

Vitamin D Supplementation for Pregnancy Complications; Systematic Literature Review

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ABSTRACT

Introduction: Vitamin D deficiency is a global health concern, particularly among pregnant women, with prevalence rates reaching up to 40%. This deficiency poses risks to both maternal and fetal health, leading to complications such as gestational diabetes, preeclampsia, and preterm labor.

Content: This study employed a literature review approach, collecting data from Google Scholar, ScienceDirect, and Technology Index (SINTA). Articles were selected based on inclusion criteria: international journals published between 2017 and 2024, focusing on the effectiveness of vitamin D during pregnancy. Exclusion criteria included journals ranked >Q3 (SJR) and >3 (SINTA). The review process involved critical appraisal, skimming, scanning, and thematic analysis.

Conclusion: Findings indicate that vitamin D supplementation reduces pregnancy complications. Future research should explore the extent of its effectiveness in optimizing maternal and fetal health outcomes.

Keywords: Vitamin D; pregnancy; complication



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Introduction

Vitamin D is essential for various physiological functions and biological processes. Optimal levels of vitamin D throughout the prenatal period are crucial for the proper progression of pregnancy and child development. Vitamin D, due to its immunomodulatory, anti-inflammatory, developmental functions, and regulation of calcium homeostasis, is anticipated to significantly impact maternal and fetal health. The correlation between vitamin D insufficiency and numerous negative pregnancy outcomes has been thoroughly examined in recent years. Vitamin D insufficiency has been hypothesized to correlate with an elevated risk of preeclampsia, gestational diabetes mellitus, cesarean delivery, and bacterial vaginosis during pregnancy. In Mediterranean nations, where vitamin D deficiency is notably more widespread (affecting 60-80% of the population), neither vitamin D supplementation nor food fortification policies are presently endorsed during pregnancy, and such measures are completely lacking in clinical practice¹. As pregnancy advances, the demand for vitamin D escalates, hence exacerbating any preexisting vitamin D insufficiency. A compromised maternal vitamin D status is linked to an approximately two-fold increase in the prevalence of congenital heart defects in offspring, as well as a heightened incidence of fetal miscarriage, gestational diabetes, bacterial vaginosis, and perinatal depression in mothers, in addition to impaired fetal and childhood growth². Recent observations indicate that hypovitaminosis D during pregnancy is becoming a significant global concern, potentially influencing the developmental programming of future generations. This suggests that the adverse effects of vitamin D deficiency may substantially impact offspring. This review aims to emphasize the significance of vitamin D as an immunomodulator, and anti-inflammatory agent, and its contributions to maternal health while mitigating the risk of developmental problems in the fetus³.

Methods

This research was a literature review study. The authors search and collect the data or literature with steps: write keywords in the journal database and choose articles according to the specified criteria. The databases were Google Scholar, Science Direct, Scientific Journal Rankings (SJR), and Technology Index (SINTA). The population was international journals examining the effectiveness of vitamin D during pregnancy. In addition, inclusion criteria were international journals researching the effectiveness of vitamin D during pregnancy and published from 2017 to 2024. The exclusion criteria were journals > Q3 for Scientific Journal Rankings (SJR) and > 3 SINTA. The journal search was carried out from 21 to 26 September 2024. Data analysis used the following methods: critical appraisal, skimming, scanning, separating irrelevant articles from relevant articles, reading relevant articles, and making notes or

summaries (including author, year, title, insight, abstract, research methods, results, conclusions, and limitations). Then we arranged the articles in the table and analyzed them.

Result

Google Scholar contained 461 publications, of which seventeen were pertinent articles. This report revealed that vitamin D's effectiveness may be valuable in mitigating the risk of pregnancy complications.

Table 1. Articles Selection

Databased	Keyword	Articles	Relevant Articles
Google Scholar	<i>Effect of Vitamin D with Common Pregnancy Complications</i>	461	17

Table 2. Summary of literature review findings

No	Title & Authors	Insight	Methods	Conclusion	Limitations
1	The Effect of Vitamin D supplementation in Pregnant Women with Overweight and Obesity: A Randomized Controlled Trial (Ku C, et al.2024) ⁴ Q1	Examines the impact of 800 IU vs. 400 IU vitamin D3 supplementation on pregnancy outcomes.	Randomized controlled trial, two-arm, parallel, non-blinded.	Increased serum 25OHD levels, but no effect on lipid profiles or pregnancy outcomes. Lower birth weight incidence in the intervention group.	Insufficient power to evaluate secondary outcomes; excluded those on lipid-lowering therapy.
2	Vitamin D supplementation and vitamin D status during pregnancy and the risk of congenital anomalies systematic review and meta-analysis (Walker K, et al. 2023) ⁵ Q1	Meta-analysis on vitamin D's role in congenital anomalies.	Review of 13 studies, meta-analysis, and narrative synthesis.	Vitamin D may influence respiratory health in children.	Selection bias in observational studies; inability to conduct meta-regressions.
3	The effects of Vitamin D on fertility, pregnancy, and polycystic ovary syndrome-a review (Varbiro S, et al. 2022) ⁶ Q1	Highlights vitamin D's role in fertility and PCOS.	Systematic review using PubMed data.	Vitamin D improves fertility in PCOS patients.	Limited research on bone mineral density and vitamin D's effect across life stages.

No	Title & Authors	Insight	Methods	Conclusion	Limitations
4	Impact of vitamin D on maternal and fetal health: A review (Arshad R, et al. 2022) ⁷ Q1	Reviews vitamin D's role in reducing pregnancy complications.	Animal and cohort studies.	Vitamin D deficiency is linked to obesity, infections, and neurological issues.	Mechanisms remain unclear; further trials are needed.
5	Vitamin D: Before, during and after Pregnancy: Effect on Neonates and Children (Mansur L, et al. 2022) ⁸ Q1	Examines vitamin D's effect on neonatal health.	Review of indexed articles from major databases.	Higher vitamin D levels are linked to reduced infection risks.	Focuses only on preconceptions in the infancy stage.
6	Evaluation of the efficacy of two doses of vitamin D supplementation on glycemic, lipidemic and oxidative stress biomarkers during pregnancy: a randomized clinical (Motamed, et al. 2020) ⁹ Q1	Compares 1000 IU vs. 2000 IU vitamin D supplementation.	Open-label randomized clinical trial.	2000 IU is more effective in increasing HDL-C and reducing iPTH levels.	No calcium supplementation; only healthy pregnancies were studied.
7	The effect of vitamin D status during pregnancy on infant neurodevelopment: the ECLIPSES study (Voltas N, et al. 2020) ¹ Q1	Investigates maternal vitamin D's impact on cognitive abilities.	Observational study using biochemical and psychological data.	Adequate prenatal vitamin D enhances cognitive, linguistic, and motor skills.	Non-mandatory prenatal visits affect data consistency.
8	Early-life effects of vitamin D: A focus on pregnancy and lactation (Wagner C, et al. 2020) ¹⁰ Q1	Links genetic polymorphisms to vitamin D metabolism.	Nested case-control, observational, and clinical trials.	Genetic variations impact gestational duration and birth weight.	Findings may not be generalizable due to study heterogeneity.
9	First Trimester Maternal Vitamin D Status and Risks of Preterm Birth and Small-For-Gestational Age (Monier I, et al. 2019) ¹¹ Q1	Examines 25-OHD levels about preterm birth.	Prospective cohort study.	There is no clear link between vitamin D deficiency and preterm birth risk.	Subgroup analysis lacks significance.
10	Immunomodulatory effects of vitamin D in pregnancy and beyond (Cyprian F, et al. 2019) ¹² Q1	Investigates vitamin D's role in immune regulation.	Laboratory-based analysis, statistical modeling.	Vitamin D may modulates the immune function in pregnancy.	Small sample size; unclear cause-effect relationships.
11	Vitamin D supplementation and incident preeclampsia:	Reviews vitamin D's role in reducing preeclampsia.	Systematic review and meta-analysis.	Vitamin D may enhance preeclampsia treatments.	Data heterogeneity; long-term effects unclear.

No	Title & Authors	Insight	Methods	Conclusion	Limitations
	A systematic review and meta-analysis of randomized clinical trials (Fogacci S, et al. 2019) ² Q1				
12	The association of vitamin D levels with common pregnancy complications (Dovnik A, et al. 2018) ¹³ Q1	Investigates vitamin D's correlation with gestational diabetes.	Observational and supplementation trials.	Vitamin D insufficiency linked to higher gestational diabetes risk.	Inconsistent evidence on supplementation efficacy.
13	The role of vitamin D in fertility and during pregnancy and lactation: a review of clinical data (Pilz S, et al. 2018) ¹⁴ Q1	Reviews vitamin D's role in pregnancy outcomes.	Systematic review of clinical data.	800-1000 IU/day is safe and beneficial.	Conflicting evidence from randomized trials.
14	Vitamin D deficiency and antenatal and postpartum depression: A systematic review (Aghajafari F, et al. 2018) ¹⁵ Q1	Investigates vitamin D's link to postpartum depression.	Systematic review of 11,888 women.	Vitamin D may lower depression risks.	Observational design limits causality.
15	Calcium and vitamin D supplementation for prevention of preeclampsia: a systematic review and network meta-analysis (Khaing W, et al. 2017) ¹⁶ Q1	Compares the effects of calcium and vitamin D on preeclampsia.	Network meta-analysis of 27 RCTs.	Vitamin D supplementation showed a 57% reduction in risk.	Bias due to outcome reporting inconsistencies.
16	The effect of vitamin D supplementation during pregnancy on the risk of having preterm birth: An evidence-based case report (Meilana I, et al. 2020) ¹⁷ SINTA 2	Examines vitamin D's role in reducing preterm birth.	Systematic review and meta-analysis.	Supplementation lowers preterm birth risk.	Limited maternal adverse event data.
17	The effect of vitamin D levels and tumor necrosis factor-alpha on normal pregnancy in the first trimester and spontaneous abortion (Prastiwi O, et al. 2022) ¹⁸ SINTA 3	Examines vitamin D levels in normal vs. spontaneous abortion cases.	Cross-sectional study of 44 patients.	Significant differences in vitamin D levels between groups.	Lacks of long-term maternal outcome data.

Discussion

Location

All investigations were conducted in the International Journal, encompassing quartiles Q1-Q4 in the SJR (Scientific Journal Ranking) and accreditation levels 1-3 in SINTA, covering Asia, Europe, and America. The research location is where researchers gather data and conduct their investigations. Site selection must account for the appeal, distinctiveness, and appropriateness of the selected subject to enable researchers to discover significant and novel insights. Furthermore, it can elucidate the attributes of the community/respondents in the study.

Research Methodology

The research strategy in this publication comprised a systematic review (42.1%), randomized controlled trial (26.3%), cross-sectional study (10.5%), statistical analysis (5.2%), systematic literature review (5.2%), case-control study (5.2%), and case report (5.2%). The design was founded on the research objectives.

Vitamin D

All publications in this literature review indicate that vitamin D may mitigate the risk of difficulties during pregnancy, including pre-eclampsia, preterm labor, neurodevelopmental issues, and congenital malformations.

Implications of Vitamin D Deficiency during Gestation

PrePreeclampsia (PE) is characterized by hypertension (systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg) diagnosed between 20 and 34 weeks of gestation, accompanied by proteinuria (urinary protein ≥ 0.3 g/24 h measured at two occasions at least 6 hours apart), as well as additional complications such as hepatic dysfunction, hematological abnormalities, and renal and neurological issues¹⁹. Pre-eclampsia is pathologically characterized as a two-stage illness, with the initial stage involving the secretion of angiogenic factors into the maternal circulation, resulting in impaired remodeling and trophoblastic invasion of spiral arteries, ultimately causing aberrant placental implantation. During the second stage, an irregular equilibrium between proangiogenic and antiangiogenic factors triggers the maternal inflammatory response, diminishes vascularization, and induces widespread endothelial dysfunction, impairing the functionality of all maternal organs²⁰. Pre-

eclampsia thus elevates the chance of fetal growth limitation and ultimately fetal demise. Vitamin D possesses anti-inflammatory properties that affect the inverse relationship between calcium levels and the incidence of preeclampsia²¹. Vitamin D3 also aids to preventing the cholesterol absorption by vascular smooth muscle cells and macrophages in the placenta of patients with pre-eclampsia. Preterm Delivery (PD) is characterized as the premature birth of a newborn before 37 weeks of gestation²². Various genetic and immunological factors are regarded as causative agents. A widely predicted idea associates Parkinson's disease with inflammation and infections, encompassing intra-amniotic, maternal extrauterine, or intrauterine infections. Vitamin D, due to its anti-inflammatory properties via nuclear factor kB inhibition, reduces the incidence of infections and periodontal disease¹¹. The correlation between vitamin D and brain development is supported by the presence of vitamin D-metabolizing enzymes, CYP27B1 and CYP24A1, in brain cells such as those in the cortex and Purkinje cells, suggesting vitamin D's autonomous function in the brain. Furthermore, VDR and a significant binding receptor protein, namely 1,25D3-MARRS, are identified in both fetal and adult brain tissue²³. Subsequent research has underscored the significant function of vitamin D in neuronal differentiation and death, dopamine synthesis, axonal integration, immune modulation, and gene transcription²⁴. Recently, comprehensive scientific literature has emerged elucidating the significance of vitamin D in cerebral development. Vinkhuyzen et al. and Lee et al. assert that maternal serum vitamin D concentration influences brain development, with shortage heightening the risk of neurological diseases²⁵.

Conclusion

All journal articles revealed that vitamin D could be of value in reducing the risk of pregnancy complications such as gestational diabetes, preeclampsia, and preterm labour. Furthermore, recent studies determining the effect of vitamin D at genetic level will also help in understanding and future design of research in the area of maternal and fetal health.

Recommendation

The researchers advise concentrating on the long-term safety and efficacy of interventions vitamin D supplements to deal with, so the public is aware in order to prevent pregnancy complications due to vitamin D deficiency by taking vitamin D supplements if necessary. Of the 42.1% of studies that used a systematic review, the majority had limited data and sources, and two studies also had different doses and duration of vitamin D supplementation.

Conflicts of Interest

There is no conflict of interest.

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