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Original Research Article

Vitamin D Status in Pregnant Women of North East India and Impact of Vitamin D Deficiency in Pregnancy on Feto-Maternal Outcome

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Abstract

Background: Despite of sufficient and stable sunny conditions across the equatorial countries, there has been a high prevalence of Vitamin D deficiency (VDD) in pregnancy. The reasons for increased prevalence of VDD are increased time spent indoors, dark skin, and adoption of covered clothing due to religious & cultural reasons, low socio-economic status that leads to chronically poor diet. The present study was undertaken to find Vitamin D deficiency in the pregnant women of North East India and to find the adverse feto-maternal outcomes associated with VDD. ***Methods:*** This prospective study was conducted in the Department of Obstetrics & Gynaecology, Gauhati Medical College & Hospital, Guwahati, Assam, and India over a period of one year. Sample size was 150 pregnant women attending antenatal clinic. ***Results:*** Out of 150 pregnant women 66 (44%) had deficient, 41 (27.3%) had insufficient and 43 (28.7%) had sufficient vitamin D levels. VDD was seen in extremes of age groups i.e. group ≤ 20 years and 31- 35 years. Multiparity and low socio-economic status was associated with vitamin D deficiency and insufficiency, no association was found between VDD and religion (Hindu & Muslim). There was significant association between Vitamin D deficiency and insufficiency and occurrence of gestational hypertensive diseases and low birth weight babies. Rate of primary caesarean section was significantly high in vitamin D deficient women. No association was found between VDD and PROM/PPROM, preterm births, gestational diabetes mellitus and neonatal jaundice.

Keywords: Vitamin D deficiency, pregnancy, gestational hypertensive diseases, preterm, gestational diabetes mellitus, LBW.

INTRODUCTION

Vitamin D is produced endogenously following exposure of the skin to ultraviolet radiation with a small proportion derived from exogeneous dietary sources. Despite of sufficient and stable sunny conditions across equatorial countries, studies have reported high prevalence of VDD in pregnant and lactating women in such areas, ranging from 26–95% during pregnancy [1,2]. Women throughout Asia, Middle East and Africa have been consistently regarded as "high risk" for VDD. Despite of abundant sunshine, VDD has been recognized to be highly prevalent in India.

This paradox is explained by the fact that dark skin pigmentation is at increased risk of VDD. Increased time spent indoors and away from sunlight, liberal sunscreen use, adoption of covered clothing due to religious, cultural or aesthetic reasons and environmental pollution are factors implicated in the increased prevalence of VDD. Women living in low socio-economic strata are unable to meet micronutrient demands of pregnancy due to chronically poor diet. Inadequate access to dietary sources of vitamin D such as fish, dairy products, eggs and having vegetarian diet makes attaining sufficient vitamin D via food sources difficult. Women with one or more of these lifestyle risk factors could be considered vulnerable to VDD.

Pregnancy represents a time period where health status affects two individuals instead of one. With monumental development and growth that occurs in fetus, optimizing health status is imperative. In the pregnant women, it is believed that the primary role of

vitamin D is immunomodulatory—rather than a calcium-regulating factor, although it would also retain that function. VDD has been associated with increased risk of a number of adverse maternal and fetal health outcomes. These includes an increased risk of gestational hypertensive diseases, gestational diabetes mellitus (GDM), preterm labour, PPROM/PROM, increased incidence of primary caesarean section. For the offspring there is increased risk of low birth weight (LBW), intrauterine growth restriction, neonatal jaundice, and neonatal tetany [3].

METHOD

This study was conducted in Department of Obstetrics and Gynaecology, Gauhati Medical College & Hospital, Guwahati over a period of one year after obtaining ethical clearance from the institute.

It was a prospective study. Sample size was 150 pregnant women attending the antenatal OPD of the Department of Obstetrics & Gynaecology. A written and informed consent was obtained from the subjects.

INCLUSION CRITERIA

All pregnant women with

- Age :18 to 35 years
- Gestational age less than 24 weeks
- Singleton pregnancy

EXCLUSION CRITERIA

- Pregnant women with history of medical disorders such as hepatic, renal, metabolic bone disease, malabsorption diseases, thyroid, parathyroid or adrenal and collagen disorders, chronic hypertension, diabetes mellitus
- Previous caesarean section cases
- History of use of drugs interfering with calcium and vitamin D metabolism like anticonvulsants, corticosteroids etc

Detailed history was recorded including complete demographic details, dietary history, past medical history, previous obstetric history and antenatal history including details of any antenatal complications. All the data was collected in the proforma and it was updated time to time during the follow period.

The pregnant women up to the gestational age of 24 weeks were advised test for determining their Serum Vitamin D levels.

Estimation of 25-hydroxy vitamin D was done by the DIAMETRA 25-OH Vitamin D quantitative solid phase ELISA technique; based on the principle of competitive binding in the Department of Biochemistry, GMCH. A 3 ml venous blood sample is needed for this test.

Diagnosis of gestational diabetes mellitus was made using DIPSI (Diabetes in Pregnancy Study Group India) test. DIPSI recommends 75 mg of oral glucose load and at 2 hours a venous sample is collected for estimating plasma glucose, irrespective of whether she is fasting or non-fasting, without regard to the last meal. GDM is diagnosed if 2 hours plasma glucose is more equal to 140mg/dl.

PPROM/PROM was diagnosed by a simple per speculum examination for the presence of amniotic fluid coming from Os.

Based on the level of Vitamin D; three groups were determined namely,
A) Vitamin D Deficient group (≤ 19.9ng/ml)
B) Vitamin D Insufficient group (20-29.9ng/ml)
C) Vitamin D Sufficient group (≥ 30ng/ml)

These groups were followed up and studied for the development of

- Maternal complications like gestational hypertension, preeclampsia and eclampsia, PPROM/PROM, gestational diabetes mellitus, preterm labour, mode of delivery.
- Fetal complications like low birth weight, neonatal jaundice.

RESULTS

Out of 150 pregnant women 66 (44%) had deficient, 41 (27.3%) had insufficient and 43 (28.7%) had sufficient vitamin D levels. The mean vitamin D level of the study population was 24.52 ± 11.06 ng/ml.

Table-1: Shows the Vitamin D status in pregnancy and mean 25(OH)D levels in the three groups.

Vitamin D status	No. of pregnant women	Mean 25(OH)D levels
Deficiency	66 (44%)	14.93 ng/ml
Insufficiency	41 (27.3%)	24.06 ng/ml
Sufficiency	43 (28.7%)	39.66 ng/ml

The mean age of study population was 25.25 ± 3.72 years. Vitamin D deficiency was seen more in extremes of age groups (≤ 20 years, 47.60%) and (31- 35 years group, 36.4%). Mean level of vitamin D in the age group 31-35 years was the lowest i.e. 21.99 ng/ml followed by that of age group 26-30 years i.e. 22.66 ng/ml. From the mean vitamin D level, it was inferred that the suboptimal level of vitamin D was present in all age groups.54.5% of the lower socio-economic population had vitamin D deficiency and only 19.5% had vitamin D sufficiency. The association between vitamin D status and lower socio-economic status was significant. In this study 50% pregnant women were primiparous and 50% multiparous and multiparity was associated with vitamin D deficiency and insufficiency.

Table-2: Shows comparison of the demographic data and parity status with their vitamin D status.

	Deficiency n=66	**Insufficiency n=41**	**Sufficiency n=43**	**P value**
Age group distribution				
Less than 20 years	10(47.60%)	6(28.60%)	5(23.80%)	
21-25 years	23(39%)	14(23.70%)	22(37.30%)	0.526
26-30 years	29(49.20%)	16(27.10%)	14(23.70%)	
31-35 years	4(36.40%)	5(45.50%)	2(18.20%)	
Religion				
Hindu	35(37.60%)	26(28%)	32(34.40%)	0.078
Muslim	31(54.40%)	15(26.30%)	11(19.30%)	
Socio-economic status				
Lower	42(54.50%)	20(26%)	15(19.50%)	
Lower Middle	16(34%)	11(23.40%)	20(42.60%)	0.027
Middle	8(30.80%)	10(38.50%)	8(30.80%)	
Parity				
Primiparous	31(41.30%)	19(25.30%)	25(33.30%)	0.044
Multiparous	35(46.70%)	22(29.30%)	18(24%)	

Out of 43 pregnant women with sufficient vitamin D levels, 32 (74.4%) women had normal blood pressure with no hypertensive crisis throughout pregnancy, 7 (16.3%) women developed PIH and only 4 (9.3%) cases developed pre-eclampsia.

Out of 66 vitamin D deficient cases 24 (36.4%) pregnant women had normal blood pressure, 24 (36.4%) pregnant women developed PIH subsequently during her antenatal course, 15 (22.7%) cases developed pre-eclampsia and 3(4.5%) cases landed up having eclampsia.

Out of 41 pregnant women who had vitamin D insufficiency,10 (24.4%) pregnant women developed PIH, only 4 (9.8%) pregnant women developed pre-eclampsia. There was significant association between vitamin D deficiency and development of gestational hypertensive disorders. (p value=0.006). The association between vitamin D status and occurrence of preterm labour and rupture of membranes, gestational diabetes mellitus and neonatal jaundice was insignificant.

Out of 66 vitamin D deficient pregnant women, 30 (45.5%) pregnant women delivered by LSCS. In vitamin D insufficient group,12(29.3%) cases delivered by LSCS, whereas in pregnant women with sufficient vitamin D levels only 11(25.6%) delivered by LSCS (p value 0.046). Higher incidence of LSCS occurred in vitamin D deficient group.

45.5% born to vitamin D deficient and 39% born to vitamin D insufficient women had LBW. Vitamin D deficiency and insufficiency was associated with LBW babies.

Table-3: Shows the comparison between feto-maternal outcomes with the vitamin D status.

	Deficiency n=66	Insufficiency n=41	Sufficiency n=43	P value
Gestational hypertensive diseases				
Normotensive PIH Pre-eclampsia Eclampsia	24(36.40%) 24(36.40%) 15(22.70%) 3(4.50%)	26(63.40%) 10(24.40%) 4(9.80%) 1(2.40%)	32(74.40%) 7(16.30%) 4(9.30%) 0(0.00%)	0.006
Gestational age at delivery				
Term (≥ 37 weeks) Preterm (<37 weeks)	51(77.30%) 15(22.70%)	32(78.00%) 9(22.00%)	37(86.00%) 6(14.00%)	0.5
PPROM/PROM				
Absent Present	52(78.80%) 14(21.20%)	33(80.50%) 8(19.50%)	38(88.40%) 5(11.60%)	0.426
Mode of delivery				
Vaginal Cesarean Instrumental	32(48.50%) 30(45.50%) 4(6.10%)	29(70.70%) 12(29.30%) 0(0.00%)	31(72.10%) 11(25.60%) 1(2.30%)	0.046
Gestational diabetes mellitus				
Non-GDM GDM	60(90.90%) 6(9.10%)	38(92.70%) 3(7.30%)	40(93%) 3(7%)	0.908
Birth weight				
Normal birth weight (≥ 2.5kg) Low birth weight (≤ 2.4 kg)	30(54.5%) 66(45.5%)	25(61.00%) 16(39.00%)	34(79.00%) 9(21.00%)	0.032
Neonatal jaundice				
Absent Present	51(77.50%) 15(22.70%)	33(80.50%) 8(19.50%)	35(81.40%) 8(18.60%)	0.854

DISCUSSION

In this study the vitamin D deficiency, insufficiency & sufficiency was found 44%, 27.3%, 28.7% of subjects respectively.

Sharma *et al*. at NEIGRIHMS, Meghalaya (India); found that vitamin D deficiency was present in 84.18% of pregnant women and vitamin D insufficiency in 12.44% [4]. Pahuja *et al*. at Himalayan Institute of Medical Science, Uttarakand (India) found that 21 % pregnant women were vitamin D deficient & 69 % were vitamin D insufficient [5].

This study had 47.6% and 28.6% of pregnant women in ≤ 20 years age-group with vitamin D deficiency & insufficiency respectively. In advanced age-groups i.e. 26-30 years, 49.2% and 27.1% women had vitamin D deficiency & insufficiency. In age-group 31-35 years vitamin D deficiency & insufficiency was seen in 36.4% and 45.5%. From this study it was concluded that vitamin D deficiency & insufficiency was present in extremes of age groups. Al Shaik *et al*. had similar finding in their study done in Saudi Arabia. They found that 52% of vitamin D deficient and 53.1% vitamin D insufficient women belong to ages between 25 to 35 years [6].

Amongst Muslim population, 54.4 % were vitamin D deficient & 19.3% had sufficient levels of vitamin D. amongst Hindu, 37.6% were vitamin D deficient and 34.4% vitamin D sufficient. There was no statistical significance between the vitamin D status of Hindu and Muslim pregnant women. Similarly, Alok Sachan *et al*. in their study on vitamin D deficiency among pregnant women in northern India found no difference between the vitamin D status of Hindu and Muslim population [7].

This study showed significantly poor vitamin D status in pregnant women belonging to lower socio-economic class. 54.5% of pregnant women of lower socioeconomic strata had vitamin D deficiency. However, Nimitphong and Holick M. in their study on vitamin D status in South Asia found that vitamin D deficiency is prevalent equally in lower and upper class [8].

Vitamin D deficiency was more in multiparous women as compared to primiparous in this study. Al-shaikh *et al*. in their study also found that 66.8% of vitamin D deficient and 75.5% of vitamin D insufficient women were multiparous [6].

Vitamin D is thought to play a significant role in preeclampsia as an immune modulator. It helps by mounting an appropriate maternal immune response to the placenta preventing the release of anti-angiogenic factors into the bloodstream and modulating hypertension.

In the present 36.4% of vitamin D deficient pregnant women suffered from PIH, 22.7% developed pre-eclampsia, 4.5% ended up having eclampsia. 24.4% of vitamin D insufficient pregnant women suffered from PIH, 9.8% developed preeclampsia, 2.4 % ended up having eclampsia. Bodnar *et al*. USA in a case control study found positive correlation between vitamin D deficiency and development of preeclampsia [9].

Worldwide studies claim that vitamin D participates in immunological processes that prevent bacterial invasion, which may indirectly influence duration of pregnancy. Cytokines released by maternal and fetal systems in response to bacterial invasion leads to production of prostaglandins which then triggers preterm contractions. However, many studies have failed to prove this association.

In this study, 22.7% of vitamin D deficient women had preterm labour and 77.3 % had it at term and 22% of vitamin D insufficient women had preterm labour and 78% had it at term. Similarly, Lixia Yang *et al*. in their prospective study conducted in China to find the correlation between vitamin D deficiency and preterm birth found no evidence of an increase in preterm birth in relation with vitamin D deficiency [10].

In this study, 21.2% of vitamin D deficient pregnancies had ROM and in vitamin D insufficient group 19.5% of pregnant women had ROM and 11.6 % of vitamin D sufficient pregnant women had ROM. This study could not prove significant association between poor vitamin D as causal for rupture of membranes. Similarly, in a prospective observational study conducted in Southern China by J. Zhou *et al*. it was found that 20.81% of vitamin D deficient, 22.73% of vitamin D insufficient and 21.04% of vitamin D sufficient pregnant women had prelabour rupture of membranes [11].

The vitamin D receptor has been identified throughout the body, including the uterine smooth muscle and skeletal muscle. Vitamin D deficiency is associated with poor muscle performance in humans leading to increase in caesarean section. Many studies conducted worldwide have successfully proven that poor vitamin D status increases the rate of primary caesarean section.

In this study, 45.5% of vitamin D deficient pregnancies landed up having caesarean section while 48.5% had vaginal delivery and 6.1% had instrumental delivery, in vitamin D insufficient group 29.3% had caesarean delivery. In this study, vitamin D deficiency had significant association with increase in the rate of primary caesarean section. In a large prospective study conducted at Boston by Anne Merewood *et al*. it was found that there exists an inverse association between caesarean section and serum 25(OH)D levels. In their study 28% pregnant women with vitamin D deficiency had caesarean section when compared to 14% pregnant women with sufficient vitamin D levels to have caesarean delivery [12].

There are several evidences supporting the role of vitamin D in maintaining glucose homeostasis and the fact that VDD can lead to glucose intolerance. But very few clinical studies conducted worldwide have proven this association.

In this study, 8% of the pregnant women were diagnosed with gestational diabetes mellitus. In vitamin D deficiency group 9.1 % pregnant women developed GDM, 7.3% of vitamin D insufficient pregnant women developed GDM, whereas 7% of pregnant women with sufficient vitamin D levels developed had GDM. There was no association between poor vitamin D status in pregnancy and occurrence of GDM in this study. A case control study was conducted by Baker et al in USA, wherein they found those 5 individuals with vitamin D deficiency in 60 GDM cases and 8 individuals with vitamin D deficiency in 120 controls. The p value was 0.90 making this association insignificant [13]. Helena H et al in their study found no difference in pregnancy 25(OH)D concentration between GDM and non-GDM women (82 vs 82 nmol/L, P= 0.99) [14].

In this study, 45.5% of vitamin D deficient and 39% of vitamin D insufficient pregnant women delivered babies weighing less than or equal to 2.4 kg (LBW) whereas only 21% of vitamin D sufficient pregnant women delivered LBW babies. So, there was a significant association between vitamin D deficiency in pregnancy and low birth weight babies in this study.

Similarly, Wang *et al*. from their study concluded that maternal vitamin D insufficiency during pregnancy is independently associated with low birth weight and have a high risk of SGA in term fetus [15]. Sharma N *et al*. in their study found that the maternal mean vitamin D level in low birth weight group was 12.17 ng/ml which was significantly low in comparison with the normal birth weight group where it was 17.45 ng/ml [4].

The metabolisms of bilirubin and vitamin D happen in two separate paths, but they may affect each other since one stage of their synthesis takes place in liver. So far, few studies have examined the relationship between neonatal hyperbilirubinemia and maternal serum vitamin D.

In one case control study conducted in Iran by Shahrokh Mehrpisheh *et al*. it was found that there was no correlationship between neonatal jaundice and maternal and neonatal vitamin D deficiency [16]. In the present study, there was no significant association between developments of neonatal jaundice in babies born to vitamin D deficient mothers.

CONCLUSION

This study showed that the prevalence of VDD in pregnancy is astonishingly high and there was significant association between hypovitaminosis D and occurrence of gestational hypertensive diseases and low birth weight babies. Rate of primary caesarean section was significantly high in vitamin D deficient women. The paucity of clinical studies on the extent of vitamin D deficiency in pregnancy and adverse impact of it on maternal and fetal health and also the high cost of vitamin D estimation makes the universal antenatal screening and even the highrisk screening of pregnant women for vitamin D an economically challenging task. Despite a dearth of interventional evidence supporting supplementation/treatment of vitamin D in randomised controlled trial settings, it is generally accepted that supplementation/treatment is not harmful and may have some significant short and long term health benefits. Treatment of vitamin D deficient women and prophylactic vitamin D supplementation is safe and is recommended for all women who are pregnant or breastfeeding. Encouragement for moderate outdoor activity for adequate exposure to sunlight is desirable.

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