

ORIGINAL RESEARCH

Study of Hypovitaminosis D in pregnancy and its correlation with preeclampsia and gestational diabetes mellitus

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ABSTRACT

Background: In developing countries, 18% of global burden of diseases has been related to pregnancy complications. Research shows significant association between Vitamin D deficiency in pregnancy and elevated risk for preeclampsia, GDM and anaemia. Regulation of Vitamin D levels and management of hypovitaminosis D is most important mainly in developing countries and low resource healthcare settings to decrease the chances of pre eclampsia and GDM and also to improve the quality of life of women. This study will also help obstetricians to consider effects of hypovitaminosis D in pregnant women and to reduce the maternal morbidity because of its complications. **Aim & Objectives:** To study the level of Vitamin D in antenatal women at 20 weeks, at term and in fetal cord serum and also to study the association of Vitamin D levels with pre eclampsia and GDM. **Material and Methods:** A hospital based study was conducted among 210 antenatal females who came at <20 weeks of gestation in Muzaffarnagar Medical College & Hospital, Muzaffarnagar, Uttar Pradesh. Study was conducted for 18 months. Data was analysed statistically and chi square test was applied. **Results:** There is a significant association between gravida status and both preeclampsia (p-value = 0.001) and GDM (p-value = 0.01). There is a significant association between the use of vitamin D supplements and preeclampsia (p-value = 0.05), but not with GDM (p-value = 0.11). The p-values for preeclampsia (<0.05) and GDM (<0.05) indicate significant associations between low vitamin D levels (<20 ng/ml) both at <20 weeks and at term and the occurrence of preeclampsia and GDM. Neonates from the control group show higher vitamin D levels in cord blood compared to those from preeclampsia and GDM groups, as supported by the significant p-values. **Conclusion:** Our findings conclude that significant association between low vitamin D levels and the occurrence of preeclampsia and GDM has been found. Primigravida women and those not using vitamin D supplements were at higher risk for these conditions. The findings highlighted the importance of monitoring and potentially supplementing vitamin D levels during pregnancy to reduce the risk of preeclampsia and GDM. Neonates from preeclamptic and GDM mothers also exhibited lower cord blood vitamin D levels.

Keywords: Hypovitaminosis D, Pre-eclampsia, GDM.

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INTRODUCTION

Vitamin D also known as calciferol, is a prohormone that plays an important role in calcium homeostasis and bone health in addition to its neuromuscular functions. Vitamin D has two major forms, vitamin D₂ and vitamin D₃. Vitamin D in the skin should undergo hydroxylation in the liver (25OHD) hydroxylation in the kidney to 1,25 dihydroxy vitamin D. This active form is required for absorption of calcium from gut and enables bone mineralization and growth.^[1]

In developing countries, 18% of global burden of diseases has been related to pregnancy complications.

Research shows significant association between Vitamin D deficiency in pregnancy and elevated risk for preeclampsia, GDM and anaemia.^[2]

Available report shows that preeclampsia complicates 2-8% of all pregnancies and has been linked with poor maternal and perinatal outcomes.^[3] Pre-eclampsia had been linked with generation ROS, decreased placental/maternal immune response, endothelial cell and trophoblast injury, altered vascular reactivity, DIC and increased production of lipid peroxides.^[4] Mechanism by which vitamin D deficiency can be a causative factor in the development of preeclampsia include impairment of the balance between Th1 and

Th2 cytokines, with higher Th1 expression adversely affecting the immunological tolerance of embryo implantation; and disruption of V-ATPase activity, which have been found to be fundamental in the pathogenesis of pre-eclampsia. [5] Other mechanism include abnormal trophoblastic invasion as a result of altered vitamin D metabolism by placental tissue. [6]

GDM had been linked with several maternal and fetal adverse pregnancy outcomes including pregnancy induced hypertension, pre-eclampsia, increased rate of caesarean section and perinatal morbidity/mortality, macrosomia, sudden intra uterine death and traumatic birth injuries.” [7] Recently vitamin D has increasingly been fingered to contribute greatly to the GDM development in pregnancy. [8]

Regulation of Vitamin D levels and management of hypovitaminosis D is most important mainly in developing countries and low resource healthcare settings to decrease the chances of pre eclampsia and GDM and also to improve the quality of life of women. This study will also help obstetricians to consider effects of hypovitaminosis D in pregnant women and to reduce the maternal morbidity because of its complications.

AIM & OBJECTIVES

1. To study the level of Vitamin D in antenatal women at 20 weeks, at term and in fetal cord serum.
2. To study the association of Vitamin D levels with pre eclampsia and GDM.

MATERIAL AND METHODS

A hospital based observational study was carried out on 265 antenatal women <20 weeks of gestation who came to the Department of Obstetrics & Gynaecology, Muzaffarnagar Medical College & Hospital, Muzaffarnagar. This study was done for 18 months. 265 women were selected on the basis of average number of antenatal patients < 20 weeks of gestation by simple Random Sampling. Among total of 265 women enrolled in the study, 22 were lost in the second trimester, 07 lost in third trimester, 5 had delivery in other hospital. 8 of subjects had preterm delivery before 32 weeks, 5 samples were contaminated and 3 samples were haemolysed. Only 200 subjects had complete serum samples i.e. one sample before 20 weeks, one at delivery and one cord blood serum sample. Therefore, out of 210 antenatal women, there were 45 pre eclampsia cases, 28 GDM and 137 served as control. Antenatal women <20 weeks of gestation with singleton pregnancy and who gave informed written consent were included in the study. All pregnant women with >20 weeks of gestation, DM, hypertension, cardiovascular problems, thrombotic diseases and who did not give consent were excluded from the study. Blood sample for vitamin D level was collected at the time of registration. Patients were followed in second and

third trimester. At the time of delivery, maternal blood and cord blood samples were collected. Then, antenatal women were categorized into preeclampsia (PE) group, gestational diabetes mellitus (GDM) group and control group. Pre-eclamptic cases had to meet the American College of Obstetrics and Gynaecology criteria for diagnosing pre-eclampsia. [9] Similarly, GDM cases had to meet the American Diabetes Association criteria to be diagnosed as Gestational diabetes mellitus. [10] Ethical approval was taken from the Institutional Ethics Committee of Muzaffarnagar Medical College, Muzaffarnagar. The P-value 0.05 was considered statistically significant. Discrete data was entered in MS-Excel sheet and data was analysed using the software SPSS 21.0.

RESULTS

The distribution of age groups, religion, sun exposure and dietary habits shows no significant association with preeclampsia (p-value >0.05) or GDM (p-value >0.05). There is a significant association between gravida status and both preeclampsia (p-value = 0.001) and GDM (p-value = 0.01). Primigravida (first-time pregnant) women have a higher percentage of preeclampsia and GDM compared to multigravida (women who have been pregnant before). This suggests that first-time pregnancies might be at higher risk for these conditions. There is a significant association between the use of vitamin D supplements and preeclampsia (p-value = 0.05), but not with GDM (p-value = 0.11) (**Table 1**).

The p-values for preeclampsia (0.007) and GDM (0.016) indicate significant associations between low vitamin D levels (<20 ng/ml) at <20 weeks and the occurrence of preeclampsia and GDM. Similarly, the p-values for preeclampsia (0.03) and GDM (0.02) also indicate significant associations between low vitamin D levels (<20 ng/ml) at term and the occurrence of preeclampsia and GDM. A significant association between low maternal vitamin D levels (<20 ng/ml) both at <20 weeks of gestation and at term with the occurrence of preeclampsia and GDM has been shown. Higher vitamin D levels (20-29 ng/ml and ≥30 ng/ml) appear to be associated with a lower incidence of these conditions, as indicated by the significant p-values (**Table 2**).

The data in Table 3 indicates a significant association between low cord blood vitamin D levels (<15 ng/ml) and the incidence of preeclampsia and GDM in mothers. Neonates from the control group show higher vitamin D levels in cord blood compared to those from preeclampsia and GDM groups, as supported by the significant p-values (**Table 3**).

Figure 1 shows the distribution of participants according to Vitamin D deficiency at term, pre eclampsia, GDM. 79.5% had Vitamin D deficiency at term, 21% women were pre-eclamptic and 13.3% were having GDM.

Table 1: Socio- demographic details of participants: (N=210)

Variable	Preeclampsia (%)	GDM (%)	Control (%)
Age group			
20-25	17	10	49
25-30	18	11	36
30-35	07	04	25
35-40	03	03	27
p value	0.12	0.45	
Religion			
Hindu	20	11	59
Muslim	25	16	75
Others	00	01	03
p value	0.60	0.87	
Gravida			
Primigravida	39	24	79
Multigravida	06	04	58
p value	0.001	0.01	
Use of Vit. D supplement			
Yes	02	01	24
No	43	27	113
p value	0.05	0.11	
Sun exposure			
Yes	18	13	74
No	27	15	63
p value	0.14	0.60	
Dietary habits			
Veg	07	4	32
Non- Veg	38	24	105
p value	0.37	0.42	

Table 2: Association of maternal vitamin D status at <20 weeks of gestation and at term in control mothers with pre- eclampsia and GDM: (N=210)

Vitamin D level (ng/ml)	Preeclampsia (%)	GDM (%)	Control (%)
At <20 weeks			
<20	42	27	97
20-29	01	01	23
>=30	02	00	17
p value	0.007	0.016	
At term			
<20	41	27	99
20-29	02	00	27
>=30	02	01	11
p value	0.03	0.02	

Table 3: Association of vitamin D status in neonates of control mothers with neonates of pre- eclampsia and GDM women: (N=210)

Vitamin D level in cord (ng/ml)	Preeclampsia (%)	GDM (%)	Control (%)
At <20 weeks			
<15	38	24	83
15-20	03	02	27
>20	04	02	27
p value	0.013	0.03	

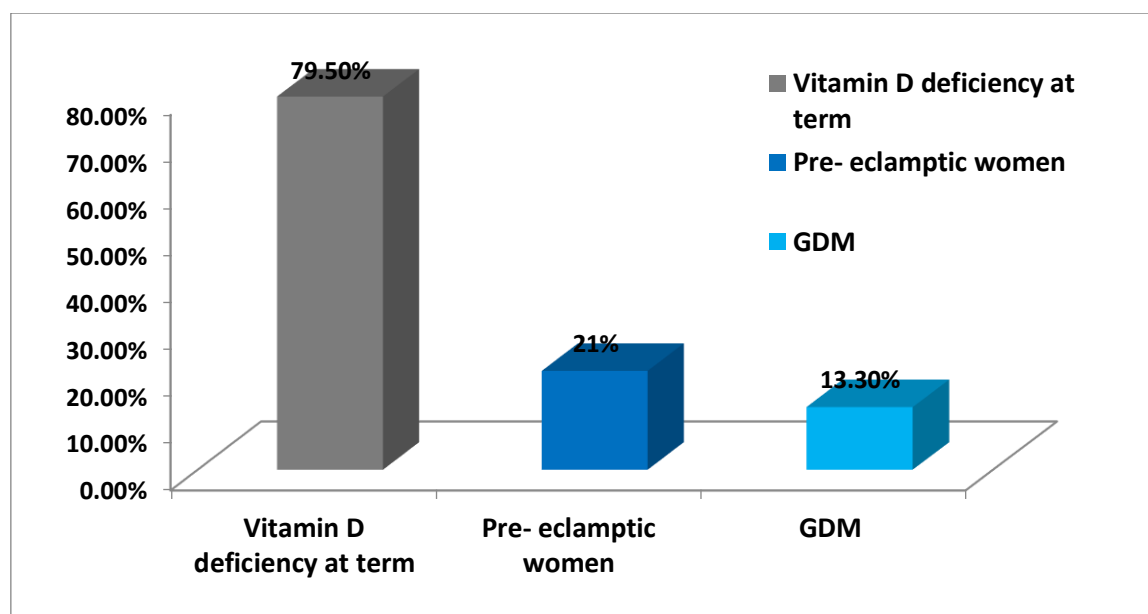


Figure 1: Bar diagram showing distribution of participants according to Vitamin D deficiency at term, pre eclampsia, GDM

DISCUSSION

In present study, the distribution of age groups, religion, sun exposure and dietary habits shows no significant association with preeclampsia (p-value >0.05) or GDM (p-value >0.05). This suggested that these were not significant factors in the occurrence of pre- eclampsia and GDM in our study. There was a significant association between gravida status and both preeclampsia (p-value = 0.001) and GDM (p-value = 0.01). Primigravida (first-time pregnant) women had a higher percentage of preeclampsia and GDM compared to multigravida (women who have been pregnant before). There was a significant association between the use of vitamin D supplements and preeclampsia (p-value = 0.05), but not with GDM (p-value = 0.11). **Lawoynto et al** did a study in Saudi Arabia showed that women at extremes of maternal age, the nulliparous women and high parity women were at an increased risk of developing preeclampsia.^[11] In a study done by **Kumari et al**, primigravida women and those with increased BMI were significantly associated with preeclampsia and GDM.^[12] These findings were almost similar to our study.

In present study, the p-values for preeclampsia (0.007) and GDM (0.016) indicate significant associations between low vitamin D levels (<20 ng/ml) at <20 weeks and the occurrence of preeclampsia and GDM. Higher vitamin D levels (20-29 ng/ml and ≥30 ng/ml) appear to be associated with a lower incidence of these conditions, as indicated by the significant p-values. In a study done by **Kumari et al**, early pregnancy maternal 25(OH)D concentration less than 20 ng/ml was significantly associated with the risk of preeclampsia (p<0.001), independent of age, prepregnancy BMI, education, gravidity, socioeconomic status, residence and religion. Vitamin

D deficiency was significantly associated with GDM when compared with control.^[12] The prevalence of hypovitaminosis D in a study done by **Okoro CC et al** was 7.0% overall, 7.7% for the preeclampsia group and 6.3% for the control groups respectively. The difference in the prevalence between the case and control groups was not statistically significant (p=0.76).^[13] **Zuhur et al** studied 234 cases of GDM and 168 controls in Turkey and reported that only severely deficient maternal serum 25(OH)D levels (<5.2 ng/ml) were significantly associated with an elevated relative risk of GDM.^[14] **Maghbooli et al** studied maternal vitamin D deficiency and GDM in a cross-sectional study of 741 pregnant women at 24-28 weeks gestation and found significantly lower levels of 25(OH)D in women with GDM compared to normo-glycaemic controls.^[15] These findings were similar to the findings of our study. **Mantoo AJ et al** found no association between Vitamin D deficiency and GDM.^[16] **Makgoba et al** examined first-trimester maternal serum 25(OH) D levels and GDM in a case-control study of 90 pregnant women and did not find an evidence of an association in women with GDM compared to 158 controls.^[17] These findings were different from our study and it can be due to different sample size.

In our study, there was a significant association between low cord blood vitamin D levels (<15 ng/ml) and the incidence of preeclampsia and GDM in mothers. Neonates from the control group show higher vitamin D levels in cord blood compared to those from preeclampsia and GDM groups, as supported by the significant p-values. In a study done by **Kumari et al**, 85.7% of neonates of GDM mothers were deficient in cord blood 25(OH)D concentration. Women with gestational diabetes mellitus and their newborns had a higher frequency of 25(OH)D

deficiency than control. The deficiencies of Vitamin D status between GDM women and control was significant ($p < 0.05$) as well as between their newborns ($p < 0.05$).^[12] These findings were similar to the findings of our study.

CONCLUSION

Our findings conclude that significant association between low vitamin D levels and the occurrence of preeclampsia and GDM has been found. Primigravida women and those not using vitamin D supplements were at higher risk for these conditions. Socio-demographic factors such as age group, religion, sun exposure, and dietary habits did not show significant associations. The findings highlight the importance of monitoring and potentially supplementing vitamin D levels during pregnancy to reduce the risk of preeclampsia and GDM. Neonates from preeclamptic and GDM mothers also exhibited lower cord blood vitamin D levels.

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