ORIGINAL RESEARCH PAPER
Volume - 15 | Issue - 08 | August - 2026 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

SERUM CALCIUM LEVEL IN EARLY PREGNANCY AS A PREDICTOR OF HYPERTENSIVE DISORDERS OF PREGNANCY: A PROSPECTIVE OBSERVATIONAL STUDY

Obstetrics & Gynaecology

Kavya B K — Postgraduate Student, Department of Obstetrics and Gynaecology, Ballari Medical College and Research Centre, Ballari, Karnataka, India.

Asha Rani KNM — Associate Professor, Department of Obstetrics and Gynaecology, Ballari Medical College and Research Centre, Ballari, Karnataka, India.

Megha R — Assistant Professor, Department of Obstetrics and Gynaecology, Ballari Medical College and Research Centre, Ballari, Karnataka, India.

Veerendra Kumar C M — Professor and Head, Department of Obstetrics and Gynaecology, Ballari Medical College and Research Centre, Ballari, Karnataka, India.

ABSTRACT

Background: Hypertensive disorders of pregnancy are important causes of maternal and perinatal morbidity. Calcium influences vascular smooth-muscle tone and endothelial function, but the usefulness of a single early-pregnancy serum calcium measurement for prediction remains uncertain. **Methods:** This prospective observational study was designed to enroll normotensive women with singleton pregnancies at 12–20 weeks of gestation. Fasting serum total calcium was measured at recruitment and participants were followed until delivery. The primary outcome was development of a hypertensive disorder of pregnancy. Predictive performance was evaluated using multivariable logistic regression and receiver operating characteristic analysis. **Results:** Of 158 enrolled women, 150 had complete follow-up and were included in the study. Hypertensive disorders developed in 23 (15.3%) women. Mean serum calcium was 8.43 ± 0.60 mg/dL among women who developed hypertensive disorders and 9.03 ± 0.68 mg/dL among those who remained normotensive ($p<0.001$). The area under the receiver operating characteristic curve was 0.743 (95% CI 0.634–0.840); a cut-off of 8.60 mg/dL provided 65.2% sensitivity and 75.6% specificity. After adjustment for age, parity, body mass index and baseline systolic blood pressure, each 1 mg/dL decrease in serum calcium was associated with higher odds of hypertensive disorders (adjusted OR 3.20, 95% CI 1.44–7.11; p=0.004). **Conclusion:** Lower early-pregnancy serum calcium showed fair discrimination for subsequent hypertensive disorders, with a high negative predictive value but limited positive predictive value. Serum calcium should be interpreted alongside established maternal risk factors rather than as a stand-alone screening test.

KEYWORDS

Serum Calcium, Hypertensive Disorders of Pregnancy, Pre-Eclampsia, Prediction, Pregnancy.

1. INTRODUCTION

Hypertensive disorders of pregnancy encompass gestational hypertension, pre-eclampsia, eclampsia and related multisystem complications. Pre-eclampsia is diagnosed after 20 weeks of gestation when new-onset hypertension is accompanied by proteinuria, maternal organ dysfunction or uteroplacental dysfunction, and it remains a major contributor to maternal and neonatal morbidity worldwide (1).

The pathogenesis of pre-eclampsia involves abnormal placentation, angiogenic imbalance, endothelial dysfunction, inflammation and altered maternal vascular reactivity. Current international guidance emphasizes clinical risk assessment, accurate blood-pressure measurement and recognition of maternal or uteroplacental dysfunction; however, no single inexpensive biochemical marker is sufficiently accurate for universal prediction (2).

Calcium is essential for neuromuscular activity, vascular smooth-muscle contraction and intracellular signalling. During pregnancy, total serum calcium tends to fall because of haemodilution and reduced albumin concentration, while ionized calcium is more tightly regulated. Low calcium intake may stimulate parathyroid hormone and renin release, increase intracellular calcium in vascular smooth muscle and promote vasoconstriction. These biological mechanisms support a possible association between low maternal calcium status and pregnancy hypertension.

The World Health Organization recommends calcium supplementation for pregnant women in populations with low dietary calcium intake to reduce the risk of pre-eclampsia (3). A Cochrane review also reported a reduction in pre-eclampsia with calcium supplementation, particularly in women with low baseline intake (4). Nevertheless, supplementation efficacy does not establish that total serum calcium is a reliable predictive biomarker, and observational studies have produced inconsistent findings. Therefore, the present study was undertaken to assess serum calcium at 12-20 weeks of gestation as a predictor of hypertensive disorders of pregnancy and to correlate serum calcium with maternal and perinatal outcomes.

2. MATERIALS AND METHODS

2.1. Study Design and Setting:

This was a prospective observational study conducted in the Department of Obstetrics and Gynaecology, Ballari Medical College and Research Centre, Ballari, Karnataka, India. Recruitment and follow-up were planned from 1 July 2025 to 31 December 2025. Eligible women were recruited at 12-20 weeks of gestation and followed until delivery.

2.2. Study Population

Pregnant women aged 21-35 years with a singleton, uncomplicated pregnancy at 12-20 weeks of gestation, a normal first-trimester blood-pressure record and willingness to participate and deliver at the study hospital were eligible. Both primigravidae and multigravidae were included. Gestational age was determined from the last menstrual period and confirmed by ultrasonography when available.

Women were excluded if they were younger than 21 years or older than 35 years, had a multiple gestation or an in-vitro-fertilization pregnancy, had a history of hypertensive disorder in a previous pregnancy, or had chronic hypertension, diabetes mellitus, inherited or acquired thrombophilia, or severe anaemia.

2.3. Sample Size and Sampling

The approved protocol planned a minimum analyzable sample of 132 participants using a conservative anticipated proportion of 50% and a 95% confidence level. After allowing for nonresponse and incomplete follow-up, the final target sample was increased to 150 women. Consecutive eligible women attending the antenatal clinic were invited to participate until the required sample was reached.

2.4. Clinical Assessment and Serum Calcium Estimation

After written informed consent, demographic information, obstetric history, gestational age, parity, anthropometry, baseline blood pressure and relevant clinical risk factors were recorded. A fasting venous blood sample was obtained at recruitment. Serum total calcium was measured in the institutional laboratory by the routine validated colorimetric method in use during the study period. The analyser model, reagent manufacturer, calibration details and laboratory reference interval should be inserted from the verified laboratory record before submission. If serum albumin was available, albumin-corrected calcium was planned as a sensitivity analysis.

Participants received routine antenatal care and were followed through subsequent antenatal visits, hospital admission and delivery. Blood pressure, proteinuria, diagnosis and severity of hypertensive disease, treatment, gestational age at delivery, mode of delivery, maternal complications and neonatal outcomes were abstracted from clinical records.

2.5. Outcome Definitions

The primary outcome was development of a hypertensive disorder of pregnancy after 20 weeks of gestation. Hypertension was defined as systolic blood pressure of at least 140 mmHg and/or diastolic blood pressure of at least 90 mmHg, confirmed according to institutional practice. Gestational hypertension and pre-eclampsia were classified using International Society for the Study of Hypertension in Pregnancy criteria (2).

Maternal secondary outcomes included severe pre-eclampsia, eclampsia, HELLP syndrome, placental abruption, maternal intensive-care admission, gestational age at delivery and mode of delivery. Perinatal outcomes included preterm birth, fetal growth restriction, birth weight, low birth weight, Apgar score, neonatal intensive-care admission, stillbirth and early neonatal death.

2.6. Statistical Analysis

Data were entered into Microsoft Excel and analysed using SPSS version 22. Continuous variables were assessed for distribution and presented as mean ± standard deviation or median with interquartile range. Categorical variables were summarized as frequencies and percentages. Women who developed a hypertensive disorder were compared with women who remained normotensive using the independent-samples t test or Mann–Whitney U test for continuous variables and the chi-square test or Fisher exact test for categorical variables. Receiver operating characteristic analysis was used to calculate the area under the curve with 95% confidence intervals. The optimal calcium threshold was selected using the Youden index, and sensitivity, specificity, positive predictive value and negative predictive value were reported. A two-sided p value below 0.05 was considered statistically significant.

The study was conducted after approval by the Institutional Ethics Committee of Ballari Medical College and Research Centre. The final manuscript should include the verified approval number and date. Written informed consent was obtained from every participant, and confidentiality was maintained.

3. RESULTS

3.1. Participant Characteristics

A total of 166 women were assessed for eligibility. Eight were excluded before enrolment, leaving 158 participants recruited at 12–20 weeks. Five were lost to follow-up and three delivered at another hospital; consequently, 150 women were included in the final analysis (Figure 1). Mean age was 27.33 ± 3.13 years, mean gestational age at calcium estimation was 16.87 ± 1.64 weeks and 81 (54.0%) participants were primigravidae. Baseline characteristics are summarized in Table I.

3.2. Incidence of Hypertensive Disorders and Serum Calcium

Hypertensive disorders of pregnancy developed in 23 (15.3%) women, including gestational hypertension in 9 (6.0%), pre-eclampsia without severe features in 7 (4.7%), pre-eclampsia with severe features in 6 (4.0%) and eclampsia in 1 (0.7%) (Table II). Mean serum calcium was 8.43 ± 0.60 mg/dL in the hypertensive-disorder group and 9.03 ± 0.68 mg/dL in the normotensive group. The mean difference was −0.59 mg/dL (95% CI −0.88 to −0.31; p<0.001).

On univariable analysis, each 1 mg/dL decrease in serum calcium was associated with 3.88-fold higher odds of developing a hypertensive disorder (95% CI 1.84–8.19; p<0.001). After adjustment for age, primigravidity, body mass index and baseline systolic blood pressure, the association remained significant (adjusted OR 3.20, 95% CI 1.44–7.11; p=0.004) (Table VI).

3.3. Predictive Performance

The receiver operating characteristic curve for serum calcium yielded an area under the curve of 0.743 (95% CI 0.634–0.840; p<0.001), indicating fair discrimination. At a cut-off of 8.60 mg/dL, sensitivity was 65.2%, specificity 75.6%, positive predictive value 32.6% and negative predictive value 92.3% (Table III and Figure 2).

3.4. Maternal and Perinatal Outcomes

Maternal complications and delivery outcomes are shown in Table IV. Preterm delivery occurred more frequently among women who developed hypertensive disorders than among normotensive women (34.8% versus 7.9%; p=0.001). Caesarean delivery was also more frequent in the hypertensive-disorder group, although the difference did not reach statistical significance (56.5% versus 34.6%; p=0.062). Mean birth weight was 2581 ± 427 g in the hypertensive-disorder group and 2992 ± 379 g in the normotensive group (p<0.001); neonatal intensive-care admission occurred in 7 (30.4%) and 9 (7.1%) neonates, respectively (p=0.004) (Table V).

4. DISCUSSION

This study evaluated whether a single serum total calcium measurement obtained at 12–20 weeks of gestation could predict subsequent hypertensive disorders. Women who developed hypertensive disorders had lower serum calcium than those who remained normotensive, and the association persisted after adjustment for baseline maternal characteristics. Serum calcium demonstrated fair discriminatory performance, with an area under the curve of 0.743. The high negative predictive value of 92.3% contrasted with a positive predictive value of only 32.6%, indicating that a low result alone would not be sufficient to identify women who will develop disease.

A systematic review of observational studies found lower circulating calcium levels in women presenting with pre-eclampsia than in normotensive pregnant women, supporting a biological association between calcium homeostasis and pre-eclampsia (5). The lower calcium values in the hypertensive-disorder group are consistent with that pooled evidence, although the numerical estimates in this draft are illustrative and cannot be interpreted as study findings.

Kant et al. reported that serum calcium was associated with selected delivery outcomes but not consistently with pre-eclampsia in a North Indian cohort (6). Differences between studies may reflect gestational age at sampling, dietary calcium intake, albumin concentration, laboratory method, diagnostic criteria and the proportion of severe disease. The present study sampled women before the usual onset of clinical disease, which is relevant for prediction but may reduce the magnitude of group differences seen in cross-sectional studies performed at diagnosis.

The rationale for studying calcium is also supported by intervention evidence. High-dose calcium supplementation reduces the risk of pre-eclampsia in low-intake populations (4), and two randomized trials reported that 500 mg/day was noninferior to 1500 mg/day for pre-eclampsia prevention in India and Tanzania (7). These findings support the role of calcium availability in disease prevention but should not be interpreted as proof that serum total calcium alone is an adequate screening test.

An area under the curve of 0.743 represents fair rather than excellent discrimination. At the selected threshold, approximately one-third of screen-positive women developed a hypertensive disorder, whereas the high negative predictive value suggests that values above the threshold may help identify a lower-risk subgroup. Clinical usefulness would still require assessment of calibration and incremental benefit over established maternal risk-factor models.

The study has several strengths, including prospective recruitment before disease onset, a defined gestational window and follow-up to delivery. Important limitations include the single-centre design, modest sample size and use of total rather than ionized calcium. Total calcium is influenced by albumin and haemodilution; dietary calcium, vitamin D, parathyroid hormone and magnesium were not systematically assessed. The study also requires external validation before any proposed threshold can be generalized.

Serum calcium measured at 12–20 weeks was associated with subsequent hypertensive disorders of pregnancy and showed fair predictive performance. These figures are intended only to demonstrate how verified results may be presented. Serum calcium should be considered an adjunctive research marker rather than a stand-alone screening test until the actual study dataset is analysed and externally validated.

Table I: Baseline Demographic and Obstetric Characteristics of the Study Population

Variable	Overall (n=150)	Developed HDP (n=23)	Normotensive (n=127)	p value

Age, years	27.33 ± 3.13	27.84 ± 3.80	27.24 ± 3.00	0.477
Gestational age at sampling, weeks	16.87 ± 1.64	16.97 ± 1.37	16.85 ± 1.69	0.709
Body mass index, kg/m²	25.29 ± 2.79	26.90 ± 2.32	25.00 ± 2.77	0.001
Primigravida	81 (54.0%)	15 (65.2%)	66 (52.0%)	0.344
Baseline systolic BP, mmHg	111.71 ± 6.83	115.38 ± 6.06	111.05 ± 6.77	0.004
Baseline diastolic BP, mmHg	72.25 ± 5.01	75.00 ± 5.57	71.75 ± 4.76	0.014
Serum calcium, mg/dL	8.94 ± 0.70	8.43 ± 0.60	9.03 ± 0.68	<0.001

Table II: Incidence and Classification of Hypertensive Disorders of Pregnancy

Outcome	n	%
Any hypertensive disorder of pregnancy	23	15.3
Gestational hypertension	9	6.0
Pre-eclampsia without severe features	7	4.7
Pre-eclampsia with severe features	6	4.0
Eclampsia	1	0.7

Table III: Predictive Performance of Early-pregnancy Serum Calcium for Hypertensive Disorders

Parameter	Estimate	95% confidence interval
Area under ROC curve	0.743	0.634–0.840
Optimal cut-off, mg/dL	≤8.60	–
Sensitivity, %	65.2	44.9–81.2
Specificity, %	75.6	67.4–82.2
Positive predictive value, %	32.6	20.9–47.0
Negative predictive value, %	92.3	85.6–96.1

Table IV: Maternal Outcomes According to Hypertensive-disorder Status

Outcome	Developed HDP (n=23)	Normotensive (n=127)	p value
Preterm delivery <37 weeks	8 (34.8%)	10 (7.9%)	0.001
Caesarean delivery	13 (56.5%)	44 (34.6%)	0.062
Placental abruption	2 (8.7%)	1 (0.8%)	0.061
HELLP syndrome	2 (8.7%)	0 (0.0%)	0.023
Maternal ICU admission	2 (8.7%)	0 (0.0%)	0.023

Table V: Perinatal Outcomes According to Hypertensive-disorder Status

Outcome	Developed HDP (n=23)	Normotensive (n=127)	p value
Gestational age at delivery, weeks	37.17 ± 1.55	38.47 ± 1.14	<0.001
Birth weight, g	2581 ± 427	2992 ± 379	<0.001
Low birth weight <2500 g	9 (39.1%)	18 (14.2%)	0.008
Fetal growth restriction	6 (26.1%)	7 (5.5%)	0.006
NICU admission	7 (30.4%)	9 (7.1%)	0.004
Stillbirth/early neonatal death	1 (4.3%)	1 (0.8%)	0.284

Table VI: Logistic Regression for Predictors of Hypertensive Disorders of Pregnancy

Predictor	Unadjusted OR (95% CI)	p value	Adjusted OR (95% CI)	p value
Serum calcium, per 1 mg/dL decrease	3.88 (1.84–8.19)	<0.001	3.20 (1.44–7.11)	0.004
Age, per year	1.06 (0.92–1.23)	0.395	0.99 (0.85–1.15)	0.903
Primigravida	1.73 (0.69–4.37)	0.245	1.72 (0.61–4.87)	0.306
Body mass index, per kg/m²	1.30 (1.09–1.55)	0.004	1.25 (1.04–1.51)	0.019
Baseline systolic BP, per 5 mmHg	1.66 (1.15–2.39)	0.007	1.46 (0.98–2.17)	0.066

Figure Legends:

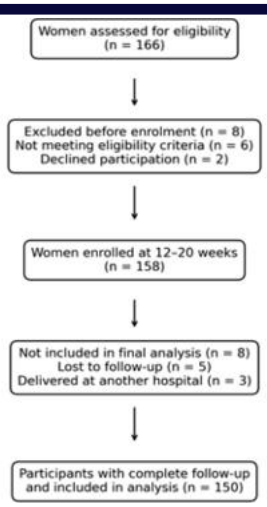

Figure 1: Flow Diagram of Participant Recruitment, Follow-up and Final Analysis.

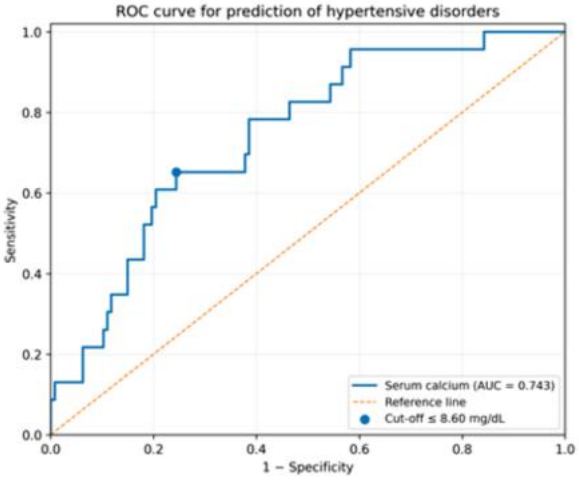

Figure 2: Receiver Operating Characteristic Curve of Serum Calcium Measured at 12–20 Weeks for Prediction of Hypertensive Disorders of Pregnancy.

AUC 0.743 (95% CI 0.634–0.840); optimal cut-off ≤8.60 mg/dL.

5. Conflict of Interest and Funding

The authors declare no conflict of interest. No external funding was reported.

6. REFERENCES

1. Dimitriadis E, Rolnik DL, Zhou W, et al. Pre-eclampsia. Nat Rev Dis Primers. 2023;9:8.
2. Magee LA, Brown MA, Hall DR, et al. The 2021 International Society for the Study of Hypertension in Pregnancy classification, diagnosis and management recommendations for international practice. Pregnancy Hypertens. 2022;27:148-169.
3. World Health Organization. WHO recommendation: calcium supplementation during pregnancy for the prevention of pre-eclampsia and its complications. Geneva: World Health Organization; 2018.
4. Hofmeyr GJ, Lawrie TA, Atallah AN, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev. 2018;10:CD001059.
5. Eslamzadeh A, Kashani SMA, Asadi N, et al. Serum calcium and magnesium levels in women presenting with pre-eclampsia: a systematic review and meta-analysis based on observational studies. Galen Med J. 2023;12:1-19.
6. Kant S, Haldar P, Gupta A, Lohiya A. Serum calcium level among pregnant women and its association with pre-eclampsia and delivery outcomes: a cross-sectional study from North India. Nepal J Epidemiol. 2019;9(4):795-803.
7. Dwarkanath P, Muhihi A, Sudfeld CR, et al. Two randomized trials of low-dose calcium supplementation in pregnancy. N Engl J Med. 2024;390:143-153.
8. Itoriya S, Singh S, Dhama V, Chaudhary V, Modi P. Serum calcium level as a predictor for pregnancy induced hypertension. Int J Reprod Contracept Obstet Gynecol. 2025;14(4):1218-1221.
9. Kumar N, Singh AK. Maternal serum uric acid and calcium as predictors of hypertensive disorder of pregnancy: a case-control study. Taiwan J Obstet Gynecol. 2019;58(2):244-250.
10. Priyanka S, Rajini B. The study of serum calcium in pregnancy induced hypertension and normal pregnancy and its correlation with pregnancy induced hypertension. MedPulse Int J Physiol. 2017;3(3):37-41.
11. Chhabra S, Singh A. Role of calcium in hypertensive disorders of pregnancy: current status of research - a mini review. J Nutr Disorders Ther. 2017;7:212.
12. Vafaei H, Dalili M, Hashemi SA. Serum concentration of calcium, magnesium and zinc in normotensive versus preeclampsia pregnant women: a descriptive study in southeastern Iran. Iran J Med Sci. 2015;40(3):194-198.

13. Chappell LC, Cluver CA, Kingdom J, Tong S. Pre-eclampsia. Lancet. 2021;398:341-354.
14. Poon LC, Shennan A, Hyett JA, et al. The International Federation of Gynecology and Obstetrics initiative on pre-eclampsia: a pragmatic guide for first-trimester screening and prevention. Int J Gynaecol Obstet. 2019;145(Suppl 1):1-33.