



Comparative Evaluation of the Effect of Vitamin D Supplementation in Pregnancy and its Correlation with Fetomaternal Outcome

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Abstract

Introduction: Vitamin D deficiency is a common and increasing problem and concerns have been raised that there may be an epidemic of such deficiency in pregnancy. Vitamin D may be important in the pathogenesis of severe preeclampsia & preterm birth.

Aim: The aim of the present study was to estimate the association between intake of vitamin D during pregnancy and the risk of preeclampsia & preterm birth.

Method: We performed a prospective observational study in 200 pregnant women with singleton pregnancy at 12-16 weeks of gestational age as cases, Serum vitamin D tested at 1st trimester & again in 3rd trimester. Observations for antenatal complications like preeclampsia and foetal outcome was done and correlated to serum vitamin D levels among those who took the supplementation and those who did not, and analyzed.

Result: The mean vitamin D level was 16.76 ± 6.56 ng/ml. Supplementation was done in 40 vitamin D deficient women. The mean vitamin D level in the 1st trimester increased from 13.74 ± 4.84 to 27.12 ± 7.19 in 3rd trimester (p value = 0.0001). According to serum vitamin D in 3rd trimester, the incidence of preeclampsia was found much higher in vitamin D deficiency (<20 ng/ml) group i.e. 28(36.36%) as compared with vitamin D insufficiency (20-30 ng/ml) group i.e. 3(4.17%). No case of preeclampsia in vitamin D sufficiency (>30 ng/ml) group. Incidence of Preterm Baby was found slightly higher in vitamin D deficiency (<20 ng/ml) group i.e. 20(25.97%) as compared with vitamin D insufficiency (20-30 ng/ml) group i.e. 16(22.22%). 2 case(3.92%) of Preterm Baby was found in vitamin D sufficiency (>30 ng/ml) group.

Conclusion: High prevalence of vitamin D deficiency in pregnancy was found in our study. Higher vitamin D levels (>30 ng/ml) is associated with better fetomaternal outcome. Supplementation of vitamin D in pregnancy is safe & should be given.

Keywords: Vitamin D supplementation; Preeclampsia; Preterm birth.

Introduction

Vitamin D deficiency or insufficiency is currently a global pandemic affecting all ages and ethnic

groups¹. Vitamin D is a fat soluble vitamin produced endogenously in the skin with exposure to sunlight. It is also obtained from consuming

fortified milk or juice, fish oils, and dietary supplements of vitamin D that is ingested or produced in the skin must undergo hydroxylation in the liver to 25 hydroxyvitamin D (25(OH)D), then further hydroxylation primarily in the kidney to the physiologically active 1,25 dihydroxyvitamin D².

Vitamin D insufficiency during pregnancy is associated with adverse maternal outcomes such as increased risk of gestational diabetes mellitus (GDM), preeclampsia, caesarean-section delivery and bacterial vaginosis³. Preeclampsia and hypertensive disorders complicate 3-10% of pregnancies and contribute to maternal and neonatal morbidity and mortality⁴.

Pathogenesis of preeclampsia involves a number of biological processes that may be directly or indirectly affected by vitamin D, including immune dysfunction, placental implantation, abnormal angiogenesis, excessive inflammation, and hypertension⁵. Vitamin D has been hypothesized to influence preeclampsia risk. Preeclampsia rates are elevated during winter months, when sunlight-dependent 25(OH) D productions are reduced.

Women with vitamin D deficiency have a 2.4 fold increased risk of having a small for gestational age baby⁶. Women who were vitamin D deficient in the 1st trimester of pregnancy 14 weeks or less were twice as likely to have babies who fell in the lower 10th percentile for weight when compared to other full term babies born in the same week of pregnancy, a condition known as “small for Gestational age”.

This study evaluates the effect of vitamin D supplementation on fetomaternal outcome in pregnant women.

Material & Methods

After approval by the Institute Ethics Committee & written informed consent from patient's parents, the study was conducted as hospital based prospective observational study in a total of 200 pregnant women with singleton pregnancy at 12-16 weeks of gestational age as cases.

Inclusion Criteria

1. All women with singleton pregnancy booked in 12-16 weeks of pregnancy.
2. Women without any medical problems, non-smokers and not taking any medication will be included in the study.

Exclusion Criteria

1. Severe anaemia
2. Twin pregnancy
3. Alcohol & tobacco use
4. Chronic hypertension
5. Angina pectoris
6. Previous myocardial infarction
7. Heart failure
8. Chronic obstructive pulmonary disease
9. Diabetes mellitus
10. Previous LSCS
11. Known case of Hypovitaminosis
12. Chronic Renal disease
13. Chronic Hepatic disease
14. Known cases of hyper parathyroid
15. Malabsorption syndrome
16. Women on anti tubercular drugs, anti epileptics, steroids

Serum vitamin D levels were tested at 12-16 weeks of pregnancy. Women found deficient (vitamin D <20ng/ml) or insufficient (vitamin D 20-30ng/ml) were counseled about the potential harms of vitamin D deficiency and supplementation, its benefits. Final choice for supplementation was left on the patient. Supplementation with 60,000 IU Cholecalciferol per week for 8 weeks followed by monthly supplemental dose of same was done in vitamin D deficient women. Only women without co morbidities, non-smokers, and before starting any medication was asked to take part in the study. Based on clinical laboratory classification, deficiency was defined as total circulating 25(OH) D level of less than 20ng/ml, insufficiency as ≥ 20 to <30ng/ml and sufficiency as ≥ 30 ng/ml. Serum vitamin D was tested again in all subjects during 32 weeks of gestational age, observation for antenatal complications like preeclampsia and preterm birth and foetal outcome was done.

Results

In our study maximum numbers of cases were in 21-25 years age group with 102 (51%) women. 26-30 years age group had 54 (27%) women, ≤20 years age group had 36 (18%) women and >30 years age group had 8 (4%) women(fig 1) . Mean age in the study was 24.185±3.552 years.

In our study, 140 women (70%) were found to have Vitamin D Deficiency (<20 ng/ml) out of which 82 (84.54%) women had taken vitamin D supplementation and 58 (56.31%) not, 45 women (22.5%) were Vitamin D Insufficiency (20-30 ng/ml) out of which 15 (15.46%) women had taken vitamin D supplementation and 30 (29.13%) not. Only 15 women (7.5%) were found to have sufficient Vitamin D Levels (>30 ng/ml) (table 1). Supplementation was done in 97 vitamin D deficient women. It increased mean vitamin D levels from 13.74 ±4.84 to 27.12±7.19 from first to third trimester (p value = 0.0001). Mean Vitamin D Levels in 3rd trimester was found slightly higher (19.95ng/ml) than the 1st trimester levels (19.61 ng/ml) in vitamin D NOT supplementation group.

The incidence of preeclampsia was found much higher in vitamin D deficiency (<20 ng/ml) group i.e. 28(36.36%) as compared with vitamin D insufficiency (20-30 ng/ml) group i.e. 3(4.17%). There was no case of preeclampsia in vitamin D sufficiency (>30 ng/ml) group (p value = 0.0001). incidence of Preterm Baby was found slightly higher in vitamin D deficiency (<20 ng/ml) group i.e. 20(25.97%) as compared with vitamin D insufficiency (20-30 ng/ml) group i.e. 16(22.22%). There was 2 (3.92%) case of Preterm Baby was found in vitamin D sufficiency (>30 ng/ml) group (p value = 0.001) (table 2,3). Maximum no. of cases (48 & 20 i.e. total 68) having birth weight >2.5 kg are in the Vitamin D supplementation group, while maximum no. of cases (34 & 39 i.e. total 73) having birth weight <2.5 kg are in the Vitamin D not supplementation group (p value=0.0033). Mean Birth Weight (in kg) was found higher (2.60±0.59 kg) in patients who were supplemented with Vitamin D than in Vitamin D NOT Supplementation Group (2.25±0.63 kg) (p value = 0.0006) (table 4).

Figure 1: Distribution of cases according to Age (in yrs)

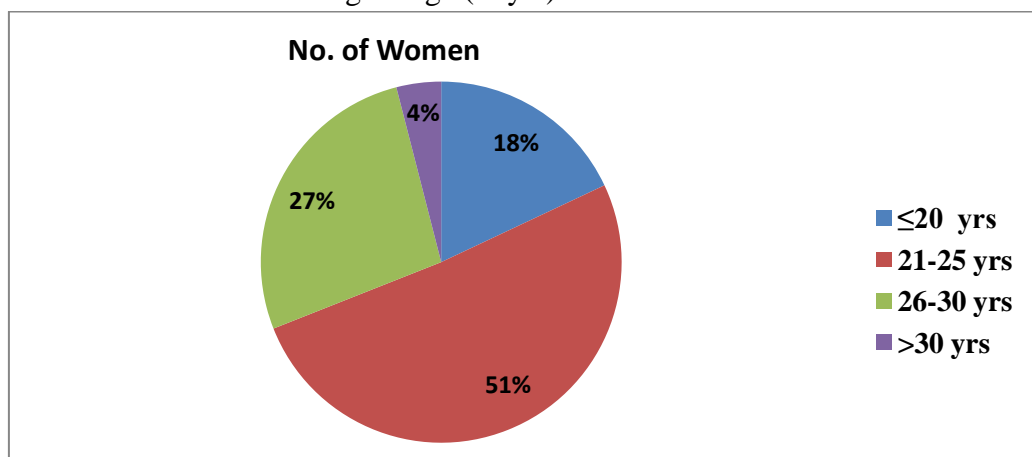


Table 1: Distribution of cases according to vitamin D Levels (ng/ml)

		1 st trimester Vitamin D Levels (ng/ml)			
		Vitamin D Deficiency (<20 ng/ml)	Vitamin D Insufficiency (20-30 ng/ml)	Vitamin D Sufficiency (>30 ng/ml)	Total
Supplementation	YES	82	15	0	97
	NO	58	30	15	103
Total		140	45	15	200

Table 2: Distribution of Incidence of Preeclampsia according to 3rd trimester Vitamin D Levels (ng/ml)

		3 rd trimester Vitamin D Levels (ng/ml)						Total
		Vitamin D Deficiency (<20 ng/ml)		Vitamin D Insufficiency (20-30 ng/ml)		Vitamin D Sufficiency (>30 ng/ml)		
		No.	%	No.	%	No.	%	
Preeclampsia	YES	28	36.36%	3	4.17%	0	0%	31
	NO	49	63.64%	69	95.83%	51	100%	169
Total		77	100%	72	100%	51	100%	200
P Value		0.001						

Table 3: Distribution of Preterm Birth according to 3rd trimester vitamin D Levels (ng/ml)

		3 rd trimester Vitamin D Levels (ng/ml)						Total
		Vitamin D Deficiency (<20 ng/ml)		Vitamin D Insufficiency (20-30 ng/ml)		Vitamin D Sufficiency (>30 ng/ml)		
		No.	%	No.	%	No.	%	
Preterm Baby	YES	20	25.97%	16	22.22%	2	3.92%	38
	NO	57	74.03%	56	77.78%	49	96.08%	162
Total		77	100%	72	100%	51	100%	200
P Value		0.001						

Table 4: Distribution of Cases According To Birth Weight & Vit D Supplementation

Birth Weight (in kg)	Vit D Supplementation		P Value
	YES	NO	
≤ 2 kg	16	34	0.0033
2.1 – 2.5 kg	13	39	
2.5 – 3.0 kg	48	18	
>3.0 kg	20	12	
TOTAL	97	103	

Discussion

The prevalence of Vitamin D deficiency in pregnancy and its association with preeclampsia and preterm birth have attracted much public health attention. In the present study, we sought to determine whether vitamin D deficiency is associated with an increased risk of adverse fetomaternal outcome. Our results confirmed our hypothesis that women who developed preeclampsia & preterm babies had significantly lower maternal serum vitamin D levels early in pregnancy compared with healthy women with uncomplicated term pregnancies.

Our findings confirm and extend earlier work by Bodnar et al⁷, where vitamin D deficiency early in pregnancy was associated with preeclampsia. The investigators reported a dose-response relationship, with 25(OH) D levels of less than 37.5 nmol/liter being associated with a 5-fold increase in the odds of preeclampsia (adjusted OR, 5.0; 95% CI, 1.7–14.1).

In a prospective cohort study by Haugen et al⁸. involving more than 20,000 nulliparous women, a 29% reduced risk of preeclampsia was observed in women who reported supplementing with 400–600 IU of vitamin D during the first half of their pregnancies.

Marya et al⁹. conducted a randomized controlled trial of calcium and vitamin D supplementation (1200 IU/d) beginning at 20–24 wk gestation in 400 women. Although the supplemented group experienced a significant reduction in blood pressure and their incidence of preeclampsia was lower than the control group (6 vs.9%), the preeclampsia results were not statistically significant.

Wei et al¹⁰ did a meta-analysis of four observational studies showed that pregnant women with vitamin D deficiency experienced an increased risk of Preterm birth (OR = 1.58, 95% CI: 1.08–2.31)

Wagner et al¹¹. showed that achieving a 25(OH)D serum concentration ≥ 40 ng/mL could significantly decrease the risk of PTB compared to concentrations ≤ 20 ng/mL after maternal supplementation with vitamin D during pregnancy.

Our study does have several methodological strengths. The maternal serum was collected well before delivery at a time when no clinical manifestations of preeclampsia were evident reducing the likelihood that subclinical disease affected vitamin D levels. In addition, we excluded all women with chronic medical illnesses, such as diabetes and chronic hypertension. These diseases have been associated with increased risk for preeclampsia.

Conclusion

Our study shows an increasingly compelling evidence for a causal relationship between low vitamin D level and adverse maternal and neonatal outcomes. As in other fields of obstetrics endocrinology, there is a need for greater research in Vitamin D therapeutics in pregnancy. Vitamin D supplementation is simple and cost effective with low likelihood of toxicity, supplementation should be done in all pregnant women to keep serum levels of vitamin D in the normal range for adults (>30 ng/ml).

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