International Journal of Contemporary Pediatrics
Thomas DJ et al. Int J Contemp Pediatr. 2020 Feb;7(2):387-392
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20200115

Original Research Article

A study on vitamin D levels in preterm and term neonates and their mothers

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Received: 21 November 2019
Revised: 24 December 2019
Accepted: 30 December 2019

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ABSTRACT

Background: Vitamin D is a fat-soluble vitamin which has immunomodulatory and anti-inflammatory effects. Vitamin D deficiency is a worldwide problem and yet is one of the most under diagnosed and under treated nutritional deficiency. Despite India being in the tropical zone with plentiful sunlight, there is a wide prevalence of vitamin D deficiency.
Methods: Cross sectional descriptive study done in a tertiary care hospital involving 30 mother baby dyads equally divided into term and preterm babies. Maternal vitamin D levels (before delivery) and cord blood vitamin D levels (after delivery) were estimated.
Results: All the mothers had low vitamin D levels, 93% having deficiency and 7% having insufficiency. The maternal vitamin D levels correlated with cord blood vitamin D levels. There was significant correlation between maternal vitamin D levels and cord blood vitamin D levels with maternal age and parity. There was no correlation between maternal vitamin D levels with gestational age, sociodemographic profile or neonatal anthropometry.
Conclusions: Vitamin D deficiency is widely prevalent even in well-nourished mothers. Vitamin D supplementation may be helpful in antenatal mothers. Larger studies are needed to study the prevalence of vitamin D deficiency in mothers and babies and look for effectiveness of supplementation.

Keywords: Cord blood, Maternal, Preterm babies, Term babies, Vitamin D levels

INTRODUCTION

Vitamin D is a fat-soluble vitamin which plays an important role in the optimal functioning of vital organ systems, it has immunomodulatory and anti-inflammatory effects. Vitamin D deficiency is a worldwide problem and yet, one of the most under diagnosed and under treated nutritional deficiency. There is a high prevalence of vitamin D deficiency in pregnant and lactating mothers. Studies have shown that mothers with vitamin D deficiency have higher rates of pre-eclampsia, gestational diabetes, bacterial vaginosis, preterm birth and caesarean section, all of which could have potential adverse effects on the neonate.[1-3]

In utero, the fetus is wholly dependent on the mother for vitamin D. The 25-hydroxy vitamin D crosses the placenta into the blood stream of the fetus with a half-life of approximately 2 months.

Thus, vitamin D is vertically transmitted.[4] Serum concentrations of 1,25 hydroxy vitamin D increase by 50-100% over pre pregnancy levels during the second trimester and by 100% during the third trimester which is required for fetal skeletal development, thus exposing the preterm more at risk for osteopenia.[5] Hence if the mother is deficient in vitamin D, the baby will be born with vitamin D deficiency and develop symptoms in infancy.

In the neonate, the clinical presentation of the deficiency may vary from short term manifestation of hypocalcemic seizures, respiratory distress syndrome, tetany in infancy, rickets in toddlers, atopic dermatitis to long term outcomes like asthma, multiple sclerosis, schizophrenia, abnormal neurocognitive outcome, type 1 diabetes mellitus and insulin resistance.[6]

Breast milk is thought to be a relatively poor source of vitamin D, making maternal vitamin D status during pregnancy important for vitamin D status of the child during infancy.

The most reliable marker of vitamin D status is the serum concentration of 25(OH) D levels.[4]

In India, there is not much data about the prevalence of hypovitaminosis D in pregnancy and in newborn and its correlation. Research has shown that even in tropical climates most of the neonates are born with deficient vitamin D levels.[7] Hence, this study aims to determine vitamin D deficiency in pregnant women and their new borns, to correlate maternal vitamin D levels with cord blood levels at various gestational ages.

METHODS

This study was a cross sectional descriptional study performed in a tertiary care hospital involving 15 term and 15 preterm inborn babies and their mothers. The study was conducted over a period of three months.

Inclusion criteria

- All pregnant women presenting with spontaneous labor with no known risk factors for preterm delivery were included after obtaining written informed consent. Maternal blood was collected for estimation of vitamin D levels along with other routine labor room investigations at the time of delivery and following delivery, 3 ml of cord blood was collected from the placental side umbilical vein for estimation of vitamin D level in the neonate.

Exclusion criteria

- Women on any drugs that affected vitamin D levels, pre-existing co morbid medical conditions, all cases of preterm delivery with known risk factors for preterm labour (previous preterm labor, multiple gestation, urinary infection, high blood pressure, developmental anomalies of fetus, placenta previa, diabetes, mothers with history of smoking or alcohol intake) and obsese mothers as vitamin D gets sequestrated in adipose tissues leading to vitamin D deficiency.

Vitamin D was estimated using Vitamin D total Elecsys Cobase 100 assay based on the principle of ECLIA-electrochemiluminescence for the quantitative determination of 25 OHD and other hydroxylated vitamin D metabolites in human serum done on automated ROCHE Cobas 6000 machine.

The cut off levels for vitamin D were assigned according to the classification by US endocrine society where a value less than 20 ng/ml was considered deficiency, 20-29 ng/ml as insufficiency and ≥30 ng/ml as sufficiency.

Relevant maternal details were obtained from the maternal case files and recorded in a proforma. Data was analyzed using Excel, SPSS 23.0 IBM Corporation. Descriptive data was summarized and presented as mean, standard deviation, frequency and percentage. Categorical data was analyzed using chi square test and fisher's exact test and inferential statistics by Pearson's correlation coefficient.

Ethical clearance was obtained from the ethical committee of the institution.

RESULTS

There were 30 mother- baby dyads as shown in (Figure 1).

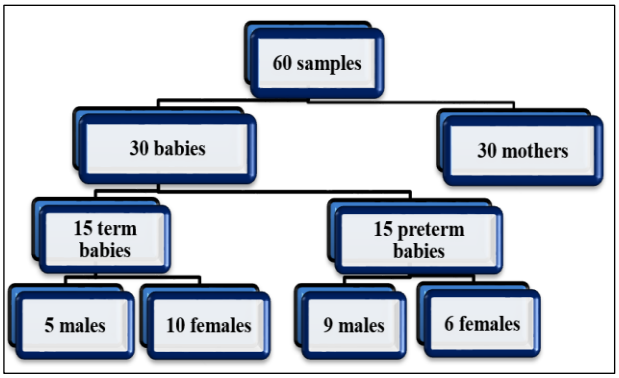

Figure 1: Flowchart of this study population.

There were 15 term babies and 15 preterm babies in this study with a mean birth weight of 3.0±0.44kg in terms and 1.61±0.72 kg in preterm. The male to female ratio in this study was 1:2 in term babies and 3:1 in preterm babies (Figure 1).

The youngest mother was 21 years old and the oldest mother was 37 years old with a mean of 24 years. The maternal serum vitamin D levels showed linear correlation with maternal age (Figure 2). This finding was statistically significant with a P value of 0.007 (R=0.48).

The cord blood vitamin D levels also showed a significant linear correlation with maternal age and the p value was 0.003 (R=0.516) (Figure 3).

In this study, 13 mothers (43%) were primiparous and 17 mothers (56%) were multiparous. The mean vitamin D levels in the primiparous mothers was 13.68±3.5 ng/ml and

in the multiparous mothers was 16.27±4.19 ng/ml. The mean cord blood vitamin D levels in these babies was 13.42±5.90 ng/ml and 18.06±4.31 ng/ml respectively. This finding was statistically significant with a p value of 0.03 (R= 0.39) (Figure 4).

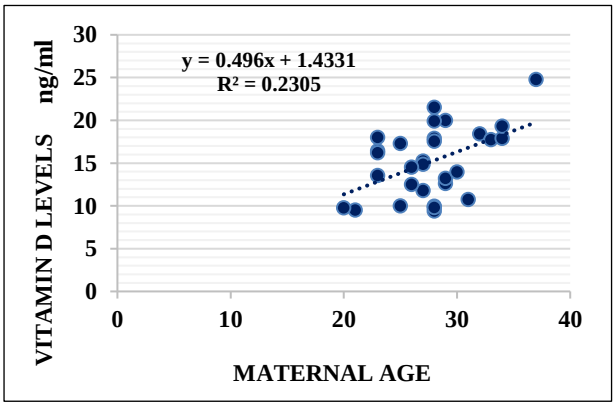

Figure 2: Correlation between maternal age and maternal vitamin D levels which was statistically significant.

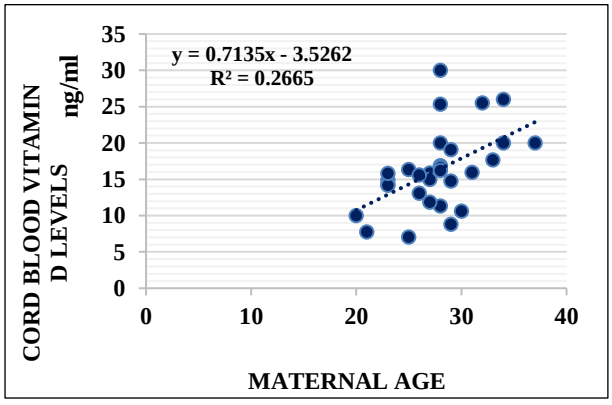

Figure 3: Correlation between the maternal age and cord blood vitamin D levels which was statistically significant.

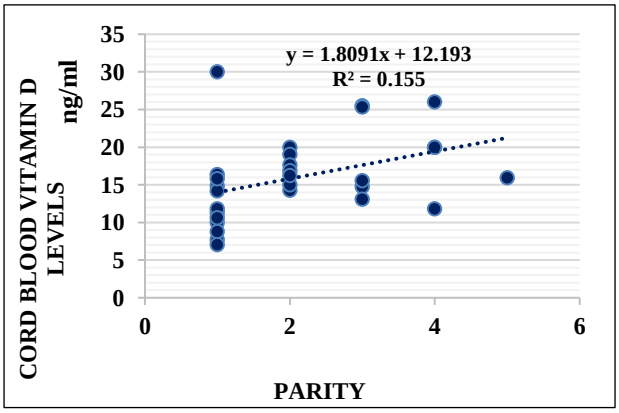

Figure 4: Correlation between parity and cord blood vitamin D levels which was statistically significant.

In this study the gestational age ranged from 25 weeks to 39 weeks with a mean gestational age of 35.73±3.9 weeks. The mean gestational age was 38.7±0.88 weeks in term and 32.7±3.39 weeks in preterm.

The mean vitamin D levels in mothers of term babies was 15.9±4.5 ng/ml and 14.3±3.52 ng/mL in mothers of preterm babies. There was no correlation between gestational ages and vitamin D levels in mothers (R= 0.08, p=0.907) nor with cord blood vitamin D levels (R=0.19, p=0.725) (Table 1, Table 2 and Table 3).

The mean cord blood vitamin D levels in term babies was 16.9±4.7 ng/mL and 15.4±6.09 ng/mL in preterm babies.

The mean BMI before pregnancy was 22.3±1.15 kg/m^2.

The sociodemographic profile in mothers (religion, dietary habits or socioeconomic class) analyzed by chi square test and fisher's exact test showed no association with cord blood vitamin D levels. None of the mothers were taking vitamin D supplements during pregnancy.

In this study all the mothers had low vitamin D levels with 93% having deficiency with 20% had severe deficiency (<10 ng/mL) and 7% having insufficient vitamin D as shown in (Table 1). The mean maternal serum vitamin D levels were 15.15±4.83 ng/ml.

The cord blood vitamin D levels were normal in only 3% of babies.83% had deficiency and 13% had insufficiency, with 13% having severe deficiency (<10 ng/mL) as shown in table 3. The mean cord blood vitamin D levels were 16.21±5.43 ng/ml.

There was no association between the cord blood vitamin D levels with birth weight (R=0.01, p=0.480), birth length (R=0.01, p=0.415) and birth head circumference (R=0.03, p=0.257).

There was a significant correlation between the maternal vitamin D levels and cord blood vitamin D levels. (R=0.77, p=0.000016) (Figure 5).

Table 1: Correlation between gestational age and maternal vitamin D levels.

Gestational age (weeks)	Vitamin D levels in mothers (ng/ml)					p value
	<20		20-29	≥30	Total	
	≤10	11- 20				
25-27	0	2	0	0	1	
28-30	0	3	0	0	3	
31-33	1	1	0	0	3	0.725
34-36	3	5	0	0	8	
37-39	2	11	2	0	15	
Total	6 (20%)	22 (73.3%)	2 (6.6%)	0	30	

Table 2: Cord blood vitamin D levels at various gestational ages.

Cord blood vitamin D levels (ng/ml)	Gestational age			p value
	Term	Preterm	Total	
<20	12(80%)	13(86.6%)	25	p=0.596
20 - 29	3(20%)	1(6.6%)	4	
≥ 30	0(0%)	1(6.6%)	1	
Total	15(100%)	15(100%)	30	

Table 3: Correlation of cord blood vitamin D levels with gestational age.

Gestational age (weeks)	Vitamin d levels in babies (ng/ml)					p value
	<20		20-29	≥30	Total	
	≤10	11-20				
25-27	0	2	0	0	1	p= 0.809
28-30	0	3	0	0	3	
31-33	2	0	0	0	3	
34-36	0	6	1	1	8	
37-39	2	10	3	0	15	
Total	4 (13%)	21 (70%)	4 (13.3%)	1 (3.3%)	30	

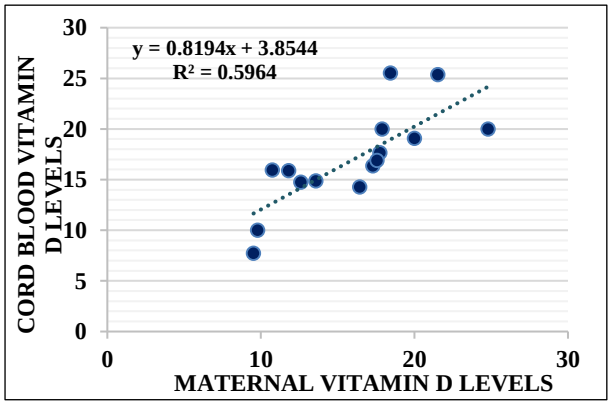

Figure 5: Correlation of maternal vitamin D levels with cord blood vitamin D levels which is statistically significant.

DISCUSSION

Equal number of term and preterm babies (15 each) along with their mothers were included in this study. The male to female ratio was 1:2 in term babies and 3:1 in preterm babies (Figure 1). The youngest mother was 21 years and the oldest mother was 37 years with a mean of 24 years. In this study younger mothers had lower levels of vitamin D. The maternal serum vitamin D levels measured before delivery showed a linear correlation with maternal age. This finding was statistically significant with a p value of 0.007. The cord blood vitamin D levels also showed a significant linear correlation with maternal age with a p value of 0.003. Similar finding was reported in a study done by Marshall et al, who stated that younger maternal age was associated with cord blood vitamin D deficiency or insufficiency.[8]

13 mothers were primiparous and 17 were multiparous. The mean vitamin D levels in the primiparous mothers was 13.68±3.5 ng/ml and in the multiparous mothers was 16.27±4.19 ng/ml. The mean cord blood vitamin D levels in these babies was 13.42±5.90 ng/ml and 18.06±4.31 ng/ml respectively. This finding was statistically significant with a p value of 0.03 (R=0.39) as shown in Figure 4. Similar finding was stated in a study done by Marshall et al, who reported that higher number of pregnancies were associated with cord blood vitamin D deficiency or insufficiency.[8]

In this study the gestational age ranged from 25 weeks to 39 weeks with a mean gestational age of 35.73±3.9 weeks. There was no correlation between gestational ages and maternal vitamin D levels (Table 1). This is in contrast to studies done by Milene Seori Kassai et al, and Shu Qin Wei et al, from Canada who concluded that mothers who had preterm babies had lower vitamin D concentrations compared to those who had term babies and their levels correlated to their baby's vitamin D status.[2,3]

This study included 15 term babies with a mean gestational age of 38.7±0.88 weeks and 15 preterm babies with a mean gestational age of 32.7±0.39 weeks. There was no correlation between gestational ages of the babies and cord blood vitamin D levels (Table 2 and 3). This was in accordance with studies done by Minoo Fallahi et al, from Iran who found no significant difference in vitamin D levels and gestational age.[9] Heather H Burris et al, from Boston found lower vitamin D levels in preterm babies <32 weeks in comparison to full term babies but they did not detect a clear linear association between vitamin D levels and gestational age.[10] Philip N Baker et al, from England reported no significant difference between the vitamin D levels in term and preterm neonates.[11] This was in contrast to a study done by Gurmeet Singh et al, who concluded that premature neonates had lower vitamin D levels when compared to mature neonates.[12]

The mean BMI in the mothers in this study was 22.3±1.15 kg/m^2. Maternal obesity during pregnancy has been associated with lower vitamin D levels in neonates at delivery.[13,14] Hence obese mothers were excluded in this study.

This study did not show any association between vitamin D levels and sociodemographic profile in mothers like religion, maternal dietary habits or socioeconomic classes. Similar results were also reported by Merewood et al.[15] This was in contrast to various studies done by Kansuda et al, from Thailand, Woolcott C et al, from Canada and El Koumi et al, who reported that key factors associated with neonatal vitamin D levels were maternal

age, dairy intake and supplement use.[16-18] None of the mothers were taking vitamin D supplements during pregnancy. It is not a common practice to supplement antenatal mothers with vitamin D as part of the routine prenatal care in India and the vitamin D levels in the mothers are a reflection of one's own diet and lifestyle.

In this study all the mothers had low vitamin D levels with 93% having deficiency with 20% had severe deficiency (<10 ng/mL) and 7% having insufficient vitamin D (Table 1). The mean maternal serum vitamin D levels were 15.15±4.83 ng/ml. Similar finding was reported by Shipra Kamal et al, from Ranchi and other authors.[19]

The cord blood vitamin D levels were normal in only 3% of our babies. 83% had deficiency and 13% had insufficiency, with 13% having severe deficiency (<10 ng/mL) (Table 3). The mean cord blood vitamin D level was 16.21±6.08 ng/mL. Various authors like Shipra et al, Sachan et al, Pradeep et al, have reported a similar finding in their studies in agreement to this finding.[19]

This study showed that maternal vitamin D levels had a strong correlation with neonatal cord blood vitamin D levels (R=0.77, p=0.000016) (Figure 5). Similar results were also reported by Kansuda et al, from Thailand and Minoo Fallahi et al, from Iran.[9,16]

This study did not show any significant correlation with cord blood vitamin D levels and anthropometry at birth. Similar results were seen in studies done by Inderpal Singh Kocher et al, and Camargo et al, who also found no association between cord blood vitamin D status and birth weight.[20,21] This is in contrast to a study done by Paulraj Sathish et al, which showed a statistically significant correlation between cord vitamin D levels and anthropometry.[22]

Limitation of this study was group comprised of mainly urban mothers and the sample size was small due to financial constraints.

CONCLUSION

Vitamin D deficiency is widely prevalent even in well-nourished mothers. Vitamin D supplementation may be helpful in antenatal mothers. Larger studies are needed to study the prevalence of vitamin D deficiency in mothers and babies and look for effectiveness of supplementation.

ACKNOWLEDGEMENTS

Authors would like to thank God Almighty, their teachers, fellow colleagues and family for their support. Authors would also like to thank Father Muller Research centre for the financial help as well as all the children and their parents involved in the study.

Funding: Partial funding from the Institution Research Fund
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Thomas DJ, Khan HU, Paul S, Jaidev MD, Hegde P. A study on vitamin D levels in preterm and term neonates and their mothers. Int J Contemp Pediatr 2020;7:387-92.