

Original Research Article

A study of relationship between maternal serum vitamin D levels during peripartum period and neonatal birth weight

Gurpreet K. Dhillon¹, Sunil K. Rai², Harpreet S. Dhillon^{3*}, Shibu Sasidharan⁴

¹Department of Pediatrics, 166 Military Hospital, Jammu, Jammu and Kashmir, India

²Department of Pediatrics, INHS ASVINI, Mumbai, Maharashtra, India

³Department of Psychiatry, 166 Military Hospital, Jammu, Jammu and Kashmir, India

⁴Department of Anaesthesiology and Critical Care, Level III Hospital, Goma, Congo

Received: 14 May 2020

Accepted: 05 June 2020

*Correspondence:

Dr. Harpreet S. Dhillon,

E-mail: harpreet5467@yahoo.com

Copyright: © the author(s), publisher and licensee Medip Academy. This 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: An observational study was undertaken to study the relationship between maternal serum vitamin D levels during peripartum period and neonatal birth weight.

Methods: This study was done on 569 patients to study the relationship between maternal serum vitamin D levels during peripartum period and neonatal birth weight. The data included was maternal serum samples (taken during peri-partum period) and neonatal birth weight. The primary objective of this project was to assess the vitamin D levels in maternal serum and to study its relationship, if any, with birth weight in the neonates.

Results: A total of 569 samples of maternal serum were analyzed for serum 25(OH)D levels out of which 457(80%) mothers were found to have sufficient, 101(18%) insufficient and 11(2%) deficient Vitamin D levels as per US Endocrinological society guidelines. Out of total 569 newborns, 104 (18.27%) were low birth weight (LBW) and 465 (81.27%) were normal birth weight (NBW). Out of total LBW (104), 19(18.27%) were born to vitamin D deficient (VDD) mothers and 85 (81.72%) were born to vitamin D sufficient (VDS) mothers. Out of total NBW(465), 86(18.45%) were born to VDD mothers and 379 (81.17%) were born to VDS mothers. These results were not statistically significant ($p=0.76456749$).

Conclusions: Maternal 25(OH)-vitamin D status during late pregnancy did not have any statistically significant effect on the neonatal birth weight.

Keywords: Low birth weight, New-born, Vitamin D deficiency

INTRODUCTION

Vitamin D deficiency is common in Indian subcontinent with a prevalence of 50-90% and is attributed to low dietary calcium along with skin color and changing lifestyle.¹ Vitamin D levels in pregnant women are on an average lower than comparable non-pregnant women's levels which may be partly explained by increased fetal demands for vitamin D.² Maternal vitamin D status depends on consumption, absorption and metabolism of dietary vitamin D, which in turn significantly affects the

fetal vitamin D status.³ Multiple neonatal complications such as neonatal hypocalcemia, impaired growth, decreased bone mineral density, skeleton deformity, seizures and low birth weight are associated with low vitamin D levels in pregnancy.⁴ Low birthweight has been defined by the World Health Organization (WHO) as the weight of neonate at birth less than 2,500 grams (or up to 2499gm), the measurement being taken preferably within 1st hour of life, before significant weight loss has occurred. This practical cut-off for international comparison is based on epidemiological observations that

infants weighing less than 2,500 g are approximately 20 times more likely to die than heavier babies.⁵ Globally, more than 20 million infants are born with low birth weight. The number of low birth weight babies is concentrated in two regions of the developing world: Asia (72%) and Africa (22%).⁶ There are more than 1 million infants born with low birthweight in China and nearly 8 million in India.⁶

The most significant cause of LBW in developing country is maternal malnutrition and anemia whereas in developed countries, it is prematurity.⁷ There are adverse consequences of being LBW in the neonatal and later period of development.⁸ There is high risk of mortality and morbidity in the neonates born weighing less than 2500 gm compared to infants born appropriate of gestational age.⁹ There is an increased risk of coronary heart disease and type II diabetes seen in LBW as compared to normal birthweight.¹⁰ Influence of vitamin D on skeletal growth provides a possible explanation for its association with LBW.^{11,12} Vitamin D has a role early in the pregnancy possibly explained by the fact that the fetal growth peaks in the third trimester but the growth trajectory sets in well before this time of pregnancy.¹³ This study was undertaken to study the impact of maternal vitamin D status on neonatal birth-weight.

METHODS

This was a cross-sectional observational study.

Inclusion criteria

- Healthy pregnant women without any co-morbidities and their newborn.

Exclusion criteria

- Pregnancy losses, spontaneous abortion and still birth were excluded.
- Twin/triplet were excluded because of their high risk of PTB, LBW, LSCS.¹⁴
- Known history or evidence of Rheumatoid arthritis, Thyroid, Parathyroid, Adrenal diseases, Hepatic or Renal failure.
- Metabolic bone disease
- Type 1 diabetes and malabsorption diseases

A total of 569 individuals were recruited into the study group after applying inclusion and exclusion criterion. The data for this observational study included maternal blood samples taken during peri-partum period and birth weight of newborn.

The primary objective of this project was to assess the vitamin D status in maternal serum and to study its relationship, if any, with birth weight in the neonates. Analysis of the data was done using SPSS software (Version 20).

Table 1: Classification of vitamin D levels as per US endocrine society.

| As per us endocrine society classification | |
|--|-----------------|
| Deficiency | ≤ 20 ng/ml |
| Insufficiency | < (21-29) ng/ml |
| Sufficiency | >30 ng/ml |
| Toxicity | >150 ng/ml |

Statistical analysis was done using Students-t test and Pearson's correlation Coefficient. A 'p' value of <0.05 was taken as statistically significant. The 25(OH) D levels as per US Endocrine Society Classification are described in Table 1. Vitamin D deficiency is defined as serum levels of 25(OH)D less than 20 ng/dL (50 nmol/liter), whereas 21- 29 ng/dL (525-725 nmol/liter) is considered to be insufficient by US Endocrine Society.¹⁵

RESULTS

Maternal vitamin D levels

A total of 569 samples of maternal serum were analyzed for serum 25(OH) D levels in this study. The levels of maternal vitamin D are shown in table 2. The mean maternal serum 25(OH) D level was 35.63ng/ml (SD 6.18, range 9.2-39.8).

Table 2: Classification of maternal 25 (OH) D levels.

| Maternal 25 (OH) levels | |
|-------------------------|-----------|
| n | 569 |
| Mean (ng/ml) | 35.629 |
| SD | 6.18 |
| Range (ng/ml) | 9.2-39.8 |
| VDS (%) | 457 (80%) |
| VDI (%) | 101(%) |
| VDD (%) | 11 (2%) |

*VDS=Vitamin D sufficient, VDI=Vitamin Insufficient, VDD=Vitamin D deficiency.

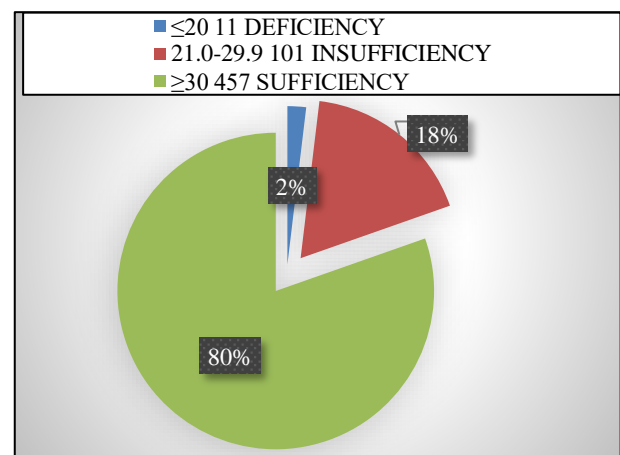


Figure 1: Classification of maternal 25(OH) D levels.

Figure 1 illustrates classification of maternal 25(OH) D levels in which 457 (80%) mothers were found to have sufficient, 101 (18%) insufficient and 11(2%) deficient Vitamin D levels as per Endocrinological Society guidelines.

Birth weight of newborns

Table 3 illustrates the distribution of newborn with respect to birth weight in which 104 (18.27%) were low birth weight (LBW) and 465 (81.72%) were normal birth weight (NBW).

Table 3: Distribution of newborns with respect to birth weight.

| | Numbers | Percentage |
|-------|---------|------------|
| LBW | 104 | 18.27% |
| NBW | 465 | 81.72% |
| TOTAL | 569 | 100% |

* LBW-Low birth weight, NBW-Normal birth weight

Table 4 describes the relationship of vitamin D in mothers and distribution of newborns as per birth weight (i.e LBW/NBW). Out of total LBW (104), 19(18.27%) were born to VDD mothers and 85 (81.72%) were born to VDS mothers.

Out of total NBW (465), 86 (18.45%) were born to VDD mothers and 379 (81.17%) were born to VDS mothers. These results were not statistically significant ($p=0.76456749$).

Table 4: Relationship between of vitamin D in mothers and LBW/NBW.

| | VDD | VDS | Percentage (VDD) | Percentage (VDS) |
|-------|-----|-----|------------------|------------------|
| LBW | 19 | 85 | 18.27% | 81.72% |
| NBW | 86 | 379 | 18.45% | 81.17% |
| TOTAL | 105 | 464 | | |

*VDD-vitamin D deficient, VDS- vitamin D sufficient, LBW-Low birth weight, NBW-Normal birth weight

Table 5: Comparison of vitamin D levels in mothers with NBW and LBW of newborns.

| | Mothers of NBW newborn | Mothers of LBW newborn |
|---------|------------------------|------------------------|
| Numbers | 465 | 104 |
| Mean | 35.6722581 | 35.471154 |
| SD | 6.20431443 | 6.1115309 |
| Median | 37 | 36.9 |
| Min | 9.2 | 9.7 |
| Max | 49 | 46.2 |

Table 5 describes the comparison of vitamin D levels in mothers of newborns with NBW (465) and LBW (104).

The median 25(OH) D concentration in maternal blood was 37 ng/ml in NBW and 36.9 ng/ml in LBW. The value of Pearson correlation coefficient between maternal vitamin D levels and LBW was not significant ($r=0.12366057$).

DISCUSSION

This study attempted to evaluate the relationship (if any) between the maternal vitamin D levels and its outcome in the form of birth weight. The maternal levels of vitamin D are shown in table 2. The mean maternal serum 25 (OH) D level was 35.63ng/ml (SD 6.18, range 9.2-39.8). The classification of maternal 25(OH) D levels was done as per US Endocrine society in which 457 (80%) mothers were found to have sufficient, 101 (18%) insufficient and 11 (2%) deficient Vitamin D levels. Majority of mothers (80%) were having sufficient Vitamin D levels. This finding is in contrast to many other studies which had found high prevalence of vitamin D deficiency during pregnancy.¹⁶⁻¹⁸

Table 3 illustrates the distribution of newborns with respect to birth weight in which 104 (18.27%) were low birth weight (LBW) and 465 (81.72%) were normal birth weight (NBW). The percentage of LBW corroborates with the prevalence of LBW in South Asia (20%) and also as reported by Indian Statistical Institute (20%) in 2011.^{19,20}

Table 4 describes the relationship of vitamin D in mothers and distribution of newborns as per birth weight (i.e LBW/NBW). Out of total LBW (104), 19 (18.27%) were born to VDD mothers and 85 (81.72%) were born to VDS mothers. Out of total NBW babies (465), 86 (18.45%) were born to vitamin D deficient (VDD) mothers and 379 (81.17%) were born to vitamin D sufficient (VDS) mothers. These differences were not statistically significant ($p=0.76456749$), as, the results indicated that percentage of LBW babies was very comparable irrespective of the maternal serum vitamin D levels.

Hence, Vitamin D status in maternal blood during peripartum period was not associated with LBW as per our study. These findings were similar to an observational study done by CR Gale et al, with the aim to estimate the association of maternal concentrations of 25(OH)-vitamin D in pregnancy and child's anthropometry.²¹ 596 pregnant women were recruited for the study and 466 (78%) children were examined at birth. Maternal 25 (OH)-vitamin D concentrations were measured in late pregnancy. There was no statistically significant association seen between maternal Vitamin D and weight at birth ($P=0.247$).

Morley and Carlin studied the relationship between maternal vitamin D and PTH concentrations at less than 16 and 28-week gestation and offspring birth size. 374 out of 475 (79%) women completed the study and they

found no evident relationship between birth size and maternal vitamin D levels.²²

However, Gernand AD et al, studied the association between maternal vitamin D and infant birth weight, (n=2146) delivering singleton, term, live births with maternal 25(OH)D measured at a gestation of 26 week or less.¹² A higher birth weight was seen in babies born to the mother with vitamin D status ≥ 37.5 nmol/L than the mothers with levels < 37.5 nmol/L and a nonlinear relation between 25(OH)D and birth weight was found in which birth weight increased by 3.6 g per 1 nmol/liter increase in maternal 25(OH)D up to 37.5 nmol/liter and then levelled off thereafter. The results obtained in this study were incongruous to our findings. The possible explanation could be large sample size, maternal serum being analyzed in first trimester as compared to our study in which the samples were drawn during perinatal period and different cut off points to classify serum vitamin D levels (37.5, 50, and 80 nmol/liter as compared to our study in which deficiency is less than 20 ng/dL whereas 21- 29 ng/dL is considered to be insufficient and more than 30 ng/dL as sufficient.

Bowyer et al, ($P < 0.001$) and Leffelaar ER (-114.4 g, 95 % CI -151.2, -77.6) in independent studies found that birth weight was lower among infants of vitamin D deficient mothers.^{23,24}

CONCLUSION

It can be concluded from the above study that maternal 25(OH)- vitamin D status during late pregnancy (peripartum period) did not have any statistically significant effect on the neonatal birth weight. However, due to conflicting results from related studies and given the significant impact of adverse neonatal outcomes in vitamin D deficient mothers, further research is warranted.

ACKNOWLEDGEMENTS

Authors would like to thank all the subjects who consented to participate in this study.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Misra M, Pacaud D, Petryk A, Collett-Solberg PF, Kappy M. Vitamin D deficiency in children and its management: review of current knowledge and recommendations. *Pediatrics*. 2008 Aug 1;122(2):398-417.
2. Holmes VA, Barnes MS, Alexander HD, McFaul P, Wallace JM. Vitamin D deficiency and insufficiency in pregnant women: a longitudinal

- study. *British J Nutrition*. 2009 Sep 1;102(06):876-81.
3. Holick MF, Mac Laughlin JA, Clark MB, Holick SA, Potts JT, Anderson RR, Blank IH, Parrish JA, Elias P. Photosynthesis of previtamin D3 in human skin and the physiologic consequences. *Science*. 1980 Oct 10;210(4466):203-5.
4. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metabolism*. 2011 Jun 6;96(7):1911-30.
5. Wardlaw TM, editor. Low birthweight: country, regional and global estimates. UNICEF. 2004.
6. UNICEF. The state of the world's children 2009: maternal and newborn health. Unicef; 2008.
7. De Bernabé JV, Soriano T, Albaladejo R, Juarranz M, Calle ME, Martínez D, et al. Risk factors for low birth weight: a review. *Europ J Obstetr Gynecol Reproductive Biol*. 2004 Sep 10;116(1):3-15.
8. Mc Cormick MC. The contribution of low birth weight to infant mortality and childhood morbidity. *New England J Med*. 1985 Jan 10;312(2):82-90.
9. Eriksson JG. Epidemiology, genes and the environment: lessons learned from the Helsinki Birth Cohort Study. *J Internal Med*. 2007 May 1;261(5):418-25.
10. Harder T, Rodekamp E, Schellong K, Dudenhausen JW, Plagemann A. Birth weight and subsequent risk of type 2 diabetes: a meta-analysis. *Am J Epidemiol*. 2007 Apr 15;165(8):849-57.
11. Dror DK. Vitamin D status during pregnancy: maternal, fetal, and postnatal outcomes. *Current Opinion Obstetr Gynecol*. 2011 Dec 1;23(6):422-6.
12. Gernand AD, Simhan HN, Klebanoff MA, Bodnar LM. Maternal serum 25-hydroxyvitamin D and measures of newborn and placental weight in a US multicenter cohort study. *J Clin Endocrinol Metabolism*. 2012 Nov 16;98(1):398-404.
13. Sultan B, Ramanathan M, Lee J, May L, Lane AP. Sinonasal epithelial cells synthesize active vitamin D, augmenting host innate immune function. *Intern forum of Allergy Rhinol*. 2013 Jan 1;3(1):26-30.
14. Clausson B, Cnattingius S, Axelsson O. Preterm and term births of small for gestational age infants: a population-based study of risk factors among nulliparous women. *BJOG: An Intern J Obstetr Gynaecol*. 1998 Sep 1;105(9):1011-7.
15. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metabolism*. 2011 Jul 1;96(7):1911-30.
16. Van der Meer IM, Karamali NS, Boeke AJ, Lips P, Middelkoop BJ, Verhoeven I, et al. High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands. *Am J Clin Nutrition*. 2006 Aug 1;84(2):350-3.

17. 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.* 2009 Mar;70(3):372-7.
18. 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. *Intern J Gynecol Obstetr.* 2011 Mar 31;112(3):229
19. Kumar M, Verma R, Khanna P, Bhalla K, Kumar R, Dhaka R, et al. Prevalence and associate factors of low birth weight in North Indian babies: A rural based study. *Int J Community Med Public Heal.* 2017 Sep;4(9):3212-7.
20. Bharati P, Pal M, Bandyopadhyay M, Bhakta A, Chakraborty S. Prevalence and causes of low birth weight in India. *Malaysian J Nutrition.* 2011 Dec 1;17(3).
21. Gale CR, Robinson SM, Harvey NC, Javaid MK, Jiang B, Martyn CN, et al. Maternal vitamin D status during pregnancy and child outcomes. *Eur J Clin Nutri.* 2008 Jan 1;62(1):68-77.
22. Morley R, Carlin JB, Pasco JA, Wark JD. Maternal 25-hydroxyvitamin D and parathyroid hormone concentrations and offspring birth size. *J Clin Endocrinol Metabolism.* 2006 Mar 1;91(3):906-12.
23. 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. *Clinical endocrinology.* 2009 Mar;70(3):372-7.
24. Leffelaar ER, Vrijkotte TG, van Eijsden M. Maternal early pregnancy vitamin D status in relation to fetal and neonatal growth: results of the multi-ethnic Amsterdam Born Children and their Development cohort. *British J Nutr.* 2010 Jul;104(1):108-17.

Cite this article as: Dhillon GK, Rai SK, Dhillon HS, Sasidharan S. A study of relationship between maternal serum vitamin D levels during peripartum period and neonatal birth weight. *Int J Contemp Pediatr* 2020;7:1584-8.