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REVIEW PAPER / OBSTETRICS

Vitamin D and calcium levels related to bone mineral density during pregnancy and postpartum

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ABSTRACT

Bone mineral density (BMD) is crucial for bone strength, with even a modest decrease significantly elevating fracture risk. Calcium imbalance during pregnancy contributes to BMD loss, as maternal stores are mobilized to support fetal skeletal development. Vitamin D deficiency exacerbates this issue, with prevalence rates alarming in various populations. Supplementation with vitamin D and calcium aims to mitigate BMD decline; however, optimal dosing and efficacy remain debated.

Studies utilizing innovative diagnostic tools like radiofrequency echographic multi spectrometry (REMS) and quantitative ultrasonometry (QUS) shed light on BMD changes during pregnancy, offering safer alternatives to traditional methods such as dual-energy X-ray absorptiometry (DEXA), prohibited during pregnancy due to fetal radiation risks. Despite methodological challenges, research reveals significant BMD reductions during pregnancy, particularly in weight-bearing bones.

In conclusion, maintaining maternal bone health during pregnancy and postpartum is critical, requiring comprehensive monitoring and support. Further research is needed to elucidate

optimal strategies for preserving BMD throughout the reproductive lifespan, reducing fracture risk and enhancing maternal well-being.

Keywords: bone mineral density (BMD); pregnancy; pregnancy complication; vitamin-d deficiency

INTRODUCTION

Bone mineral density (BMD) is one of the most important elements in determining bone strength. A 10% reduction in BMD has been demonstrated to double the fracture risk [1]. It is conceivable that their prolongation (e.g. in the form of multiparity, prolonged lactation) may contribute to bone deterioration and consequently increase the risk of fracture.

Many factors during pregnancy and lactation cause calcium imbalance in the female body and lead to a decrease in BMD. Loss of BMD During pregnancy is the result of mobilisation and absorption of calcium from the mother's skeleton for fetal bone growth. The resulting maternal osteoporosis leads to sustained low back pain which may be correlated with higher number of fractures. To avoid fetal exposure to radiation, most examinations have been conducted before and after pregnancy. The cause of that is very restricted information on maternal BMD changes during pregnancy.

The purpose of this review is to gather existing knowledge on vitamin D3 and calcium supplementation, their effects on BMD and the impact of pregnancy on BMD, as well as to identify changes in BMD during pregnancy, primarily using new, safe diagnostic methods.

VITAMIN D AND CALCIUM STATUS — DEFICIENCY AND SUPPLEMENTATION

Bone metabolism and its minerals are strongly influenced by vitamin D. Increasing the supply and/or supplementing it reduces bone turnover and helps increase bone mineral density. However, it should be noted that excessive vitamin D supplementation and/or supply can negatively affect health, as it belongs to the group of fat-soluble vitamins that have the ability to accumulate in the body [2]. As a biomarker of vitamin D status, 25-hydroxycholecalciferol is used due to its longer half-life [3]. In Europe, vitamin D is produced in the skin under the influence of sunlight from April to September, when the sun is more than 50°N above the horizon. People with darker skin pigment absorb UV light, so that sun exposure does not have the same effect on vitamin D production [4].

The essence of testing vitamin D, calcium and bone density measurements is the impact of mineral disorders and their negative effects on the mother and child's body. A paper

involving as many as 42 meta-analyses published between 2018 and 2023 on the relationship between serum 25-hydroxycholecalciferol levels and outcome of pregnancy found that vitamin D deficiency increases the likelihood of spontaneous miscarriage, preterm labor, especially in multiple pregnancies, pre-eclampsia (PE), gestational anemia, postpartum depression, autism spectrum disorders in early childhood [5]. In contrast, a reduced risk of low birth weight and gestational diabetes was correlated with higher vitamin D levels. Kurmangali et al. [5] demonstrated that the development of insulin resistance and bronchial asthma in the first years of life, as well as pre-eclampsia, is prevented by vitamin D supplementation during gestation at least 2000 IU. Pregnant women should maintain serum levels of 25-hydroxycholecalciferol above 30 mg/mL.

During pregnancy, the need for calcium supply increases. Calcium absorption from the intestine is increased. In the duodenum, active transport, dependent on 1,25-dihydroxylcholecalciferol, predominates. It is further subject to active transport to the foetus via the placenta. Calcium absorption from the maternal bones becomes prevalent in late gestation if calcium consumption is poor [6]. This can lead to lower BMD, the risk of delayed bone maturation in the newborn, and reduced BMD or hardness of the offspring's teeth in later life [7].

The WHO has advised calcium supplementation of 1500–2000 mg daily since 2011 [8]. A study involving 18 064 women (27 studies) showed that, especially in women with calcium-poor diets, high-dose Ca supplementation (≥ 1 g/day) reduces the risk of preeclampsia as well as premature labour [9]. On the other hand, there are two randomized trials of low-dose calcium supplementation during pregnancy, involving 11 000 non-pregnant women in each study. These 2 studies indicated that high-dose calcium supplementation did not provide a significant advantage in terms of preeclampsia risk, relative to low-dose supplementation [10].

As far as the importance of calcium in pregnancy is concerned, only pre-eclampsia appears, however other important health effects should not be overlooked. One paper indicated that vitamin D supplementation along with calcium leads to significant weight loss, primarily as a result of reduced fat mass in the body's central areas [11]. Maternal Ca deficit during gestation may affect gene expression and thereby contribute to altered metabolic phenotype, causing insulin resistance in the offspring [12].

The data does not converge and require further investigation into the effects of vitamin D3 and calcium concentrations on BMD.

RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY (REMS)

The utilize of double vitality X-ray absorptiometry (DXA) is disallowed in pregnancy, not at all like ultrasound, which is commonly utilized in the conclusion of pregnant women. Radiofrequency echographic multispectrometry (REMS) is considered as an advanced tool for diagnostic evaluation of bone health (Fig. 1). A study from Siena, Italy, showed that REMS has an even higher capacity to diagnose osteoporosis compared to DXA [13]. This and other works [14] have led researchers to use the REMS technique to examine BMD in pregnant women as a safe alternative to DXA.

Researchers from Parma, Italy, studied 78 pregnant women at 39.1 ± 1.5 weeks using REMS. They found that femoral BMD decreased by up to 8.1% compared to the control group. BMD of the femoral neck showed a positive association with BMI before pregnancy and a negative association with the mother's age. In a further note, femoral neck BMD was reported to be lower in Caucasians compared to non-Caucasians [15].

Another study from Italy in 2024 examined 65 female patients using REMS. The study found that there is a considerable decrease in bone mineral density in the femoral neck from early to late in pregnancy [16]. Other work using REMS also indicates a decrease in BMD during pregnancy [17, 18].

Radiofrequency echographic multispectrometry is a new technology which has just begun in obstetrics. More studies on its use are needed, as the primary results are very promising.

X-RAY, QUS AND OTHER METHODS OF MEASUREMENTS

Quantitative ultrasonometry (QUS) is an affordable, radiation-free way to evaluate bone mineral density and the quality of bone, which may be applied during pregnancy (Fig. 1). Hellmeyer et al. [19] conducted QUS of the phalanges in 60 women without disease during gestation. They found a substantial decrease in the speed of sound (AdSOS) in the first, second and third trimesters. Moreover, they observed that AdSOS was substantially lower in the second and third trimesters in comparison to the first trimester. This reduction had a major impact on the t-score and Z-score of the QUS in this trial and thus shows potential clinical significance. Study published in 2021, as well as other papers, also showed a significant decrease in QUS parameters in pregnant women [20, 21].

Dual energy X-ray absorptiometry scan (DXA) is forbidden in pregnancy due to potential risk for fetus. Therefore, there are not many studies using this method during pregnancy. The largest DXA study during pregnancy on a group of 153 women was

conducted by U. K. Møller et al. [22], measuring BMD in women planning pregnancy and then during each trimester of gestation and at 15, 129 and 280 days postpartum. In comparison with the control group, BMD declined markedly during gestation by 3.2 ± 0.5% in the total hip, 1.8 ± 0.5% in the lumbar spine, 2.4 ± 0.3% in the whole body and 4.2 ± 0.7% in the ultra-distal forearm. After delivery, BMD declined under the influence of breastfeeding. One study analyzed the correlation of 25-hydroxycholecalciferol and BMD in patients with gestational diabetes mellitus (GDM). Elevated blood glucose levels relate to reduced 25-hydroxycholecalciferol expression, which reduces BMD and leads to impaired bone metabolism [23].

N-telopeptides (NTX), pyridinoline (PYD) or deoxypyridinoline (DPYD) as markers of bone resorption in urine during lactation seem interesting (Fig. 1). Erin M Kyle et al. [24] found that these 3 urinary markers decreased from early postpartum to 12 months postpartum. Urine markers may be a more affordable and available measurement of BMD and better illustrate present bone status in comparison with DXA, which only offers a static picture of BMD [25].

MINERAL STATUS DURING PREGNANCY

The aim of this work was to present available data concerning the correlation between blood vitamin D levels and BMD. The main role of vitamin D is to preserve normal calcium and phosphorus concentrations, as phosphorus and calcium are both necessary for bones. Adequate proof of the impact of vitamin D and calcium supplementation on mother's bone mass is still lacking in the literature.

In 2019. Eroglu et al. [26] assessed BMD values among 93 women aged 18–40 years at 30 days postpartum using DEXA technology. They found that low levels of 25-hydroxycholecalciferol were directly proportionately associated with low BMD, as well as with reporting postpartum back pain.

Paper published by William W K To et al. [27] present data on 450 pregnancies with gestational hypertension using QUS. The patients with hypertension had a slightly higher mean BMD loss compared to patients with blood pressure in reference values, probably due to the small number of women with gestational hypertension 4.8% (n = 22).

Dahlman et al. [28] examined the relationship between blood vitamin D concentrations and BMD in 60 women using DXA at 12 weeks' gestation and 6–12 months postpartum. They found no statistically relevant connection between 25-hydroxycholecalciferol concentrations and BMD measurements. Also, a study by Wei Wei et al. [29] using DXA on a group of 301

pregnancies who had BMD measurements at 12–20 weeks of pregnancy and then at 0–14 week postpartum, discovered that vitamin D supplementation had no significant effect on BMD changes. On the other hand, a study on 160 pregnant Japanese women indicated that 25-hydroxycholecalciferol blood concentrations and BMI in the first trimester of pregnancy were associated with bone mass in breastfeeding women from the time of delivery to 1 year postpartum [30].

Furthermore, the calcium supplementation in pregnancies with insufficient calcium intakes could disturb metabolic adjustment and could not favor the health of maternal bone [31]. A systematic review conducted in Finland analysed the titles and abstracts of 3555 records, including seven randomised controlled trials did not confirm a beneficial effect of calcium supplementation on maternal BMD after childbirth or during lactation, or on offspring BMD, even with low dietary calcium intake. The effect of calcium supplementation on maternal and offspring bone health was considered unclear due to ambiguous study results [7]. Contradictory to these studies is the Chinese DXA study, which concluded that Ca and/or milk supplementation during gestation is linked with higher BMD [3]. The Shanghai work suggested that Ca levels should be included in the routine examination of pregnant women, but correlations between Vitamin D and BMD were not statistically significant [21].

Shao et al. [21] in a trial of 130 women demonstrated that BMD decrease, measured by QUS of the heel bone between the start and end of pregnancy, was not associated with vitamin D status. Levels of calcium, phosphorus and alkaline phosphatase were significantly negatively correlated with BMD during gestation.

Another less invasive method of testing is the measurement of the bone resorption marker, C-terminal telopeptide of type I collagen (CTX) in the urine. In one study on approximately 400 women, CTX and 25-hydroxycholecalciferol were measured in early and late pregnancy. Cholecalciferol reduces the increase in CTX in maternal urine but continues to increase during pregnancy [33].

Most of the work published to date has shown a relationship between vitamin D3 concentration and calcium on maternal bone mass. However, their effect on BMD is still not fully understood.

CONCLUSION

It's important for healthcare providers to monitor and support women's bone health during the postpartum period to minimize the risk of osteoporosis and other bone-related complications later in life.

Overall, available data suggest that bone turnover increases during pregnancy, especially during the third trimester. There are real but small declines in BMD throughout the skeleton that require a sufficiently large cohort to be detected with confidence. Increased bone resorption occurs during the third trimester of pregnancy and is likely to result in some bone loss, with most women experiencing a moderate decline in BMD until delivery. Increased bone resorption and loss are more likely in women who do not absorb enough calcium to meet the combined needs of themselves and their offspring. Inadequate dietary calcium intake probably contributes to the increased risk of osteoporosis associated with pregnancy.

Article information and declarations

Author contributions

Wiktor Wojczakowski — 50%, concept, analysis and interpretation of data, article draft, corresponding author. Konrad Futyma — concept, analysis and interpretation of data, article draft.

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Conflict of interest

Wiktor Wojczakowski and Konrad Futyma declare no conflict of interest.

Supplementary material

None.

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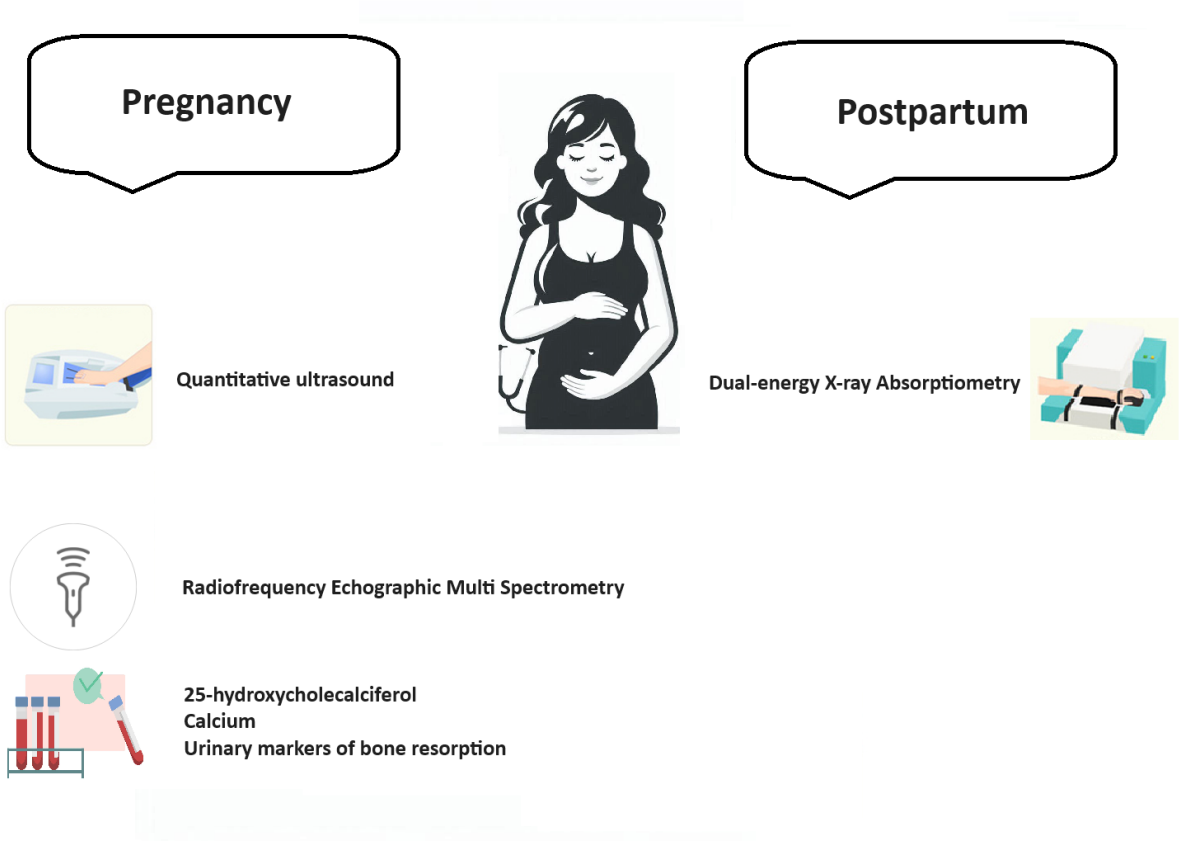

Figure 1. Methods of measurements of bone mineral density during pregnancy and postpartum