



## A STUDY TO ASSESS THE ASSOCIATION OF VITAMIN D INSUFFICIENCY AND DEFICIENCY WITH ADVERSE PREGNANCY OUTCOMES

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### ABSTRACT

The objective of this study was to determine the incidence of vitamin D deficiency and insufficiency and study its association with adverse pregnancy outcomes.

**Methods:** 200 consecutive patients presenting to labour room for delivery were tested for serum Vitamin D levels. Data containing socio-demographic and personal details, vitamin D levels and adverse pregnancy outcomes in terms of Gestational Diabetes, Hypertensive Disorders of Pregnancy before delivery and Preterm birth, Primary LSCS, IUGR, NICU admission after birth of the baby were collected and analysed using Chi Square and the One way ANOVA score.  $p < 0.05$  was considered statistically significant.

**Results:** 58.50% of the antenatal patients were insufficient in their Serum Vitamin D levels, 20.50% were deficient in their Vitamin D levels and only 21% had normal Vitamin D levels. No significant association was found between maternal serum Vitamin D levels and Adverse Pregnancy outcomes.

**Conclusion:** The study findings revealed that vitamin D insufficiency and deficiency is highly common in the pregnant women. No significant association could be brought out between maternal serum vitamin D levels and adverse pregnancy outcomes.

**KEYWORDS :** Adverse Pregnancy Outcomes; Vitamin D Deficiency; Vitamin D Insufficiency; Pregnant Women

### 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.<sup>1,2</sup> The main function of Vitamin D is to maintain serum calcium levels through its action on the gut, osteoblasts and osteoclasts.<sup>3,4</sup>

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.<sup>5,6,8</sup> The role and metabolism of vitamin D in the pregnant state is not well understood.<sup>7</sup> 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.

### MATERIALS AND METHODS

This observational study was conducted at Command Hospital Air Force Bengaluru between 1st January 2016 to 1st July 2017. 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 assay. 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 following criteria were used to define and stratify Vitamin D levels.

**Table 1: Reference levels of Serum Vitamin D**

Serum Vitamin D level	
> 30 ng/ml (> 75 nmol/L)	Normal
20-30 ng/ml (50-75 nmol/L)	Insufficiency
< 20 ng/ml (< 50 nmol/L)	Deficiency

The outcome variables were studied against the levels of Vitamin D Stratified as Normal, Insufficiency and Deficiency. The continuous variables such as age of the patient and Vitamin D levels were represented as mean. The nominal outcome variables were represented as percentage. The Chi Square test and the One Way ANOVA test was used to analyse 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 The maximum patients (26.50%) were in the gestational age group of 39 weeks to 40 weeks (Range 32 weeks to 41 weeks). The study population is stratified according to their Serum Vitamin D levels. Only 42 out of 200 patients (21%) in the study group had normal Vitamin D level. 41 out of 200 patients (20.50%) were deficient in Vitamin D and 117 out of 200 patients (58.50%) were insufficient in Vitamin D levels.

The incidence of neonatal outcomes in terms of non complicated vaginal deliveries, primary caesarean sections, IUGR, preterm delivery, preterm primary Caesarean sections and NICU admissions is shown in Table 1. 162 out of 200 patients had no adverse neonatal outcome, as is evident from Table 1. 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 01. Of the 41 women who had Deficient Vitamin D levels 11 had adverse pregnancy outcomes enlisted in Table 01. 117 women had Insufficient Vitamin D levels and 18 of these women had adverse pregnancy outcomes enlisted in Table 2.

**Table 2: Outcome Variables stratified according to Vitamin D levels**

Neonatal outcome	Normal Vitamin D	%	Deficiency Vitamin D	%	Insufficiency Vitamin D	%	Total
No Complication & Normal Vaginal birth	33	78.57	32	78.05	99	84.61	162
IUGR	1	2.38	0	0.00	0	0.00	1
LSCS	1	2.38	2	4.88	2	1.71	5
Preterm	1	2.38	3	7.32	8	6.84	12
Preterm, LSCS	2	4.76	0	0.00	0	0.00	2
NICU Admission	4	9.52	6	14.63	8	6.84	18
Total	42	100.00	41	100.00	117	100.00	200

The strength of 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: Strength of Association as measured in terms of 'p' value**

Out Come Studied	'p' Value	'p' Value
	Normal Vitamin D v/s Insufficient Vitamin D levels	Normal Vitamin D v/s Deficient Vitamin D levels
Fetal Growth Restriction	0.2642	1.000
Primary LSCS	1.000	0.6158
Preterm Labour	0.4469	0.3597
Preterm LSCS	0.0661	0.4947
NICU Admission	0.5181	0.5195

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

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

A total of 26 out of 200 patients had GDM (13%). 05 of these 26 patients (19.23%) had normal Vitamin D level, 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 between the Vitamin D Sufficient and Insufficient group and that for Vitamin D Sufficient and Deficient is 1.000 which are 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 level (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 between the Vitamin D Sufficient and Insufficient group is 0.4529 and that for Vitamin D Sufficient and Deficient is 0.6028 which are 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% urban women and 83.6% rural women suffered from vitamin D deficiency.<sup>[11,15]</sup>

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. There was no lady who had occupational exposure to sunlight. The serum calcium and serum Vitamin D levels in our study are consistent with the findings of study of Sahu M et al.<sup>[11]</sup>

In our study we also found high incidence of vitamin D insufficiency and deficiency. Only 21% patients in the study group had normal Vitamin D level. 20.50% were deficient in Vitamin D 58.50% 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 wide spread 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.<sup>[9]</sup> In contrast to above finding, Bodnar et al (2007) reported that maternal vitamin D insufficiency in early pregnancy maybe an independent risk factor for preeclampsia.<sup>[10]</sup> 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 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 level to those with vitamin D deficiency and insufficiency respectively. Likewise the p values obtained after comparing the incidences of the individual adverse neonatal outcomes, in patients with FGR, Primary LSCS, Preterm birth, Preterm LSCS, 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 in the normal, deficiency and insufficiency sub groups. This finding is inconsistent as compared to the findings of the studies by Gupta T et al<sup>[14]</sup>, and Katherine J et al<sup>[12]</sup>. However these findings are similar to a previous meta analysis done by

Nassar et al<sup>[3]</sup>, which showed no relation of serum calcium with the serum Vitamin D levels in pregnant women. In pregnancy, there is as such 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 for their normal serum calcium levels.

Indian data on studies on vitamin D in pregnancy is extremely lacking. Whatever study exists, the participating population is very small, thus indicating 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.<sup>[6]</sup>

Hence the relation of serum calcium levels with adverse pregnancy outcomes cannot be expected. Various hormones like calcitonin, parathormone are interacting in the milieu interia 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 with respect to calcium metabolism and skeletal health.

## 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, preterm birth, rate of primary LSCS 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.

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