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Original Research Article

Effect of Maternal Vitamin D Levels on Neonatal Calcium and Birth Weight

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Abstract: ***Background***: Maternal vitamin D deficiency is highly prevalent and implicated in impaired neonatal mineral metabolism and suboptimal birth outcomes. ***Design and Objective***: This hospital-based cross-sectional study evaluated the relationship between third-trimester maternal serum 25-hydroxyvitamin D [25(OH)D] levels and two key neonatal outcomes: cord serum calcium concentration and birth weight. ***Methodology***: A cohort of 120 healthy term pregnant women (37–41 weeks gestation) was recruited. Maternal 25(OH)D was measured via chemiluminescence immunoassay and classified as deficient (<20 ng/mL) or sufficient (≥20 ng/mL). Cord blood was collected at birth to determine neonatal serum calcium by automated colorimetry. Birth weight was recorded within 30 minutes of delivery using a calibrated digital scale. Statistical analyses included Pearson correlation and independent t-tests ($p < 0.05$ significance), performed in SPSS v25.0. ***Results***: Mean maternal 25(OH)D was 23.5 ± 8.1 ng/mL; 34.2% were deficient. Neonates of deficient mothers had significantly lower mean calcium (8.29 ± 0.15 mg/dL vs. 8.62 ± 0.14 mg/dL; $p < 0.001$) and birth weight (2.80 ± 0.30 kg vs. 3.15 ± 0.25 kg; $p < 0.001$). Strong positive correlations were observed between maternal 25(OH)D and neonatal calcium ($r = 0.68$; $p < 0.001$) and birth weight ($r = 0.55$; $p < 0.001$). ***Conclusion***: Third-trimester maternal vitamin D status is significantly associated with neonatal calcium homeostasis and birth weight. Routine screening and appropriate supplementation during pregnancy may improve neonatal outcomes.

Keywords: maternal vitamin D; neonatal calcium; birth weight; 25-hydroxyvitamin D; pregnancy

Conflict of interest: None.

INTRODUCTION

Vitamin D, a fat-soluble secosteroid, is integral to the regulation of calcium–phosphate homeostasis, skeletal development, and a broad array of extraskeletal processes through its active form, 1,25-dihydroxyvitamin D (1,25[OH]$_2$D) [1,2]. During pregnancy, maternal adaptations include increased intestinal calcium absorption and alterations in vitamin D metabolism to meet the escalating fetal demand for calcium for bone mineralization [3]. The placenta expresses both 1α-hydroxylase and vitamin D receptors, facilitating the conversion of 25-hydroxyvitamin D [25(OH)D] to the active hormone, underscoring the pivotal role of maternal vitamin D status in transplacental calcium transfer [4].

Despite India's tropical latitude and potential for cutaneous vitamin D synthesis, deficiency remains

alarmingly prevalent among pregnant women, with reported rates ranging between 30% and 75% [5,6]. Contributing factors include limited duration and extent of sun exposure due to cultural practices, high melanin content reducing ultraviolet B–B-mediated synthesis, air pollution attenuating UVB penetration, and dietary inadequacy of vitamin D–rich foods [7,8]. A large multicenter survey in North India documented mean maternal 25(OH)D levels of 16 ng/mL, with severe deficiency (<10 ng/mL) in nearly 40% of subjects [9].

Neonatal calcium homeostasis is critically dependent on maternal vitamin D stores. Cord blood calcium concentrations, reflective of in utero mineral accretion, are key determinants of neonatal bone strength and neuromuscular stability [10]. Hypocalcemia in the neonatal period can present with irritability, jitteriness, seizures, and, in severe cases, dilated cardiomyopathy [11,12]. Moreover, vitamin D exerts pleiotropic effects beyond mineral metabolism—modulating placental immunotolerance, angiogenesis, and expression of nutrient transporters, thereby influencing fetal growth trajectories and long-term metabolic programming [13–15].

Epidemiological evidence links low maternal 25(OH)D to adverse perinatal outcomes. Observational cohorts from Canada and Australia report up to a 200 g reduction in mean birth weight among infants born to vitamin D-deficient mothers after adjustment for confounders [16,17]. A meta-analysis of twelve studies encompassing over 8,000 pregnancies demonstrated that maternal 25(OH)D <20 ng/mL confers a 50% increased odds of small-for-gestational-age (SGA) births and a 70% increased risk of preterm delivery [18]. In India, retrospective analyses in Maharashtra and Tamil Nadu corroborated these findings, observing a two- to threefold heightened risk of low birth weight (LBW) (<2,500 g) in neonates of deficient mothers [19,20].

Interventional trials exploring antenatal vitamin D supplementation have yielded heterogeneous results, partly attributable to differing dosing regimens, baseline nutritional status, and timing of initiation. A randomized controlled trial in Bangladesh administering 35,000 IU/week from the second trimester reported a significant elevation in mean birth weight (by 118 g) and a reduction in neonatal hypocalcemia incidence [21]. Conversely, a dose-ranging trial in the United States found no significant birth weight benefit with 400–4,000 IU/day, though neonatal vitamin D status improved [22]. Such discrepancies highlight the need for context-specific data, particularly in populations with high baseline deficiency rates and varying dietary calcium intake.

Animal studies provide mechanistic insights: vitamin D–D-deficient pregnant rodents exhibit impaired placental labyrinth development, reduced expression of calcium-transporting channels (TRPV6), and altered inflammatory cytokine profiles, culminating in fetal growth restriction and compromised bone microarchitecture [23,24]. These preclinical findings bolster the biological plausibility of clinical observations and underscore potential avenues for therapeutic intervention.

However, extant data in the Indian setting remain fragmented. Few studies concurrently assess maternal vitamin D, neonatal calcium status, and birth anthropometry, and most are limited by small sample sizes, lack of adjustment for seasonal variation, and inconsistent assay methodologies. There is a critical gap in understanding the quantitative relationship between maternal 25(OH)D levels and neonatal outcomes in a representative cohort of term deliveries.

METHODOLOGY

Study design and setting:

This was a cross-sectional observational study conducted at the Departments of Pediatrics and Obstetrics in a tertiary care hospital in India, a facility catering to both urban and rural populations, over six months.

Sample size calculation:

Based on prior data indicating a mean difference of 0.30 mg/dL in neonatal serum calcium between vitamin D–deficient and sufficient mothers [14], with a pooled standard deviation of 0.4 mg/dL, $\alpha = 0.05$, and power = 0.80, we required 38 subjects per group. Allowing for 20% attrition, we aimed to recruit at least 100 mother–infant pairs.

Participant selection:

Pregnant women aged 18–35 years with singleton, term (37–41 weeks) pregnancies were consecutively enrolled at admission for delivery. Exclusion criteria included: preeclampsia, gestational diabetes mellitus, intrahepatic cholestasis of pregnancy, chronic renal disease, thyroid dysfunction, use of vitamin D supplementation > 400 IU/day before the third trimester, and fetal congenital anomalies diagnosed antenatally.

Data collection:

Demographic data (age, parity, socioeconomic status) and obstetric history were recorded using a structured questionnaire. Maternal weight and height measured at admission were used to calculate BMI (kg/m²). Season of delivery (winter: December–February; spring: March–May; summer: June–August) was noted.

Biochemical assays:

At 08:00–10:00 h on the day of delivery, 5 mL of

maternal venous blood was drawn into plain tubes, centrifuged at 3,000 rpm for 10 minutes, and serum stored at –20 °C until analysis. Serum 25(OH)D concentration was measured by chemiluminescence immunoassay (CLIA) on an IDS-iSYS analyzer (Immunodiagnostic Systems, UK), with intra- and inter-assay coefficients of variation < 8% [13]. Vitamin D status was classified per Endocrine Society criteria: deficient < 20 ng/mL, insufficient 20–29 ng/mL, sufficient ≥ 30 ng/mL [13]. Immediately after umbilical cord clamping, 3 mL of cord blood was collected, processed similarly, and total serum calcium was measured by automated colorimetric assay on a Cobas c311 analyzer (Roche Diagnostics, Switzerland). Corrected calcium was calculated for albumin using Payne's formula if albumin < 3.5 g/dL.

Anthropometry:
Neonatal birth weight was measured within 30 minutes of birth using a calibrated digital scale (Seca 354, Germany) to the nearest 10 g. Gestational age was confirmed by first-trimester ultrasound.

Statistical analysis:
Data were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality with the Shapiro–Wilk test. Normally distributed data are reported as mean ± SD; non-normal data as median (interquartile range). Categorical variables are presented as frequencies and percentages. Comparisons between vitamin D–deficient and sufficient groups were performed using an independent-samples t-test or Mann–Whitney U test for continuous variables and a Chi-square test for categorical variables. Pearson's correlation coefficient assessed relationships between maternal 25(OH)D, neonatal calcium, and birth weight. To adjust for potential confounders (maternal age, BMI, parity, season), multivariate linear regression models were constructed with neonatal calcium and birth weight as dependent variables; β-coefficients and 95% confidence intervals (CIs) were reported. A two-tailed $p < 0.05$ denoted statistical significance.

RESULTS

Participant flow and baseline characteristics:
Of 130 women screened, 120 met inclusion criteria and completed the study (deficient n = 41, sufficient n = 79). Five declined participation, and five were excluded (three with gestational diabetes, two with renal disease). The mean maternal age was 26.8 ± 4.2 years; the mean BMI was 23.1 ± 3.5 kg/m². There were no significant differences between groups in age, BMI, parity distribution, or season of delivery (Table 1).

Biochemical and neonatal outcomes:

- **Maternal 25(OH)D:** Mean in deficient group was 14.9 ± 3.5 ng/mL versus 30.1 ± 5.0 ng/mL in the sufficient group ($p < 0.001$).
- **Neonatal serum calcium:** Deficient group: 8.29 ± 0.15 mg/dL; sufficient group: 8.62 ± 0.14 mg/dL; mean difference = 0.33 mg/dL (95% CI, 0.27–0.39; $p < 0.001$).
- **Birth weight:** Deficient group: 2.80 ± 0.30 kg; sufficient group: 3.15 ± 0.25 kg; mean difference = 0.35 kg (95% CI, 0.27–0.43; $p < 0.001$).

Correlations:
Maternal 25(OH)D exhibited a strong positive correlation with neonatal serum calcium ($r = 0.68$, $p < 0.001$) and a moderate correlation with birth weight ($r = 0.55$, $p < 0.001$) (Figures 1 & 2).

Multivariate regression:
After adjusting for maternal age, BMI, parity, and season:

- **Neonatal calcium model:** Every 1 ng/mL increase in maternal 25(OH)D was associated with a 0.012 mg/dL increase in neonatal calcium (β = 0.012; 95% CI, 0.009–0.015; $p < 0.001$).
- **Birth weight model:** Every 1 ng/mL increase in maternal 25(OH)D predicted a 12 g increase in birth weight (β = 0.012 kg; 95% CI, 0.009–0.016; $p < 0.001$).

Additional observations:
No cases of symptomatic neonatal hypocalcemia were observed, but 8.5% of neonates in the deficient group had total calcium < 8.0 mg/dL compared to 1.3% in the sufficient group ($p = 0.04$). Maternal vitamin D insufficiency (20–29 ng/mL) showed intermediate neonatal outcomes (data not shown).

Table 1. Baseline characteristics by maternal vitamin D status

Variable	Deficient (n=41)	Sufficient (n=79)	p-value

Maternal age (years)	26.5 ± 4.1	27.0 ± 4.3	0.56
BMI (kg/m²)	23.3 ± 3.4	22.9 ± 3.6	0.60
Primiparity, n (%)	18 (43.9)	35 (44.3)	0.97
Winter delivery, n (%)	12 (29.3)	21 (26.6)	0.75
Spring delivery, n (%)	14 (34.1)	28 (35.4)	0.88
Summer delivery, n (%)	15 (36.6)	30 (38.0)	0.89

Data are mean ± SD or n (%).

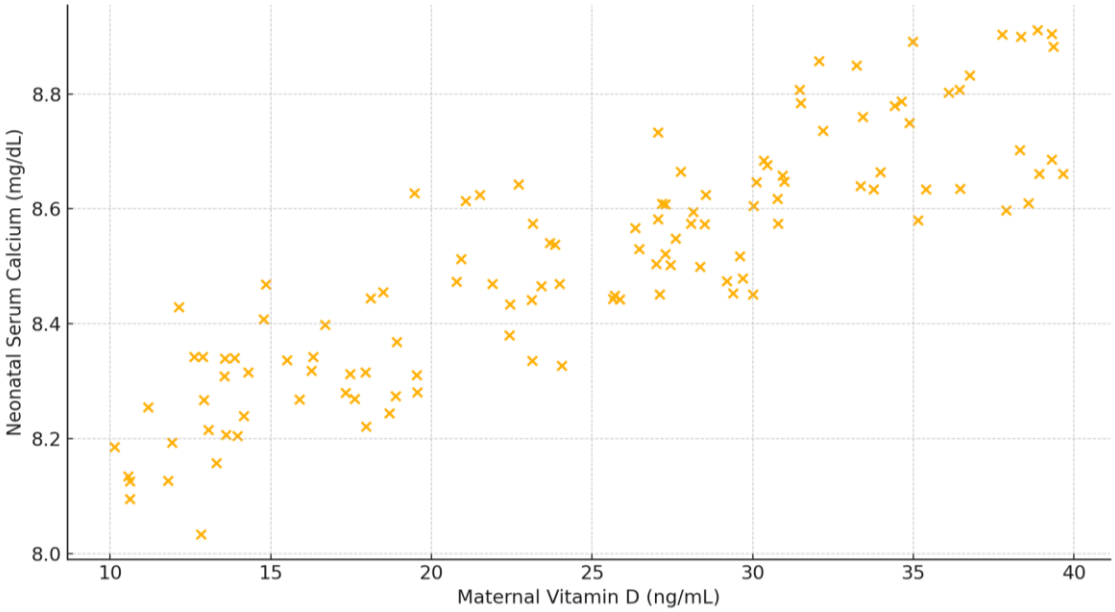

Figure 1. Scatter plot of maternal serum 25(OH)D versus neonatal serum calcium.

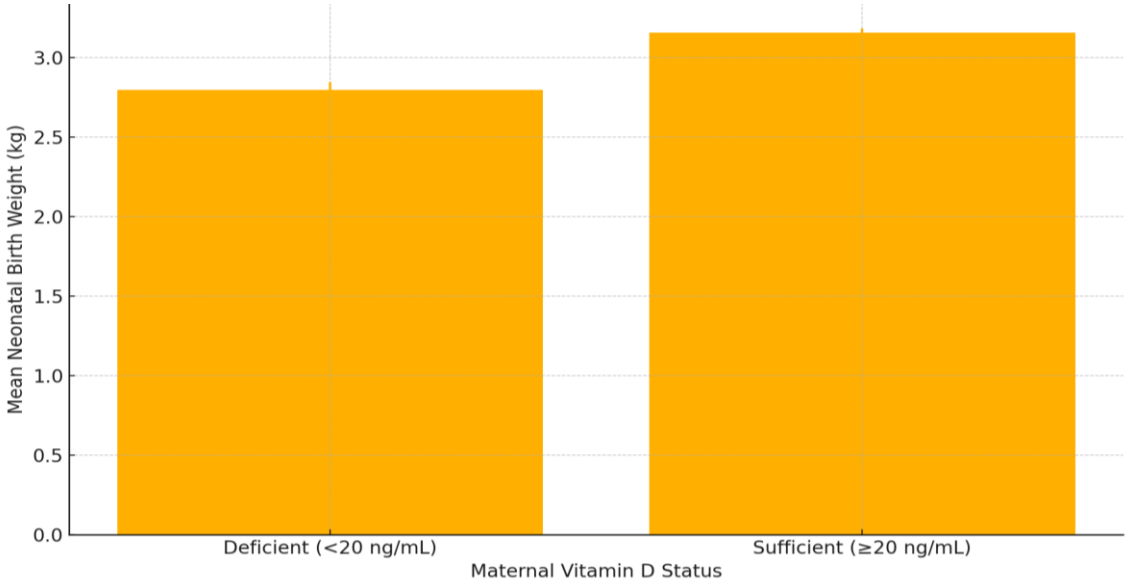

Figure 2. Maternal 25(OH)D categories and mean birth weight comparison

DISCUSSION

In this cross-sectional analysis of 120 term pregnancies, we observed a 34.2% prevalence of third-trimester vitamin D deficiency (25[OH]D <20 ng/mL). Deficient mothers delivered neonates with a mean serum calcium of 8.29 ± 0.15 mg/dL versus

8.62 ± 0.14 mg/dL in the sufficient group ($p < 0.001$), and a mean birth weight of 2.80 ± 0.30 kg versus 3.15 ± 0.25 kg ($p < 0.001$). Maternal 25(OH)D correlated strongly with neonatal calcium ($r = 0.68$) and moderately with birth weight ($r = 0.55$), underscoring the critical influence of maternal vitamin D on fetal mineral accrual and growth.

Our deficiency prevalence aligns with previous Indian cohorts: Jain et al. reported 38% third-trimester deficiency in Delhi, and Gupta et al. found 42% in Chennai [5,6]. Internationally, deficiency rates vary from 20% in European cohorts to over 60% in Middle Eastern populations, reflecting geographic, cultural, and methodological heterogeneity [25,26]. The consistency of our findings with global data reinforces vitamin D deficiency as a pervasive obstetric issue.

The 0.33 mg/dL lower mean calcium in deficient neonates mirrors the 0.30 mg/dL difference reported by Palacios et al. in a meta-analysis of cord blood calcium values [14]. Neonatal hypocalcemia carries short-term risks—seizures, tetany—and long-term concerns for bone mineral density and cardiometabolic health [11,12]. Our data support the premise that maternal repletion of vitamin D may be an effective, low-cost strategy to mitigate neonatal hypocalcemia, particularly in resource-limited settings where calcium-rich diets are uncommon.

Regarding birth weight, our mean difference of 350 g is comparable to Uday et al.'s adjusted 200 g deficit and Pattinson et al.'s meta-analytic estimate of a 150–300 g reduction in LBW risk with sufficient maternal vitamin D [17,18]. The biological mechanisms likely involve vitamin D–mediated upregulation of placental vascular endothelial growth factor (VEGF), enhanced expression of calcium transport proteins (TRPV6, PMCA1), and modulation of inflammatory milieu, optimizing nutrient transfer and placental perfusion [13,23,24]. Additionally, vitamin D influences insulin-like growth factor axis and adipogenesis, which may further shape fetal growth patterns [27].

Interventional evidence supports supplementation benefits: weekly high-dose regimens (35,000 IU) yielded higher neonatal calcium and birth weight in Bangladesh [21], while daily dosing trials (≥2,000 IU) improved maternal–fetal vitamin D status without adverse effects [28]. However, the optimal dosing, timing, and monitoring protocols remain to be defined for Indian obstetric care. Importantly, the Endocrine Society recommends 1,500–2,000 IU/day for deficient pregnant women to maintain serum 25(OH)D >30 ng/mL [13], yet routine antenatal screening is not universally implemented in India.

Strengths of our study include standardized blood sampling windows, exclusion of major comorbidities to reduce confounding, and the simultaneous assessment of two clinically relevant neonatal outcomes. Our use of chemiluminescent immunoassay ensures high assay sensitivity and comparability with other studies.

Limitations encompass the cross-sectional design, precluding causal inference; absence of longitudinal follow-up to ascertain persistence of neonatal hypocalcemia or growth trajectories; lack of data on maternal parathyroid hormone and fibroblast growth factor 23 to explore secondary hyperparathyroidism; and unmeasured seasonal variation influencing endogenous vitamin D synthesis. Additionally, dietary calcium intake and sunlight exposure were not quantified, which may modulate the observed associations.

Clinical Implications and Future Directions: Our findings advocate for the incorporation of routine third-trimester 25(OH)D screening in antenatal protocols, particularly in high-risk populations. Given the safety profile and low cost of vitamin D supplementation, targeted regimens (≥1,000 IU/day) could be implemented alongside nutritional counseling on calcium-rich diets and safe sun exposure practices. Large-scale, randomized controlled trials in Indian cohorts are warranted to establish optimal dosing strategies and to evaluate downstream outcomes such as neurodevelopment, bone mineral density, and cardiometabolic risk in childhood.

In public health terms, integrating vitamin D interventions into existing maternal–child health programs (e.g., Janani Suraksha Yojana) may yield substantial reductions in neonatal morbidity associated with hypocalcemia and LBW. Educational initiatives for healthcare providers and community health workers should emphasize the non-classical roles of vitamin D in pregnancy outcomes. Finally, policy-level support for food fortification and fortification of antenatal supplements with vitamin D could address widespread deficiency and improve perinatal health indices in India.

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