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Association Between Preeclampsia and Hypovitaminosis D in Females Presenting During Third Trimester of Pregnancy

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Abstract

Background: Preeclampsia is a major cause of maternal and perinatal morbidity, while vitamin D deficiency is highly prevalent among pregnant women in developing countries. Emerging evidence suggests a possible association between hypovitaminosis D and hypertensive disorders of pregnancy. **Objective:** To determine the association between vitamin D deficiency and preeclampsia among women presenting during the third trimester of pregnancy. **Methods:** This was a hospital-based case–control comparative study conducted at the Outpatient Department of Obstetrics and Gynaecology, Services Hospital, Lahore, from March 2025 to June 2025. A total of 200 pregnant women presenting during the third trimester were enrolled in the study. **Results:** Women with preeclampsia were older (30.8 ± 5.6 vs 28.9 ± 5.1 years) and had higher BMI (29.2 ± 4.3 vs 26.7 ± 3.9 kg/m²). Mean vitamin D levels were significantly lower in cases (15.2 ± 6.1 ng/mL) compared with controls (22.8 ± 7.3 ng/mL) ($p<0.001$). Vitamin D deficiency was present in 72% of cases versus 33% of controls. Deficient women had over fivefold higher odds of developing preeclampsia (OR 5.21, 95% CI 2.79–9.72). Adverse outcomes including preterm delivery (38% vs 14%), low birth weight (44% vs 18%), and NICU admission (36% vs 11%) were significantly more frequent among cases. **Conclusion:** Vitamin D deficiency is significantly associated with preeclampsia and poorer fetomaternal outcomes. Early identification and supplementation may help reduce pregnancy-related complications.

Introduction

Preeclampsia is a pregnancy-related hypertensive condition that develops hypertension that is new and sometimes comes with proteinuria or dysfunction of end-organs after gestation period of 20 weeks. It is associated with almost 5-15 percent

pregnancy and continues to be a leading cause of maternal and perinatal morbidity and mortality globally [1]. The pathogenesis of it is complicated and includes abnormal placentation, endothelial dysfunction, oxidative stress, and inflammatory responses that are overactive [2]. Although obstetric care has improved, there are still no effective preventive measures that are in place. Although vitamin D is still considered a significant regulator of calcium and bone metabolism, it is recognized that it also plays a significant role in regulating immunity, vascular and metabolic processes [3]. In pregnancy, vitamin D is crucial in growth of the placenta and fetus, and lack of it has been linked to such negative effects as gestational diabetes, intrauterine growth retardation, and hypertensive illnesses [4]. There is also systematic evidence to show that maternal hypovitaminosis D is a contributing factor to maternal and neonatal complications [5]. The level of vitamin D deficiency is very high among the South Asians especially in Pakistan where lifestyle, nutritional, and cultural factors restrict the exposure to sun and nutritional intake [6]. At the same time, gestational hypertensive diseases represent a large percentage of maternal mortality, highlighting the local problem in the health of the population [7]. There can also be genetic and environmental factors that can alter the susceptibility of disease on this population [8]. Preeclampsia complicates between 2- 8 percent of pregnancies in the world, and it raises the risk of cardiovascular diseases in women who have had preeclampsia [9].

Vitamin D is mainly produced in the skin after exposure to ultraviolet rays, and there is an insignificant contribution from dietary intake [10]. It has immunomodulatory and anti-inflammatory effects, suggesting a biologically plausible role in maintaining normal placental function [11]. Deficiency could thus facilitate endothelial damage and trophoblastic invasive invasion, which plays a pivotal role in the commencement of preeclampsia [12]. Observational studies have reported that serum vitamin D levels are lower in preeclamptic women than in normotensive controls, and this may be associated with the condition [13]. Additionally, trials of supplementation indicate that it is possible to reduce relapses and/or disease burden by increasing vitamin D levels, but the evidence in this area is inconsistent [14].

Objective

To determine the association between vitamin D deficiency and preeclampsia among women presenting during the third trimester of pregnancy

Methodology

This was a hospital-based case–control comparative study conducted at the Outpatient Department of Obstetrics and Gynaecology, Services Hospital, Lahore, from March 2025 to June 2025. A total of 200 pregnant women presenting during the third trimester were enrolled in the study. Non-probability consecutive sampling was used to recruit all eligible participants. Based on their clinical status, women were categorized into two groups:

Group A (n = 100): Pregnant women diagnosed with preeclampsia

Group B (n = 100): Normotensive pregnant women without proteinuria (controls)

The participants that were eligible were pregnant women with an age range of 25-45 years, primigravida or multigravida, and in the third trimester. The cases were established as women who met the diagnostic criteria of preeclampsia and the controls as women who were healthy pregnant women who had normal blood and showed no signs of proteinuria. Preeclampsia was diagnosed when systolic blood pressure [?]140 mmHg or diastolic blood pressure [?]90 mmHg was achieved on at least 2 readings at least 4 hours apart, as well as proteinuria [?]0.3 g in 24 hour urine collection or [?]1+ on the dipstick test. The definition of vitamin D deficiency was the serum level of 25-hydroxyvitamin D at less than 20 ng/mL. Women who had chronic hypertension, eclampsia, chronic renal disease, a history of preterm birth or having bone or

metabolic conditions were excluded. Patients who were not willing to give informed consent were not included as well.

Data Collection

All the eligible women were recruited sequentially after receiving ethical approval and informed written consent. A structured proforma was used to document baseline demographic and clinical data such as age, parity, residence, maternal education and socioeconomic status. Blood pressure was taken in a standard sphygmomanometer and urine protein analysis was done to diagnose it. About 5 mL of aseptic venous blood was taken. Samples were left to clot and centrifuged within two hours to separate serum and stored at [?]20degC till analysis. The level of serum 25-hydroxyvitamin D was determined with the aid of the enzyme-linked immunosorbent assay (ELISA). All preeclamptic patients got routine obstetric care as per the hospital guidelines. Clinical monitoring and documentation of outcomes were followed by following the participants till delivery.

Data Analysis

Data were entered and analyzed using SPSS version 25.0. Quantitative variables such as maternal age and gestational age were expressed as mean ± standard deviation, while qualitative variables were presented as frequencies and percentages. Independent sample t-test was used to compare continuous variables and chi-square test for categorical variables. Odds ratios with 95% confidence intervals were calculated to determine the association between vitamin D deficiency and preeclampsia. Stratification was performed for potential confounders including age, residence, education, and socioeconomic status. A p-value ≤ 0.05 was considered statistically significant.

Results

Women with preeclampsia were slightly older than controls (30.8 ± 5.6 vs 28.9 ± 5.1 years, p=0.012) and presented at an earlier gestational age (33.7 ± 2.1 vs 34.5 ± 1.8 weeks, p=0.004). Primigravidity was more frequent among cases (58% vs 41%, p=0.018). A higher proportion of preeclamptic women belonged to rural areas (64% vs 49%, p=0.031), had low socioeconomic status (61% vs 38%, p=0.002), and lower education levels (67% vs 46%, p=0.006). Mean BMI was also significantly higher in cases (29.2 ± 4.3 vs 26.7 ± 3.9 kg/m², p<0.001).

Table 1. Baseline Demographic and Obstetric Characteristics of Study Participants (n = 200)

Variable	Preeclampsia (n=100)	Controls (n=100)	Total (n=200)	p-value
Age (years, mean ± SD)	30.8 ± 5.6	28.9 ± 5.1	29.9 ± 5.4	0.012
Gestational age (weeks, mean ± SD)	33.7 ± 2.1	34.5 ± 1.8	34.1 ± 2.0	0.004
Primigravida, n (%)	58 (58%)	41 (41%)	99 (49.5%)	0.018
Multigravida, n (%)	42 (42%)	59 (59%)	101 (50.5%)	0.018
Rural residence, n (%)	64 (64%)	49 (49%)	113 (56.5%)	0.031
Low socioeconomic status, n (%)	61 (61%)	38 (38%)	99 (49.5%)	0.002
Education ≤ matric, n (%)	67 (67%)	46 (46%)	113 (56.5%)	0.006
BMI (kg/m², mean ± SD)	29.2 ± 4.3	26.7 ± 3.9	27.9 ± 4.2	<0.001

Preeclamptic patients demonstrated markedly elevated blood pressures, with mean systolic pressure of 154.6 ± 11.8 mmHg compared with 116.3 ± 9.2 mmHg in controls,

and diastolic pressure of 98.7 ± 8.9 vs 74.5 ± 6.8 mmHg (both p<0.001). Mean arterial pressure was similarly higher (117.3 ± 9.5 vs 88.4 ± 7.1 mmHg, p<0.001). All cases exhibited proteinuria, while none of the controls did. Edema (71% vs 22%) and neurological symptoms (46% vs 8%) were significantly more common among cases (p<0.001). Hemoglobin was slightly lower (10.6 ± 1.4 vs 11.2 ± 1.3 g/dL, p=0.002), and platelet counts were reduced (164 ± 48 vs 212 ± 55 $\times 10^9$/L, p<0.001), reflecting hematological involvement.

Table 2. Clinical and Hemodynamic Profile at Presentation

Parameter	Preeclampsia (n=100)	Controls (n=100)	p-value
Systolic BP (mmHg, mean ± SD)	154.6 ± 11.8	116.3 ± 9.2	<0.001
Diastolic BP (mmHg, mean ± SD)	98.7 ± 8.9	74.5 ± 6.8	<0.001
Proteinuria ≥1+, n (%)	100 (100%)	0 (0%)	—
Edema, n (%)	71 (71%)	22 (22%)	<0.001
Headache/visual symptoms, n (%)	46 (46%)	8 (8%)	<0.001
Mean arterial pressure (mmHg)	117.3 ± 9.5	88.4 ± 7.1	<0.001
Hemoglobin (g/dL, mean ± SD)	10.6 ± 1.4	11.2 ± 1.3	0.002
Platelet count ($\times 10^9$/L, mean ± SD)	164 ± 48	212 ± 55	<0.001

Serum vitamin D levels were substantially lower in preeclamptic women, with a mean of 15.2 ± 6.1 ng/mL compared to 22.8 ± 7.3 ng/mL in controls (p<0.001). Severe deficiency was three times more common in cases (29% vs 9%), while overall deficiency (<20 ng/mL) affected nearly three-quarters of cases (72%) compared with one-third of controls (33%) (p<0.001).

Table 3. Serum Vitamin D Levels and Deficiency Status

Vitamin D Parameter	Preeclampsia (n=100)	Controls (n=100)	Total	p-value
Vitamin D level (ng/mL, mean ± SD)	15.2 ± 6.1	22.8 ± 7.3	19.0 ± 7.6	<0.001
Severe deficiency (<10 ng/mL), n (%)	29 (29%)	9 (9%)	38 (19%)	<0.001
Deficiency (10–19 ng/mL), n (%)	43 (43%)	24 (24%)	67 (33.5%)	0.004
Insufficiency (20–29 ng/mL), n (%)	18 (18%)	36 (36%)	54 (27%)	0.006
Normal (≥30 ng/mL), n (%)	10 (10%)	31 (31%)	41 (20.5%)	<0.001
Overall deficiency (<20 ng/mL), n (%)	72 (72%)	33 (33%)	105 (52.5%)	<0.001

Women with deficiency had over five times higher odds of developing preeclampsia (OR 5.21, 95% CI 2.79–9.72, p<0.001). Severe deficiency conferred a fourfold increased risk (OR 4.19, p<0.001), while moderate deficiency tripled the risk (OR 3.02, p=0.001). These findings indicate a dose–response relationship, where lower vitamin D levels corresponded with higher disease likelihood.

Table 4. Association Between Vitamin D Deficiency and Preeclampsia (Odds Ratio Analysis)

Vitamin D Status	Cases (n=100)	Controls (n=100)	Odds Ratio (95% CI)	p-value
Deficient (<20 ng/mL)	72	33	5.21 (2.79–9.72)	<0.001
Not deficient (≥20 ng/mL)	28	67	Reference	—
Severe deficiency (<10 ng/mL)	29	9	4.19 (1.82–9.61)	<0.001
Moderate deficiency	43	24	3.02 (1.61–5.66)	0.001

Preterm delivery occurred in 38% of cases compared with 14% of controls (p<0.001). Cesarean section rates were higher (63% vs 39%, p=0.001), and low birth weight infants were more common (44% vs 18%, p<0.001). Mean birth weight was lower in the case group (2.31 ± 0.48 vs 2.89 ± 0.52 kg), and Apgar scores were reduced (7.1 ± 1.2 vs 8.4 ± 0.9) (both p<0.001). NICU admissions (36% vs 11%) and maternal complications (27% vs 6%) were also significantly increased, indicating poorer fetomaternal outcomes.

Table 5. Maternal and Perinatal Outcomes in Both Groups

Outcome	Preeclampsia (n=100)	Controls (n=100)	p-value
Preterm delivery (<37 weeks), n (%)	38 (38%)	14 (14%)	<0.001
Cesarean section, n (%)	63 (63%)	39 (39%)	0.001
Low birth weight (<2.5 kg), n (%)	44 (44%)	18 (18%)	<0.001
NICU admission, n (%)	36 (36%)	11 (11%)	<0.001
Mean birth weight (kg ± SD)	2.31 ± 0.48	2.89 ± 0.52	<0.001
Apgar score at 5 min (mean ± SD)	7.1 ± 1.2	8.4 ± 0.9	<0.001
Maternal complications, n (%)	27 (27%)	6 (6%)	<0.001

Discussion

The current research showed the evident correlation of maternal hypovitaminosis D and preeclampsia, and there is a considerable demographic and clinical disparity between the groups. Preeclamptic women were older (30.8 vs 28.9 years, p=0.012), taller (29.2 vs 26.7 kg/m 2, p<0.001), and more likely to be primigravida (58% vs 41%). The percentage of rural location and low socioeconomic class was also higher (64% vs 49 and 61% vs 38% respectively), which suggests that both biological and social factors can be risk factors. The same trends have been observed in other studies in which obesity, primigravidity, and low socioeconomic status were often associated with hypertension disorders of pregnancy [15]. Abnormalities in hemodynamics and systemic cases were noted. The mean systolic and diastolic blood pressure was significantly higher (154.6 ± 11.8 /98.7 ± 8.9 mmHg) than the controls (116.3 ± 9.2/74.5 ± 6.8 mmHg, p<0.001). They were also more common with edema (71% vs 22%), and neurological symptoms (46% vs 8). Also, there were low hemoglobin (10.6 ± 1.4 vs 11.2 ± 1.3 g/dL) and low platelet (164 ± 48 vs 212 ± 55 $\times 10^{-}$/L) indicating systemic and hematological involvement. Other studies have reported similar levels of clinical severity, which is an indication of multisystem endothelial dysfunction that is typical of preeclampsia [16]. One of the significant conclusions in this study was the substantially low serum vitamin D level in preeclamptic women (15.2 + 6.1 ng/mL m vs. 22.8 + 7.3 ng/mL m) (p<0.001). The overall deficiency in vitamin D (<20 ng/mL) was found in 72 percent of cases and 33 percent of controls and severe deficiency

(<10 ng/mL) in 29 percent and 9 percent, respectively. Other earlier studies also reported reduced vitamin D levels and increased deficiency in preeclamptic women, which confirms the hypothesis that vitamin D deficiency could lead to poor placental vascularity development and immune response [17][18].

The association was also strong with vitamin D-deficient women having more than five times higher chances of developing preeclampsia (OR 5.21, 95 percent confidence interval, 2.79-9.72, p=.001). The degree of deficiency of severe (OR 4.19) and moderate (OR 3.02) also showed a dose-response relationship. Past studies have shown similar meanings of association which strengthens vitamin D deficiency as an independent and possibly modifiable risk factor [19]. There was also significant higher adverse fetomaternal outcomes in cases. The proportions were preterm birth (38 vs. 14), cesarean (63 vs. 39) and low birth weight (44 vs. 18) (all $p<0.001$). There was a lower means birth weight (2.31 ± 0.48 vs 2.89 ± 0.52 kg), lower Apgar scores (7.1 ± 1.2 vs 8.4 ± 0.9) and increased NICU admissions (36% vs 11%). The same negative results have been indicated in past studies which show the severe neonatal effects of preeclampsia and related micronutrient deficiencies [20]. In general, the current results provide a quantitative agreement that vitamin D deficiency is closely associated with the development and intensity of preeclampsia along with the worse maternal and neonatal outcomes. Given that hypovitaminosis D is very common in our population, the simple prevention measure is early screening and supplementation that is done during pregnancy.

Limitations

This single-center case–control study with consecutive sampling may limit generalizability and introduce selection bias. Vitamin D was measured only once, and factors such as diet, sun exposure, and supplementation were not fully controlled. The observational design precludes causal inference.

Conclusion

It is concluded that maternal hypovitaminosis D is strongly associated with preeclampsia and significantly increases the risk of adverse fetomaternal outcomes. Women with preeclampsia had markedly lower serum vitamin D levels (15.2 ± 6.1 vs 22.8 ± 7.3 ng/mL), with deficiency observed in 72% compared with 33% of controls, conferring over fivefold higher odds of disease (OR 5.21). Preeclampsia was also linked with higher rates of preterm birth (38%), low birth weight (44%), and NICU admission (36%).

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