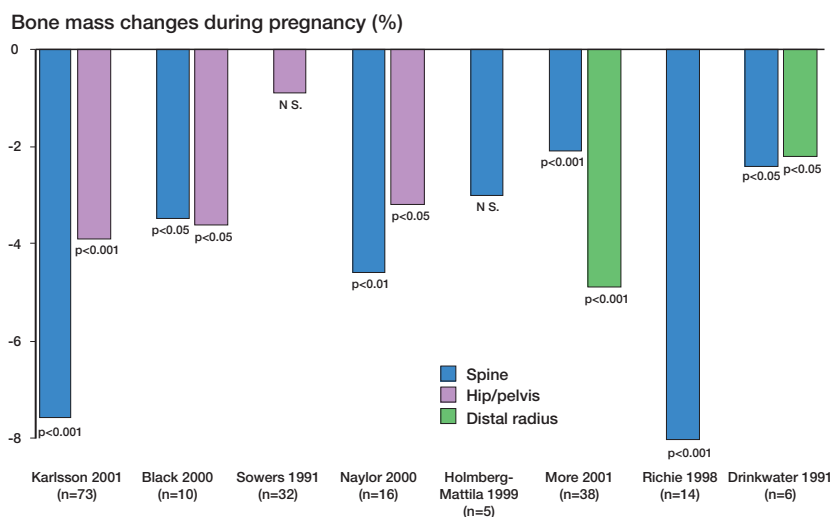


Figure 1. Relative changes in bone mass during a pregnancy evaluated in several original studies. The data are presented with first author and reference number in this review, numbers of women included, and level of significance for the comparison between the pre-pregnancy and the post-pregnancy values.

follow-up period was 475 days for the cases and 669 days for the controls in the study of Sowers et al. (1991a), and the risk of making a type II error must be regarded as high in the study of Cross et al. (1995). Only Karlsson et al. (2001) and Sowers et al. (1991a) performed the follow-up measurements close to delivery, 3 days and 15 days after parturition, respectively. The other studies used baseline measurements done up to 12 months before conception and follow-up measurements done up to 12 months after delivery, inevitably including the effect of lactation. Moreover, only 3 studies were controlled and only one study adjusted for differences in soft tissue composition when pregnant and non-pregnant women were compared. In spite of all these methodological problems, if we summarize published studies—including a recent large review (Ensom et al. 2002)—it seems feasible to conclude that during a pregnancy there is a loss of maternal BMD of around 5% (Figure 1). It also seems reasonable to conclude that general intervention has little or no effect on this loss, except perhaps in cases with a low nutritional intake of calcium.

Changes in factors that can influence BMD during lactation

Calcium metabolism undergoes dramatic changes during lactation. During full breast feeding, 200

mg calcium is transferred from the mother to the infant every day, so that the total calcium transfer through the breast milk in one lactation period of 3–6 months is greater than the calcium content transferred across the placenta during a pregnancy (Prentice 2000a). However, the maternal absorption of calcium adapts to the required level, and a general calcium supplement appears to have no or only minor effects on the BMD during lactation. Randomized, controlled intervention studies of lactating women have mainly shown no effects of an increased calcium supply on bone turnover markers (Cross et al. 1995, Prentice 2000a, b, Kalkwarf and Specker 2002). Similar findings have been found when the BMD was followed. In a study involving 274 lactating mothers, Polatti et al. (1999) reported that any effects of calcium intervention were only transient, with no long-term benefits on BMD. Kalkwarf et al. (1997) found no effect of calcium supplementation and Prentice et al. (1995) even stated that even women with low calcium intake did not benefit from calcium supplementation during lactation. The few studies which have reported a small effect of calcium intervention postpartum have usually found the same beneficial effect in non-lactating mothers (Kent et al. 1990, Cross et al. 1995, Prentice et al. 1995). It seems that calcium supplementation does not influ-

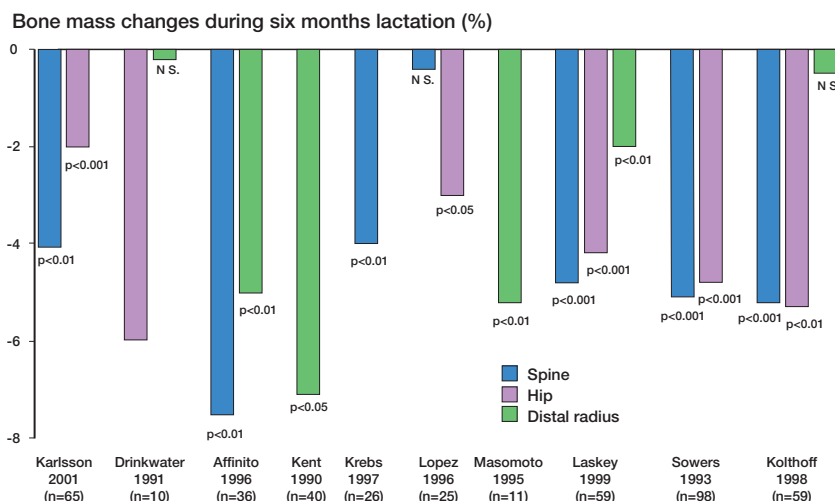


Figure 2. Relative changes in bone mass during 6 months of lactation evaluated in several original studies. The data are presented with first author and reference number in this review, numbers of women included, and level of significance for the comparison of values found directly after delivery and 6 months post-pregnancy.

ence the loss of BMD induced by lactation. There have been no studies that indicate that vitamin D requirements are greater in lactating women than in non-lactating women (Specker 1994). Finally, we cannot exclude the possibility that the intake of other dietary components, associated with the arrival of a new baby, influence BMD. Many women reduce smoking, coffee and alcohol intake and as these nutritionally exert a negative influence on BMD (Anderson 1992, Ilich and Kerstetter 2000), these changes may, if anything, influence the BMD in an anabolic way.

During lactation there is also a decrease in maternal weight and fat content, which is most obvious during the first weeks after a delivery. The decreased weight results in a decreased mechanical load on the skeleton, and the decreased fat content results in a decreased periferal production of estrogen, which may both (hypothetically) influence the BMD in a catabolic way (Sowers et al. 1991b, Lindsay et al. 1992). The negative effects on BMD are further accentuated if breast feeding is started. This is due to suppression of the hypothalamus-pituitary axis, resulting in a lactation-induced amenorrhea with low estrogen levels (McNeilly et al. 1994). Ovarian dysfunction has been proposed to be one of the main factors that would explain loss of BMD during lactation (Honda et al. 1998). Also,

a high prolactin level is sustained during lactation (McNeilly 2001). Prolactin concentrations remain elevated during the first three to four months of lactation, and it has been suggested that this high level may have a role in the depression of BMD, by suppressing the hypothalamus-pituitary axis (Sowers et al. 1996). There are further changes in levels of a variety of other hormones during lactation which may affect BMD, a set of circumstances which, in practice, makes it unfeasible either to calculate the specific contribution of each hormone or to estimate the final change in BMD. Again, as estrogen is probably the most important hormone regulating the BMD level (Turner et al. 1994), hypothetically this would, if anything, lead to a decreased BMD. After weaning, estrogen levels return to normal, which should lead to a recovery in BMD—a notion supported in the majority of published studies (Turner et al. 1994, Kalkwarf and Specker 1995, Kolthoff et al. 1998).

After delivery, many women gradually increase their level of physical activity, a change which would be beneficial for BMD. By contrast, some women find that they lack spare time after a new baby has arrived, so that their level of physical activity becomes reduced. Thus, it is not possible to draw any general conclusions regarding the effect of physical activity during lactation, and

the question of exercise may tend either way, with active exercise resulting in increased BMD, or the opposite.

Are there any changes in BMD during lactation?

Biochemical markers of bone resorption and bone formation suggest that there is an elevated bone turnover during the first months of lactation, with a decrease after 6–12 months, even in women who continue to breast feed (Prentice 2000a, b). This is strong indirect evidence that the level of BMD changes during lactation (Figure 2). In a cross-sectional case-control study involving 65 breast feeding women, Karlsson et al. (2001) reported a 4.1% lower lumbar spine BMD and a 2.0% lower femoral neck BMD after 5 months of lactation, after adjustment for differences in soft tissue composition. So far, this is the only study to present the BMD data adjusted for differences in soft tissue composition, in the evaluation of the effect of lactation. Moreover, the BMD of the spine 12 months after delivery had completely recovered in this cohort, while the BMD in the femoral neck had only partly recovered (Karlsson et al. 2001) (Figure 3). Several prospective, controlled and non-controlled studies support the results of the study of Karlsson et al. (Figure 2). In a study of 10 women with 6 months of lactation, Drinkwater et al. (1991) reported a 6% reduction in femoral neck BMD. Affinito et al. (1996), comparing 18 lactating mothers with 36 non-lactating mothers, reported a 7.5% reduction in lumbar spine BMD and a 5% reduction in distal radius BMD, with an incomplete recovery found 6 months after weaning. Kent et al. (1990), in a study involving 40 mothers who were breast feeding and 40 age-matched controls, found a 7.1% reduction in the ultradistal radius BMD. Krebs et al. (1997), investigating 26 lactating women and 8 non-lactating controls, reported a 4.0% decline in spine BMD after 7 months of lactation, with an almost complete recovery found after weaning. Similar findings, with a decline in maternal BMD of 3–6% after 3–6 months of lactation—most obvious in the axial skeleton—have been confirmed in a variety of other prospective, controlled studies (Lopez et al. 1996, Kolthoff et al. 1998, Laskey and Prentice 1999) (Figure 2). The conclusions have been strengthened further by the finding of a

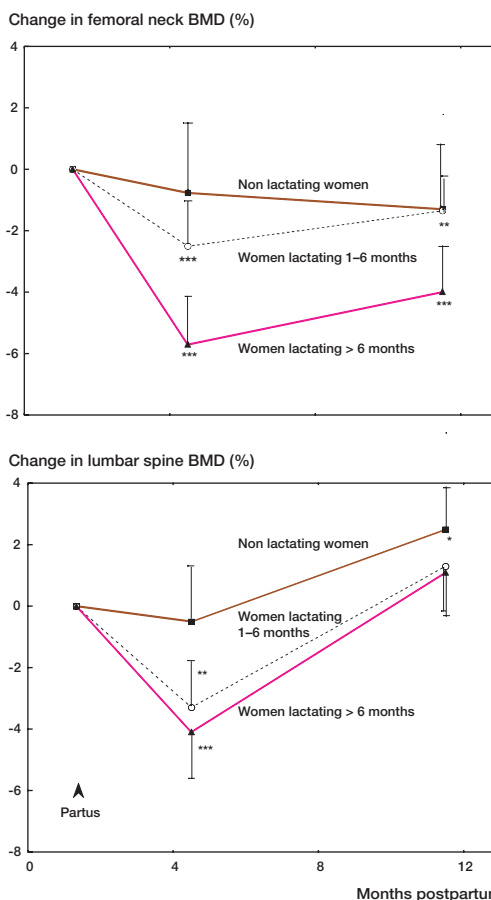


Figure 3. Relative changes in bone mass during the first year following delivery in women not breast feeding, and in women breast feeding for a duration of more than and of less than 6 months.

dose-response relationship that a longer period of lactation is associated with a larger loss in BMD, a finding that strengthens the view that lactation does lead to a reduction in BMD (Laskey and Prentice 1999, More et al. 2001). It also seems reasonable to conclude that general interventions have little or no effect on BMD loss during lactation, except perhaps calcium supplementation for women with a low nutritional intake of calcium.

The clinically most relevant question then becomes: does BMD recover after weaning? Matsumoto et al. (1995), studying 22 women, reported a complete recovery 24 months after delivery. In a study of 25 women, Sowers et al. (1993) reported a complete recovery 12 months after delivery, while Kalthoff et al. (1998) and Turner et al. (1994) found

a complete recovery 12–18 months after delivery. A transient bone loss with lactation, at a magnitude similar to the deficits described above but with a total recovery after 6–18 months of weaning, has been supported in most publications (Kalkwarf and Specker 1995), including the large review by Enson et al. (2002) (Figure 3). It has also been suggested that closely spaced pregnancies may be a risk factor for osteoporosis later in life, due to additive periods with a loss of BMD in quick succession (Affinito et al. 1996). There have been studies investigating mothers with short intervals between childbirth and lactation periods longitudinally, but all of these studies imply that these women do not risk failure of bone recovery to pre-lactation levels after the last period of lactation (Sowers et al. 1995, Laskey and Prentice 1997).

Pregnancy-related osteoporosis and transient osteoporosis of the hip

A minor loss of BMD occurs during most pregnancies, but pregnancy-related osteoporosis is considered to be a rare complication with unknown incidence (Alderman et al. 1986). A pregnancy-related, transient osteoporosis of the hip probably reflects the same condition, albeit localized to the hip only (Samdani et al. 1998, Axt-Flidner et al. 2001). Our knowledge regarding the condition is based on two published case series, including 24 patients (Smith et al. 1995) and 35 patients (Dunne et al. 1993) respectively, and a number of case reports. The condition affects predominantly slightly built, primigravid, lactating women and is usually diagnosed during the third trimester. The disease does not usually recur during subsequent pregnancies. Little is known about its pathogenesis, or the dynamics of BMD decrement when the disease develops and the BMD increment during the recovery phase (Dunne et al. 1993, Smith, et al. 1995, Smith and Phillips 1998, Anai et al. 1999). The disease is regarded as a benign condition since, without treatment, patients are expected to return to normal BMD 6–12 months after weaning. Usually the condition does not lead to long-term deficits, except in cases complicated by a vertebral, sacrum or hip fracture during the period with osteoporosis (Breuil et al. 1997, Smith and Phillips 1998, Anai et al. 1999).

Do pregnancies and lactation lead to an increased incidence of osteoporosis in the long run?

Perhaps the clinically most relevant question as regards female reproductive history and its association with decreased BMD, is whether the reduction in BMD described during a pregnancy and lactation is associated with an increased risk of developing osteoporosis and fragility fractures in old age. Only cross-sectional observational or case-control studies have been published which evaluate the effect of multiple pregnancies and lactation on BMD. In a study involving 39 pre-menopausal women with a minimum of four pregnancies, and after adjustment for differences in soft tissue composition, Karlsson et al. (2001) reported that BMD was no lower in these women than in 58 age-matched controls with a maximum of 2 pregnancies (Figure 4). Furthermore, there was no correlation between the total duration of lactation and BMD. A similar conclusion was drawn by Kojima et al. (2002), who had included 465 pre- and 713 post-menopausal Japanese women in a cross-sectional study and by Johansson et al. (1993) including 70 year-old Swedish women, and in a recently published review (Ensom et al. 2002), including 23 different citations.

In contrast, in a study involving 1855 post-menopausal women, Cure-Cure et al. (2002) reported that women with two deliveries or more had a 3% higher total body BMD, an 8% higher femoral neck BMD and a 4% higher leg BMD than women with no children. This is similar to the results of Forsmo et al. (2001), who included 1652 peri- and post-menopausal Norwegian women, to those of Grainge et al. (2001), including 580 English women aged 45–61 years, Tuppuvainen et al. (1995), including 3126 Finnish women aged 47–56 years, Murphy et al. (1994), including 825 English women aged 41–76 years, Sowers et al. (1992), including 217 white American women aged 22–54 years, and to those of Mariconda et al. (1997), including 320 Italian women (Figure 4). These studies concluded that in general, women with a history of one or several children had 3–5% higher BMD than nulliparous women. Murphy et al. (1994) further strengthened this view by reporting that the lowest BMD values were found in nulliparous women, intermediate values were found

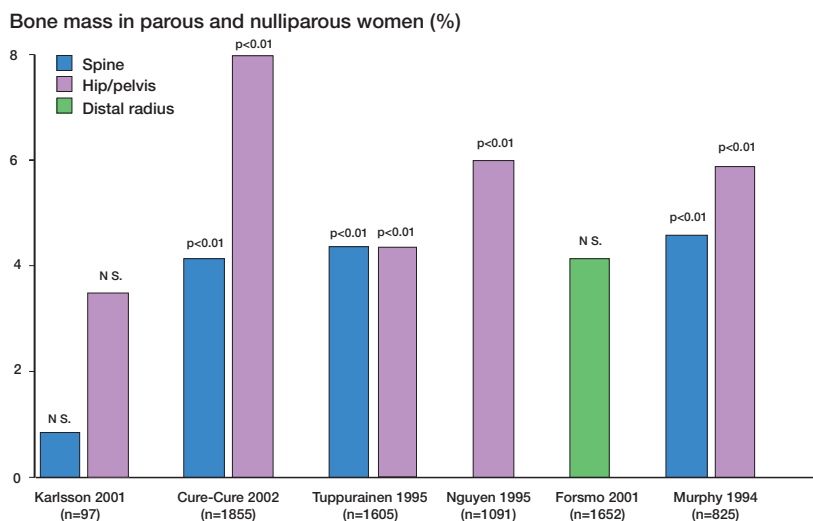


Figure 4. Relative difference in bone mass in parous women compared with nulliparous women evaluated in several original studies. The data are presented with first author and reference number in this review, numbers of women included, and level of significance for the comparison between the parous and the nulliparous women.

in primiparas, and the highest values in women with two or more children.

This finding is surprising, as both pregnancy and lactation are associated with an increased BMD loss. Apparently, in the long-term perspective, this is overshadowed by other factors that influence BMD, as mothers with many children and long periods of lactation have similar or higher BMD than their peers who have not given birth (Figure 4). The causality is unclear, but probably changes in lifestyle associated with large families account for this outcome. Another explanation that cannot be excluded is that shared genetic factors may account for the finding, so that women with a high BMD are also likely to have many children.

Do pregnancies and lactation lead to an increased incidence of fractures in the long run?

Hypothetically, there could be an increased risk of sustaining fractures in the postpartum period when BMD is still low and when women regain her former level of BMD. However, even if they lose BMD during a pregnancy, most women still have a BMD of sufficiently high level to withstand fractures, and to date there have been no studies specifically evaluating fracture risk during the months following delivery.

But what about the long-term risk of fracture? It is only when we are able to provide reports with the clinically relevant endpoint, namely a fracture, that we can make stronger inferences regarding risk factors and fractures. Alderman et al. (1986), including 355 post-menopausal women with a fracture and 562 matched women with no history of fracture, reported that the incidence of hip and forearm fractures was no higher in women who had given birth to four or more children than in women who had not given birth (Figure 5) Also, women who had breast fed for more than 2 years did not have a higher fracture risk than women who had never breast fed. The notion that fracture incidence for women with multiple pregnancies was no different from that of nulliparous women has been supported by several studies: Johansson et al. (1993) with a cohort of 70-year old Swedish women; the Study of Osteoporotic Fractures (SOF), a longitudinal study of 9704 American women over 65 years of age (Cummings et al. 1995); the Mediterranean Osteoporosis study (MEDOS), a cross-sectional study including 2086 women with a hip fracture from 14 centres in six countries in Southern Europe and 3532 non-fractured controls (Johnell et al. 1995); and the European Vertebral Osteoporosis Study (EVOS), a longitudinal study including 6646 women aged 50–79 years (O'Neill et al. 1997).

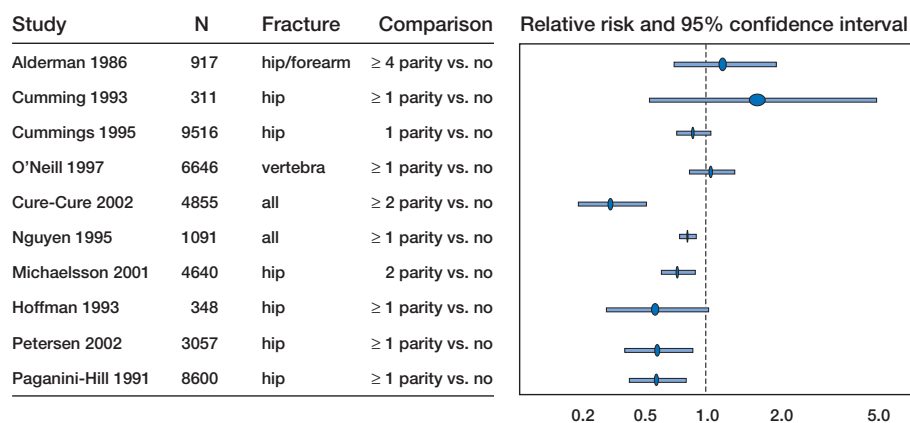


Figure 5. Relative risk of sustaining a fracture in parous women compared with nulliparous women. The data are presented with first author and reference number in this review, numbers (N), type of fracture evaluated, and numbers of pregnancies with 95% confidence interval for the risk ratio presented.

In contrast, Cure-Cure et al. (2002) reported a 59% lower fracture risk in women with two or more deliveries than in nulliparous women. In the prospective Dubbo Epidemiological Osteoporosis Study, Nguyen et al. (1995) found a 6% lower fracture incidence in parous women than in nulliparous women. Michaelsson et al. (2001), including 1328 post-menopausal Swedish women aged 50–81 years with a hip fracture and 3312 matched controls, found a 10% lower hip fracture risk per child (5% after adjustment for body mass index), but no association between lactation and fracture risk. Hoffman et al. (1993), including 174 cases aged 54 years and over and 74 matched controls, found evidence that a live birth was associated with a 35% reduction in hip fracture risk compared to having no births. A reduced risk of hip fracture associated with having one or more children has also been reported in the Leisure World Study, a prospective study of 8 600 post-menopausal women (Paganini-Hill et al. 1991), and in a Danish twin study involving 3 057 twins aged 66–99 years who were followed for a total of 29 112 person-years (Petersen et al. 2002). Thus, to summarize, half of the studies suggest that there is no association between parity and fractures, while the other half imply that a history of one or several pregnancies is associated with a reduced risk of fracture (Figure 5). Virtually no study has suggested an association between lactation and fracture risk. It appears that having many children leads to a situation that, if anything, leads to not only a higher

BMD, but also a reduced fracture risk. The causality cannot be proven, but the association between number of children and fracture risk may operate through a different mechanism than is detected by BMD, as the association remains even after adjusting for differences in BMD in women with no or many children (Hillier et al. 2003, 2004, Robbins et al. 2004).

To summarize the answers to our four specific questions: (i) since a variety of factors can influence skeletal changes during both a pregnancy and a period of lactation, it is virtually impossible to predict the development in BMD during these conditions; (ii) it appears that there is a loss of BMD of up to 5% during both a pregnancy and a 6-month period of lactation, but that the BMD recovers with weaning; (iii) women with multiple pregnancies and long total duration of lactation have no different or higher BMD than women who have had no or few pregnancies; (iv) women with several pregnancies and long total duration of lactation have no different or lower fracture incidence than their peers with no or few children. The current data do not support that a pregnancy or a period of lactation can be regarded as risk factors for future osteoporosis and fragility fractures.

No competing interests declared.

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