Original Article

Vitamin D status in pregnant women visiting a tertiary care center of North Eastern India

Nalini Sharma[1], Chandan Nath[2], Jamil Mohammad[3]

Departments of [1]Obstetrics and Gynaecology, [2]Biochemistry and [3]Medicine, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India

Abstract

Background: Studies of vitamin D (VD) physiology suggest that effects of vitamin D deficiency (VDD) could be much broader than rickets including cardiovascular disease, cancers, diabetes, infection, and allergy and pregnancy complications. Data regarding the prevalence of hypovitaminosis in pregnancy are scanty especially in north eastern part of India. Therefore, this study has undertaken with the intention to find out prevalence and outcome of hypovitaminosis of VD in pregnancy. **Materials and Method:** In total, 177 pregnant women with singleton pregnancy, <16 weeks of gestational age, visited to antenatal clinic of our institute were consecutively enrolled for the study. The serum VD was estimated by Beckman coulter unicel DXI immunoassay system using the principle of Chemiluminescence. Incidence of vitamin deficiency and insufficiency calculated. VDD was defined as 25(OH)D levels in blood <20 ng/mL, and insufficiency of VD was defined as 25(OH)D levels <32 ng/mL. Antenatal complications, such as intrauterine growth restriction (IUGR), oligohydramnios, pre-eclampsia, preterm labor, gestational diabetes, if any, were noted. Labor and delivery information including induction of labor, mode of delivery, and newborn birth weight were noted. **Result:** In total, 177 women recruited for the study. Mean age and parity of the subjects were 26.71 ± 9.96 and 2.10 ± 1.8, respectively. For detailed statistical analysis, women were divided into three groups depending upon their VD levels: deficiency group [25(OH)D level <20 ng/mL], insufficiency group [25(OH)D level <32 ng/mL], and sufficient group [25(OH)D level >32 ng/mL]. VDD was present in 84.18% subjects. VD insufficiency was present in 12.44% of cases. There is association of preeclampsia, cesarean section, and low birth weight babies with lower level of VD. **Conclusion:** This study showed that the prevalence of VDD in pregnancy is astonishingly high till now there is no guideline to screen antenatal women for VDD. As the test is costly even, offering it to all at-risk women may not be cost effective compared with offering universal supplementation, particularly as treatment is regarded as being very safe.

Keywords: Cesarean section, vitamin D, vitamin D deficiency, vitamin D insufficiency, pregnancy outcome, pre-eclampsia

Introduction

Vitamin D (VD) is part of complex steroid hormone system long known to be involved in the bone metabolism. Recently, the prevalence of rickets has increased sparking a new interest in vitamin D deficiency (VDD). In addition, studies of VD physiology suggest that effects of VDD could be much broader than rickets including cardiovascular disease, cancers, diabetes, infection, and allergy and pregnancy complications.

Address for correspondence: Dr. Nalini Sharma, Department of Obstetrics and Gynecology, B 1 D, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India.
E-mail: Nalinisharma100@rediffmail.com

Access this article online

Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/jfmpc.jfmpc_404_18

During pregnancy, serum level of 1,25(OH)D increase up to twofold starting at 10–12 weeks of gestation and reaching a maximum in the third trimester.[1]

Given an increase in the active form of VD pregnant women likely have a higher cellular exposure to VD during second and third trimesters suggesting a role for VD in obstetrics well-being. Perinatal outcome to be related to VDD preeclampsia, gestational diabetes mellitus, low birth weight, preterm delivery, and cesarean section.[2-5] There is wide range of actions of VD in pregnancy, including its effects on placental function and inflammatory response.[6] Proinflammatory cytokines, such as tumor necrosis

How to cite this article: Sharma N, Nath C, Mohammad J. Vitamin D status in pregnant women visiting a tertiary care center of North Eastern India. J Family Med Prim Care 2019;8:356-60.

factor-a, interleukin-6, and interferon-gama have been reported to be increased in pregnancies with VDD.[7] Having important immune-modulated property VD may help to setup a proper maternal immune response to placenta.[8] It also regulates key target genes associated with proper implantation of placenta.[9] VD regulates expression of human chorionic gonadotropin in syntiotrophoblast and stimulate production of sex steroids. Many studies also suggested VD has important role in glucose and insulin metabolism.[8]

Pancreatic β-cells express 1α-hydroxylase; the active form of VD binds on VD receptor on pancreatic β-cells; the VD response element is present in the human insulin gene promoter. There is also a number of evidences about the role of VD in maintaining glucose tolerance through its influence on insulin secretion and sensitivity.

The exact mechanism of altered VD metabolism in patients with preeclampsia and hypertensive disorders is not fully understood. It may be related with inflammatory mediator and effects on blood vessels.

VD could influence the pathophysiology of preterm labor as it affects the processes of inflammation and immunomodulation. The susceptibility to infection is increased in cases of VDD because of impairment of toll-like mediated induction of antimicrobial peptide cathelicidin from macrophages.[10]

A possible reason for the potential higher risk of cesarean delivery in women with lower VD concentrations was hypothesized to be reduced pelvic muscle strength leading to prolonged labor.[10]

India being a tropical country with ample sunlight throughout the year, people still suffering from VDD and it will worsen in pregnancy.

Data regarding the prevalence of hypovitaminosis in pregnancy are scanty especially in north eastern part of India. Therefore, this study has undertaken with the intention to find out prevalence and outcome of hypovitaminosis of VD in pregnancy.

Materials and Method

This prospective study was conducted in two and half-year period in one of the teaching institute of hilly north eastern India.

In total, 177 pregnant women with singleton pregnancy, <16 weeks of gestational age, visited to antenatal clinic of our institute were consecutively enrolled for the study. Gestational age of the subject was determined using definite menstrual history and or first trimester ultrasonographic scan. Written informed consent was taken from the recruited subjects. Approval was taken from the institute ethical board. Exclusion criteria were pregnant patient with >16 weeks, known history or evidence of medical disorder such as thyroid, parathyroid, or adrenal, collagen disorder, hepatic or renal dysfunction, metabolic bone disease, type 1 diabetes mellitus, and malabsorption. Women were also excluded if they had history of medication with drugs interfering with calcium and VD metabolism like anticonvulsants, corticosteroids, thiazides, and not willing to participate in the study. Detailed history was recorded from the recruited pregnant women including complete demographic details, dietary history, past medical history, previous obstetric history, and antenatal history including details of any antenatal complications. Women were advised to give 3-cc blood samples along with routine antenatal investigation. The serum VD was estimated by Beckman coulter unicel DXI immunoassay system using the principle of chemiluminescence.

Incidence of vitamin deficiency and insufficiency calculated. VDD was defined as 25(OH)D levels in blood <20 ng/mL, and insufficiency of VD was defined as 25(OH)D levels <32 ng/mL.[11] Antenatal complications such as intrauterine growth restriction (IUGR), oligohydramnios, preeclampsia, preterm labor, gestational diabetes, if any, were noted. Labor and delivery information including mode of delivery, and newborn birth weight were noted.

Statistical analysis

Descriptive statistics was used to calculate the mean ± SD. *t*-test unequal variance was performed to compare the mean value between the groups. All *P* value <0.05 within 95% confidence interval and at 5% level of significance were considered to be statistically significant.

Result

In total, 177 women recruited for the study. Mean age and parity of the subjects were 26.71 ± 9.96 and 2.10 ± 1.8, respectively [Table 1]. For detailed statistical analysis, women were divided into three groups depending upon their VD levels: deficiency group [25(OH)D level <20 ng/mL], insufficiency group [25(OH)D level <32 ng/mL], and sufficient group [25(OH)D level >32 ng/mL]. Mean VD level was 15.53 ± 7.65 ng/dL. VDD was present in 84.18% subjects. Mean VD level in this group was 12.91 ng/dL. VD insufficiency was present in 12.44% of cases. Mean VD level was 24.175 ng/dL in this group. only six subjects had sufficient VD level. There is no association of age, education, religion, rural, versus urban area. VDD and insufficiency were present in almost all (96.62%) women. There is inverse relationship between parity and VD. Mean VD level was less in women with hypertensive disorder of pregnancy (13.52 ng/dL) as compared with women with normal blood pressure (16.02) ($P < 0.01$) [Table 2].

Table 1: Demographic profile

Parameters	Mean
Mean age	26.71±9.96
Mean parity	2.10±1.8
Mean vitamin D level in insufficient group	24.175±2.17
Mean vitamin D level in deficient group	12.91±4.06

Table 2: Vitamin D (VD) level in various groups

Mean VD value	Mean VD value	*P*
VD level in PIH group 13.52 ng/dl	VD level in normotensive group 16.02 ng/dl	*P* 0.01
VD level in LSCS group 13.51 ng/dl	VD level in vaginal delivery group 17.57 ng/dl	*P* 0.000
VD level in low birth weight group 12.17 ng/dl	VD level not in low birth weight group 17.45 ng/dl	*P* 0.001

About 54.25% delivered vaginally and 47.14% delivered by LSCS. Women who underwent LSCS have deficiency and insufficiency of 90% and 7%, respectively, as compared with vaginal delivery who are having deficiency and insufficiency of 80% and 11%, respectively. Mean VD level in women who underwent normal vaginal delivery was 17.57 and women who underwent LSCS was 13.51. There was statistical significance difference between two groups (*P*-value 0.000) by *t*-test unequal variance.

Mean VD level was 12.17 in mothers whose babies were low birth weight as compared with 17.45 in mothers who are having no low birth weight babies (*P*-value = 0.001).

Discussion

In this prospective study, prevalence of VDD and insufficiency in pregnancy was 96.62%. Sunlight exposure is often the major influence on the VD status and is influenced by skin color, latitude, season as well as life style and cultural practices. Shillong is at 25.57°N 91.88°E. In the summer, the temperature varies from 23°C (73°F). In the winter, the temperature varies from 4°C (39°F). the city features a subtropical highland climate. Its summers are cool and very rainy, while its winters are cool and dry. Shillong is subject to vagaries of the monsoon. The monsoons arrive in June and it rains almost until the end of August. People keep cover themselves almost throughout the year. Staple diet is rice. Diet is also not rich in VD.

This finding of high prevalence correlating very well with other studies done in various parts of the world. In London in antenatal population, a VD level was <25 nmol/L (10 ng/mL) was found in 47% of Indian Asian women, 64% of middle eastern women, 58% in black women, and 13% of Caucasian.[12] In this study, cutoff was less; therefore, extent of deficiency was not that high. This high prevalence of VDD <20 ng/mL also observed among pregnant women in northeastern United States.[13] VDD is also noted in gulf state.[14]

There are studies which showed wide spread prevalence of VDD in India.[15,16] Various reason for this high deficiency may be poor sun exposure due to modern life style, vegetarian diet, skin pigmentation, and some cultural practice, such as pardah and burkhah.

In our study, age has no relation with VDD. Parity has direct association with VDD. Repeated and unspaced pregnancy can also exaggerated the VDD, which is already present in these women.

In present study, VD level was very low in pre-eclampsic women as compared with normotensive women ($P < 0.01$). This finding correlating well with another study that documented VD insufficiency was associated with increased risk of pre-eclampsia, gestational diabetes mellitus, and small for gestational age babies.[17] In two other studies, women who developed pre-eclampsia were found to have lower level of VD than women who did not with <50 nmol/L associated with a fivefold increased risk of severe pre-eclampsia.[18,19]

A study from Canada demonstrated that women with low circulating maternal VD level are more likely to have hypertension on pregnancy in the univariate analysis, but not the multivariate analysis.[13,20] Two meta-analyses, including a meta-analysis of 31 studies, demonstrated that VD insufficiency was associated with pre-eclampsia and SGA infants.[17,21]

In our study, mother of low birth weight babies were VD insufficient or deficient. There is positive association in these two parameters.

Maternal VD levels have been shown to positively correlate with birthweight centile.[22] One study from Holland showed that women with VDD had a 2.4-fold increased risk of having an SGA baby.[23] One more study found that maternal VD levels of <37.5 nmol/L in the first half of pregnancy were associated with an adjusted odds ratio of 7.5 for SGA infants in white women, but not in black women.[24] Another study from Australia found that mean birthweight was 200 g lower ($P < 0.001$) in babies of VDD mothers.[25] However, other studies demonstrated no relationship between maternal VD levels in the first trimester and birthweight but revealed that low VD levels in late pregnancy were linked with reduced intrauterine long bone growth and lower gestational age at delivery.[26]

Randomized controlled trials of VD supplementation in British mothers of Asian descent suggest a greater incidence of small-for-gestational-age infants born to mothers who received placebo than to mothers who received 1,000 IU of VD per day during the final trimester of pregnancy.[27,28]

Mean VD level in women who underwent normal vaginal delivery was 17.57 and women who underwent LSCS was 13.51. There was statistical significance difference between two groups (*P*-value 0.000) in this study. Similar to our observation, one study from Boston found that VD level <37.5 ng/L had four times the odds of a Cesarean delivery than those with higher level.[29] Contrary to this study a study from Northern California found no difference in mean VD levels between women who underwent Cesarean delivery and those who did not.[30] In one randomized control trial with VD supplementation, they observed no difference in Cesarean section rates between supplemented and control group.[31] However, one study showed that there is no correlation of VDD and various adverse pregnancy outcome, such as gestational diabetes mellitus, hypertension, pre-eclampsia, intrauterine growth restriction, preterm labor,

antenatal infection, bacterial vaginosis, and anemia, and neonatal outcomes, such as low birth weight baby, and neonatal intensive care unit admission.[32]

This study showed that the prevalence of VDD in pregnancy is astonishingly high. VDD is known to be linked with an increased prevalence of pre-eclampsia, Cesarean delivery, and with small infant size. Current recommendations for daily VD intake (200 IU) are inadequate to maintain serum levels of 25(OH)D in the normal range during pregnancy and lactation. Further studies are desirable to establish the serum levels and the amount of supplementation that is necessary to optimize maternal and fetal outcomes. However, VD supplementation is easy and cost-effective with a low probability of toxicity.[33] ACOG and RCOG advocate increased supplementation in antenatal women to keep serum levels of 25(OH)D in the normal range for adults (>32 ng/mL).[34,35]

Limitation of the studies lies in the fact that sample size was very small and single center study.

Conclusion

This study showed that the prevalence of VDD in pregnancy is astonishingly high till now there is no guideline to screen antenatal women for VDD. As there are no data to support routine screening for VDD in pregnancy in terms of health benefits or cost effectiveness, there is a disagreement that women at high risk for VDD should have a screening test, such as, dark skin color or coverage, obesity, risk of pre-eclampsia, or gastroenterological conditions limiting fat absorption. As the test is costly even, offering it to all at-risk women may not be cost effective compared with offering universal supplementation, particularly as treatment is regarded as being very safe.

Financial support and sponsorship

This study was funded by Intramural fund for faculty North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences Shillong, Meghalaya.

Conflicts of interest

There are no conflicts of interest.

References

1. Brannon PM, PiccianoMF. Vitamin D in pregnancy and lactation in humans. Annu Rev Nut 2011;31:89-115.
2. Wei SQ. Vitamin D and pregnancy outcome: Current Opi Obstet Gynecol 2014;26:438-47.
3. Kassai MS, Cafeo FR, Affonso-Kaufman FA, Suano-Souza FI, Sarni ROS. Vitamin D plasma concentrations in pregnant women and their preterm newborns. BMC Pregnancy Childbirth 2018;18:412.
4. Bondar LM, Platt RW, Simhan HN. Earlypregnancy Vitamin D deficiency and risk of preterm birth subtypes. Obstet gynecol 2015;125:439-47.
5. Song Hong-Bi, Xu Yin, Yang Xiaowu, Wang Ying, Xu Yang, Cao Ting, *et al.* High prevalence of vitamin D deficiency in pregnant women and its relationship with adverse pregnancy outcomes in Guizhou, China. J Int Med Res 2018;46:4500-5.
6. Shin JS, Choi MY, Longtine MS, Nelson DM. Vitamin D effects onpregnancy andtheplacenta. Placenta 2010;31:1027-34.
7. Dıaz L, Noyola-Martınez N, Barrera D, Hernandez G, Avila E, Halhali A, *et al.* Calcitriol inhibits TNF-alpha-induced inflammatory cytokinesin human trophoblasts. J Reprod Immunol 2009;81:17-24.
8. Bodnar LM, Krohn MA, Sinhan HN. Maternal Vit D may be link to black white disparity in adverse birth outcome. Obstet Gynecol Syrv 2010;65:273-284
9. Evnas KN, Bulmer JN, Kilby MD. Hewison M. Vitamin D and placental decidual function. J Soc Grnecol Investig 2004;11:263-71.
10. Dovnik A, Mujezinović F. The association of Vitamin D levels with common pregnancy complications. Nutrients 2018;10:867-79.
11. Lips P. Vitamin D physiology. Prog Biophys Mol Biol 2006;92:4-8.
12. Yu CK, Sykes L, Sethi M, Teoh TG, Robinson S. Vitamin D deficiency and supplementation during pregnancy. Clin Endocrinol 2009;70:685-90.
13. Johnson DD, Wagner CL, Hulsey TC, McNeil RB, Ebeling M, Hollis BW. Vitamin D Deficiency and insufficiency is common during pregnancy. Am J Perinatol 2011;28:7-12.
14. Saadi HF, Dawodu A, Afandi BO, Zayed R, Benedict S, Nagelkerke N. Efficacy of daily and monthly high dose calciferol in vitamin deficient nulliparrous and lactating women. Am J Clin Nutr 2007;85:1565-71.
15. Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High paevalence of Viamin D deficiency among pregnant women and their newborn in northern India. Am J Clin Nutr 2005;81:1060-4.
16. Jain V1, Gupta N, Kalaivani M, Jain A, Sinha A, Agarwal R. Vitamin D deficiency in healthy breastfed term infant at 3 months and their mothers in India. Seasonal variation and determinants. Indian J Med Res 2011;3:267-73.
17. Aghajafari F, Nagulesapillai T, Ronksley PE, Tough SC, O'Beirne M, Rabi DM. Association between maternal serum 25-hydroxyvitamin D level and pregnancy and neonatal outcomes: Systematic review and meta-analysis of observational studies. BMJ 2013;346:1169-80.
18. Baker Am, Haeri S, Camargo CA Espinola JA, Stube AM. A nested case control study of midgestation Viamin D deficiency and risk of severe preeclampsia. J Clin Endocrinol 2010;95:5105-9.
19. Bodnar LM, Catov JM, Simhan HN, Holick MF, Powers RW, Roberts JM. Maternal vitamin D deficiency increases the risk of preeclampsia. J Clin Endocrinol Metab 2007;92:3517-22.
20. Ringrose JS, Paus Jenssen AM, Wilson M, Blanco L, Ward H, Wilson TW. Vitamin D and hypertension in pregnancy. Clin Invest Med 2011;34:E147-54.
21. Wei SQ, Qi HP, Luo ZC, Fraser WD. Maternal vitamin D status and adverse pregnancy outcomes: A systematic review and meta-analysis. J Matern Fetal Neonatal Med 2013;26:889-99.
22. Robinson CJ, Wagner CL, Hollis BW, Baatz JE, Johnson DD. Maternal vitamin D and fetal growth in early-onset severe preeclampsia. Am J Obstet Gynecol 2011;204:556.e1-4.
23. 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. Br J Nutr 2010;104:108-17.

24. Bodnar LM, Catov JM, Zmuda JM, Cooper ME, Parrott MS, Roberts JM, *et al.* Maternal serum 25-hydroxyvitamin D concentrations are associated with small-for-gestational age births in white women. J Nutr 2010;140:999-1006.
25. 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;70:372-7.
26. Morley R, Carlin JB, Pasco JA, Wark JD. Maternal 25-hydroxyvitamin D and parathyroid hormone concentrations and offspring birth size. J Clin Endocrinol Metab 2006;91:906-12.
27. Brooke OG, Wood C. Growth in British Asians: Longitudinal data in the first year. J Hum Nutr 1980;34:355-9.
28. Brooke OG, Brown IR, Cleeve HJ, Sood A. Observations on the vitamin D state of pregnant Asian women in London. BJOG 1981;88:18-26.
29. Merewood A Mehta SD, Chen TC, Bauchner H, Holick MF. Association between vitamin D deficiency and primary cesarean section. J Clin Endocrinol Metab 2009;94:940-5.
30. Dror DK, King JC, Duarnd DJ, Allen LH. Association of modifiable and nonmodifiable factors with vitamin D status in pregnant women and neonates in Oakland, CA. J Am Diet Assoc 2011;111:111-6.
31. Hollis BW, Johnson D, Hulsey TC, Ebeling M, Wagner CL. Vitamin D supplementation during pregnancy: Double-blind, randomized clinical trial of safety and effectiveness. J Bone Miner Res 2011;26:2341-57.
32. Lee CL, Ng BK, Wu LL, Cheah FC, Othman H, Ismail NAM. Vitamin D deficiency in pregnancy at term: Risk factors and pregnancy outcomes. Horm Mol Biol Clin Investig 2017;31. doi: 10.1515/hmbci-2017-0005.
33. Barebring L, Schoenmakers I, Glantz A, Jagner A, Ellis J, Barebring M, *et al.* Vitamin D status during pregnancy in a multiethnic population –representative Swedish cohort. Nutrients 2016;8:655-65.
34. ACOG Committee on Obstetric Practice. ACOG Committee Opinion No. 495: Vitamin D: Screening and supplementation during pregnancy. Obstet Gynecol 2011;118:197-8.
35. RCOG statement: New NICE public health guidance on Vitamin D supplementation. Royal College Of Obstetrician Gynecologist; 2014.