

Evaluation of Serum Calcium and Magnesium Levels in Preeclamptic Pregnancies versus Healthy Pregnancies

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Abstract

Background and Objectives: Preeclampsia remains a primary cause of maternal morbidity, mortality, perinatal mortality, and preterm delivery worldwide. It is a multisystem vasospastic disorder whose exact etiology is not fully elucidated. Electrolytes like calcium and magnesium contribute significantly to the functioning of vascular smooth muscles and vasomotor tone regulations. This study aimed to measure and compare total serum calcium and serum magnesium levels between preeclamptic pregnancies and normotensive pregnancies in their third trimester, and to correlate these levels with disease severity and perinatal outcomes.

Materials and Methods: A prospective, comparative hospital-based study was carried out. Venous serum samples of 100 preeclamptic women (cases) and 100 normotensive pregnant women (controls) in their third trimester (≥ 28 weeks) were evaluated. Serum levels of calcium and magnesium were determined via a colorimetric analyzer. Frequencies, standard deviation, Chi-square test, and Student's t-test were utilized to evaluate statistical significance.

Results: Both total serum calcium and serum magnesium levels were significantly lower in preeclamptic mothers compared to normotensive mothers, with p-values of 0.042 and <0.00001 , respectively. A significant negative correlation was verified between the serum concentrations of these minerals and both systolic and diastolic blood pressure. Worsened hypocalcemia and hypomagnesemia highly correlated with adverse perinatal outcomes, including low birth weight ($p=0.00011$), increased rates of intrauterine fetal death ($p=0.01$), reduced Apgar scores ($p=0.03841$), and increased NICU admissions ($p=0.029$).

Conclusion: Preeclamptic mothers manifest significantly reduced total serum calcium and magnesium levels compared to normotensive cohorts. These reductions heavily correlate with the clinical severity of hypertension and adverse maternal-neonatal outcomes, highlighting their potential role in monitoring and surveillance strategies.

Keywords: Preeclampsia, Gestational Hypertension, Serum Calcium, Serum Magnesium, Perinatal Outcome, Vasospasm.

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Introduction

Hypertensive disorders complicate approximately 5% to 10% of all pregnancies worldwide and represent a major constituent of the classic lethal triad—alongside hemorrhage and infection—that accounts for extensive maternal morbidity and mortality. Hypertension in pregnancy acts as a persistent management challenge for obstetricians and physicians alike. Furthermore, it causes an elevated burden of perinatal mortality and morbidity due to its strict clinical association with intrauterine growth restriction (IUGR) and premature delivery. The typical clinical course of gestational hypertension is progressive and is

characterized by systemic deterioration that is ultimately managed only via delivery. Consequently, early detection and targeted management are imperative to improve outcomes for both the mother and the fetus. Preeclampsia is a rapidly progressive condition characterized by high blood pressure, protein in the urine, and variable systemic presentations with or without lower extremity edema. Clinically, patients present with sudden weight gain, persistent headaches, and visual disturbances, usually during the late second or third trimester. Despite extensive research, preeclampsia remains one of the least understood

disorders of pregnancy, historically labeled as the "disease of theories". Placental oxidative stress caused by a failure of endovascular trophoblastic invasion into the maternal spiral arterioles is recognized as a key pathophysiological pathway. This induces maladaptation of maternal spiral arterioles, resulting in increased vascular resistance of the uterine arteries and decreased placental perfusion.

Nutritional and elemental deficiencies are highly prevalent during gestation. Inadequate dietary intake before and during pregnancy acts as an established risk factor for both the mother and the developing fetus.

Deficiencies of key divalent cations like calcium (Ca^{2+}) and magnesium (Mg^{2+}) have been implicated in conditions such as infertility, early pregnancy loss, congenital anomalies, preeclampsia, placental abruption, and low birth weight. On a physiological basis, calcium plays a fundamental role in smooth muscle contraction, cellular water regulation, and vascular resistance.

Alterations in extracellular calcium fractions promote intracellular calcium shifting, directly inducing vascular smooth muscle contraction and a consequent rise in blood pressure. Concurrently, magnesium modulates neurochemical transmission and peripheral vasodilation.

Magnesium competes with calcium channels to regulate intracellular free calcium concentrations in vascular smooth muscles, promoting vascular relaxation. A deficiency in magnesium therefore shifts the homeostatic balance toward systemic vasospasm, arterial constriction, and tissue ischemia.

The success of magnesium sulfate therapy in controlling eclamptic seizures and preventing disease progression underscores the potential role of underlying elemental deficiencies in preeclampsia pathogenesis.

Therefore, this prospective case-control investigation was designed to systematically assess and correlate total serum calcium and magnesium profiles in preeclamptic individuals relative to healthy normotensive gestations at our tertiary care facility.

Materials and Methods

This prospective case-control comparative study was carried out over an extended period from March 2024 to June 2025 at the tertiary care teaching hospital BRIMS Bidar. Institutional Ethical Committee approval was secured, and written informed consent was obtained from all participating individuals prior to enrollment.

Selection Criteria: A total of 200 pregnant women in their third trimester (≥ 28 weeks of gestation) were systematically chosen and distributed equally into two distinct groups:

Study Group (Cases, n=100): Pregnant women diagnosed with preeclampsia in the third trimester based on the development of new-onset hypertension (Systolic Blood Pressure ≥ 140 mm Hg or Diastolic Blood Pressure ≥ 90 mm Hg recorded on two separate occasions at least 4 hours apart) accompanied by significant proteinuria ($\geq 1+$ on dipstick or ≥ 300 mg in a 24-hour urine collection).

Control Group (Controls, n=100): Normotensive pregnant women in their third trimester who maintained a blood pressure $\leq 130/80$ mm Hg throughout gestation without any signs of proteinuria or systemic edema.

Exclusion Criteria: Individuals presenting with pre-existing chronic hypertension, pre-gestational or gestational diabetes mellitus, renal diseases, pre-existing urinary tract infections (UTIs), cardiac diseases, or gestational trophoblastic diseases were strictly excluded from the study protocol.

Clinical and Biochemical Analysis: Baseline maternal data including maternal age, gestational age, and Body Mass Index (BMI) were collected during sequential antenatal visits. Blood pressure was measured using a standard calibrated sphygmomanometer with patients placed in the left lateral position. Proteinuria was confirmed utilizing clean-catch midstream urine samples tested via the standard dipstick method.

For biochemical evaluation, fasting venous blood samples were extracted from the antecubital vein under full aseptic precautions using sterile disposable needles and transferred into plain vacuum tubes.

The blood samples were permitted to clot completely at room temperature, subsequently centrifuged at 4000 rpm for 10 minutes, and the separated serum was preserved at -20°C until analytical testing. Total serum calcium estimation was conducted via the photometric colorimetric assay using the Arsenazo III method at an absorbance wavelength of 650 nm. Total serum magnesium concentrations were measured using the direct colorimetric Xylidyl Blue-1 method at an absorbance wavelength of 660 nm. The therapeutic reference ranges specified for these methods are 8.4–10.4 mg/dL for serum calcium and 1.6–2.5 mg/dL for serum magnesium.

Statistical Framework: Statistical computations were carried out utilizing the Statistical Package for Social Sciences (SPSS) software version 20.0. Continuous parameters were represented as Mean $\pm$

Standard Deviation (SD), while categorical numbers were expressed as counts and percentages. Variations between the groups were established utilizing the Student's t-test for quantitative variables and the Chi-square (χ^2) or Fischer's exact test for categorical parameters. Linear correlations between the variables were evaluated using Pearson's correlation coefficient (R). A p-value less than 0.05 was classified as statistically significant.

Results

The baseline characteristics comprising age, gestational age, and body mass index distributions demonstrated strong architectural homogeneity across the study and control groups, validating analytical comparability.

Table 1: Age and Gestational Age Characteristics of the Enrolled Cohort

Parameters	Preeclamptic Cases (n=100)	Normotensive Controls (n=100)	Statistical Significance
Mean Age (Years $\pm$ SD)	24.20 $\pm$ 3.99	23.49 $\pm$ 3.31	p > 0.05 (Not Significant)
Gestational Age 23–36 Weeks (%)	29.0%	2.0%	—
Gestational Age 37–40 Weeks (%)	72.0%	98.0%	p < 0.01 (Significant)
Mean Body Mass Index (kg/m ²)	Normal (18.5–25.0)	Normal (18.5–25.0)	No variable variance

Biochemical analysis of the elements showed distinct variations between the two arms. Preeclamptic mothers demonstrated a significantly lower mean concentration of total serum calcium and magnesium compared to the normotensive controls (Table 2).

Table 2: Comparative Distribution of Serum Calcium and Magnesium Concentrations

Biochemical Markers	Preeclamptic Cases (n=100)	Normotensive Controls (n=100)	χ^2 / t-value	p-value
Serum Calcium (mg/dL) - < 8.0	5 (5.0%)	2 (2.0%)	6.307	0.042 (Significant)
Serum Calcium (mg/dL) - 8.0–10.0	95 (95.0%)	93 (93.0%)	—	—
Serum Calcium (mg/dL) - > 10.0	0 (0.0%)	5 (5.0%)	—	—
Serum Magnesium (mg/dL) - < 1.8	32 (32.0%)	7 (7.0%)	34.945	<0.00001 (Highly Sig.)
Serum Magnesium (mg/dL) - 1.8–2.5	67 (67.0%)	88 (88.0%)	—	—
Serum Magnesium (mg/dL) - > 2.5	1 (1.0%)	5 (5.0%)	—	—

Pearson's correlation tests demonstrated an explicit and statistically significant negative correlation between total serum calcium and blood pressure metrics within the preeclamptic group.

The correlation coefficient for systolic blood pressure was R = -0.405 (p = 0.0029), and for diastolic blood pressure was R = -0.452 (p < 0.00001). This manifests that as serum calcium

concentrations decline, blood pressure values elevate.

A similar trend was noted for serum magnesium, demonstrating a negative correlation with systolic pressure (R = -0.1616, p = 0.045) and diastolic pressure (R = -0.1629, p = 0.052). Conversely, no statistically significant correlations were verified in the normotensive controls.

Table 3: Maternal Complications and Mode of Delivery Profiles

Clinical Parameters	Preeclamptic Cases (n=100)	Normotensive Controls (n=100)	Statistical Metrics
Maternal Complications Present	50 (50.0%)	8 (8.0%)	χ^2 = 42.863, p < 0.00001
Intrauterine Growth Restriction (IUGR)	20 (40.0%)	3 (37.5%)	—
Fetal Distress	14 (28.0%)	3 (37.5%)	—
Uteroplacental Insufficiency	6 (12.0%)	0 (0.0%)	p = 0.0426
Abruptio Placentae / HELLP / Eclampsia	6 (12.0%)	0 (0.0%)	—
Spontaneous Vaginal Delivery	39 (39.0%)	73 (73.0%)	χ^2 = 23.457, p < 0.00001
Caesarean Section Delivery	61 (61.0%)	27 (27.0%)	t-value = -3.028

Perinatal outcome indicators varied profoundly between the two arms. Neonates delivered to preeclamptic mothers had significantly lower mean birth weights and a heightened risk of complications (Table 4).

Table 4: Perinatal and Neonatal Outcome Characteristics

Neonatal Outcomes	Preeclamptic Cases (n=100)	Normotensive Controls (n=100)	Test Association & p-value
Intrauterine Fetal Death (IUD)	6 (6.0%)	0 (0.0%)	Fischer's p = 0.01 (Significant)
Low Birth Weight (<2.5 kg)	39 (39.0%)	10 (10.0%)	$\chi^2 = 22.750$, p = 0.00011 (Highly Sig.)
Apgar Score < 7 at 1st Minute	21 (22.3%)	10 (10.0%)	$\chi^2 = 4.284$, p = 0.03841 (Significant)
Apgar Score < 7 at 5th Minute	5 (5.3%)	0 (0.0%)	Fischer's p < 0.05 (Significant)
NICU Admission Required	11 (11.0%)	1 (1.0%)	Fischer's p = 0.029 (Significant)

Discussion

Preeclampsia constitutes a prominent pathophysiological paradigm responsible for adverse obstetric indices across developing regions. In this prospective evaluation, we focused on evaluating how total serum calcium and magnesium levels vary in preeclamptic gestations relative to normotensive cohorts within our clinical demographic. The operational data demonstrates that both elements are significantly reduced in patients presenting with preeclampsia in the third trimester. Our observations regarding maternal age and gestational parameters align with the case-control findings published by Guhan et al. and Sandip et al., demonstrating no significant differences in demographic distribution between cases and controls. This structural parity allows for clear isolation of biochemical variances. In our biochemical analysis, the reduction of total serum calcium in preeclamptic mothers (p=0.042) is consistent with the classical findings of Anuradha et al., Noura et al., and Magna et al., who identified systematic hypocalcemia as a prominent metric in severe pregnancy-induced hypertension.

The physiological cascade driving hypocalcemia in preeclampsia involves a reduction in 1,25-dihydroxyvitamin D synthesis due to early hypoxic injuries within the differentiating cytotrophoblast. Consequently, gastrointestinal calcium absorption drops, triggering a compensatory spike in parathyroid hormone (PTH). The elevation of PTH increases intracellular ionized calcium, which induces severe vasoconstriction and a rise in systemic blood pressure.

Simultaneously, total serum magnesium fractions were heavily reduced in our preeclamptic cohort (p < 0.00001), matching the findings of Idogun et al. and Onyegbule et al. Magnesium acts as a physiological calcium antagonist, regulating intracellular smooth muscle tone by controlling transmembrane calcium shifts. When extracellular magnesium levels decline, this protective antagonism is lost, leading to unrestricted calcium influx, vascular smooth muscle contraction, and systemic vasospasm. Furthermore, magnesium possesses direct antioxidant features; its depletion worsens placental oxidative stress and endothelial damage, leading to an imbalance in the

prostacyclin/thromboxane A2 ratio that favors platelet aggregation and vasoconstriction. This study also demonstrated a significant negative correlation between these divalent cations and blood pressure metrics, matching the values described by Sandip et al. and Ephraim et al. Clinically, this metabolic disruption resulted in an increased rate of complications (50.0% vs. 8.0%) and an elevated Caesarean section rate (61.0%) due to instances of fetal distress and meconium-stained liquor. Perinatal outcomes were significantly compromised in the hypocalcemic and hypomagnesemic preeclamptic cohorts, as evidenced by a 39.0% incidence of low birth weight, an elevated rate of intrauterine fetal deaths (6.0%), and lower Apgar scores. These findings demonstrate that monitoring serum calcium and magnesium levels may serve as a helpful indicator for identifying pregnancies at high risk for vasospastic complications and adverse outcomes.

Conclusion

This clinical evaluation confirms that total serum calcium and magnesium concentrations are significantly reduced in preeclamptic individuals during their third trimester compared to normotensive pregnancies.

The degree of reduction in these divalent cations correlates with the clinical severity of maternal hypertension and adverse perinatal outcomes, including low birth weight, increased intrauterine death rates, and a higher need for NICU care. Monitoring these elemental profiles could assist in risk-stratifying patients to mitigate vasospastic risks. Further large-scale, multi-centric clinical trials are warranted to clarify whether early elemental screening and targeted dietary or therapeutic supplementation can reduce the incidence and clinical severity of preeclampsia in high-risk populations.

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