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Research Article

Association Of Vitamin D With Adverse Pregnancy Outcomes

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ABSTRACT

Background: Vitamin D deficiency is prevalent in India with 70-100% prevalence in the general population. This study investigated the association between serum 25(OH) vitamin D levels and adverse pregnancy outcomes.
Objectives: To assess vitamin D levels during pregnancy and evaluate the association of vitamin D insufficiency/deficiency with adverse pregnancy outcomes.
Methods: This observational study was conducted at 7 Air Force Hospital, Kanpur from August-December 2023. 200 consecutive patients presenting to labour room for delivery were tested for serum vitamin D levels using chemiluminescence immunoassay. Participants were assessed for gestational diabetes, hypertensive disorders, preterm birth, primary cesarean section, fetal growth restriction, and NICU admissions. Outcomes were stratified according to vitamin D levels (Normal: >30ng/ml, Insufficient: 20-30ng/ml, Deficient: <20ng/ml).
Results: Among 200 participants (mean age 25.90 years), only 21% had normal vitamin D levels, while 20.5% were deficient and 58.5% were insufficient. The incidence of gestational diabetes was 13% and pregnancy-induced hypertension was 17%. No statistically significant associations were found between vitamin D levels and adverse pregnancy outcomes including gestational diabetes (p=1.000), pregnancy-induced hypertension (p=0.4529-0.6028), mean birth weight (p=0.8314), or serum calcium levels (p=0.7364). NICU admissions, preterm births, and primary cesarean sections showed no significant correlation with vitamin D status.
Conclusion: Despite high prevalence of vitamin D insufficiency/deficiency (79%) among pregnant women, no statistically significant association was established with adverse pregnancy outcomes. However, considering the beneficial effects and high prevalence of deficiency, routine vitamin D supplementation during pregnancy is recommended. Larger multicentric studies are needed to definitively establish these associations.

Keywords*: Vitamin D deficiency, Pregnancy outcomes, Gestational diabetes, Pregnancy-induced hypertension, Preterm birth.*

INTRODUCTION

Vitamin D is a fat-soluble vitamin that is naturally present in very few foods, obtained through sun exposure and diet supplements. Vitamin D thus obtained is biologically inert and undergoes two hydroxylations in the body for activation. [1,2] The main function of Vitamin D is to maintain serum calcium levels through its action on the gut, osteoblasts and osteoclasts. [3,4]

Apart from its primary role Vitamin D has an increasingly recognised repertoire of nonclassical actions, such as promoting insulin action and secretion, immune modulation and lung development. It therefore has the potential to influence many factors in the developing fetus through its non-classical actions. [5,6,8] The role and metabolism of vitamin D in the pregnant state is not well understood. [7] This study investigates the association of serum 25 (OH) vitamin D levels with adverse pregnancy outcomes.

AIMS AND OBJECTIVES

The aim of this study is to assess the levels of vitamin D during pregnancy and also assess the association of Vitamin D insufficiency and deficiency with adverse pregnancy outcome.

MATERIAL AND METHOD

This observational study was conducted at a zonal hospital in central Indiabetween 1st August 2023 to 31st December 2023. 200 consecutive patients presenting to labour room for delivery were tested for serum Vitamin D levels. The participants were studied for presence of Gestational Diabetes, Hypertensive Disorders of pregnancy before delivery and Preterm birth , Primary LSCS, FGR , NICU admission after delivery. The outcomes as mentioned above were stratified according to their Vitamin D levels.

In all the patients Vitamin D (25 Hydroxy Cholecalciferol) levels were estimated using Chemiluminescence Immunoassay. The inclusion for the study was patient presenting in labour. The exclusion criteria were Post LSCS patients, Patients with chronic hypertension, Patients with overt or pre existing Diabetes Mellitus, Patients with mal presentations of fetus.

Primary Outcomes Recorded was Incidence of vitamin D insufficiency and deficiency in the cohort stratified according to vitamin D levels. Secondary outcomes in the cohort were Incidence of hypertensive disorders of pregnancy, Gestational diabetes mellitus, FGR, Preterm Delivery and NICU admissions and the levels of serum calcium, all stratified according to vitamin D levels.

The criteria used to define and stratify Vitamin D levels is shown in Table 1.
The outcome variables were studied against the levels of Vitamin D Stratified as Normal, Insufficiency and Deficiency. The continuous variables such as the age of the patient and Vitamin D levels were represented as mean. The nominal outcome variables were represented as percentages. The Chi-Square test and the One Way ANOVA test was used to analyze the data.

RESULTS

A total of consecutive 200 patients presenting to labour room for delivery were enrolled in the study and they all participated. The mean age of participation was 25.90 years (Range 18- 35 years). The gestational age of the study population varied from 32 weeks to 41 weeks. Maximum patients (26.50%) were in the gestational age group of 39 weeks to 40 weeks. The study population was stratified according to their Serum Vitamin D levels. Only 42 out of 200 patients (21%) in the study group had normal Vitamin D levels. 41 out of 200 patients (20.50%) were deficient in Vitamin D and 117 out of 200 patients (58.50%) were insufficient in Vitamin Dlevels.

Table 1 : Reference Serum Vitamin D Level	
Serum Vitamin D Level	
> 30 ng/ml (> 75 nmol/L)	Normal
20-30 ng/ml (50-75 nmol/L)	Insufficient
< 20 ng/ml (<50 nmol/L)	Deficient

The incidence of neonatal outcomes in terms of noncomplicated vaginal deliveries, primary caesarean sections, IUGR, preterm delivery, preterm primary Caesarean sections, and NICU admissions is shown in Table 2. 162 out of 200 patients had no adverse neonatal outcome, as is evident from Table 2. Out of the 42 women who had Normal Vitamin D levels, 33 (78.57%) had Normal Vaginal Delivery without any adverse pregnancy outcomes and 09 had adverse pregnancy outcomes enlisted in Table 2. Of the 41 women who had Deficient Vitamin D levels, 11 had adverse pregnancy outcomes enlisted in Table 2. 117 women had Insufficient Vitamin D levels and 18 of these women had adverse pregnancy outcomes enlisted in Table 2.

Table 2: Distribution of Pregnancy Outcomes by Vitamin D Status

Vitamin D Status	**Total Patients**	**Normal Vaginal Delivery (No adverse outcomes)**	**Adverse Pregnancy Outcomes**
Normal	42 (21%)	33 (78.57%)	9 (21.43%)
Deficient	41 (20.5%)	30 (73.17%)	11 (26.83%)
Insufficient	117 (58.5%)	99 (84.62%)	18 (15.38%)
Total	**200 (100%)**	**162 (81%)**	**38 (19%)**

The strength of the association of vitamin D levels with each of the above-mentioned adverse neonatal outcome was measured using the Chi-Square test and One-way Anova Test. The strength of association was measured in terms of 'p' value as shown in Table 3.

Table 3: Statistical Analysis of Outcomes

Parameter	Normal Vitamin D	Deficient Vitamin D	Insufficient Vitamin D	P-value	Statistical Significance
Mean Birth Weight (kg)	2.88	2.82	2.86	0.8314	Not significant
Mean Serum Calcium (mEq/L)	5.31	5.34	5.37	0.7364	Not significant
Gestational Diabetes Mellitus (n=26)	5 (19.23%)	5 (19.23%)	16 (61.54%)	1.000	Not significant
Pregnancy-induced Hypertension (n=34)	8 (23.53%)	10 (29.41%)	16 (47.06%)	0.4529-0.6028	Not significant

The mean birth weight of the neonates born to mothers with normal vitamin D levels was 2.88 kg, the mean birth weight of the neonates born to mothers with deficient vitamin D levels was 2.82 kg and that of those mothers with insufficient levels was 2.86 kg. The p-value of this association is 0.8314.

The mean Serum Calcium was 5.31, 5.34 and 5.37 mEq/L for the normal, deficient, and Insufficient group respectively. The p-value of this association is 0.7364.

A total of 26 out of 200 patients had Gestational Diabetes Mellitus (13 %). 05 of these 26 patients (19.23%) had normal Vitamin D levels, 05 of 26 (19.23%) had deficient levels and 16 of 26 (61.54%) had insufficient vitamin D levels. The calculated p-value of the association of gestational Diabetes mellitus between the Vitamin D Sufficient and Insufficient group and that for Vitamin D Sufficient and Deficient is 1.000 which is statistically insignificant.

A total of 34 patients out of 200 (17%) had Pregnancy-induced Hypertension. In that, 8 out of 34 had normal vitamin D levels (23.53%), 10 out of 34 had Vitamin D deficiency (29.41%) and 16 out of 34 had vitamin D insufficiency (47.06%). The calculated p-value of the association of Pregnancy Induced Hypertension between the Vitamin D Sufficient and Insufficient group is 0.4529 and that for Vitamin D Sufficient and Deficient is 0.6028 which is statistically insignificant.

DISCUSSION

Vitamin D deficiency prevails in epidemic proportions all over the Indian subcontinent, with a prevalence of 70%–100% in the general population. Studies from Northern, Central, and Southern states of the country revealed that 76% of reproductive-age women and 70% of post-menopausal women were vitamin D deficient and that 84.3% of urban women and 83.6% of rural women suffered from vitamin D deficiency. [11,15]

The population in our study consisted of pregnant ladies from middle-class socio-economic strata, most of whom were homemakers by occupation or were involved in office work. No lady had occupational exposure to sunlight. The serum calcium and serum Vitamin D levels in our study are consistent with the findings of the study of Sahu M et al.[11]

In our study, we also found a high incidence of vitamin D insufficiency and deficiency. Only 21% of patients in the study group had normal Vitamin D level. 20.50% were deficient in Vitamin D and 58.50% of patients were insufficient in Vitamin D levels. It is evident that despite improvements in the socio-economic demography of the Indian population, there is still widespread prevalence of Vitamin D insufficiency and deficiency. The results of our study are consistent with studies that have been done time and again on the subject.

Marya et al (1987) reported no meaningful difference in the incidence of pre-eclampsia between the groups that were administered vitamin D and calcium supplements in the antenatal period and the group that was not given any supplements. [9] In contrast to the above finding, Bodnar et al (2007) reported that maternal vitamin D insufficiency in early pregnancy may be an independent risk factor for preeclampsia.

In our study, we also assessed the association of Vitamin D levels with the incidence of Hypertension in Pregnancy and Gestational Diabetes and found no statistically important association between maternal Vitamin D levels and Gestational Hypertension and Gestational Diabetes. The national incidence of Hypertensive Disorders of Pregnancy is 15.2% in India. Results from our study (17%) are comparable to the national data. The Overall incidence of GDM in India is 16.55% which is higher than the incidence calculated in our study population (13%).

Statistical analysis revealed p values of 0.799 and 0.4722 respectively on comparing the incidence of adverse neonatal outcomes in patients with normal Vitamin D levels to those with vitamin D deficiency and insufficiency respectively. Likewise, the p values obtained after comparing the incidences of individual adverse

neonatal outcomes, in patients with Fetal Growth restriction, Primary Cesarean, Preterm birth, Preterm Cesarean, and NICU admissions amongst those with normal, insufficient, and deficient Vitamin D, showed insignificant results (details in results).

The mean serum calcium values in the three subgroups, normal, deficiency, and insufficiency groups were comparable. i.e. the serum calcium values were 5.31, 5.34, and 5.37 mEq/L in the normal, deficiency, and insufficiency subgroups. This finding is inconsistent as compared to the findings of the studies by Gupta T et al [14], and Katherine J et al [12]. However, these findings are similar to a previous meta-analysis done by Nassar et al [13], which showed no relation between serum calcium and serum Vitamin D levels in pregnant women. In pregnancy, there is hemodilution and there is a progressive fall in all the micronutrients in the body including elements like calcium, zinc, etc. However, due to regular calcium supplementation in adequate dosage in our patients during their antenatal period, there is less likelihood of calcium deficiency in them. This might be a contributing factor to their normal serum calcium levels.

Indian data on studies on vitamin D in pregnancy is extremely lacking. The participating population is very small in the presently existing studies, thus indicating the low power of these studies.

RCOG mentions in its Scientific Impact Paper No 43, June 2014 that Vitamin D expresses its effects on pregnancy outcomes mainly through the non-calcium i.e. immunological actions.[8]

Hence the relation of serum calcium levels with adverse pregnancy outcomes cannot be expected. Various hormones like calcitonin and parathormone interact in the milieu interne to maintain adequate serum calcium levels. Vitamin D is responsible for the intestinal absorption of Calcium. Slight changes in the serum calcium concentrations can result in catastrophic organ system failure. Hence the body maintains serum calcium within a narrow range. This may be the reason why no statistically significant relation was observed between the vitamin D level in pregnancy with serum calcium levels.

Given that adult calcium and bone metabolism depend on vitamin D sufficiency, vitamin D sufficiency would seem to be especially critical during pregnancy and lactation. However, the maternal adaptations during pregnancy, lactation, and fetal development provide the necessary calcium relatively independently of vitamin D. It is only after birth that dependency on vitamin D becomes evident, at least for calcium metabolism and skeletal health.

All studies done on the topic so far seem to agree upon one common point, namely , the insufficient and deficient levels of Vitamin D in Indian Women in reproductive age group. Through its calcium and non calcium actions , Vitamin D maintains general well being of the lady throughout pregnancy. It does help in reducing muscular cramps, nocturnal calf muscle pains, generalized aches and pains and improves the mood of the lady in general. It is noteworthy that the cost of test for vitamin D in India is far greater than the actual cost of the treatment. Hence with view to its profound beneficial effects and the background knowledge of high prevalence of Deficiency/Insufficiency in target population, Vitamin D can be safely supplemented during pregnancy.

CONCLUSION

In our study, we established the presence of low levels of vitamin D amongst the pregnant ladies. The incidence of vitamin D insufficiency and deficiency as calculated in our observational study is comparable to that in the general population as computed in the Indian studies. However, we found no statistically significant association of vitamin D levels with the incidences of Pregnancy-Induced Hypertension, Gestational Diabetes Mellitus, preterm birth, rate of primary Cesarean or neonatal admission to the NICU. No statistical significance of vitamin D levels was noted while assessing its association with these adverse pregnancy outcomes. The serum Calcium levels were comparable in all the three groups of patients- i.e. the one with normal vitamin D level, those with deficient and those with insufficient Vitamin D levels.

As no statistical significance could be elicited between vitamin D levels and the occurrence of adverse pregnancy outcomes, further multi centric studies with much larger sample size becomes essential to either prove or disprove the association of vitamin D with adverse pregnancy outcomes. However with view to its profound beneficial effects and the background knowledge of high prevalence of Deficiency/Insufficiency in target population, Vitamin D should be routinely supplemented to all pregnant women.

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