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Original Research Article

# Vitamin D as a Novel Biomarker for Grading the Severity of Preeclampsia: A Cross-Sectional Case Control Study

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**Abstract**

**Introduction:** Preeclampsia remains a leading cause of maternal and perinatal morbidity worldwide. The importance of vitamin D for placental function, endothelial integrity, and immunological regulation is increasing. The purpose of this study was to measure serum vitamin D levels in pregnant women with preeclampsia and normotension and to see if it could be used as a biomarker to rate the severity of the condition.

**Aims and objectives:** The objectives of this study were: (i) to estimate serum vitamin D levels in pregnancies with normotension, severe pre-eclampsia, and mild pre-eclampsia, (ii) to determine the relationship between the severity of the disease and vitamin D levels.

**Material and Methods:** A tertiary care teaching hospital served as site of this cross-sectional case-control study. A total of 120 third-trimester pregnant women has been recruited and split into three groups: 40 normotensive controls, 40 with mild preeclampsia, and 40 with severe preeclampsia. Competitive enzyme-linked immunoassay (ELISA) was used to measure serum vitamin D levels. Biochemical and clinical parameters were compared among groups. One-way ANOVA and Pearson correlation were used for statistical analysis.

**Results:** Women with preeclampsia have been significantly lower mean serum vitamin D levels than normotensive controls ($p < 0.00001$). As the severity of preeclampsia increased, vitamin D levels gradually decreased. Diastolic blood pressure (DBP), systolic blood pressure (SBP), and proteinuria were all significantly correlated negatively with serum vitamin D.

**Conclusion:** Serum vitamin D levels are markedly lower in preeclampsia and show a negative correlation with the severity of the illness. One possible biomarker for identifying high-risk pregnancies and grading preeclampsia is vitamin D.

**Keywords:** Preeclampsia, Vitamin D, Placental Function.

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## Introduction

Pre-eclampsia, a hypertensive condition specific to pregnancy, is defined as new-onset hypertension with or without proteinuria after 20 weeks of pregnancy. The etiology of pre-eclampsia is complex.

A widely accepted two-phase model, as outlined by Roberts and Hubel, suggests that an abnormal placenta at the beginning of pregnancy causes oxidative stress and placental ischemia, followed by a systemic inflammatory response in the mother and widespread endothelial dysfunction. [1] It remains one of the leading causes of morbidity and mortality among mothers and newborns around the world. [1, 2] Despite progress in maternal care, it is still difficult to detect serious disease early and delivery is often the only effective treatment. Clinically, these changes manifest themselves as proteinuria, hypertension, and multiple organ involvement. The search for biomarkers that reflect these pathophysiological processes could help in early diagnosis and disease surveillance.

Fat-soluble vitamin D is necessary for immuno logical control, vascular homeostasis, and the metabolism of calcium and bone. Vitamin D receptors and activating enzymes are expressed in the placenta, suggesting a possible function in

trophoblast invasion and placental development. [3] Vitamin D deficiency has been linked to endothelial dysfunction, dysregulated immune responses, and poor placental implantation—all of which are characteristics of pre-eclampsia. Even in areas with sufficient sun exposure, vitamin D deficiency is very common among pregnant women worldwide. [4] Low maternal serum vitamin D levels have been linked to a higher risk of hypertensive disorders of pregnancy, including pre-eclampsia, according to a number of observational studies. [5-9] Systematic reviews and meta-analyses showing an inverse relationship between maternal vitamin D status and pre-eclampsia risk further corroborate these findings. [10-13]

The relationship between vitamin D deficiency and the severity of pre-eclampsia, however, has received little attention. Grading disease severity is clinically significant because severe pre-eclampsia is linked to higher risks of maternal complications like HELLP syndrome, eclampsia, acute kidney injury, and unfavorable perinatal outcomes. Therefore, there would be significant clinical value in finding a single, reasonably priced biomarker that could stratify the severity of the disease. This study aimed to assess the potential of vitamin D as a biomarker for disease severity grading by measuring serum vitamin D levels in pregnant women with mild and severe pre-eclampsia and comparing them with normotensive women.

## Materials and Methods

This Case-control research was carried out by the clinical biochemistry and obstetrics departments of the ESIC Medical College and Hospital, Indore, M.P., with the permission of the ethics committee. One hundred and twenty pregnant women, ages 18 to 35, have been "selected from obstetrics and gynecology department. Cases included 40 pregnant women with severe preeclampsia and 40 pregnant women with mild preeclampsia. Forty pregnant women" of the same age who had normal blood pressure (BP) were used as the control group. Every study participant gave written informed consent.

**Inclusion Criteria:** Each case had to be a singleton, occur in 3rd trimester of pregnancy, between the ages of 18 and 35, have normal blood pressure for 1st 20 weeks of pregnancy, and have no history of hypertension (more than 28 weeks of gestation).

**Exclusion Criteria**, include having multiple fetuses during a pregnancy, taking medication for diabetes, having a hepatic or chronic renal condition, having chorioamnionitis, a urinary tract infection, or a comparable illness, as well as smoking and drinking together. Five milliliters of blood were drawn from the patient while they were fasting using aseptic techniques and placed in a clot activator tube. Serum was separated and analyzed in order to perform biochemical experiments. Serum vitamin D was measured using ELISA, which is based on competitive binding principle.

**Analysis of statistics:** The quantitative and statistical analyses were performed using Microsoft Excel and IBM SPSS version 15. With a ± standard deviation, data were presented as mean. After post-hoc Tukey and one-way variance analysis of the data, the mean values of the 3 groups were compared. The Pearson correlation coefficient was used to evaluate the correlation between variables. We considered something statistically significant when the p-value was $< 0.05$.

## Results and Observations

Both Table 1 and Table 2 present the biochemical and demographic details of the research participants. Table 1 and Figure 1: According to the study's findings, people with extreme preeclampsia had significantly higher mean BP (157.6/117.2 mmHg). The blood pressure of patients with mild preeclampsia was 132/89.2 mmHg. Pregnant women with normal blood pressure, on the other hand, had a reading of 108.6/75.1 mmHg. Serum uric acid levels for pregnant women with severe preeclampsia were 6.27 ± 0.47 mg/dl. In contrast, the serum uric acid level in pregnant women with mild preeclampsia was 4.16 ± 0.30 mg/dl. Finally, pregnant women with normotensive had a blood uric acid level of 2.92 ± 0.54 mg/dl. Pregnant women with severe preeclampsia had an average urine albumin level of 1.11 ± 0.08 grams per day. On the other hand, pregnant women with moderate preeclampsia had a mean value of 0.64 ± 0.08 g/day. Pregnant women with normotensive preeclampsia had an average daily value of 0.17 ± 0.03 grams. The mean "serum uric acid, BP, and urine albumin level of pregnant women with extreme preeclampsia, mild preeclampsia, normotensive" circumstances were found to differ significantly ($P<0.00001$ across the three groups) Figure 2 and Table 2. Serum vitamin D levels were 29.72±2.46ng/ml on average in control group, 23.68±0.96ng/ml in mild preeclampsia group, and 15.79±0.41ng/ml in extreme preeclampsia group.

An analysis of the data revealed that pregnancy with extreme preeclampsia had a considerably lower blood vitamin D level ($P < 0.00001$). A matched comparison of research participants' blood vitamin D levels is displayed in Table 3. When comparing "mean serum vitamin D levels of normotensive preeclampsia and mild preeclampsia, a statistically significant outcome ($P < 0.00001$) was found. In contrast to pregnant women with moderate preeclampsia, normotensive women have higher vitamin D levels. Comparing mean serum vitamin D levels of 2 groups with normotensive

and extreme preeclampsia produced a statistically significant outcome (P < 0.00001). The findings indicated that pregnant women with severe preeclampsia have lower vitamin D levels than pregnant women with normal BP. A comparison of mean serum vitamin D levels" among moderate and extreme preeclampsia revealed statistical significance (P < 0.00001). Compared to cases with moderate preeclampsia, those with extreme preeclampsia have a decreased vitamin D level. The degree of proteinuria (r = -0.946), DBP (r = -0.9512), and SBP (r = -0.959) all significantly correlated negatively with serum vitamin D levels (Table 4).

**Table 1: Comparison of demographic & clinical profile between cases and controls.**

| Variables | Normotensive Pregnancies (n=40) | Pregnancies with mild Preeclampsia (n=40) | Pregnancies with severe Preeclampsia (n=40) | F- value | P- value |
|---|---|---|---|---|---|
| Age (Years) | 24.72±1.11 | 24.71±1.07 | 24.31±1.05 | 1.8738 | 0.1581 |
| SBP (mmHg) | 108.6±2.57 | 132±3.39 | 157.6±1.98 | 3271.71 | <0.00001 |
| DBP (mmHg) | 75.1±4.41 | 89.2±2.06 | 117.2±2.25 | 1911.30 | <0.00001 |
| Serum Uric acid (mg/dl) | 2.92±0.54 | 4.16±0.30 | 6.27±0.47 | 569.75 | <0.00001 |
| Urine albumin (gm/day) | 0.17±0.03 | 0.64±0.08 | 1.11±0.08" | 1862.81 | <0.00001 |

**Table 2: Comparison of mean serum vitamin D between in study subjects.**

| Study Subjects | N | Mean serum vitamin D (ng/ml) | Standard Deviation | F Test | P value | Result |
|---|---|---|---|---|---|---|
| Normotensive | 40 | 29.72 | 2.46 | 817.68 | <0.00001 | Significant |
| Mild Preeclampsia | 40 | 23.68 | 0.96 | | | |
| Severe Preeclampsia | 40 | 15.79 | 0.41 | | | |

**Table 3: Pair-wise comparison of mean serum vitamin D.**

| Pair | F factor | P value | Interpretation |
|---|---|---|---|
| Normotensive- Mild Preeclampsia | 208.58 | <0.00001 | Significant |
| Normotensive- Severe Preeclampsia | 1245.82 | <0.00001 | Significant |
| Mild Preeclampsia -Severe Preeclampsia | 2272.19 | <0.00001 | Significant |

**Table 4: Correlation analysis between clinical variables.**

| | SBP | | DBP | | Urine albumin | |
|---|---|---|---|---|---|---|
| | r | p | r | p | r | p |
| Serum vitamin D (ng/ml) | -0.959 Strong negative | <0.00001 | -0.9512 Strong negative | <0.00001 | -0.946 Strong negative | <0.00001 |

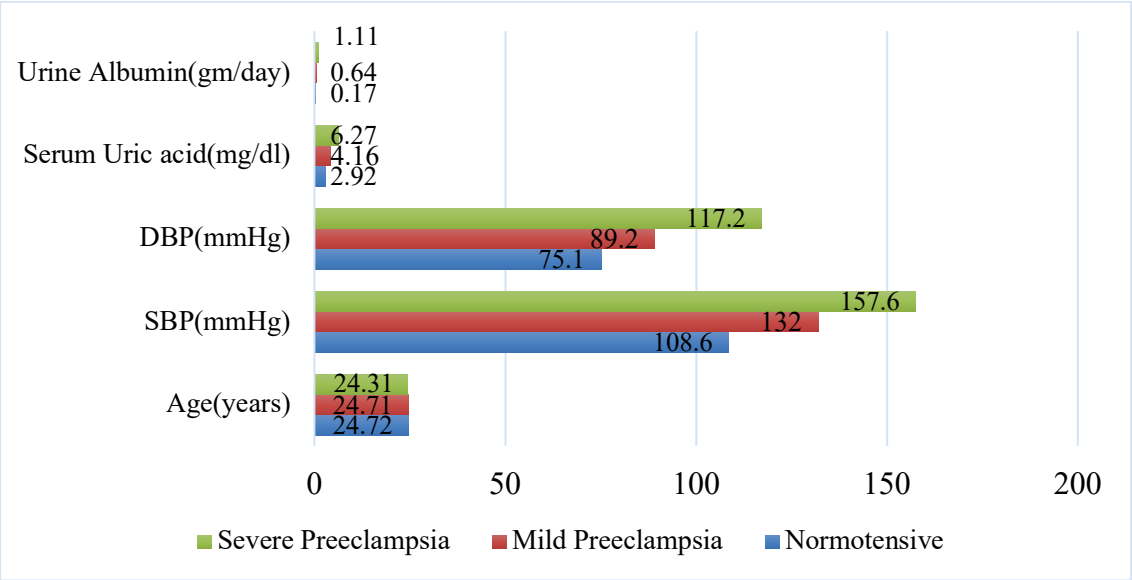


**Figure 1: Comparison of Demographic & Clinical profile between cases and controls.**

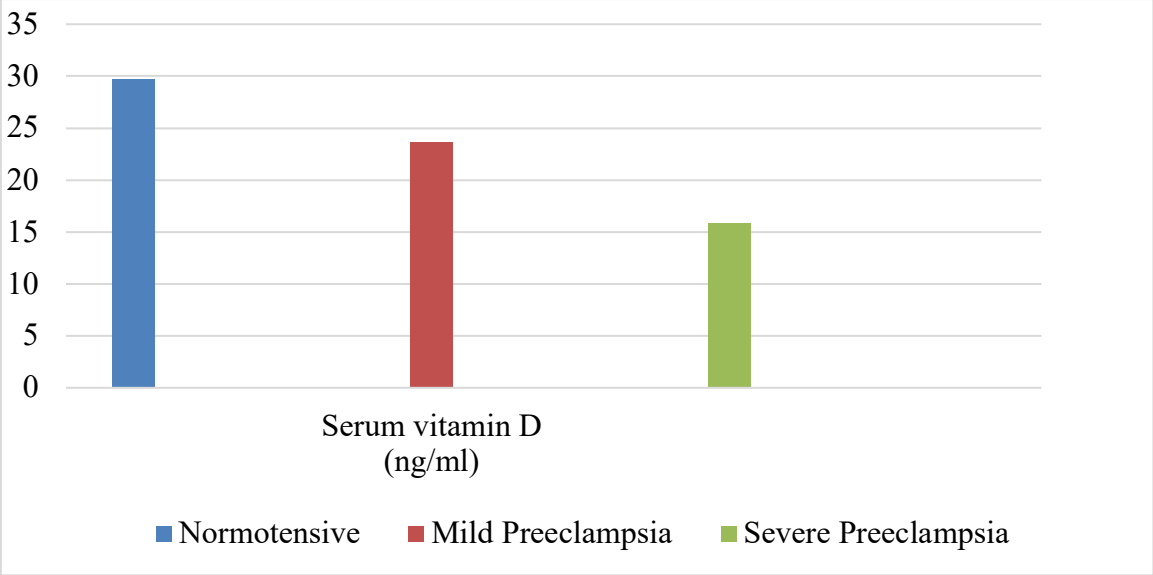


**Figure 2: Comparison of mean Serum vitamin D in study subjects**

## Discussion

The present study demonstrates a strong inverse association between serum vitamin D levels and both the presence and severity of pre-eclampsia. Vitamin D levels were significantly lower in women with pre-eclampsia compared with normotensive pregnant women, with the lowest concentrations observed among those with severe disease. These findings suggest that declining vitamin D levels may reflect increasing disease severity.

Our results align with previous research conducted by Wei et al. [5] and Bodnar and associates, [6] showed that a higher risk of pre-eclampsia is linked to lower maternal serum vitamin D levels. Ullah et al. [7] reported similar findings, who found that vitamin D deficiency is a risk factor for eclampsia and pre-eclampsia. Robinson and others., [8] found that women with early-onset severe pre-eclampsia had significantly lower vitamin D levels, confirming the link between vitamin D deficiency and the severity of the illness. Achkar and others., [9] discovered that a higher risk of pre-eclampsia was linked to low vitamin D status in the early stages of pregnancy. This association has been reinforced by evidence from meta-analyses and systematic reviews. Christesen et al., [10] found that by controlling placental growth factor and vascular endothelial growth factor, which are both dysregulated in pre-eclampsia, vitamin D affects placental function and angiogenic balance. By controlling cytokine production and fostering immune tolerance at the mother-fetal interface, vitamin D plays a crucial role in immune modulation. This limits excessive inflammatory responses that lead to endothelial dysfunction and vasoconstriction. Purswani and associates, [11] emphasized in their systematic review how vitamin D deficiency contributes to the onset of pre-eclampsia. Further evidence connecting vitamin D deficiency to the increasing incidence of pre-eclampsia came from Hyppönen's [12] population-based study. Additionally, Zhou et al., [13] demonstrated by a meta-analysis that a significant risk of pre-eclampsia is associated with a vitamin D deficiency. By demonstrating a graded decline in vitamin D levels with increasing disease severity, the current study adds to the body of evidence and supports the potential role of vitamin D as a severity-related biomarker. The biological plausibility of this association is supported by mechanistic evidence.

The current study's serum vitamin D levels showed a significant inverse relationship with blood pressure parameters, offering more proof of vitamin D's role in vascular regulation. Severe pre-eclampsia is characterized by significant endothelial dysfunction, which can be exacerbated by vitamin D deficiency through increased oxidative stress and decreased nitric oxide synthesis. These mechanisms may account for the observed association between lower vitamin D levels and more severe clinical manifestations. Evidence from interventional studies, like the most recent meta-analysis by Rezavand N et al. [14] and Palacios et al. [15] suggests that taking vitamin D supplements during pregnancy may reduce the risk of pre-eclampsia, although results vary based on study type and population.

The cross-sectional design of this study hinders causal inference, and the single-center design may limit generalizability. Nonetheless, the study is strengthened by standardized laboratory measurements, strong statistical analysis, and the inclusion of both mild and severe pre-eclampsia groups.

## Conclusion

Pregnant women with preeclampsia must be identified and treated as soon as possible in order to improve their pregnancy. Clinical criteria that rely on clinical signs are commonly used to diagnose pre-eclampsia. There isn't currently a clinically accepted standard diagnostic test. According to this study, women with preeclampsia had significantly lower serum vitamin D levels, which progressively drop as the condition gets worse. The observed inverse relationship between vitamin D levels and clinical parameters such as blood pressure and proteinuria suggests that vitamin D deficiency may be associated with more severe disease manifestations.

These findings support the use of serum vitamin D as a novel, readily available, and affordable biomarker for grading the severity of preeclampsia. In addition to enabling closer monitoring and timely intervention, routine prenatal screening that includes a vitamin D assessment may help identify women who are more likely to develop severe illness. More thorough prospective studies are required to establish causality and determine whether vitamin D supplementation may be influencing the course of the disease or improving maternal and perinatal outcomes.

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## References:

1. Roberts JM, Hubel CA. The two stage model of preeclampsia: variations on the theme Placenta. 2009;30 Suppl A: S32-S37.
2. American College of Obstetricians and Gynecologists. Gestational hypertension and preeclampsia. Obstet Gynecol. 2020;135(6): e237-e260.
3. Tamblyn JA, Hewison M, Wagner CL, et al. Immunological role of vitamin D at the maternal-fetal interface. J Endocrinol. 2015: 224(3):R107-R121.
4. Urrutia RP, Thorp JM. Vitamin D in pregnancy: current concepts. Curr Opin obstet Gynecol. 2012;24(2):57-64.
5. Wei SQ. Audibert F, Hidiroglou N, et al. Longitudinal vitamin D status in pregnancy and the risk of preeclampsia. BJOG. 2012;119(7):832-839.
6. Bodnar LM, Catov JM, Simhan HN, et al. Maternal vitamin D deficiency increases the risk of preeclampsia. J Clin Endocrinol Metab. 2007:92(9):3517-3522.
7. 7.Ullah MI, Koch CA, Tamanna S, et al. Vitamin D deficiency and the risk of preeclampsia and eclampsia. Clin Endocrinol. 2013;78(3):381-387.
8. Robinson CJ, Wagner CL, Hollis BW, et al. Maternal vitamin D and fetal growth in early-onset severe preeclampsia. Am J Obstet Gynecol. 2011;204(6): 556.e1-556.e4.
9. Achkar M, Dodds L, Giguère Y, et al. Vitamin D status in early pregnancy and risk of preeclampsia. Am J Obstet Gynecol. 2015:212(4): 511.e1-511.e7.
10. Christesen HT, Falkenberg T, Lamont RF, et al. The impact of vitamin D on pregnancy: a systematic review. Acta Obstet Gynecol Scand. 2012:91(12):1357-1367.
11. Purswani JM. Gala P, Dwarkanath P, et al. The role of vitamin D in pre-eclampsia: a systematic review. BMC Pregnancy Childbirth. 2017; 17:231.
12. Hyppönen E. Vitamin D and increasing incidence of preeclampsia. Nutrients. 2015;7(7):5558- 5572.
13. Zhou J, Wang J, Xiong Y, et al. Association between vitamin D deficiency and preeclampsia: a meta-analysis. J Hum Hypertens. 2017:31(10):695-704.
14. Rezavand N, Veisi F, Zangeneh M, et al. Association between vitanmin D deficiency and preeclampsia: a case-control study. Int J Reprod Biomed. 2019;17(8):581-586.
15. Palacios C, De-Regil LM, Lombardo LK, et al. Vitamin D supplementation during pregnancy: updated meta-analysis. BMJ. 2019; 366:14733.