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Original Article

Factors affecting Umbilical Cord Vitamin D Concentration and Its Association with Maternal Vitamin D Level

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Abstract

Objective: To analyze factors affecting maternal and umbilical cord levels of vitamin D and to understand the correlation between maternal and umbilical cord vitamin D levels.

Methods: This was a cross-sectional study conducted at the department of pediatrics of Dr. D. Y. Patil Medical College and Research Centre, Pune, India. Maternal and umbilical cord vitamin D levels were examined in 300 pairs of mother and child over a period of two years. Informed consent was obtained from all participants. The vitamin D level was measured using chemiluminescent immunoassay and classified as either deficient, insufficient or adequate depending on specific cut-offs. Correlations between maternal and neonatal vitamin D levels and demographic factors like religion, socioeconomic status, and sun exposure were also exlored. Statistical tests were performed using the SPSS 21.0 software, with p<0.05 deemed p-valueas significant.

Results: There was significantly high prevalence of vitamin D deficiency in neonates, (78.67%). Key factors influencing maternal vitamin D levels were religion (p=0.027), maternal education (p=0.003), gravida status (p=0.035), and sunlight exposure, with sunlight exposure showing a very strong correlation to the deficiency (p<0.001). Moreover, maternal serum calcium levels significantly affected vitamin D status (p<0.001). A significant association was observed between maternal and cord blood vitamin D levels, with the maternal vitamin D level strongly predicted vitamin D status in neonates (p<0.001).

Conclusion: The umbilical cord vitamin D level strongly correlates with the maternal vitamin D level, which is significantly affected by maternal education, residence, pregnancy status, gestational age, and sun exposure.

Keywords: Fetal development, neonate, pregnancy, vitamin D

Introduction

Vitamin D is a fat-soluble vitamin (secosteroid) obtained by the human body in two ways: through dietary intake, mainly from fatty fish, eggs, and fortified foods, and through endogenous production in the skin after ultraviolet-B exposure. This vitamin involved in the uptake and degradation of calcium and phosphorus in bones from serum. In addition, vitamin D has been shown to play a role in cell differentiation, cell growth, metabolism, and immunity. There is an increasing interest in analyzing the role of vitamin D in these non-classical functions.[1]

A population of particular interest in the emerging vitamin D narrative is the pregnant women. The role of vitamin D during pregnancy is particularly crucial due to the dependence of the growing fetus on its mother for sufficient vitamin D.[2] Since vitamin D levels tend to be lower during pregnancy than in comparable non-pregnant women.[3], there is controversy surrounding the optimal vitamin D levels for the fetus, its effects on various outcomes, and the relationship between maternal and fetal vitamin D. During pregnancy, maternal serum concentrations of 25(OH)D3 correlate with dietary vitamin D intake as well as vitamin D supplementation.[4]

It has been demonstrated that the maternal serum concentration of 1,25-dihydroxyvitamin D_3, the circulating and active form of vitamin D is significantly elevated during pregnancy.[5] During fetal intrauterine development, the production of the 1,25-dihydroxyvitamin D3 is primarily done by the placental decidual cells, which facilitates enhanced calcium absorption. The fetus relies entirely on maternal 25(OH) D3, which is thought to cross the placenta. After birth, both full-term and preterm neonates experience hypocalcemia, which, along with increased secretion of parathyroid hormone, stimulates the production of 1,25-dihydroxyvitamin D.

Adequate intake of vitamin D is important during pregnancy due to possible associations between maternal vitamin D levels and fetal and infant outcomes. Insufficient or deficient levels of vitamin D in mothers have been linked to an increased risk of gestational diabetes and preeclampsia.[7] Also, vitamin D deficiency during pregnancy has been associated with various negative health outcomes in offsprings, including a higher incidence of abortion, low birth weight, neonatal hypocalcemia, impaired development, and rickets.[8]

Many studies have reported a significant association between cord blood vitamin D levels and maternal serum vitamin D levels; however, it remains unclear how strong these two are interrelated. Furthermore, there is a lack of studies regarding these associations, particularly in the Indian population. If a significant association between maternal vitamin D levels and cord vitamin D levels can be established, it could have important implications for both maternal and child health. These findings could be crucial for a country like India, where infant mortality rates are high, in its progress toward achieving Millennium Development Goals in these parameters.[9]

This study was undertaken to analyze the factors affecting both maternal and cord vitamin D levels and to determine the correlation between them

Methods

It was a cross-sectional study carried out in the Department of Pediatrics at Dr. D. Y. Patil Medical College and Research Centre, Pimpri, Pune, India. The duration of the study was 2 years, extending from December 2021 to November 2023. The study comprised healthy women aged between 18 and 40 years and their newborns delivered at this institute, with all mothers providing informed and written consent to participate.

Exclusion criteria included refusal to give consent, mothers below 18 years or above 40 years, and those with a history of thyroid or parathyroid hormone abnormalities, chronic renal failure, or chronic liver disease. Informed and written consent was obtained from all participants. The sample size was calculated based on pilot studies conducted on the estimation of cord vitamin D in newborns. Considering a 90% power and a 95% confidence interval, the required sample size was determined to be 250 samples. Based on the central limit theorem, a sample size of more than 250 was assumed to be sufficient. Thus, 300 blood samples were included in this study. A detailed maternal history was obtained to identify the presence of disorders known to affect maternal serum calcium levels, such as thyroid and parathyroid diseases, chronic renal failure, or liver diseases. After ruling out any significant maternal illness, 300 pairs of cord blood samples and maternal blood samples were collected from mothers who met the inclusion criteria and provided written consent after the procedure was fully explained to them. For each neonate, 3 mL of blood from the umbilical cord was collected in an EDTA-containing tube, then centrifuged at 3,000 rpm for 10 minutes. The serum was separated and stored as 1 mL aliquots at −20°C until analysis; the same process was followed for the maternal samples. The serum levels of 25-hydroxy vitamin D were measured using chemiluminescent immunoassay (CLIA). Vitamin D levels were categorized based on the following cut-offs: below 30 nmol/L as deficient, 30–50 nmol/L as insufficient, and above 50 nmol/L as adequate.

The correlation between cord blood and maternal vitamin D levels was examined. Additionally, the variation of vitamin D levels with different gestational ages and neonatal birth weights was assessed. The relationship between maternal and neonatal vitamin D levels and various demographic and lifestyle factors—including the mother's religion, habitat, socioeconomic status, education, number of pregnancies, parity, sun exposure, and dietary habits—was also analyzed.

Data were presented as mean ± standard

Table 1 Mean Age of Mothers and Its Correlation with Maternal Levels of Vitamin D

		Deficient	Insufficient	Sufficient	p-value
Age	Mean ± SD	24.58±3.03	25.11±3.65	25.25±4.37	0.483
	Min.-max.	19–35	20–35	21–32	

deviation (X±SD) or percentage (%). Linear correlation and regression were used to test the relationships between the measured parameters. Cut-off values were calculated from the receiver operating characteristics (ROC) curve as mean±2 SD of the control group. For comparisons of quantitative data between groups, an unpaired t-test was applied. Data were tabulated and statistically analyzed using the Statistical Package for Social Sciences (SPSS) version 21.0 software. A p-value of less than 0.05 was considered statistically significant.

Results

The maternal ages of women whose babies were sampled for cord vitamin D levels ranged from 19 to 35 years. The mean age for the deficient group was 24.58±3.03 years, for the insufficient group it was 25.11±3.65 years, and for the sufficient group it was 25.25 ± 4.37 years. The mother's age as a factor influencing variability in cord blood vitamin D levels was found to be statistically insignificant (p= 0.483) (Table 1).

The analysis of cord vitamin D levels in neonates showed that the majority, 236 (78.67%), were found to be deficient in cord blood vitamin D at the cut-off point of serum calcidiol levels (25(OH)D) <20 ng/mL (< 50 nmol/L). Out of a total of 300 cord blood samples, only 8 had sufficient vitamin D levels >30 ng/mL (>75 nmol/L), while 56 samples had insufficient levels between 20–30 ng/mL (50–75 nmol/L) (Table 2).

Analysis on the factors affecting maternal vitamin D levels revealed a significant correlation with religion (p-value of 0.027). Hindu participants showed higher sufficiency rates (6.8%) compared to Muslims, who had no sufficient cases. However, the area of residence did not show a significant correlation with vitamin D levels, as indicated by a p-value of 0.938, suggesting that living in either rural or urban areas does not significantly affect vitamin D status. Maternal education approached significance (p-value of 0.051), indicating a potential influence, with higher education groups showing lower sufficiency rates. Socioeconomic status, with a p-value of 0.090, also suggested a possible effect but was not statistically significant, indicating minor variations across economic groups. Maternal gravida status (p-value of 0.027) showed a notable distinction, with primigravida mothers having a higher sufficiency rate (10.8%) compared to multigravida mothers (3.2%), highlighting how the number of pregnancies may affect vitamin D levels. Conversely maternal parity (p-value of 0.584) showed no significant influence, indicating that parity does not significantly alter vitamin D levels. Dietary habits of the mother were not significantly correlated with vitamin D levels (p-value of 0.093), although vegetarian mothers exhibited slightly higher sufficiency (9.6%). A strong correlation was observed with maternal exposure to sunlight, evidenced by a highly significant p-value of <0.001; inadequate sun exposure resulted in a 94.9% deficiency rate. Gestational age and birth weight both showed no significant differences in vitamin D levels, with p-values of 0.093 and 0.908, respectively (Table 3).

Table 2 Status of Cord Vitamin D Levels

Cord Vitamin D Level	Frequency (n=300)	%
Deficient	236	78.67
Insufficient	56	18.67
Sufficient	8	2.67

The study of various factors influencing cord blood vitamin D levels among the cases examined revealed significant findings for several variables. Religion (p-value=0.151) and socioeconomic status (p-value=0.597) did not significantly impact vitamin D levels, despite differences in deficiency rates between religious groups and across socioeconomic categories. In contrast, area of residence (p-value=0.026) demonstrated a notable difference, with rural residents experiencing higher deficiency rates than urban dwellers. Maternal education significantly influenced vitamin D status (p-value=0.003), with higher education levels correlating with better vitamin D levels. Maternal gravida status (p-value=0.035) and gestational age (p-value

=0.046) also demonstrated significant associations, indicating that physiological changes during pregnancy affect vitamin D synthesis. Meanwhile, maternal parity (p-value=0.819) and the gender of the neonate (p-value=0.390) did not present significant differences. Dietary habits did not significantly affect the vitamin D levels (p-value=0.080). Most strikingly, inadequate maternal sun exposure (p-value <0.001) resulted in a 100%

Table 3 Factors Affecting Maternal Serum Vitamin D Levels

Factors Affecting Maternal Serum Vitamin D Levels		Total (n=300)	Maternal Serum Vitamin D Levels			p-value
			Deficient (n=236) (%)	Insufficient (n=56) (%)	Sufficient (n=18) (%)	
Religion	Hindu	266	167 (62.8)	81 (30.5)	18 (6.8)	0.027
	Muslim	34	29 (85.3)	5 (14.7)	0 (0.0)	
Area of residence	Rural	157	104 (66.2)	44 (28)	9 (5.7)	0.938
	Urban	143	92 (64.3)	42 (29.4)	9 (6.3)	
Maternal education	Primary	19	15 (78.9)	4 (21.1)	0 (0.0)	0.051
	Secondary	61	35 (57.4)	19 (31.1)	7 (11.5)	
	Senior secondary	85	55 (64.7)	26 (30.6)	4 (4.7)	
	Graduate	101	61 (60.4)	33 (30.6)	7 (4.7)	
	Above	34	30 (88.2)	4 (11.8)	0 (0.0)	
Socio economic status of the family	Lower	2	2 (100.0)	0 (0.0)	0 (0.0)	0.090
	Upper lower	82	57 (69.5)	20 (24.4)	5 (6.1)	
	Lower middle	86	46 (53.5)	36 (41.9)	4 (4.7)	
	Upper middle	124	85 (68.5)	30 (24.2)	9 (7.3)	
	Upper	6	6 (100)	0 (0.0)	0 (0.0)	
Maternal gravida	Primigravida	111	59 (53.2)	40 (36)	12 (10.8)	0.027
	Multigravida	189	137 (72.5)	46 (24.3)	6 (3.2)	
Maternal parity	Nulliparous	238	154 (64.7)	68 (28.6)	16 (6.7)	0.584
	Multiparous	62	42 (67.7)	18 (29)	2 (3.2)	
Maternal dietary habits	Vegetarian	114	74 (64.9)	29 (25.4)	11 (9.6)	0.093
	Non-vegetarian	186	122 (65.6)	57 (30.6)	7 (3.8)	
Maternal exposure to sun	Inadequate	117	111 (94.9)	6 (5.1)	0 (0.0)	<0.001
	Adequate	183	85 (46.4)	80 (43.7)	18 (9.8)	
Gestational age	Pre-term	79	52 (65.8)	21 (26.6)	6 (7.6)	0.093
	Term	152	104 (68.4)	41 (27)	7 (4.6)	
	Post-term	38	24 (63.2)	14 (36.8)	0 (0.0)	
	Post	31	16 (51.6)	10 (32.3)	5 (16.1)	
Birth weight	Very low	29	19 (65.5)	8 (27.6)	2 (6.9)	0.908
	Low	69	47 (68.1)	20 (29)	2 (2.9)	
	Normal	201	129 (64.2)	58 (28.9)	14 (7.0)	
	Above	1	1 (100)	0 (0.0)	0 (0.0)	

deficiency rate, emphasizing the critical role of sunlight in vitamin D synthesis. Additionally, maternal serum calcium (p-value < 0.001) and maternal serum alkaline phosphatase (p-value =0.050) highlighted biochemical factors that significantly affect vitamin D levels, with calcium showing nearly universal deficiency among those with inadequate levels, and

Table 4 Factors Affecting Cord Vitamin D Levels

Factors Affecting Cord Blood Vitamin D Level		Total (n=300)	Cord Blood Vitamin D Level			p-value
			Deficient (n=236) (%)	Insufficient (n=56) (%)	Sufficient (n=18) (%)	
Religion	Hindu	266	205 (77.1)	53 (19.9)	8 (3)	0.151
	Muslim	34	31 (91.2)	3 (8.8)	0 (0.0)	
Area of residence	Rural	157	130 (82.8)	21 (13.4)	6 (3.8)	0.026
	Urban	143	106 (74.1)	35 (24.5)	2 (1.4)	
Maternal education	Primary	19	17 (89.5)	2 (10.5)	0 (0.0)	0.003
	Secondary	61	46 (75.4)	11 (18)	4 (6.6)	
	Senior Secondary	85	66 (77.6)	15 (17.6)	4 (4.7)	
	Graduate	101	73 (72.3)	28 (27.7)	0 (0.0)	
	Above	34	34 (100)	0 (0.0)	0 (0.0)	
Socio economic status of the family	Lower	2	2 (100)	0 (0.0)	0 (0.0)	0.597
	Upper Lower	82	62 (75.6)	18 (22)	2 (2.4)	
	Lower Middle	86	63 (73.3)	19 (22.1)	4 (4.7)	
	Upper Middle	124	103 (83.1)	19 (15.3)	2 (1.6)	
	Upper	6	6 (100)	0 (0.0)	0 (0.0)	
Maternal gravida	Primigravida	111	80 (72.1)	29 (26.1)	2 (1.8)	0.035
	Multigravida	189	156 (82.5)	27 (14.3)	6 (3.2)	
Maternal parity	Nulliparous	238	186 (78.2)	46 (19.3)	6 (2.5)	0.819
	Multiparous	62	50 (80.6)	10 (16.1)	2 (3.2)	
Maternal dietary habits	Vegetarian	114	89 (78.1)	19 (16.7)	6 (5.3)	0.080
	Non-Vegetarian	186	147 (79)	37 (19.9)	2 (1.1)	
Maternal exposure to sun	Inadequate	117	117 (100)	0 (0.0)	0 (0.0)	<0.001
	Adequate	183	119 (65)	56 (30.6)	8 (4.4)	
Gender of neonate	Male	165	131 (79.4)	28 (17)	6 (3.4)	0.390
	Female	135	105 (77.8)	28 (20.7)	2 (1.5)	
Gestational age	Pre-Term	79	58 (73.4)	17 (21.4)	4 (5.1)	0.046
	Term	159	128 (84.2)	20 (13.2)	4 (2.6)	
	Post-Term	38	30 (78.9)	18 (21.1)	0 (0.0)	
	Post Dated	31	20 (64.5)	11 (35.5)	0 (0.0)	

Table 4 Continued

Factors Affecting Cord Blood Vitamin D Level		Total (n=300)	Cord Blood Vitamin D Level			p-value
			Deficient (n=236) (%)	Insufficient (n=56) (%)	Sufficient (n=18) (%)	
Birth weight	Very Low	29	21 (72.4)	6 (20.7)	2 (6.9)	0.602
	Low	69	58 (84.1)	9 (13)	2 (2.9)	
	Normal	201	156 (77.6)	41 (20.4)	4 (2)	
	Above	1	1 (100)	0 (0.0)	0 (0.0)	
Maternal serum calcium	Inadequate	78	75 (96.2)	3 (3.8)	0 (0.0)	
	Normal	222	161 (72.5)	53 (23.9)	8 (3.6)	<0.001
Maternal serum alkaline phosphatase	Normal	21	19 (61.9)	8 (38.1)	0 (0.0)	
	Excess	279	223 (79.9)	48 (17.2)	8 (2.9)	0.050

alkaline phosphatase levels correlating with higher deficiencies, possibly due to their roles in metabolic health (Table 4).

Cord blood vitamin D levels were shown to be significantly associated with vitamin D levels in maternal blood. Among 300 maternal blood samples, only 18 were found to have sufficient vitamin D levels (>30 ng/mL). Of the babies born to mothers in the deficient group, 98.5% were found to be deficient in vitamin D levels. In contrast, none of the neonates born to mothers with sufficient vitamin D levels were found to be deficient. The correlation between maternal vitamin D levels and cord blood vitamin D levels was found to be statistically highly significant ($p<0.001$) (Table 5).

Discussion

Vitamin D deficiency in pregnant women is considered a major global health problem, and despite abundant sunlight, its prevalence is high in Asian countries, including India. Many recent studies have concluded that low levels of vitamin D in maternal serum depend on a number of factors, including climate, culture, and dietary habits. Numerous studies document that newborns receive their vitamin D entirely from their mothers' vitamin D stores. Both low maternal and cord blood vitamin D levels have been linked to adverse outcomes in pregnant mothers and neonates. Therefore, the importance of early detection and correction of low maternal vitamin D levels may lead to improvements in maternal and child health indices.[10]

In this study, religion was found to significantly correlate with vitamin D levels, with Hindu mothers exhibiting higher sufficiency rates compared to Muslim mothers, who had none. Additionally, maternal gravida status played a notable role; primigravida

Table 5 Correlation Between Maternal and Cord Vitamin D Levels

Maternal Vitamin D	Total (n=300)	Cord Blood Vitamin D Level			p-value
		Deficient	Insufficient	Sufficient	
		Frequency (n=236) (%)	Frequency (n=56) (%)	Frequency (n=18) (%)	
Deficient	196	193 (98.5)	3 (1.5)	0 (0.0)	<0.001
Insufficient	86	43 (50)	43 (50)	0 (0.0)	
Sufficient	18	0 (0.0)	10 (55.6)	8 (44.4)	

mothers had higher vitamin D sufficiency than multigravida mothers. Other factors, such as area of residence, maternal education, socioeconomic status, maternal parity, dietary habits, gestational age, and birth weight, did not show a significant impact on vitamin D levels. Notably, maternal exposure to sunlight was strongly correlated; inadequate sun exposure was associated with a high deficiency rate. While this study provides significant insights into the correlation between maternal and neonatal vitamin D levels, it is important to acknowledge additional factors that may contribute to vitamin D deficiency. Factors such as maternal BMI, physical activity, skin pigmentation, and seasonality are crucial determinants of vitamin D status. Higher BMI has been associated with lower vitamin D levels due to the sequestration of the vitamin in adipose tissue. Similarly, limited physical activity, darker skin pigmentation, and lack of seasonal sunlight exposure are known to affect the synthesis of vitamin D.[11]

Aji conducted a study to assess the serum levels of 25-hydroxyvitamin D (25(OH)D) in the first trimester and its associated factors, including socio-demographics, pregnancy profiles, dietary intake, and maternal anthropometric measurements.[12] The study identified significant independent predictors such as being unemployed, having nulliparous parity, engaging in less than an hour of outdoor activity daily, and not taking supplements prior to pregnancy. Similar observations were reported by authors such as Brian-D Adinma *et al*.[13] and Ates *et al*.[14]

Significant maternal factors affecting cord blood vitamin D levels included area of residence, maternal education, maternal gravida status, gestational age, maternal serum calcium, maternal serum alkaline phosphatase, and maternal sun exposure. In contrast, maternal factors that did not significantly affect vitamin D levels were religion, socioeconomic status, maternal parity, gender of the neonate, and dietary habits. Fink *et al*. undertook a review study to assess factors affecting vitamin D status in infancy, such as the intake of antenatal and postnatal vitamin D supplementation.[15] The review found significant associations between dietary intake, UV exposure, latitude, seasonal variation, and infants' vitamin D status. Although some associations between genetic variation, ethnicity, socioeconomic status, and vitamin D levels have been reported, these were not found to be significantly associated. Similar findings were also reported by authors such as Jamali *et al*[16] and Aletayeb *et al*.[17]

Cord blood vitamin D levels were significantly associated with maternal vitamin D levels; 98.5% of babies born to deficient mothers were also deficient in vitamin D levels. None of the neonates born to mothers with sufficient vitamin D levels were found to be deficient in their vitamin D levels. The correlation between maternal vitamin D levels and cord blood vitamin D was found to be statistically highly significant. Ariyawatkul K *et al*. conducted a study to determine the prevalence of vitamin D deficiency in the cord blood of newborns and its association with maternal vitamin D status.[18] The study found that the mean maternal and cord blood 25OHD levels were 25.42±8.07 ng/mL and 14.85±5.13 ng/mL, respectively. Vitamin D deficiency (25OHD <12 ng/mL) and insufficiency (25OHD 12-20 ng/mL) in cord blood were observed in 20.2% and 69.1% of newborns, respectively. A significant correlation was found between maternal and cord blood vitamin D levels ($r=0.86$; $p<0.001$). This strong correlation aligns with the findings of similar positive correlations reported by authors such as Wierzejska *et al*.[19] and Treiber *et al*.[20]

The limitations of this study included its cross-sectional nature, the absence of a control group, and a relatively small number of cases. Furthermore, factors that may affect cord vitamin D levels, such as gestational age and weight, were not considered. Randomized controlled trials or comparative studies with a larger number of cases are required to further substantiate the findings of this study. The study demonstrated a strong correlation between maternal and cord blood vitamin D levels, highlighting that deficiencies in mothers are likely to result in deficiencies in neonates. Significant factors influencing vitamin D levels included maternal education, area of residence, gravida status, gestational age, sun exposure, and biochemical indicators like serum calcium and alkaline phosphatase. In contrast, religion, socioeconomic status, maternal parity, dietary habits, and the gender of the neonate were not found to have a significant impact on neonatal vitamin D levels.

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