

A Study of Vitamin D Level in Newborn with Special Reference to Correlation with Gestational Age, Morbidity and Maternal Vitamin D Level.

Bela Shah¹, Dhara Gosai², Urvi Ladumor³

¹Professor and Head of Unit, Department of Paediatrics, B. J. Medical College, Ahmedabad.

²Assistant Professor, Department of Paediatrics, B. J. Medical College, Ahmedabad.

³Resident, Department of Paediatrics, B. J. Medical College, Ahmedabad.

Received: August 2017

Accepted: August 2017

Copyright: © the author(s), publisher. It is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Recently the high prevalence of vitamin D level deficiency in general population. Pregnancy and preterm deliveries are known as risk Factors for vitamin d deficiency. In the study we aimed to compare vitamin D level in term and preterm newborn mother pair. **Methods:** We prospectively collected vitamin D blood level in term and preterm newborn with their mother's vitamin D level in neonatal ICU at tertiary health care centre. **Results:** Total 80 newborn mother pair was recruited in study, including 44 preterm (55%) and 36 term (45%) newborns In total 41.9% and 55.9% of preterm and term newborn had vitamin D deficiency, respectively and 47.6% & 32.5% of preterm and term newborn had vitamin D insufficiency, respectively. Among all newborns, 48.9% had vitamin D deficiency, although the difference between term and preterm newborn was not statistically significant. Based on findings, serum vitamin D levels in mother and newborns were significantly correlated ($p < 0.001$). The Data suggest that preterm & term newborn with vitamin D deficiency have higher incidence of ROP & sepsis respectively as compared to others ($p < 0.001$). **Conclusion:** According to present study, vitamin D level in mother and newborn were significantly correlated and vitamin D level deficiency in preterm and term newborn is associated with higher chances of development of ROP and early onset septicemia respectively, there is no significant correlation between gestational age and vitamin D level in newborn mother pair.

Keywords: Vitamin D, Newborn, Preterm, Morbidity.

INTRODUCTION

Preterm birth constitutes 5-18% of all deliveries and very low birth weight infants comprise 4-8% of all live births.^[1,2] Significant advances in neonatal care have increased the survival rate of premature infants. However, the associated morbidity continues to affect these infants despite the increased 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.^[3]

Based on recent studies, a significant percentage of the general population suffers from vitamin D deficiency. The overall prevalence of vitamin D deficiency has been estimated at 41.6% in several studies, with the highest rate reported among black people (82.1%).^[4] In addition, pregnancy is an identified risk factor for vitamin D deficiency.

Overall, vitamin D deficiency has been reported among 47.0% and 83.5% of white and black pregnant women, respectively.

On the other hand, in a previous study, the prevalence of vitamin D deficiency was estimated at 65.3% among both white and black pregnant women.^[5] Considering the association between vitamin D deficiency and preterm delivery and the difference in vitamin D level between women with preterm and term deliveries,^[6] in this study, we aimed to compare vitamin D level in term and preterm infant-mother pairs.

The active metabolite of vitamin D, 1,25-dihydroxyvitamin D₃ (1,25(OH)₂D₃), exerts its biological actions by binding to a nuclear receptor, the vitamin D receptor (VDR) and these are present in almost every organ system in the body. It is speculated that there is a physiologic role for vitamin D and its metabolites in general health.^[9,12,13] The awareness of a role for vitamin D in the regulation of immune responses was triggered by the discovery of VDRs in almost all immune cells of the innate and adaptive immune system.¹⁰ Moreover, immune signals can regulate expression levels of the VDR

Name & Address of Corresponding Author

Dr. Urvi Ladumor

Resident,

Department of Paediatrics,

B. J. Medical College, Ahmedabad.

and the enzymes involved in vitamin D metabolism.^[11]

The VDRs and vitamin D metabolizing enzymes have also been identified in both the vasculature and the heart including cardiac myocytes, vascular smooth muscle cells, and endothelial cells. 1,25(OH)2D3 also inhibits angiogenesis, by inhibiting the proliferation of endothelial cells and/or by repressing the release of angiogenic factors such as TGF- α , epidermal growth factor, and vascular endothelial growth factor (VEGF).^[20] The association of vitamin D levels to clinical outcome in VLBW infants has not been well studied. Objectives of the study were to determine the vitamin D levels in the cord blood of preterm infants, supplement vitamin D in two doses 400 IU daily and 800-1000 IU daily to randomly assigned preterm infants and to correlate the serum vitamin D levels to neonatal morbidity.

MATERIALS AND METHODS

This cross-sectional study was conducted in the neonatal intensive care unit (NICU) at tertiary care centre. The 25hydroxy vitamin D level of preterm infant-mother pairs (≤ 37 weeks of gestation and birth weight ≤ 1500 g) was compared with vitamin D level in term infant-mother pairs within the first 24 hours following birth. Blood samples of mothers and newborns were stored at -80°C , and vitamin D level was determined.

Vitamin D level was categorized into three groups:

- 1) Sufficient (> 30 ng/ml);
- 2) Insufficient (10-30 ng/ml);
- 3) Deficient (< 10 ng/ml).

Variables such as gestational age, maternal age, birth weight, neonate's gender, and vitamin D level were analyzed,

RESULTS

A total of 80 newborn-mother pairs were enrolled in this study. Out of which 45% were term and 55% were preterm newborn.

Table 1: Demographic Characteristics of Newborn Mother Pair

		Preterm	Term
1	Gestational Age(Week)	30.6	37.93
2	Birth Weight(Gm)	1146	2947
3	Maternal Age(Year)	26.5	24.9
4	Newborn Vitamin D Level (Ng/ml)	12.4	11.9
5	Mothers Vitamin D Level(Ng/ml)	13.4	12.7

In preterm newborn 43% have vitamin D deficiency, 48% have vitamin d insufficiency and 9% have vitamin D sufficiency. Whereas in term newborn 56% have vitamin D deficiency, 33% have vitamin

D insufficiency and 11% have vitamin D sufficiency.

Table 2: Comparison of Vitamin D Level in Preterm Newborn & Mother

	Mother				
	VIT.D DEF.	VIT.D INSUFF.	VIT.D SUFF.	TOTAL	
Newborn	Vit.D Def.	12	6	1	19
	Vit.D Insuff.	4	16	1	21
	Vit.D Suff.	1	1	2	4
	Total	17	23	4	44

Table 3: Comparison of Vitamin D Level in Term Newborn & Mother

	MOTHER				
	VIT.D DEF.	VIT.D INSUFF.	VIT.D SUFF.	TOTAL	
Newborn	Vit.D Def.	15	3	2	20
	Vit.D Insuff.	3	8	1	12
	Vit.D Suff.	1	1	2	4
	Total	19	13	4	36

The serum vitamin D levels in mothers and newborns were significantly correlated ($P < 0.001$). In term newborn with vitamin D deficiency, lower vitamin D levels were detected in mothers, unlike mothers of infants with higher vitamin D levels (8.3 ± 5.3 vs. 23.9 ± 15).

In vitamin D deficient mother there are 70% chances of preterm deliveries where as in vitamin D insufficient mother have 49% of chances of preterm deliveries. Mother with vitamin D sufficiency have 34% chances of preterm deliveries. So from this analysis it shows that there is correlation between mothers vitamin D level and preterm deliveries.

Table 4: Vitamin D Level Related Morbidity in Preterm Newborn

	Septicemia	HMD	ROP	RDS
Vit D suff	3	4	2	5
Vit D insuff	12	6	13	9
Vit D def	10	8	14	4

Table 5: Vitamin D Level Related Morbidities in Term Newborn

	Septicaemia	HMD	ROP	RDS
Vit D suff	2	3	0	3
Vit D insuff	16	6	2	6
Vit D def	14	9	3	5

The Data suggest that preterm newborn with vitamin D deficiency have higher incidence of ROP and in term newborn sepsis is more common in vitamin D deficient newborn as compared to others ($p < 0.001$).

DISCUSSION

In this study, we briefly assessed the serum level of 25-hydroxy vitamin D in mothers and newborns at tertiary health centre, Ahmedabad. According to recent studies, a significant percentage of the general population has vitamin D deficiency.^[4] Pregnancy and preterm delivery are regarded as risk factors for vitamin D deficiency.^[5,6] Therefore, in this study, we aimed to compare vitamin D level in term and preterm newborn–mother pairs. Based on the present findings, there was no significant difference between term and preterm newborn–mother pairs.

In consistence with the present study, there is no significant association between vitamin D level and preterm delivery, there was no significant difference between term and preterm newborn.^[8]

In the present study, we found no significant relationship between low birth weight and mothers' vitamin D level. Also, according to a recent systematic review of five randomized clinical trials, which focused on the role of vitamin D level in pregnancy and neonatal outcomes, the protective effects of supplements on low birth weight of infants were reported in three studies, while two studies did not present such findings. In general, little information is available on the effects of vitamin D intake during pregnancy on maternal, perinatal, or neonatal health outcomes.^[8]

The major limitation of the present study was the small sample size and measurement of vitamin D level only at birth. Since preterm infants are at risk of vitamin D deficiency and osteopenia of prematurity (due to the limited passage of vitamin D through the placenta in the third trimester of pregnancy), they may require higher levels of vitamin D in the first months of life, compared to term neonates. Therefore, it is recommended that these newborns be assessed in terms of vitamin D deficiency

Our data indicate that babies with low vitamin D levels have higher incidence of ROP and late onset sepsis.

Retinopathy of prematurity occurs when abnormal new blood vessels develop in response to angiogenic stimuli from hypoxia. The factors that lead to this include HIF 1- α and VEGF. The newly formed blood vessels are fragile and may leak which can give rise to scarring fibrous tissue resulting in retinal detachment in severe cases. Therefore, there is great interest in the development and identification of agents that can inhibit the growth of new blood vessels. The anti-angiogenic properties of calcitriol (1,25dihydroxyvitamin D₃), has been studied in the mouse model and it has been mentioned as a potent inhibitor of retinal neovascularization and may be of benefit in the treatment of a variety of eye diseases with a neovascular component like ROP.^[9,10,14] How calcitriol affects angiogenesis has been unclear.

It was also found that there is an association of vitamin D deficiency and late onset sepsis. Vitamin D has a role in regulating inflammation and chemokine production as well as an important role in immunomodulation. Nearly all cells display a specific vitamin D receptor (VDR),^[11-13,15] including B and T lymphocytes (both resting and activated), monocytes and dendritic cells. Vitamin D also facilitates neutrophil motility and phagocytic function.^[16] A major component of the antimicrobial action of Vitamin D is through the production of peptides which have antimicrobial as well as anti-endotoxin activity. Vitamin D stimulates the expression of potent antimicrobial peptides, such as cathelicidin and β defensin which exist in neutrophils, monocytes, natural killer (NK) cells and epithelial cells lining the respiratory tract. Macrophages,^[17,18] lymphocytes and monocytes have VDRs that, with 25(OH)D stimulation, increase the expression of these antimicrobial peptides.^[2]

Cathelicidin is effective against gram-positive and gram-negative bacteria, fungi and mycobacteria at a variety of pathogen entry sites, including the skin and the mucosal linings of the respiratory and gastrointestinal system. Patients with 25(OH) D levels less than 20 ng/mL may be unable to fully express cathelicidin, which could be associated with increased susceptibility to nosocomial infections such as pneumonia, sepsis and central line infections.^[19,20] In-vitro studies have shown that vitamin D₃ has inhibitory activity on strains of *Staphylococcus aureus*, *Streptococcus pyogenes*, *Klebsiella pneumoniae*, *Escherichia coli* (*E. coli*) and other bacteria. Grant had reported that vitamin D supplementation of mother and infant can reduce the risk of sepsis in infants and neonates.

The results of our study also indicate that the usual recommended dose of 400 IU Vitamin D in preterms is not sufficient to maintain normal physiological levels in our cohort of Indian infants. This has been observed in other Indian studies also. It is quite possible that these infants had very low vitamin D levels at birth perhaps due to maternal vitamin D deficiency and required a higher dose of vitamin D supplementation postnatally. Although none of the infants in our study who received 800-1000 IU of vitamin D very high levels of serum vitamin D we recommend that serum vitamin D levels should be monitored at least once within a month of supplementation of this high dose of vitamin D.

CONCLUSION

Based on the findings, vitamin D levels in mothers and newborns were significantly correlated, there was no significant correlation between gestational age and vitamin D level in newborn and mother. Further research is required to identify the relationship between preterm birth and vitamin D deficiency.

These data suggest that severe vitamin D deficiency is common in preterm newborns at birth and postnatally. In newborn with low levels of vitamin D, incidences of late onset sepsis and ROP are significantly higher.

Retinal maturation of infants with low levels of vitamin D is delayed perhaps increasing their risk for development of ROP even in the absence of supplemental oxygen administration.

REFERENCES

1. Preterm birth Fact sheet N 363. World Health Organization. Available at: URL: <http://www.who.int/mediacentre/factsheets/fs363/en/>; 2015.
2. Afjeh SA, Sabzehei MK, Fallahi M, Esmaili F. Outcome of very low birth weight infants over 3 years report from an Iranian center. *Iran J Pediatr.* 2013; 23(5):579-87.
3. Rustico SE, Calabria AC, Garber SJ. Metabolic bone disease of prematurity. *J Clin Transl Endocrinol.* 2014; 1(3):85-91.
4. Forrest KY, Stuhldreher WL. Prevalence and correlates of vitamin D deficiency in US adults. *Nutr Res.* 2011; 31(1):48-54.
5. ACOG Committee on Obstetric Practice. ACOG committee opinion No. 495: vitamin D: screening and supplementation during pregnancy. *Obstet Gynecol.* 2011; 118(1):197-8.
6. Bodnar LM, Platt RW, Simhan HN. Early-Pregnancy vitamin D deficiency and risk of preterm birth subtypes. *Obstet Gynecol.* 2015; 125(2):439-47.
7. Baker PN, Wheeler SJ, Sanders TA, Thomas JE, Hutchinson CJ, Clarke K, et al. A prospective study of micronutrient status in adolescent pregnancy. *Am J Clin Nutr.* 2009; 89(4):1114-24.
8. Thorne-Lyman AI, Fawzi WW. Vitamin D during pregnancy and maternal, neonatal and infant health outcomes: a systematic review and metaanalysis. *Paediatr Perinat Epidemiol.* 2012; 26(0 1):75-90.
9. Shoshan BM, Amir S, Dang DT. 1alpha,25-dihydroxyvitamin D3 (calcitriol) inhibits hypoxia-inducible factor-1/vascular endothelial growth factor pathway in human cancer cells. *Mol Cancer Ther.* 2007;6:1433-9.
10. Albert DM, Scheef EA, Wang S. Calcitriol is a potent inhibitor of retinal neovascularization. *Invest Ophthalmol Vis Sci.* 2007;48:2327-34.
11. Kamen DL, Tangpricha V. Vitamin D and molecular actions on the immune system: modulation of innate and autoimmunity. *J Mol Med.* 2010;88:441-50.
12. Veldman CM, Cantorna MT, Deluca HF. Expression of 1,25-dihydroxyvitamin D(3) receptor in the immune system. *Arch Biochem Biophys.* 2000;374:334-8.
13. Bartley J. Vitamin D: emerging roles in infection and immunity. *Expert Rev Anti Infect Ther.* 2010;8:1359-69.
14. Alitalo A. Human anti-infectious defence may be enhanced by vitamin D. *Duodecim.* 2010;126:1127-34.
15. Jeng L, Yamshchikov AV, Judd SE, Blumberg HM, Martin GS, Ziegler TR, et al. Alterations in vitamin D status and antimicrobial peptide levels in patients in the intensive care unit with sepsis. *J Transl Med.* 2009;7:28.
16. Bikle DD. Vitamin D and the immune system: role in protection against bacterial infection. *Curr Opin Nephrol Hypertens.* 2008;17:348-52.
17. Urashima M, Segawa T, Okazaki M, Kurihara M, Wada Y, Ida H. Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren. *Am J Clin Nutr.* 2010;91:1255-60.
18. Feindt E, Stroder J. Studies on the antimicrobial effect of vitamin D. *Klin Wochenschr.* 1977;55:507-8.
19. Grant WB. Vitamin D supplementation of mother and infant could reduce risk of sepsis in premature infants. *Early Hum Dev.* 2010;86:133.
20. Calcium and vitamin D requirements of enterally fed preterm infants. Available at <https://pediatrics.aappublications.org/content/pediatrics/early/2013/04/24/peds.2013-0420.full.pdf>. Accessed on 14 July 2016.

How to cite this article: Shah B, Gosai D, Ladumor U. A Study of Vitamin D Level in Newborn with Special Reference to Correlation with Gestational Age, Morbidity and Maternal Vitamin D Level. *Ann. Int. Med. Den. Res.* 2017; 3(6):PE08-PE11.

Source of Support: Nil, **Conflict of Interest:** None declared