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Research Article

Relationship between Maternal Vitamin D and Calcium Status and Neonatal Calcium Homeostasis in Pregnancies Complicated by Hypertensive Disorders

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ABSTRACT
Background: Hypertensive disorders of pregnancy can lead to maternal and fetal complications and can affect the transfer of nutrients from the placenta. Vitamin D and calcium play a crucial role in maternal mineral balance, fetal skeletal development and neonatal calcium regulation. Changes in maternal vitamin D and calcium levels might consequently influence the development of neonatal hypocalcemia, especially during preeclampsia and other hypertensive disorders.
Objective: To determine the relationship between maternal vitamin D and calcium status and neonatal calcium homeostasis in pregnancies complicated by hypertensive disorders.
Methodology: This analytical cross-sectional study was carried out in January-June 2025 in Khalifa Gul Nawaz Teaching Hospital, Bannu. The pregnant women with hypertensive disorders and neonates were selected by consecutive sampling, with a total number of 75. Serum 25-hydroxyvitamin D, calcium, phosphate, magnesium and albumin levels were measured. Data recorded included: Neonatal birth weight, Apgar scores, cord blood calcium, neonatal serum calcium, phosphate, magnesium, and neonatal hypocalcemia status. Correlation analysis, Chi-square/Fisher's exact test and multivariable logistic regression were used to evaluate the associations between maternal biochemical status and neonatal calcium homeostasis. One-sided p-value of < 0.05 was regarded as statistically significant.
Results: The mean maternal serum 25(OH)D level was 20.46 ± 8.17 ng/mL, while mean maternal serum calcium was 8.42 ± 0.71 mg/dL. Vitamin D deficiency was observed in 45.3% of mothers and low maternal calcium in 34.7%. The mean neonatal serum calcium concentration was 8.21 ± 0.76 mg/dL, and neonatal hypocalcemia occurred in 25.3% of newborns. Maternal vitamin D and serum calcium were positively correlated with neonatal calcium levels ($r = 0.46$ and $r = 0.52$, respectively; both $p < 0.001$). Neonatal hypocalcemia was significantly more frequent among vitamin D-deficient mothers, mothers with low serum calcium, and women with severe preeclampsia.
Conclusion: Lower maternal vitamin D and calcium levels were significantly associated with impaired neonatal calcium homeostasis in hypertensive pregnancies. Maternal vitamin D deficiency, low calcium status, and severe preeclampsia may identify neonates at increased risk of hypocalcemia and may warrant closer biochemical monitoring after birth.

Keywords: Vitamin D, Calcium, Neonatal Hypocalcemia, Preeclampsia, Gestational Hypertension, Neonatal Calcium Homeostasis.

INTRODUCTION

The hypertensive disorders of pregnancy are still significant causes of maternal and fetal morbidity throughout the world such as gestational hypertension and preeclampsia. These disorders include high blood pressure

during pregnancy with, in more severe cases, proteinuria, endothelial dysfunction and multi-organ involvement. In addition to the direct effect on the cardiovascular system, HPD can decrease uteroplacental blood flow and affect the exchange of nutrients and minerals between the mother and developing fetus. These changes may affect fetal growth, metabolic adaptation, and biochemical stability in the neonatal period (1-3).

Vitamin D plays a significant role in calcium and phosphate homeostasis, bone metabolism, immune function, and placental function. Vitamin D needs are higher in pregnancy due to the increased rate of fetal bone mineralization and increased calcium demand. Active transport of calcium across the placenta is necessary for the maintenance of fetal mineral stores, especially in the last trimester of pregnancy when the rate of fetal mineralization is highest. Maternal vitamin D deficiency may decrease intestinal calcium absorption, and have the potential to interfere with maternal calcium balance, which may lead to changes in calcium available to the fetus (4-6).

Calcium metabolism is also intimately involved with vascular function and blood pressure regulation. However, low calcium status has been linked with changes in the activity of vascular smooth muscle cells, as well as an increase in vascular resistance, which could be important in the hypertensive disorders of pregnancy. Meanwhile, abnormal placentation, endothelial dysfunction, and decreased uteroplacental blood flow are all linked to preeclampsia. The abnormalities could interfere with normal maternal fetal mineral exchange and may exacerbate the impact of maternal vitamin D and calcium deficiency on fetal and neonatal mineral status (7-9).

The physiological transition of neonatal calcium homeostasis is significant just after birth. There is active transport of calcium across the placenta, resulting in a higher level of calcium in the fetus than in the mother during intrauterine life. After birth, it is suddenly withdrawn and the infant must immediately adjust the serum calcium level by secretion of parathyroid hormone, activation of vitamin D, reabsorption by the kidney, and mobilization of bone mineral. Therefore, neonates that are low in mineral stores or have poor adaptive response are more susceptible to early hypocalcemia, which can be expressed as jitteriness, poor feedings, irritability, seizures, or may be clinically silent (10-12).

Despite the biological relationship between maternal vitamin D, calcium, placental function, and neonatal mineral metabolism, limited local data are available regarding these associations in pregnancies complicated by hypertensive disorders. Most available studies have assessed maternal vitamin D or calcium in relation to preeclampsia alone, while fewer have examined their combined effect on neonatal calcium regulation. Therefore, the present study aimed to evaluate the relationship between maternal vitamin D and calcium status and neonatal calcium homeostasis in pregnancies complicated by hypertensive disorders, with particular emphasis on neonatal serum calcium and the occurrence of neonatal hypocalcemia.

METHODOLOGY

This analytical cross-sectional study was conducted at Khalifa Gul Nawaz Teaching Hospital, Bannu**, from** January 2025 to June 2025. The study was designed to evaluate the relationship between maternal vitamin D and calcium status and neonatal calcium homeostasis among pregnancies complicated by hypertensive disorders. A total of 75 pregnant women with hypertensive disorders and their respective neonates were enrolled through non-probability consecutive sampling. Before inclusion, informed consent was obtained from all participants, and confidentiality of clinical and laboratory information was maintained throughout the study.

Singleton pregnant women diagnosed with gestational hypertension/Preeclampsia and presenting in the third trimester or for delivery were included. The classification of hypertensive disorders was based on the standard clinical criteria, in terms of blood pressure, proteinuria, and presence or lack of severe features. Patients who had a history of chronic renal disease, parathyroid disorders, severe hepatic disease, malabsorption syndromes, disorders of calcium metabolism, or were actively receiving medications to significantly alter calcium and/or vitamin D metabolism were excluded. Major fetal congenital anomalies were also excluded because they could, by themselves, impact the neonatal biochemical status.

The structured data collection form was used to record maternal demographic and obstetric data. Information provided was maternal age, body mass index, gravidity, parity, place of birth, gestational age at delivery, mode of delivery, systolic and diastolic blood pressure,

proteinuria, type of hypertension and severity, and antihypertensive therapy. The maternal venous blood samples were taken prior to delivery or on admission to the hospital for delivery. Concentrations of serum 25-hydroxyvitamin D (25(OH)D), total calcium, albumin, phosphate, and magnesium were measured on the hospital laboratory using standard laboratory methods. Vitamin D status was classified as deficient, insufficient or sufficient based on pre-established laboratory reference values. The same laboratory reference range was also applied to categorise maternal calcium levels as low or normal.

Immediate and early assessment of the neonatal period was conducted. Data on neonatal variables were obtained, such as sex, birth weight, gestational age, Apgar score at 1 minute and 5 minutes, and requirement for NICU admission. Cord blood calcium was measured at delivery as available; serum calcium was measured in the newborn within 24–48 hours of birth. Additionally, when available, neonatal levels of phosphate and magnesium were measured. Neonatal hypocalcemia was identified by reference value for neonatal serum calcium, as determined from the institutional laboratory. Serum calcium levels in the mother and calcium and vitamin D levels in the neonate were then compared and the incidence of neonatal hypocalcemia determined.

The data was entered and analyzed in IBM SPSS Statistics. The mean ± standard deviation (SD) (categorical variables: Frequencies and percentages) were used to summarize data. One-way ANOVA, an independent-samples t-test or an appropriate non-parametric test was used to test differences among the biochemical parameters of the mother and the neonates based on category of the hypertensive disorders, depending on data distribution. The categorical variable associations were analyzed by Chi-square test or Fisher's exact test between maternal vitamin D status, maternal calcium status, severity of hypertension and neonatal hypocalcemia. Pearson's or Spearman's correlation analysis was employed to measure relationships between maternal 25(OH)D, maternal calcium and neonatal serum calcium. Factors that were clinically relevant or of significance from bivariate analysis were included in a multivariable binary logistic regression model to determine independent variables associated with neonatal hypocalcemia. The odds ratios with 95% CI were presented and the value of $p<0.05$ was given as statistically significant.

RESULTS

A total of 75 pregnant women suffering from hypertensive disorders and their neonates participated in the study. The mean maternal age and mean gestational age at delivery were found to be 29.84 ± 5.21 years and 36.91 ± 1.84 weeks, respectively. The majority of the participants were multigravida (61.3%), while majority of them were Cesarean section (57.6%). The most common method of delivery was an section (65.3%). Gestational hypertension was seen in 25.3%, preeclampsia with no severe features in 36.0% and preeclampsia with severe features in 38.7% of women.

Table 1. Maternal demographic and obstetric characteristics (n = 75)

Variable	n (%) / Mean ± SD
Maternal age, years	29.84 ± 5.21
Age group	
≤25 years	17 (22.7)
26–30 years	26 (34.7)
31–35 years	21 (28.0)
>35 years	11 (14.7)
Residence	
Urban	43 (57.3)
Rural	32 (42.7)
BMI, kg/m²	28.16 ± 3.72
Gravidity	
Primigravida	29 (38.7)
Multigravida	46 (61.3)
Gestational age at delivery, weeks	36.91 ± 1.84
Mode of delivery	
Vaginal delivery	26 (34.7)
Cesarean section	49 (65.3)

The severity of the hypertensive disease was quite variable among the subjects. The mean SBP and DBP were 151.87 ± 14.26 mmHg and 96.45 ± 9.31 mmHg, respectively. Proteinuria was present in 46 (61.3%) women. Almost 20% of those who participated had severe preeclampsia.

Table 2. Clinical characteristics of maternal hypertensive disorders (n = 75)

Variable	n (%) / Mean ± SD
Systolic blood pressure, mmHg	151.87 ± 14.26
Diastolic blood pressure, mmHg	96.45 ± 9.31
Hypertensive disorder	
Gestational hypertension	19 (25.3)
Preeclampsia without severe features	27 (36.0)
Preeclampsia with severe features	29 (38.7)
Proteinuria present	46 (61.3)
Antihypertensive treatment	58 (77.3)

The mean maternal serum 25(OH)D level was 20.46 ± 8.17 ng/mL and the mean serum calcium level was 8.42 ± 0.71 mg/dL. Of the participants, 34 (45.3%) were found to have vitamin D deficiency and 25 (33.3%) others were found to have vitamin D insufficiency. Vitamin D level was sufficient in only 16 (21.3%) women. Twenty-Six (34.7%) participants had low maternal serum calcium.

Table 3. Maternal vitamin D and biochemical calcium status (n = 75)

Biochemical variable	n (%) / Mean ± SD
Serum 25(OH)D, ng/mL	20.46 ± 8.17
Vitamin D status	
Deficient	34 (45.3)
Insufficient	25 (33.3)
Sufficient	16 (21.3)
Total serum calcium, mg/dL	8.42 ± 0.71
Low maternal calcium	26 (34.7)
Normal maternal calcium	49 (65.3)
Serum phosphate, mg/dL	3.61 ± 0.58
Serum magnesium, mg/dL	1.86 ± 0.31
Serum albumin, g/dL	3.42 ± 0.47

The mean neonatal birth weight was 2.68 ± 0.54 kg, and 24 (32.0%) neonates had a birth weight below 2.5 kg. The mean serum calcium of the newborn was 8.21 ± 0.76 mg/dL. Twenty-five.3% (19) of newborns had been diagnosed with neonatal hypocalcemia. In 21 (28.0%) cases the child was admitted to NICU.

Table 4. Neonatal characteristics and calcium homeostasis (n = 75)

Variable	n (%) / Mean ± SD
Birth weight, kg	2.68 ± 0.54
Low birth weight (<2.5 kg)	24 (32.0)
Male neonate	39 (52.0)
Female neonate	36 (48.0)
Apgar score at 1 minute	7.18 ± 1.24
Apgar score at 5 minutes	8.43 ± 0.91
Cord blood calcium, mg/dL	8.36 ± 0.74
Neonatal serum calcium, mg/dL	8.21 ± 0.76
Neonatal hypocalcemia	19 (25.3)
Neonatal serum phosphate, mg/dL	5.41 ± 0.83
Neonatal serum magnesium, mg/dL	1.79 ± 0.28
NICU admission	21 (28.0)

Maternal vitamin D concentration was found to show significant positive correlation with the neonatal serum calcium ($r = 0.46$, $p < 0.001$). Maternal serum calcium also was positively related to neonatal calcium concentration ($r = 0.52$; $p < 0.001$). Mothers with vitamin D deficiency had significantly more than the other two groups of mothers with neonatal hypocalcemia (14, 41.2% versus 4, 16.0% vs 1, 6.3%; $p = 0.008$). Likewise, 12/26 (46.2%) neonates were neonatally hypocalcemic when their mothers had low serum calcium and 7/49 (14.3%) were hypocalcemic when their mothers had normal calcium ($p = 0.002$). Neonatal hypocalcemia was also significantly associated with severe preeclampsia ($p = 0.021$).

Table 5. Relationship of maternal vitamin D and calcium status with neonatal calcium homeostasis

Maternal factor	Neonatal outcome	Statistical result	p-value
Maternal 25(OH)D	Neonatal serum calcium	$r = 0.46$	<0.001
Maternal serum calcium	Neonatal serum calcium	$r = 0.52$	<0.001
Vitamin D status	Neonatal hypocalcemia	$\chi^2 = 9.72$	0.008
Maternal calcium status	Neonatal hypocalcemia	$\chi^2 = 9.81$	0.002
Severity of hypertensive disorder	Neonatal hypocalcemia	$\chi^2 = 7.70$	0.021
Gestational age	Neonatal serum calcium	$r = 0.29$	0.012
Birth weight	Neonatal serum calcium	$r = 0.31$	0.007

Vitamin D and calcium levels in the mother's blood were found to be lower as the severity of the hypertensive disease increased when the participants were classified by severity of the disease. The mean serum 25(OH)D levels were 24.83 ± 7.46 ng/mL in women with GH, 20.74 ± 7.52 ng/mL in preeclampsia without severe features and 17.34 ± 7.62 ng/mL in preeclampsia with severe features ($p = 0.004$). A similar pattern was observed for maternal serum calcium and neonatal serum calcium.

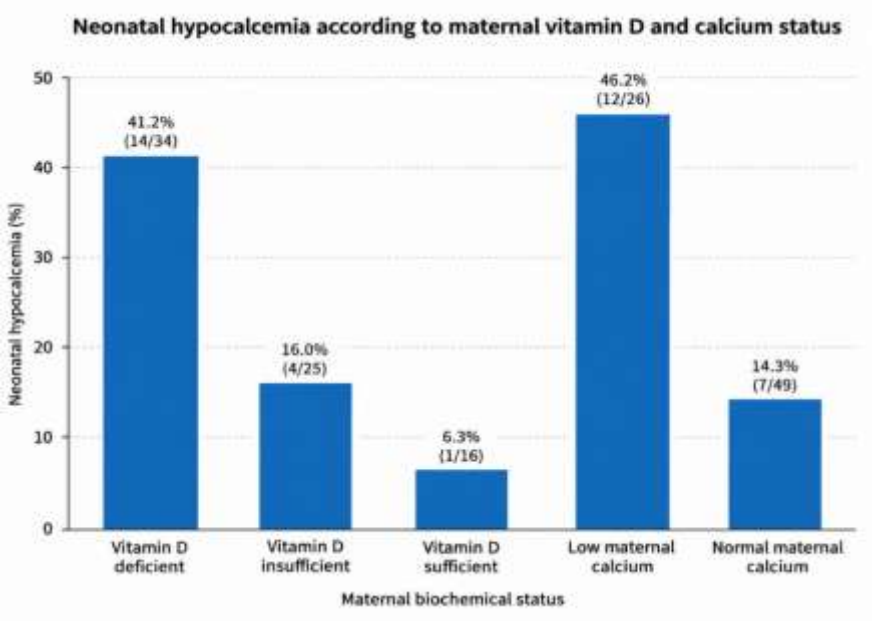
Table 6. Maternal and neonatal biochemical parameters according to hypertensive disorder severity

Parameter	Gestational hypertension (n=19)	Preeclampsia without severe features (n=27)	Preeclampsia with severe features (n=29)	p-value
Maternal 25(OH)D, ng/mL	24.83 ± 7.46	20.74 ± 7.52	17.34 ± 7.62	0.004
Maternal calcium, mg/dL	8.73 ± 0.60	8.47 ± 0.64	8.16 ± 0.74	0.011
Neonatal calcium, mg/dL	8.55 ± 0.62	8.24 ± 0.70	7.96 ± 0.82	0.015
Neonatal hypocalcemia	2 (10.5)	5 (18.5)	12 (41.4)	0.021

Maternal vitamin D deficiency, low level of maternal serum calcium, and severe preeclampsia were associated with neonatal hypocalcemia in multivariable logistic regression analysis. The odds of neonatal hypocalcemia were found to be about three times higher among neonates of mothers with vitamin D deficiency (AOR = 3.42, 95% CI: 1.10–10.63; $p = 0.034$). Low maternal calcium showed a similarly strong association (AOR = 3.78, 95% CI: 1.22–11.69; $p = 0.021$).

Table 7. Multivariable predictors of neonatal hypocalcemia

Predictor	Adjusted OR	95% CI	p-value
Maternal vitamin D deficiency	3.42	1.10–10.63	0.034
Low maternal serum calcium	3.78	1.22–11.69	0.021
Severe preeclampsia	2.91	1.01–8.42	0.048
Gestational age, per week	0.78	0.59–1.03	0.079
Low birth weight	1.84	0.61–5.55	0.278



The figure shows a higher frequency of neonatal hypocalcemia among mothers with **vitamin D deficiency (41.2%)** and **low maternal calcium (46.2%)**, while lower frequencies were observed among mothers with vitamin D insufficiency, sufficient vitamin D levels, and normal maternal calcium status.

DISCUSSION

The present study demonstrated a clear relationship between maternal vitamin D and calcium status and neonatal calcium homeostasis among pregnancies complicated by hypertensive disorders. Maternal 25-hydroxyvitamin D and serum calcium levels were positively correlated with neonatal serum calcium concentrations, suggesting that poorer maternal mineral status may adversely influence calcium availability to the fetus and newborn. Neonatal hypocalcemia was observed more frequently among mothers with vitamin D deficiency and low serum calcium levels. These findings are biologically plausible because vitamin D plays an important role in intestinal calcium absorption and maintenance of maternal calcium balance, while adequate maternal calcium availability is essential for placental transfer and fetal skeletal mineralization. Disturbances in these pathways may become more pronounced in pregnancies complicated by hypertension and placental dysfunction (13, 14).

Vitamin D deficiency was prevalent in the study population, with almost half of the mothers exhibiting deficiency and another proportion being vitamin D insufficient. The prevalence of hypocalcemia was significantly greater in neonates born to vitamin D deficient mothers than in the neonates born to mothers with sufficient vitamin D levels. Such a pattern suggests that vitamin D status of the mother at time of birth may play a significant role in the regulation of calcium level in the infant during the early postnatal period. Vitamin D needs during pregnancy are higher than normal due to the increased calcium requirements for fetal development and bone mineralisation. Low maternal vitamin D levels can decrease calcium absorption and impair the regulation of calcium/parathyroid hormone, which can restrict calcium availability for the transfer across the placenta. Following birth, interruption of the placenta's calcium supply could further predispose newborns with insufficient calcium stores to developing early neonatal hypocalcemia (15, 16).

Maternal serum calcium also correlated positively and significantly with the neonatal serum calcium, and low calcium levels in the mother were associated with higher frequencies of neonatal hypocalcemia. This discovery lends further credence to the idea that maternal calcium status directly affects neonatal calcium balance. While fetal calcium levels are controlled by active transport into the fetus, maternal biochemical disturbances can have an effect on mineral stores, especially if the placenta is dysfunctional. In addition to blood pressure abnormalities, the hypertensive disorders of pregnancy are associated with abnormal placentation, endothelial dysfunction and changes in uteroplacental perfusion. The

role of these pathological changes in the normal exchange of mineral between mother and fetus remains unclear but may be part of the explanation for the decreased calcium levels in the neonatal circulation seen in more severe cases of hypertensive disease (17, 18).

Other significant findings were the gradual decline in maternal vitamin D, maternal calcium and neonatal calcium levels with advancing degrees of hypertensive disorder. Maternal vitamin D and calcium levels were lowest in women who developed preeclampsia with severe features, and serum calcium levels were also lowest in their neonates, and the most common was hypocalcemia. These findings indicate that the severity of maternal hypertensive disease may have a modulating effect on maternal nutritional and biochemical conditions, in determining mineral homeostasis in the neonate. In addition, vitamin D deficiency in mothers, low calcium concentration in maternal serum and severe preeclampsia were independently associated with neonatal hypocalcemia in the multivariable analysis. This suggests that the associations between their relationships and neonatal calcium status were not fully accounted for by the effects of gestational age and birth weight (19, 20).

The results are clinically relevant as the measurement of vitamin D and calcium in the mother could help to identify pregnancies where the neonate is at higher risk of calcium homeostasis disturbance. Women who have severe hypertensive disorders and biochemical evidence of vitamin D or calcium deficiency should be monitored more carefully during the pregnancy and their neonates should have early calcium monitoring after delivery. There are a few caveats, however. This study carried out at one centre, with a relatively small number of 75 mother–neonate pairs, may be less generalizable. Because of the cross-sectional design of this study, any definite causal relationships cannot be determined and some dietary calcium, vitamin D intake, sun exposure, seasonality, maternal levels of parathyroid hormone and detailed information on neonatal feeding practices were not well studied. There is a need for more prospective multicenter studies to further clarify the timeline of maternal vitamin D, calcium metabolism and severity of HDP, and the subsequent timeline of calcium metabolism in the neonate.

CONCLUSION

Maternal vitamin D and calcium status were significantly associated with neonatal calcium homeostasis in pregnancies complicated by hypertensive disorders. Lower maternal 25(OH)D and serum calcium concentrations were associated with reduced neonatal serum calcium and a greater frequency of neonatal hypocalcemia. The risk appeared to be particularly high in pregnancies complicated by severe preeclampsia. These findings support the importance of assessing maternal nutritional and mineral status in hypertensive pregnancies and suggest that neonates born to mothers with vitamin D deficiency, low calcium levels, or severe hypertensive disease may require closer biochemical monitoring during the early neonatal period.

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