

Original Research Article

Correlation of neonatal cord blood with corresponding maternal blood levels of vitamin D3 at birth-a prospective observational study

Mahavir Jain¹, Abhishek Kulkarni^{2*}, Rahul Verma¹, Joewin Monteiro²

¹Department of Paediatrics, Sir H N Reliance foundation Hospital, Mumbai, Maharashtra, India

²Department of Paediatric and Adolescent Endocrinology, Sir H N Reliance Foundation Hospital, Mumbai, Maharashtra, India

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*Correspondence:

Dr. Abhishek Kulkarni,

E-mail: cpedndc@gmail.com

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ABSTRACT

Background: Vitamin D has a pivotal role in bone metabolism and the functioning of the body's immune, respiratory, endocrine, and cardiovascular systems. Synthesis of vitamin forms the major part of vitamin D stores in the body while dietary sources contribute to a much lesser extent. Vitamin D deficiency in infancy can lead to soft, malformed bones (rickets), seizures due to low blood calcium, and respiratory difficulties. Pregnant women and children are considered a high-risk group for vitamin D deficiency. The level of 25 (OH) D in neonates at birth depend entirely on their mothers' levels and several studies have shown a correlation between cord blood 25(OH)D levels and those of their mothers. We designed an observational study to assess the correlation between cord blood 25 (OH) D levels of the neonate at birth and the corresponding maternal blood 25 (OH) D levels.

Methods: A prospective observational study was conducted between June 2022 to June 2023 at the in-patient department of Sir HN Reliance Foundation Hospital and Research Centre, with prior institutional ethical clearance. A cohort consisting of mother-baby dyads, where the baby was a full term, healthy, singleton of either gender, irrespective of the mode of delivery was studied. Residual cord blood serum, taken for routine testing, was collected for study. Maternal serum procured routinely before deliveries for serology studies was used for estimation of 25 (OH) D levels.

Results: A total of 54 dyads of mother-baby were enrolled during the study period. 15 (27.78 percent) mothers had insufficient vitamin D levels, 6 (11.11 percent) were vitamin D deficient and 33 (61.11 percent) had sufficient vitamin D levels. The mean 25 (OH) D level among newborns was 26.37 (± 10.92) ng/ml. 19 (35.19 percent) newborns had insufficient vitamin D levels, whereas 17 (31.48 percent) were vitamin D deficient. There was a significant correlation observed between maternal and newborn vitamin D status ($p=0.013$).

Conclusion: A significant correlation was observed between the vitamin D levels of mothers and their neonates at birth, highlighting the crucial role of maternal vitamin D levels. Since fetuses rely entirely on their mothers for vitamin D, it is essential to ensure that antenatal vitamin D levels in pregnant woman are sufficient.

Keywords: Neonate, Maternal vitamin D, Neonatal vitamin D deficiency

INTRODUCTION

Vitamin D has a pivotal role in bone metabolism and the functioning of the body's immune, respiratory, endocrine, and cardiovascular systems. It is synthesized naturally in the body and can also be obtained through consumption

of foods such as fatty fish, which contain cholecalciferol (vitamin D3), as well as plants and fungi that provide ergocalciferol (vitamin D2). Synthesis of vitamin forms the major part of vitamin D stores in the body while dietary sources contribute to a much lesser extent. Optimal levels of vitamin D 25 (OH) for are considered

to be above 30 ng/ml (75 nmol/l); levels between 21–29 ng/ml (51–74 nmol/l) indicate insufficiency, while concentrations under 20 ng/ml (50 nmol/l) are suggestive of deficiency. Vitamin D deficiency in infancy can lead to soft, malformed bones (rickets), seizures due to low blood calcium, and respiratory difficulties.¹

Pregnant women and children are considered a high-risk group for vitamin D deficiency. Global reports suggest that 20-80 percent of pregnant women may suffer from inadequate vitamin D levels. Similarly, infants around the world show evidence of vitamin D deficiency, across different geographic regions and cultures.² The developing fetus relies solely on the mother's diet and nutrient reserves. Recent studies indicate that pregnant women often experience deficiencies in vitamins D, C, A, K, B-6, and E.³

Vitamin D freely crosses the placenta during pregnancy. The level of 25 (OH) D in neonates at birth depend entirely on their mothers' levels and several studies have shown a correlation between cord blood 25(OH)D levels and those of their mothers.⁴ Since a fetus is unable to synthesize vitamin D, it needs to be transferred across the placenta. Maternal vitamin D levels have been linked to fetal bone growth and birth weight, and these effects persist after birth.⁵ We designed an observational study to assess the correlation between cord blood 25 (OH) D levels of the neonate at birth and the corresponding maternal blood 25 (OH) D levels.

Aims and objectives

The primary aim of the study was to assess the correlation between cord blood 25 (OH) D levels of the neonate at birth and the corresponding maternal blood 25 (OH) D levels.

METHODS

A prospective observational study was conducted between June 2022 to June 2023 at the in-patient department of Sir HN Reliance Foundation Hospital and Research Centre, with prior institutional ethical clearance. A cohort consisting of mother-baby dyads, where the baby was a full term, healthy, singleton of either gender, irrespective of the mode of delivery was studied. Prior consent was taken before enrolling into the study. Pre and post term babies, mothers with non-singleton pregnancy were excluded from the study.

Based on the study by Subbarao & Mahabala, the correlation between maternal vitamin D levels and vitamin D levels in the newborn was 0.49. The sample size was calculated using this paper as a reference and assuming the following parameters: $\alpha=0.05$, Power $(1-\beta)=0.95$. Based on this, the estimated sample size was 48. The sample size was calculated using the formula: $N=((Z\alpha+Z\beta)/C)^2+3$. Where: The standard normal deviate

for $\alpha=Z\alpha=1.96$ The standard normal deviate for $\beta=Z\beta=1.64$ $C=0.5 \times \ln(1+r)/(1-r)=0.5361$

Residual cord blood serum, taken for routine testing, was collected for study. Maternal serum procured routinely before deliveries for serology studies was used for estimation of 25 (OH) D levels. All statistical analyses were performed using STATA.17 (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp L.L.C).

RESULTS

A total of 54 dyads of mother-baby were enrolled during the study period. Of the 54 mothers enrolled 29 were primi-parous and 25 were multiparous. The mean birth weight was 3043 grams (± 462.55). The mean 25 (OH) D level of the maternal cohort was 36.87 (± 16.10) ng/ml. 15 (27.78 percent) mothers had insufficient vitamin D levels, 6 (11.11 percent) were vitamin D deficient and 33 (61.11 percent) had sufficient vitamin D levels. The mean 25 (OH) D level among newborns was 26.37 (± 10.92) ng/ml. 19 (35.19 percent) newborns had insufficient vitamin D levels, whereas 17 (31.48 percent) were vitamin D deficient. 18 (33.33 percent) out of the 54 neonates had sufficient levels of 25 (OH) D. There was a significant correlation observed between maternal and newborn vitamin D status ($p=0.013$).

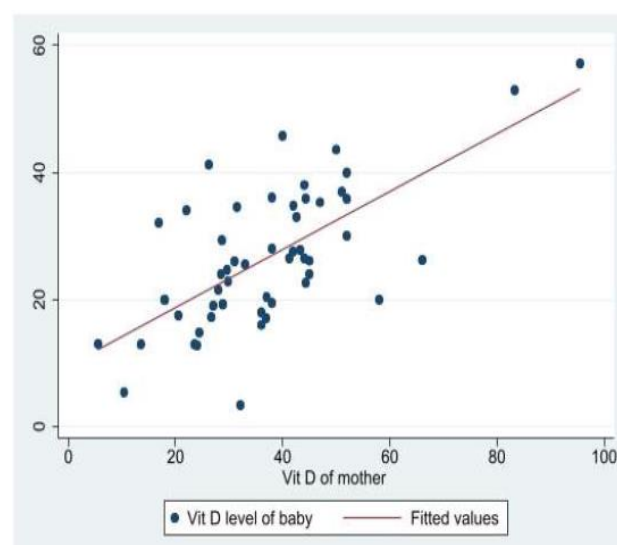


Figure 1: Scatter diagram depicting correlation between maternal and neonatal cord blood 25 (OH) D levels.

A linear relationship between 25 (OH) D level of the mother and that of the neonatal cord blood was observed on the scatterplot. A Pearson correlation was run to assess the relationship between 25 (OH) D level of the mother and neonatal cord blood 25 (OH) D of 54 participants. A strong positive correlation between the two with $r=0.67$ (p value= 0.000) was noted (Figure 1).

Table 1: Covariates and 25 OH D levels of the maternal-neonatal dyad.

Covariates	Maternal 25 (OH) D levels			Total	P value
	Deficient N (%)	Insufficient N (%)	Sufficient N (%)		
Age of mother (in years)					
20-25	0 (0.0)	1 (100.0)	0 (0.0)	1	0.6
26-30	3 (15.0)	5 (25.0)	12 (60.0)	20	
31-35	2 (7.41)	8 (29.63)	17(62.96)	27	
36-40	1 (16.67)	1 (16.67)	4 (66.67)	6	
Gravida					
1	2 (6.9)	7 (24.14)	20 (68.97)	29	0.208
2	3 (18.75)	7 (43.75)	6 (37.50)	16	
3	0 (0.0)	1 (33.3)	2 (66.67)	3	
4	0 (0.0)	0 (0.0)	4 (100.0)	4	
5	1 (50.0)	0 (0.0)	1 (50.0)	2	
Type of delivery					
Assisted	0 (0.0)	1 (11.11)	8 (88.89)	9	0.486
LSCS	4 (12.9)	9 (29.03)	18 (58.06)	31	
NVD	2 (14.29)	5 (35.71)	7 (50.0)	14	
Birth weight in grams					
Less than 2000	0 (0.0)	0 (0.0)	1 (100.0)	1	0.054
2000 to 2499	3 (60.0)	1 (20.0)	1 (20.0)	5	
2500 to 3499	3 (7.89)	10 (26.32)	25 (65.79)	38	
3500 or more	0 (0.0)	4 (40.0)	6 (60.0)	10	
Gender					
Male	4 (10.81)	10 (27.03)	23 (62.16)	37	
Female	2 (11.76)	5 (29.41)	10 (58.82)	17	
Neonatal cord blood 25 (OH) D					
Deficient	4 (23.53)	8 (47.06)	5 (29.41)	17	0.013
Insufficient	1 (5.26)	5 (26.32)	13 (68.42)	19	
Sufficient	1 (5.56)	2 (11.11)	15 (83.33)	18	

DISCUSSION

Vitamin D deficiency is common in the Indian population.⁷ The relationship between low vitamin D and adverse maternal outcomes such as pregnancy induced hypertension, hypertension in diabetic pregnancy, gestational diabetes mellitus, recurrent loss of pregnancy, preterm delivery, primary caesarian section and depression during postpartum period has been documented in recent years.⁸ Maternal secondary hyperparathyroidism and osteomalacia, neonatal hypocalcemia and tetany, delayed ossification of the cranial vertex, wide fontanelle and impaired fetal bone ossification has been reported by various authors, and reviewed in detail by others.⁹ In the present observational study, we considered the mother-baby as a dyad. A total of 54 dyads were included in the study. In our study, 29 (53.70 percent) of the mothers were primigravida and 16 (29.63 percent) were second gravida. 1,25 (OH)₂ D via the vitamin D receptor (VDR) improves skeletal muscle function. Deficiency of vitamin D can lead to proximal muscle weakness and reduced lower extremity muscle function, potentially increasing the risk of requiring a

caesarean section. However, our study did not find a significant correlation between 25 (OH) D levels and the mode of delivery. The average birth weight in our study was 3043 grams, with only 11 percent of infants weighing less than 2500 grams. There was no significant association between maternal 25 (OH) D levels and low neonatal birth weight.

Approximately 15 mothers (27.78 percent) had insufficient vitamin D levels, while 6 mothers (11.11 percent) were vitamin D deficient. Amongst the newborns, 19 (35.19 percent) had insufficient vitamin D levels, and 17 (31.48 percent) were vitamin D deficient.

Since maternal 25 (OH) D is the sole source of vitamin D for the fetus, pregnant women must maintain adequate vitamin D levels to ensure their infants have sufficient vitamin D levels at birth. Sathish et al found vitamin D deficiency in 63 percent of pregnant women and 63 percent of newborns.¹⁰ Arya et al also found that 63 percent of pregnant women were vitamin D deficient amongst newborns, the deficiency was 81.0 percent. Karim et al also observed that nearly 88 percent of

pregnant women are vitamin deficient, which is also relatively high.^{11,12}

Doses of vitamin D3 between 1000 to 2000 IU per day can be supplemented in the mid and late trimesters to pregnant women, without risk of toxicity or teratogenicity. Deficiency of vitamin D in pregnancy is treated with a dose of 4000 units/day.⁹ The present study observed a significant association ($p < 0.05$) between maternal and newborn cord blood vitamin D levels. There was a positive correlation between maternal and newborn vitamin D levels ($r = 0.67$). The findings reaffirm the dependency of the fetus on its mother for the supply of this vitamin.

This is a single centre study which was taken up limiting the inclusion of dyads from a small geographic location. The vitamin D levels have not been serially monitored in the mothers. This offers an avenue to include better monitoring of vitamin D levels during pregnancy in future studies and postulating safe vitamin supplementation threshold in pregnancy.

CONCLUSION

The current study underscores the prevalence of vitamin D deficiency among mothers and their neonates at birth. A significant correlation was observed between the vitamin D levels of mothers and their neonates at birth, highlighting the crucial role of maternal vitamin D levels. Since fetuses rely entirely on their mothers for vitamin D, it is essential to ensure that antenatal vitamin D levels in pregnant woman are sufficient.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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