Original Article

Correlation of Serum Vitamin D Levels in Lactating Mothers and Their Infants

Minhaz Husain, Manish Verma[1], Rakesh Jora[2], Jai Prakash Soni[2], Pramod Sharma[2]

Department of Paediatrics, Banaras Hindu University, Varanasi, Uttar Pradesh, [1]Department of Paediatrics, JLN Medical College, Ajmer, [2]Department of Paediatrics, Dr. S. N. Medical College, Jodhpur, Rajasthan, India

Abstract

Background: Although Vitamin D deficiency is highly prevalent in Indians, data on Vitamin D eficiency in lactating mothers and exclusively breast fed infants is inadequate. **Objective:** This study was done to evaluate the prevalence of Vitamin D deficiency in lactating mothers and their infants and to find out any correlation between them. **Materials and Methods:** This hospital based, cross sectional study included 200 healthy infants between 1-30 days and their mothers. Serum sample was collected from both for Ca, inorganic phosphate (IP), alkaline phosphatase (ALP), and 25(OH)D. **Results:** Mean serum 25(OH)D level of mothers was 11.33 ± 5.86 ng/ml with a range of 2–37 ng/ml. Hypovitaminosis D was defined as serum 25(OH)D level <10 ng/ml. Almost 94 (47%) of mothers were having hypovitaminosis D. Mean serum 25(OH)D level of infants was 11.92 ± 7.89 ng/dl with a range of 2.5–68 ng/dl. Ninety (45%) infants were having hypovitaminosis D. There was a moderate positive correlation between individual mothers' and infants' serum 25(OH)D values (Pearson coefficient = 0.516, $P < 0.001$). Using logistic regression, it was found that infants born to mothers with hypovitaminosis D carry a 4.47 times more risk of developing hypovitaminosis D as compared to infants born to mothers with normal serum 25(OH)D (Odds ratio = 4.47, $P < 0.001$). **Conclusion:** This study shows a high prevalence of Vitamin D deficiency in lactating mothers and their breastfeeding infants with a positive correlation between them. These results provide a justification for adequate Vitamin D supplementation of all exclusively breastfeeding infants and highlight the urgent need to improve maternal Vitamin D status.

Keywords: Alkaline phosphate, calcium, infants, lactating mother, sunlight, Vitamin D

Introduction

Vitamin D is required to maintain calcium (Ca) and phosphorus balance. It plays an important role in the maintenance of strong skeleton. Vitamin D deficiency was considered to be rare among Indians because of plenty of sunshine.[1] However, recent studies have shown that serum 25-hydroxy (25[OH]) levels are remarkably subnormal in Asian Indians.[2] Such Vitamin D deficiency has been reported in all the age groups, i.e., neonate to adults. We have seen that Vitamin D deficiency is widely prevalent in India, especially during pregnancy. This will have an impact on Vitamin D content of breast milk. As newborn is exclusively breastfed during first 6 months of life, so totally dependent on Vitamin D content of breast milk. As this deficiency is a continuum of deficiency during pregnancy, fetal storage of Vitamin D will also be very limited. Combination of these two factors, low fetal reserve of Vitamin D as well as low intake of Vitamin D from breast milk will put infants at very high risk of Vitamin D deficiency.

In a population that already has a high prevalence of Vitamin D deficiency and poor dietary Ca intake, the problem is likely to worsen during pregnancy because of the active transplacental transport of Ca to the developing fetus. The prevalence of newborn Vitamin D deficiency ranges from 11% to 93%, depending on the definition of deficiency used and the population studied.[3] Because Vitamin D crosses the placenta, Vitamin D level of the newborn is entirely dependent on the maternal Vitamin D level.[4] Therefore, a high prevalence of Vitamin D deficiency in pregnant women correlates with a

Address for correspondence: Dr. Manish Verma,
IW/3/7, Behind Isolation Ward, JLN Hospital,
Ajmer - 305 001, Rajasthan, India
E-mail: mverma83@gmail.com

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correspondingly high prevalence of Vitamin D deficiency in newborns. Although some studies indicate low neonatal levels of Vitamin D may be associated with adverse neonatal outcomes.[5]

An American study found that serum 25(OH) Vitamin D (25[OH] D) <37.5 nmol/L was a significant risk factor for infants being born small for gestational age (SGA) among white but not black women.[6] A Dutch study of 3730 mothers found that infants born to mothers with serum 25(OH) D <29.9 nmol/L were more likely to be born SGA and had a significantly lower birth weight than those born to mothers with serum 25(OH)D >50 nmol/L.[7] Information generated by this research will help identify sociodemographic, obstetric, and personal health factors that combine to influence Vitamin D levels in the lactating mothers.

Subjects and Methods

The present study was a prospective, hospital based, cross-sectional study. Healthy, exclusive breastfed infants aged between 1 and 30 days and their mothers admitted in the postnatal ward or outborn admitted in the pediatric ward were evaluated clinically and biochemically for asymptomatic Vitamin D deficiency. This study has been conducted in the Department of Paediatrics, Dr. S. N. Medical College, Jodhpur, Rajasthan, over 1 year duration. Two hundred healthy breastfed infants and their mothers were included in this study. Mothers were evaluated for any clinical features suggestive of Vitamin D deficiency. These features include bone pains, muscle cramp, and signs such as bow legs and knock knee. Renal function tests, liver function tests, serum Ca, phosphorus, alkaline phosphates, and serum 25(OH)D3 estimation were done. Random urine sample has been taken for Ca: creatinine ratio. Infants were evaluated for clinical features of rickets such as wide anterior fontanelle and frontal bossing. Serum Ca, phosphorus, alkaline phosphates, and serum 25(OH)D of infants were calculated. Infants were subjected to a detailed anthropometry and clinical examination. Inclusion criteria of infants were full-term singleton deliveries, exclusively breastfed, aged 1–30 days, no gross congenital malformation, and no congenital cardiac, renal, liver, or bone disease. Exclusion criteria for mothers were preexisting diabetes mellitus, hypertension, parathyroid disease, chronic renal or liver impairment, uncontrolled thyroid disease, psychological instability (concurrent treatment with antipsychotic drugs), and any condition requiring surgery during the study period.

A detailed history was taken focusing on factors that could influence the Vitamin D nutrition of women. These included age, parity, socioeconomic status, education status, nutrition status (body mass index [BMI]), dietary habits, religion (sun exposure), and dietary evaluation were done using 24 h recall method. Oral informed consent was obtained from all subjects. Approval from the Institutional Ethics Committee was obtained.

Biochemical analysis

Serum sample was collected by venepuncture for Ca, inorganic phosphate (IP), alkaline phosphatase (ALP), and 25(OH)D. The serum sample was analysed with spectrophotometry. Morning nonfasting urine sample was collected from mothers for measurement of urine Ca to creatinine ratio. Serum Ca was corrected for serum albumin.

The normal upper limit for maternal ALP was taken 240 U/L, and the normal upper limit for cord blood ALP was taken as 1076 U/L.[8] Serum 25(OH)D was assayed using a quantitative chemiluminescent immunoassay method by DiaSorin, IDS, Siemens, Abbott Diagnostic (ARCHITECT) Vitamin D testing method by Roche. At a concentration below 13 ng/mL (which is the lower limit based on linearity), coefficient of variation was within 10%. The assay has a measuring range of 13–96 ng/mL.[9] The normal range of maternal as infants 25(OH)D was similarly taken as 10–80 ng/mL.

Statistical analysis

All the results were analyzed using Windows SPSS software (Version 25.0, IBM Corp, Armonk, NY) and *t*-test was used for comparison of means. Chi-square test was used for comparison of proportion. Pearson coefficient was used to find a correlation between two variables. Logistic regression was applied to find the odds ratio. Significance at $P \leq 0.05$ was taken for two-sided tests.

Results

In total, 200 mother–infant pairs participated in this study. Maternal and newborn characteristics are summarized in Table 1. The mean serum ALP level of mother was 246 ± 93.13 IU/L with a range of 119–960. Forty-eight percentage mothers were having elevated ALP levels, indicating the presence of biochemical osteomalacia (ALP ≥240 IU/L). Only 15% of the women had symptoms suggestive of Vitamin D deficiency in the form of muscle cramps and bone pains. Levels of maternal and infants' blood biochemical markers are summarized in Table 2. The mean serum ALP level of infants was 246.29 ± 105.90 IU/L with a range of 103–870 IU/L. None of the infants were having elevated ALP levels (≥1076 IU/L). Fourteen (7%) of infants had hypocalcemia (total Ca <8 mg/dl), and all these infants had serum 25(OH)D level <10 ng/ml.

Table 1: Maternal and newborn characteristics (*n*=200)

Parameter	Value
Age of mother (year)	23.16±3.96
Weight of mother (kg)	56.02±10.33
Parity	1.84
Hindu/muslim	148/52
Infants age (day)	5.48±3.34
Male:Female	0.92:1
Gestational age (week)	38.60±0.98
Term AGA/SGA	118/82

x±SD (all such values). AGA: Appropriate for gestational age, SGA: Small for gestational age, SD: Standard deviation

Table 2: Levels of maternal and cord blood biochemical markers

	Maternal	Infants
25(OH)D (ng/ml)	11.33±5.86	11.92±7.89
ALP (IU/L)	246±93.13	246±105.9
Calcium (mg/dl)	9.35±1.16	9.46±1.03
Phosphorus (mg/dl)	4.24±0.55	4.83±0.62
Hypovitaminosis D, *n* (%)	94 (47)	90 (45)

ALP: Alkaline phosphatase, 25(OH)D: 25-hydroxy vitamin D

Twenty-two (11%) of mothers had low total serum Ca levels (<8 mg/dl) and 18 of these mothers had hypovitaminosis D (<10 ng/ml). Seventy-two (36%) mothers had normal serum total Ca despite serum hypovitaminosis D <10 ng/ml. The mean serum IP level in infants was 4.83 ± 0.62 mg/dl. Two (1%) infants found hypophosphatemic (<3 mg/dl). The mean serum IP level in mothers was 4.24 ± 0.55 mg/dl. Nearly 4.5% mothers had low IP level.

Mean serum 25(OH)D level of mothers was 11.33 ± 5.86 ng/ml with a range of 2–37 ng/ml. Hypovitaminosis D was defined as serum 25(OH)D level <10 ng/ml. Almost 94 (47%) of mothers were having hypovitaminosis D. Mean serum 25(OH)D level of infants was 11.92 ± 7.89 ng/dl with a range of 2.5–68 ng/dl. Ninety (45%) infants were having hypovitaminosis D. The mean serum 25(OH)D levels in the mothers and infants in our study were 11.33 ± 5.86 ng/ml and 11.92 ± 7.89 ng/ml, respectively. There was a moderate positive correlation between individual mothers' and infants' serum 25(OH)D values (Pearson coefficient = 0.516, P <.001). The mean serum Ca levels in the mother and infant in our study were 9.35 ± 1.16 and 9.43 ± 1.03 mg/dl, respectively. There was no statistically significant difference between mean serum Ca levels in mother and infants (P = 0.486). Correlation between serum ALP and IP was not studied due to the difference in normal levels in young infants and adults. Ninety-four mothers had hypovitaminosis D. Sixty (63.38%) of their infants also had low serum 25(OH)D levels. In contrast, only thirty (28.3%) born to 106 mothers with normal serum 25(OH)D levels had hypovitaminosis D. Using logistic regression, it was found that infants born to mothers with hypovitaminosis D carry a 4.47 times more risk of developing hypovitaminosis D as compared to infants born to mothers with normal serum 25(OH)D (Odds ratio = 4.47, P < 0.001). There was no significant correlation between maternal serum Vitamin D levels with age, BMI, socioeconomic status, parity, dietary habits, and education status. There is no significant difference of mean Vitamin D levels of Muslim (45.9%) and Hindu (50%). Infants with hypovitaminosis D did not had increased serum ALP level (≥1076 IU/L), so it seems that ALP is less sensitive in detection of hypovitaminosis D in infants. No significant correlation was observed between infants' Vitamin D level and their characteristics such as weight, gestational age, and appropriate for gestational age (AGA)/SGA.

Discussion

Deficiency of Vitamin D is widely prevalent worldwide. Most of the studies related to this subject are from American and European Nations. However, population found to be at highest risk in these studies has predominantly been immigrants from Asia.[10] A study from Glasgow[11] showed florid rickets occurred most commonly among Asian children. There is a paucity of data on the prevalence and manifestations of Vitamin D deficiency from India and rest of Asia. However, there are few reports that indicate Vitamin D deficiency is quite prevalent here as well. Most of the studies have been done on pregnant women and cord blood Vitamin D. Our study presents the first of its kind in Western Rajasthan to date, in which we have done serum Vitamin D level in lactating women and exclusively breastfed infants from a population in a tropical country. In the present study, we have taken the cutoff value to define hypovitaminosis D is <10 ng/ml. This is in accordance with most studies done on this subject. Accordingly, ninety-four (47%) mothers had hypovitaminosis D (<10 ng/ml), out of them 68 (34%) had moderate hypovitaminosis D (5–9.9 ng/ml) and 26 (13%) had severe hypovitaminosis D (<5 ng/ml). The normal range of serum 25(OH)D in adults was taken as 15–80 ng/ml.[12] According to Lips,[13] hypovitaminosis D is considered to severe, if serum 25(OH)D is < 5 ng/ml, moderate, if serum 25(OH)D is 5–10 ng/ml, and mild, if serum 25(OH)D is 10–20 ng/ml. In our study, the mean Vitamin D of mother was 11.33 ± 5.86 ng/ml with a range of 2–37 ng/ml. The mean 25(OH)D level was on lower side, may be due to darker skin pigment, low dietary intake of Ca, higher atmospheric pollution in Indian cities, and less use of milk or milk products. Dawodu *et al*.[14] conducted a study in the United Arab Emirates and reported 61% of mothers deficient in Vitamin D. In this study, sample size was small and high prevalence of hypovitaminosis D was due to less outdoor activity and covering of body by women (use of burqa). Sachan *et al*.[15] conducted a study in Northern India and found 42.5% women were having hypovitaminosis D (<10 ng/ml), whereas 66% had value <15 ng/ml. On regression analysis, they had found the cutoff value for hypovitaminosis D was <22.5 ng/ml. On this basis, in their study, 84% women had hypovitaminosis D and higher as compared to our study. Seth *et al*.[16] similar to our study, the prevalence of hypovitaminosis D was 47.8%. The mean Vitamin D was 10.9 ± 5.8 ng/ml. However, in our study, the mean serum 25(OH)D level was 11.33 ± 5.86 ng/ml, more as compare to this study with a range of 2–37 ng/ml. Hypovitaminosis D and osteomalacia among pregnant South Asian women had been widely reported in studies done by various other authors.[2,17,18] However, a few of them[2,17] were from temperate regions such as the United Kingdom[10] and Norway[19] where the already low availability of overhead sun is compounded for Asian women by poor outdoor activity, pigmented skin, and excessive clothing. In the present study, we have tried to find out the risk factors that could lead to hypovitaminosis D in mothers. However, we found no statistically significant difference of these factors on Vitamin

D status of mothers. Seth *et al*.[16] and Sachan *et al*.[15] found similar results.

In our study, serum 25(OH)D deficiency was found in 45.9% of Muslims and 50% in Hindu, the difference is statistically insignificant ($P = 0.63$). Opposite to our study by Seth *et al*.[16] found that Muslim women had 2.71 times more risk of developing hypovitaminosis D as compared to non-Muslims (odds ratio: 2.71, $P = 0.091$). Sociocultural practices in Muslims restrict adequate sun exposure in women, but Western Rajasthan which is located at high altitude with good sunlight and increased UV exposure might be responsible for less prevalence of hypovitaminosis D in Muslim population.

The normal range of serum 25(OH)D in infants is 7.4–53 ng/ml. The cutoff value to define hypovitaminosis D is taken as 10 ng/ml. Ninety (45%) infants had hypovitaminosis D. According to the classification proposed by Lips,[13] forty (20%) infants had severe (<5 ng/ml), 50 (25%) had moderate (5–10 ng/ml), and 92 (46%) had mild hypovitaminosis D (10–20 ng/ml). Mean serum 25(OH)D level of infants was 11.92 ± 7.89 ng/ml in our study. Worldwide, several studies have shown a high prevalence of hypovitaminosis D in infants. In a study from Leeds,[10] 68% of cord blood samples and 36% of newborn infants had serum Vitamin D levels <10 ng/ml. There was no significant difference between mean 25(OH)D level in T_{AGA} and T_{SGA} ($P = 0.895$).

The mean serum 25(OH)D levels in the mothers and infants were 11.33 ± 5.86 ng/ml and 11.92 ± 7.89 ng/ml, respectively. There was no statistically significant difference between the two. However, a moderate positive correlation was found between individual mothers' and infants' serum 25(OH)D values (Pearson coefficient = 0.516, $P < 0.001$) [Figure 1]. Earlier most of the studies[4,18] done on pregnant women and cord blood Vitamin D status and they found that cord blood Vitamin D is strongly correlated with maternal values. In our study, 94 mothers had hypovitaminosis D and 60 (63.38%) of their infants also had hypovitaminosis D. In contrast, only thirty (28.3%) infants born to 106 mothers with normal serum 25(OH)D levels had hypovitaminosis D. Using logistic regression, it was found that infants born to mothers with hypovitaminosis D carry a 4.47 times more risk of developing hypovitaminosis D as compared to infants born to mothers with normal serum 25(OH)D (Odds ratio = 4.47, $P < 0.001$). Sachan *et al*.[15] similar to our study found that cord blood Vitamin D is strongly correlated with maternal values ($r = 0.79$, $P < 0.001$). In our study, the mean serum Ca levels in the mother and infant were 9.35 ± 1.16 mg/dl and 9.43 ± 1.03 mg/dl, respectively, with no statistically significant difference.

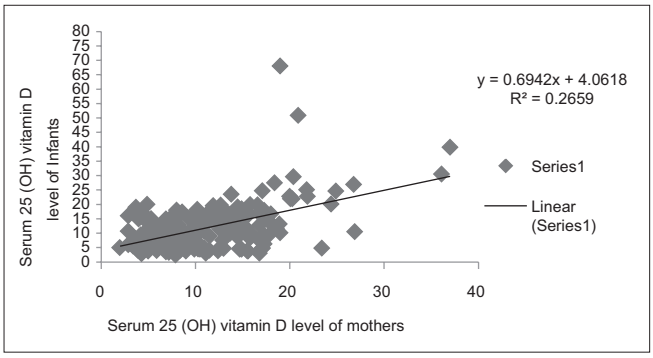

Figure 1: Correlation of 25(OH) Vitamin D among mothers and infants

In the present study, the mean total serum Ca was 9.35 ± 1.16 mg/dl with a range of 6.2–14.2 mg/dl. Only 22 (11%) mothers had low total serum Ca levels (<8 mg/dl) and 18 (9%) of these mothers had hypovitaminosis D (<10 ng/ml). Seventy-two (36%) mothers had normal serum total Ca despite serum hypovitaminosis D <10 ng/ml.

Conclusions

Our study showed that there is an increased prevalence of Vitamin D deficiency in lactating mothers and their breastfeeding infants which have been proved by other authors also. This study is one of few studies, may be first in Western Rajasthan, in which we have tried to find out the correlation between Vitamin D levels of lactating mothers and their infants. Infants born to mothers with hypovitaminosis D had 4.47 times higher risk of developing hypovitaminosis D as compared to those born to mothers with normal Vitamin D levels. The results of our study provide a justification for adequate Vitamin D supplementation of all exclusively breastfeeding infants and highlight the urgent need to improve maternal Vitamin D status. Hence, we conclude from our study that there is a high prevalence of physiologically hypovitaminosis D among lactating women and their newborns, the magnitude of which warrants public health intervention.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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