



## VITAMIN D DEFICIENCY IN PREGNANCY AND ITS ASSOCIATION WITH MATERNAL COMPLICATIONS.

**Dr. Meenu Rai**

Senior Resident, Ndmc Medical College And Hindu Rao Hospital

**Dr. Archna R. Verma**

Assistant Professor Ndmc Medical College And Hindu Rao Hospital

### ABSTRACT

**Introduction:** Vitamin D deficiency and insufficiency have been associated with a variety of adverse maternal and fetal outcomes, ranging from Gestational hypertension, preeclampsia, gestational diabetes, preterm delivery, intrauterine growth restriction, and cesarean section. The study was done to determine whether vitamin D deficiency in pregnant women was associated with complications. **Methods:** In this prospective observational study, vitamin D levels were estimated in 100 pregnant women from gestational age 32 to 40 weeks in a teaching hospital in Delhi, India. All the subjects were further followed up for the appearance of pregnancy associated complications mostly focusing on the appearance of Gestational Hypertension, Pre-eclampsia, Gestational Diabetes, IUGR, Preterm labour or landing up in Caesarean section. **Results:** 84% had suboptimal vitamin D level i.e serum vitamin D < 30ng/ml. Common complications were gestational hypertension (47%), caesarean section (47%) and gestational diabetes (41%). Significantly low vitamin D levels were found in women with obstetric complications as compared to controls with no complications. Also, significant association was found between suboptimal vitamin D levels and complications. **Conclusion:** The routine measurement of vitamin D in pregnancy can be of great help in identifying patients at risk for development of these complications, early intervention and prevention of occurrence of these complications. Cost effective and timely treatment can prevent the complications in expecting mothers.

**KEYWORDS :** Vitamin D, Gestational hypertension, Pre-eclampsia, gestational diabetes, preterm labour

### INTRODUCTION

Vitamin D deficiency is recognized as the most untreated nutritional deficiency currently in the world.<sup>1</sup> Although India is a tropical country with abundant of sunshine; still vitamin D deficiency is very common in India in all age groups and both sexes across country.

The concentration of 25(OH) D is relatively constant throughout pregnancy.<sup>2</sup> The mother is the only source of vitamin D for the foetus.<sup>3</sup> The abnormalities of the action of vitamin D receptor could manifest in signs and symptoms of vitamin D deficiency. During pregnancy, this may present as gestational diabetes, preeclampsia, preterm birth or miscarriage in early stages of pregnancy.<sup>4</sup> However, its concentrations in the mother's blood are doubled in pregnancy, probably because of its production in foetal tissues and placenta.<sup>5,6</sup>

At this time there is insufficient evidence to support a recommendation for screening all pregnant women for vitamin D deficiency. For pregnant women thought to be at increased risk of vitamin D deficiency, maternal serum 25(OH)D levels can be considered and should be interpreted in the context of the individual clinical circumstances. The study was aimed to determine the prevalence of vitamin D deficiency in pregnancy and to know the incidence of maternal complications in relation to vitamin D deficiency.

### MATERIAL AND METHODS

#### Study Design

Prospective observational study

#### Study Population

All the antenatal patients reporting in the outpatient and inpatient department of Obstetrics and Gynaecology and fulfilling the inclusion criteria formed the study population.

#### Study duration

This study was conducted from September 2019 to May 2020.

#### Sample Size

Taking an estimate of vitamin D deficiency as 50% with a precision of 10%, study design as 1 and alpha error of 5%, sample size was calculated as 97 ANC Females which was rounded off to 100 subjects.

All pregnant women from 32 weeks to 40 weeks period of gestation irrespective of age and parity were included in the study. Those with active thyroid disease like thyroiditis or graves diseases, preexisting calcium or parathyroid condition or who require diuretic or cardiac medication, taking treatment for chronic hypertension, diabetes mellitus, renal disease and previous caesarean section were excluded.

#### Study Method:

All antenatal women were explained about the study procedure in detail in their own vernacular language. Once they approved verbally to participate in the study, then a written voluntary informed consent was obtained. Only after getting the voluntary informed consent, the study related procedures were conducted.

After approval of institutional ethical committee (JGH/DNB/MS/2019 dated 24.09.2019), 100 consenting patients fulfilling the inclusion criteria were considered for the study. A thorough checkup was done for all patients which includes a detailed history including demographic details, chief complaints, history of presenting illness, medical history and obstetrical history, general physical, systemic examination and obstetrical examination. Basic antenatal investigation (if not done), focusing on BP if it was > 140/90 mmHg on two different occasions six hours apart to diagnose gestational hypertension, along with urine albumin to diagnose pre-eclampsia. 75gm oral glucose tolerance test was done to diagnose GDM, and serum vitamin D i.e 25(OH)D level was done. The detailed work up of all cases with vitamin D deficiency was done.

#### Laboratory techniques

Serum 25-OH Vitamin D levels were measured using VIDAS® 25 OH. Vitamin D total manufactured by Bio Mérieux SA. It is an automated quantitative test for use on the instruments of the VIDAS family for the determination of 25-hydroxy vitamin D Total in human serum or plasma using the ELFA technique (Enzyme Linked Fluorescent Assay). The assay principle combines an enzyme immunoassay competition method with a final fluorescent detection (ELFA). All of the assay steps were performed automatically by the instrument.

(ACOG), serum 25(OH)D concentration below 20 ng/ml used as a cut-off for deficiency and below 30ng/ml as a cut-off for insufficiency.

**Statistical analysis**

Data was analyzed using SYSTAT software version 13.2 for Windows. Quantitative data were presented as mean and standard deviation whereas qualitative data were presented as ratio and proportions. For qualitative data, Chi-square test for proportion was used to measure the difference. Normally distributed quantitative data was analyzed using t-test and Mann Whitney U test was used for non-normal quantitative data. For statistical significance, p-value less than 0.05 was taken as point of statistical significance. Results

The mean age of subjects enrolled was 28.76 years (SD=2.71). Two third (67%) of the subjects were in the age group of 26-30 years. Primigravida constituted 58% whereas 16% were third gravida and above. Lower and middle socio-economic status was constituted by 13% and 74% respectively. Nearly three fourth of subjects (74%) had gestational age of 32-36 weeks. Pregnancy related complications included gestational hypertension & caesarean section (47% each), gestational diabetes (41%), intrauterine growth retardation (37%), pre-eclampsia (36%) and preterm labor (24%).

Out of 100 pregnant women 80% had vitamin D level less than 20ng/ml, 4% had vitamin D level between 20-30ng/ml and only 16% had vitamin D level more than 30 ng/ml. Table 1 is showing the levels of vitamin D in various complication with statistical significance. Except for pre-term labor, all the obstetric complication had significantly lower levels of vitamin D.

**Table 1: Comparison of vitamin D levels in presence and absence of complications**

Complication	Vitamin D levels in complication status		P-value*
	Yes	No	
Gestational hypertension (n=47)	9.96±3.34	21.11±14.82	<0.001
Pre-eclampsia (n=36)	10.11±3.48	19.11±14.22	0.0003
GDM (n=41)	10.81±5.57	19.38±14.32	0.0045
IUGR (n=37)	11.41±4.72	18.49±14.51	0.005
Preterm labor (n=24)	10.27±3.55	17.64±13.53	0.073
LSCS (n=47)	11.07±6.31	20.12±14.64	0.003

\*Mann-whitney test

On univariate analysis, it was found that complications in pregnant subjects had significant association with sub-optimal vitamin D levels. This has been tabulated in table 2.

**Table 2: Association of complication with optimal levels of vitamin D**

Complication	Status	Suboptimal Vitamin D	Vitamin D Normal	P-value*
Gestational hypertension	Yes	47 (56.0%)	0	0.001
	No	37 (44.0%)	16 (100%)	
Pre-eclampsia	Yes	36(42.86%)	0	0.0004
	No	48(57.14%)	16(100%)	
Gestational Diabetes mellitus	Yes	40(47.62%)	1(6.25%)	0.0008
	No	44(52.38%)	15(93.75%)	
IUGR	Yes	37 (44.03%)	0	0.0004
	No	47 (55.95%)	16 (100%)	
Pre-term labor	Yes	24 (28.6%)	0	0.011
	No	60 (71.4%)	16 (100%)	
Caesarean section	Yes	46 (54.8%)	1 (6.3%)	<0.001
	No	38 (45.2%)	15 (93.8%)	

\*Chi-square test

**DISCUSSION**

Vitamin D is traditionally supposed to be involved in bone and calcium metabolism. In the last two decades many studies have demonstrated its role in various other physiological processes. Recent studies worldwide have demonstrated a high prevalence of vitamin D deficiency in pregnant women at or near term.<sup>7,8</sup> The optimum level of vitamin D and maternal vitamin D requirements during pregnancy has been poorly studied.

In our study, 84% pregnant women had low vitamin D level. A study done by Marwaha et al<sup>9</sup>, hypovitaminosis D (25(OH)D <50 nmol/l) was observed in 96.3% of the pregnant subjects. In another study done by Sachin et al showed 84.3% of urban and 83.6% of rural women had 25(OH)D values below cut-off level (22.5ng/ml).<sup>10</sup> Lower levels of vitamin D were in subjects with gestational hypertension in the present study. Study done by Samantha et al showed that there was significant negative association between blood pressure and serum 25(OH)D levels.<sup>11</sup> Another prospective interventional study done by Goel et al in 2010 revealed that administration of vitamin D3 had a role in reducing blood pressure in hypertensive patients which corroborate with the results of the current study.<sup>12</sup>

Pre-eclampsia was present in 36% subjects with levels of vitamin D as 10.11 ng/ml. Similar results were reported by Gupta et al where median levels of vitamin D were found to be 3.9 and 9.0 ng/ml in cases and controls respectively.<sup>13</sup> Another study by Kumari et al found lower levels of vitamin D among pre-eclamptic and GDM women as compared to controls. Vitamin D deficiency was significantly higher in pregnant women GDM (94.28% vs 68.3%) and preeclampsia (96.67% vs 68.3%) when compared to uncomplicated group.<sup>14</sup> On the other hand, Goel et al reported contradictory findings when they found similar prevalence of vitamin D deficiency among pre-eclamptic and control subjects.<sup>15</sup>

Regarding gestational diabetes mellitus (41%) in the present study, similar results have been reported by Pratibha et al<sup>16</sup> and Song et al.<sup>17</sup> It was concluded by Pratibha et al that low plasma vitamin D in early pregnancy was associated with high risk of GDM.<sup>16</sup> The finding of the above studies further substantiates our results. In the present study, 37 pregnant women gave birth to low birth weight newborns. They had low levels of vitamin D (11.41 ng/ml). Studies conducted in Iran also reported the same findings of low vitamin D levels among mothers with low birth weight newborns.<sup>18,19</sup>

Preterm birth of newborn and lower segment caesarean section happened in 24% and 47% women respectively. The mean vitamin D levels among preterm and caesarean section mothers was 10.27 and 11.07 ng/ml respectively. A nested case control study done among 27 pregnant women reported that 61.5% subjects had spontaneous preterm delivery who had insufficient vitamin D levels.<sup>20</sup> Similar finding were reported by Leticia et al in a case control study.<sup>21</sup> Study conducted in Boston by Merewood et al reported that women with vitamin D deficiency were about 4 time as likely to have primary caesarean section as compared to women with normal levels (OR 3.84).<sup>22</sup> Vitamin D deficiency has been associated with proximal muscle weakness as well as suboptimal muscle performance and strength vitamin D deficiency might be related to specific types of cesareans such as cephalopelvic disproportion or failure to progress, disproportion or failure to progress.

The study findings had some limitations which included less representation of lower socio-economic strata and limited patient enrollment due to time constraints.

**CONCLUSION**

The present study reported a high prevalence of vitamin D deficiency among pregnant women and complications of pregnancy which had significant association with vitamin D deficiency. Routine measurement of vitamin D levels is warranted keeping in view of study results. With these findings, it becomes imperative that deficiency of vitamin D be met through dietary sources and as well as cost effective therapeutic management options should be instituted among expecting mothers especially who are near term in order to prevent complications.

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