

Original Research Article

Vitamin D supplementation reduces the risk of preeclampsia in high-risk pregnant females

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ABSTRACT

Background: Maternal vitamin D insufficiency has been linked with increased risk of preeclampsia. Despite this, the evidence regarding the efficacy of vitamin D supplementation in preventing preeclampsia is controversial. The aim of study was to collate the incidence of preeclampsia in high-risk females with vitamin D supplementation versus placebo.

Methods: The present study was a randomized controlled trial. The study was conducted in the department of obstetrics and gynecology, Madinah Teaching Hospital affiliated with University Medical and Dental College Faisalabad. The study was collected over one year from July 2019 to June 2020. Patients were randomly assigned to two groups. Patients in group-A were given vitamin D supplementation of 600 IU daily. The control group (group-B) was given placebo. If blood pressure (BP) $\geq 140/90$ mmHg and proteinuria found positive in urine, then preeclampsia was labeled (as per operational definition). Both groups were compared for preeclampsia by using Chi-square test. P value <0.05 was taken as significant.

Results: The incidence of preeclampsia was 4% (n=2/150) in group A and 8% (n=6/150) in group B developed preeclampsia. The difference was (p value=0.3) insignificant difference.

Conclusions: Vitamin D addition in pregnancy did not demonstrate a statistically significant effect of vitamin D on the prevention of preeclampsia.

Keywords: Vitamin D supplementation, Preeclampsia, Pregnancy

INTRODUCTION

Vitamin D is a significant component for human health.¹ There is widespread presence of vitamin D insufficiency all over the world. Studies reported from different countries have shown prevalence of vitamin D deficiency in pregnant women ranging from 4% to 60%.² Pakistan has the highest incidence of adult vitamin D deficiency in South Asia at 73%.³ Vitamin D deficiency has been recently reported to be associated with hypertension, coronary artery disease, diabetes, asthma, rheumatoid

arthritis, other autoimmune diseases, and certain cancers.⁴ Vitamin D deficiency has been associated with immune and endothelial disorder and intricately in the pathophysiology of preeclampsia.^{5,6}

Preeclampsia is a multi-organ disease defined by raised blood pressure of $\geq 140/90$ mm of Hg and proteinuria of 300 mg in 24-hour urine collection after 20 weeks of pregnancy.⁷ The occurrence of severe preeclampsia is 1-2%, and may be complicated by placental abruption, acute renal failure, haemolysis, elevated liver enzymes, low

platelet count (HELLP) syndrome, and increased chance of unfortunate pregnancy outcomes.⁸

Several studies explored the relationship between maternal vitamin D level and preeclampsia, and a relationship between maternal vitamin D deficiency and severe preeclampsia has been observed in some studies. Contrarily, other studies have not observed any relationship.⁹

The aim of study was to evaluate the effect of vitamin D supplementation on the incidence of preeclampsia in the high-risk pregnancies.

METHODS

This study was a randomized controlled trial, conducted in the department of obstetrics and gynaecology department of Madina Teaching Hospital Faisalabad from January 2019 to June 2019. Sampling technique was non-probability, consecutive sampling. Total 150 pregnant high-risk females of age 18-40 years, parity <5, at or more than 16 weeks of gestation were included in the study. Pregnant women having first pregnancy, history of chronic hypertension, pregnancy induced hypertension, previous history of pre-eclampsia, body mass index (BMI) >25, twin gestation was categorized as high-risk females. Females already taking vitamin D, allergic to vitamin D, having preterm labor and not willing to follow the study protocol were excluded. Ethical review of the study was acquired from ethical committee of University Medical and Dental College Faisalabad.

Patients meeting the inclusion criteria were randomly split in two groups. Patients in group-A were given vitamin D supplementation of 600 IU daily. The control group (group B) was given placebo. Both groups were given a study drug (vitamin D or placebo) from day of enrolment in study till 36 weeks of gestation.

Diagnosis of preeclampsia was made by clinical examination and biochemical tests (blood pressure of $\geq 140/90$ mm of Hg and proteinuria of greater than +1 on urine complete examination). Blood pressure was recorded twice weekly. If blood pressure was $\geq 140/90$ mm of Hg, urine was sent for proteinuria. If the blood pressure was normal, the patient was recalled after 14 days.

Data was analyzed through statistical package for the social sciences (SPSS) 21. Quantitative variables like age, gestational age, BMI, BP, and proteinuria were calculated as mean and SD. Qualitative variables like preeclampsia was presented as frequency. Parity was also presented as frequency. Both groups were compared for preeclampsia by using Chi-square test. P value ≤ 0.05 was taken as significant. Data was stratified for age, gestational age, BMI, and parity. Post-stratification, chi-square test was applied to compare stratified groups. P value ≤ 0.05 was taken as significant.

RESULTS

150 patients (75 in each group) fulfilling the selection criteria were enrolled to compare the incidence of preeclampsia with vitamin D supplementation versus placebo. Age distribution showed that 86.67% (n=65) in group A and 85.33% (n=64) in group B were between 18-30 years of age whereas 13.33% (n=10) in group A and 14.67% (n=11) in group B were between 31-40 years of age, mean and SD was calculated as 26.4 ± 3.60 years in group A and 26.83 ± 3.29 years in group B (Table 1).

Table 1: Age distribution (n=150).

Age (years)	Group A (n=75)		Group B (n=75)	
	No. of patients	%	No. of patients	%
18-30	65	86.67	64	85.33
31-40	10	13.33	11	14.67
Total	75	100	75	100
Mean \pm SD	26.4 ± 3.60		26.83 ± 3.29	

Mean blood pressure in group A was 124.58 ± 11.51 mmHg in group A and 126.73 ± 10.87 mmHg in group B. Mean proteinuria in group A was 0.68 ± 0.19 and 0.73 ± 0.23 in group B (Table 2).

Table 2: Mean blood pressure (n=150).

Parameter	Group A (n=75)		Group B (n=75)	
	Mean	SD	Mean	SD
Blood pressure (mmHg)	124.58	11.51	126.73	10.87

Comparison of the frequency of preeclampsia in patients with vitamin D supplementation versus placebo shows that 4 % (n=2) in group A and 8 % (n=6) in group B developed preeclampsia (Table 4). P value was 0.30 showing insignificant difference.

Table 3: Mean proteinuria (n=150).

Parameter	Group A (n=75)		Group B (n=75)	
	Mean	SD	Mean	SD
Proteinuria	0.68	0.19	0.73	0.23

Table 4: Comparison of frequencies of preeclampsia in high-risk females with vitamin D supplementation versus placebo (n=150).

Preeclampsia	Group A (n=75)		Group B (n=75)	
	No. of patients	%	No. of patients	%
Yes	2	4	6	8
No	72	96	69	92
Total	75	100	75	100

P value=0.30

DISCUSSION

Preeclampsia is related to detrimental maternal and fetal outcome, so there is increased need to recognize clinical and laboratory predictors of preeclampsia.¹⁰ It is also important to spot effective methods to prevent its development. Preeclampsia is the common reason of maternal and perinatal morbidity and mortality. Vitamin D supplementation has been considered to reduce the risk of preeclampsia.

Evidence to assess the efficacy of vitamin D supplementation in preventing pregnancy preeclampsia is not sufficient. We know it is observational rather than experimental, therefore, currently vitamin D supplementation is not customarily suggested in pregnancy.¹¹ In the current study, we evaluated the role of vitamin D addition in decreasing the chance of preeclampsia. Our results showed that the rate of occurrence of preeclampsia in case group, who get vitamin D, was less than control group but this dissimilarity between case and control groups was not statistically non-significant.

A current Cochrane review observing the impact of vitamin D addition on threat of preeclampsia included two RCTs.¹² The meta-analysis of the results from these trials did not demonstrate any significant trend to decrease chance of preeclampsia in females who get the vitamin D supplementation.

Stougaard et al in 2018 also found no confirmation to hold up the role of vitamin D in lowering preeclampsia risk.¹³

Mirzakhani et al found that vitamin D supplementation did not decrease the incidence of preeclampsia, which also support our results.¹⁴ Our results are in contrary to the study conducted in Iran which concluded that significantly lower probability of preeclampsia in intervention group (vitamin D supplementation).¹⁵

Purwani et al also concluded that there is no independent impact of vitamin D supplementation to stop the development of preeclampsia.¹⁶

Our results are disagreed with a study conducted by Fogacci in which results indicate that vitamin D supplementation may be helpful in preventing preeclampsia.¹⁷

Further well-designed, prospective, randomized trials of vitamin D with adequate sample size that manages dietary submission will be mandatory to settle a probable function of vitamin D in the prevention of preeclampsia.

Limitations

The study was conducted in single center. If the same study is conducted in multiple centers than more elaborated and better results can be achieved.

CONCLUSION

There is consistent documentation of association between low vitamin D level and detrimental preeclampsia outcomes. Results from vitamin D supplementation during pregnancy did not demonstrate a statistically significant impact of vitamin D on the threat of preeclampsia. And further trials are required to further clarify the impact of vitamin D augmentation to reduce the incidence of preeclampsia.

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