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Research Article

## Correlation between maternal and neonatal blood vitamin D levels and its effect on the newborn anthropometry

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### ABSTRACT

**Background:** Vitamin D deficiency during pregnancy has important implications for the new born and infant. In India, there were few data about the prevalence of hypovitaminosis D in pregnancy and in new-born and its correlation. Hence, this study aim was to determine vitamin D deficiency in pregnant women and their new-borns and to assess the correlation between maternal and new born serum levels of the vitamin D3 and also to study its effect on the newborn anthropometry.

**Methods:** This cross-sectional, hospital based study was conducted with 54 consecutive women in labour presenting with a singleton term pregnancy at a large tertiary centre in Tamilnadu, India. Data were recorded on a special form and 25-hydroxy vitamin D3 was assessed before delivery in mothers and after delivery in their infant's umbilical cord blood.

**Results:** The mean vitamin D levels were 20.21 ng/mL for the participants and 20.07 ng/mL for the newborns. Vitamin D severe deficiency was noted in 3 (6%), deficiency 31 (57%), insufficiency 12 (22%) and sufficiency in 8 (15%) of 54 participants whereas severe deficiency, insufficiency and sufficiency respectively, were noted in 4 (7%), 30 (56%), 11 (20%) and 9 (17%) of the newborns. Maternal vitamin D level significantly associated with socioeconomic status, term of delivery and type of delivery respectively were  $p=0.000$ ,  $p=0.000$  and  $p=0.038$  whereas age ( $p=0.081$ ), BMI ( $p=0.085$ ) and parity ( $p=0.038$ ) was not significant at  $p < 0.05$  level by chi-square analysis. Similarly, the new born characteristics of birth weight ( $p=0.000$ ), birth length ( $p=0.016$ ), head and chest circumference ( $p=0.001$ ,  $p=0.000$ ) exists significant association at  $p < 0.05$  level by analysis of variance (ANOVA) method and also there was a strong positive correlation between the vitamin D levels in maternal and cord blood ( $r=0.898$ ;  $P < 0.05$ ).

**Conclusions:** There was a high prevalence of vitamin D deficiency in the south Indian pregnant women and their newborns. Vitamin D deficiency increased the risk of low birth weight neonate and it also had an effect on the length of the baby, head circumference and chest circumference. This public health problem needs urgent attention.

**Keywords:** Pregnancy, New born, Vitamin D, Birth weight, Socioeconomic status

### INTRODUCTION

Vitamin D deficiency is unexpected in a tropical country like India, where there is abundant sunshine throughout year. Vitamin D is one of the essential ingredients in

terms of metabolic and physiological processes in the human body. The main source of vitamin D is its synthesis in dermis and epidermis, which is affected by ultraviolet B (UVB) rays, including approximately 90 percent of the entire body need<sup>1</sup>. However, sources of this vitamin exist in foods such as egg yolk, fatty fish,

fish oil, fortified foods and vitamin supplements but diet provides only part of body needs. Thus, inadequate radiation or lack of UVB and in turn reduced dermal synthesis is considered as one of the main determinants of vitamin D deficiency.<sup>2</sup>

During pregnancy, a woman maintains her vitamin D requirements to support her own health, but also needs the extra amount to support her foetus. Thus, achieving and maintaining adequate vitamin D is much more critical in pregnant women than in any other population.<sup>3</sup> There is increasing evidence showing that vitamin D status during pregnancy is integral to maternal health, fetal development and optimal neonatal outcomes as well as future health of the offspring.<sup>4-7</sup>

Studies have shown a high prevalence of vitamin D deficiency among Turkish women and their infants and among pregnant women and their newborns (as assessed from cord blood) in Greece and Iran.<sup>8-10</sup> An Australian study concluded that insufficient prenatal and postnatal levels of vitamin D were found to place breastfed infants at high risk for vitamin D deficiency and poor bone formation and a study from Pakistan reported widespread vitamin D deficiency among pregnant women and a correlation between maternal and cord blood levels of vitamin D.<sup>11-13</sup> People of Indian origin, especially pregnant women, are known to have a high prevalence of vitamin D deficiency.<sup>14-16</sup>

The present study was conducted with women presenting in labour in a tertiary-care centre at Tamilnadu, India. Its objective was to determine the vitamin D deficiency in pregnant women and their newborns and look for a correlation between maternal and neonatal vitamin D deficiency and also to note its effect on the newborn anthropometry.

## METHODS

This cross-sectional, hospital based study was conducted at the obstetrics and gynaecology department of SRM medical college hospital and research centre, Kanchipuram, India (Tertiary care centre predominantly catering to the needs of the poorer population of Tamilnadu). A total of 54 consecutive singleton pregnant women admitted in labour were included. Twin or multiple pregnancies, congenital anomalies in the newborn and liver and kidney disorder subjects were excluded from the study. Informed consent was obtained from each study subject after the nature of the study was fully explained. The Institutional ethical clearance was obtained to conduct the study (No: 502/IEC/2013).

Maternal characteristics such as age, height, weight, parity, level of education, occupation, total income of family and obstetrical history (gestational weeks, term of delivery) were recorded in a standardized questionnaire. Cord blood was obtained at the time of delivery, vitamin D levels were determined. Newborn anthropometric

measurements like birth weight, height, head and neck circumference were measured at birth. Socioeconomic status was categorized according to the total score of education, occupation and monthly per capita family income.<sup>17</sup>

## Estimation of 25 (OH) D3 procedure

Circulating 25(OH) D was measured as 25 hydroxyvitamin D3 (25(OH)D3) by HPLC in serum using a kit marketed by Chromosorb (Germany). Briefly, to 0.5 mL of serum are added 350  $\mu$ L of methanol-2-propanol (80:20 by volume) and the 25(OH)D extracted by mixing three times with 2 mL of hexane. The phases were separated by centrifugation, and the upper organic phases combined and dried under nitrogen. The residue was then dissolved in 100  $\mu$ L of mobile phase. Calibration curves were constructed using four concentrations of 25(OH)D (15-120 nmol/L) and human serum albumin (50 g/L). For the chromatography we used a Waters millennium HPLC (Waters Inc., Milford MA) FITTED with a LiChrospher 60 RP select B column (4 $\times$ 250 mm; 5  $\mu$ m bead size; EMD, Bridgewater, NJ) maintained at 40 °C. The separation was achieved using 760 mL/L methanol in water as the mobile phase with a flow rate of 1 mL/min and detection at 265 nm. The injected volume was 50  $\mu$ L. The 25(OH)D3 and 25(OH)D2 peaks are completely resolved with retention times of 20.8-21.1 min and 23.1 min, respectively. The within-assay and between assay CVs were <8%. Serum 25(OH) D3 was analysed by high performance liquid chromatography, according to the protocol of Turpeinen et al.<sup>18</sup>

The cut offs utilised to define vitamin D deficiency were based on Institute of Medicine. Subjects were grouped into different categories, based on the serum level of 25(OH)D3 as per the guidelines of Institute of Medicine (IOM). The IOM defines 25(OH)D3 serum level of <10 ng/mL as severe deficiency, <20 ng/ml as deficiency, 20-30 as insufficiency and >30 ng/mL as sufficiency.<sup>19</sup>

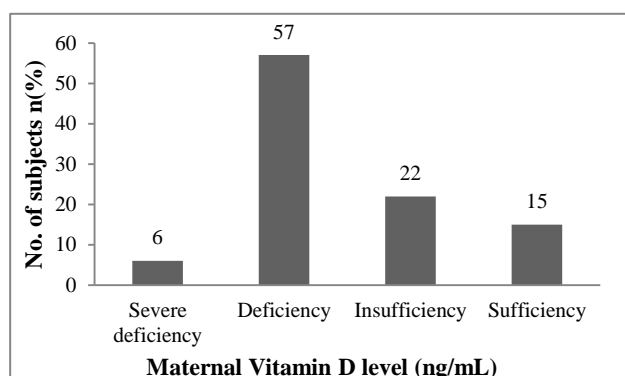
## Statistical analysis

Data analyses were performed using SPSS (version 16:0, SPSS Inc., Chicago, IL). The chi-square test was used to compare vitamin D levels including between mothers and newborns and to explore relationships between vitamin D deficiency and possible predictors of the deficiency. P <0.05 was considered significant.

## RESULTS

The demographic characteristics of the 54 participants were shown in Table 1. Most participants were between 25 and 35 years old (mean $\pm$ SD, 20.21 $\pm$ 3.74 years). In the present study, most of the subjects 24 (44.44%) were from lower socioeconomic status. The participants mean body mass index (calculated as weight in kilograms divided by height in meters squared) was 24.45 $\pm$ 5.65.

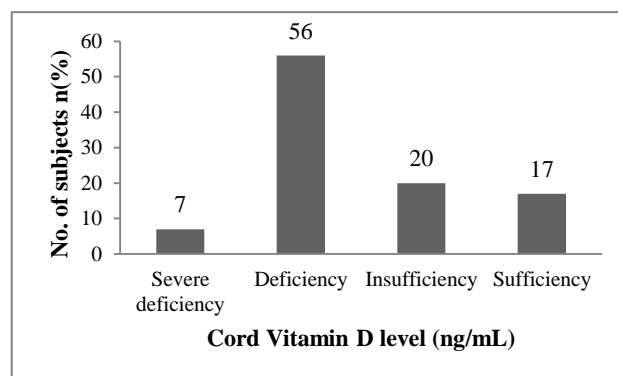
The mean birth weight was 2660.61±353.27 g, the mean birth height was 45.52±8.05 cm, and the newborns' mean head and chest circumference was 31.44±3.99 cm and 28.88±4.3 cm, respectively.



**Figure 1: Distribution of maternal serum levels of 25(OH)D3 in the study subjects (N=54).**

Figure 1 and Figure 2 show the distribution of maternal and cord blood vitamin D concentrations. The mean concentrations were, approximately, 20.21 ng/mL for maternal blood and 20.07 ng/mL for cord blood 25(OH)D3. Vitamin D severe deficiency was noted in 3 (5.56%), deficiency in 31 (57.41%), insufficiency in 12 (22.22%) and sufficiency in 8 (14.81%) of 54 participants whereas severe deficiency, deficiency, insufficiency and sufficiency respectively, were noted in 4 (7%), 30 (56%), 11 (20%) and 9 (17%) of the newborns. The study

showed a deficiency of vitamin D in a total of 34 (63%) pregnant women and a similarity in vitamin D deficiency also exists in their offspring.



**Figure 2: Newborn serum levels of 25(OH)D3 in the study subjects (N=54).**

Table 1 illustrates the maternal vitamin D level significantly associated with socioeconomic status, term of delivery and type of delivery. They were p=0.000, p=0.000 and p=0.038 whereas age (p=0.081), BMI (p=0.085) and parity (p=0.038) was not significant at p<0.05 level by chi-square analysis. Similarly, Table 2 shows the newborn characteristics of birth weight (p=0.000), birth length (p=0.016), head and chest circumference (p=0.001, p=0.000) which has a significant association at p <0.05 level by analysis of variance (ANOVA) method.

**Table 1: Maternal vitamin D level association with demographic, economic and obstetrical characteristics.**

Characteristics	Vitamin D				p-value
	Severe deficiency (N=3)	Deficiency (N=31)	Insufficiency (N=12)	Sufficiency (N=8)	
<b>Age (Yrs)</b>					
18-22	0	6 (19.35)	5 (41.67)	4 (50)	0.081
23-27	0	4 (12.91)	0	3 (37.5)	
30-34	2 (66.67)	3 (9.67)	4 (33.33)	0	
35-39	0	4 (12.91)	1 (8.33)	0	
≥40	1 (33.33)	14 (45.16)	2 (16.67)	1 (12.5)	
<b>Socioeconomic status</b>					
Upper class	0	1 (3.22)	1 (8.33)	0	0.000*
Upper middle	0	7 (22.58)	3 (25)	2 (25)	
Lower middle	1 (33.33)	5 (16.13)	4 (33.33)	4 (50)	
Upper lower	0	2 (6.45)	0	0	
Lower	2 (66.67)	16 (51.62)	4 (33.33)	2 (25)	
<b>Body mass index (Kg/m<sup>2</sup>)</b>					
Underweight (<19)	3 (100)	10 (32.26)	3 (25)	2 (25)	0.085
Healthy weight (19-24)	0	5 (16.13)	5 (41.67)	5 (62.5)	
Overweight (25-29)	0	3 (9.67)	1 (8.33)	0	
Obese (30-35)	0	13 (41.94)	3 (25)	1 (12.5)	
<b>Term of delivery</b>					
Very preterm (<32 weeks)	3 (100)	10 (32.26)	3 (25)	0	0.000*
Mildly preterm (32-36 weeks)	0	21 (67.74)	6 (50)	0	
In-term (≥37 weeks)	0	0	3 (25)	8 (100)	

Parity					
Primiparous	1 (33.33)	19 (61.29)	7 (58.33)	3 (37.5)	0.724
Multiparous	2 (66.67)	12 (38.71)	5 (41.67)	5 (62.5)	
Type of delivery					
Normal	0	13 (41.94)	8 (66.67)	2 (25)	0.038*
Caesarean	3 (100)	18 (58.06)	4 (33.33)	6 (75)	

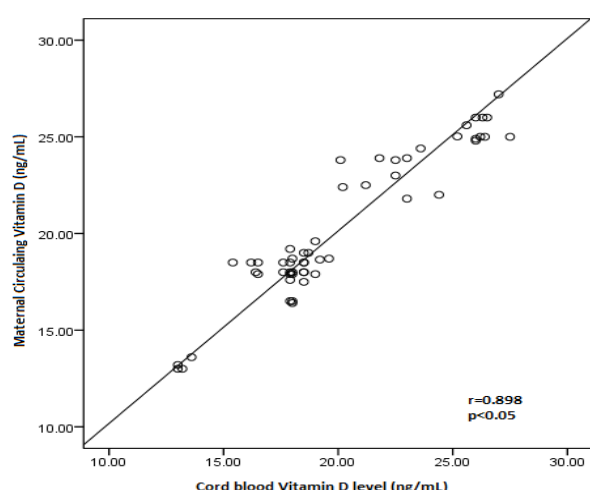
\*Statistically significant at  $p < 0.05$  level by chi-square analysis.

**Table 2: New born characteristics association with cord vitamin D level.**

Characteristics	Vitamin D				p-value
	Severe deficiency (N=4)	Deficiency (N=30)	Insufficiency (N=11)	Sufficiency (N=9)	
Birth weight (g)	2080±237.627	2584.9±245.67	2624.44±83.98	3064.25±332.63	0.000*
Birth length (cm)	35.3±0.68	44.06±7.24	44.82±6.78	53±6.36	0.016*
Head circumference (cm)	26.1±1.80	30.87±3.18	30.31±3.37	35.44±3.5	0.001*
Chest circumference (cm)	24.02±1.74	28.53±3.49	26.68±4.17	33±3.65	0.001*

\*Statistically significant at  $p < 0.05$  level by ANOVA analysis

Figure 3 revealed the strong positive correlation between the vitamin D levels in maternal and cord blood ( $r=0.898$ ;  $P < 0.05$ ) by Pearson correlation coefficient method.



**Figure 3: Correlation of maternal vitamin D and umbilical cord vitamin D level.**

## DISCUSSION

The dependence of newborns on maternal reserves of vitamin D is reflected in the high level of correlation between maternal and cord blood levels of 25-hydroxy vitamin D<sub>3</sub>, and these observations were consistent with previous reports.<sup>20,21</sup> In the present study, 34 (63%) pregnant women and 34 (63%) newborn were vitamin D deficient. Similarly, Arya et al found in his study that 63% of pregnant women were vitamin D deficient but in contrary 81.0% of the newborns were vitamin D deficient. In India, the intake of a vitamin D<sub>3</sub>-rich diet is poor and vitamin D<sub>3</sub>-fortified food is not available. In addition, affluent women prefer to avoid exposure to

direct sunlight, using umbrellas or protective shields outdoors and thick curtains indoors, thus minimizing the production of vitamin D.<sup>22</sup>

Maternal vitamin D deficiency had been associated with adverse pregnancy outcome. VDR and 1, 25 (OH)<sub>2</sub>D normally increase skeletal muscle function. Conversely, vitamin D deficiency results in proximal muscle weakness and decreased lower extremity muscle function, perhaps contributing to the risk for cesarean section.<sup>23</sup> The present study also revealed that type of delivery had significant association with vitamin D level.

Trans placental passage of maternal 25(OH)D is the only source of vitamin D. Accordingly, pregnant women need to be vitamin D replete at the time of giving birth to ensure sufficient levels of this vitamin in their baby to last the first 4-6 months of life. Hypovitaminosis D during pregnancy and in turn neonatal period and infancy is of special concern.<sup>24-25</sup>

Our study showed a statistically significant association between cord vitamin D levels and newborn characteristics like birth weight, birth length head circumference and chest circumference. A study among Chinese population demonstrated that newborns of mothers with severe vitamin D deficiency had lower birth length and weight, with lower head circumference and birth weight in vitamin D-deficient newborns than in other neonates.<sup>26</sup> A meta-analysis of observational studies, published in 2013, reinforced the association between vitamin D deficiency and risk of low birth weight babies.<sup>27</sup> In a U.S. study of over 2,000 births, 25-hydroxyvitamin D levels, 15 ng/mL before 26 weeks gestational age was associated with higher birth weight and larger head circumference.<sup>28</sup>



The present study showed the strong correlation of cord serum vitamin D level with maternal vitamin D level ( $r=0.898$ ;  $P<0.05$ ). Similarly, the hospital based Pakistani study showed a strong correlation between vitamin D levels in maternal and cord blood. This finding reminds us that the fetus is solely dependent on its mother for the supply of this vitamin. This suggests that for normal vitamin D concentrations to be maintained in fetal blood, the normal vitamin D concentration is higher during than before pregnancy.<sup>12</sup>

In conclusion, there was a high prevalence of vitamin D deficiency in the south Indian pregnant women and their newborns. Vitamin D deficiency increased the risk of low birth weight neonate and it also had an effect on the length of the baby, head circumference and chest circumference. Hence, this public health problem needs urgent attention.

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