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Original Research Article

The sunshine vitamin D: ubiquitous source, still so deficient in mother and baby duo

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ABSTRACT

Background: Vitamin D is a fat-soluble vitamin, a sunshine vitamin. Vitamin D deficiency is now recognized as a pandemic. Fetus depends on mother for its need of vitamin D, thus there is growing concern for its impact on neonates. This study was designed to determine the correlation between 25-hydroxyvitamin D (vitamin D3) levels in maternal blood and in cord blood.
Methods: A total 50 term pregnant women attending antenatal clinic at SVS medical college, Telangana and their neonates were included in the study. At term after taking written consent, maternal and cord blood vitamin D3 were measured, and values were correlated. Antenatal and neonatal complications were noted, and correlated with vitamin D3 levels.
Results: In this study 80% of pregnant women and 88% of neonates were vitamin D3 deficient. Mean maternal blood vitamin D3 was 17.62±10.01 and cord blood vitamin D3 was 12.84±7.68. Maternal blood vitamin D3 correlated positively with cord blood vitamin D3 ($r=0.951$, $p<0.001$). Antenatal and neonatal complications were observed, but statistically significant association with vitamin D3 deficiency could not be established.
Conclusions: This study has demonstrated a very high prevalence of vitamin D deficiency in apparently healthy, young, pregnant women despite abundant sunlight leading to deficiency in their neonates. To establish strong association between vitamin D3 deficiency and various antenatal and neonatal complications further studies with large subject groups are required.

Keywords: Antenatal, Complications, Cord blood, Deficiency, Neonatal, 25-hydroxyvitamin D

INTRODUCTION

Vitamin D is a fat-soluble vitamin, a secosteroid, a prohormone, a sunshine vitamin. Vitamin D deficiency is now recognized as a pandemic.[1] There is a growing awareness that vitamin D sufficiency is required for optimal health. Study by Hodgkin et al published in Lancet resulted in the belief that vitamin D deficiency did not exist in sun abundant countries.[2] But many recent epidemiological studies indicate that there is currently a worldwide vitamin D deficiency in various populations, including infants, pregnant and lactating mothers.[3-8] In India both urban and surprisingly rural women are vitamin D deficient which is paradoxical to conventional science and to the name "sunshine vitamin".[7,9]

The two principal driving forces for heightened interest in study of vitamin D are: The worsening, worldwide trend to nutritional vitamin D insufficiency and new knowledge regarding the non-classical, nonhormonal actions of vitamin D metabolites in humans.[10]

Despite the fact that pregnant women in most countries are encouraged to take a daily prenatal vitamin supplement containing vitamin D, a disturbingly high prevalence of vitamin D deficiency has been

demonstrated.[11,12] Because the human fetus is entirely dependent on the maternal pool of vitamin D, there is growing concern about the functional impacts that hypovitaminosis D during pregnancy may have on the offspring in utero, in infancy, and later in life.

Vitamin D deficiency during pregnancy has important health implications for the mother and infant. Intrauterine programming is important for neonatal and adult health, which depends on adequate vitamin D status and calcium homeostasis during pregnancy. Many recent studies have shown association of vitamin D deficiency with increased incidence of bacterial vaginosis infection in first trimester, pre- eclampsia, gestational diabetes. Neonatal complications include impaired growth, small for gestational age, hypocalcaemia seizures, dilated cardiomyopathy, rickets, craniotabes. Complications in childhood and in later life include delayed bone ossification, abnormal enamel formation, LRTI, asthma, schizophrenia, and type 1 diabetes.

This study was designed to determine the correlation between 25-hydroxyvitamin D (vitamin D3) levels in maternal blood and in cord blood. Over the last 20 years, there has been an increasing realization of the role played by maternal vitamin D status during pregnancy and lactation in influencing the vitamin D status of the new-born and young infant.

There have been many studies suggesting a high prevalence of physiologically significant vitamin D deficiency among pregnant women and their neonates. Cord blood vitamin D3 levels depend on the maternal serum vitamin D3 levels, the magnitude of which warrants public health intervention. Thus, this study is planned in our hospital which will assess the need to screen and treat pregnant women for Vitamin D deficiency thus preventing problems in neonates and children.

METHODS

This is a prospective observational study conducted at Shri Venkata Sai Medical College, Mahabubnagar, Telangana between October 2018 and December 2019. A total 50 term pregnant women and their neonates were included in the study with following inclusion and exclusion criteria.

Inclusion criteria

- Pregnant women of age group 18 to 40 years, singleton pregnancy, at term, women planning to deliver at SVS medical college hospital and their neonates.

Exclusion criteria

- Women with chronic liver disease, renal disease, known hyperparathyroidism, malabsorption syndrome, women using drugs like antitubercular drugs, antiepileptic drugs, steroids. Neonates with any structural and chromosomal anomalies, inborn errors of metabolisms were excluded from study.

Informed and written consent was taken from mother for measuring vitamin D3 in herself and the cord blood of her neonate. Vitamin D3 was measured in maternal blood sample at term during antenatal check-up or during labour and cord blood vitamin D3 was measured after delivery. The above samples were assessed by using ELISA kit (IDS 250 vit D EIAKIT).

A questionnaire was used to collect data regarding demographical characteristics, antenatal complications, delivery details, neonatal complications. Primary aim and objective of the study was to measure vitamin D3 levels in term pregnant women and cord blood of their neonates and to correlate them. Secondary objective of the study was to observe antenatal complications in these pregnant women and complications in their neonates and then to correlate them with vitamin D3 levels.

Endocrine society's practice guideline was followed to define the following

- Vitamin D3 deficiency <20 ng/ml
- Insufficiency 21-29 ng/ml and
- Sufficiency >30 ng/ml.

Statistical analysis

Statistical analysis was conducted by using SPSS software (version 20; SPSS). Data are presented as mean and SD. Correlations of serum vitamin D3 (25 OH D) levels between term pregnant women and cord blood of their neonates were studied by using linear regression analysis. A p-value of <0.05 was considered significant. Proportions were compared by using the chi-square test.

RESULTS

In the present study, out of 50 pregnant term women, vitamin D3 deficiency was found in 40 women that accounts for 80%. 6 (12%) women had vitamin D3 insufficiency and 4 (8%) women had vitamin D3 sufficiency.

In cord blood of neonates 44 (88%) had vitamin D3 deficiency, 3 (6%) had vitamin D3 insufficiency and 3 (6%) had vitamin D3 sufficiency (Table 1).

In this study 80% of pregnant women and 88% of neonates were vitamin D3 deficient. Mean maternal blood vitamin D3 was 17.62±10.01 and cord blood vitamin D3 was 12.84±7.68.

Maternal blood vitamin D3 correlated positively with cord blood vitamin D3 ($r=0.951$, $p<0.001$).

Table 1: Vitamin D3 levels in maternal and cord blood samples.

Vitamin D3 levels	No. of pregnant women	No. of cord blood
Deficiency-<20 ng/ml	40 (80%)	44 (88%)
Insufficiency-20-30 ng/ml	6 (12%)	3 (6%)
Sufficiency->30 ng/ml	4 (8%)	3 (6%)
Mean vitamin D level	17.62	12.84
Range	27.63-7.61	20.52-5.16
p value	<0.001	
r value	0.951	
r^2	0.905	

Antenatal complications in these pregnant women were observed. Out of 50 women, 2(4%) women had bacterial vaginosis infection in first trimester. 2(4%) women developed GDM and 3 (6%) women developed pre-eclampsia. Statistically significant association between these complications and vitamin D3 deficiency could not be established (Table 2). A total 32 (64%) women had normal vaginal delivery (NVD) and 18 (36%) had lower segment caesarean section (LSCS) (Table 3). 84% of women who had NVD were vitamin D3 deficient (<20 ng/ml) and 72% of women who had LSCS were deficient as well. Statistically significant association between vitamin D3 deficiency and incidence of LSCS could not be established (Table 3).

Table 2: Antenatal complications observed and vitamin D3 levels.

	Vitamin D3 levels						Total %
	<20 ng/ml		20-30 ng/ml		>30 ng/ml		
Preeclampsia	3	6%	0	0%	0	0%	6%
GDM	2	4%	0	0%	0	0%	52%
BV	2	4%	0	0%	2	4%	20%

Table 3: Mode of delivery.

Type of delivery	Vitamin D levels						Total %
	<20 ng/ml		20-30 ng/ml		>30 ng/ml		
NVD	27	54%	4	8%	1	2%	64%
LSCS	13	26%	2	4%	3	6%	36%
Total	40	80%	6	12%	4	8%	100%

DISCUSSION

The present study is a prospective observational study of 50 term pregnant women and their neonates delivered at SVS medical college, Mahabubnagar, Telangana. Demographic characteristics of the study group were as follows. Out of total 50 pregnant women, majority 56% were in the age group 20-25 years, 28% were in 26-30 years age group and 10% were in 31-35 years age group and 6% were in <20 years age group. More than half, 56% of them were primigravidae, 34% were second gravida, 10% were third gravida and their mean BMI was 24.88/kg/m².

In this study, out of 50 term pregnant women, vitamin D3 deficiency was found in 40 women that accounts for 80%. 6 (12%) women had vitamin D3 insufficiency and 4 (8%) women had vitamin D3 sufficiency. In cord blood of neonates 44 (88%) had vitamin D3 deficiency, 3 (6%) had vitamin D3 insufficiency and 3(6%) had vitamin D3 sufficiency. 80% of pregnant women and 88% of neonates were vitamin D3 deficient (Table 1). Mean maternal blood vitamin D3 was 17.62±10.01 and cord blood vitamin D3 was 12.84±7.68. Maternal blood vitamin D3 correlated positively with cord blood vitamin D3 ($r=0.951$, $p<0.001$) which is consistent with following Indian studies. Sachan et al in their study reported, a total 84.3% of urban and 83.6% of rural women had 25(OH) D values <22.5 ng/ml cut off, below which PTH raised. Goswami et al reported from Delhi high prevalence of subnormal levels of 25 (OH) D.[7,13] Sahu et al in their study from rural place near Lucknow reported the high prevalence of vitamin D deficiency in adolescent girls about 88.6% and in pregnant women 74%.[14] They also reported seasonal variation of vitamin D status which showed lower values in winter. Marwaha et al found high prevalence of vitamin D deficiency in lactating mothers and exclusively breast-fed infants about 47.8% and 43.2% respectively.[15] Kumar P et al and Arora et al also have documented high prevalence of vitamin D deficiency among pregnant women and their neonates.[16,17]

There are studies reported across the world depicting vitamin D3 deficiency in mother and their neonates

Dror et al, and Bodnar et al reported high prevalence of vitamin D3 deficiency in both white and black pregnant

women and neonates.[3,18] More severe deficiency in blacks. Dror et al reported 54% deficiency in pregnant women across all racial group, Bodnar et al found vitamin D deficiency and insufficiency in 29.2% and 54.1% of black women and 45.6% and 46.8% black neonates, 5% and 42.1% of white women and 9.7% and 56.4% of white neonates respectively. They also reported seasonal variation with vitamin D levels higher in summer and also found that vitamin D insufficiency was present in spite of compliance with prenatal vitamins. Both the above studies showed positive correlation between maternal and neonatal vitamin D levels. In present study, authors did not find statistically significant differences in seasonal variation in vitamin D3 status in mother and cord blood. This difference could be because authors do not have significant difference in hours of sunshine during days in various seasons throughout the year.

Ginde et al, another study from USA reported high prevalence of vitamin D insufficiency in pregnant (69%) and nonpregnant (78%) women of childbearing age.[19] Davis et al and associates found high prevalence of vitamin D insufficiency in 80 pregnant African American adolescents (<18 years of age) at Johns Hopkins Hospital.[20] They also found inverse associations between 25(OH) D and bacterial vaginosis. In present study, we had only 3 subjects who were <20 years and all of them were vitamin D3 deficient. Regarding bacterial vaginosis in pregnant women, our study did not show any statistically significant correlation between vitamin D3 deficiency and bacterial vaginosis.

Holmes et al found high prevalence of hypovitaminosis D in Caucasian pregnant women about 75% compared to non-pregnant women 42%.[21] They also reported higher mean serum 25(OH) D values in supplemented group but were still in insufficient range. Meer V et al reported high prevalence of vitamin D deficiency in pregnant non-western women about 84%in Netherland.[22] Nicolaidou et al from Greece concluded that abundant sunlight exposure in Athens was not sufficient to prevent hypovitaminosis D in pregnant women and their babies.[23] Thus, this study results are consistent with results of above studies from USA and Europe.

Study from Australia by Devika et al reported 78% of vitamin D insufficiency in immigrant pregnant women.[8] They also found correlation between maternal and cord blood vitamin D levels consistent with this study results. Kalbani et al reported from Oman 65% of vitamin D insufficiency in pregnant women and Maghbooli et al reported from Iran the high prevalence of vitamin D insufficiency about 66.8% and 93.3% in mothers and their neonates.[24,25] Serenius et al reported from Saudi Arabia reported undetectable vitamin D levels in about 9.2% and 42% of pregnant women and cord blood respectively.[26] These are studies from Middle East showing high prevalence of vitamin D insufficiency and also maternal and cord blood vitamin D correlation, our results are consistent with these results.

There are studies from many Asian countries like Hossain et al from Pakistan, Shrestha et al from Nepal documenting vitamin D deficiency among pregnant women and their neonates.[27,28] All these studies from across the world including our study only reiterates that vitamin D deficiency is pandemic and further large-scale studies regarding interventions to prevent and treat it are required.

Cause for such high prevalence of vitamin D deficiency despite abundant sunshine in our study could be because of dark skin colour of study subjects, modest clothing exposing only head, neck and hands precluding adequate sun exposure, insufficient outdoor activity in urban areas, poor dietary calcium causing secondary vitamin D deficiency, and environmental pollution.

Antenatal complications in these pregnant women were observed. Out of 50 women, 2 (4%) women had bacterial vaginosis infection in first trimester (BV). 2 (4%) women developed gestational diabetes mellitus (GDM) and 3 (6%) women developed pre-eclampsia (Table 2).

Out of 50 pregnant women, only 4(8%) had bacterial vaginosis infection in first trimester. Out of these 4 women, 2 had vitamin D3 deficiency (<20 ng/ml) and 2 other women had vitamin D3 sufficiency (>30 ng/ml). This study results did not show statistically significant association between vitamin D3 deficiency and bacterial vaginosis infection in first trimester. Hensel et al, Bodnar et al, Davis et al found inverse associations between vitamin D3 and bacterial vaginosis.[21,29,30] Bodnar et found dose-response association between vitamin D3 and the prevalence of bacterial vaginosis and reported 1.65-fold and 1.26-fold increases in prevalence of BV associated with a serum vitamin D3 concentration of 20 and 50 nmol/L, respectively.

Second complication which was observed in pregnant women was gestational diabetes mellitus (GDM). Only 2 (4%) developed GDM and both of them had vitamin D3 deficiency (<20 ng/ml). But statistically significant association between them could not be established because of small number of subjects. This study result is consistent with results of study by Makgoba et al.[31] They did not find any statistically significant differences in baseline maternal mean vitamin D3 levels between GDM cases and controls. Zhang et al, Soheilykhah et al, Wang Ou et al reported statistically significant association between vitamin D3 deficiency and GDM.[32-34] Zhang et al found each 5 ng/ml decrease in vitamin D3 concentrations was related to a 1.29-fold increase in GDM risk. Soheilykhah et al found that the women with GDM had a 2.66-fold increased risk of vitamin D3 deficient status (<15 ng/mL) compared with control group. Wang Ou et al, reported from China that subjects with vitamin D3 levels <25 nmol/L had a 1.8-fold higher

risk of GDM compared with subjects with higher vitamin D levels.

In present study only 3 (6%) women developed pre-eclampsia and all 3 had vitamin D3 deficiency (<20 ng/ml). But statistically significant association between them could not be established. Powe et al, reported that first trimester vitamin D3 levels were not independently associated with first trimester blood pressure or subsequent preeclampsia because they found first trimester total vitamin D3 levels were similar in cases and controls.[35] This result is consistent with the present study.[36,37] Whereas Bodnar et al and Baker et al found correlation between vitamin D3 deficiency in mid-gestation and subsequent development of preeclampsia. Bodnar et al reported that early-pregnancy maternal vitamin D3 concentration <37.5 nmol/litre was associated with a 5-fold increase in the odds of preeclampsia. Baker et al reported that mid-gestation maternal vitamin D3 of less than 50 nmol/litre was associated with almost 4-fold odds of severe preeclampsia.

These pregnant women were followed till delivery. 32 (64%) women had normal vaginal delivery (NVD) and 18 (36%) had lower segment caesarean section (LSCS) (Table 3). 84% of women who had NVD were vitamin D3 deficient (<20 ng/ml) and 72% of women who had LSCS were deficient as well, thus our study could not show any statistically significant association between vitamin D3 deficiency and incidence of LSCS. Merewood et al, in their study reported vitamin D3 deficiency was associated with increased odds of primary caesarean section.[38]

Out of 50 neonates, only 4(8%) had low birth weight (LBW) (<2.5 kgs), all 4 neonates and their mothers had vitamin D3 deficiency (<20 ng/ml). But mothers of 2 of these neonates had pre-eclampsia complicating pregnancy, thus LBW could have been because of pre-eclampsia in mothers. This study did not show any statistically significant association between vitamin D3 deficiency and LBW. Farrant et al and Bodnar et al reported no association between vitamin D deficiency and birth weight, our result was consistent with their results.[39,40] In present study, neonates did not have complications of hypocalcaemia seizures or dilated cardiomyopathy.

The present study concludes that there is correlation between maternal and cord blood vitamin D3 levels ($p<0.001$, $r=0.951$, $r^2=0.905$) and there is high prevalence of vitamin D3 deficiency (<20 ng/ml) in both mothers (80%) and their neonates (88%).

This higher rate of deficiency in neonates compared to mothers is because neonates of vitamin D3 insufficient (20-30 ng/ml) mothers shifted to deficient range. Ante natal and neonatal complications were not correlated with vitamin D3 deficiency due to small size of study group.

CONCLUSION

This study has demonstrated a very high prevalence of vitamin D3 deficiency in apparently healthy, young, pregnant women despite abundant sunlight leading to deficiency in their neonates. This study reaffirms the belief that vitamin D deficiency is a pandemic. Vitamin D supplementation for pregnant and lactating women in adequate doses, for adequate length of time is required to prevent deficiency in their neonates. To establish strong association between vitamin D3 deficiency and various ante natal and neonatal complications further studies with large subject groups are required. To eradicate this pandemic, further larger studies documenting interventions to prevent and treat vitamin D deficiency are required.

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