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REVIEW

Pregnancy- and lactation-related bone fragility: The hidden risk

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ABSTRACT

Pregnancy and lactation significantly alter bone homeostasis, potentially leading to impaired bone quality and mineralization due to the increased metabolic demands of the developing offspring. While most women with osteopenia during these periods experience a return to baseline bone density after weaning, some may remain at risk for fractures, particularly in cancellous bone. There are inconsistencies in current reports on fracture risk and appropriate treatment strategies. In this review, we discuss the existing evidence on the diagnosis, clinical presentation, and approaches for preventing and managing bone fragility in this unique population.

Keywords: Fracture, fragility, gynecology, lactation, osteoporosis, pregnancy.

Pregnancy and lactation are periods of significant physiological change for females that have been linked to alterations in bone quality and mineralization. Although pregnancy and lactation-related bone fragility are considered uncommon, they may be underdiagnosed and underreported, resulting in an unclear understanding of its actual incidence. The increased fetal demand for calcium during pregnancy leads to alterations in maternal bone homeostasis. While most women experience a return to their baseline bone mineral density (BMD) eventually, there remains a risk of fragility fractures during the third trimester of pregnancy or the early postpartum period.[1-3] Additionally, vitamin D deficiency, affecting 40 to 98% of pregnant individuals globally, and low calcium levels have been associated with adverse maternal and child health outcomes, although it remains uncertain whether these deficiencies are causative or merely indicative of poor overall maternal health.[4]

Changes in BMD related to reproduction occur within ±5% of those seen in healthy women who are not pregnant or lactating.[5] The existing evidence indicates that lactation is linked to a decrease in bone strength and volume due to lactation-induced bone resorption, which supplies additional calcium to meet the increased demands of the offspring, along with an elevated rate of bone turnover.[6,7] Elevated bone turnover leads to uncoupled bone resorption, where the new deposition is also weaker and less mineralized, thereby resulting in decreased BMD and impaired microstructural integrity, which peaks at the point of weaning.[8,9]

Osteopenia is typically reversible and ceases after the peak at the time of weaning.[10] However, longitudinal studies have demonstrated that extended lactation periods, particularly those exceeding six

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months, may lead to notable bone loss, with 12 to 18 months identified as a threshold beyond which BMD may not fully recover.[11-13] An intriguing outtake from lactation-related osteoporosis phenomenon is that several animal and clinical studies suggest that the bone loss is observed predominantly in cancellous bone, such as vertebrae and calcaneus, due to their higher metabolic activity, thereby primarily providing for the increased demand.[10,14,15] In contrast, cortical bone has been shown to undergo bone accumulation rather than bone loss, possibly secondary to the anabolic phase experienced during post-lactation period.[6,16] This accumulation can confer a protective effect at load-bearing skeletal sites composed primarily of cortical bone, namely the hip joint. Unlike postmenopausal osteoporosis, hip fracture risk may even be reduced in women with longer duration of lactation where lumbar fractures are observed with an increased risk.[17-19] It should be highlighted that, despite preclinical studies indicate that pregnancy and lactation may contribute to bone loss, clinical evidence on this matter remains inconclusive. While bone loss during these periods is anticipated based on existing research, there is contrasting evidence on the associated risk of fracture.[18-23] Moreover, considering the postmenopausal osteoporotic fractures, history of lactation has been associated with a decreased risk of fracture in recent meta-analyses.[18,19]

Understanding these effects is essential for effectively managing changes in bone quality associated with lactation and pregnancy. Therapeutic options for treating osteoporosis during pregnancy or breastfeeding are still limited.[24] There is a paucity of scientific literature to guide clinical decisions. There is also concern about the potential deleterious impact of treatment on future pregnancies.[24]

In the United States, the current recommendations for pregnant and lactating individuals include a daily calcium intake of 1,000 to 1,300 mg, depending on age, along with supplementation of 600 international units of vitamin D.[25] However, the use of pharmacotherapy in this population remains a topic of considerable debate. Several studies have explored the potential of various interventions to address these concerns. To illustrate, one study investigated the use of pamidronate during pregnancy and lactation, which demonstrated favorable outcomes in preserving maternal bone mass by preventing bone loss associated with these reproductive stages.[26] Additionally, estrogen therapy or combined estrogen-progestin therapy has been identified as the key treatment option for menopausal symptom relief and osteoporosis prevention.[27] By reducing bone resorption and improving bone quality, bisphosphonates lead to an enhanced quality of life.[28] Daily teriparatide is considered a potential treatment for young patients with pregnancy- and lactation-associated osteoporosis, particularly in cases involving multiple vertebral fractures, to reduce the risk of long-term complications.[29]

It is of utmost importance to recognize that women with breastfeeding and pregnancy-related bone loss should be regarded as a distinct group from women with postmenopausal osteoporosis, as the expected trajectory of bone loss differs between these two populations. While bone loss is anticipated to persist in postmenopausal women, it is unlikely to continue in those who have recently undergone pregnancy and lactation. This distinction underscores the potential risks associated with the use of antiresorptive agents to mitigate bone loss in patients with pregnancy- or lactation-related osteoporosis. Additionally, it highlights the necessity for the development of novel therapeutic modalities for this specific group.

The development of novel treatment methods is contingent upon the continuation of research and clinical trials. The primary goal is to develop safe pharmacological interventions that do not adversely impact the fetus or nursing infant. The formulation of targeted dietary supplements aims at addressing the specific nutritional needs of women during pregnancy and lactation. An enhanced comprehension of the underlying mechanisms that give rise to alterations in bone density during pregnancy and lactation is required.

In conclusion, while current guidelines emphasize on calcium and vitamin D supplementation, nutritional counseling, exercise, and lifestyle modifications, there is a clear need for further development of pharmacological treatments and personalized approaches. The establishment of more effective and safe treatment modalities for addressing bone quality alterations during gestation and lactation would be contingent upon the outcomes of ongoing research and clinical trials.

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