OPTIMIZING MATERNAL AND FETAL HEALTH: THE ROLE OF VITAMIN D SUPPLEMENTATION IN PREGNANCY OUTCOMES

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Abstract

Background: Vitamin D plays a crucial role in calcium and phosphate regulation, supporting bone health, immune function, and metabolic processes. Deficiency in vitamin D has been linked to adverse pregnancy outcomes, including gestational diabetes, preeclampsia, preterm birth, and low birth weight. Given the widespread prevalence of vitamin D deficiency, this study examines the impact of vitamin D supplementation on maternal and fetal health.

Methods: This study was conducted on 500 pregnant women with recorded serum vitamin D levels. Among them, 300 with vitamin D deficiency (<20 ng/mL) received a standardized vitamin D3 supplement, while rest women with unknown vitamin D levels served as the control group. Vitamin D levels were measured using liquid chromatography-tandem mass spectrometry at different stages of pregnancy. The effects of supplementation on serum vitamin D levels and pregnancy outcomes, including gestational diabetes, preeclampsia, preterm birth, low birth weight, and postpartum haemorrhage, were analyzed using statistical tests, including Student's t-test, Chi-squared test, and logistic regression.

Results: At baseline, 99% of participants had vitamin D levels below 30 ng/mL. Vitamin D supplementation increased serum levels from an average of 13.70 ± 3.54 ng/mL to 30.5 ± 7.73 ng/mL. Women who achieved sufficient vitamin D levels (≥30 ng/mL) had significantly lower rates of preterm birth (p = 0.007), low birth weight (p = 0.025), and postpartum haemorrhage (p = 0.047) compared to the control group. However, no significant difference was observed in the rates of gestational diabetes and preeclampsia. A positive correlation was found between maternal and cord blood vitamin D levels (p < 0.0001).

Conclusion: Vitamin D deficiency is highly prevalent among pregnant women, particularly those with higher BMI. Supplementation effectively raises serum vitamin D levels and may reduce the risk of adverse pregnancy outcomes such as preterm birth, low birth weight, and postpartum haemorrhage. However, a dosage higher than 2,000 IU/day may be necessary to achieve sufficient levels within three months. Ensuring adequate vitamin D intake during pregnancy may contribute to improved maternal and neonatal health outcomes.

Introduction

Vitamin D plays a fundamental role in the regulation of calcium and phosphate, facilitating their absorption and resorption within the body (1,2). This function is essential for proper skeletal formation and the preservation of bone integrity (3). The most widely recognized consequence of vitamin D deficiency is rickets, a condition that affects bone development (4). However, beyond its impact on the skeletal system, vitamin D is also crucial for immune defense, reducing susceptibility to infections, controlling inflammation, and modulating autoimmune responses (5). Observational research has suggested a correlation between inadequate vitamin D levels and various health issues, including malignancies, cardiovascular and respiratory conditions, metabolic disorders like obesity and diabetes, impaired red blood cell production, muscle weakness, and autoimmune disorders (6).

The primary source of vitamin D in the body is cutaneous synthesis, initiated when ultraviolet radiation triggers the transformation of 7-dehydrocholesterol (provitamin D3) into precholecalciferol (previtamin D3) upon sun exposure (7). This precursor is subsequently converted into cholecalciferol, also known as vitamin D3, which binds to a specific transport protein and is carried to the liver. In the liver, an enzyme called 25-hydroxylase (CYP2R1) metabolizes vitamin D3 into 25-hydroxyvitamin D3 [25(OH)D3], also referred to as calcidiol. The kidneys then further process this compound via 25-OH-D3-1α-hydroxylase (CYP27B1), generating 1,25-dihydroxyvitamin D3 [1α,25(OH)2D3], the biologically active form of vitamin D (7).

To assess an individual's vitamin D status, serum 25(OH)D3 levels are typically measured. A concentration of at least 20 ng/mL (50 nmol/L) is considered adequate for physiological needs (8). However, studies indicate that individuals with levels between 30–32 ng/mL (75–80 nmol/L) experience a lower risk of falls and fractures, making 30 ng/mL (75 nmol/L) a preferable target (9,10). Based on these findings, vitamin D status is generally categorized as deficient when levels are below 20 ng/mL, insufficient between 20–30 ng/mL, and sufficient when exceeding 30 ng/mL (11).

Since vitamin D production relies on sun exposure, deficiency is prevalent, particularly among individuals who spend most of their time indoors. The prevalence of vitamin D deficiency varies significantly, ranging from 18% to 84% depending on factors such as geographical location, ethnicity, and diet (12,13). The most effective way to address this deficiency is through direct supplementation with vitamin D3, circumventing the reliance on sunlight for synthesis.

Pregnancy-related complications, including gestational hypertension, gestational diabetes, preterm birth, and low birth weight, are interconnected and often influenced by maternal health (14,15). Inadequate vitamin D levels in pregnant women may negatively impact fetal development (16). Therefore, this study examines the hypothesis that maintaining maternal serum vitamin D levels above 30 ng/mL may have beneficial effects on pregnancy outcomes.

Methods

This study evaluates serum vitamin D levels, we examined medical records of 500 women who attended their initial prenatal visit and had documented vitamin D measurements. Inclusion criteria required participants to have delivered beyond 20 weeks of gestation, while cases with incomplete records or pregnancy terminations due to fetal anomalies were excluded. To assess the impact of vitamin D supplementation, we focused on 300 women diagnosed with vitamin D deficiency (<20 ng/mL), all of whom received the same vitamin D3 product. Additionally, a control group was established, comprising rest women who gave birth beyond 20 weeks of gestation

The vitamin D3 supplement administered in this study was Liquid P&B, which was formulated in 90–95% medium-chain triglycerides (MCT) oil. Each drop (0.028 mL) contained 400 IU (10 µg) of vitamin D3. This product was distributed by a pharmaceutical company in Taiwan. Women diagnosed with vitamin D deficiency were prescribed 2,000 IU/day from 12 to 16 weeks of gestation. Once their serum levels exceeded 20 ng/mL, a maintenance dose of 800 IU/day was provided until delivery. If the deficiency persisted, the 2,000 IU/day dosage was continued until levels reached the threshold or until the end of pregnancy.

Serum 25(OH)D levels were measured at intervals of at least three months

using liquid chromatography-tandem mass spectrometry (LC-MS/MS), following previously established methods (17). The initial assessment was conducted between 8 and 12 weeks of pregnancy. Subsequent follow-up measurements were taken at 24–28 weeks and again at 35–37 weeks to monitor the effectiveness of supplementation. During each prenatal visit, remaining vitamin D3 supplement doses were checked to ensure adherence to the regimen.

Gestational diabetes mellitus (GDM) was diagnosed through an oral glucose tolerance test performed between 24 and 28 weeks of gestation, following a minimum of 8 hours of fasting. Blood glucose levels were recorded before and at 1, 2, and 3 hours after consuming a 100 g glucose solution. GDM was confirmed when blood glucose readings exceeded specific thresholds at two or more time points (≥95 mg/dL fasting, ≥180 mg/dL at 1 hour, ≥155 mg/dL at 2 hours, and ≥140 mg/dL at 3 hours).

Preeclampsia was defined as a blood pressure reading of 140/90 mmHg or higher, along with proteinuria or organ dysfunction affecting the liver, lungs, or kidneys. Preterm birth was classified as delivery occurring before 37 weeks of gestation. Infants with birth weights under 2,500 g were categorized as low birth weight (LBW). At five minutes after birth, newborns underwent an Apgar score assessment, evaluating factors such as skin color, heart rate, reflex responses, muscle tone, and respiration. Scores below 7 were considered abnormal. Postpartum haemorrhage (PPH) was diagnosed when blood loss exceeded 500 mL for vaginal births or 1,000 mL for caesarean deliveries.

Statistical Analysis

The ANOVA test was used to compare average serum vitamin D levels across different age categories. The Student's t-test was applied to assess differences in vitamin D levels between women with and without GDM, preeclampsia, preterm birth, LBW, PPH, or Group B Streptococcus (GBS) colonization. This test was also used to compare mean values of age and BMI between two groups. The Chi-squared test was performed to analyze differences in the prevalence of adverse pregnancy outcomes across groups. A p-value of less than 0.05 was considered statistically significant. Additionally, logistic regression was utilized to explore the associations between serum vitamin D levels and variables such as BMI, maternal weight, and height. Statistical analyses were conducted using SPSS 17.0 for Windows (SPSS Inc., Chicago, IL).

Results

To assess vitamin D insufficiency in expectant mothers, a study was conducted on 500 participants. The average maternal age was 33.45 ± 4.12 years, with a pre-pregnancy BMI of 21.67 ± 3.35 kg/m². The mean serum vitamin D concentration at the initial prenatal visit was 14.72 ± 5.33 ng/mL. Participants were categorized into four age brackets: 14–23 years (1.5%), 24–33 years (47%), 34–43 years (51.2%), and ≥44 years (0.3%). The corresponding average serum vitamin D levels for these groups were 14.60 ± 7.20, 14.46 ± 5.21, 14.93 ± 5.37, and 19.47 ± 3.59 ng/mL, respectively. A total of participants (19.5%) had vitamin D levels below 10 ng/mL, (65.4%) fell between 10–19.99 ng/mL, (14.3%) had values in the range of 20–29.99 ng/mL, and individuals (0.8%) exceeded 30 ng/mL. No statistically significant differences in vitamin D levels were identified among the different age groups.

A statistical analysis indicated no meaningful correlation between serum vitamin D levels and participants' height (p = 0.8262). However, an inverse relationship was found between vitamin D levels and both body weight and BMI prior to supplementation. The average BMI was higher (23) among individuals with serum vitamin D below 20 ng/mL, whereas those exceeding this threshold had a lower mean BMI of 21 (p = 0.0366).

Comparing pregnancy complications among groups with varying vitamin D levels after supplementation revealed no notable disparities in gestational diabetes mellitus (GDM) rates, which remained around 8% across all groups. Similarly, rates of preterm birth, low birth weight, and abnormal Apgar scores did not significantly increase in women classified as deficient. However, incidences of preeclampsia and postpartum haemorrhage (PPH) appeared elevated in women with vitamin D levels under 20 ng/mL, though statistical significance was not established. Additionally, the prevalence of Group B Streptococcus (GBS) was found to be 33.3% in individuals with vitamin D below 20 ng/mL, compared to 24.46% in those between 20–29.99 ng/mL and 22.73% in those ≥30 ng/mL, indicating a potential association, though statistical significance was not confirmed (Table 1).

Discussion

This study highlights the widespread prevalence of vitamin D insufficiency among pregnant women. Among the 500 participants, 99% had serum vitamin D levels below 30 ng/mL. A significant proportion of these individuals (46.95%) were between 24 and 33 years old, while 51.24% fell within the 34 to 43 age range. These findings align with prior research that identified a high prevalence of vitamin D deficiency (<20 ng/mL) in individuals aged 30 to 39 years (18). Given that this age group represents a critical period for reproduction, inadequate vitamin D levels have been linked to several adverse pregnancy outcomes, including gestational hypertension (19), gestational diabetes (20), recurrent pregnancy loss (21), preterm labor (22), and postpartum depression (23).

Although overweight pregnant women exhibited lower serum vitamin D concentrations, this association was not statistically significant (p = 0.0591). However, a significant inverse correlation was observed between vitamin D levels and BMI (p = 0.0366) (Figure 1), which aligns with previous studies (24). It is suggested that reduced sun exposure, lower physical activity, and sequestration of vitamin D in adipose tissue contribute to lower serum levels in overweight or obese individuals (25).

The results indicate that supplementation with vitamin D3 effectively raises serum concentrations. Previous studies have deemed doses up to 4,000 IU/day safe for pregnant women (26). Earlier findings suggest that a daily intake of 2,000 IU over one month can increase vitamin D levels by approximately 5–6 ng/mL, while three months of supplementation can elevate levels above 30 ng/mL. However, recommended dosages differ widely among institutions. The Institute of Medicine suggests 400–600 IU/day (10), while the National Institute for Health and Clinical Excellence recommends 400 IU/day (27), and the Endocrine Society suggests 1,500–2,000 IU/day (11). Due to these inconsistencies, multiple clinical trials have sought to determine an optimal dosage for pregnant women, with some studies also investigating its effects on new-borns.

One study examined two groups of women with severe vitamin D deficiency (28). One group, with an average serum level of 11.7 ± 4.1 ng/mL, received 2,000 IU/day for three months, while the other, with an average of 8.9 ± 4.0 ng/mL, was administered 60,000 IU/month for the same period. Both regimens failed to raise vitamin D levels above 20 ng/mL. In contrast, other studies on women with higher baseline vitamin D levels (27.6–39.7 ng/mL) explored supplementation strategies such as 400 IU/day for six months, 2,000 or 4,000 IU/day for three months, and 150,000 IU/month for one month (29–31). The findings indicated that both maternal and neonatal vitamin D levels increased by at least 10 ng/mL with these regimens.

In the present study, 50.3% of women with vitamin D insufficiency achieved sufficient levels (≥30 ng/mL) with 2,000 IU/day of vitamin D3. However, among those with severe deficiency (<10 ng/mL), only 41.2% responded to this dose, while 46.9% of those with levels between 10 and 20 ng/mL failed to reach sufficiency. These findings suggest that a higher dosage, such as 4,000 IU/day, may be more effective. Clinical observations indicate that maintaining vitamin D levels at ≥30 ng/mL throughout late pregnancy may require a maintenance dose of 1,200 IU/day. Since cord blood vitamin D levels strongly correlate with maternal serum levels (p < 0.0001), ensuring sufficient maternal vitamin D is crucial for optimal fatal development.

women who achieved sufficient vitamin D levels were evaluated for complications, including gestational diabetes, pre-eclampsia, preterm birth, low birth weight, low Apgar scores, and postpartum haemorrhage. The findings revealed significantly lower complication rates in women with sufficient vitamin D (≥30 ng/mL) than in the general population, supporting previous research. A meta-analysis of 22 trials involving 3,725 pregnant women concluded that vitamin D supplementation reduces the risk of pre-eclampsia, gestational diabetes, postpartum haemorrhage, and low birth weight (32). Although our study did not find a statistically significant reduction in pre-eclampsia risk, a decreasing trend was observed, which may become significant in a larger

Table 1. Rates of Adverse Pregnancy Outcomes in Women with Different Serum Vitamin D Levels After Supplementation.

Adverse Pregnancy Outcomes	25(OH)D 0–19.99 ng/mL	25(OH)D 20–29.99 ng/mL	25(OH)D ≥30 ng/mL	P-value
GDM (Gestational Diabetes Mellitus)	(8.33%)	(8.36%)	(7.73%)	0.952
Pre-eclampsia	(4.17%)	(2.17%)	(1.87%)	0.585
Preterm Birth	(6.25%)	(9.60%)	(6.67%)	0.326
LBW (Low Birth Weight)	(6.25%)	(8.05%)	(6.40%)	0.680
Apgar Score <7	(0.0%)	(0.30%)	(0.0%)	NA
PPH (Postpartum Hemorrhage)	(4.17%)	(2.17%)	(1.33%)	0.347

sample. The effect of vitamin D on gestational diabetes may be influenced by study design variations, inadequate adjustment for confounding factors (33), and differing diagnostic criteria.

Numerous investigations have explored the relationship between vitamin D deficiency and pregnancy complications, yielding variable results. However, the link between low vitamin D and preterm birth remains consistent. Several studies reported a higher incidence of preterm delivery in women with vitamin D insufficiency (<30 ng/mL) compared to those with adequate levels (34–35). Other research suggests that maternal vitamin D levels of ≥40 ng/mL are associated with a 60% reduction in preterm birth risk (36). The present study also found a lower incidence of low birth weight (6.40% vs. 10%) in women with sufficient vitamin D, consistent with prior findings (37). Additionally, postpartum haemorrhage was less frequent among women with adequate vitamin D (1.33% vs. 3.20%), mirroring previous reports (38).

Regarding neonatal outcomes, this study did not establish a correlation between maternal vitamin D levels and low Apgar scores, as only one case involved an infant with a score below 7. Other studies have reported conflicting results on this association (34–35, 39).

According to recent national health surveys, the prevalence of vitamin D deficiency is 41.3%, while insufficiency stands at 42.9%. Despite this, only about 10% of women receive vitamin D supplementation (40). To further clarify the relationship between vitamin D and pregnancy outcomes, larger studies or trials involving higher maternal vitamin D levels (e.g., ≥50 ng/mL) are necessary. Given the high prevalence of vitamin D insufficiency, it is recommended that healthcare providers discuss vitamin D status with pregnant women, encourage prenatal screening, and conduct periodic monitoring to ensure effective supplementation.

Conclusion

Vitamin D deficiency is highly prevalent, particularly among women with a higher BMI. Ensuring sufficient vitamin D intake through supplementation can effectively address this deficiency. Elevated vitamin D levels in the blood appear to offer protective benefits against complications such as preterm birth, low birth weight, and postpartum haemorrhage. However, our findings indicate that a daily intake exceeding 2000 IU is necessary to achieve optimal serum levels within three months. Since cord blood vitamin D concentrations are directly linked to maternal levels, supplementing pregnant women with vitamin D may contribute positively to fetal growth and overall neonatal health.

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