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Original Research Article

Vitamin D levels in preterm and term neonates at birth

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ABSTRACT

Background: Vitamin D deficiency is a significant health problem throughout India irrespective of gender, age, race and geography. It plays important role in neonatal period in fetal skeletal growth, prevention of rickets, sepsis, respiratory tract infections, cancer, cardiovascular diseases, diabetes and other endocrine disorders. Thus, we aim to study vitamin D levels in neonates at birth and its relationship with gestational age.
Methods: This was a hospital based prospective observational study. Total 300 neonates born at SGRDIMSR, Amritsar were enrolled out of which 150 were term and 150 preterm.
Results: Overall 85.67% neonates were found to be deficient in vitamin D. Mean 25 (OH) levels in <32, 32≤37, ≥37 weeks gestation was 12.46, 17.96, 19.36 ng/dl respectively. Deficiency was present in 94.74%, 87.78%, 82.67% and neonates born <32 weeks, 32≤37 weeks, ≥37 weeks gestation respectively. No significant relationship was found between vitamin D and gestational age. Vitamin D levels were higher in neonates born by LSCS and mothers without vitamin D supplementation.
Conclusions: Vitamin D deficiency was prevalent in neonates. Premature neonates had low levels as compared to the mature ones however the association between two was found to be insignificant.

Keywords: Deficiency, Vitamin D, Neonates, Preterm, Term

INTRODUCTION

Vitamin D deficiency is a significant health problem prevalent in India despite plentiful sunshine. Vitamin D deficiency is widespread in individuals irrespective of gender, race, geography and age. Vitamin D plays important role in neonatal period. Effects of vitamin D deficiency on fetal health are plenty; some being short term and others may become apparent in later life. Vitamin D has direct effects on neonatal immune system effecting both innate and adaptive immunity. Vitamin D has well documented role in causation of rickets. With severe maternal vitamin D deficiency, the fetus rarely may develop rickets in utero with manifestation at birth.[1] Throughout gestation, it does play a role to certain extent in fetal skeletal development, tooth enamel formation and general fetal growth and development.[2] Further, it has been seen that cardiovascular risk factors may have origin in fetal vitamin D deficiency.[3] Vitamin D plays an important role in prevention of sepsis and morbidities in neonatal period.[4]

The manifestations of deficiency may vary from hypocalcemic seizures, tetany in infancy and adolescence to florid rickets in toddlers. Vitamin D deficiency is associated with increased risk for infants to develop type 1 diabetes mellitus, cancers and other endocrine disorders in later life. Vitamin D deficiency is also associated with respiratory tract infections in newborns and wheezing episodes later in life.[5] Vitamin D deficiency at birth is also associated with higher risk of developing atopic dermatitis.[6] Low vitamin D levels has also been considered as one of the risk factor for respiratory distress syndrome.[7]

The objective of this study was to determine vitamin D levels in neonates both preterm and term and its relationship to gestational age.

METHODS

The present study was prospective observational conducted at Sri Guru Ram Das Institute of Medical Sciences and Research, Vallah, Sri Amritsar. Total 300 cases were enrolled out of which 150 were preterm and remaining 150 were term Cord blood sample of new-borns were collected 3 ml in two separate red topped vials (with clot activator), one for 25 (OH) D and the other for alkaline phosphatase (ALP) and total serum calcium. These were sent to biochemistry lab of SGRDIMSR hospital after labelling the vials with patient's name and MRD number. After centrifugation, serum was separated and stored at -20 degree Celsius until analysed. Vitamin D was estimated by Direct ELISA method, serum calcium by cresolphthalein complexone method and serum ALP by PNPP (para nitro phenyl phosphate) method.

Informed written consent was obtained from parents / guardian of the children providing all the necessary information about the study. Serum levels of vitamin D >30 ng/ml were taken as sufficient, insufficiency is said to be present between 20 - 30 ng/ml and <20 ng/ml levels are designated as deficiency.[8] Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean±SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then non parametric test was used.

Statistical tests were applied as follows

- Quantitative variables were compared using ANOVA/Kruskal Wallis Test (when the data sets were not normally distributed) between the three groups
- Qualitative variables were correlated using Chi-Square test /Fisher's exact test
- Spearsman correlation coefficient was used to assess the association of gestational age in weeks with serum Vitamin D.

A p value of <0.05 was considered statistically significant.

RESULTS

Out of total 300 cases enrolled, overall deficiency was seen in 85.67%. Out of total cases 69% had levels below 20 ng/dl, 16.67% had insufficient levels (20-29 ng/dl) and 14.33% had sufficient levels (>30 ng/dl). Mean serum vitamin D in severely deficient group was 11.24ng/dl, in deficient group was 24.49 ng/dl and sufficient group was 45.17 ng/dl. Overall mean valve in both groups is 18.31ng/dl.

Table 1: Relationship of vitamin d levels with gestational age.

		Vitamin D levels (ng/dl)			P-value
		< 20	**20 - 30**	**>30**	
Gender	Male	142 (68.60%)	32 (64.00%)	22 (51.16%)	0.09
	Female	65 (31.40%)	18 (36%)	21 (48.84%)	
Gestational age (weeks)	<32	17 (89.47%)	1 (5.26%)	1 (5.26%)	0.223
	32≤37	90 (68.70%)	25 (19.08%)	16 (12.21%)	
	≥37	100 (66.67%)	24 (16.00%)	26 (17.33%)	
Type of delivery	NVD	80 (38.65%)	24 (48.00%)	25 (58.14%)	0.047
	LSCS	127 (61.35%)	26 (52.00%)	18 (41.86%)	
Vitamin D supplementation in mother	Yes	100 (48.31%)	49 (98.00%)	42 (97.67%)	<0.001
	No	107 (48.31%)	1 (2.00%)	1 (2.33%)	

In the present study it was found that in age group less than 32 weeks overall 94.74% had levels <30 ng/dl with deficiency in 89.47% and insufficiency in 5.26%. In age group 32 to 37 weeks overall 87.78% had levels below 30ng/dl with deficiency in 68.70% and insufficiency in 19.08%. In term neonates overall 82.67% had levels below 30 ng/dl cases with deficiency in 66.67% and insufficiency in 16%. Mean vitamin D levels in <32 week age group was 12.46 ng/dl, in 32≤ 37 week age group was 17.96 ng/dl and ≥37 weeks age group was 19.36 ng/dl. Thus, vitamin D levels were low in more premature neonates as compared to more mature ones however the difference between them is not significant (p = 0.223).

Out of 207 cases with levels below 20 ng/dl (deficient cases), 38.64% (n = 80) were born by NVD and 61.35% (n = 127) were born by LSCS. Among 50 vitamin D insufficient cases, 48% (n = 24) were born by NVD and 52% (n = 26) were delivered by LSCS. Out of 43 vitamin D sufficient cases, 58.13% (n = 25) were delivered by NVD and 41.86% (n = 18) were born by LSCS. Thus

cases born by LSCS had more prevalence of low vitamin D. The difference between them was significant though not highly significant (p = 0.047).

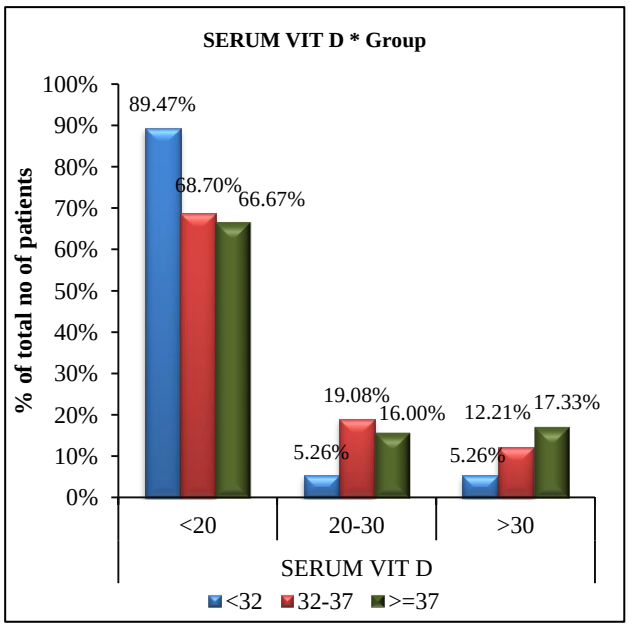

Figure 1: Relationship of vitamin d levels with gestational age.

In the present study it was found that out of 109 cases whose mothers had not received vitamin D supplementation 107 (98.16%) had levels below 20 ng/dl, 1 had insufficient levels (20-29 ng/dl) and one had sufficient levels. Out of 191 neonates whose mother had vitamin D supplementation in antenatal period, 100 (52.35%) had levels <20 ngdl, 49 (25.65%) had insufficiency (20-30 ng/dl), 42 (21.98%) had sufficient (>30 ng/dl) levels. Thus neonates born to mothers who had not received vitamin D supplementation in antenatal period had high prevalence of severe vitamin D deficiency as compared to those who had received vitamin D supplementation and the difference between the two is highly significant (p = <0.001).

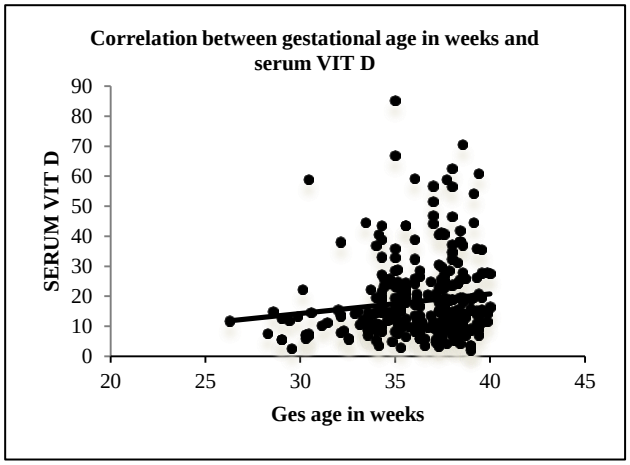

Figure 2: Scatter diagram (r = 0.115).

No association was found between serum calcium levels and 25 (OH) D levels as in spite of low levels of vitamin D serum calcium was within normal limits in 99% cases. Similarly in our study we found no significant association between 25 (OH) D and ALP.

DISCUSSION

In this study it was found that 85.67% of the neonates were deficient (20-30ng/dl) in serum 25 (OH) D levels whereas severe deficiency (<20 ng/dl) was present in 69% with mean serum vitamin D levels of 18.32ng/dl and median 14.4 ng/dl, which was comparable to various studies which have been conducted throughout the world. This higher deficiency in newborns is attributed to the fact that such higher deficiency ranging from 67% to 96% is prevalent in mothers as depicted in various studies on pregnant mothers from southern and northern states of India.[9,10] As already discussed fetal and newborn concentrations of 25 (OH) D deficiency depend on and correlate with maternal serum levels. Thus, newborns born to vitamin D insufficient mothers are at greater risk of developing vitamin D deficiency.[11] However even if mothers are marginally sufficient infants still have a risk of vitamin D deficiency, while those born to insufficient mothers are almost certainly deficient.[12] Kumar P et al found that 83% of the newborns had hypovitaminosis with mean cord blood level was 12.8 ng/dl.[13] Similar results were found found in study done by Khuri N in Jordan, Park S in Korea, Xiaodon in China, with deficiency in 94%, 91.7%, 84.1% neonates respectively.[14-16] Sachan A et al found low levels of cord blood 25 (OH) D (8.4±5.7 ng/mL).[17] Zeghoud F et al found 63.7% of the infants had calcidiol concentrations < or = 30 nmol/L at birth.[18] Dawodu et al found 44% of Arab infants had moderately severe deficiency with mean serum vitamin D levels 14.5nmol/.[19] Fallahi M found 56% of neonates had vitamin D deficiency in Trehan.[20]

In the present study it was found that higher prevalence of vitamin D deficiency and severe deficiency was present in more premature infants as compares to mature ones but the difference was not found to be significant. Similar results were found in studies Park S had found 51.1% of preterm infants were having severe vitamin D deficiency (25-OHD<10 ng/mL).[15] The serum 25-OHD concentrations did not correlate with gestational age. There were no significant differences in serum 25-OHD concentrations or incidence of severe vitamin D deficiency among early, moderate, and late preterm infants. Similarly study by Xiaodan showed no association between vitamin D and gestational age.[16] Monangi et al found that mean vitamin D level was lower in infants born <28 weeks than that born between 28- 32 weeks. Burris et al found that infants born before 32 weeks' gestation have an increased risk of low 25 (OH) D levels (below 20 ng/ml) as compared with more mature infants.[21,22] They found that there was no linear correlation of cord blood vitamin D with gestational age. Minoo F showed 48.5% of preterm and 65.5% of term

neonates had vitamin D deficiency showing more deficiency in term which was contrary to our study but the difference of vitamin D levels between term and preterm neonates was not significant.[20]

In present study, we found that neonates born by lower segment cesarean section were having higher prevalence of severe vitamin D deficiency as compared to those born by normal vaginal delivery. It can be attributed to the fact as found by Stephen J that maternal vitamin D deficiency influences mode of delivery.[23] Vitamin D deficiency has been linked to increased odds of primary cesarean delivery as well as a higher likelihood of emergency cesarean section.[24,25] So as maternal vitamin D levels has direct correlation with neonatal vitamin D levels as found in studies by Nicolaidou P, Bowyer L, Song J, neonates born by LSCS will have low vitamin D levels.[26-28] However studies by Skowrońska-Jóźwiak E, Gernand reveal no association of vitamin D deficiency with mode of delivery.[29,30]

In study it was found that mothers who had not received vitamin D supplementation had higher prevalence of vitamin D deficiency in cord blood as compared to those who had received supplementation and the difference was statistically significant ($p \leq 0.001$). Similar results were stated by Mirjam E in that cord blood 25-OHD concentrations were strongly associated with maternal vitamin D3 supplementation during pregnancy.[31] However Maghbooli Z differed and found no significant correlation between maternal and cord blood serum vitamin D levels with vitamin D intake during pregnancy.[32] In this study we have found that in cases with vitamin D deficiency serum alkaline phosphatase levels were within normal limits in 96% cases. Similar results were found in studies by Dijkstra SH, Shaheen S, Park S.[15,33] In present study, no correlation was found between 25 (OH) D and serum calcium levels which is comparable to the results shown by Park.[15]

CONCLUSION

Significant vitamin D deficiency (85.67%) was found in our study. Prevalence of vitamin D deficiency was found more in premature neonates as compared to the mature ones however the difference was not statistically significant. Prevalence of vitamin D deficiency was more in neonates born by LSCS than those delivered by NVD. Prevalence of vitamin D deficiency was more in male subjects as compared to the females even though difference was insignificant. So as the subnormal 25 (OH) D levels are not always related to hypocalcemia and raised ALP and no association was found in our study so these biochemical parameters should not be relied upon for diagnosis of vitamin D deficiency.

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