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Original Research Article

Prevalence of vitamin D deficiency and effect of vitamin D supplementation on feto-maternal outcome in tertiary care centre

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ABSTRACT

Background: Vitamin D deficiency is widely prevalent throughout the world. Pregnant women, neonates and infants form most vulnerable groups for vitamin D deficiency. Hypovitaminosis D in pregnancy has been reported to cause various fetomaternal effect, i.e. increased risk of preeclampsia (PE), gestational diabetes mellitus (GDM), caesarean section, hypocalcemia, subclinical myopathy, neonatal tetany, hyperbilirubinemia congenital rickets and infantile rickets, etc. Only few Indian studies are available in this regard. The objectives are to find prevalence of vitamin D deficiency in pregnant women and to evaluate the effect of supplementation with cholecalciferol in improving vitamin D levels in pregnant women and evaluate its correlation with feto-maternal outcome.

Methods: A prospective observational was conducted on 120 Pregnant women on their first visit to hospital irrespective of gestational age were offered the test and on the basis of inclusion and exclusion criteria are included in study and vitamin D level was done to know the prevalence of vitamin D deficiency. Apart from routine obstetrical investigation, serum vitamin D (total) level was estimated. All results were recorded and analyzed statically.

Results: Out of 120 patients 101 (84.1%) were found to be vitamin D deficient. Mean age of vitamin D deficient group was 28.31±3.86 and sufficient group was 26.37±2.83.81 (67.5%) were vegetarian and 39 (32.5%) were nonvegetarian.75 (92.59%) vegetarian and 26 (66.66%) non-vegetarian found to be vitamin D deficient. ($p<0.05$). Vitamin D supplementation has been observed to reduce risk of preeclampsia. ($p<0.05$) and vitamin D sufficiency associated with reduced risk of low birth weight babies.

Conclusions: Vitamin D supplementation reduces risk of maternal comorbidities and helps improve neonatal outcomes.

Keywords: Feto-maternal outcome, Hypovitaminosis D, Vitamin D status in pregnancy, Maternal blood vitamin D

INTRODUCTION

Vitamin D, a lipid-soluble vitamin and prohormone, is known to play an important role in bone metabolism through regulation of calcium and phosphate homoeostasis.[1] Vitamin D traditionally known as "anti-ricketic or sunshine vitamin".

It is a unique nutrient because it can be synthesized endogenously (skin) and it function as a hormone.[2]

Vitamin D deficiency is prevalent worldwide, and its unrecognized epidemic is common in all age groups ranging from 46-90%.[3-9] Various Indian studies have reported vitamin D deficiency in all age groups and involving both sexes. Its prevalence ranging between 40-93%.[10-12] During pregnancy high prevalence of vitamin D deficiency has been reported from various region of world, ranging from 45-100%.[7-9] And in Indian population it has been reported to the tune of 42-93%.[13-16]

Studies regarding prevalence of vitamin D deficiency in antenatal women in India are mainly from Northern and southern India and very a few from central Part of India, thus this study has been undertaken in order to know the prevalence of vitamin D deficiency of antenatal women in present institute.[13-16] Vitamin D functions in both classical and non-classical ways: The action of 1, 25$(OH)_2$D are mediated through specific, high affinity binding to the vitamin D receptor (VDR). The classical way to regulate calcium and phosphorus absorption and help in bone synthesis and metabolism via its action on kidney-liver- intestine.[17] Recent data of non-classical way of function of Vitamin D is via the target organ in the endocrine system which include adaptive and immune system, β- pancreatic cell, cardiovascular system and brain.[18]

Vitamin D deficiency during pregnancy is associated with the non- classical action of this hormone, being linked with preeclampsia, insulin resistance, gestational diabetes mellitus, and risk of Caesarean section, impaired calcium metabolism and fetal growth.[19-22]

Studies reported in India are mainly from Northern and southern India and` very a few from central Part of India, thus this study has been undertaken in order to know the prevalence and its maternal and fetal outcome in present institute.

METHODS

This study was a prospective observational study conducted in the Department of Obstetrics and Gynaecology in collaboration with the department of nuclear medicine of Jawahar Lal Nehru Hospital and Research Centre, Bhilai, Chhattisgarh, India, from October 2015 to November 2016 after approval from the hospital ethical committee.

Inclusion criteria

- Antenatal women on their first visit to hospital, irrespective of period of gestational age.
- Patient's willingness to get test done.

Exclusion criteria

- Patients on vitamin D supplementation in early pregnancy before attending ANC OPD/ IPD
- Patients with essential hypertension and known case of Diabetes mellitus.

Written informed consent was taken from patient or guardian/ relatives prior to enrolment in the study.

Methodology

Pregnant women (Antenatal women) on their first visit to hospital irrespective of gestational age were offered the test and on the basis of inclusion and exclusion criteria are included in study and vitamin D level was done to know the prevalence of vitamin D deficiency. Apart from routine obstetrical investigation, serum vitamin D level estimation was done by fully automated chemiluminescent immunoassay and radioimmunoassay (RIA).

Table 1: Reference range-recently revised institute of medicine's (IOM) criteria 2010.[23]

	Vit D3 level	
	ng/ml	**nmol/l**
Vitamin D sufficiency	>30	75-80
Vitamin D insufficiency	21-29	49-75
Vitamin D deficiency	<20	50

1 nmol/l=0.4 ng/ml

Antenatal women having vitamin D level below 30ng/ml were supplemented with 60,000 IU of cholecalciferol weekly. As vitamin D deficient women belonged to different period of gestation at the start of therapy hence, period of supplementation with vitamin D was variable. To achieve normalcy of vitamin D level 8 weeks of therapy is considered adequate, taking reference of study done by Malbanan and Goswami.[24,25]

For the study purpose all antenatal women will be divided in to two groups:

Group 1 (vitamin D sufficient group)

- Women with vitamin D level ≥30ng/ml on first visit.
- Vitamin D deficient women who will be supplemented with 60,000IU of cholecalciferol weekly for 8 weeks to normalize their vitamin D level in sufficient range.

Group 2 (vitamin D deficient group)

- This group included antenatal women diagnosed with deficiency in late pregnancy where in spite of weekly supplementation with vitamin D, duration of therapy was <8 weeks. Hence, these women were taken in deficient group.

Sample size: 120 cases.

Cochran formula for sample size for descriptive analysis,

Equation: Sample size N = $\frac{1.96^2 \times p \times (1-p)}{e^2}$

P - Percentage of pregnant women having vitamin D deficiency from a previous study=72.1%=0.721.

Statistical analysis

Data thus collected were entered in Microsoft Excel Sheet by investigator himself on same day so as to minimize data entry bias if any analysed using SPSS version 24. The results were presented as percentages and Chi-square test was used to assess the association. P-value of less than 0.05 was taken as the level of significance.

RESULTS

The present study was undertaken in order to determine the vitamin D level in 120 pregnant women, age range of 19-39 years with first visit to hospital irrespective of their gestational age. Out of these 101 cases (84.1%) were found vitamin D deficient. The prevalence of vitamin D deficiency was found 84.1% or 841.66 per thousand women. The mean age of vitamin D deficient group was found 28.31±3.86 years. The mean age of vitamin D sufficient group was found 26.37±2.83 years. Maximum number of patients were Hindu 114 (95%) and out of this, 97 (85.08%) were vitamin D deficient and 17 (14.9%) were vitamin D sufficient.

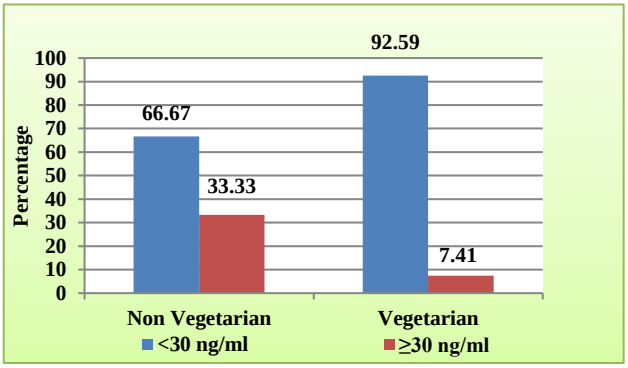

Figure 1: Distribution of cases according to diet.

Only 6 (5%) cases were Muslim out of this 4 (66.66%) were vitamin D deficient and 2 (33.33%) were vitamin D sufficient. Maximum number 81(67.5%) patients were vegetarian, out of this 75(92.5%) were vitamin D deficient and only 6(31.58%) were vitamin D sufficient.39 patients were non-vegetarian, out of this 26 (66.66%) were vitamin D deficient and 13 (33.33%) were vitamin D sufficient. This correlation of vegetarian diet with vitamin D deficiency is found statistically significant (p <0.001).

Table 2: Distribution of cases according to sunscreen lotion/ cream uses.

Sunscreen	Vitamin D			
	<30 ng/ml	≥30 ng/ml	Total	
Yes	65 (94.5%)	4 (21.05%)	69 (57.5%)	Chi square value=12.27
No	36 (70.59%)	15 (78.95%)	51 (42.5%)	DF=1 P=0.00046 HS
Total	101 (100%)	19 (100%)	120 (100%)	

69 (57.75%) patients used sunscreen lotion/cream out of this 65 (94.5%) patients were found vitamin D deficient and 4 (21.05%) were vitamin D sufficient.51 (42.5%) patients were not used sunscreen lotion/cream out of this 36 (70.59%) patients were found vitamin D deficient and 15 (78.95%) were vitamin D sufficient. This association between vitamin D deficiency and uses of sunscreen lotion/cream found to be statistically significant (p<0.05).

Maximum 49 (40.83%) patient's first visit was in 28-36 weeks of gestational age. Minimum 6 (5%) patient's first visit was in first trimester (<12 week). Majority of patients, 84 (70%) were belonged to primipara, out of this 71 (84.52%) found vitamin D deficient and 13 (15.48%) were vitamin D sufficient.

Rest 36 (30%) were multipara. Out of this 30 (25%) were vitamin D deficient and 8 (31.5%) were vitamin D sufficient.

Table 3: Distribution of cases according to development of preeclampsia.

PE	Vit D deficient	Vit D sufficient	Total	P value
Yes	26 (78.8%)	07 (21.1%)	33 (27.5%)	Chi square value=22.52
No	25 (28.7%)	62 (71.2%)	87 (72.5%)	DF=1 P<0.0001 HS
Total	51 (42.5%s)	69 (57.5%)	120 (100%)	

In a population of 120 antenatal patients 33(27.5%) patients developed preeclampsia and rest 87 (72.5%) patients were normotensive. Out of 33 patients of preeclampsia 26 (78.8%) were vitamin D deficient and only 7 (21.21%) were vitamin D sufficient.

Total 69 patients were vitamin D sufficient out of this only 7 (10.1%) patient developed preeclampsia and 62(89.8%) were normotensive. This correlation between vitamin D deficient and sufficient patients with preeclampsia found statistically significant (p<0.001). In the study of 120 patients only 2 (1.6%) patients developed GDM out of which one was vitamin D sufficient and another one was vitamin D deficient. As number of cases who developed GDM was only 2 and majority (98.01%) of patients were euglycemics.

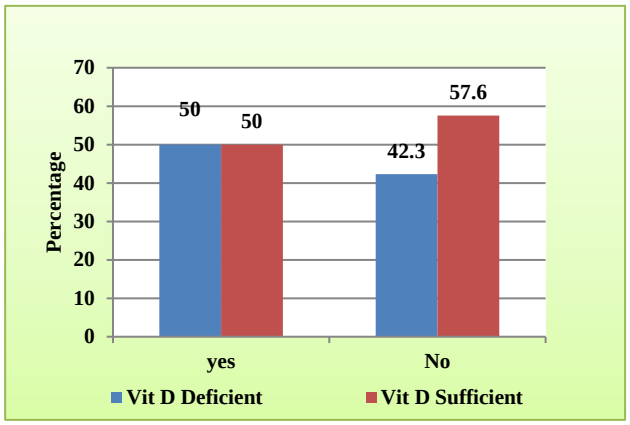

Figure 2: Distribution of case according to development of gestation diabetes mellitus.

Total of 60 (50%) patients delivered by LSCS, out of this 23 (38.3%) were vitamin D deficient and 37 (61.66%). 60 (50%) patients delivered normal vaginally, out of this 28 (46.6%) were vitamin D deficient and 32 (53.3%) were vitamin D sufficient This association was statistically not significant (p>0.4).

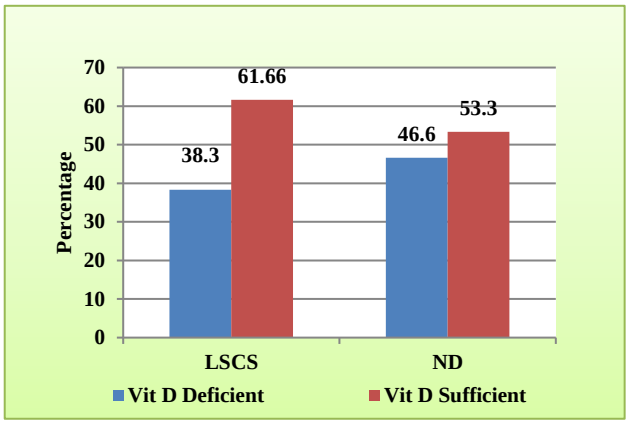

Figure 3: Distribution of cases according to mode of delivery.

In the study of 120 patients 108 (90%) patients delivered at term and 12 (10%) patients gave birth to preterm baby. Out of 108 mothers who delivered term baby, 41 (37.96%) were vitamin D deficient and 67 (62.03%) were vitamin D sufficient. Out of 12 mothers of preterm baby, 10 (83.3%) were vitamin D deficient and only 2 (16.37%) were vitamin D sufficient. This correlation was found to be significant (P<0.01).

Table 4: Distribution of cases according to period of gestation.

POG	Vit D deficient	Vit D sufficient	Total	P value
Preterm	10 (83.33%)	2 (16.37%)	12 (10%)	Chi square value=7.335
Term	41 (37.96%)	67 (62.03%)	108 (90%)	DF=1 P=0.007 HS
Total	51 (42.5%)	69 (57.5%)	120 (100%)	

Table 5: Distribution of cases according to birth weight of new born.

Birth weight	Vit D deficient	Vit D sufficient	Total	P value
≤2.5 kg	27 (77.14%)	8 (22.8%)	35 (29.1%)	Chi square value=22.306
>2.5 kg	24 (35.41%)	61 (71.1%)	85 (70.08%)	DF=1 P<0.01 Significant
Total	51 (42.5%)	69 (57.5%)	120 (100%)	

35 (29.1%) patients delivered low birth weight babies, out of this 27 (77.14%) were vitamin D deficient and only 8 (22.8%) were vitamin D sufficient. 85 (70.08%) had normal birth weight babies, out of this 24 (35.41%) were vitamin D deficient and 61 (71.1%) were vitamin D sufficient. This correlation between vitamin D deficient and vitamin D sufficient patients with birth weight of babies found statistically significant (p<0.01).

DISCUSSION

It has been estimated that 1 billion people worldwide, across all ethical and age group, have vitamin D deficiency and insufficiency. There is widespread prevalence of varying degree ranging from 36-94% involving all age group both sexes and pregnant women. Vitamin D deficiency is also not uncommon in India in

spite of receiving ample sunlight throughout the year. [10-12] Vitamin D deficiency in Indian pregnant women ranging from 42-93%.[13-16]

The present study was undertaken in order to determine the vitamin D level in 120 pregnant women on their first visit to hospital irrespective of their gestational age. In present study the prevalence of vitamin D deficiency was 84.1% or 841.66 per thousand women. Similarly, prevalence of vitamin D deficiency in pregnant women reported by Jani R et al, Sachan A et al and Dasgupta et al, Chauhan R et al was 100%, 84.3% and 42%, 72.1% respectively.[11,13,14,26] In present study, age range was 19-39 years. Vitamin D deficiency was found most common in 25-29 years (51.67%) with mean age 28.31±3.86 years.

Johnson D et al conducted study on 310 pregnant women and also found mean age 24.3 (range 18-40 year) of vitamin D deficient patients.[27] Mallah et al conducted a study in Jordanians at national level revealed that women who wear hijab or niqab were more likely to have low levels vitamin D.[28] In present study of 120 patients, 114(95%) cases were Hindu; out of this 97(85%) had vitamin D deficiency. Only 6 (5%) cases were Muslim out of which 4(66.66%) had vitamin D deficiency. In present study out of 81 (67.5%) vegetarian patients, 75 (92.59%) were vitamin D deficient.

Out of 39 (32.5%) non-vegetarian, 26 (66.6%) were vitamin D deficient. Hence, vitamin D deficiency was more pronounce in vegetarian compare to non-vegetarian. This association between vitamin D deficiency and diet was found to be statistically significant ($p<0.005$). Similarly, Crowel et al found that plasma 25(OH)D concentration were lower in vegetarian than meat and fish eater.[29] In present study patients who used sunscreen cream/lotion, 94.2% were vitamin D deficient and on other hand 51 (42.5%) patients who were not used sunscreen cream vitamin D deficiency observed in 36 (70.56%) patients.

Thus, cases who used sunscreen cream are more prone to developed vitamin D deficiency than who do not. This association with sunscreen cream found statistically significant ($p<0.05$). Holick MF et al in 1977 also found that the most important source of vitamin D is skin's synthesis of vitamin D from sunlight and use of sun-block and time spend indoor increases the risk of vitamin D deficiency.[22]

In the present study of 120 antenatal patients, 33 (27.5%) patients developed preeclampsia and rest 87 (72.5%) patients were normotensive. Out of 33 patients of preeclampsia, 26 (78.8%) were vitamin D deficient. Total 69 patients had vitamin D level in sufficient range, which included 19 patients having vitamin D in normal range on first visit and 50 patients who were supplemented with 8 weeks of vitamin D in early pregnancy to normalise their vitamin D level. Amongst these 69 patients, only 7 (10.1%) patients developed preeclampsia. This correlation between vitamin D deficient and sufficient patients with preeclampsia found statistically significant ($p<0.001$). Thus, vitamin D deficiency has been observed to be a factor for development of preeclampsia and supplementation with vitamin D for minimum of 8 weeks likely to reduce risk of preeclampsia

Similarly, Bodnar et al in 2007, Baker et al in 2010, Robinson et al in 2011 and Chauhan R in 2015 also found that prevalence of vitamin D deficiency is more prevalent in preeclamptic women.[19,26,30,31] As Malbanan and Goswami reported successful normalization of serum 25(OH)D at 8 weeks after supplementing with 60,000IU orally cholecalciferol each week to vitamin D deficient patients.[24,25] Similarly, in present study authors have supplemented all vitamin D deficient patients with 60,000 IU weekly. These patients who can be supplemented with 8 weeks of weekly vitamin D were considered as vitamin D sufficient and rest where therapy was given in late pregnancy (<8 weeks) were considered as vitamin D deficient.

According to the studies done by Marya et al, Emadi et al and Taheri M et al vitamin D supplementation associated with significant reduction in the risk of preeclampsia.[32-34] Similarly, in present study out of 69 patients of vitamin D sufficient level only 7 patients developed preeclampsia, thus there may be a possible association of vitamin D supplementation and reduced risk of pre-eclamsia.

In present study out of 120 patients only 2 developed gestational diabetes mellitus, 99 patients were euglycemic. The number is too less to draw any conclusion about association. In present study LSCS was done in 60 patients, out of which 23(38.3%) were vitamin D deficient and 37(61.66%) were vitamin D sufficient. Out of normal vaginal delivery patients (60/120), 28 (46.6%) were vitamin D deficient and 32 (53.3%) were vitamin D sufficient.

Dror DK et al in 2011 also found no change in mean vitamin D level between women who underwent caesarean delivery and who did not.[35] Contrary to this Merewood et al in 2008 found that women with low vitamin D level had four times the odds of caesarean delivery.[28] In present study maximum 108 (90%) out of 120 patients delivered at term and Only 12 (10%) patients had preterm delivery. Out of 108 mother who delivered term baby, 67 (62.03%) were vitamin D sufficient and 41 (37.96%) were vitamin D deficient. 12 mothers of preterm baby,10 (83.3%) were vitamin D deficient and only 2 (16.2%) were vitamin D deficient. Wagner et al in 2013 that supplemented 257 pregnant women for 12-16 week of gestational age with vitamin D (2000 IU) found risk reduction in preterm infection and preterm birth.[36]

In the present study of 120 patients a total of 35 patients had low birth weight babies out of this 77.14% (27) were vitamin D deficient and only 8 patients (22.6%) patients were vitamin D sufficient. Total of 69 vitamin D

sufficient patients only 8 (11.5%) delivered low birth weight babies. Here the p value for low birth weight patients was statistically significant ($p<0.05$).

Thus, vitamin D deficiency has been observed to be linked with low birth weight newborns and vitamin D supplementation may reduce the risk of supplementation. Similarly, Brook et al in 1980 also reported reduced incidence of low birth weight babies in vitamin D supplement Asian mother. [37]

CONCLUSION

Vitamin D deficiency has high prevalence in Indian pregnant women and investigation during first trimester to diagnose deficient patients and timely supplementation during pregnancy can significantly reduce the chance of preeclampsia and low birth weight babies.

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