VOLUME-6 | ISSUE-4 | APRIL - 2017 • ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46

ROLE OF VITAMIN D IN PREDICTING THE RISK OF PREECLAMPSIA

Gynaecology

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

Baror Sangeeta	Final year Postgraduate Student, Department of Obstetrics and Gynecology, S.M.S. Medical College, Jaipur-302012 (Rajasthan).
Rajoria Lata	Senior Professor and HOD, Department of Obstetrics and Gynecology, S.M.S. Medical College, Jaipur-302012 (Rajasthan).
Hemani Sunita	Assistant Professor, Department of Obstetrics and Gynecology, S.M.S. Medical College, Jaipur-302012 (Rajasthan).
Sharma Anita	Final year Postgraduate student, Department of Obstetrics and Gynecology, S.M.S. Medical College, Jaipur-302012 (Rajasthan).
Vyas Jyotsna	Professor, Department of Obstetrics and Gynecology, S.M.S. Medical College, Jaipur-302012 (Rajasthan).
Baghotia Priyanka	Department of Obstetrics and Gynecology, S.M.S. Medical College, Jaipur-302012 (Rajasthan).

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 ± 6.91ng/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 Chemiluminisent 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%) had 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 > 20 ng/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 Pre-eclampsia		Without Pre-eclampsia		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

x^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 Pre-eclampsia	Without Pre-eclampsia	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 Pre-eclampsia		Severe Pre-eclampsia	
	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

x^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 al[9] in their study observed that there is widespread prevalence of varying degrees (50-90%) of Vitamin D deficiency in Indian population.

Dave A. et al 10 revealed that in India vitamin D deficiency prevalence was 48.2% among pregnant women.

Bassir M et al[10] 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 al[11], 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 al[12] 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 al[13] 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 al[14] 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 al[12] 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 al [15], 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 al[16] 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 likehood 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.

References

1. Lo JO, Mission JF, Caughey AB. Hypertensive disease of pregnancy and maternal mortality. Curr Opin Obstet Gynecol, 2013 Feb 11 [Epub ahead of print].
2. National High Blood Pressure Education Program. Working group report on high blood pressure in pregnancy. Am J Obstet Gynecol, 2000; 183 : S1.
3. Cardus A, Parisi E, Gallego C, Aldea M, Fernandez E, Valdivielso JM. 1,25-Dihydroxyvitamin D3 stimulates vascular smooth muscle cell proliferation through a VEGF-mediated pathway. Kidney Int, 2006; 69 : 1377–1384.
4. Evans KN, Bulmer JN, Kilby MD, Hewison M. Vitamin D and placental-decidual function. J Soc Gynecol Investig, 2004; 11 : 263–271.
5. Hewison M. Vitamin D and the immune system. J Endocrinol, 1992; 132 : 173–175.
6. 14. Li YC, Kong J, Wei M, Chen ZF, Liu SQ, Cao LP. 1,25-Dihydroxyvitamin D3 is a negative endocrine regulator of the renin-angiotensin system. J Clin Invest, 2002; 110 : 229–238.
7. Daftary GS, Taylor HS. Endocrine regulation of HOX genes. Endocr Rev, 2006; 27 : 331–355.
8. Muller K, Diamant M, Bendtzen K. Inhibition of production and function of interleukin-6 by 1,25-dihydroxyvitamin D3. Immunol Lett, 1991; 28 : 115–120.
9. Harinarayan CV, Joshi SR. Vitamin D Status in India - Its implications and remedial measures. JAPI, 2009; Vol. 57 : 40-48.
10. Bassir M, Laborie S, Lapillonne A, Claris O, Chappuis MC, Salle BL. Vitamin D deficiency in Iranian mothers and their neonates: a pilot study. Acta Paediatr, 2001; 90 : 577-9.
11. Bodnar LM, Catov JM, Simhan HN, Holick MF, Powers RW, Roberts JM. Maternal vitamin D deficiency increases the risk of preeclampsia. J Clin Endocrinol Metab, 2007; 92 : 3517–22.
12. Baker AM, Haeri S, Camargo CA, Jr., Espinola JA, and Stuebe AM. A Nested Case-Control Study of Midgestation Vitamin D Deficiency and Risk of Severe Preeclampsia.

J Clin Endocrinol Metab, November 2010; 95(11) : 5105–5109.
13. Singal R, Gurung P, Aggarwal N, Dutta U, Kochhar R . Relationship between preeclampsia and vitamin D deficiency: a case control study. Arch Gynecol Obstet, 2015 Jun; 291(6) : 1247-51.
14. Achkar M, Dodds L, Giguère Y, Forest JC, Armson BA, Woolcott C, Agellon S, Spencer A, Weiler HA. Vitamin D status in early pregnancy and risk of preeclampsia. Am J Obstet Gynecol, 2015 Apr; 212(4) : 511.e1-7.
15. Haugen M, Brantsaeter AL, Trogstad L, Alexander J, Roth C, Magnus P, et al. Vitamin D supplementation and reduced risk of preeclampsia in nulliparous women. Epidemiology, 2009; 20 : 720–6.
16. Robinson CJ, Alanis MC, Wagner CL, Hollis BW, Johnson DD. Plasma 25-hydroxyvitamin D levels in early-onset severe pre-eclampsia. Am J Obstet Gynecol, 2010; 203 : 366.