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PRENATAL PREDICTORS OF VITAMIN D DEFICIENCY IN NEONATES

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ABSTRACT

Background: Vitamin D plays a vital role in fetal skeletal development and immune regulation. During pregnancy, the fetus is entirely dependent on maternal 25(OH)D levels, which are influenced by sun exposure, dietary intake, and maternal health. Deficiency in vitamin D has been associated with adverse outcomes in both mother and neonate.

Objective: To assess the prevalence of vitamin D deficiency in pregnant women and its correlation with neonatal cord blood vitamin D levels, as well as evaluate associated maternal factors such as parity, BMI, and sun exposure.

Methods: This prospective observational study included 100 pregnant women (20–40 years) with singleton term pregnancies, conducted at Government Medical College, Srinagar. Maternal and cord blood samples were analyzed for 25(OH)D levels using ELISA. Vitamin D status was categorized as deficient (<30 nmol/L), insufficient (30–50 nmol/L), or sufficient (>50 nmol/L). Associations were examined using Chi-square and Pearson correlation tests.

Results: Vitamin D deficiency was observed in 56% of mothers and 58% of neonates. A significant correlation existed between maternal and neonatal vitamin D levels ($p = 0.001$). Deficiency was highest in underweight (78.6%), nulliparous (83.3%), and women with no sun exposure (71.4%). Statistically significant associations were noted for parity ($p = 0.047$), BMI ($p = 0.047$), and sun exposure ($p = 0.0002$), but not for maternal age ($p = 0.5241$).

Conclusion: Maternal vitamin D status significantly influences neonatal levels. Routine antenatal screening, supplementation, and promoting sun exposure should be prioritized, especially in high-risk subgroups, to prevent deficiency-related complications.

Keywords: Vitamin D deficiency, pregnancy, neonatal outcome, 25-hydroxyvitamin D.

INTRODUCTION

Vitamin D, particularly in its most active form - 1,25 dihydroxyvitamin D3 is vital not only for maintaining calcium balance and supporting bone health but also for regulating endocrine function, immune response, and cellular growth and differentiation.[1] During pregnancy, the maternal levels of 25(OH)D3, which is the circulating precursor of vitamin D, are largely influenced by dietary intake.[2] Additionally, levels of the active hormone, 1,25-dihydroxyvitamin D3, are naturally elevated during gestation.[2] This hormone is primarily produced by decidual cells of the placenta and plays a key role in enhancing calcium absorption to meet fetal skeletal demands. Since the fetus is incapable of synthesizing vitamin D, it relies solely on maternal 25(OH)D3 which crosses the placenta.[3] After birth, both term and preterm neonates begin producing 1,25-dihydroxyvitamin D in response to hypocalcemia and elevated parathyroid hormone levels. However, the concentration of 25(OH)D3 in neonates—a critical precursor for active vitamin D synthesis is often higher than that seen in older infants.[4] In countries where dairy fortification with vitamin D is uncommon, supplementation during pregnancy is essential to prevent deficiency.[5] Throughout gestation, total serum calcium tends to decline, reaching its lowest point around the second month, typically between 2 to 2.2 mmol/L.[4] This decrease is partly due to reduced albumin levels from plasma volume expansion, although ionized calcium levels tend to remain stable. Maternal 25(OH)D3 levels are known to vary based on sun exposure, dietary sources, seasonal changes, and geographic location.[6] Inadequate vitamin D during pregnancy has been associated with multiple fetal complications, including miscarriage, intrauterine growth restriction, neonatal hypocalcemia, and developmental delays, as well as rickets in later infancy.[1-7] During the third trimester, demands for calcium markedly increase due to the fetal skeleton's rapid development. Alarmingly high rates of vitamin D deficiency have been reported among pregnant women in several countries such as the United Kingdom, India, Pakistan, Norway, and Saudi Arabia, often mirrored by deficiencies in their neonates.[8]

Key contributors to maternal deficiency include insufficient sunlight exposure and poor dietary intake of vitamin D.[9] Moreover, pregnancy itself has been proposed as a risk factor, especially in women residing in high-altitude regions.[10,11] Adverse maternal and neonatal outcomes linked to low vitamin D include gestational diabetes, preeclampsia, intrahepatic cholestasis of pregnancy, cesarean deliveries, preterm labor, postpartum hemorrhage, and suboptimal immune, neural, and skeletal development in the fetus. For adequate vitamin D synthesis, 5–30 minutes of sun exposure to the face, arms, legs, or back without sunscreen between 10 AM and 3 PM at least twice a week is sufficient.

Limited sunlight exposure and inadequate dietary intake are major contributors to maternal vitamin D deficiency.[9] Additionally, pregnancy itself is considered a predisposing factor, particularly among women living at higher altitudes.[10,11] Deficient maternal vitamin D levels have been associated with various negative outcomes, including gestational diabetes, preeclampsia, intrahepatic cholestasis of pregnancy, increased risk of cesarean delivery, preterm birth, and postpartum hemorrhage. In the fetus, insufficient vitamin D can impair immune function and hinder proper neurological and skeletal development. To support optimal vitamin D production, it is generally recommended to have sun exposure without sunscreen on the face, arms, legs, or back for about 5 to 30 minutes between 10 AM and 3 PM, at least two times per week.[12]

Other complications may include neonatal cardiovascular and respiratory dysfunction, type I diabetes, and rickets.[13-15] Elevated maternal 25(OH)D levels have been associated with extended gestational duration. For instance, 25(OH)D concentrations below 40 ng/mL have been shown to increase the risk of preterm delivery by 60% in general obstetric populations at urban medical centers.[16] In the Middle Eastern region, vitamin D deficiency prevalence in pregnant women ranges from 24.5% to 98%, while in neonates it spans 22% to 100%.[13] Evidence from clinical trials indicates that a daily dose of 30 mg of vitamin D during pregnancy can ensure adequate vitamin D levels in both mother and newborn.[17] Moreover, supplementation has been shown to reduce complications associated with maternal and neonatal deficiency.[15] The vitamin D content of breast milk is also critical, and maternal supplementation during lactation can enhance infant vitamin D status.[18]

Vitamin D deficiency is now recognized as one of the most common and under-treated nutritional deficiencies globally.[19,20] Deficiency during pregnancy is particularly concerning due to its heightened risk for both mother and child. Approximately one billion individuals worldwide are either vitamin D deficient or insufficient. Globally, deficiency prevalence is estimated between 54% and 100%, while insufficiency rates fall between 39% and 76%.[21] In Asia, including sunlight-rich countries like India, deficiency remains highly prevalent. Studies report rates of 93% in Delhi, 97% in Bangalore, and 94% in Mumbai.[22,23] Vitamin D status is commonly assessed by measuring circulating 25(OH)D levels, the biomarker of nutritional sufficiency. There is, however, no universal consensus on the exact cut-off for defining deficiency during pregnancy, with thresholds ranging between 10 and 32ng/mL. According to the American College of Obstetricians and Gynecologists

(ACOG), a minimum of 20 ng/mL is necessary to prevent bone-related complications, while deficiency is identified at levels below 32 ng/mL. The Endocrine Society classifies serum levels below 20 ng/mL as deficient and those between 20 and 30 ng/mL as insufficient.[24] Although evidence for outcomes with levels above 30 ng/mL is still evolving, maintaining a minimum of 30 ng/mL during pregnancy is generally recommended to ensure better maternal and fetal outcomes.
This study aims to evaluate the prevalence of vitamin D deficiency among pregnant women and its direct correlation with neonatal vitamin D levels in a North Indian tertiary care center.

AIMS AND OBJECTIVES

1. To assess the relationship between maternal vitamin D levels and neonatal cord blood vitamin D levels.
2. To evaluate the association of maternal vitamin D status with neonatal outcomes, including birth weight and NICU admission.

MATERIAL AND METHODS

The present prospective observational study was conducted in the Postgraduate Department of Paediatrics and Neonatology, Government Medical College, Srinagar, Jammu and Kashmir. A total of 100 pregnant women aged 20-40 years, at ≥37 weeks of gestation, presenting in active labor, were recruited after informed consent.

Inclusion Criteria:

- Singleton pregnancy
- Gestational age between 37–42 weeks
- No known chronic illness or supplementation with high-dose vitamin D

Exclusion Criteria:

- Pre-existing metabolic or endocrine disorders
- History of preeclampsia, GDM, or multiple gestation
- Neonatal anomalies

Demographic information, obstetric history, and supplementation practices were recorded. Blood samples were collected from mothers during labor and cord blood was drawn post-delivery. Serum 25(OH)D levels were measured using enzyme-linked immunosorbent assay (ELISA). Vitamin D was classified as per Aly H et al., (2013)[25] wherein vitamin D of <30nmol/L was considered as deficient, 30-50nmol/L as insufficient and >50nmol/L as sufficient.
Data obtained was saved in Microsoft Excel Spreadsheet and analysed using Statistical Package for Social Science (SPSS Ver. 23). Correlation between maternal and neonatal vitamin D was assessed using Pearson's correlation. Chi-square test was used for categorical variables. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Maternal serum 25(OH)D3 (nmol/L) and Neonatal serum 25(OH)D3 (nmol/L)

Variables	Categories	No. of Patients	Percentage	P Value
Maternal serum 25(OH)D3 (nmol/L)	Deficient (<30nmol/l)	56	56.00	0.001
	Insufficient (30-50 nmol/l)	34	34.00	
	Sufficient (>50 nmol/l)	10	10.00	
Neonatal serum 25(OH)D3 (nmol/L)	Deficient (<30nmol/l)	58	58.00	
	Insufficient (30-50 nmol/l)	31	31.00	
	Sufficient (>50 nmol/l)	11	11.00	

The table presents the distribution of vitamin D status among 100 mother–infant dyads, categorized based on serum 25(OH)D_3 levels into three groups: deficient (<30 nmol/L), insufficient (30–50 nmol/L), and sufficient (>50 nmol/L), for both mothers and neonates. Among mothers, 56% (n=56) were vitamin D deficient, 34% (n=34) had insufficient levels, and only 10% (n=10) had sufficient vitamin D levels. In neonates, 58% (n=58) were found to be vitamin D deficient, 31% (n=31) insufficient, and 11% (n=11) sufficient. A comparison between maternal and neonatal vitamin D status demonstrated a statistically significant association with a p-value of 0.001. This finding suggests a strong correlation between maternal serum 25(OH)D_3 levels during pregnancy and the corresponding neonatal vitamin D status at birth. The results reinforce the importance of optimizing maternal vitamin D levels to prevent neonatal deficiency.

Table 2: Maternal Age Distribution by Vitamin D Groups

Age Group	**Maternal serum 25(OH)D3 (nmol/L)**			**Total**	**P value**
	Deficient (<30nmol/l)	**Insufficient (30-50 nmol/l)**	**Sufficient (>50 nmol/l)**		
20-30 years	30	22	5	57	0.524
30-40 years	26	12	5	43	
Total	56	34	10	100	

Table illustrates the distribution of maternal age across three categories of maternal serum 25(OH)D_3 levels—Deficient (<30 nmol/L), Insufficient (30–50 nmol/L), and Sufficient (>50 nmol/L)—in a cohort of 100 pregnant women. Out of 57 women aged 20–30 years, 30 (52.6%) were vitamin D deficient, 22 (38.6%) had insufficient levels, and only 5 (8.8%) had sufficient vitamin D levels. Among the 43 women aged 30–40 years, 26 (60.5%) were vitamin D deficient, 12 (27.9%) had insufficient levels, and 5 (11.6%) had sufficient vitamin D. Although a higher proportion of vitamin D deficiency was observed in the older age group (30–40 years), the difference in age distribution across the three vitamin D status groups was not statistically significant, with a p-value of 0.5241. This suggests that maternal age did not have a significant association with vitamin D status in this study population.

Table 3: Parity Distribution by Vitamin D Groups

Parity	**Maternal serum 25(OH)D3 (nmol/L)**			**Total**	**P value**
	Deficient (<30nmol/l)	**Insufficient (30-50 nmol/l)**	**Sufficient (>50 nmol/l)**		
Nulliparous (0)	10	2	0	12	0.047
Primiparous (1)	15	13	3	31	
Multiparous (≥2)	31	19	7	57	
Total	56	34	10	100	

Above table shows the distribution of parity among 100 pregnant women in relation to their maternal serum 25(OH)D_3 levels, categorized as Deficient (<30 nmol/L), Insufficient (30–50 nmol/L), and Sufficient (>50 nmol/L). Among the 12 nulliparous women (Parity 0), 10 (83.3%) were vitamin D deficient, 2 (16.7%) were insufficient, and none had sufficient levels. In the primiparous group (Parity 1, n=31), 15 women (48.4%) were deficient, 13 (41.9%) were insufficient, and 3 (9.7%) were sufficient. In the multiparous group (Parity ≥2, n=57), 31 (54.4%) were deficient, 19 (33.3%) insufficient, and 7 (12.3%) sufficient. The association between parity and maternal vitamin D status was statistically significant, with a p-value of 0.047, indicating that parity may influence vitamin D levels during pregnancy. Notably, vitamin D deficiency was most prominent among nulliparous women.

Table 4: Maternal Pre-Pregnancy BMI Distribution by Vitamin D Groups

BMI (kg/m^2)	**Maternal serum 25(OH)D3 (nmol/L)**			**Total**	**P value**
	Deficient (<30nmol/l)	**Insufficient (30-50 nmol/l)**	**Sufficient (>50 nmol/l)**		
Underweight (<24.9)	22	4	2	28	0.047
Normal weight (25–29.9)	14	12	4	30	
Overweight (≥30)	20	18	4	42	
Total	56	34	10	100	

Table presents the distribution of maternal pre-pregnancy Body Mass Index (BMI) among 100 pregnant women categorized according to their serum 25(OH)D_3 levels as Deficient (<30 nmol/L), Insufficient (30–50 nmol/L), and Sufficient (>50 nmol/L). Among the 28 underweight women (BMI <24.9), 22 (78.6%) were vitamin D deficient, 4 (14.3%) were insufficient, and only 2 (7.1%) were sufficient. Of the 30 women with normal BMI (25–29.9), 14 (46.7%) were deficient, 12 (40.0%) insufficient, and 4 (13.3%) sufficient. In the overweight group (BMI ≥30, n=42), 20 women (47.6%) were deficient, 18 (42.9%) were insufficient, and 4 (9.5%) had sufficient levels. The association between BMI and maternal vitamin D status was statistically significant with a p-value of 0.047, indicating that pre-pregnancy BMI may influence maternal vitamin D levels. Notably, underweight women showed the highest proportion of deficiency, suggesting a possible nutritional vulnerability in this group.

Table 5: Sun Exposure Distribution by Vitamin D Groups

Sun Exposure	**Maternal serum 25(OH)D3 (nmol/L)**			**Total**	**P value**
	Deficient (<30nmol/l)	**Insufficient (30-50 nmol/l)**	**Sufficient (>50 nmol/l)**		
Positive	6	18	6	30	0.0002
Negative	50	16	4	70	
Total	56	34	10	100	

Table displays the distribution of maternal serum 25(OH)D_3 levels in relation to sun exposure among 100 pregnant women. Participants were categorized into three vitamin D status groups—Deficient (<30 nmol/L), Insufficient (30–50 nmol/L), and Sufficient (>50 nmol/L). Among women who reported positive sun exposure (n=30), only 6 (20%) were vitamin D deficient, whereas 18 (60%) were insufficient, and 6 (20%) had sufficient vitamin D levels. In contrast, among those with negative sun exposure (n=70), a significantly higher proportion, 50 (71.4%), were vitamin D deficient, with only 16 (22.9%) insufficient and 4 (5.7%) sufficient. The association between sun exposure and maternal vitamin D status was found to be highly statistically significant with a p-value of 0.0002, indicating that lack of sunlight exposure is strongly associated with a higher risk of vitamin D deficiency in pregnancy.

DISCUSSION

The present study was conducted to examine how maternal vitamin D levels influence neonatal vitamin D status, and the findings not only reaffirm existing evidence but also draw attention to specific demographic and clinical contributors to vitamin D deficiency among both mothers and their newborns.

A substantial proportion of both mothers (56%) and neonates (58%) were found to be deficient in vitamin D, with only 10% of mothers and 11% of neonates showing sufficient levels. A significant statistical association ($p = 0.001$) between maternal and neonatal vitamin D status was identified, supporting the hypothesis that neonatal vitamin D levels are closely linked to maternal status. These observations are consistent with those by **Aly et al. (2013)**[25], who reported a strong positive correlation ($r = 0.89$, $p = 0.01$) between maternal and neonatal 25(OH)D_3 levels. They demonstrated that fetal vitamin D reserves depend directly on maternal concentrations. Similarly, **Ghafarzadeh et al. (2021)**[26] found a deficiency rate of 60.9% in mother–infant pairs and reported a statistically significant relationship ($p = 0.001$) between maternal serum 25(OH)D and neonatal cord blood levels, highlighting the importance of supplementation during pregnancy. According to **Seth et al. (2024)**[27], neonates born to vitamin D-deficient mothers were more likely to require NICU care, and maternal deficiency was associated with complications such as low birth weight and intrauterine growth restriction. **Chien et al. (2024)**[28], in their umbrella review, further confirmed that maternal hypovitaminosis D significantly elevates the risk of neonatal deficiency and related morbidities. Their analysis emphasized that maternal supplementation above 400 IU/day helps mitigate these risks.

This study also explored the relationship between maternal age and vitamin D status among 100 participants. Of the women aged 20–30 years (n = 57), 52.6% were deficient, 38.6% insufficient, and

8.8% sufficient. In the 30–40 year age group (n = 43), deficiency increased to 60.5%, insufficiency was 27.9%, and sufficiency was slightly higher at 11.6%. However, the association between age and vitamin D status was not statistically significant (p=0.5241). These results align with findings from **Aly et al. (2013)**[25], who reported that vitamin D deficiency occurred across all age groups without significant differences, implying that age alone may not be a determinant. **Ghafarzadeh et al. (2021)**[26] similarly found no significant age-related variation in vitamin D levels among Iranian women. Although **Seth et al. (2024)**[27] observed that a majority of deficient mothers were under 30, they did not find a statistically meaningful correlation between age and serum levels, pointing instead to socio-demographic variables like rural residence and absence of supplementation. **Nageshu et al. (2016)**[29] also reported widespread deficiency among pregnant women, regardless of age group, indicating that other modifiable risk factors are more impactful.

Parity was found to be significantly related to maternal vitamin D levels (p = 0.047). Among nulliparous women (n = 12), 83.3% were deficient and none had sufficient levels. Primiparous women (n = 31) showed 48.4% deficiency and 9.7% sufficiency, while among multiparous women (n = 57), 54.4% were deficient and 12.3% were sufficient. These data suggest that vitamin D levels tend to be lower in first-time mothers. This observation corresponds with the study by **Aly et al. (2013)**[25], who found that nulliparous women had significantly lower serum 25(OH)D_3 levels than multiparous women, potentially due to greater awareness and supplement use in subsequent pregnancies. **Seth et al. (2024)**[27] also found a significant relationship between parity and deficiency, noting that the most severe deficiencies were common among nulliparous women. **Ghafarzadeh et al. (2021)**[26], however, reported no significant parity-wise difference in vitamin D status, reinforcing the idea that universal risk factors like poor sun exposure and dietary intake might overshadow parity as a variable.

The study also showed a significant link between pre-pregnancy BMI and maternal vitamin D status (p = 0.047). Among underweight women (BMI <24.9; n = 28), 78.6% were deficient. For women with normal BMI (25–29.9; n = 30), the deficiency rate dropped to 46.7%, and in the overweight group (BMI ≥30; n = 42), 47.6% were deficient. Notably, vitamin D sufficiency was highest in the normal BMI group (13.3%), compared to the underweight (7.1%) and overweight (9.5%) groups. These findings are consistent with those of **Ghafarzadeh et al. (2021)**[26], who found lower serum 25(OH)D levels in women with lower BMI. Although their study did not present BMI-stratified percentages, the 60.9% overall deficiency rate closely mirrors our findings. **Aly et al. (2013)**[25] similarly noted higher deficiency rates in women with low BMI or poor nutritional status. **Seth et al. (2024)**[27] also observed that a majority of deficient cases were from rural, undernourished populations, again reinforcing the association between low BMI and vitamin D deficiency.

Sunlight exposure was found to have a highly significant association with maternal vitamin D levels (p = 0.0002). Among women with regular sun exposure (n = 30), only 20% were deficient, compared to 71.4% of those with little or no sun exposure (n = 70). Furthermore, vitamin D sufficiency was more prevalent in the sun-exposed group (20%) than the non-exposed (5.7%). These results are well-supported by **Ghafarzadeh et al. (2021)**[26], who found that 84.6% of women with deficiency reported inadequate sun exposure, whereas 77.4% of sufficient cases had adequate exposure. **Aly et al. (2013)**[25] also highlighted that reduced sunlight exposure significantly impacted both maternal and neonatal vitamin D status. **Seth et al. (2024)**[27], while not directly quantifying sun exposure, linked high deficiency rates to rural residence and cultural clothing practices that reduce UV exposure. **Chien et al. (2024)**[28] further validated these findings in their review, identifying inadequate UVB exposure as one of the most modifiable and impactful risk factors for hypovitaminosis D during pregnancy. The disparity observed in the current study, deficiency rates of 71.4% vs. 20% clearly illustrates the protective effect of sunlight.

CONCLUSION

Routine screening and supplementation of vitamin D should be integrated into antenatal care, with special focus on women with low sun exposure, abnormal BMI, or first-time pregnancies, alongside health education promoting safe sun exposure and nutritional counseling to prevent maternal and neonatal vitamin D deficiency. The study conclusively establishes that maternal vitamin D status is significantly influenced by sun exposure, pre-pregnancy BMI, and parity, and directly determines neonatal vitamin D levels. Deficiency was most severe in underweight, nulliparous women with poor sun exposure. These findings emphasize the need for routine vitamin D screening and targeted supplementation during pregnancy to prevent neonatal deficiency and its associated risks.

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