International Journal of Contemporary Pediatrics
Narayan R et al. Int J Contemp Pediatr. 2020 Mar;7(3):582-587
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20200683

Original Research Article

A study of pattern of vitamin D deficiency in newborns with reference to its gestational age and birth weight

Raghvendra Narayan[1], Shivani Singh[2]*, Om Prakash Singh[1]

[1]Department of Pediatrics, [2]Department of Dentistry, Heritage Institute of Medical Sciences, Varanasi, Uttar Pradesh, India

Received: 27 November 2019
Revised: 02 January 2020
Accepted: 27 January 2020

***Correspondence:**
Dr. Shivani Singh,
E-mail: docshivs716@gmail.com

ABSTRACT

Background: Deficiency of Vitamin D is a prominent health problem globally and its severity is significant in countries like India regardless of age, gender, race and geographical distribution. It is presently the most untreated nutritional deficiency worldwide. Vitamin D during pregnancy has an increasingly recognized range of functions such as immune modulation, lung development etc. Hence, having the potential to influence many factors in the developing fetus. Effects of vitamin D deficiency on fetal health is abundant; some being for brief period of time and others may become apparent in later life. Objectives of this study the pattern of vitamin D deficiency in newborns with reference to its gestational age and birth weight.
Methods: This was a hospital-based prospective observational study. Total 100 neonates born at MMIMSR, Ambala were enrolled out of which 50 were term and 50 preterm.
Results: Out of 100 newborns delivered, 53 newborns were vitamin D deficient. Premature newborns having 32 (60%) and term newborn having 21 (40%) were found to be deficient in vitamin D. Mean 25 (OH) levels were 21.81 ng/dl.
Conclusions: More than half newborns were deficient in vitamin D. Premature newborns had relatively low levels as compared to the term newborns and the difference between two were found statistically significant.

Key words: Gestation period, Low birth weight, Pattern, Preterm, Vitamin D

INTRODUCTION

Vitamin D is a fat-soluble vitamin that that have important role in calcium and bone metabolism. It has action like steroid hormone that has various function in many organ systems and may be a risk modifying factor in many chronic conditions like osteomalacia, rickets, multiple sclerosis, Schizophrenia, cardiac diseases, diabetes and carcinomas.[1-3]

Deficiency of Vitamin D is a universal health problem and its prevalence and severity is a major concern in developing countries like India regardless of age, gender, race and topographical distribution. It is currently the most untreated nutritional deficiency worldwide.[4-6] The location of India is between 8.4°N and 37.6°N latitude with the population predominantly living in regions experiencing optimum sunlight throughout the year. In India, despite plenty of sunlight, Vitamin D deficiency prevalence has been well documented in the range of 50-90% among all the age groups.[7]

The high prevalence of vitamin D deficiency is present not only in children and adults but also in pregnant women and their neonates. Vitamin D in neonates is of paramount importance. Vitamin D in pregnancy has an increasingly recognized range of functions such as lung development, Immune modulation, etc. Hence, having

the potential to influence many factors in the developing fetus. Effects of vitamin D deficiency on fetal health are abundant; some being for a brief period and others may become apparent in later life. Vitamin D affects the newborn's immune response in turn affecting innate response and adaptive immunity. It also has a key role in causing rickets. A fetus can seldom develop rickets in-utero with clinical features at birth because of severe maternal vitamin D deficiency.[8] Throughout the gestation, it plays a role to a certain limit in the development of the skeleton, tooth enamel formation and overall fetal growth and development.[9] Further, it has been noticed that cardiovascular risk factors may lead to vitamin D deficiency in newborns.[10] Vitamin D plays an important role in the preclusion of sepsis and morbidities during neonatal period of life.[11] The deficiency signs may differ from hypocalcemic seizures, tetany in early period and puberty to florid rickets in toddlers .Vitamin D deficiency is linked with increased risk for infants to develop Diabetes Mellitus type 1 and other endocrine disorders in later part of life and atopic dermatitis at birth.[12] Vitamin D deficiency is also associated with respiratory tract Infections in newborns and wheezing events in later life.[13] Lower vitamin D levels have also been considered as one of the risk factors for respiratory distress syndrome.[14]

Studies on Pregnant mothers from northern and southern states of India have reported vitamin D deficiency levels ranging from 67% to 96%. A study conducted amongst pregnant mothers in India, showed that 74% of the mothers had a deficiency of vitamin D. Vitamin D status of pregnant mothers (20-40 years) showed 20% of the mothers had vitamin D deficiency and 24% had vitamin D insufficiency.[12] However, few studies have investigated maternal risk factors for having Newborn with low levels of Vitamin D.

The vitamin D level of the Newborn is totally dependent on the maternal vitamin D level because vitamin D crosses the placenta during the last trimester of gestation.[15]

This develops the fetal vitamin D stores. If the mother having vitamin D deficient, then less vitamin D will be transported across the placenta and the fetus will have a low vitamin D store at birth. Preterm birth in India constitutes more than 60% of all deliveries and significant advances in neonatal care have increased the survival rate. One of the adverse outcomes of prematurity is osteopenia of prematurity and one of the risk factors for this condition is vitamin D deficiency. Perinatal complications can precipitate preterm birth and thus preterm newborns may be at higher risk of vitamin D deficiency.[16] However, Studies regarding distribution of 25(OH) D levels at birth among neonates across the gestational age spectrum is not much known.

Aim of study to see pattern of vitamin D with reference to gestational age and birth weight.

METHODS

The present prospective observational study was conducted on 100 newborns delivered during February 2018 to August 2019 at M. M. Institute of Medical Sciences and Research, Mullana, Ambala. After consent was obtained, the questionnaire containing about the mother's health and demographic information were collected in pre-defined performa. Cord blood was collected just after delivery and stored in a refrigerator until transported to the laboratory. The medical records of labor and the infant were used to collect information about the pregnancy and delivery as well as anthropometric measurements and health status of the baby at birth. This information was entered into an electronic database. Standard definitions were applied regarding parity, gestation, birth weight and prematurity.

Cord blood sample of new-born were collected. Minimum 2ml in one separate red- topped vial(with clot activator) for 25 (OH) D. These were sent to the biochemistry lab of hospital after labeling the vials with the patient's name and IP number.

After allowing it to settle for 10-15 minutes and later centrifuged, serum was separated and were used for Vitamin D estimation.

The samples were stored at 4 degree Celsius until analyzed if it had to be preserved for a few days.

Vitamin D levels were estimated by chemiluminescence immunoassay (CLIA) method. The method had been fully automated, high throughput immunoassay system. The machine used was SIEMENS ADVIA Centaur® XP.

Inclusion criteria

Babies delivered between February 2018 to August 2019 in this Institute.

Exclusion criteria

Those babies having major congenital anomalies, critically sick babies, any pre-existing disease in mother or on any drug affecting vitamin D level in newborn were excluded from study.

Serum levels of Vitamin D classified according to severity as:[17]

Sufficient- >30ng/ml
Insufficiency- 20-30ng/ml
Deficiency- <20ng/ml

Statistical analysis

Data were entered in Microsoft Excel and all statistical tests were performed using SPSS (Statistical Package for Social Sciences) version 20 software. Categorical

variables were presented in number and percentage (%). Chi-Square test was used for the test of significance and a p value of <0.05 was considered statistically significant. The Study was approved by the institutional ethics committee (IEC) of this institute. Informed consent was obtained from the mother/family included in the study. Data and samples were coded and stored securely.

RESULTS

This table shows out of 100 newborns 51 (51%) were males and 49 (49%) were females with male:female ratio is 1.04:1 (Table 1).

Table 1: Distribution of newborns according to gender.

Gender	Percentage	Number of cases
Female	49%	49
Male	51%	51
Total	100%	100

Table 2: Distribution of newborns according to vitamin D levels.

Vitamin D (25-OH) levels	Percentage	Frequency
Sufficient	23%	23
Insufficiency	24%	24
Deficient	53%	53
Total	100%	100

Table 3: Distribution of newborns according to gestational age.

Gestational age	Percentage	Number of cases
<32 weeks	2%	2
32-37 weeks	50%	50
>37 weeks	48%	48
Total	100%	100

Table 2 shows that out of 100 newborns 53 (53%) newborns were deficient, 24 (24%) having insufficiency and 23 (23%) were having sufficient levels of Vitamin D (Table 2). This table shows that the maximum number of newborns were fall into gestational age of 32-37 weeks 50 (50%), 48 (48%) newborns of >37 weeks and only 2 (2%) were of less than 32 weeks of gestation (Table 3).

The maximum number of newborns were belonged to AGA 83 (83%), 11 (11%) newborns of SGA and 6 (6%) were LGA (Table 4).

Table 5 shows that most of the newborns were NBW 54 (54%), 44 (44%) newborns of LBW, 1 (1%) of VLBW and 1 (1%) of ELBW (Table 5).

Table 4: Distribution of newborns according to gestational age and birth weight.

Gestational age and birth weight	Percentage	Number of cases
Appropriate for gestational age(AGA)	83%	83
Small for gestational age (SGA)	11%	11
Large for gestational age (LGA)	6%	6
Total	100%	100

Table 5: Distribution of newborns according to birth weight.

Birth weight	Percentage	Frequency
ELBW	1%	1
VLBW	1%	1
LBW	44%	44
NBW	54%	54
Total	100%	100

Table 6 shows the relationship of the period of gestation with Vitamin D levels. Vitamin D deficiency was seen in a majority of newborns born between 32-37 weeks of period of gestation 32 (60%) followed by 20 (38%) born >37 weeks of period of gestation and the difference was found to be statistically significant (Table 6).

Table 7 shows the relationship of gestational age with Vitamin D levels. Most of the newborns having vitamin D deficiency were AGA 44 (83%) followed by SGA 4 (9%) and LGA 4(8%) and the difference was found to be statistically insignificant (Table 7).

Table 6: Relationship of period of gestation with vitamin D levels.

Vitamin D(25-OH) levels (ng/ml)								Total	Chi-square value	p-value
		Deficiency		Insufficiency		Sufficient				
Period of gestation	<32 weeks	1	2%	0	0%	1	4%	2	13.235	0.010
	32-37 weeks	32	60%	14	58%	4	17%	50		
	>37 weeks	20	38%	10	42%	18	78%	48		
Total		53	100%	24	100%	23	100%	100		

Table 7: Relationship of gestational age with birth weight with vitamin D levels.

		Vitamin D(25-OH) levels (ng/ml)						Total	Chi-square value	p-value
		Deficiency		Insufficiency		Sufficient				
Gestational age with birth weight	AGA	44	83%	19	79%	20	87%	83	2.150	0.708
	LGA	4	8%	2	8%	0	0%	6		
	SGA	5	9%	3	13%	3	13%	11		
Total		53	100%	24	100%	23	100%	100		

Table 8: Relationship of birth weight with vitamin D levels.

		Vitamin D(25-OH) levels (ng/ml)						Total	Chi-square value	p-value
		Deficiency		Insufficiency		Sufficient				
Birth Weight	ELBW	0	0%	0	0%	1	4%	1	6.47	0.373
	LBW	27	51%	9	38%	8	35%	44		
	NBW	25	47%	15	63%	14	61%	54		
	VLBW	1	2%	0	0%	0	0%	1		
Total		53	100%	24	100%	23	100%	100		

Table 8 shows that vitamin D deficiency was mostly seen in LBW babies 27 (51%), followed by NBW 25 (47%), VLBW 1 (2%) and the difference was found to be statistically insignificant (Table 8).

DISCUSSION

Vitamin D deficiency is a worldwide problem that prevails in developing as well as developed countries. Vitamin D deficiency is closely related to multiple disease states. It may influence obstetrical complications as gestational diabetes, preeclampsia, preterm birth, low birth weight bacterial vaginosis, and cesarean section. Long term outcomes in the neonate including asthma, schizophrenia, multiple sclerosis, type 1 diabetes mellitus, abnormal neurocognitive outcome, and insulin resistance can occur with vitamin D deficiency.[18]

In this study, the maximum number of newborns were fall into gestational age 32-37 weeks 50(50%) followed by 48 (48%) of >37 weeks and 2 (2%) were of less than 32 weeks of gestation (Table 3). Vitamin D deficiency was seen in a majority of newborns born between 32-37 weeks of period of gestation 32 (60%) followed by 20 (38%) born in >37 weeks of period of gestation and the difference was found statistically significant (p value =0.010) (Table 6).

Vitamin D deficiency was seen in term newborn in 20(42%). Vitamin D deficiency was seen in one preterm of <32 weeks of period of gestation. However, the difference was not statistically linked (p value = 0.073). It was found that higher prevalence of vitamin D deficiency with more severe deficiency was present in premature infants as compared to term neonates and the difference was found statistically significant. The serum 25-OHD concentrations did not correlate with gestational age.

Authors did not find significant differences in serum 25-OHD concentrations among early and late preterm infants. As reported by Singh G et al, they found 82.67% term newborns had vitamin D levels below 30 ng/dl with deficiency in 66.67% and insufficiency in 16%.[19] However, the difference between them was found statistically not significant (p = 0.223) which is similar to this study. Other studies done by Xiaodan et al and Burris et al showed no association between vitamin D level and gestational age.[20,21] In a study done by Fallahi M et al. showed 48.5% of preterm and 65.5% of term neonates had vitamin D deficiency showing more deficiency in term babies than in preterm babies which was contrary to this study.[22]

In this study, the maximum number of newborns were belonging to AGA group 83 (83%) followed by SGA 11 (11%) and LGA 6(6%) (Table 4). Vitamin D deficiency was seen more in preterm 6 (67%) than term 18 (41%) newborns with AGA (appropriate for gestational age) and was found to be significant (p value=0.004) followed by 3 (60%) of preterm and 1(100%) with LGA (large for gestational age) and 3(50 %) of preterm and 2 (40%) of term newborns with SGA (small for gestational age) (Table 7). In contrast to this findings, Burris et al. reported and found no statistically significant differences (p value =0.98) between cord blood 25(OH)D levels in infants born small-for-gestational-age (SGA) and those born appropriate for-gestational-age (AGA).[16]

In this study, vitamin D deficiency was mostly seen in preterm 23 (72%) and term 4 (33%) newborns those fall into low birth weight, followed by preterm 8 (50%) and term 4 (33%) newborns in Normal Birth Weight group and the difference was found to be statistically significant (p value = 0.007) (Table 8). Similar results were seen in some studies. In a study done by Morgan et

al they found vitamin D levels of <50 nmol/L were associated with lower odds of LBW, though with only 13 cases of LBW with 25(OH)D levels <50 nmol/ L. Weiler et al. produced findings similar to the present study with regard to birth-weight, finding that mean birth weight was 299 g lower in 32 neonates with cord blood 25(OH)D levels above 37.5 nmol/L relative to 18 neonates with levels below 37.5 nmol/L (p = 0.02).[23,24] In a distinct setting (Pakistan), Hossain et al. also observed a significant inverse correlation between cord blood 25(OH)D concentration and birth weight.[25] In contrast, Bowyer et al. found no significant difference in mean birth weight among neonates with cord blood 25(OH)D concentrations below versus above 25 nmol/L.[26]

Limitations of this study include:

- The number of newborns were small, which limits this power to see relations with these outcomes.
- Authors do not have data on maternal plasma vitamin D (25-OH) levels during pregnancy which would have helped in associating vitamin D level in their newborns.
- Authors have only analyzed one single blood sample taken from the umbilical cord at birth. This may not reflect vitamin D levels over time.
- Lack of follow up.

CONCLUSION

Out of 100 newborns included in the study, 51 (51%) were males and 49 (49%) were females with male:female ratio 1.04:1. Vitamin D deficiency was seen in 53 newborns out of which females were 28 (53%) and males 25 (47%). Insufficiency was seen in 24 newborns out of which 10 (42%) were females and 14 (58%) were males. Out of 25 males who are vitamin D deficient, 14 (56%) were preterm and 11 (42%) were term newborns. Insufficiency was seen in 10 females out of which 5 (20%) were preterm and 5 (21%) were term newborns. Insufficiency was seen in 14 males out of which 9 (36%) were preterm and 5 (19%) were term newborns. However, the difference of both the term and preterm newborns was found to be statistically significant (p value-0.035,0.033).

This study again supports the recommendation of routine supplementation of vitamin D3 in neonates, especially in preterm.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Holick MF. Vitamin D. A d-lightful solution for health. J investing Med. 2011 Aug 1;59(6):872-80.
2. Nagpal S, Na S, Rathnachalam R. Noncalcemic action of Vit D receptors ligands. Endocr Rev. 2005;26:662-87.
3. Holick MF. Vitamin D: Importance in the prevention of cancers, type 1 diabetes, Heart Disease and Osteoporosis. Am J Clinical Nutr. 2004 Mar 1;79(3):362-71.
4. Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B, Eisman JA, et al. Global vitamin D status and determinants of hypovitaminosis D. Osteoporos Int. 2009;20(11):1807-20.
5. van der Meer IM, Middelkoop BJ, Boeke AJ, Lips PT. Prevalence of vitamin D deficiency among Turkish, Moroccan, Indian and sub-Sahara African populations in Europe and their countries of origin: an overview. Oste Int. 2011 Apr 1;22(4):1009-21.
6. Natasja M, Lips P. Worldwide vitamin D status. Best Pract Res Clin Endocrinol Metab. 2011;25:671-80.
7. Harinarayan CV, Joshi SR. Vitamin D status in India- its implications and remedial measures. JAPI. 2009 Jan; 57:40-8.
8. Hollis BW, Wagner CL. Assessment of dietary vitamin D requirements during pregnancy and lactation. Am J Clin Nutr. 2004;79(5):717-26.
9. Brooke OG, Brown IR, Bone CD, Carter ND, Cleeve HJ, Maxwell JD, et al. Vitamin D supplements in pregnant Asian women: effects on calcium status and fetal growth. Br Med J. 1980;280(6216):751-4.
10. Gezmish O, Black MJ. Vitamin D deficiency in early life and the potential programming of cardiovascular disease in adulthood. J Cardiovasc Transl Res. 2013;6(4):588-603.
11. Cetinkaya M, Cekmez F, Buyukkale G, Erener-Ercan T, Demir F, Tunc T, et al. Lower vitamin D levels are associated with increased risk of early-onset neonatal sepsis in term infants. J Perinatol. 2015;35(1):39-45.
12. Uriu-Adams JY, Obican SG, Keen CL. Vitamin D and maternal and child health: overview and implications for dietary requirements. Birth Defects Res Part C Embryo Today Rev. 2013;99(1):24-44.
13. Pacifici GM. Effects of vitamin D in neonates and young infants. Int J Pediatr. 2016;4(1):1273-85.
14. Ataseven F, Aygün C, Okuyucu A, Bedir A, Kücük Y, Kücüködük S. Is vitamin d deficiency a risk factor for respiratory distress syndrome. Int J Vitam Nutr Res. 2013;83(4):232-7.
15. Hillman LS, Haddad JG. Human perinatal vitamin D metabolism I: 25-hydroxyvitamin D in maternal and cord blood. J Pediatr. 1974;84(5):742-9.
16. Burris HH, Van Marter LJ, McElrath TF, Tabatabai P, Litonjua AA, Weiss ST, et al. Vitamin D status among preterm and full-term infants at birth. Pediatr Res. 2014;75(1-1):75-80.
17. Holick MF, Binkley NC, Bischoff - Ferrari HA, Gordon CM, Hanley DA, Heany RP et al. Evaluation, treatment and prevention of vitamin D

deficiency : An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011;96(7):1911-30.
18. Aly H, Abdel-Hady H. Vitamin D and neonate: An update J Clin Neonatol. 2015;4(1):1-7.
19. Singh G, Singh G, Brar H, Malik S. Vitamin D levels in preterm and term neonates at birth. Int J Contemp Pediatr. 2016;4(1):48-52.
20. Yu X, Wang W, Wei Z, Ouyang F, Huang L, Wang X, et al. Vitamin D status and related factors in newborns in Shanghai, China. Nutrients. 2014;6(12):5600-10.
21. Burris HH, Van Marter LJ, McElrath TF, Tabatabai P, Litonjua AA, Weiss ST, Christou H. Vitamin D status among preterm and full-term infants at birth. Pediatr Resea. 2014 Jan;75(1):75-80.
22. Fallahi M, Afjeh A, Saneifard H, Namazi N, Kazemian M, Tabatabaee S. Comparison of vitamin D level in preterm and term infant–mother pairs: a brief study. Iran J Neonatol IJN. 2016;7(1):32-6.
23. Morgan C, Dodds L, Langille DB, Weiler HA, Armson BA, Forest JC, et al. Cord blood vitamin D status and neonatal outcomes in a birth cohort in Quebec, Canada. Arch Gynecol Obstet. 2016;293(4):731-8.
24. Weiler H, Fitzpatrick-Wong S, Veitch R, Kovacs H, Schellenberg J, McCloy U, et al. Vitamin D deficiency and whole-body and femur bone mass relative to weight in healthy newborns. CMAJ. 2005;172(6):757-61.
25. Hossain N, Khanani R, Hussain-Kanani F, Shah T, Arif S, Pal L. High prevalence of vitamin D deficiency in Pakistani mothers and their newborns. Int J Gynecol Obstet. 2011;112(3):229-33.
26. Bowyer L, Catling-Paull C, Diamond T, Homer C, Davis G, Craig ME. Vitamin D, PTH and calcium levels in pregnant women and their neonates. Clin Endocrinol (Oxf). 2009;70(3):372-7.

Cite this article as: Narayan R, Singh S, Singh OP. A study of pattern of vitamin D deficiency in newborns with reference to its gestational age and birth weight. Int J Contemp Pediatr 2020;7:582-7.