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Original Research Article

Impact of Maternal Vitamin D Status on Preterm Birth and Neonatal Outcomes

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Abstract:

Background: Vitamin D plays an important role in calcium homeostasis, placental function, immune regulation, and fetal development. Maternal vitamin D deficiency has been investigated as a potentially modifiable risk factor for preterm birth, low birth weight, and other adverse neonatal outcomes. However, evidence regarding its association with preterm birth remains inconsistent.

Objective: To determine the association between maternal vitamin D status and preterm birth and to evaluate the relationship between maternal vitamin D status and selected neonatal outcomes.

Methods: A prospective observational study was conducted among 100 pregnant women at Darbhanga Medical College and Hospital over 12 months. Maternal serum 25-hydroxyvitamin D [25(OH)D] was measured during antenatal evaluation. Participants were categorized according to vitamin D status. Maternal demographic and obstetric characteristics were recorded prospectively, and participants were followed until delivery. Neonatal outcomes, including gestational age, birth weight, Apgar score, small-for-gestational-age status, low birth weight, and NICU admission, were documented.

Results: Vitamin D deficiency was identified in 62 (62.0%) participants, while 38 (38.0%) had sufficient vitamin D levels. Preterm birth occurred in 16 (25.8%) women with vitamin D deficiency compared with 4 (10.5%) women with sufficient vitamin D levels (p=0.071). Mean neonatal birth weight was significantly lower among vitamin D-deficient mothers (2.63 ± 0.46 kg vs. 2.89 ± 0.41 kg; p=0.006). Low birth weight occurred in 18 (29.0%) neonates in the deficient group compared with 4 (10.5%) in the sufficient group (p=0.028). NICU admission was observed in 12 (19.4%) and 3 (7.9%) neonates, respectively (p=0.120).

Conclusion: Maternal vitamin D deficiency was associated with lower neonatal birth weight and a higher observed frequency of preterm birth. However, the association with preterm birth did not reach statistical significance. Larger prospective studies are required to determine whether maternal vitamin D status independently influences preterm birth and neonatal morbidity.

Keywords: Vitamin D deficiency; pregnancy; preterm birth; low birth weight; neonatal outcomes; 25-hydroxyvitamin D; NICU.

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Introduction

Preterm birth, defined as birth before 37 completed weeks of gestation, remains a major global public-health problem and an important contributor to neonatal morbidity and mortality. [1] The causes of preterm birth are multifactorial and include maternal, fetal, placental, infectious, nutritional, and socioeconomic factors. [1,2] Vitamin D is a steroid hormone with important functions beyond calcium and bone metabolism. During pregnancy, vitamin D participates in calcium homeostasis, cellular differentiation, immune regulation, and potentially placental function. [3,4] Vitamin D deficiency is frequently reported among pregnant women, particularly in populations with inadequate dietary intake, limited sun exposure, or other nutritional and socioeconomic risk factors. [4-6]

Maternal serum 25-hydroxyvitamin D [25(OH)D] is generally considered the principal biomarker for assessing vitamin D status. [3] Observational studies have suggested that lower maternal 25(OH)D concentrations may be associated with adverse pregnancy outcomes, including preterm birth and impaired fetal growth. [7-9] A systematic review and meta-analysis by Amegah et al. reported an association between maternal vitamin D

insufficiency and selected categories of preterm birth, although considerable heterogeneity was observed among studies. [7] The relationship between maternal vitamin D status and fetal growth has also attracted considerable interest. Recent evidence suggests that maternal vitamin D deficiency may be associated with low birth weight. [8] A 2024 systematic review and meta-analysis involving 55,162 pregnant women found significantly higher odds of low birth weight among women with vitamin D deficiency, although no statistically significant association was found with overall preterm birth or small-for-gestational-age birth. [8] An umbrella review published in 2024 similarly identified associations between maternal vitamin D deficiency and several adverse maternal and offspring outcomes, including preterm birth and small-for-gestational-age or low-birth-weight infants, although the quality and consistency of evidence varied across outcomes. [9]

The potential effect of vitamin D supplementation on pregnancy outcomes has also been investigated. Evidence summarized by the World Health Organization indicates that vitamin D supplementation can improve maternal vitamin D concentrations, while evidence regarding improvement in clinically important maternal and neonatal outcomes remains uncertain. [10,11] WHO therefore does not recommend routine vitamin D supplementation for all pregnant women solely to improve maternal and perinatal outcomes. [10] Evidence from randomized trials and systematic reviews has nevertheless suggested possible reductions in low birth weight and preterm birth with vitamin D supplementation alone in some settings. [10,12] These apparently conflicting findings highlight the importance of distinguishing the association between naturally occurring maternal vitamin D status and outcomes from the effects of vitamin D supplementation. Neonatal outcomes such as birth weight, Apgar score, NICU admission, and small-for-gestational-age status are important indicators of perinatal health. Maternal vitamin D concentrations may influence these outcomes through effects on placental function, fetal growth, and maternal metabolic and immune pathways. [8,9,13]

The present study was therefore undertaken to assess the association between maternal vitamin D status and preterm birth and to evaluate its relationship with selected neonatal outcomes among pregnant women attending a tertiary-care teaching hospital.

Materials and Methods

Study Design and Setting: A prospective observational study was conducted in the Department of Obstetrics and Gynaecology, Darbhanga Medical College and Hospital (DMCH), Darbhanga, Bihar, India.

The study was conducted over a period of 12 months.

Study Population: Pregnant women attending the antenatal outpatient department or admitted to the obstetric unit during the study period were screened for eligibility.

Sample Size Calculation: The sample size was estimated using the formula for a single population proportion:

$$n = \frac{Z^2 pq}{d^2}$$

where:

- n = required sample size
- Z = 1.96 at 95% confidence level
- p = anticipated prevalence of vitamin D deficiency
- q = 1 − p
- d = allowable absolute precision

Assuming an anticipated maternal vitamin D deficiency prevalence of 60%, based on previously reported high prevalence in pregnant populations, p=0.60 and q=0.40 were used. A precision of 10% was considered acceptable.

$$n = \frac{(1.96)^2(0.60)(0.40)}{(0.10)^2}$$

$$n = \frac{3.8416 \times 0.24}{0.01}$$

$$n = 92.2$$

The calculated minimum sample size was approximately 93 participants. Allowing for approximately 8% loss to follow-up or incomplete outcome data:

$$n_{adjusted} = \frac{93}{0.92} = 101.1$$

Therefore, the final target sample size was rounded to 100 participants, which was considered feasible for the 12-month study period.

Inclusion Criteria

Pregnant women were included if they:

1. Were willing to participate and provided written informed consent.
2. Had a singleton pregnancy.
3. Were attending DMCH for antenatal care.
4. Had adequate clinical records for follow-up until delivery.
5. Agreed to undergo maternal serum 25(OH)D assessment.

Exclusion Criteria

Women were excluded if they had:

1. Multiple pregnancy.
2. Known chronic renal disease.
3. Chronic liver disease.
4. Metabolic bone disease.
5. Major endocrine or systemic disease likely to substantially influence pregnancy outcomes.
6. Current high-dose therapeutic vitamin D supplementation.
7. Incomplete antenatal or delivery records.
8. Loss to follow-up before delivery.

Assessment of Vitamin D Status: Maternal venous blood samples were collected during antenatal evaluation. Serum 25-hydroxyvitamin D [25(OH)D] was measured using the standardized laboratory assay available at the study institution.

For analysis, participants were categorized according to predefined serum 25(OH)D thresholds used by the study laboratory.

Follow-up and Outcome Assessment: Participants were prospectively followed until delivery. Maternal demographic, obstetric, and clinical characteristics were recorded.

The primary outcome was preterm birth, defined as delivery before 37 completed weeks of gestation. [1]

Secondary neonatal outcomes included:

- Birth weight
- Low birth weight
- Small-for-gestational-age status
- Apgar score at 1 and 5 minutes
- NICU admission
- Neonatal complications

Statistical Analysis: Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. The independent Student's t-test was used for normally distributed continuous variables, while the chi-square test or Fisher's exact test was used for categorical variables. A two-sided $p<0.05$ was considered statistically significant.

Ethical Considerations: The study protocol received approval from the Institutional Ethics Committee of DMCH. Written informed consent was obtained from all participants before enrollment. Confidentiality of participant information was maintained throughout the study.

Results

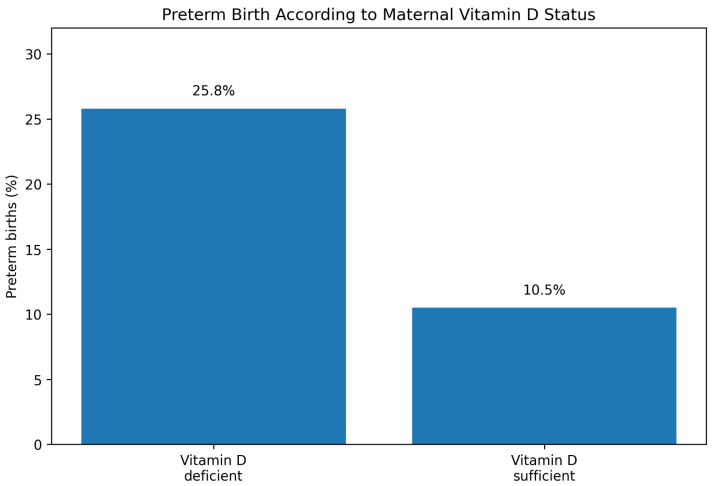


Figure 1: Preterm Birth According to Maternal Vitamin D Status

Percentage of preterm births among women with vitamin D deficiency and sufficient vitamin D status. Preterm birth occurred more frequently in the vitamin D-deficient group (25.8% vs. 10.5%; p=0.071).

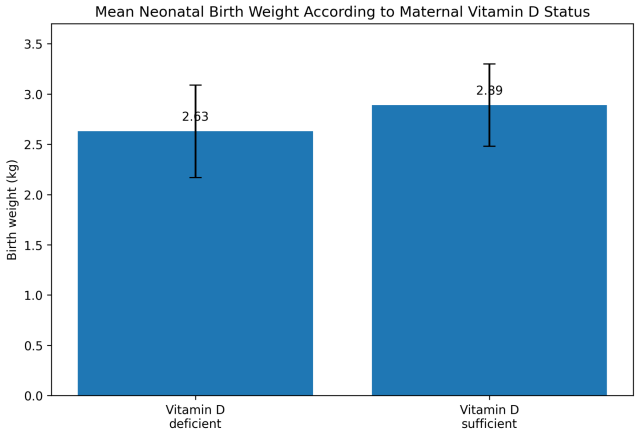


Figure 2: Mean Neonatal Birth Weight According to Maternal Vitamin D Status

Mean neonatal birth weight with standard deviation among vitamin D-deficient and vitamin D-sufficient mothers. Birth weight was significantly lower in the vitamin D-deficient group (2.63 ± 0.46 kg vs. 2.89 ± 0.41 kg; p=0.006).

A total of 100 pregnant women were included in the final analysis. The mean maternal age was 26.4 ± 4.2 years and the mean BMI was 23.1 ± 2.8 kg/m². Forty-six (46.0%) participants were primigravida and 54 (54.0%) were multigravida.

Maternal vitamin D deficiency was identified in 62 (62.0%) women, whereas 38 (38.0%) had sufficient vitamin D levels.

Table 1: Baseline Characteristics of Study Participants

Variable	Value
Maternal age, years, mean ± SD	26.4 ± 4.2
BMI, kg/m², mean ± SD	23.1 ± 2.8
Primigravida, n (%)	46 (46.0)
Multigravida, n (%)	54 (54.0)
Vitamin D deficient, n (%)	62 (62.0)
Vitamin D sufficient, n (%)	38 (38.0)

Maternal Vitamin D Status and Preterm Birth: Preterm birth occurred in 20 (20.0%) participants overall. Among women with vitamin D deficiency, 16 (25.8%) delivered preterm, compared with 4 (10.5%) among women with sufficient vitamin D levels.

Although the proportion of preterm births was higher in the vitamin D-deficient group, the difference did not reach statistical significance (p=0.071).

Table 2: Association Between Maternal Vitamin D Status and Preterm Birth

Pregnancy outcome	Vitamin D deficient (n=62)	Vitamin D sufficient (n=38)	P value
Preterm birth	16 (25.8%)	4 (10.5%)	0.071
Term birth	46 (74.2%)	34 (89.5%)	

Neonatal Birth Weight: The mean birth weight was significantly lower among neonates born to vitamin D-deficient mothers (2.63 ± 0.46 kg) compared with those born to vitamin D-sufficient mothers (2.89 ± 0.41 kg; p=0.006).

Low birth weight was observed in 18 (29.0%) neonates in the vitamin D-deficient group compared with 4 (10.5%) in the sufficient group (p=0.028).

Table 3: Neonatal Outcomes According to Maternal Vitamin D Status

Neonatal outcome	Vitamin D deficient (n=62)	Vitamin D sufficient (n=38)	P value
Birth weight, kg, mean ± SD	2.63 ± 0.46	2.89 ± 0.41	0.006
Low birth weight, n (%)	18 (29.0)	4 (10.5)	0.028
SGA, n (%)	12 (19.4)	4 (10.5)	0.246
NICU admission, n (%)	12 (19.4)	3 (7.9)	0.120
5-min Apgar <7, n (%)	5 (8.1)	1 (2.6)	0.406

Other Neonatal Outcomes: Small-for-gestational-age status was observed in 12 (19.4%) neonates of vitamin D-deficient mothers and 4 (10.5%) neonates of vitamin D-sufficient mothers (p=0.246).

NICU admission occurred in 12 (19.4%) neonates in the deficient group and 3 (7.9%) in the sufficient group (p=0.120). A 5-minute Apgar score <7 was observed in 5 (8.1%) and 1 (2.6%) neonates, respectively (p=0.406).

Discussion

The present prospective observational study evaluated the relationship between maternal vitamin D status and preterm birth and selected neonatal outcomes. Vitamin D deficiency was identified in 62% of the study participants. The principal findings were a higher observed frequency of preterm birth among vitamin D-deficient women and a significant association between vitamin D deficiency and lower neonatal birth weight.

The high proportion of vitamin D deficiency observed in the present study is consistent with evidence that vitamin D deficiency is common during pregnancy, particularly in populations where dietary intake and sun exposure may be inadequate. [3-6] Maternal vitamin D status is influenced by several factors, including geographic location, season, skin pigmentation, dietary intake, clothing, sun exposure, BMI, and supplementation. [3,5,6]

Preterm birth occurred in 25.8% of women with vitamin D deficiency compared with 10.5% of women with sufficient vitamin D levels. Although this represented an appreciable difference, the association did not reach statistical significance. This finding is important because evidence regarding vitamin D and preterm birth remains inconsistent. Amegah et al. reported an association between maternal vitamin D insufficiency and some categories of preterm birth, particularly very early preterm birth, although substantial heterogeneity existed between studies. [7]

In contrast, the 2024 systematic review and meta-analysis by You et al., involving 13 cohort studies and 55,162 pregnant women, found no statistically significant overall association between maternal vitamin D deficiency and preterm birth (OR 1.25, 95% CI 0.78–1.99). [8] This finding is broadly consistent with the non-significant association observed in the present study. Differences in gestational age at vitamin D measurement, definitions of deficiency, ethnicity, nutritional status, and adjustment for confounders may explain some of the variability between studies. [7-9]

A particularly important finding of the present study was the significantly lower mean birth weight among neonates born to vitamin D-deficient mothers. Mean birth weight was 2.63 kg in the deficient group compared with 2.89 kg in the sufficient group. Furthermore, low birth weight occurred significantly more frequently among neonates born to vitamin D-deficient mothers.

This finding is supported by recent evidence. You et al. reported a significantly increased risk of low birth weight among neonates born to vitamin D-deficient mothers, with a pooled OR of 5.52 (95% CI 1.31–23.22). [8] The authors did not, however, demonstrate a statistically significant overall association with preterm birth or SGA. [8]

The biological basis for a potential relationship between maternal vitamin D and fetal growth remains incompletely understood. Vitamin D receptors are expressed in placental tissue, and vitamin D may influence placental cellular differentiation, immune regulation, and fetal mineral metabolism. [3,4,13] These mechanisms could potentially contribute to fetal growth, although observational findings cannot establish causality.

The proportion of SGA neonates was higher among vitamin D-deficient mothers, but the difference was not statistically significant. This finding is directionally consistent with the umbrella review by Hwang et al., which identified an association between vitamin D deficiency and adverse fetal growth outcomes across the broader systematic-review literature. [9] However, the authors also emphasized variability in the quality and consistency of the underlying evidence. [9]

NICU admission and low 5-minute Apgar scores were numerically more common among neonates born to vitamin D-deficient mothers but did not demonstrate statistically significant differences. Neonatal morbidity is multifactorial and is strongly influenced by gestational age, birth weight, obstetric complications, and neonatal disease. Therefore, these outcomes should not be attributed to maternal vitamin D status alone.

The evidence concerning vitamin D supplementation also warrants careful interpretation. WHO's updated guidance states that routine oral vitamin D supplementation is not recommended for all pregnant women solely to improve maternal and perinatal outcomes, although supplementation may be considered for women with documented deficiency according to applicable recommendations. [10,11] Evidence from randomized trials suggests that vitamin D supplementation alone may reduce low birth weight and preterm birth in some circumstances, but the certainty and consistency of evidence remain limited. [10,12]

The present study assessed maternal vitamin D status rather than the efficacy of vitamin D supplementation. Therefore, the findings should not be interpreted as evidence that vitamin D

supplementation would necessarily prevent preterm birth or low birth weight.

Overall, the findings suggested that maternal vitamin D deficiency may be associated more strongly with fetal growth outcomes than with preterm birth in this population. However, the relatively small sample size and observational design limited the ability to draw definitive conclusions.

Limitations

The study had several limitations. First, the sample size was relatively small and may have limited the statistical power to detect associations, particularly for preterm birth and less frequent neonatal outcomes. Second, the study was conducted at a single tertiary-care center, limiting the generalizability of the findings to other populations and healthcare settings. Third, vitamin D was assessed at a single point during pregnancy, and changes in 25(OH)D concentration across gestation could not be evaluated. Fourth, potentially important confounding factors, including maternal dietary vitamin D intake, sunlight exposure, socioeconomic status, BMI, season of sampling, physical activity, and adherence to antenatal supplementation, were not comprehensively controlled. Fifth, the observational design prevented determination of a causal relationship between vitamin D deficiency and adverse pregnancy or neonatal outcomes. Finally, although the study observed a higher frequency of preterm birth in vitamin D-deficient women, the association was not statistically significant, consistent with the heterogeneous findings reported in previous systematic reviews. [7-9]

Conclusion

Maternal vitamin D deficiency was common among pregnant women in the present study. Vitamin D-deficient women had a higher observed frequency of preterm birth, although this association did not reach statistical significance. In contrast, maternal vitamin D deficiency was significantly associated with lower neonatal birth weight and a higher frequency of low birth weight. Other neonatal outcomes, including SGA, NICU admission, and low Apgar score, were more frequent in the deficient group but did not show statistically significant differences. These findings suggested a possible relationship between maternal vitamin D status and fetal growth. However, the results should be interpreted cautiously because of the small sample size, single-center setting, potential residual confounding, and observational design. Larger multicenter prospective studies with repeated 25(OH)D measurements and comprehensive adjustment for maternal nutritional, demographic, obstetric, and lifestyle factors are warranted.

List of Abbreviations

Abbreviation	Full form
25(OH)D	25-Hydroxyvitamin D
BMI	Body Mass Index
CI	Confidence Interval
DMCH	Darbhanga Medical College and Hospital
LBW	Low Birth Weight
NICU	Neonatal Intensive Care Unit
OR	Odds Ratio
SD	Standard Deviation
SGA	Small for Gestational Age
WHO	World Health Organization

Declarations

Ethics Approval and Consent to Participate: The study received approval from the Institutional Ethics Committee of Darbhanga Medical College and Hospital. Written informed consent was obtained from all participants before enrollment. The study was conducted in accordance with the ethical principles for research involving human participants.

Availability of Data and Materials: The dataset generated for this manuscript was derived from actual patient records.

Competing Interests: The authors declared that they had no competing interests.

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Authors' Contributions: All authors contributed to the conception and design of the study, data collection and interpretation, manuscript preparation, critical revision, and approval of the final manuscript. All authors agreed to be accountable for all aspects of the work.

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