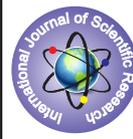


ROLE OF VITAMIN D IN PREDICTING THE RISK OF PREECLAMPSIA



Gynaecology

KEYWORDS: Vitamin D, preeclampsia, NICU, low birth weight.

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ABSTRACT

Aims and objectives - To find out the correlation of serum Vitamin D levels in early pregnancy with subsequent development of preeclampsia (PE).

Material and methods - This observational study was done in Department of Obstetrics & gynaecology, SMS Medical College, Jaipur on 800 pregnant women between 13-20 weeks gestation. Serum Vitamin D levels were assessed, all women were followed till delivery and development of preeclampsia was observed.

Results - Serum 25(OH)D concentrations in early pregnancy were lower in women who subsequently developed preeclampsia as compared to women who did not develop preeclampsia [mean, 13.58 ± 7.61 ng/ml, vs. 17.14 ± 6.91 ng/ml, and 95% confidence interval 1.54-5.37; p value < 0.001]. Serum vitamin D levels showed a decrease as the severity of hypertensive disorders increased.

Conclusion - It was thus concluded that Low serum Vitamin D levels were associated with increased incidence of preeclampsia.

Introduction

Hypertensive disorders represent the most common medical disorder of pregnancy affecting between 7-15% of all the gestations.¹ The national high blood pressure education programme (2000) working group on high blood pressure in pregnancy defined preeclampsia as BP ≥ 140/90 mm hg 6 hours apart on two separate occasions with proteinuria greater than 0.3 gm/dl in a 24 hours urine collection or greater than or +1 on urine dipstick examination after 20 weeks of gestation.²

Vitamin D is a hormone rather than a vitamin. Vitamin D is involved in many aspect of human life such as bone metabolism, cell functioning and reproduction. Vitamin D is involved in implantation and placental development and displays anti proliferative and immunomodulatory actions. Low serum 25(OH) D levels have been related to adverse obstetric and neonatal outcomes such as preterm birth, low birth weight, low Apgar score, increased NICU admissions, hypertensive disorder in pregnancy and gestational diabetes mellitus.

The pathogenesis of preeclampsia involves a number of biological processes that may be directly or indirectly affected by vitamin D.^{3,4,5,6} The active form of vitamin D, 1, 25-dihydroxyvitamin D₃, has been shown to regulate the transcription and function of genes associated with placental invasion, normal implantation and angiogenesis.^{4,7} Furthermore abnormal implantation has been proposed to be mediated by an appropriate immune response between mother and baby. The immunomodulatory properties of 1, 25-dihydroxy vitamin D₃ may be relevant in this regard.^{5,8} Proteinuria of preeclampsia is thought to be mediated by renal vascular endothelial growth factor (VEGF). 1, 25-dihydroxy vitamin D₃ has been shown to regulate angiogenesis process through direct effects on VEGF genes transcription.³

Aim & Objectives

The aim of our study was to evaluate the effect of Vitamin D deficiency in early pregnancy and subsequent development of

preeclampsia.

Material & Methods

This prospective Hospital based study was conducted in Department of Obstetrics & Gynecology, SMS Medical College, Jaipur .800 pregnant women with gestational age between 13-20 weeks, singleton pregnancy and age up to 35 years, attending the antenatal clinic were included in study. Women >35 year, with multifetal pregnancy, history of chronic hypertension, diabetes mellitus, liver, cardiac or renal disease, collagen disorder, molar pregnancy or any other major illness were excluded from study.

All selected women underwent a blood test to assess their serum level of 25(OH) Vitamin D. Patients were categorized as vitamin D deficient or sufficient as per these reference values- Deficiency was considered when Vitamin D levels were < 20ng/ml; Insufficiency 20-30ng/ml; Sufficiency >30ng/ml.

All selected women followed till delivery and development of preeclampsia were noted.

Women were considered to have mild preeclampsia if systolic blood pressure (SBP) was between 140-159 mmHg and diastolic blood pressure (DBP) between 90-109 mmHg and in severe preeclampsia if SBP ≥ 160 mmHg or DBP ≥ 110 mmHg. Follow up was done for perinatal outcomes.

Assessment of serum 25(OH) D was done by Chemiluminiscent Immune Assay method in department of biochemistry SMS medical college Jaipur.

Observation

Out of 800 women, 61(7.6%) developed PE. All women of study population were non smoker and housewives. Maximum number of study subjects belonged to age group 21-30 years (81%) maximum had BMI in the range 18.5-29.9kg/m² (70%). Mean gestational age at the time of sample collection was 14.55±1.32 weeks.

In our study it was observed that 60.37% study population had Vitamin D deficiency, 36.13% had Vitamin D insufficiency. Only 3.5% women showed Vitamin D sufficiency. This result showed that there is widespread prevalence of Vitamin D deficiency in India, especially in pregnant women. There was a statistically significant increase in percentage of women who developed preeclampsia when the Vitamin D levels were <20ng/ml. Mean Vitamin D levels of women who developed preeclampsia was significantly lower than women who did not developed preeclampsia. Our study showed significant increase in severity of hypertensive disorder of pregnancy as the vitamin D levels decreases.

Table – 1
Distribution of Study Population According to Maternal Vitamin D Levels and development of preeclampsia

Vitamin D Levels (ng/ml)	With Preeclampsia		Without Preeclampsia		Total	
	No.	%	No.	%	No.	%
Deficient (<20)	44	72.13	439	59.41	483	60.37
Insufficient (20-30)	16	26.23	273	36.94	289	36.13
Sufficient (>30)	1	1.64	27	3.65	28	3.50
Total	61	100	739	100	800	100.00

$\chi^2 = 12.42$ $d.f. = 3$ $p = 0.006$ *Sig*

Table no. 2
Distribution of study population according to mean vitamin D levels

Vitamin D Levels (ng/ml)	With Preeclampsia	Without Preeclampsia	95% CI	p-value
Mean±SD	13.58 ± 7.61	17.14 ± 6.91	1.54-5.37	0.001 (Sig)

Table no. 3
Association of Vitamin D Levels with severity of hypertensive Disorder of Pregnancy

Vitamin D Levels (ng/ml)	Normotensive		Gestational Hypertension		Mild Preeclampsia		Severe Preeclampsia	
	No.	%	No.	%	No.	%	No.	%
Deficient (<20)	394	81.60	45	9.30	31	6.40	13	2.70
Insufficient (20-30)	261	90.30	12	4.20	11	3.80	5	1.70
Sufficient (>30)	24	85.70	3	10.70	1	3.60	0	0.00
Total	679	84.90	60	7.50	43	5.40	18	2.20

$\chi^2 = 12.32$ $d.f. = 6$ $p = 0.045$ *Sig*

Discussion

There is widespread vitamin D deficiency in India despite plenty of sunshine. Due to lifestyle changes there is a decrease in outdoor activities, which can lead to decreased synthesis of Vitamin D. Vitamin D deficiency could also be due to low dietary intake of calcium and decreased intestinal absorption.

Harinarayan CV et al⁹ in their study observed that there is widespread prevalence of varying degrees (50-90%) of Vitamin D deficiency in Indian population.

Bassir M et al¹⁰ in their study in Iranian mothers and their neonates, observed that 80% of the women had Vitamin D < 25nmol/L.

In this study we sought to determine whether midgestation vitamin D deficiency is associated with an increased risk of preeclampsia. Our results confirmed our hypothesis that women who developed preeclampsia had significantly lower vitamin D level in early pregnancy.

Bodnar LM et al¹¹, in their study concluded that in early pregnancy Vitamin D deficiency was more common among women who later developed PE as compared to women who did not developed PE. Early pregnancy maternal Vitamin D deficiency < 37.5 nmol/l was associated with 5 fold increase in the odds of PE.

Baker AM et al¹² observed that midgestation (15-20 weeks) maternal 25(OH) D concentration was lower in women who subsequently developed PE than women who did not [Median (interquartile range), 75 (47-107) nmol/l vs. 98 (66-113) nmol/l; p-value=0.001].

Singal R et al¹³ also reported significantly lower mean vitamin D levels in cases of PE as compared to controls (9.7 ± 4.95 ng/ml and 14.8 ± 4.95 ng/ml respectively).

Achkar M et al¹⁴ in a study reported that women who develop PE had a significantly lower Vitamin D concentration at a mean gestational age of 14 weeks compared with women in control (mean ± SD - 47 17.7 vs. 52.3 17.2 nmol/l). Baker AM et al¹² observed that midgestation maternal 25(OH) D level <50 nmol/L was associated with almost 4 fold odds of severe preeclampsia (unadjusted odds ratio, 3.63; 95% CI, 1.52-8.65) when compared with midgestation levels of 25(OH) D 75 nmol/L.

Several studies have provided evidence that vitamin D supplementation may reduce the risk of preeclampsia.

In a prospective cohort study by Haugen et al¹⁵, a 29% reduced risk of preeclampsia was observed in women who reported supplementing with 400-600IU of vitamin D during the first half of their pregnancy.

Robinson CJ et al¹⁶ observed 70% reduction in severe preeclampsia risk per 25 nmol/L increase in 25(OH) D.

Our study does have some methodological strength. The maternal serum was collected well before delivery at a time when no clinical manifestation of preeclampsia were evident, reducing likelihood of that subclinical diseases affected vitamin D levels. In addition we excluded all women with chronic medical illnesses, multifetal pregnancy, age >35 year. These all associated with increased risk for preeclampsia.

Conclusion

To conclude serum Vitamin D levels has significant association with development of preeclampsia. It can be used as a prognostic tool for assessing the development of preeclampsia. So it can be suggested that maternal Vitamin D level should be assessed in early pregnancy and all the deficient women should be given Vitamin D supplementation in appropriate doses.

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