

Relationship between maternal Vitamin D levels and neonatal Vitamin D levels with delayed neonatal hypocalcemia - A hospital-based observational study



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ABSTRACT

Background: Vitamin D has important role in regulating various metabolic processes in the body including calcium metabolism. Fetuses and neonates are dependent on their mothers to get adequate supply of Vitamin D. Maintaining adequate maternal Vitamin D levels may be highly beneficial for their fetuses and the babies. **Aims and Objectives:** The aim of the study was to find a correlation, if any, between maternal Vitamin D status and neonatal Vitamin D levels and delayed neonatal hypocalcemia. **Materials and Methods:** Fifty mother infant pairs with neonatal late onset hypocalcemia were included in the study. Detailed clinical history along with simultaneous maternal and neonatal blood samples were taken for estimation of calcium, phosphorus, parathormone (intact), and Vitamin D levels. **Results:** Mean maternal and neonatal serum Vitamin D (25-OH Vitamin D) levels were 19.5 ± 7.5 and 15 ± 8.5 , respectively. There was a statistically significant correlation between maternal and neonatal Vitamin D levels ($P=0.001$). There was also a direct correlation between low maternal Vitamin D levels and delayed hypocalcemia in neonates ($P=0.048$). Mean maternal and neonatal serum calcium levels were 9 ± 1.5 mg/dl and 6.2 ± 0.4 mg/dl, respectively. There was no significant statistical correlation between the two ($P>0.05$). **Conclusion:** Maternal Vitamin D level appears to be an important determinant of neonatal Vitamin D and serum calcium levels.

Key words: Delayed hypocalcemia; Vitamin D deficiency; Hyperphosphatemia; Mother-infant pair

INTRODUCTION

By definition neonatal hypocalcemia is total serum calcium <8 mg/dl (2 mmol/dl) in term and <7 mg/dl (1.75 mmol) in preterm neonates.¹ Conventionally, it is classified based on the onset of symptoms as early onset which manifests within the first 72 h of birth and late onset after 3 days of birth. The causes of neonatal late-onset hypocalcemia are hypoparathyroidism, hypomagnesemia, high phosphate intake, maternal hyperparathyroidism, and more commonly Vitamin D deficiency. Ionized calcium is essential for many biochemical functions. During pregnancy and breast

feeding, fetus and neonate are supplied with a large amount of maternal calcium. This transfer is very much dependent on adequacy of Vitamin D in the mother.¹ Studies have shown not only negative pregnancy and neonatal outcome in maternal Vitamin D deficiency but have also shown high prevalence of hypovitaminosis D in neonates.²⁻⁶

Maternal Vitamin D deficiency is more common in women because of nutritional inadequacy, poor sun exposure.¹ This is accentuated in rural populations where women are compelled to stay inside or be dressed differently for social, cultural, and religious compulsions.² Union territory of Jammu and

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Kashmir is having similar ethno religious background, paying attention to this issue will be very important. Hence, this study was conducted to find a correlation, if any, between maternal Vitamin D status and neonatal Vitamin D levels and late onset hypocalcemia in this part of the country.

Aims and objectives

The aim of the study was to find a correlation, if any, between maternal Vitamin D status and neonatal late onset hypocalcemia in this part of the country.

MATERIALS AND METHODS

This was a hospital-based study conducted from July 2015 to June 2016 at GB Pant Children's hospital Srinagar, which is a tertiary care pediatric associated hospital of Medical College Srinagar. The study was approved by institutional ethics and scientific committee.

Inclusion criteria

Infants admitted after day 3rd of life but <1 month old who has a seizure and a documented hypocalcemia (serum total calcium <7.5 mg/dl) were enrolled for the study.

Exclusion criteria

Mother baby pairs with maternal diabetes mellitus, neonatal asphyxia, renal insufficiency, blood transfusions, or use of diuretics, anticonvulsants, Di George syndrome or ventilator care.

As only those babies were enrolled for the study that had a hypocalcemic seizure, sampling method employed was purposive in nature. After enrollment simultaneous maternal and neonatal blood samples were taken for the estimation of Ca, P, parathormone(intact), and Vitamin D. Hypocalcemia was taken as <8 mg/dl (2 mmol/L) and <7 (1.75 mmol) for term and preterm neonates respectively. Vitamin D levels <20 ng/ml was taken as low. Data thus obtained were tabulated as per the pre-designed pro forma and analyzed using SPSS version 21. P<0.05 was taken as significant.

RESULTS

A total of 50 neonates with delayed hypocalcemia (after 72 of post-natal life) were enrolled for the study having the mean age of 6.25 days. Majority of the study population consisted of male infants (n=27; 54%) and most of them were of term gestation (n=35; 70%). Forty (80%) neonates were exclusively breastfed and the rest of the infants were either on mixed feeding (n=5; 10%) or on breast milk substitutes (n=5; 10%). There was a striking relation with the period of year when the hypocalcemic babies were born. During winter (Dec–Feb) we recorded 22 births, while as during summer we had just 2 hypocalcemic neonates (Table 1).

Mean serum calcium for infants and mothers was 6.2 ± 0.4 mg/dl and 9 ± 1.5 mg/dl, respectively. Mean serum phosphorus in neonates and mothers was 5 ± 1.8 mg/dL and 4.5 ± 0.50 mg/dL; serum alkaline phosphatase (ALP) 461.0 ± 197.57 U/L and 400.70 ± 110.84 U/L; and mean serum parathyroid hormone (PTH) 50.99 ± 20.49 pg/dL and 52.41 ± 29.4 pg/dL, respectively. None of these levels had a significant correlation between maternal and neonatal levels. Thirty-seven neonates (74%) and 32 mothers (65%) had Vitamin D deficiency. All the 32 neonates born to mothers with Vitamin D deficiency had hypocalcemia. Mean serum neonatal Vitamin D (25-OH Vitamin D₃) was 15 ± 8.5 nmol/L. Mean maternal serum Vitamin D (25-OH Vitamin D) was 19.5 ± 7.5 . There was a statistically significant correlation between maternal and neonatal serum Vitamin D levels ([P=0.001]; Table 2).

Out of mothers of 50 neonates with seizures and late onset hypocalcemia, 32 were having low Vitamin D levels. The proportion of mothers with low Vitamin D level was significant higher (Table 3).

DISCUSSION

Late onset hypocalcemia is an important cause of neonatal morbidity and mortality.¹ There are many causes of

Table 1: Characteristics of neonates with delayed hypocalcemia

Demographic variable	Value
Age (onset of hypocalcemia) days	6±2.5
Gender (n)	
Female	27
Male	23
Type of feeding (n)	
Breast milk	40
Mixed feeding	10
Breast milk substitutes	10
Season of birth time (Number of babies)	
Spring (March-May)	18
Summer (June-August)	2
Autumn (September-November)	8
Winter (December-February)	22
Birth weight (grams)	2250–3950

Table 2: Comparison of paired maternal and neonatal sera for Vitamin D, calcium, phosphorus, alkaline phosphatase

Variable	Maternal	Neonatal	P-value
	Mean±SD	Mean±SD	
Phosphorus	4.5±0.50	5±1.8	>0.05
Serum total calcium	9±1.5	6.2±0.4	>0.05
Alkaline phosphatase	400±110.84	461±197.57	>0.05
25 OH D	19±7.5	15±8.5	<0.001
Parathyroid hormone	52.41±29.4	50.99±20.49	>0.05

Table 3: Comparison of paired maternal and neonatal sera for Vitamin D and calcium

Neonates (n=50)	Hypocalcemia	Chi-square	P-value
Mothers (n=50)			
Low Vitamin D3	32	3.92	0.048
Normal Vitamin D3	18		
Total	50		

neonatal hypocalcemia and maternal hypovitaminosis D is one of them. Maternal Vitamin D levels are also an important determinant of neonatal Vitamin D levels because fetuses are unable to synthesis Vitamin D and are dependent on placental transfer for the same. Hence, the maternal Vitamin D level has great importance in determining the neonatal Vitamin D levels. Vitamin D plays directly and indirectly important roles in many important metabolic pathways and by improving maternal Vitamin D status; neonatal outcomes are likely to improve.

In our study, 37 (74%) neonates and 32 (65%) mothers had Vitamin D deficiency. All the mothers with Vitamin D deficiency had babies with Vitamin D deficiency. Khalesi et al.,² reported similar findings of hypovitaminosis D prevalence and these findings are higher in comparison with other studies.^{7,8} This may reflect differences in Vitamin D levels in different populations for environmental and socio-cultural factors. Nevertheless, the findings of our study, similar to most of the previous ones,^{9,10} have shown a strongly positive correlation between level of 25(OH) D in mothers and neonates. This reflects the importance of maternal Vitamin D levels in maintaining the fetal and subsequently the neonatal Vitamin D levels.

The mean serum calcium levels (9 ± 1.5) were within normal limits and the mean neonatal serum calcium levels were in hypocalcemia range. This possibly reflects the fact that the maternal Vitamin D levels and not the maternal serum calcium levels determine the serum calcium levels of neonates in neonatal period. There is a considerable accretion of calcium during the third trimester and through breastfeeding in a neonate. Levels around 10 mg/kg/day which are required to support an active skeletal growth are supplied in the third trimester.⁹ If mother suffers from Vitamin D deficiency, the neonate encounters this deficiency due to reduced placental Vitamin D transmission and in case of extended maternal Vitamin D deficiency during breast feeding, the neonate will be at risk of rickets.¹⁰

Both ALP and phosphorus levels were well within the normal limits. No elevation of ALP or parathyroid hormone was observed in neonates with late-onset hypocalcemia despite maternal Vitamin D deficiency. Similar findings have been reported by other researchers.¹¹

This is partly because newborns do not have developed a fully mature parathyroid sensitivity to low Vitamin D and hypocalcemia.

Gender had no effect on the prevalence of delayed hypocalcaemia which is similar to findings of the previous studies.⁹ This may be for the fact that it is the mother's Vitamin D levels and not the genetic makeup of babies that determines Vitamin D level and serum calcium levels of the babies. Majority of the babies with documented hypocalcemia was born during winter months. This may be reflective of lack of sufficient sun exposure during winters.¹¹

Exclusive breastfeeding was a risk factor in late onset hypocalcemia when the mother was Vitamin D deficient. Other researchers have documented similar results.¹¹ Usually babies achieve a full RDA of Vitamin D when they reach to the ages of around 3–4 months. Low levels of Vitamin D in breast milk compounded with insufficient accretion of Vitamin D and calcium during 3rd month of gestation for low maternal levels of Vitamin D result in higher incidence of hypocalcaemia in early neonatal period.

Limitations of the study

Only 50 mother infant pairs from a limited population catchment area have been enrolled for the study. This limits the generalizability of our study findings.

CONCLUSION

Maternal Vitamin D levels appear to be an important determinant of neonatal Vitamin D and serum calcium levels.

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AAW - Conceiving the idea of study and data collection; **AAW, SHT,** and **MAB** - Contributed in data analysis, critical appraisal, preparation of manuscript, and final approval.

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