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# The impact of maternal vitamin D deficiency on fetal development and long-term health outcomes in offspring

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**Abstract**

Introduction: Vitamin D is a vital micronutrient that supports mineral balance, modulates immune activity, and contributes to healthy fetal development. Adequate maternal vitamin D levels are essential for proper placental function and optimal intrauterine growth. Nevertheless, deficiency of this nutrient remains common among pregnant women worldwide, posing potential risks for both maternal and child health [1]. The purpose of this review is to critically evaluate current evidence regarding the influence of maternal vitamin D insufficiency on

fetal growth, perinatal outcomes, and the longer-term health of offspring — particularly its implications for skeletal integrity, immune system maturation, metabolic regulation, and neurodevelopment.

Materials and methods: Literature from 2015–2025 was systematically searched through PubMed, Scopus, and Google Scholar using the terms: “thoracic outlet syndrome,” “overhead athletes,” “Paget-Schroetter syndrome,” “effort thrombosis,” “vascular compression,” and “rehabilitation.” Priority was given to systematic reviews, clinical trials, and high-quality case studies

Summary: Evidence suggests that low maternal vitamin D levels are associated with impaired fetal bone mineralization, increased risk of preeclampsia and preterm birth, and lower birth weight. Beyond the neonatal period, maternal deficiency has been linked to higher susceptibility to respiratory infections, allergic and autoimmune diseases, insulin resistance, and neurodevelopmental disorders in children.

Conclusions: Insufficient maternal vitamin D levels constitute a modifiable determinant that may influence offspring health well beyond the perinatal period. Ensuring adequate vitamin D status during pregnancy—through targeted supplementation programs and evidence-based public health initiatives—can contribute to improved maternal and neonatal outcomes and may help lower the risk of chronic diseases later in life.

Keywords: vitamin D deficiency; pregnancy; fetal development; maternal health; child health; immune development; neurodevelopment; autoimmune diseases; allergic disorders; supplementation; public health

## Introduction

Vitamin D, a fat-soluble secosteroid hormone, exerts broad biological effects that extend beyond its traditional role in calcium and phosphorus metabolism. It modulates immune responses, regulates cellular differentiation, and contributes to vascular and metabolic homeostasis. During pregnancy, vitamin D assumes additional significance as it supports placental development, trophoblast invasion, and the establishment of adequate uteroplacental circulation—processes essential for normal fetal growth and survival [1].

Deficiency of vitamin D during gestation remains a widespread global health concern, affecting an estimated 40–80% of pregnant women, depending on geographic region, sun exposure, dietary habits, and skin pigmentation. Physiological changes in pregnancy, such as increased maternal adiposity and hemodilution, can further lower circulating concentrations of 25-hydroxyvitamin D [25(OH)D], the primary biomarker of vitamin D status [2]. These deficiencies may have important clinical consequences, influencing not only maternal well-being but also fetal development and subsequent health trajectories in offspring.

Emerging evidence indicates that inadequate maternal vitamin D levels are associated with adverse pregnancy outcomes, including preeclampsia, gestational diabetes, low birth weight, and preterm delivery. Furthermore, growing interest has focused on potential long-term consequences for the child, such as impaired skeletal mineralization, altered immune programming, and increased susceptibility to metabolic or neurodevelopmental disorders later in life. The biological plausibility of these associations is supported by the presence of vitamin D receptors (VDRs) and metabolizing enzymes in the placenta, fetal tissues, and developing organs, suggesting that maternal vitamin D directly influences gene expression and cellular signaling during critical developmental windows. [3]

The accumulating body of literature underscores the importance of maintaining adequate vitamin D levels during gestation as a potentially modifiable factor influencing both immediate and lifelong health outcomes in offspring [4].

This review aims to synthesize current knowledge regarding the impact of maternal vitamin D deficiency on fetal growth, neonatal health, and the long-term development of children. It also explores underlying biological mechanisms, evaluates evidence from observational and interventional studies, and highlights emerging areas of research relevant to public health and prenatal care.

## Fetal Development and Skeletal Outcomes

Vitamin D plays a pivotal role in fetal skeletal growth and mineralization through its regulation of calcium and phosphate homeostasis. During pregnancy, maternal 25-hydroxyvitamin D [25(OH)D] crosses the placenta and serves as the primary source of vitamin D for the

developing fetus. The active form, 1,25-dihydroxyvitamin D [1,25(OH)$_2$D], contributes to calcium absorption and mobilization, ensuring adequate supply for fetal bone formation, particularly during the third trimester when rapid skeletal mineralization occurs [5].

Maternal vitamin D deficiency has been consistently associated with impaired fetal bone development and suboptimal birth outcomes. Epidemiological studies demonstrate that low maternal serum 25(OH)D concentrations are linked to decreased neonatal bone mineral content, reduced femur length, and lower birth weight [6]. For instance, cohort studies such as the Southampton Women's Survey have shown that maternal vitamin D insufficiency during late pregnancy correlates with reduced bone mass in offspring at birth and even at later stages of childhood, suggesting a "fetal programming" effect on skeletal health [7].

Clinical outcomes of maternal vitamin D deficiency extend beyond immediate neonatal effects. Infants born to vitamin D–deficient mothers have a higher risk of developing rickets, delayed growth, and skeletal deformities. Furthermore, longitudinal studies suggest that low prenatal vitamin D exposure may contribute to lower peak bone mass and increased fracture risk in adolescence and adulthood [8]. These findings underscore the long-term skeletal consequences of insufficient maternal vitamin D levels during pregnancy.

In summary, adequate maternal vitamin D levels are critical for healthy fetal skeletal development and for the prevention of adverse skeletal outcomes later in life. Ensuring sufficient vitamin D status before and during pregnancy represents a modifiable factor that may contribute to improved maternal and child health across generations.

**Immune Development and the Risk of Allergic and Autoimmune Diseases**

Vitamin D is increasingly recognized as an important immunomodulatory molecule, exerting significant effects on both the innate and adaptive immune systems. Its active form, 1,25-dihydroxyvitamin D [1,25(OH)$_2$D], binds to the vitamin D receptor (VDR), which is expressed in numerous immune cells, including macrophages, dendritic cells, T lymphocytes, and B cells. Through this pathway, vitamin D regulates the expression of genes involved in cytokine production, antigen presentation, and immune tolerance [9]. During pregnancy, these mechanisms are crucial not only for maintaining maternal-fetal immune balance but also for shaping the development of the fetal immune system.

Emerging evidence suggests that maternal vitamin D deficiency during pregnancy may predispose offspring to an increased risk of allergic and autoimmune diseases [10]. Observational studies have reported associations between low maternal 25(OH)D levels and higher incidence of asthma, eczema, allergic rhinitis, and autoimmune disorders such as type 1 diabetes and multiple sclerosis in children. These associations are thought to be mediated through early-life immune programming, where insufficient vitamin D exposure alters T-cell differentiation and immune tolerance mechanisms [11].

In summary, maternal vitamin D status during pregnancy appears to play a critical role in immune system programming and may influence susceptibility to allergic and autoimmune diseases in offspring. Although causal relationships have not been definitively established, the available evidence supports the biological plausibility of vitamin D–mediated immune regulation [12]. Ensuring sufficient maternal vitamin D levels through targeted supplementation and public health strategies may represent a simple yet impactful approach to promoting immune resilience and reducing the burden of immune-mediated diseases in future generations [13].

**Neurodevelopmental Outcomes and Cognitive Function**

Beyond its well-established skeletal and immunological roles, vitamin D has emerged as a key neurosteroid influencing brain development and function. The vitamin D receptor (VDR) and the enzyme 1α-hydroxylase, responsible for converting 25(OH)D to its active form, are widely expressed in the developing human brain, including regions such as the hippocampus, cerebellum, and cortex [14]. These findings suggest that vitamin D is involved in neuronal differentiation, synaptogenesis, and neurotransmission, processes that are crucial for cognitive and behavioral development. During pregnancy, adequate maternal vitamin D levels support normal neurodevelopment by modulating neurotrophic factors, regulating calcium signaling, and protecting neural tissue from oxidative stress and inflammation. Conversely, maternal vitamin D deficiency may disrupt these pathways, leading to altered brain structure and function in the offspring [15]. Human studies have provided evidence linking low maternal vitamin D status during pregnancy with adverse neurodevelopmental and behavioral outcomes in children. The biological mechanisms underlying these associations are multifactorial [16]. Vitamin D regulates the expression of neurotrophins such as nerve growth factor (NGF) and glial-derived

neurotrophic factor (GDNF), both of which support neuronal survival and synaptic plasticity [17]. Furthermore, vitamin D modulates inflammatory cytokines and oxidative stress markers, maintaining a neuroprotective environment within the developing brain. Deficiency during pregnancy may therefore result in subtle alterations in brain circuitry that manifest as cognitive and behavioral deficits later in life.

In summary, maternal vitamin D appears to play a vital role in brain development and cognitive function, with deficiency potentially contributing to an increased risk of neurodevelopmental disorders in children.

**Vitamin D Supplementation and Incident Preeclampsia**

Preeclampsia is a pregnancy-specific hypertensive disorder characterized by new-onset hypertension and proteinuria after 20 weeks of gestation, often accompanied by systemic endothelial dysfunction and organ damage. It remains one of the leading causes of maternal and perinatal morbidity and mortality worldwide [18]. Although its precise etiology is multifactorial, involving abnormal placentation, oxidative stress, and dysregulated immune responses, growing evidence implicates maternal vitamin D status as a potentially modifiable risk factor [19].

Vitamin D exerts pleiotropic effects that extend beyond calcium metabolism, influencing endothelial function, angiogenesis, and immune regulation — all of which are critical in the pathogenesis of preeclampsia. The active form, 1,25-dihydroxyvitamin D [$1,25(OH)_2D$], enhances vascular health by stimulating nitric oxide production, suppressing renin gene expression, and modulating inflammatory cytokines [20]. It also regulates placental implantation and trophoblast invasion through interactions with the vitamin D receptor (VDR), which is highly expressed in placental tissue. Deficiency in vitamin D may therefore contribute to abnormal placental development and increased oxidative stress, leading to impaired perfusion and the clinical manifestation of preeclampsia [21].

Despite promising mechanistic and epidemiological data, current clinical guidelines do not universally recommend vitamin D supplementation solely for the prevention of preeclampsia. Instead, supplementation is generally advised to maintain adequate maternal vitamin D levels for overall pregnancy health. The World Health Organization (WHO) and several obstetric

societies recommend daily doses of 600–2000 IU during pregnancy, depending on regional deficiency prevalence [22]. In summary, vitamin D supplementation during pregnancy shows potential in reducing the risk of preeclampsia through its effects on placental function, angiogenesis, and immune modulation. Maintaining sufficient maternal vitamin D status remains a prudent and low-risk strategy with potential benefits extending beyond preeclampsia prevention to overall maternal and fetal health.

## Summary and conclusion

Maternal vitamin D deficiency during pregnancy has emerged as a significant determinant of both short-term and long-term health outcomes in offspring. Evidence from epidemiological, clinical, and experimental studies highlights its influence on fetal skeletal development, immune system maturation, and neurocognitive function. Although observational data strongly suggest that inadequate vitamin D exposure in utero may increase the risk of bone abnormalities, allergic and autoimmune diseases, and neurodevelopmental disorders, causality remains to be fully established.

Despite the biological plausibility of these associations, inconsistencies in study design, supplementation protocols, and population characteristics continue to limit definitive conclusions. Nevertheless, the prevention of maternal vitamin D deficiency is a low-cost, safe, and potentially far-reaching public health intervention. Universal screening, tailored supplementation strategies, and increased awareness among healthcare providers may substantially improve pregnancy outcomes and promote long-term health in children.

Future research should focus on high-quality randomized controlled trials, standardized measurement protocols, and mechanistic studies exploring the epigenetic and molecular pathways by which vitamin D influences fetal programming. Strengthening this evidence base will be essential to refine clinical guidelines and optimize maternal and child health across generations.

## Disclosure

The authors declare no conflict of interest in relation to this study.

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