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MATERNAL VITAMIN D SUPPLEMENTATION AND ITS ASSOCIATION WITH PREGNANCY OUTCOMES, NEONATAL PHYSIOLOGICAL ADAPTATION, AND EARLY INFANT HEALTH: AN ANALYTICAL CROSS-SECTIONAL STUDY"

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ABSTRACT

Background: Maternal vitamin D deficiency remains a prevalent global health concern linked to adverse maternal, fetal, and neonatal health outcomes. Despite growing awareness, variations in regional clinical practices and adherence to maternal supplementation continue to impact developmental trajectories. This study evaluated the association between maternal vitamin D supplementation during pregnancy and key metrics of maternal pregnancy outcomes, neonatal physiological adaptation, and early infant health.

Methods: An analytical cross-sectional study was conducted among mothers and their full-term singleton infants (N = 350) presenting at tertiary care facilities over a 06 months period. Maternal vitamin D status and supplementation history (dose, timing, and consistency) were documented alongside maternal serum 25-hydroxyvitamin D [25(OH)D] levels measured at delivery. Primary outcomes included maternal gestational complications (gestational diabetes, preeclampsia), neonatal physiological adaptation at birth (APGAR scores, umbilical cord blood gas analysis, neonatal serum calcium), and early infant health outcomes (birth weight, incidence of early-onset neonatal infections, and 6-week infant growth indices). Multivariate logistic regression and linear regression models were utilized to adjust for confounding variables including maternal age, baseline BMI, socioeconomic status, and gestational age at birth.

Results: Mothers who received consistent vitamin D supplementation (600 IU/day or more) demonstrated significantly higher mean delivery 25(OH)D levels compared to non-supplemented mothers (28.4 ± 6.2 ng/mL vs. 14.1 ± 4.8 ng/mL, $p < 0.001$). Maternal vitamin D supplementation was associated with a reduced risk of preeclampsia (AOR = 0.42, 95% CI: 0.21–0.84) and lower rates of low birth weight (AOR = 0.38, 95% CI: 0.19–0.76). Neonates born to supplemented mothers exhibited superior physiological adaptation, characterized by higher 5-minute APGAR scores ($p = 0.008$), reduced rates of neonatal hypocalcemia (3.2% vs. 14.8%, $p < 0.001$), and higher mean cord serum 25(OH)D levels. At the 6-week follow-up, infants of supplemented mothers showed improved weight-for-age z-scores and a lower incidence of acute respiratory tract infections (AOR = 0.51, 95% CI: 0.29–0.90).

Conclusion: Adequate maternal vitamin D supplementation during pregnancy is strongly associated with a reduced incidence of maternal gestational complications, improved neonatal physiological transition at birth, and favorable early infant health and growth metrics. These findings support routine monitoring and targeted maternal supplementation protocols to optimize perinatal and early infant health outcomes.

KEYWORDS: Maternal Health, Vitamin D Supplementation, Pregnancy Outcomes, Neonatal Adaptation, Infant Health, 25-hydroxyvitamin D, Perinatal Outcomes.

INTRODUCTION

Vitamin D, a secosteroid hormone primarily known for regulating calcium-phosphate homeostasis and bone mineralization, is now recognized as a critical immunomodulatory and vascular signaling factor during gestation [1].

Maternal 25-hydroxyvitamin D [25(OH)D] readily crosses the placental barrier, serving as the sole source of vitamin D for the developing fetus [2]. Despite the physiological increase in 1,25-dihydroxyvitamin D synthesis

driven by placental 1-alpha-hydroxylase activity, maternal hypovitaminosis D remains a pervasive global public health issue [3]. Recent global estimates indicate that vitamin D deficiency (serum 25(OH)D less than 20 ng/mL) affects between 40% to 80% of pregnant women across various geographic regions, largely influenced by limited sun exposure, dietary deficiencies, and regional healthcare disparities [2,4].

During gestation, adequate maternal serum concentrations of 25(OH)D are necessary to support systemic physiological adaptations. Insufficient maternal vitamin D levels have been implicated in dysregulated placental angiogenesis, enhanced systemic inflammation, and impaired glucose tolerance [1,5]. Epidemiological evidence links maternal deficiency to heightened risks of major gestational complications, including preeclampsia, gestational diabetes mellitus, and fetal growth restriction [1,6]. Furthermore, because the primary transfer of maternal vitamin D and calcium to the fetus occurs during the third trimester, maternal deficiency directly compromises fetal bone mineralization, limits neonatal vitamin D reserves, and increases the vulnerability of the newborn to acute physiological disturbances at birth [3,7].

At birth, the transition from intra-uterine to extra-uterine life demands rapid physiological adaptation across the neonatal cardiovascular, respiratory, and metabolic systems. Maternal vitamin D status plays a key role in facilitating this transition. Adequate neonatal 25(OH)D levels support early neuromuscular function, stabilize serum calcium levels—preventing neonatal tetany and early-onset hypocalcemia—and regulate early immune responses [3,5]. Beyond the immediate perinatal window, the immunomodulatory effects of maternal vitamin D supplementation extend into early infancy. Infants born to mothers with optimal vitamin D status demonstrate reduced rates of early-onset respiratory infections, improved growth trajectories, and lower long-term cardiometabolic risk profiles [6,7].

Despite widespread recognition of these pathways, significant clinical ambiguity persists regarding the optimal dose, timing, and regional effectiveness of prenatal vitamin D supplementation. Current national and international clinical guidelines offer varying recommendations, ranging from 600 IU/day to over 2000 IU/day, with limited cross-sectional data evaluating how maternal supplementation directly influences the continuum of maternal outcomes, neonatal adaptation at delivery, and early infant health metrics within real-world clinical settings [4,6].

Therefore, this analytical cross-sectional study was conducted to evaluate the relationship between maternal vitamin D supplementation, delivery serum 25(OH)D concentrations, maternal pregnancy complications, neonatal physiological adaptation at birth, and health outcomes in early infancy.

MATERIALS AND METHODS

Study Design and Setting. An analytical cross-sectional study was conducted at the Department of Obstetrics and Gynaecology in collaboration with the Department of Paediatrics at Tertiary Care Hospital from June 2025 to November 2025 (a period of 6 months).

Ethical clearance was obtained from the Institutional Ethics Committee prior to the commencement of data collection. Written informed consent was obtained from all participating mothers before enrollment.

Study Population The study population comprised pregnant women admitted for delivery at the tertiary care facility along with their newborn infants.

- **Inclusion Criteria:**
- Pregnant women aged 18 to 40 years.
- Full-term singleton deliveries (gestational age between 37 weeks 0 days and 41 weeks 6 days determined by first-trimester ultrasound or last menstrual period).
- Mothers providing documented history of prenatal care and supplementation.
- **Exclusion Criteria:**
- Multiple gestations (twins, triplets).
- Pre-existing maternal chronic illnesses (such as pre-gestational diabetes, chronic hypertension, renal or hepatic disorders, primary hyperparathyroidism).
- History of maternal intake of medications known to alter vitamin D metabolism (such as anticonvulsants, systemic corticosteroids).
- Major congenital anomalies detected in the neonate at birth.

Sample Size and Sampling Technique A non-probability consecutive sampling method was utilized. The sample size was calculated using OpenEpi oftware based on an estimated maternal vitamin D deficiency prevalence of 65% in the region, a 95% confidence level, and a 5% margin of error. Accounting for potential non-response or loss to follow-up at the 6-week post-natal visit, a final sample size of 350 mother-infant dyads was targeted and enrolled.

Data Collection Procedure Data were recorded using a pre-designed, structured questionnaire administered by trained healthcare personnel.

1. **Maternal Demographic and Clinical Parameters:** Information regarding maternal age, parity, socioeconomic status, baseline Body Mass Index (BMI), sun exposure habits, and dietary intake was documented. Detailed records of maternal vitamin D supplementation during pregnancy—including dosage, timing of initiation (trimester), and compliance—were recorded.

2. **Laboratory Analyses:** Maternal venous blood samples (5 mL) were collected upon admission for delivery. Umbilical cord blood samples (5 mL) were drawn immediately following delivery. Serum 25-hydroxyvitamin D [25(OH)D] concentrations were quantified using enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassay (CLIA). Maternal vitamin D status was categorized as deficient (less than 20 ng/mL), insufficient (20 to 29.9 ng/mL), or sufficient (30 ng/mL or more).
3. **Assessment of Pregnancy Outcomes:** Gestational complications such as preeclampsia, gestational diabetes mellitus (GDM), pre-labor rupture of membranes (PROM), and mode of delivery were recorded from hospital clinical files.
4. **Neonatal Physiological Adaptation at Birth:** Immediate physiological transition was evaluated via 1-minute and 5-minute APGAR scores. Neonatal anthropometric measurements (birth weight, length, head circumference) were taken within 1 hour of birth. Umbilical cord blood gas parameters and neonatal serum calcium levels were measured within the first 24 hours of life.
5. **Early Infant Follow-up (6 Weeks):** Infants were re-evaluated at 6 weeks post-partum during routine immunization visits. Parameters assessed included physical growth indices (weight-for-age z-scores), developmental milestones, and occurrences of early infant morbidity (such as acute respiratory tract infections, neonatal jaundice, or hypo calcemic tetany).

Statistical Analysis Data were entered and analyzed using SPSS (Statistical Package for the Social Sciences) version 26.0. Continuous variables were presented as mean ± standard deviation or median (interquartile range) based on normality tests (Shapiro-Wilk test). Categorical variables were expressed as frequencies and percentages.

- Comparisons between supplemented and non-supplemented groups were performed using the Independent Student's t-test or Mann-Whitney U test for continuous data, and the Chi-square test or Fisher's exact test for categorical parameters.
- Multivariate logistic regression analysis was conducted to assess the independent association between maternal vitamin D supplementation and maternal/neonatal outcomes, adjusting for potential confounders such as maternal age, BMI, socioeconomic status, and gestational age. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 350 mother–infant dyads were enrolled and evaluated during the six-month study period from June 2025 to November 2025. Based on documented prenatal vitamin D intake, participants were classified into two groups: the Supplemented group (n = 210), comprising mothers who received ≥600 IU/day of vitamin D, and the Non-Supplemented/Irregular group (n = 140), comprising mothers with no supplementation or irregular intake. Baseline demographic characteristics were broadly comparable between the two groups, suggesting a relatively balanced study population.

1. Baseline Demographic and Clinical Characteristics

The mean maternal age was comparable between the supplemented and non-supplemented groups (27.4 ± 4.1 vs. 26.9 ± 4.5 years, respectively; p = 0.284). Similarly, no significant between-group differences were observed in primiparity, maternal BMI, or socioeconomic status (all p > 0.05).

In contrast, maternal vitamin D status at delivery differed markedly between the groups. Mean serum **25-hydroxyvitamin D [25(OH)D]** concentration was substantially higher among supplemented mothers than among non-supplemented/irregularly supplemented mothers (28.4 ± 6.2 vs. 14.1 ± 4.8 ng/mL; p < 0.001). Vitamin D deficiency (<20 ng/mL) was observed in **10.5%** of mothers in the supplemented group compared with **91.4%** in the non-supplemented group. Conversely, vitamin D sufficiency (≥30 ng/mL) was achieved by 35.2% of supplemented mothers compared with only 1.4% of mothers in the non-supplemented group. Overall, **42.8% of mothers had vitamin D deficiency**, indicating a substantial burden of deficiency in the study population.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Participants

Parameter	Supplemented (n = 210)	Non-Supplemented/Irregular (n = 140)	Test statistic	p-value
Maternal age, years	27.4 ± 4.1	26.9 ± 4.5	t = 1.07	0.284
Primiparous, n (%)	118 (56.2)	75 (53.6)	$\chi^2 = 0.23$	0.630
BMI, kg/m²	25.1 ± 3.4	25.6 ± 3.8	t = 1.28	0.201
Low socioeconomic status, n (%)	62 (29.5)	51 (36.4)	$\chi^2 = 1.81$	0.178
Maternal serum 25(OH)D, ng/mL	28.4 ± 6.2	14.1 ± 4.8	t = 23.11	<0.001
Vitamin D status, n (%)			$\chi^2 = 224.5$	<0.001
Deficient (<20 ng/mL)	22 (10.5)	128 (91.4)		

Parameter	Supplemented (n = 210)	Non-Supplemented/Irregular (n = 140)	Test statistic	p-value
Insufficient (20–29.9 ng/mL)	114 (54.3)	10 (7.1)		
Sufficient (≥30 ng/mL)	74 (35.2)	2 (1.4)		

Values are presented as mean ± SD or n (%), as appropriate.

2. Maternal Gestational Outcomes

Maternal vitamin D supplementation was associated with a more favorable gestational outcome profile. Preeclampsia occurred in 5.7% of mothers in the supplemented group compared with 14.3% in the non-supplemented/irregular group (p = 0.006). After adjustment for maternal age, BMI, socioeconomic status, and parity, supplemented mothers had lower odds of preeclampsia (adjusted OR 0.42, 95% CI 0.21–0.84).

A similar pattern was observed for gestational diabetes mellitus. GDM occurred in 7.1% versus 15.0% of supplemented and non-supplemented mothers, respectively (p = 0.019), with adjusted odds of 0.48 (95% CI 0.24–0.96). Although pre-labor rupture of membranes and cesarean delivery were numerically less frequent in the supplemented group, these differences did not reach statistical significance.

Table 2. Maternal Gestational Complications According to Vitamin D Supplementation Status

Gestational outcome	Supplemented (n = 210)	Non-Supplemented/Irregular (n = 140)	Adjusted OR (95% CI)	p-value
Preeclampsia	12 (5.7%)	20 (14.3%)	0.42 (0.21–0.84)	0.006
Gestational diabetes mellitus	15 (7.1%)	21 (15.0%)	**0.48 (0.24–0.96)**	**0.019**
Pre-labor rupture of membranes	18 (8.6%)	19 (13.6%)	0.61 (0.31–1.21)	0.141
Cesarean delivery	58 (27.6%)	51 (36.4%)	0.71 (0.45–1.12)	0.082

Adjusted for maternal age, baseline BMI, socioeconomic status, and parity.

3. Neonatal Physiological Adaptation at Birth

Neonates born to mothers receiving regular vitamin D supplementation demonstrated more favorable biochemical and clinical parameters at birth. Mean cord serum 25(OH)D concentration was significantly higher among neonates in the supplemented group than in the non-supplemented/irregular group (22.1 ± 5.4 vs. 10.8 ± 3.9 ng/mL; p < 0.001), demonstrating a clear relationship between maternal and neonatal vitamin D status.

Mean birth weight was also significantly greater among infants born to supplemented mothers (3120 ± 410 vs. 2890 ± 450 g; p < 0.001). Correspondingly, low birth weight (<2500 g) was less frequent in the supplemented group (6.7% vs. 16.4%; p = 0.004).

Neonatal calcium concentrations were significantly higher in the supplemented group (9.4 ± 0.7 vs. 8.5 ± 0.9 mg/dL; p < 0.001), while early neonatal hypocalcemia occurred in only 3.3% of supplemented infants compared with 14.8% of infants in the non-supplemented group (p < 0.001). In addition, a 5-minute APGAR score <7 was less frequent among infants in the supplemented group (2.9% vs. 9.3%; p = 0.011).

Table 3. Neonatal Physiological Parameters and Birth Outcomes

Neonatal parameter	Supplemented (n = 210)	Non-Supplemented/Irregular (n = 140)	p-value
Birth weight, g	3120 ± 410	2890 ± 450	<0.001
Low birth weight (<2500 g), n (%)	14 (6.7)	23 (16.4)	0.004
5-minute APGAR <7, n (%)	6 (2.9)	13 (9.3)	0.011
Cord serum 25(OH)D, ng/mL	22.1 ± 5.4	10.8 ± 3.9	<0.001
Neonatal serum calcium, mg/dL	9.4 ± 0.7	8.5 ± 0.9	<0.001
Early hypocalcemia (<8.0 mg/dL), n (%)	7 (3.3)	21 (14.8)	<0.001

Values are presented as mean ± SD or n (%), as appropriate.

4. Infant Growth and Early Morbidity at Six Weeks

Of the 350 enrolled mother–infant dyads, 328 (93.7%) completed the six-week postnatal follow-up, including 196 infants in the supplemented group and 132 in the non-supplemented/irregular group.

At six weeks, infants born to supplemented mothers demonstrated significantly better early growth, with a higher mean weight-for-age z-score than infants in the non-supplemented group (0.12 ± 0.84 vs. −0.28 ± 0.91; p < 0.001).

Early morbidity also differed between the groups. Acute respiratory tract infection was documented in 8.2% of infants in the supplemented group compared with 17.2% in the non-supplemented group (adjusted OR 0.51, 95% CI 0.29–0.90; p = 0.013). Phototherapy-treated neonatal jaundice was less frequent in the supplemented group, although the difference was not statistically significant (6.1% vs. 11.4%; p = 0.089).
Hypo calcemic tetany/seizures were observed exclusively in the non-supplemented group (0% vs. 2.3%; p = 0.038), although the small number of events warrants cautious interpretation.

Table 4. Infant Growth and Morbidity at Six-Week Follow-up

Infant outcome	Supplemented (n = 196)	Non-Supplemented/Irregular (n = 132)	Adjusted OR (95% CI)	p-value
Weight-for-age z-score	0.12 ± 0.84	−0.28 ± 0.91	—	<0.001
Acute respiratory tract infection, n (%)	16 (8.2)	23 (17.2)	0.51 (0.29–0.90)	0.013
Phototherapy for jaundice, n (%)	12 (6.1)	15 (11.4)	0.56 (0.26–1.22)	0.089
Hypo calcemic tetany/seizures, n (%)	0 (0.0)	3 (2.3)	—	0.038

Overall, regular maternal vitamin D supplementation was associated with higher maternal and neonatal 25(OH)D concentrations, lower rates of preeclampsia and gestational diabetes mellitus, greater birth weight, improved neonatal calcium status, reduced early neonatal hypocalcemia, and more favorable infant growth and respiratory morbidity outcomes at six weeks.

DISCUSSION

The findings of this analytical cross-sectional study demonstrate a significant positive association between consistent maternal vitamin D supplementation during pregnancy and improved maternal gestational outcomes, superior neonatal physiological adaptation at birth, and favorable early infant growth metrics. Maternal vitamin D deficiency remains a widespread public health challenge, with over 40% of the non-supplemented maternal cohort demonstrating serum 25(OH)D levels below 20 ng/mL at delivery. These results align with recent global epidemiologic data highlighting the vulnerability of pregnant populations to hypovitaminosis D in the absence of routine supplementation [1,2].
The reduction in maternal gestational complications observed among supplemented mothers supports the established immunomodulatory and endovascular roles of vitamin D during pregnancy [1]. Preeclampsia and gestational diabetes mellitus were significantly less frequent in women receiving regular supplementation. Placental tissue relies heavily on sufficient 25(OH)D concentrations for vascular endothelial growth factor expression, proper trophoblast invasion, and down-regulation of pro-inflammatory cytokines [1,5]. By preserving placental vascular integrity and systemic insulin sensitivity, vitamin D supplementation serves as a key protective factor against pregnancy-induced hypertensive and metabolic disorders [1,6].
At delivery, the neonate is entirely dependent on transplacental transfer of 25(OH)D for immediate metabolic stability. In this study, cord blood 25(OH)D levels strongly correlated with maternal delivery concentrations [2,3]. Neonates born to supplemented mothers exhibited marked advantages in early physiological transition, characterized by higher 5-minute APGAR scores and a low rate of early-onset neonatal hypocalcemia. Vitamin D plays a crucial role in maintaining extracellular calcium concentrations required for neuromuscular function and surfactant response during extra-uterine adaptation [3,5]. The observed high rate of hypocalcemia (14.8%) in the non-supplemented group underscores the clinical risk of uncorrected maternal deficiency on immediate newborn adaptation [3,7].
Furthermore, the protective effects of prenatal maternal supplementation extended into early infancy. At the 6-week post-natal evaluation, infants of supplemented mothers demonstrated superior weight-for-age z-scores and significantly fewer presentations for acute respiratory tract infections [6,7]. Vitamin D regulates the expression of antimicrobial peptides, such as cathelicidin, within the respiratory epithelium, strengthening the infant's innate immune barrier during the vulnerable early post-natal weeks [3,7]. These findings emphasize that adequate prenatal supplementation benefits both immediate delivery parameters and early childhood developmental trajectories [6,7].

LIMITATIONS

Several limitations should be considered when interpreting these findings. First, the cross-sectional design restricts the ability to establish direct causal relationships. Second, dietary vitamin D intake and seasonal sun exposure were assessed via self-reported questionnaires, which may introduce recall bias. Finally, while key confounding variables were controlled using multivariate models, unmeasured socioeconomic or lifestyle factors could have influenced early infant health metrics.

CONCLUSION

Maternal vitamin D supplementation during pregnancy is strongly associated with elevated delivery serum 25(OH)D levels, reduced risks of preeclampsia and gestational diabetes, improved neonatal physiological adaptation at delivery, and reduced infant respiratory morbidity at 6 weeks of age.

Recommendations

1. **Routine Screening & Supplementation Protocols:** Healthcare facilities should integrate routine screening of serum 25(OH)D into antenatal care or implement standardized daily supplementation (at least 600 IU/day) for pregnant women.
2. **Public Health Policy Integration**: Maternal health policies in high-risk regions should emphasize prenatal vitamin D awareness to reduce preventable perinatal and early neonatal complications.
3. **Future Research**: Prospective cohort studies and randomized controlled trials are recommended to establish optimal trimester-specific dosage regimens tailored to diverse populations.

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