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Research Article

Association of vitamin D deficiency during pregnancy with preeclampsia and eclampsia

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ABSTRACT

Background: Vitamin D was considered important for bone and calcium. Historically thought to be important for bone and calcium metabolism but recent studies have redefined its role. There is some evidence now that low levels of Vitamin D are associated with the risk of preeclampsia but more studies are needed to prove the same. This study was done to determine whether vitamin D deficiency is an independent risk factor for preeclampsia/eclampsia.

Methods: In this prospective case control study vitamin D levels were estimated in 92 women divided into two groups. Group 1(n = 42) included pregnant women with preeclampsia/eclampsia and group 2(n = 50) included uncomplicated pregnant women admitted in labour ward for delivery. The frequency of risk factors for preeclampsia/eclampsia were compared in two groups. Statistical analysis was done using the multivariate logistic regression analysis.

Results: Almost 100% women in both groups had low vitamin D levels. Mean serum 25(OH)D levels were significantly less in Group 1(6.7236ng/ml) as compared to group 2(9.8862 ng/ml, p = 0.004). 83.3% of women in group 1 had severe deficiency (25(OH)D levels <10 ng/ml) compared to 68% women in group 2. All women (100%) in group 1 had vitamin D deficiency (<20 ng/ml) as compared to 92% in group 2 but this was not statistically significant.

Conclusions: Although mean serum 25(OH)D levels were significantly less in preeclampsia/eclampsia group, prevelance of vitamin D deficiency was not significantly different in pregnant women with preeclampsia/eclampsia as compared to women who did not have preeclampsia/eclampsia.

Keywords: Vitamin D, Pregnancy, Preeclampsia, Eclampsia

INTRODUCTION

Adequate Vitamin D level is important not only for bone and calcium metabolism but also for maintenance of other systems. Studies have shown that Hypovitaminosis D may be associated with chronic illnesses like type 2 diabetes, infections, malignancy, some immune problems, cardiovascular disease etc.[1] Similarly vitamin D deficiency (VDD) during pregnancy have shown to be associated with many maternal and fetal complications thus increasing morbidity in mother, infant and child.[2,3,4]

Prevalence of Vitamin D deficiency is quite high in our country. The reason for this in spite of enough sunlight. The reasons for this is dark complexion of Indians, wearing of covered clothing, no stringent food fortification policy, vegetarian diet etc.[5] Data is sparse as regards the prevalence of Vitamin D deficiency during pregnancy in India is concerned.[5,6,7]

Studies related to outcomes in pregnancy have shown that inadequate vitamin D during pregnancy is associated with gestational diabetes mellitus, preterm labour, increased chances of cesarean section and bacterial vaginosis although the studies are inconclusive.[4] Similarly the role of vitamin D in preeclampsia is still unclear.

Preeclampsia and eclampsia are serious disorder complicating approximately 5% of all pregnancies and is an important cause of maternal as well as fetal morbidity and mortality There are some risk factors for preeclampsia like primigravidas, age (women younger than 20 and older than 40), obesity, multiple pregnancy, diabetes, gestational diabetes, renal disease, certain autoimmune disorders, family history of preeclampsia and previous history of preeclampsia.[8] Knowledge of risk factors is important as treatment can be directed towards these for reducing the morbidity and mortality associated with this disorder.

There is also some evidence now that low levels of Vitamin D and insufficient vitamin D intake increases the risk of preeclampsia but other studies have not shown any association of preeclampsia with hypovitaminosis D.[9,10,11,12,13] Preeclampsia rates are elevated during winter months, when sunlight-dependent 25(OH)D production is reduced.[14]

As studies have shown that VDD may be a risk factor for preeclampsia and that vitamin D supplements above the dose recommended in prenatal vitamin in early pregnancy could play a role in prevention of preeclampsia, this study was planned to find out the association of Vitamin D and preeclampsia.

METHODS

This was a prospective case control study conducted among pregnant women attending the labour ward of our hospital with a diagnosis of preeclampsia and eclampsia. The study was approved by the Research Ethics Committee of our hospital. After an informed consent 50 pregnant women with preeclampsia and eclampsia (group 1) at delivery were enrolled in the study. Uncomplicated pregnant patients admitted in labour ward (age and parity matched) for delivery were taken as controls in 1:1 ratio (group 2).A detailed socio-demographic characteristics, obstetric, medical and family histories were recorded of the women enrolled in the study. Maternal and fetal outcomes were also recorded. 25(OH) D was assessed in cases and controls by radioimmunoassay. The frequency of the risk factors for preeclampsia and eclampsia were compared in two groups (cases and controls). Stasitical analysis was done to find the association of hypovitaminosis D with preeclampsia and eclampsia. Vitamin D deficiency was defined as 25(OH) D levels in blood < 30 ng/ml.

RESULTS

Table 1: Demographic parameters.

		Group 1 (n = 42)	Group 2 (n = 50)	p-value
Mean age (years)		25.48±4.232	24.30±3.066	0.127
Backg-round	Rural	25 (59.5%)	15 (30%)	0.003
	Urban	17 (40.5%)	35 (70%)	
	Total	42 (100.0%)	50 (100%)	

In our study total 100 patients (50 in each group) were booked but in group 1, compete details of 42 patients are available. In group 2 details of all patients are available.

Table 2: Obstetric history.

Obstetric history		Group 1 (n = 42)	Group 2 (n = 50)
Gravida (G)	1	26 (61.9%)	28 (56.0%)
	2	9 (21.4%)	15 (30.0%)
	3	4 (9.5%)	6 (12.0%)
	4	2 (4.8%)	1 (2.0%)
	5	1 (2.4%)	0 (0.0%)
Parity (P)	0	32 (80.0%)	35 (70.0%)
	1	7 (17.5%)	14 (28.0%)
	2	0 (0.0%)	1 (2.0%)
	3	1 (2.5%)	0 (0.0%)

Table 3: Risk factors for preeclampsia/eclampsia.

Risk factors		Group 1	Group 2	p-value
BMI	Underweight	5 (11.9)%	0 (0.0%)	0.053
	Normal	24 (57.2%)	38 (76.0%)	
	Overweight	12 (28.5%)	11 (22.0%)	
	Obese	1 (2.4%)	1 (2.0%)	
	Total	42 (100.0%)	50 (100.0%)	
Previous history of preeclampsia or eclampsi		11 (26.2%)	0 (0.0%)	<0.001
History or renal disease		0 (0.0%)	0 (0.0%)	
Autoimmune disease		1 (2.4%)	0 (0.0%)	0.467
Chronic hypertension		0 (0.0%)	1 (2.0%)	1.000
Multiple pregnancy		17 (40.5%)	0 (0.0%)	<0.001

Demographic details

Mean age in group 1 was 25.48 years and in group 2 was 24.30 years (p = 0.127). Significantly more women who developed preeclampsia or eclampsia belonged to rural background (p = 0.003).

There was no statistically significant difference between the two groups as regards the gravidity and parity and similarly there was no difference in the BMI of the women between the two groups (p=0.053) (Table 1, 2).

Table 4: Vitamin D levels.

Group	Mean (ng/ml)	N	Std. Deviation	Minimum (ng/ml)	Maximum (ng/ml)
1 (cases)	6.7236	42	3.81028	<4.20	19.50
2 (controls)	9.8862	50	6.03511	<4.20	31.95
Total	8.4424	92	5.35371	4.20	31.95

Table 5: Vitamin D insufficiency/deficiency.

	Vitamin D levels (ng/ml)	Group 1 (n = 42)	Group 2 (n = 50)	Total
Type of deficiency	<10	35 (83.3%)	34 (68.0%)	69 (75.0%)
	10-19	7 (16.7%)	12 (24.0%)	19 (20.7%)
	20-30	0 (0.0%)	3 (6.0%)	3 (3.3%)
	>30	0 (0.0%)	1 (2.0%)	1 (1.1%)

Vitamin D insufficiency serum 25(OH) D levels 20-30ng/ml, Vitamin D deficiency <20 ng/ml

Risk factors for Preeclampsia and Eclampsia (Table 3)

Previous history of preeclampsia and eclampsia was present in 11 women in group 1 and none of the women in group 2 and it was statistically significant (p<.001). There was no stastically difference in the occurrence of autoimmune disease, previous history of renal disease and chronic hypertension between group 1 and group 2. More women in group 1 had multiple pregnancy (17) as compared to group 2 and the difference was statistically significant.

Vitamin D levels in subjects recruited (Table 4, 5)

100% women who developed preeclampsia and Eclampsia had low Vitamin D levels (42/42 in group 1) and 98% in controls (49/50 in group 2). Mean serum 25 (OH)D levels were significantly lower in Group 1 (6.7236ng/ml) as compared to group 2 (9.8862ng/ml(p=0.004). 83.3% of women in group 1 had severe deficiency (25(OH)D levels <10 ngm/ml) and 68% women in group 2. All women (100%) in group 1 had Vitamin D deficiency (vit D <20ngm/ml) as compared to 92% in group 2 but this was not statistically significant.

Maternal and Fetal outcomes

Gestational age at the time of delivery was lower in the group 1(37.85 weeks vs 40.30 weeks, p<0.001). The rate of cesarean delivery was more in the pre-eclamptic group and eclamptic group (19/42) than the control group (4/50) and it was statistically significant. The one minute and five minute Apgar score of neonates (less than 7) was significantly low in the group 1 (p<0.001,p<.001). Low birth weight babies were significantly more in group 1 as compared to group 2.

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 pregnant women at or near term are vitamin D-deficient.[15,16] The optimum level of vitamin D and maternal vitamin D requirements during pregnancy has been poorly studied.

The studies on relationship of low levels of 25-hydroxy vitamin D with adverse pregnancy outcomes have also not given conclusive results. Clinical studies have correlated hypovitaminosis D and high incidence of maternal and fetal complications such as preeclampsia, gestational diabetes, low birth weight, preterm labor, cesarean delivery and infectious diseases.[17,18,19,20]

The value used to define vitamin D deficiency in different studies are different; therefore, levels of 'vitamin D deficiency' in various populations cannot be directly compared.[21,22] According to American College of Obstetrics and Gynecology (ACOG), serum 25(OH)D

concentration below 20 ng/ml used as a cut-off for deficiency and below 32ng/ml as a cut-off for insufficiency[22]. According to Canadian Paediatric Society, serum 25(OH) D concentration below 10ng/ml used as a cut-off for deficiency and below 30ng/ml as a cut -off for insufficiency.[23] According to Institute of Medicine (IOM) recommendations, below 12 ng/l (30 nmol/l) of serum 25(OH) D levels used as a cut -off for deficiency and 20ngm/ml for insufficiency.[24]

Studies estimating the prevalence of hypovitaminosis in pregnancy are few from India but have found a very high prevalence of VDD. A study done by R.K. Marwaha, hypovitaminosis D (25(OH)D <50 nmol/l) was observed in 96·3% of the pregnant subjects.[7] In the study done by Sachin A et al ,showed 84.3% of urban and 83.6% of rural women had 25(OH)D values below cutoff (22.5ng/ml).[6] Prevalance of hypovitaminosis D studied in 98 pregnant women (by vandita jain et al in 2009), showed vitamin D deficiency in 81.1% of pregnant women and insufficiency in 11.6% of subjects (cut-off taken for hypovitaminosis D deficiency ≤15 ng/ml and insufficiency 15-20 ng/ml).[5] Our study also revealed a very high prevalence of hypovitaminosis D, 92% of the women with uncomplicated pregnancies had Vitamin D deficiency(vit D <20ngm/ml) and 98% had Vitamin D insufficiency(vit D <30ngm/ml).The higher prevalence as compared to other studies may be due to the recruitment of subjects and sampling for Vitamin D estimation was done in winter months.

Various studies have corelated the association of preeclampsia with hypovitaminosis and the results are inconclusive. In a study by Bodhar et al where association between maternal vitamin D status at ≤26 weeks gestation and the risk of preeclampsia by clinical subtype was studied and they concluded that maternal vitamin D deficiency may be a risk factor for severe preeclampsia but not for its mild subtypes.[9]

D.Robinson et al in a case control study revealed that circulating 25(OH)D levels were significantly decreased in early-onset severe pre-eclampsia (EOSPE) individuals.[12] 83.3% of women had severe deficiency of Vitamin D (<10 ngm/ml) as compared to 68% women in the control group in our study. All women (100%) with preeclampsia or eclampsia had Vitamin D deficiency (vit D <20ngm/ml) as compared to 92% in the control group but this was not statistically significant. Powe C et al performed a case-control study measuring first trimester total 25-hydroxyvitamin D. They compared these levels from pregnancies complicated by subsequent preeclampsia (cases, n=39) with those from normotensive pregnancies (controls, n=131). First trimester total 25(OH)D levels were similar in cases and controls (27.4±1.9 versus 28.8±0.80 ng/mL; p=0.435).[10] Mean Vitamin D levels were significantly less in women with preeclampsia or eclampsia (6.7236ng/l) as compared to the control group (9.8862ng/l,p=0.004) in our study.

Our study revealed significant risk factors for severe preeclampsia and eclampsia being rural background, multiple pregnancy and history of pre-eclampsia during antecedent pregnancy. In our study mean serum 25(OH)D levels were significantly less in women who developed preeclampsia and eclampsia as compared to controls. This study showed a very high prevalence of vitamin D deficiency in pregnant women, 100% women with preeclampsia and eclampsia had Vitamin D deficiency (vit D <20ngm/ml) as compared to 92% in the control group.

Whether Vitamin D deficiency or insufficiency is a risk factor for the development of preeclampsia or eclampsia cannot be concluded from our study as there was no statistically significant difference in the prevalence of VDD or Vitamin D insufficiency in women with preeclampsia and eclampsia as compared to controls although the mean 25(OH) D levels were significantly less in cases as compared to controls. Other already proven risk factors which were studied in our study were BMI, history of chronic hypertension, history of renal disease, autoimmune disease, pre-gestational diabetes and GDM in present pregnancy but we did not find them significantly more in the cases as compared to the control group, may be because of small sample size. Age and parity as risk factors couldn't be studied as we have taken age and parity matched controls. Seasonal variations also could not be studied as recruitment of subjects was done in winter season only. More large scale studies are required to study VDD as a risk factor for preeclampsia and eclampsia.

CONCLUSION

Significant risk factors for preeclampsia and eclampsia in our study were rural background, previous history of preeclampsia and multiple pregnancy. Our study revealed a very high prevalence of VDD in pregnant women. Mean serum 25(OH)D levels were less than 10 ng/l in all pregnant women recruited in the study. There was significant difference in the mean serum 25(OH)D levels in women who developed preeclampsia/eclampsia (6.7236ng/l in women with preeclampsia and eclampsia9.8862ng/l in the control group,p=0.004) as compared to controls. Prevalence of VDD or Vitamin D insufficiency was not significantly different in pregnant women with preeclampsia or eclampsia as compared to women who did not have preeclampsia or eclampsia.

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Conflict of interest: None declared

Ethical approval: This study was based on ethical guidelines for biomedical research on human subjects as given in the "Declaration of Helsinki" and by Central Ethics Committee on Human Research (CEHER) of ICMR, New Delhi

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