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Comparative Evaluation of Maternal and Fetal Outcomes in Hypertensive Disorders of Pregnancy with Normal and Low Serum Calcium Levels

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Abstract

Background: Hypertensive disorders of pregnancy (HDP) are a major cause of maternal and perinatal morbidity and mortality worldwide. Calcium deficiency has been implicated as a potential factor in the pathogenesis and severity of HDP due to its role in vascular smooth muscle contractility and endothelial regulation. This study aimed to compare maternal and fetal outcomes among women with hypertensive disorders of pregnancy based on serum calcium levels. **Methods:** A hospital-based cross-sectional comparative study was conducted among 120 pregnant women diagnosed with hypertensive disorders of pregnancy at a tertiary care center between January 2023 and June 2024. Participants were divided into two groups based on serum calcium levels: normal calcium (≥8.5 mg/dL; n=73) and low calcium (<8.5 mg/dL; n=47). Clinical profiles, maternal complications, and fetal outcomes were recorded and compared using standard statistical methods, with a p-value <0.05 considered significant. **Results:**The mean serum calcium level in the study population was 8.45 ± 0.64 mg/dL, with 39.2% showing hypocalcemia. Women with low calcium had significantly higher mean systolic (151.1 ± 11.0 mmHg) and diastolic (96.2 ± 8.1 mmHg) blood pressures compared to those with normal calcium (146.3 ± 10.2 mmHg and 93.1 ± 7.9 mmHg, respectively; p<0.05). The mean gestational age at delivery was significantly lower in the low-calcium group (36.9 ± 1.9 weeks) than in the normal-calcium group (37.6 ± 1.7 weeks; p=0.040). Although maternal complications such as severe preeclampsia and eclampsia were more frequent in the low-calcium group, differences were not statistically significant. Neonates of hypocalcemic mothers had lower mean birth weights (2.58 ± 0.42 kg vs. 2.73 ± 0.39 kg; p=0.046) and higher NICU admissions (34.0% vs. 19.2%).**Conclusion:** Low serum calcium levels were associated with increased severity of hypertensive disorders and poorer perinatal outcomes. Routine assessment of calcium levels during pregnancy and timely correction of deficiency through supplementation and dietary guidance may contribute to improved maternal and neonatal outcomes.

Keywords: Serum calcium, Hypertensive disorders of pregnancy, Maternal outcome, Fetal outcome

INTRODUCTION

Hypertensive disorders of pregnancy (HDP) remain among the leading causes of maternal and perinatal morbidity and mortality worldwide, particularly in developing countries. They encompass a spectrum of conditions, including gestational hypertension, preeclampsia, eclampsia, and chronic hypertension with superimposed preeclampsia. These disorders complicate approximately 5-10% of all pregnancies and significantly contribute to adverse outcomes such as intrauterine growth restriction (IUGR), placental abruption, preterm delivery, and increased perinatal mortality. Despite advances in antenatal surveillance and obstetric management, the pathophysiology of HDP is complex and not yet completely understood.[1]

One of the emerging biochemical factors implicated in the development of hypertensive disorders of pregnancy is serum calcium. Calcium plays a vital role in vascular smooth muscle contractility, neuromuscular transmission, and intracellular signaling. Hypocalcemia has been hypothesized to increase vascular smooth muscle excitability, leading to heightened vasoconstriction and elevated blood pressure. In normal pregnancy, maternal calcium levels tend to decrease physiologically due to hemodilution, increased renal excretion, and transplacental calcium transfer to the growing fetus. However, in some cases, a further reduction beyond physiological limits may predispose pregnant women to hypertension and preeclampsia.[2]

Several studies have demonstrated a significant association between low serum calcium levels and preeclampsia, suggesting that hypocalcemia may impair endothelial function, reduce prostacyclin synthesis, and increase intracellular

calcium in vascular smooth muscle, all of which contribute to vasospasm and hypertension. Conversely, adequate dietary calcium intake has been associated with a lower risk of preeclampsia and improved maternal outcomes. Maternal calcium status has also been shown to influence fetal growth, placental function, and neonatal well-being, with hypocalcemia being linked to lower birth weights, preterm deliveries, and higher neonatal morbidity rates.[3]

In low- and middle-income countries, where dietary calcium deficiency is common, understanding the relationship between serum calcium levels and HDP is of particular relevance. Evaluating maternal and fetal outcomes in women with hypertensive disorders based on calcium status may provide insights into potential preventive and therapeutic strategies. Early identification of women at risk and timely correction of calcium deficiency could reduce complications and improve pregnancy outcomes.[4]

Aim:
To compare maternal and fetal outcomes in hypertensive disorders of pregnancy with normal and low serum calcium levels.

Objectives:
1. To assess serum calcium levels among pregnant women diagnosed with hypertensive disorders of pregnancy.
2. To compare maternal complications and outcomes between women with normal and low serum calcium levels.
3. To evaluate fetal outcomes such as birth weight, gestational age at delivery, and perinatal morbidity and mortality in relation to maternal calcium status.

MATERIALS AND METHODS

Source of Data: The study utilized data collected from pregnant women admitted to the Department of Obstetrics and Gynaecology at a tertiary care teaching hospital. Patients diagnosed with hypertensive disorders of pregnancy were included after obtaining informed consent.
Study Design:A hospital-based cross-sectional comparative study.
Study Location: Department of Obstetrics and Gynaecology, at tertiary care hospital.
Study Duration: The study was conducted over a period of 18 months, from January 2023 to June 2024.
Sample Size:A total of 120 pregnant women diagnosed with hypertensive disorders of pregnancy (HDP) were included in the study.

Inclusion Criteria:
- Pregnant women diagnosed with hypertensive disorders (gestational hypertension, preeclampsia, eclampsia).
- Singleton pregnancies beyond 28 weeks of gestation.
- Women who gave informed consent for participation.

Exclusion Criteria:
- Pregnant women with chronic hypertension prior to conception.
- Multiple gestations.
- Patients with renal, hepatic, endocrine, or parathyroid disorders affecting calcium metabolism.
- Those on calcium supplements beyond routine antenatal prophylaxis.

Procedure and Methodology: Eligible participants were evaluated through detailed clinical history, physical examination, and relevant laboratory investigations. Blood pressure was recorded using a calibrated sphygmomanometer in a sitting position. Diagnosis and classification of HDP were based on the American College of Obstetricians and Gynecologists (ACOG) criteria. Venous blood samples were collected under aseptic precautions for serum calcium estimation, performed using an automated chemistry analyzer by the o-cresolphthalein complexone method. Based on serum calcium values, participants were divided into two groups:
- **Group A:** Normal serum calcium (≥8.5 mg/dL)
- **Group B:** Low serum calcium (<8.5 mg/dL)

Maternal outcomes recorded included the development of complications such as severe preeclampsia, eclampsia, HELLP syndrome, abruptio placentae, and mode of delivery. Fetal outcomes assessed included birth weight, Apgar scores, intrauterine growth restriction (IUGR), preterm birth, stillbirth, and neonatal intensive care unit (NICU) admissions.

Sample Processing: Blood samples were centrifuged at 3000 rpm for 10 minutes, and serum was separated immediately for biochemical analysis. Calcium levels were estimated using colorimetric assay kits validated for clinical use. All samples were processed within two hours of collection to avoid degradation.

Statistical Methods: Data were compiled and analyzed using SPSS software version 26.0. Quantitative variables were expressed as mean ± standard deviation (SD) and compared using the independent Student's t-test. Categorical variables were expressed as percentages and compared using the Chi-square test or Fisher's exact test. A p-value <0.05 was considered statistically significant. Correlation between serum calcium levels and clinical parameters was analyzed using Pearson's correlation coefficient.

Data Collection: Patient data, including demographic details, clinical findings, biochemical parameters, and obstetric and neonatal outcomes, were recorded in a predesigned proforma. All laboratory reports were verified by qualified personnel, and ethical clearance was obtained from the Institutional Ethics Committee before study initiation.

RESULTS

Table 1. Baseline profile & key outcomes by maternal calcium status (N = 120; Normal n=73, Low n=47)

Measure	Normal Ca (≥8.5 mg/dL) Mean ± SD / n (%)	Low Ca (<8.5 mg/dL) Mean ± SD / n (%)	Effect & Test of Significance	95% CI	p-value
Age (years)	27.9 ± 4.3	29.4 ± 4.1	Mean diff = +1.5; Welch t=1.92 (df=101.7)	−0.05 to +3.05	0.056
BMI (kg/m²)	24.7 ± 3.4	26.1 ± 3.6	Mean diff = +1.4; Welch t=2.12 (df=94.2)	+0.10 to +2.70	0.034
SBP at enrollment (mmHg)	146.3 ± 10.2	151.1 ± 11.0	Mean diff = +4.8; Welch t=2.40 (df=92.8)	+0.84 to +8.76	0.016
DBP at enrollment (mmHg)	93.1 ± 7.9	96.2 ± 8.1	Mean diff = +3.1; Welch t=2.07 (df=96.5)	+0.13 to +6.07	0.039
Gestational age at delivery (weeks)	37.6 ± 1.7	36.9 ± 1.9	Mean diff = −0.7; Welch t=−2.05 (df=90.3)	−1.38 to −0.02	0.040
Primigravida	39 (53.4%)	29 (61.7%)	RR = 1.15; χ^2=0.86 (df=1)	0.82-1.61	0.354
Any maternal complication†	24 (32.9%)	21 (44.7%)	RR = 1.36; χ^2=1.89 (df=1)	0.87-2.11	0.169
Any adverse fetal outcome‡	28 (38.4%)	22 (46.8%)	RR = 1.22; χ^2=0.94 (df=1)	0.81-1.83	0.332

†Maternal complication: severe preeclampsia/eclampsia/HELLP/abruption/PPH.
‡Adverse fetal: preterm birth/IUGR/LBW/NICU/stillbirth.

Table 1 presents the baseline maternal profile and overall outcomes according to serum calcium status in 120 women with hypertensive disorders of pregnancy (HDP). Of these, 73 had normal calcium levels (≥8.5 mg/dL) and 47 had low calcium levels (<8.5 mg/dL). The mean maternal age was slightly higher in the low calcium group (29.4 ± 4.1 years) compared to those with normal calcium (27.9 ± 4.3 years), though this difference was only borderline significant (p = 0.056). Women with low calcium had significantly higher mean BMI (26.1 ± 3.6 kg/m² vs. 24.7 ± 3.4 kg/m², p = 0.034) and higher systolic and diastolic blood pressures (SBP = 151.1 ± 11.0 mmHg, DBP = 96.2 ± 8.1 mmHg) compared to the normal calcium group (SBP = 146.3 ± 10.2 mmHg, DBP = 93.1 ± 7.9 mmHg), both differences reaching statistical significance (p < 0.05). Gestational age at delivery was significantly lower in the low calcium group (36.9 ± 1.9 weeks vs. 37.6 ± 1.7 weeks, p = 0.040), indicating earlier deliveries among women with hypocalcemia. The distribution of primigravidas was similar across groups (53.4% vs. 61.7%, p = 0.354). Although maternal and fetal complications were more frequent in the low calcium group (44.7% and 46.8%, respectively) than in the normal calcium group (32.9% and 38.4%).

Table 2. Serum calcium profile among HDP (distribution, subgroup means, and correlations) (N = 120)

Measure	Value
Mean total serum calcium (mg/dL), overall	8.45 ± 0.64 (95% CI: 8.33-8.57)
Proportion with low calcium (<8.5 mg/dL)	47 (39.2%) (95% CI: 30.4%-47.9%)
HDP subtype distribution	Gestational HTN 38 (31.7%); Preeclampsia 66 (55.0%); Eclampsia 16 (13.3%)
Mean calcium by subtype (mg/dL)	Gest HTN: 8.7 ± 0.5; Preeclampsia: 8.3 ± 0.7; Eclampsia: 8.1 ± 0.8
One-way ANOVA (Ca by subtype)	F(2,117) = 6.37; p = 0.002; between-group mean differences favor higher Ca in gestational HTN

Low Ca prevalence by subtype	Gest HTN: 9/38 (23.7%); Preeclampsia: 29/66 (43.9%); Eclampsia: 9/16 (56.3%); χ^2=8.14 (df=2), p=0.017
Correlation: serum Ca vs SBP	r = −0.27 (95% CI: −0.43 to −0.10); t=−3.05 (df=118); p=0.003
Correlation: serum Ca vs DBP	r = −0.22 (95% CI: −0.39 to −0.04); t=−2.43 (df=118); p=0.017

Table 2 summarizes serum calcium profiles among the study population. The mean total serum calcium was 8.45 ± 0.64 mg/dL (95% CI: 8.33-8.57). Low calcium levels were observed in 39.2% of participants (95% CI: 30.4%-47.9%). Among the subtypes of HDP, preeclampsia was most common (55.0%), followed by gestational hypertension (31.7%) and eclampsia (13.3%). The mean calcium levels were progressively lower across the severity spectrum: 8.7 ± 0.5 mg/dL in gestational hypertension, 8.3 ± 0.7 mg/dL in preeclampsia, and 8.1 ± 0.8 mg/dL in eclampsia. This difference was statistically significant (F = 6.37, p = 0.002). The prevalence of low calcium also increased with severity (23.7% in gestational hypertension, 43.9% in preeclampsia, and 56.3% in eclampsia; p = 0.017). Furthermore, serum calcium showed a significant negative correlation with both systolic (r = −0.27, p = 0.003) and diastolic (r = −0.22, p = 0.017) blood pressure values.

Table 3. Maternal complications & delivery outcomes by calcium status (N = 120; Normal n=73, Low n=47)

Outcome	Normal Ca n (%)	Low Ca n (%)	Effect & Test of Significance	95% CI	p-value
Severe preeclampsia	21 (28.8%)	21 (44.7%)	RR = 1.55; χ^2=3.18 (df=1)	0.96-2.51	0.074
Eclampsia	3 (4.1%)	6 (12.8%)	RR = 3.11; χ^2=3.09 (df=1)	0.82-11.82	0.079
HELLP syndrome	3 (4.1%)	5 (10.6%)	RR = 2.59; χ^2=1.96 (df=1)	0.65-10.33	0.162
Abruptio placentae	2 (2.7%)	4 (8.5%)	RR = 3.11; χ^2=2.00 (df=1)	0.59-16.29	0.157
Postpartum hemorrhage	5 (6.8%)	7 (14.9%)	RR = 2.17; χ^2=2.06 (df=1)	0.73-6.45	0.152
Cesarean delivery	33 (45.2%)	27 (57.4%)	RR = 1.27; χ^2=1.71 (df=1)	0.89-1.81	0.190
Length of stay (days), Mean ± SD	3.8 ± 1.2	4.3 ± 1.3	Mean diff = +0.5; Welch t=2.08 (df=110.7)	+0.02 to +0.98	0.040

Table 3 compares maternal complications and delivery outcomes between women with normal and low serum calcium levels. Severe preeclampsia and eclampsia occurred more frequently in women with low calcium (44.7% and 12.8%) compared to those with normal calcium (28.8% and 4.1%), showing an increasing trend though not reaching conventional statistical significance (p = 0.074 and 0.079, respectively). Similar trends were observed for HELLP syndrome (10.6% vs. 4.1%), abruptio placentae (8.5% vs. 2.7%), postpartum hemorrhage (14.9% vs. 6.8%), and cesarean delivery (57.4% vs. 45.2%), suggesting that low calcium may predispose to more obstetric complications. The mean hospital stay was significantly longer among women with low calcium levels (4.3 ± 1.3 days vs. 3.8 ± 1.2 days, p = 0.040).

Table 4. Fetal & neonatal outcomes by calcium status (N = 120; Normal n=73, Low n=47)

Outcome	Normal Ca n (%) or Mean ± SD	Low Ca n (%) or Mean ± SD	Effect & Test of Significance	95% CI	p-value
Birth weight (kg), Mean ± SD	2.73 ± 0.39	2.58 ± 0.42	Mean diff = −0.15; Welch t=−2.02 (df=86.4)	−0.29 to −0.01	0.046
Low birth weight (<2.5 kg)	17 (23.3%)	18 (38.3%)	RR = 1.64; χ^2=3.12 (df=1)	0.95-2.86	0.077
Preterm birth (<37 wks)	18 (24.7%)	19 (40.4%)	RR = 1.64; χ^2=3.33 (df=1)	0.96-2.79	0.068
IUGR	13 (17.8%)	14 (29.8%)	RR = 1.67; χ^2=2.35 (df=1)	0.86-3.24	0.125
5-min Apgar <7	6 (8.2%)	8 (17.0%)	RR = 2.07; χ^2=2.14 (df=1)	0.75-5.68	0.144
NICU admission	14 (19.2%)	16 (34.0%)	RR = 1.78; χ^2=3.37 (df=1)	0.96-3.29	0.066
Stillbirth	2 (2.7%)	3 (6.4%)	RR = 2.33; χ^2=0.95 (df=1)	0.40-13.42	0.330

Table 4 highlights fetal and neonatal outcomes in relation to maternal calcium status. The mean birth weight was significantly lower in neonates born to mothers with low calcium levels (2.58 ± 0.42 kg) compared to those with normal calcium (2.73 ± 0.39 kg; p = 0.046). Correspondingly, the incidence of low birth weight (<2.5 kg), preterm births (<37 weeks), and intrauterine growth restriction (IUGR) was higher in the low calcium group (38.3%, 40.4%, and 29.8%, respectively) than in the normal calcium group (23.3%, 24.7%, and 17.8%). Although these associations did not reach statistical significance (p > 0.05), the consistent pattern suggested poorer fetal growth and gestational outcomes with hypocalcemia. NICU admission rates were also higher in the low calcium group (34.0% vs. 19.2%, p = 0.066), indicating increased neonatal morbidity. The incidence of stillbirths was relatively low overall but slightly higher among hypocalcemic mothers (6.4% vs. 2.7%).

DISCUSSION

Baseline profile (Table 1). The low-calcium group exhibited higher SBP (+4.8 mmHg, p=0.016) and DBP (+3.1 mmHg, p=0.039), and a modestly higher BMI (+1.4 kg/m², p=0.034). This profile dovetails with clinic-based series from South Asia where hypocalcaemia co-segregates with greater hypertensive severity and adiposity Zhu Qet al.(2024)[5]. The slightly younger age in the normal-calcium group and comparable primigravidity suggest that the BP differences are not simply parity- or age-driven confounding. Consistent with endothelial hypotheses, multiple cross-sectional studies have reported lower mean calcium in HDP versus normotensive pregnancies, with stepwise worsening across gestational hypertension → preeclampsia → eclampsia Jaiswal Vet al.(2024)[6].

Serum calcium distribution and gradients across HDP subtypes (Table 2). Mean calcium was 8.45 ± 0.64 mg/dL, with 39.2% below 8.5 mg/dL. The graded decline (gestational HTN 8.7 ± 0.5; preeclampsia 8.3 ± 0.7; eclampsia 8.1 ± 0.8; ANOVA p=0.002) mirrors prior Indian and regional reports showing progressive hypocalcaemia with increasing clinical severity Grzeszczak Ket al.(2023)[7]. The rising prevalence of low calcium from gestational hypertension (23.7%) to preeclampsia (43.9%) and eclampsia (56.3%) (χ^2 p=0.017) echoes centre-based cohorts where low calcium clusters with proteinuria, neurological irritability, and lab markers of severe disease. Importantly, we observed significant inverse correlations of serum calcium with SBP (r=−0.27, p=0.003) and DBP (r=−0.22, p=0.017). Similar magnitudes (r=−0.20 to −0.35) have been reported in hospital cohorts and small community samples, supporting a dose-response relationship between calcium status and blood pressure in late gestation Ajong ABet al.(2023)[8].

Maternal complications and delivery outcomes (Table 3). Although the risks of severe preeclampsia (RR 1.55, p=0.074) and eclampsia (RR 3.11, p=0.079) did not cross conventional significance thresholds—likely reflecting sample size—they point in the same direction as meta-analytic evidence that improving calcium intake lowers preeclampsia risk, especially in low-intake populations Chen Det al.(2022)[9]. Trends toward more HELLP, abruption, PPH, and a higher caesarean rate in low-calcium participants are biologically plausible given vasoconstriction, placental malperfusion, and coagulopathic cascades described in HDP Bano Ret al.(2022)[10]. The significantly longer hospital stay (+0.5 days, p=0.040) in the low-calcium group is a clinically relevant composite signal of increased monitoring and intervention needs. WHO guidance recognises settings with low dietary calcium (<800 mg/day) as high-yield contexts for calcium supplementation (1.5-2.0 g/day) to reduce severe HDP endpoints Gebreyohannes RDet al.(2021)[11].

Fetal and neonatal outcomes (Table 4). We found lower mean birthweight in the low-calcium group (−0.15 kg, p=0.046) and numerically higher risks of LBW, preterm birth, IUGR, low 5-min Apgar, NICU admission, and stillbirth. While several RRs were borderline (p=0.07-0.15), the consistency across endpoints strengthens causal plausibility. Prior trials and systematic reviews suggest that calcium supplementation can reduce preterm birth and may modestly improve fetal growth in low-intake populations, largely mediated by improved maternal haemodynamics and placental perfusion Enebe JTet al.(2020)[12]. Observational studies from South Asia similarly link lower maternal calcium with LBW and higher NICU use Ajong ABet al.(2022)[13].

CONCLUSION

The present study concludes that low maternal serum calcium levels are significantly associated with increased blood pressure, reduced gestational age at delivery, and unfavorable maternal and fetal outcomes among women with hypertensive disorders of pregnancy. Hypocalcemic mothers demonstrated higher incidences of severe preeclampsia, eclampsia, and postpartum complications, as well as a greater frequency of low birth weight and preterm births in their neonates. Although some associations did not achieve statistical significance, the consistent trend across parameters indicates that hypocalcemia may play an important contributory role in the pathophysiology and severity of hypertensive disorders. Early identification and correction of calcium deficiency through nutritional counseling and supplementation during antenatal care could help mitigate complications, improve maternal well-being, and enhance neonatal outcomes.

Limitations of the Study

1. The study was conducted at a single tertiary care hospital, which may limit generalization of the results to other populations.
2. Dietary calcium intake and vitamin D status, which could influence serum calcium levels, were not assessed.
3. The cross-sectional study design precludes establishing a causal relationship between low calcium and hypertensive disorders.
4. The sample size (n=120) was relatively small, which may have limited statistical power for detecting smaller effect sizes.
5. Serial calcium measurements were not performed throughout pregnancy, preventing evaluation of temporal trends or dynamic changes.

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