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Prevention of Preeclampsia with Vitamin D supplement in Pregnant Women

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ABSTRACT

Objective: *to evaluate the effectiveness of vitamin D supplementation in preeclampsia prevention in pregnant women.*

Methods: *A total of 250 patients with diagnosis of preeclampsia were enrolled. The study focused on analyzing the vitamin D levels of these patients, and individuals with 25-hydroxy vitamin D levels ≥25 ng/ml were included. Exclusions comprised patients with immunological diseases, lack of confidence in cooperation, pre-existing renal insufficiency, hypertension before conception, cardiac disease, and those who left during the study.*

Results: *In the intervention group, 78 females 62.4% experienced normal vaginal delivery, 33.6% underwent cesarean section (C/S), and 4.0% opted for abortion. Similarly, in the control group, 62 females 49.6% had normal vaginal delivery, 45.6% had C/S, and 4.8% chose abortion. However, it is noteworthy that the observed differences between the two groups were deemed statistically insignificant, 24.8% preeclampsia presented in intervention versus 18.4% in control groups, ($p<0.001$).*

Conclusion: *Vitamin D supplementation during pregnancy is helpful in reduction of preeclampsia and gestational hypertension.*

Keywords: *Gestational hypertension, Vitamin D, Preeclampsia, Proteinurea, Pregnant women.*

1. INTRODUCTION

Preeclampsia, characterized by proteinuria and high blood pressure after 20 weeks of pregnancy, affects approximately

8% of pregnancies and contributes to 25% of maternal deaths, making it a leading cause of perinatal morbidity and mortality[1,2]. It is important to note that preeclampsia is not merely hypertension during pregnancy with associated proteinuria; rather, it is diagnosed when proteinuria exceeds 300mg in a 24-hour urine collection or when there is continuous protein excretion in randomly collected urine samples (30mg per deciliter)[3,4]. A 2018 national survey in Pakistan revealed a high prevalence of vitamin D deficiency, reaching up to 79.9%, especially among the reproductive-age population[5].

Multiple instances in previous literature have documented the occurrence of calcium metabolism abnormalities or hypocalciurea, coupled with vitamin D deficiency, which later manifested as preeclampsia[6]. Contributing factors to the development of preeclampsia encompass diabetes mellitus, hypertension[7], diploid pregnancy, multi gravidity, family history of preeclampsia, nulliparous women, obesity, immune disorder and renal insufficiency[8]. Noteworthy that the occurrence of preeclampsia in a particular pregnancy does not necessarily serve as a predictive indicator for its recurrence in subsequent pregnancies[9].

The development of low birth weight in early pregnancy is linked to a higher likelihood of recurrence in subsequent pregnancies[10]. Throughout pregnancy, vitamin D assumes a paramount role, surpassing other nutritional factors, as its deficiency is correlated with increased risks of low birth weight and maternal comorbidities[11]. Vitamin D deficiency is widespread globally, with prevalence rates ranging from 18% to 84%, contingent on factors such as geographical location, local clothing customs, ethnicity, and dietary habits[12]. Numerous studies have investigated the connection between vitamin D levels and pregnancy outcomes, yielding conflicting results on associations with mode of delivery, preterm labor, and diabetic status[13].

In previous studies, disruptions in the Th1 and Th2 immune responses were reported, indicating their role in the overexpression of cytokines and subsequent immunological tolerance of embryo implantation[14]. Several hypotheses have been proposed linking the etiology of preeclampsia to a deficiency of vitamin D during pregnancy. In this study, we administered vitamin D supplements to women with a history of preeclampsia, specifically focusing on a population in South Punjab, aiming to address the local reference gap evident in the existing literature.

2. METHODOLOGY

Study initiated after approval from the departmental ethical committee and informed consent was from patients attending the outpatient department and with a history of previous preeclampsia. The study focused on analyzing the vitamin D levels of these patients, and individuals with 25-hydroxy vitamin D levels ≥25 ng/ml were included. Exclusions comprised patients with immunological diseases, lack of confidence in cooperation, pre-existing renal insufficiency, hypertension before conception, cardiac disease, and those who left during the study.

Patients were randomly assigned to case or control group through a lottery method, and after a 12-hour fasting period, blood samples were collected for vitamin D level assessment upon obtaining patient consent. The samples were then sent to the laboratory. In the intervention group, patients received 50000 IU capsules of vitamin D3 after 15 days, and all participants were instructed to continue

taking the assigned medication (placebo or vitamin D) until the 36th week of gestation. Preeclampsia diagnosis was determined through clinical examination or laboratory investigation, with criteria including blood pressure readings of 140/90 mmHg and proteinuria of +1. Blood pressure monitoring occurred every 15 days throughout the medication period. SPSS version 24 was used for analysis of data, P value less than or equal to 0.05 was taken as significant.

3. RESULTS

The study comprised a total of 250 patients, one receiving interventions and the other serving as controls. Notably, the baseline characteristics and demographic, BMI, age, gestational age, number of pregnancies, diastolic and systolic blood pressure, proteinuria at 24-hour, exhibited remarkable similarity between the two groups, with p-values exceeding 0.050, as detailed in Table I.

In the intervention group, 78 females (62.4%) experienced normal vaginal delivery, 42 (33.6%) underwent cesarean section (C/S), and 5 (4.0%) opted for abortion. Similarly, in the control group, 62 females 57 (45.6%) had C/S, (49.6%) had normal vaginal delivery, and 6 (4.8%) chose abortion. However, it is noteworthy that the observed differences between the two groups were deemed statistically insignificant, as indicated in Table II.

Comparison of preeclampsia was shown in table. III. 31 (24.8%) preeclampsia presented in intervention versus 23 (18.4%) in control groups, ($p<0.001$). (Table. III).

Table-I: Demographics and study characteristics

Characteristic	Intervention Group N (%)	Control Group N (%)	p-value*
Age (years)	36.12±9.56	35.36±8.82	0.515
BMI (kg/m^2)	25.87±7.38	26.08±9.12	0.837
Gravidity	3.15±1.25	3.41±1.19	0.089
Gestational age	14.53±2.41	14.21±2.58	0.301
Blood pressure systolic (mm Hg)	121.52±3.33	119.87±3.41	0.412
Blood pressure diastolic (mm Hg)	76.86±3.01	76.78±2.95	0.840
Proteinuria/24 hours (mg/cc)	135.64/1864.02±2.21	135.76/1969.11±2.31	0.687

Table-II: Pregnancy type

Termination of Pregnancy	Study Group N (%)	Control Group N (%)	p-value*
NVD	78 (62.4)	62 (49.6)	0.063
C/S	42 (33.6)	57 (45.6)	0.052
Abortion	5 (4.0)	6 (4.8)	0.843

Table-III: Comparison of outcomes (preeclampsia) for the study groups

Preeclampsia	Intervention Group N (%)	Control Group N (%)	p-value
Preeclampsia	23 (18.4)	31 (24.8)	<0.001
Non-Preeclampsia	102 (81.6)	94 (75.2)	

4. DISCUSSION

This study suggests that early pregnancy supplementation with vitamin D can significantly reduce the incidence of preeclampsia, with a strong observed association between preeclampsia and vitamin D concentration. Preeclampsia occurred in 18.4% of patients who received vitamin D supplementation, compared to 24.8% in the control group. Supporting our findings, a study by Behjat Sasam et al[15] concluded that vitamin D therapy is highly beneficial in decreasing preeclampsia and hypertension due to pregnancy, particularly when administered in the early stages of pregnancy, effectively inhibiting the recurrence of preeclampsia.

In 2002, Li et al[16] conducted a study suggesting that vitamin D deficiency is linked to hypertension, and they found that adequate vitamin D supplementation during pregnancy may prevent the onset of preeclampsia and gestational hypertension. Additionally, a study by Cardus A et al[17] concluded that vitamin D has the capability

to regulate renal vascular endothelial growth factor (VEGF), a factor associated with proteinuria in pregnancy, as VEGF influences gene transcription and governs the overall transportation of protein urea.

Mackay et al[18] conducted a study indicating that the measurement of 25-hydroxy vitamin D levels in pregnant women is a viable method to assess vitamin D status, and their research highlights associations between low vitamin D levels and adverse pregnancy outcomes such as the development of preeclampsia, preterm labor, and fetomaternal mortality, consistent with findings from various observational studies. Past literature has consistently reported an association between preeclampsia and low vitamin D levels, suggesting that this relationship may be addressed through the use of vitamin supplementation[19].

In a study conducted by Ramon et al[20] it was revealed that numerous clinical trials funded by the National Institute of Health aimed to assess the vitamin D role in preventing preeclampsia. The findings consistently indicated a positive association between vitamin D deficiency during pregnancy and the occurrence of gestational hypertension associated preeclampsia. Additionally, Lai et al[21] reported a significant positive correlation between preeclampsia and levels of vitamin D, with a CI 95%, odds ratio of 4.2, and a p-value of 0.04. The study suggested the potential benefits of administering vitamin D from the first trimester of pregnancy.

Olsen et al's[22] study suggested that vitamin D alone is not effective in preventing preeclampsia, but when combined with multivitamins and minerals, it proves to be useful; they recommended a daily dose of vitamin D (900 IU) in the form of liver oil. In a trial conducted by Marya et al[23] with 400 pregnant women, the administration of 1200 IU of vitamin D and a daily calcium supplement of 375 mg resulted in a significant reduction in blood pressure ($p<0.001$), although the decrease in preeclampsia incidence compared to the placebo was not statistically significant.

Limitations: The study may have a small sample size, limiting the finding generalizability to a larger population. If the targeted population is not represented by sample., there may be selection bias, and the results may not be applicable to all pregnant women.

Other factors that may influence the development of preeclampsia, such as dietary habits, socioeconomic status, and pre-existing health conditions, may not be adequately controlled for in the analysis.

Recommendations: Provide comprehensive education to pregnant women about the importance of maintaining optimal Vitamin D levels and the potential benefits in preventing preeclampsia. This includes dietary sources, sunlight exposure, and adherence to prescribed supplements.

5. CONCLUSION

Vitamin D supplementation during pregnancy is helpful in reduction of preeclampsia and gestational hypertension. Worldwide low vitamin D levels are prevalent, pregnant women and their neonates are especially vulnerable.

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