A study of pattern of vitamin D deficiency in preterm and term newborns at rural teaching hospital, Haryana, India

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Abstract

Background: Deficiency of Vitamin D is currently the most untreated nutritional deficiency worldwide. In India, despite plenty of sunlight, VDD prevalence is 50-90% in all age groups. The neonatal vitamin D level depends wholly on the maternal vitamin D level because vitamin D crosses the placenta during the last trimester of pregnancy

Objectives*:* To study the pattern of VDD in preterm and term newborns delivered at M.M. Institute of Medical Sciences and Research (MMIMSR), Mullana, Haryana, India.

Method: This was a hospital-based prospective observational study. Total of 100 neonates born at MMIMSR was enrolled out of which 50 were term and 50 preterm.

Results: Out of the 100 newborns, 53 had VDD. Of the 53 newborns with VDD, 32 (60%) were preterm and 21(40%) were term. Mean 25 (OH) level was 21.81 ng/dl.

Conclusions: In this study carried out at MMIMSR, 53% newborns had VDD. VDD was significantly more in preterm babies compared to term babies ($p<0.01$).

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(Key words: Preterm, term, vitamin D, newborns, pattern)

Introduction

Vitamin D deficiency (VDD) is currently the most untreated nutritional deficiency worldwide[1-3]. In India, despite plenty of sunlight, VDD prevalence is 50-90% in all age groups[4]. A fetus can rarely develop rickets in utero with clinical features at birth due to severe maternal VDD[5]. Throughout gestation, vitamin D plays a role in the development of the skeleton, tooth enamel formation and overall fetal growth[6]. Further, cardiovascular risk factors can lead to VDD in neonates[7]. Vitamin D is critical in the preclusion of sepsis and morbidities in the neonate[8]. VDD is linked to increased risk for infants developing diabetes mellitus type 1 and other endocrine disorders in later life, and atopic dermatitis at birth[9]. VDD is also associated with respiratory tract infections in newborns and wheezing events in later life[10]. Decreased vitamin D levels are considered as one of the risk factors for respiratory distress syndrome[11].

Vitamin D status of pregnant mothers (20-40 years) showed that 20% of the mothers had VDD and 24% had vitamin D insufficiency[12]. However, maternal risk factors for having newborn with decreased vitamin D levels have not been studied very much. The neonatal vitamin D level depends wholly on the maternal vitamin D level because vitamin D crosses the placenta during the last trimester of pregnancy[12]. If the mother has VDD, less vitamin D will be transported across the placenta with resultant low vitamin D stores at birth. Preterm neonates are at higher risk of VDD[13]. Current knowledge of 25(OH) D levels at birth among preterm and term neonates is scanty.

Objectives

To study the pattern of VDD in preterm and term newborns delivered at M.M. Institute of Medical Sciences and Research (MMIMSR), Mullana, Haryana, India.

Method

A prospective observational study was conducted on 100 newborns delivered from February 2018 to August 2019 at MMIMSR. After consent was obtained, the questionnaire regarding maternal health and demographic information was collected in a pre-defined proforma. Cord blood was collected just after delivery, stored in a refrigerator and transported to the laboratory. Medical records were utilised to obtain information regarding the pregnancy and delivery, as well as anthropometric

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measurements and health of infant at birth. This information was entered into an electronic database. Standard definitions were applied regarding parity, gestation, birth weight and prematurity. Babies having major congenital anomalies, critically sick babies, babies with any pre-existing disease in mother and babies of mothers on any drug affecting vitamin D level in newborn were excluded from the study.

Cord blood samples of newborns were collected with a minimum of 2 ml in one separate red-topped vial (with clot activator) for 25 (OH) D. These were sent to the biochemistry laboratory of the hospital after labelling the vials with the patient's name and internet protocol (IP) number. After allowing the blood to settle for 10-15 minutes, it was centrifuged, serum was separated and used for vitamin D estimation. The samples were stored at 4^0C until analysed if it had to be preserved for a few days. Vitamin D levels were estimated by the chemiluminescence immunoassay (CLIA) method. The method had been fully automated, high throughput immunoassay system. The machine used was SIEMENS ADVIA Centaur® XP. Serum levels of vitamin D were classified according to severity[14]:

1. Sufficient - >30ng/ml
2. Insufficiency- 20-30ng/ml
3. Deficiency- <20ng/ml

Statistical analysis: Data were entered into Microsoft Excel and all statistical tests were performed using Statistical Package for Social Sciences (SPSS) version 20. Categorical variables were presented as numbers and percentages. Chi-Square test was utilised to test for significance, p <0.05 being regarded as statistically significant.

Ethical issues: The study was approved by the institutional ethics committee (IEC). Informed consent was obtained from the mother/family included in the study. Data and samples were coded and stored securely.

Results

Table 1 shows the distribution of newborns into preterm and term.

Table 1
Distribution of newborns

Group	Number (%)
Preterm	50 (50)
Term	50 (50)
Total	100 (100)

Table 2 shows the distribution of newborns according to gender. The male: female ratio is 1.04:1.

Table 2
Distribution of newborns according to gender

Gender	Number (%)
Male	51 (51)
Female	49 (49)
Total	100 (100)

Table 3 shows the distribution of newborns according to vitamin D levels. In our study, the overall mean serum vitamin D level was 21.81 ng/dl and the overall median vitamin D level was 19.21ng/dl.

Table 3
Distribution according to vitamin D levels

Vitamin D (25-OH) level	Number (%)
Sufficient	23 (23)
Insufficiency	24 (24)
Deficient	53 (53)
Total	100 (100)

Table 4 shows the relationship of vitamin D to distribution of newborn. VDD was present in 53 newborns of whom 32 (60%) were preterm and 21(40%) were term and the difference was statistically significant (p=0.002).

Table 4: ***Relationship of vitamin D to distribution of newborns***

Group	Vitamin D (25-OH) levels (ng/ml)			Total	Chi square value	p-value
	Deficiency	Insufficiency	Sufficient			
Preterm	32 (60%)	14 (58%)	04 (17%)	50	12.732	0.002
Term	21 (40%)	10 (42%)	19 (83%)	50		
Total	53 (100%)	24 (100%)	23 (100%)	100		

Table 5 shows the relationship of gender with vitamin D levels among preterm and term newborns. The differences in the gender variable of both the term and preterm newborns were found to be significant (p<0.05).

Table 5: ***Relationship of gender with vitamin D levels among preterm and term newborns***

Gender	Vitamin D (25-OH) levels (ng/ml)			Total	Chi square value	p-value
	Deficiency	Insufficiency	Sufficient			
Female						
Preterm	18 (64.3%)	05 (50.0%)	02 (18.2%)	25		
Term	10 (35.7%)	05 (50.0%)	09 (81.8%)	24	6.723	0.035
Total	28 (100%)	10 (100%)	11 (100%)	49		
Male						
Preterm	14 (56.0%)	09 (64.3%)	02 (16.7%)	25		
Term	11 (44.0%)	05 (35.7%)	10 (83.3%)	26	6.819	0.033
Total	25 (100%)	14 (100%)	12 (100%)	51		

Discussion

Long term outcomes of VDD in the neonate include asthma, schizophrenia, multiple sclerosis, type 1 diabetes mellitus, abnormal neurocognitive outcome, and insulin resistance[15]. In our study of 100 newborns, 53 had VDD, 24 were vitamin D insufficient and 23 had sufficient levels of vitamin D. Of the 53 newborns with VDD, 32 (60%) were preterm and 21 (40%) were term. Of the 24 newborns who were vitamin D insufficient, 14 (58%) were preterm and 10 (42%) were term. Of the 23 newborns who had sufficient levels of vitamin D, 4 (17%) were preterm and 19 (83%) were term. The differences in vitamin D levels among preterm and term newborns were statistically significant (p=0.002).

In our study, the overall mean serum vitamin D level was 21.81 ng/dl and the overall median vitamin D level was 19.21ng/dl. In an Italian study by Cadario *et al*[16], mean vitamin D level was 21.4±11 ng/ml in cord blood and 14.9±7 ng/ml in serum postnatally. In a Turkish study by Terek *et al*.[17], mean vitamin D level was 27.4±19.3 ng/ml. A UK study in summer by Sulaiman *et al*.[18] showed significantly lower serum levels in South Asian infants, compared to Caucasians. In a study by Fallahi *et al*[19], mean serum vitamin D level in preterm infants was 13.91 ng/ml. and 13.39 ng/ml. in term infants.

In a study by Singh G *et al*[27]conducted in north India, out of a total 300 cases enrolled, overall VDD was seen in 85.7%. Out of total cases, 69% had levels below 20 ng/dl, 16.7% had insufficient levels (20-29 ng/dl) and 14.3% had sufficient levels (>30 ng/dl). Overall mean value in both groups was 18.3 ng/dl. Premature newborns had low levels as compared to the term newborns. All these studies closely resemble our study results. Newborn vitamin D level depends on maternal serum level. Thus, neonates who are born to vitamin D insufficient mothers are at greater risk of developing VDD[20]. Zeghoud F, *et al*[21] found that 63.7% of neonates had calcidiol concentrations ≤30 nmol/L at birth. Fallahi *et al*[19] found that 56% of newborns had a deficiency of vitamin D in Trehan. Park S *et al*.[22] found that 51% of preterm babies had severe VDD (<10 ng/ml).

In our study of 100 newborns, 51 (51%) were males with a male: female ratio of 1.04:1. VDD was seen in 53 newborns of whom 28 (53%) were female. Insufficiency was seen in 24 newborns of whom 14 (58%) were male. The gender of the newborns was not significantly linked to vitamin D levels (p =0.657). Of 28 female newborns with VDD, 18 (64.3%) were preterm and 10 (35.7%) were term. Insufficiency was seen in 10 female newborns, of whom 5 (50%) were preterm and 5 (50%) were term. Insufficiency was seen in 14 male newborns, of whom 9 (64.3%) were preterm and 5 (35.7%) were term. The gender prevalence too has been reported to vary in different studies. Hameed *et al*.[26] showed no association between vitamin D level and gender in both study groups (p >0.05). A study by Gernand *et al.* documented that there is an interrelationship between vitamin D and placental vascular pathology differentiated by infant sex. They found dissimilarities by infant sex; mothers with high serum vitamin D level (≥80 nmol/L) were associated with a 49% reduced risk of developing a vascular pathology in the placenta in pregnancies in comparison to women with insufficient vitamin D level (<50 nmol/L) if they were pregnant by male infant and those women with normal serum vitamin D level in comparison to those with insufficient level had 44% reduced risk of placental vascular pathology (95% confidence interval is 0.45- 0.97). This association did not exist if women were pregnant by female infant[23]. In a study by Singh G *et al*[27], the majority of the newborns were male 142 (68.60%) than females 81(31.40%) but the difference was statistically insignificant (p=0.09). Both sexes are theoretically equally vulnerable in other studies[24].

There were some limitations. Number of newborns was small, limiting our ability to see relations with these outcomes. There was no data on maternal plasma vitamin D levels during pregnancy which would have helped associate vitamin D levels in their newborns. We only analysed a single blood sample from the umbilical cord at birth which may

not reflect vitamin D levels over time. There is also lack of follow up.

Conclusions

In this study at the M.M. Institute of Medical Sciences and Research, 53% newborns were VDD. VDD was significantly more in preterm babies compared to term babies ($p<0.01$).

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