Calcium Metabolism in Pregnancy and Lactation

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Abstract

Pregnancy and lactation are periods of high calcium requirement. Around 200-300 mg of calcium/day is either transferred via the placenta to the fetus or excreted in breast milk. The provision of this calcium is made by the physiological adaptations of calcium absorption, urinary calcium excretion, and maternal bone calcium turnover. So woman of child-bearing age will meet their own needs of calcium and those of their infants if they regularly consume adequate amounts of calcium (1,000mg/ day). Additional calcium supplementation during pregnancy appears to have the greatest impact in women who chronically consume < 500 mg calcium /day.

Hypertensive disorders of pregnancy are more frequent in countries where the customary calcium intake is low. In such areas, World Health Organization recommended calcium supplementation as part of the antenatal care for the prevention of preeclampsia in pregnant women, particularly among those at higher risk of developing hypertension.

Keywords: Calcium metabolism; Pregnancy; Lactation; Preeclampsia; Osteoporosis.

Introduction

Pregnancy and lactation are periods of high calcium requirement. Significant trans-placental calcium transfer occurs during pregnancy, to meet the demands of the rapidly mineralizing skeleton of the fetus & neonate. Similarly, there is an obligate loss of calcium in breast milk during lactation. These result in considerable stress on the bone mineral homeostasis in the mother. Potential adaptations include increased intake of mineral, increased efficiency of intestinal absorption of mineral, mobilization of mineral from the skeleton, and increased renal conservation of mineral. Despite a similar magnitude of calcium demand by pregnant and lactating women, the adjustments made in each of these reproductive periods differ significantly.

These hormone - mediated adjustments normally satisfy the needs of the fetus and infant with short-term depletions of maternal skeletal calcium content, but without long-term consequences to the maternal skeleton. In states of maternal malnutrition and vitamin D deficiency, however, the depletion of skeletal mineral content may be proportionately more severe and may be accompanied by increased skeletal fragility.[1]

The average calcium demand of a developing fetus is 30 gm by the end of gestation. 80 % of this calcium amount is acquired during the third trimester while the fetal skeleton is rapidly developing.[2] The total calcium accretion rate of the fetus increases from approximately 50 mg/ day at 20 weeks gestation to 330 mg/ day at 35 weeks . For the third trimester of pregnancy, 200 mg/day is considered the average accretion rate.[3] This demand for calcium is largely met by a doubling of maternal

Fig 1: Calcium homeostasis in human pregnancy and lactation compared with normal. The thickness of arrows indicates a relative increase or decrease with respect to the normal and non pregnant state.[1].
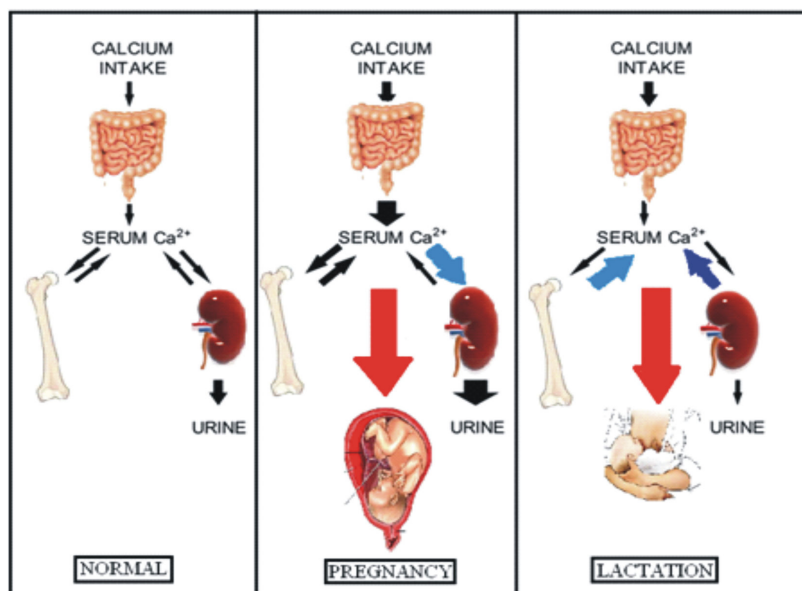
	Normal	Pregnancy	Lactation
Intake	N	↑	↑
Gi Absorption	N	↑↑	↑
Renal Excretion	N	↑	⇓
Tubular Resorption	N	↑	↑↑
Bone Resorption	N	↑	↑↑

intestinal calcium absorption, mediated by 1,25-dihydroxyvitamin D3 (1,25(OH)2D3), or calcitriol, and possibly by other factors.[1]

Physiological changes in calcium metabolism during pregnancy

One of the earliest changes in calcium metabolism during pregnancy is a decrease in total serum calcium. This change is not physiologically significant. This fall is due to the decrease in serum albumin that accompanies the normal hemodilution of pregnancy. The ionized calcium (the physiologically important fraction of calcium) remains constant throughout pregnancy. PTH levels fall into a low-normal range during the first trimester, but rise throughout the pregnancy to reach normal level by the end of gestation.[4] Calcitonin levels are increased throughout the pregnancy preventing extreme

calcium loss from the maternal skeleton. However, some calcium from the mother's skeleton is used for fetal development & is not completely spared.[4] The most adaptive change protecting the maternal skeleton from bone density loss may be the shift in levels of 1,25(OH)2D3. Total 1, 25(OH) 2D3 levels double early in pregnancy and maintain this increase until term; free 1, 25(OH) 2D3 levels are increased from the third trimester and possibly earlier. This increase can occur as early as 12 weeks gestation & researchers hypothesize, the maternal skeleton starts absorbing more calcium early & stores it in preparation for when the fetus will need the calcium during skeleton development in the third trimester.[2] The increase in 1, 25(OH) 2D3 may be largely independent of changes in PTH because PTH levels typically are decreasing at the time of the increase in 1, 25(OH) 2D3. The maternal kidneys likely

account for most, if not all, of the increase in 1, 25(OH) 2D3 during pregnancy, although the decidua, placenta, and fetal kidneys may contribute a small amount.[5]

Parathormone related peptide (PTHrP) is a prohormone that produces multiple N-terminal, mid-molecule & C-terminal peptides which differ in their biological activities & specificities. However, none of these peptides have been systematically measured during pregnancy. The most studied is the large molecule which comprises 1 – 86 amino acids. The levels start rising usually around the mid-second to third trimester of pregnancy. Because PTHrP is produced by many tissues in the mother and fetus (including the placenta, amnion, decidua, umbilical cord, fetal parathyroids, and breast), it is unclear which sources contribute to the increase detected in the maternal circulation. Several roles of PTHrP are postulated from animal studies, including fetal calcium transfer & stimulating 1- alpha hydoxylase activity. Further, the carboxy terminal of PTHrP called "osteostatin" may suppress osteoclastic activity & may have a possible bone protection role in the mother.[5,6,7]

Other hormones

Many other hormones, growth factors, and cytokines are elevated in the maternal circulation during pregnancy that could stimulate or drive the observed changes in calcium absorption, 1, 25-dihydroxyvitamin D synthesis, and bone turnover. These include prolactin, oestrogen, progesterone, placental lactogen, placental growth hormone, tumor necrosis factor alpha, and insulin-like growth factor-1. Their relative contributions to calcium and bone metabolism in human pregnancy have yet to be established.[5,8,9]

Intestinal calcium absorption

The total body calcium content is 1000–2000 g, and 99% of the calcium in the body of adult individuals is in the skeleton. About 200–400 mg of calcium are absorbed daily by active transport from the proximal small bowel in the non-pregnant adult. During pregnancy, however, intestinal absorption increases twofold, particularly during the third trimester.[2–4] Increased intestinal calcium absorption is already present at 12 weeks, which is the earliest gestational age that has been studied. It is associated with higher serum levels of 1-alpha-25-dihydroxyvitamin D (1,25-(OH)2D3) as well as increased intestinal expression of the vitamin D-dependent calcium-binding protein calbindin-9K. Prolactin (PRL) and human placental lactogen (HPL) are believed to be other factors contributing to the increased intestinal calcium absorption. Because the increased intestinal calcium absorption starts so early in gestation and well before the peak demands of the third trimester, it is thought that some calcium is stored in the maternal skeleton in anticipation for subsequent demands.[10] This is something that has been observed in some animal models, but has not been possible to directly asses in humans.

Renal calcium excretion

Under normal circumstances, 98% of calcium filtered by the kidney is reabsorbed, mostly in the proximal tubules. However, in pregnancy the urinary calcium excretion is higher than outside pregnancy and correlates with the increased glomerular filtration rate (GFR).[11] The increased urinary calcium excretion has also been detected as early as 12 weeks of gestation. The increased intestinal calcium absorption and the higher calcitonin (CT) levels of pregnancy are also believed to be contributing factors favoring renal calcium excretion.[10] In the fasted state, the calcium excretion is normal or even low.[2]

Skeletal calcium metabolism
Serum Markers

Most human studies of skeletal calcium metabolism in pregnancy have examined changes in serum markers of bone formation (bone-specific alkaline phosphatase, osteocalcin, procollagen I and carboxypeptidase) & urine markers of bone

resorption (24-hour collection of deoxypyridinoline, hydroxyproline and pyridinoline). These studies indicate that bone formation indices are decreased and bone resorption markers are increased. Based on those results, it has been assumed that there is decreased bone formation and accelerated bone resorption. These studies are fraught with a number of confounding variables, including lack of pregpregnancy baseline values, effects of hemodilution in pregnancy on serum markers; increased GFR & renal clearance; altered creatinine excretion ; placental, uterine, & fetal contribution to the markers; degradation and clearance by the placenta; and lack of diurnally timed or fasted specimens. Therefore these markers may not be accurate indicators of bone metabolism in pregnant women.[12]

Imaging

Changes in maternal bone mineral content (BMC) and bone mineral density (BMD) resulting from gestation have been studied using three different imaging techniques: dual x-ray absorptiometry (DXA), quantitative ultrasound, and peripheral quantitative computed tomography (pQCT). pQCT is the only technique available formeasuring changes in trabecular bone, the type of bone most likely to be mobilized in the adult skeleton during pregnancy.[13]

Bone mineral density (BMD) studies by Dual Energy X-ray Absorptiometry (DXA) scan or its other versions are contraindicated during pregnancy. Few studies in pregnant women where it was done immediately after delivery or after an abortion at various periods of gestation showed variable results precluding any concrete conclusions. Such studies are confounded by the changes in body composition and weight during pregnancy which may also interfere with bone density estimation by DXA.[5,14]

Quantitative ultrasound is able to measure bone without the use of ionizing radiation, allowing it to be used during pregnancy, primarily at the calcaneus and phalanges. Evidence has shown that the speed of sound,

an indication of the density and structure of the trabecular bone, decreases significantly at the phalanges ($P < 0.05$)[15,16] and the calcaneus ($P < 0.001$)[17] between the first and third trimesters. A limitation of quantitative ultrasound is its greater variability in measurement than either DXA or pQCT; since pregnancy is a time period in which changes in fluid status and body size occur, the variability in the quantitative ultrasound measurements may increase.[18]

To date, Wisser *et al* are the only investigators to use pQCT to measure gestational changes in trabecular and cortical bone. The measurement was performed at only one site, the non dominant distal radius. Cortical bone volume and density did not change between the first and third trimesters of pregnancy, but a significant decrease was seen in trabecular bone density (mean of -3.1%, with some women losing up to 20.7%). Trabecular bone density is more sensitive to bone turnover, particularly that resulting from hormonal changes in women, such as what occurs during gestation.[19]

It seems certain that any acute changes in bone metabolism during pregnancy do not normally cause long-term changes in skeletal calcium content or strength. Numerous studies of osteoporotic or osteopenic women have failed to find a significant association of parity with bone density or fracture risk[2,20]; however, a few studies of women with extremely low calcium or vitamin D intake found that pregnancy may compromise skeletal strength and density. Although most clinical studies could not separate out the effects of parity from the effects of lactation, it may be reasonable to conclude that if parity has any effect on bone density or fracture risk, it normally must be only a modest effect. A more recent study of twins indicated that there may be a small protective effect of parity and lactation on maintaining bone mineral content.[21]

A few examples exists in which calcium balance between maternal skeleton, intestine and renal conservation are not equal, possibly putting the mother at greater risk for bone

density loss:

1. *Adolescent Mothers:* Studies have shown that bone mass density decreases as much as 10% in adolescent mothers during pregnancy and lactation. This decrease did not occur in women over the age 18 years.[22] This loss can be offset by increasing the adolescent's dietary calcium intake.[22]

2. *Heparin Use:* Women who are using heparin injections to prevent deep vein thromboses during pregnancy have reported several cases of vertebral osteoporosis. Heparin inhibits the synthesis of 1,25-dihydroxyvitamin D. Without the compensation mechanism of increased intestinal calcium absorption with 1,25-dihydroxyvitamin D, greater risk of bone density loss occurs.[22]

3. *Low Calcium Intake:* There are limited data that low calcium intake in the mother may adversely affect fetal mineral accretion and maternal bone mineral metabolism.[23]

In a longitudinal study researchers hypothesized that if the mother's calcium intake was too low the body would not completely compensate and a greater bone loss would occur. They found that the level of bone turnover markers negatively correlated with the calcium intake. Women with lower dietary calcium intakes had greater turnover. One turnover marker; beta CTX , doubles in women who consume recommended daily amount of calcium during the third trimester. For women who had half of the recommended amount of calcium, their turnover marker was eight times as high as a non pregnant woman. Thus, the body's physiological response to calcium metabolism to pregnancy may not be enough to cover all the calcium needs of the fetus in women with low dietary calcium intake.[4]

In women with low dietary calcium intake there are differing results as to whether or not calcium supplementation during pregnancy improves maternal or neonatal bone density.[23] There is a short term evidence that maternal turnover was reduced when 1.2 gm of calcium was given for 20 days to 31 Mexican women with a mean calcium intake of 1 g during weeks 25-30 of gestation.[24]

Preeclampsia

1980 Epidemiological Study conducted in Guatemala were Scientists noted that Mayan Indians exhibited high Calcium intakes and low incidence of preeclampsia and eclampsia.[25]

Eclampsia is more common in countries where the dietary calcium intake is low.[26]

Low calcium intakes during pregnancy may:

1. Stimulate PTH secretion, increasing intracellular calcium levels. This leads to smooth muscle vessel contraction and hypertension. And/ or

2. Releases Renin from the Kidney, leading to vasoconstriction and retention of sodium and fluids. These physiological changes can lead to the development of preeclampsia.[18]

A meta analysis of the role of calcium supplementation during pregnancy in the prevention of gestational hypertensive disorders found a 45 % reduction in the development of preeclampsia in women receiving calcium versus placebo. (Relative risk [RR]: 0.55; 95% confidence interval [CI] 0.36-0.85).[27]

The World Health Organization conducted a calcium supplementation trial (1500 mg/ day or Placebo) during pregnancy in women who habitually consumed <600 mg calcium/ day. Women (n=8325) began supplementation at 20 weeks of gestation and where monitored until delivery. The difference in the incidence of the preeclampsia between the control group (4.5%) and the calcium group (4.1%) was not significantly different. However, the relative risks of severe preeclampsia (RR 0.76; 95% C.I.0.66-0.89) and eclampsia (1.2 % calcium vs. 2.8% placebo, P= 0.04) were both significantly lower in women supplemented with calcium.[28]

A large randomized controlled trail, involving 4,589 nulliparous pregnant women

in United States demonstrated that in a population with an average calcium intake of 1100 mg/day, calcium supplement of 2000 mg/day did not reduce the incidence of either preeclampsia or raised blood pressure.[29] However , it should be noted that this study included women who were at low risk for gestational hypertension. Also all women, even the control group received some calcium in their regular prenatal vitamins.[8]. This may support that calcium supplements only show results when the daily intake is lower than the amount that would provide maximum benefit.[30]

A Cochrane review of 13 trials involving 15730 pregnant women reported that the average risk of preeclampsia was reduced in those receiving calcium supplements (RR=0.45) and that the effect was greatest in women with low baseline calcium intakes (RR=0.36).

The review concluded that pregnant women consuming low amount of calcium could reduce their risk of preeclampsia by 31 -65% if they consumed an additional 1000 mg of calcium/day.[31]

Whether calcium supplementations during pregnancy could prevent childhood hypertension?

The Researchers believed that later blood pressure could be programmed during fetal development. The study conducted by Belizain and colleagues included 591 children, ages 5-9 years old, whose mothers either took 2 g/ day calcium supplements or a placebo. The Researchers found that the systolic blood pressure was lower in the calcium group by an average of 1.4 mm Hg. The most significant blood pressure changes were found in overweight children who had body mass indices above 17.5. Their systolic blood pressure dropped an average of 5.8 mm Hg. [32]

Preterm delivery

Calcium supplementation has shown effectiveness in reducing risk of preterm delivery in women with low calcium intake.

Amongst the pregnant women whose calcium intake is less than 600 mg/ day were supplemented with additional calcium (1500 mg/day). A decrease in the risk of preterm delivery, maternal morbidity and neonatal mortality index were observed following the above.[28]

Infant growth

Maternal malnutrition has a major impact on fetal growth and birth weight and hence on skeletal mass. Poor nutrition during pregnancy may reduce neonatal bone density as well as size. Calcium intake during pregnancy may have positive effect, but the research has provided conflicting results.[32,33,34]

A positive relationship between maternal calcium intake and infant length or mid upper arm circumference has been shown[33,34] but the reasons have not been reproduced in other studies.[34,35]

Calcium metabolism during lactation

During lactation, the mother undergoes a continued stress on calcium demand with production of breast milk. Human milk contains two to three times the maternal serum level of calcium, and it is estimated that between 280 and 400 mg of calcium go into breast milk daily.[36] Women breastfeeding twins might lose up to 1000 mg per day.[10] Except in mothers with vitamin D deficiency and low serum calcium levels, the calcium concentration in milk does not change. [5,37] During the first 6 months after delivery the mean calcium concentration in breast milk is slightly higher than during the succeeding 6 months but calcium loss in breast milk remains significant throughout lactation [38]. Calcium losses during lactation are even greater than in late pregnancy when calcium transfer to the fetus is greatly increased.[10] In contrast to the pregnant state, this demand is met mainly by increased resorption of calcium from the bone and partly by increased reabsorption from the kidneys.

Minerals & hormones

During lactation, PTH, serum calcium, ionized calcium, and urinary calcium excretion levels to normal pre-pregnancy ranges.[22]

Calcitonin levels fall to normal within six weeks postpartum.[2]

The high levels of 1,25-(OH)2D3 decrease rapidly after delivery and remain in the normal range afterwards.[39]

As a result, no increase in intestinal absorption of calcium occurs to compensate for the loss to the neonate. Without this mechanism, the primary source of extra calcium becomes the maternal skeleton.[4]

PTH

Intact PTH, as determined by a two-site IRMA, has been found to be reduced 50 % or more in lactating women in the first several months postpartum. It rises to normal level at weaning, but may rise above normal post weaning.[2]

PTH is believed to play an important role in the rapid recovery of bone mass that takes place after weaning and also in the renal conservation of calcium and phosphorus. [40,41]

Parathyroid hormone-related protein

The most striking of the hormonal changes observed during lactation is the marked increase in PTHrP levels in breast milk.[10]

The source of PTHrP may be the breast, because PTHrP has been detected in breast milk at concentrations exceeding 10,000 times the level found in the blood.[2] Though it is biologically weak when compared with PTH, the high levels result in bone resorption and increased tubular re absorption of calcium and also suppress PTH.[42]

Intestinal absorption of calcium

Intestinal calcium absorption decreases to the non pregnant rate from the increased rate of pregnancy. This decrease in absorption

corresponds to the decrease in 1, 25(OH) 2D3 levels to normal.[12]

Renal calcium excretion

In humans, the GFR decreases during lactation, and the renal excretion of calcium typically is reduced to very low levels. This situation suggests that tubular reabsorption of calcium must be increased, to account for reduced calcium excretion in the setting of increased serum calcium. [12]

Skeletal calcium metabolism

Serum markers of bone formation and urinary markers of bone resorption have been assessed in numerous cross-sectional and prospective studies of lactation. Some confounding factors discussed with respect to pregnancy apply to the use of these markers in lactating women. During lactation, GFR is reduced, and the intravascular volume is more contracted. Urinary markers of bone resorption (24-hour collection) increase two to three times above normal during lactation and are higher than the levels attained in the third trimester. Serum markers of bone formation (not adjusted for hemoconcentration or reduced GFR) are generally high during lactation and increase over the levels attained during the third trimester. Total alkaline phosphatase declines immediately postpartum owing to loss of the placental fraction, but still may remain above normal because of the elevation in the bone-specific fraction. Despite the confounding variables, these findings suggest that bone turnover is significantly increased during lactation.[12]

The combination of high PTHrP and prolactin with rapidly decreasing estrogen levels is believed to be the main reason for the skeletal changes in lactating women.[43] It is estimated that lactation causes a 3–10% decline in bone mineral content after breastfeeding for 6 months, as reported by studies measuring serial bone density changes. The loss is greater in trabecular (lumbar spine, femur, and distal radius) than in cortical

bone.[44,45,46,47]. Taller women have been reported to have greater bone loss during lactation [44&48]. The loss occurs at a peak rate of 1-3% per month, far exceeding the rate of 1-3% per year that can occur in women with postmenopausal osteoporosis who are considered to be losing bone rapidly. Loss of bone mineral from the maternal skeleton seems to be a normal consequence of lactation and may not be preventable by raising the calcium intake above the recommended dietary allowance. Several studies have demonstrated that calcium supplementation does not significantly reduce the amount of bone density lost during lactation.[2] Not surprisingly, the lactational decrease in bone mineral density correlates with the amount of calcium lost in the breast milk output.[48]

The mechanisms controlling the rapid loss of skeletal calcium content are not fully understood. The reduced estrogen levels of lactation are important, but are unlikely to be the sole explanation.[13]

All bone losses are regained 3-6 months after weaning, regardless of how much was lost, at a rate of 0.5 – 2 % per month.[12]

The mechanism for this restoration of bone density is uncertain and largely unexplored, but preliminary evidence from animal models suggests that PTH, calcitriol, calcitonin, and estrogen may not be required to achieve that restoration.[2]

Osteoprosis associated with Pregnancy and Lactation

Osteoporosis associated with Pregnancy and Lactation has been recognized for more than five decades.

Osteoporosis is difficult to diagnose during pregnancy as DXA scan, the gold standard for diagnosing the condition, cannot be done during in pregnancy.[5] It usually presents during late pregnancy or early post partum. Clinical manifestation usually includes severe back pain especially in the lumbar area and may be associated with collapse of the vertebrae. In most instances, the possibility that the woman had low bone density before

conception cannot be excluded. Some cases may be confounded by chronic therapy with heparin, anticonvulsants, or corticosteroids, among other causes of secondary osteoporosis.[2]

In a series of 35 women with osteoporosis in pregnancy, majority had a maternal history of fracture, possibly implicating a genetic basis.[49] However, pregnancy and lactation itself are states of relatively high bone turnover and may thus cause further deterioration in bone density in an already predisposed individual. Another point in favor of the role of pregnancy in this condition is that most cases recover within few months of delivery.[5,49,50,51] Management is conservative and most patients recover clinically & radiologically in 3-6 months postpartum. Myriad pharmacologic agents have been used in individual cases, including calcium, vitamin D, testosterone, estrogen, calcitonin, and bisphosphonates, with increments in bone mineral density reaching 27 % at the spine and 7 % at the hip in patient case treated with alendronate for six months.[52]

In severe cases of osteoporosis, it may be prudent to discourage breast feeding, the rationale being that the skeleton may not be able to tolerate the normal demineralization that lactation would induce. Patients should be cautioned against carrying heavy weights to avoid additional stress on the spine, and the use of a supportive corset may be helpful.[1]

Transient osteoporosis of hip (TOH)

This is a distinct condition seen in pregnancy. It is also called algodystrophy of the hip.[5,49,53] The pathophysiology is more related to local factors. The theories proposed to explain the condition include femoral venous stasis due to gravid uterus, reflex sympathetic dystrophy, ischemia, trauma, viral infections, immobilization, and fetal pressure on the obturator nerve. These patients present with unilateral or bilateral hip pain, limp, and/or hip fracture in the third

trimester. There is objective evidence of reduced bone density of the symptomatic femoral head and neck that has been shown by MRI to be the consequence of increased water content of the femora head and the marrow; a joint effusion may also be present. The symptoms and the radiological appearance usually resolve within 2-6 months postpartum.[2]

Calcium recommendations

During Pregnancy and Lactation calcium is needed for fetal growth and breast milk production. The amount required, approximately 200 mg/ day is substantial in relation to the daily calcium intake for many women. It has long been assumed that the extra calcium needed for pregnancy and lactation must be satisfied by increasing dietary calcium intake. However, the recent evidence detailed in this review, is that human pregnancy and lactation are accompanied by physiological changes sufficient to make calcium available for fetal growth and breast milk production without necessitating increase in maternal calcium intake. Physiological hyper absorption of calcium occurs in pregnancy, preceding the demands of the fetus for calcium, whereas renal conservation of calcium and temporary liberation of calcium from the skeletal occur in lactation.

It would appear; therefore, that pregnancy and lactation in human are characterized by physiological adaptive processes that provide the calcium necessary for fetal growth and breast milk production. So no extra calcium is needed from the diet.

Women of child bearing age group will meet their own needs and those of their infants if they regularly consume adequate amounts of calcium. (1,000 mg/day). Additional calcium supplementation during pregnancy appears to have the greatest impact in women who chronically consume <500 mg calcium per day, demonstrating the importance of adequate calcium intake before pregnancy begins.

W.H.O. recommendation for prevention of preeclampsia

In populations where calcium intake is low, calcium supplementation as part of the antenatal care is recommended for the prevention of preeclampsia in pregnant women, particularly among those at higher risk of developing hypertension (*strong recommendation*).[54,55]

A suggested scheme for supplementation in pregnant women is presented in Table 1.

If they have one or more of the following risk factors: obesity, previous pre-eclampsia, diabetes, chronic hypertension, renal disease, autoimmune disease, nulliparity, advanced maternal age, adolescent pregnancy and conditions leading to hyperplacentation and large placentas (e.g. twin pregnancy). This is not an exhaustive list, but can be adapted/

Table 1: Suggested scheme for calcium supplementation in pregnant women	
Dosage	1.5–2.0 g elemental calcium/day[a]
Frequency	Daily, with the total daily dosage divided into three doses (preferably taken at mealtimes)
Duration	From 20 weeks' gestation until the end of pregnancy
Target Group	All pregnant women, particularly those at higher risk of gestational hypertension[b]
Settings	Areas with low calcium intake

By WHO. *Guideline: Calcium supplementation in pregnant women.* Geneva, World Health Organization, 2013
a-1 g of elemental calcium equals 2.5 g of calcium carbonate or 4 g of calcium citrate.
b-Women are regarded as being at high risk of developing gestational hypertension and pre-eclampsia

complemented based on the local epidemiology of preeclampsia.

Implementation of this recommendation requires close monitoring of women's total daily calcium intake (diet, supplements and antacids). The overall intake of calcium per day should not exceed the locally established upper tolerable limit. In the absence of such reference standards, an upper limit of calcium intake of 3 g/day can be used.

Conclusion

Maternal adaptations during pregnancy and lactation meet the increased mineral demand of the growing fetus. Increased intestinal absorption of calcium during pregnancy and skeletal resorption of calcium during lactation form the main maternal adaptation mechanisms to meet this raised requirements.

It may be important to optimize dietary calcium intake of women prior to conception. Appropriate calcium nutrition should be focused on young women before child bearing instead of targeting only pregnant and lactating women, as is the common practice currently.

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