

Study of Vitamin D Levels in Pregnancy With Relation To Obstetrical and Medical Complications

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DOI: [10.36347/sjams.2020.v08i06.016](https://doi.org/10.36347/sjams.2020.v08i06.016)

| Received: 01.06.2020 | Accepted: 15.06.2020 | Published: 20.06.2020

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Abstract

Original Research Article

Background: Historically vitamin D was thought to be important for bone and calcium metabolism only but recent studies have redefined its role. There is some evidence now that low levels of vitamin D are associated with many pregnancy related complications. Hence this study was done to estimate vitamin D levels in pregnancy and its correlation with medical and obstetrical complications. This was a cross sectional study conducted among pregnant women attending OPD or IPD of our hospital. In this study vitamin D levels of 100 pregnant females were estimated and these were divided into two groups. Group A (n=50) included the women with normal course of pregnancy and Group B(n=50) included pregnancy with complication. Mean of the vitamin D levels were compared in both the groups. Statistical analysis was done by using SPSS software. Almost 94% women in both groups had low vitamin D levels. Mean serum 25(OH) D levels were significantly less in group B (10.9ng/ml, p = 0.0002) as compared to group A (19.49ng/ml). 100% of women in group B had deficiency of 25(OH)-D levels (<10 ng/ml) compared to 96% women in group A. Vitamin D deficiency was significantly associated with maternal complications like gestational diabetes mellitus and preeclampsia. Although mean serum levels of vitamin D were significantly less in pregnancy with complication as compared to those who had normal course of pregnancy. But overall most of the patients were vitamin D deficient in both the groups.

Keywords: vitamin D, metabolism, OPD.

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INTRODUCTION

The prevalence of vitamin D deficiency is quite high in our country and majority of the antenatal women have vitamin D insufficiency or deficiency. The reasons for this in spite of enough sunlight are dark complexion of Indians, wearing of covered clothing, no stringent food fortification policy and vegetarian diet etc [1]. Maternal vitamin D deficiency is especially common during pregnancy and is a widespread public health problem [2]. It has been reported that 40%–100% of vitamin D deficiency during pregnancy are found in Sweden, Oman, UK, USA, Australia, Pakistan, urban India, Japan and China [3].

Poor vitamin D status during pregnancy has been associated with increased risk of adverse obstetric outcomes such as insulin resistance, gestational diabetes mellitus, preeclampsia, bacterial vaginosis, preterm delivery and caesarean section. Adverse new-born outcomes related with low levels of maternal vitamin D

in pregnancy include increased risk of preterm birth and foetal growth restriction resulting in low birth weight and small for gestational age neonates [4].

Vitamin D has traditionally been viewed as a key regulator of bone mineralization and calcium homeostasis however, the documented effects are far more pleiotropic. Vitamin D also inhibits angiogenesis and is involved in the regulation of insulin secretion and possibly insulin action [5]. Furthermore vitamin D also has immunomodulatory roles during pregnancy that enables successful implantation and stimulates antimicrobial activity. From early in pregnancy, there are high demands for calcium to support both maternal calcium homeostasis and foetal skeletal development and growth [6].

Vitamin D deficiency (VDD) during pregnancy is shown to be associated with many maternal and foetal complications thereby increasing

morbidity in mother, infant and child. Therefore there is an increasing interest in studying the impact of maternal vitamin D status on diverse pregnancy and birth outcomes.

Developing foetus acquires its vitamin D across the placenta and thus maternal vitamin D status may influence the intrauterine foetal development and infant health later. During pregnancy vitamin D values tend to decrease from their optimal requirement for the body for several reasons. This phenomenon may lead to development of either vitamin D insufficiency or deficiency, which may affect the mother directly and later the offspring. Therefore attaining adequate vitamin D status during pregnancy is important for maternal as well as infant health [7].

The most reliable indicator of individual's vitamin D status is considered to be the circulating plasma concentration of 25-(OH)-D. An adequate 25-OH-D level has been determined to be 30ng/mL. Vitamin D insufficiency and deficiency are diagnosed at levels of less than 30ng/mL and less than 20ng/mL 25-OH-D respectively [8]. The deficiencies and insufficiencies of vitamin D complicate nearly 67% of pregnancies. Studies have reported prevalence that range from 18-84%, depending on the country of residence and local clothing custom.

Hence the present study aims to assess 25-(OH)-D levels in pregnant women attending the antenatal OPD, and its correlation to the possible obstetrical and medical complications.

Inclusion Criteria

1. ≥ 18 years of age
2. Singleton pregnancy
3. Period of gestation >28 weeks
4. Pregnancy with complications like hypertensive disorders (Preeclampsia), GDM, and preterm labour, intrauterine growth restriction.

Exclusion Criteria

1. History of chronic medical disorder (pre-existing diabetes mellitus, chronic hypertension), intestinal malabsorption, any evidence of liver, kidney, or gastrointestinal diseases.)

2. Patients on medication that affects 25(OH) D levels like anticonvulsants, anti-tuberculosis drugs.
3. History of intake of vitamin D supplements.

MATERIALS AND METHODS

This was a cross sectional study performed in the department of Obstetrics and Gynaecology, Dr RPGMC Tanda at Kangra during July 2017 to June 2018,

A total of 100 patients with their written consent were enrolled in the study after ethical clearance from ethical committee of the institution. All the patients in their third trimester were classified into two groups and their vitamin D3 levels were estimated.

GROUP A: Consisted of antenatal patients having normal course of pregnancy till date and fulfilling the inclusion criteria.

GROUP B: Consisted of antenatal patients who presented to us with complications like PE, GDM, preterm labour and IUGR and fulfilling inclusion criteria.

Both the groups were comparable in the ratio of 1:1. All were subjected to an estimation of serum 25 hydroxy vitamin D levels and accordingly were classified as sufficient, insufficient and deficient. Blood samples were collected for vitamin D estimation and sera was processed and stored at -80°C until analysed. Comparative study was done and quantification of serum 25(OH) D was performed using chemiluminescence assay. The range of detection was 5–300nmol/L. Patients vitamin D status was evaluated according to the 25(OH) D concentrations and classified into three categories:

- Deficient [Levels below 50nmol/L (20ng/ml)],
- Insufficient [concentrations between 51 and 74 nmol/L (21–29 ng/ml)]
- Normal [25(OH)D ≥ 75 nmol/L (≥ 30 ng/ml)].

RESULTS

In the present study we enrolled total 100 participants according to our inclusion criteria. We divided these participants in to study group and control group.

Table-1: Socio demographic profile of the patients

S. No	Variables		Frequency n (%)	95% CI
1	Locality	Rural	62(62)	51.75-71.52
		Urban	38(38)	28.48-48.25
2	Education	Illiterate	6(6)	2.23-12.60
		1-5 th	27(27)	18.61-36.80
		6-10 th	31(31)	22.13-41.03
		Graduate	29(29)	20.36-38.93
		Postgraduate	7(7)	2.86-13.89
3	Occupation	Homemaker	38(38)	28.48-48.25
		Agriculturist	32(32)	23.02-42.08
		Professional	30(30)	21.24-39.98
4	Parity	First	41(41)	31.26-51.29
		Second	42(42)	32.20-52.29
		Third	12(12)	32.20-52.29
		Fourth	3(3)	0.62-8.52
		Fifth	2(2)	0.24-7.04

In our study, out of total 100 participants 62% were from rural background and 38% were from urban background. According to education status, it was observed that 6% of the participants were illiterate, 27% were educated up to primary, and 31% were up to metric, 29% graduated. Only 7% of the patients were

post graduate. In our study, it was found that 38% of the patients were homemaker, 32% were agriculturist and 30% of the patients were professionals. It was observed that out of total 100 patients most of the patients were either primigravida or secondpara. 12% patients were with parity 3.

Table-2: Distribution of patients according to Vitamin D levels in both the groups

S. No	Vitamin D levels(ng/ml)	Frequency	Percentage	95%CI
1	≤20 Deficient	81	81	71.93-88.16
2	20-29 Insufficient	13	13	7.11-21.20
3	≥30 Sufficient	6	6	2.23-12.60

After getting the results of serum vitamin D levels it was found that 81% of the patients were deficient in vitamin D, 13 % were insufficient and only

6% of patients were having sufficient level of vitamin D.

Table-3: Comparison of Vitamin D deficiency in cases and controls

Vitamin D levels(ng/ml)	Frequency (%) Cases n=50	Frequency (%) Controls n=50
≤20 Deficient	47(94)	34(68)
20-29 Insufficient	3(6)	10(20)
≥30 Sufficient	0	6(12)

Table-4: Comparison of mean vitamin D levels

Groups	N=100	Mean±SD	P value
Normal pregnancy	50	19.4960± 12.92	0.0002
Pregnancy with complication	50	10.94±4.37	

Mean vitamin D level of the study group that is pregnancy with complication was significantly low as

compared to control group that is normal pregnancy (p value 0.0002).

Table-5: Comparison of mean vit D levels with different complications

S. No	Group	N=100	Mean±SD	P value
1	Normal Pregnancy	75	17.25±11.33	0.0006
	Pregnancy with PE	25	9.10±2.90	
2	Normal pregnancy	85	15.85±11.22	0.04
	Pregnancy with GDM	15	11.62±3.22	
3	Normal pregnancy	95	15.37±10.69	0.4
	Pregnancy with PL	5	12.20±6.12	
4	Normal pregnancy	95	15.13±10.70	0.2
	Pregnancy with IUGR	5	16.86±6.38	

In the present study it was found that the mean level of vitamin D in pregnancy without preeclampsia (n=75) was found to be 17.25 ± 11.33 and pregnancy with preeclampsia (n=25) was found to be 9.10 ± 2.90 .

The p value was 0.0006 which was significant hence showing a strong association between preeclampsia and vitamin D deficiency.

In our study it was found that mean level of vitamin D in pregnancy without GDM (n=85) was found to be 15.85 ± 11.22 and pregnancy with GDM was (n=15) was found to be 11.62 ± 3.22 .

The p value was 0.04 which was significant hence revealing a strong association between pregnancy associated with GDM with vitamin D deficiency. In the present study it was found that the mean level of vitamin D in pregnancy without IUGR (n=95) was found to be 15.37 ± 10.69 and pregnancy with IUGR (n=5) was found to be 16.86 ± 6.38 .

The p value was 0.2 which was not significant hence showing no association between IUGR and vitamin D deficiency.

DISCUSSION

Our study found that 96 % of the total participants were deficient in vitamin D. Deficiency was significantly higher with those patients who were having medical / obstetrical complications.

In our study, 25 out of 100 patients were having preeclampsia and all of these were vitamin D deficient. Preeclampsia patients had low mean vitamin D levels, mean (9.1 ± 2.9 ng/ml).

A case control study was carried out by Gupta T *et al.*, [9] on 100 patients. They found more incidence of severe vitamin D deficiency (90%) in preeclampsia patients as compared to normotensive patients (62%). Also preeclampsia group had lower median vitamin D levels (3.9ng/ml) when compared to normotensive group (9ng/ml). They concluded that preeclampsia is indeed associated with lower vitamin D levels. Similarly in a study conducted by Merewood *et al.*, [10], the risk of preeclampsia was 5-fold increased among women with 25-(OH)-D levels below 15ng/mL.

In the present study vitamin D deficiency was also associated with a significantly increased risk of GDM (p value = 0.04). In our study, 15 out of 100 patients were diagnosed with GDM and all of them had significantly lower levels (mean 11.6 ± 3.2 ng/ml) of vitamin D. Our results are in concordance with several other published studies reporting an association between low maternal vitamin D status and GDM. Soheilykhah *et al.*, [11] in case control study in Iran found that maternal 25-(OH)-D concentrations at 24–28 weeks of gestation were significantly lower in women with GDM and with impaired glucose tolerance than

non GDM controls. Maghbooli Z *et al.*, [12] found in a study of 741 women in Iran that among the 29 % of participants with 25-(OH)-D levels < 15 nmol/L, the prevalence of GDM was significantly higher compared to women with 25-(OH)-D levels ≥ 35 nmol/L. Clifton-Bligh RJ *et al.*, [13] found in a study of 264 women that among the 32% of women with GDM, 25-(OH)-D levels were significantly lower than among women without gestational diabetes.

Jain M *et al.*, in 2015 in Banaras, India did a study and found a high incidence of vitamin D deficiency (72.8%) in pregnancy. They studied a total of 550 antenatal cases and found serum 25-(OH)-D concentrations significantly lower (46% less) in women who subsequently developed GDM compared with controls [mean: 11.93 ± 3.42 ng/ml, 95% CI: 10.7-13.17ng /ml]. They concluded that maternal vitamin D deficiency is highly prevalent in early pregnancy and is an independent risk factor for GDM in North India [14].

In the present study vitamin D deficiency was not found to be associated with preterm labour. Baker AM *et al.*, [15] found no differences in the prevalence of first-trimester maternal vitamin D deficiency [25-(OH)-D < 50 nmol/l] or in the median circulating 25-(OH)-D concentration between groups. Rodriguez A *et al.*, [4] also found 4.6% of the pregnant women in their study had preterm delivery, but this outcome was not associated with maternal circulating 25-(OH)-D concentration in early pregnancy.

In present study no association was found between vitamin D deficiency and intrauterine growth restriction. Bodnar *et al.*, [16] reported that the relationship among Caucasian women between maternal serums 25-(OH)-D levels before the 22nd week of pregnancy and the risk of a small for gestational age (SGA) birth is U-shaped. The lowest risk was observed at 25-(OH)-D levels between 24 and 32 ng/mL. Leffelaar ER *et al.*, [17] reported data from the Amsterdam born children and their development cohort, which included 3730 women of various ethnicities. Women with first-trimester 25-(OH)-D levels of 12 ng/mL or less were at higher risk (odds ratio 2.4) of delivering SGA infants with lower birth weights (-114 g) than were women with first-trimester 25-(OH)-D levels of 20 ng/mL or more. However A. M. Fernandez-Alonso *et al.*, found no correlation between first-trimester 25-(OH)-D levels and neonatal gestational age or weight [18].

CONCLUSION

Our results suggest that third trimester 25-(OH)-D levels may be associated with a significantly increased risk of complications such as gestational diabetes mellitus and preeclampsia. Apparently, low 25-(OH)-D concentrations were not associated with birth and neonatal adverse effects like preterm labour and intrauterine growth restriction (IUGR).

Due to the presence of an alarmingly high prevalence of insufficiency and deficiency of vitamin D, there is a compelling need to study the causal relation between low 25-OH-D levels and thereby preventing pregnancy related complications besides establishing guidelines for necessary supplementation.

There is an extreme lack of awareness regarding the importance of vitamin D and its sources, especially in the population of Himachal Pradesh. Organizations involved in women's health care, such as the World Health Organization and the International Federation of Gynaecology and Obstetrics (FIGO), should make recommendations focused on pregnant and breastfeeding women to maximize maternal and child health, given the almost epidemic status of hypovitaminosis D.

RECOMMENDATIONS

Based on the present study, reducing the proportion of women of childbearing age with vitamin D deficiency is important and vitamin D supplementation in pregnancy could be explored as a safe and effective means of preventing adverse maternal health outcomes like gestational diabetes mellitus and preeclampsia.

REFERENCES

- Goel P, Garg G, Kaur J, Mehra R, Tandon R, Huria A. Association of vitamin D deficiency during pregnancy with preeclampsia and eclampsia. *Int J Reprod Contracept Obstet Gynecol.* 2016 Sep;5(9):3046-50.
- Wei SQ, Audibert F, Hidiroglou N, Sarafin K, Julien P, Wu Y, Luo ZC, Fraser WD. Longitudinal vitamin D status in pregnancy and the risk of pre-eclampsia. *BJOG: An International Journal of Obstetrics & Gynaecology.* 2012 Jun;119(7):832-9.
- Zhang MX, Pan GT, Guo JF, Li BY, Qin LQ, Zhang ZL. Vitamin D deficiency increases risk of gestational diabetes mellitus: A meta-analysis of observational studies. *Nutrients.* 2015;7(10):8366-75.
- Rodríguez A, García-Esteban R, Basterretxea M, Lertxundi A, Rodríguez-Bernal C, Iniguez C, Rodríguez-Dehli C, Tardon A, Espada M, Sunyer J, Morales E. Associations of maternal circulating 25-hydroxyvitamin D3 concentration with pregnancy and birth outcomes. *BJOG: An International Journal of Obstetrics & Gynaecology.* 2015 Nov;122(12):1695-704.
- Pleskačová A, Bartáková V, Pácal L, Kuricová K, Bělobrádková J, Tomandl J, Kaňková K. Vitamin D status in women with gestational diabetes mellitus during pregnancy and postpartum. *BioMed research international.* 2015;2015.
- Schneuer FJ, Roberts CL, Guilbert C, Simpson JM, Algert CS, Khambalia AZ, Tasevski V, Ashton AW, Morris JM, Nassar N. Effects of maternal serum 25-hydroxyvitamin D concentrations in the first trimester on subsequent pregnancy outcomes in an Australian population. *The American journal of clinical nutrition.* 2014 Feb 1;99(2):287-95.
- Shand AW, Nassar N, Von Dadelszen P, Innis S, Green T. Maternal vitamin D status in pregnancy and adverse pregnancy outcomes in a group at high risk for preeclampsia. *BJOG.* 2010;117:1593-8.
- Robinson CJ, Alanis MC, Wagner CL, Hollis BW, Johnson DD. Plasma 25-hydroxyvitamin D levels in early-onset severe preeclampsia. *American journal of obstetrics and gynecology.* 2010 Oct 1;203(4):366-e1.
- Gupta T, Wahi S, Gupta N, Arora S, Gupta S, Bhatia P. Correlation of Vitamin D Levels in term normotensive and preeclamptic patients in labor. *J Obstet Gynaecol India.* 2015; 42(3):1-6.
- Merewood A, Mehta SD, Chen TC, Bauchner H, Holick MF. Association between vitamin D deficiency and primary cesarean section. *J Clin Endocrinol Metab.* 2009;94(3):940-5.
- Soheilykhah S, Mojibian M, Moghadam MJ, Shojaoddiny-Ardekani A. The effect of different doses of vitamin D supplementation on insulin resistance during pregnancy. *Gynecol. Endocrinol.* 2013;29:396-9.
- Maghbooli Z, Hossein-nezhad A, Mirzaei K, Karimi F, Besharati A, Omidfar K, Larijani B. Association between retinol-binding protein 4 concentrations and gestational diabetes mellitus and risk of developing metabolic syndrome after pregnancy. *Reproductive Sciences.* 2010 Feb;17(2):196-201.
- Clifton-Bligh RJ, McElduff P, McElduff A. Maternal vitamin D deficiency, ethnicity and gestational diabetes. *Diabet Med.* 2008; 25:678-84.
- Jain M, Karp S, Jain S, Singh SK, Singh TB, Jain. Maternal vitamin D Deficiency. A risk factors for Gestational Diabetes Mellitus in North India. *Gynecol Obstet.* 2015;5(1):94-101
- Baker AM, Haeri S, Camargo CA, Stuebe AM, Boggess KA. A nested case-control study of first-trimester maternal vitamin D status and risk for spontaneous preterm birth. *Am J Perinatol.* 2011;28:667-72.
- Bodnar LM, Catov JM, Simhan HN, Holick MF, Powers RW, Roberts JM. Maternal vitamin D deficiency increases the risk of preeclampsia. *The Journal of Clinical Endocrinology & Metabolism.* 2007 Sep 1;92(9):3517-22.
- Leffelaar ER, Vrijkotte TG, van Eijsden M. Maternal early pregnancy vitamin D status in relation to fetal and neonatal growth: results of the multi-ethnic Amsterdam Born Children and their Development cohort. *British Journal of Nutrition.* 2010 Jul;104(1):108-17.
- Fernández-Alonso AM, Dionis-Sánchez EC, Chedraui P, González-Salmerón MD, Pérez-López FR, Spanish Vitamin D and Women's Health Research Group. First-trimester maternal serum 25-hydroxyvitamin D3 status and pregnancy outcome. *International Journal of Gynecology & Obstetrics.* 2012 Jan;116(1):6-9.