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Effects of Maternal 25-Hydroxyvitamin D Levels during Pregnancy on Offspring Health

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Abstract

Vitamin D is a crucial vitamin that regulates human metabolism, and its deficiency or insufficiency significantly impacts human health. Maternal vitamin D deficiency during pregnancy can affect both the mother's and her offspring's health to varying degrees. Whether routine screening for vitamin D nutritional status in pregnant women and their offspring is necessary requires further large-scale clinical research to provide scientific evidence aimed at enhancing the health outcomes for both mothers and their offspring.

Keywords

Vitamin D, Maternal, Offspring, Newborn

1. Introduction

With the advancement of research on vitamin D metabolism in pregnant women, the relationship between maternal 25-hydroxyvitamin D levels and offspring health has become an increasingly significant issue in perinatal medicine. This review examines the current status of maternal vitamin D nutritional status during pregnancy worldwide and its impact on offspring health. It aims to provide scientific evidence for determining whether routine screening and early intervention for vitamin D nutritional status in both mothers during pregnancy and their offspring are necessary, thereby enhancing maternal and infant safety and promoting healthy development in the next generation.

2. Current Status of Vitamin D Nutritional Status in the Population

Vitamin D is a key hormone regulating calcium and phosphorus metabolism. The

human body primarily obtains vitamin D through direct sunlight exposure on the skin, which converts 7-dehydrocholesterol into vitamin D3 [1], with exogenous intake via the digestive tract being a secondary source [2]. A study on vitamin D nutrition among Chinese elderly individuals indicated that vitamin D deficiency is a widespread issue in China's aging population [3]; A Malaysian survey of 25-hydroxyvitamin D levels in the elderly found that 83% of participants were deficient in vitamin D [4]. A Hangzhou study on serum 25-hydroxyvitamin D status in children aged 0 - 14 years revealed a gradual decrease in serum 25-hydroxyvitamin D levels with increasing age within this age group [5]. A cross-sectional survey by Xie Xiaolian *et al.* [6] in Yinchuan City found a vitamin D deficiency rate of 66.9% among students in the region. This indicates that vitamin D deficiency is also prevalent among the elderly and children. The vitamin D nutritional status of special populations such as the elderly, children, and pregnant women warrants attention. Vitamin D requirements significantly increase during pregnancy [7], but are influenced by factors including skin tone, latitude, clothing, and dietary habits. Multiple studies indicate that vitamin D insufficiency/deficiency is prevalent among pregnant women and newborns globally [8] [9]. Maternal vitamin D levels directly or indirectly influence fetal vitamin D status via the placenta [1] [10], and its effects on newborns post-birth warrant systematic review.

3. Current Research on Maternal Vitamin D Levels during Pregnancy and Their Effects on Pregnant Women

3.1. Current Status of Vitamin D Levels during Maternal Pregnancy

A retrospective study by Yakar, Burkay [11] from Turkey found that the prevalence of vitamin D deficiency among pregnant women was 73% during seasons with sufficient sunlight exposure and 90% during seasons with insufficient sunlight exposure. A 2021 study from Western Australia on maternal vitamin D nutritional status and its influencing factors found that 19% of pregnant women were deficient in vitamin D, with 14% experiencing severe deficiency [12]. Another study from Shanghai on maternal vitamin D nutritional status and its influencing factors revealed that 97.6% of the 953 pregnant women participating in the study exhibited varying degrees of vitamin D deficiency [13]. These studies indicate that maternal vitamin D levels vary across different countries, regions, and seasons. Furthermore, diagnostic criteria for vitamin D deficiency remain inconsistent globally, with no consensus on the normal range for pregnant women—a vulnerable population—as most studies adopt standards for the general population. Current research on normal maternal vitamin D levels is limited. Future multi-center, large-scale studies are needed to establish the normal range and variation patterns of vitamin D in pregnant women across different regions and ethnicities.

3.2. Effects of Maternal Vitamin D Levels during Pregnancy on the Mother

Multiple studies indicate that maternal vitamin D deficiency during pregnancy

correlates with the occurrence of pregnancy complications and comorbidities. An Arab research revealed that women with vitamin D deficiency had a fourfold increased risk of preeclampsia compared to those with normal vitamin D levels [14]. George Dahma *et al.* [15] also noted that pregnant women with low vitamin D levels in early pregnancy had an increased risk of preeclampsia. Another Indian cross-sectional study found that vitamin D supplementation during pregnancy reduced the incidence of complications such as gestational diabetes [16]. Mei-Chun Chien *et al.* [17] demonstrated that vitamin D deficiency during pregnancy was associated with an increased risk of bacterial vaginosis and gestational diabetes in pregnant women. A cohort study indicated that maternal 25(OH)D levels below 20 ng/mL elevate preterm birth risk, potentially through VitD's role in regulating inflammatory responses [8]. Chen Yufen *et al.*'s research revealed widespread vitamin D deficiency among pregnant women in high-altitude regions, with higher levels in full-term pregnancies compared to preterm births, suggesting vitamin D deficiency may contribute to preterm birth incidence in such areas [18].

4. Effects of Maternal Vitamin D Levels during Pregnancy on Newborns

4.1. Maternal Vitamin D Levels and Preterm Birth

A retrospective study examining the relationship between vitamin D deficiency in pregnant women from developing countries and neonatal complications revealed a significant association between maternal vitamin D levels and adverse neonatal health outcomes, including preterm birth [19]. A meta-analysis by Monica Tous *et al.* also indicated a strong correlation between maternal vitamin D insufficiency and the risk of preterm birth [20]. However, differing perspectives exist. A study from Guangzhou examining maternal 25-hydroxyvitamin D levels and pregnancy outcomes found that higher maternal vitamin D levels were associated with a greater likelihood of preterm birth [21]. Conversely, a study by Fan Yanqin *et al.* did not identify a correlation between low maternal vitamin D levels and preterm birth [22].

4.2. Maternal Vitamin D Levels and Low Birth Weight

The mechanism by which maternal vitamin D insufficiency or deficiency leads to low birth weight in fetuses remains unclear. Some studies suggest it may be associated with reduced fetal bone size and density after birth due to low maternal vitamin D levels during pregnancy [23]. Other research indicates that lower vitamin D levels in pregnant women may increase the risk of placental inflammation during gestation, thereby causing intrauterine growth restriction [24]. A study by Pei Lijun *et al.* [25] indicated that vitamin D deficiency at any stage of pregnancy increases the risk of low birth weight in newborns. This finding was corroborated by a retrospective study by Fang Kehong *et al.* [26], another retrospective study by Tsenkova-Toncheva [27], and a cross-sectional study conducted by Singh, Mayank *et al.* at a large tertiary hospital in India [28]. The relationship between ma-

ternal vitamin D insufficiency/deficiency during pregnancy and low birth weight in newborns remains controversial at present. A study by Eyad Almidani *et al.* on vitamin D levels in Saudi Arabian pregnant women and newborn birth weight found no correlation between maternal vitamin D levels and newborn birth weight [29].

4.3. Maternal Vitamin D Levels and Neonatal Hypocalcemia

Neonatal hypocalcemia is defined as serum total calcium < 1.75 mmol/L (7 mg/dL) or serum free calcium < 0.9 mmol/L (3.5 mg/dL) [30]. Based on the timing of onset, hypocalcemia occurring within 1 - 2 days postpartum is defined as early-onset hypocalcemia, while hypocalcemia developing after 3 days postpartum is termed late-onset hypocalcemia. Literature indicates that maternal vitamin D levels can influence neonatal vitamin D concentrations via the umbilical cord-placental pathway [31] [32]. This suggests maternal vitamin D deficiency may increase the risk of neonatal hypocalcemia. As early as 2014, a Korean study demonstrated that delayed-onset neonatal hypocalcemia may be influenced by maternal vitamin D deficiency and insufficiency [33]. Another meta-analysis shown that maternal vitamin D levels influence fetal vitamin D status via the umbilical cord pathway, and vitamin D-deficient newborns exhibit a higher risk of hypocalcemia, with maternal vitamin D levels playing a crucial role in this association [34].

4.4. Maternal Vitamin D Levels and Neonatal Bone Development

During fetal development, vitamin D can only be obtained from the mother. A study conducted in Japan by Junko Yorifuji *et al.* [35] indicated that neonatal cranial softening is associated with intrauterine vitamin D deficiency. Rita M. Pita *et al.* [36] also analyzed four cases of full-term newborns with cranial softening, concluding that maternal vitamin D levels play a critical role in fetal skeletal development. While these studies conclude neonatal cranial softening as a pathological manifestation of vitamin D deficiency, some view it as a normal physiological phenomenon requiring no intervention [37]. Therefore, whether neonatal cranial softening can serve as an early warning sign for vitamin D deficiency remains to be validated by further clinical research.

4.5. Maternal Vitamin D Levels and Neonatal Neurodevelopment

In 2004, Darryl W. Eyles *et al.* first reported the distribution of 1,25-dihydroxyvitamin D3 receptors (VDR) and 1α-hydroxylase (1α-OHase) (the enzyme responsible for forming active vitamin D in the brain) in the human brain [38], providing direct evidence that vitamin D influences nervous system function. Thus, we have reason to speculate that maternal vitamin D nutritional status may influence fetal neurodevelopment. Studies suggest maternal vitamin D deficiency correlates with reduced brain volume in newborns; persistent vitamin D deficiency during pregnancy may also hinder children's learning and cognitive processes. Consequently, maternal vitamin D levels during pregnancy can serve as a predictor of offspring

neurodevelopment [39]. A 2023 prospective study indicated that umbilical cord blood 25(OH)D levels showed a significant positive correlation with cognitive, language, and motor development at 24 months of age in offspring [40]. Furthermore, research by Melissa M Melough *et al.* [41] revealed a positive correlation between maternal vitamin D nutritional status during pregnancy and children's IQ at ages 4 - 6. This provides stronger evidence that maternal vitamin D levels during pregnancy are associated with offspring's neurological development, with effects extending beyond the perinatal period.

4.6. Maternal Vitamin D Levels and Long-Term Diseases in Offspring

The long-term effects of maternal vitamin D status during pregnancy extend beyond the musculoskeletal system, potentially impacting respiratory, endocrine, and immune systems. A study in the northeastern United States found that higher maternal vitamin D intake during pregnancy may reduce the risk of recurrent wheezing in early childhood among offspring [42]; Chantal Mathieu *et al.* [43], through research on vitamin D receptors, proposed that maternal vitamin D deficiency during pregnancy may increase the incidence of autoimmune diseases (such as type 1 diabetes) in genetically susceptible offspring. A meta-analysis indicated a negative correlation between maternal vitamin D levels in Asia and the occurrence of atopic dermatitis in offspring [44].

Globally, diagnostic criteria for vitamin D deficiency vary across different ethnicities, latitudes, skin tones, and religious contexts. According to the Chinese Expert Consensus on Clinical Application of Vitamin A and Vitamin D in Children (2024) [45], serum 25-(OH)D levels below 30 nmol/L indicate vitamin D deficiency, levels between 30 - 50 nmol/L indicate vitamin D insufficiency, and levels ≥50 nmol/L are considered adequate. The Institute of Medicine (IOM) defines vitamin deficiency as: 25-(OH)D < 20 ng/mL (50 nmol/L) for vitamin D deficiency; 25-(OH)D > 21 ng/mL and <29 ng/mL (52.5 - 72.5 nmol/L) for vitamin D insufficiency; and 25-(OH)D levels greater than 30 ng/mL but less than 100 ng/mL (75 - 250 nmol/L) indicate vitamin D sufficiency [46].

China has yet to incorporate maternal vitamin D levels into routine prenatal screening, and further research is needed to define the optimal range for maternal vitamin D status. Studies examining the impact of maternal vitamin D deficiency during pregnancy on offspring health are even more limited. Future efforts should include large-scale, nationwide surveys of maternal vitamin D levels and multicenter, large-sample clinical studies examining the effects of maternal vitamin D levels on offspring health. This research is essential to determine the optimal dosage for vitamin D supplementation during pregnancy and to provide robust evidence for improving offspring health and reducing disease incidence.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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