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Comparison of serum calcium and magnesium levels in women with hypertensive disorders of pregnancy versus normotensive pregnant females and fetomaternal outcome in both groups

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Abstract

Background: Hypertensive disorders of pregnancy are a major cause of maternal and perinatal morbidity and mortality. Altered calcium and magnesium metabolism has been implicated in the pathogenesis of these disorders, but their association with Maternal and Fetal Outcome remains inadequately defined.

Aim: To compare serum calcium and magnesium levels and evaluate Maternal and Fetal outcomes in women with hypertensive disorders of pregnancy and normotensive pregnant women.

Methods: This prospective observational study was conducted at Lalla Ded Hospital, Government Medical College, Srinagar. A total of 240 third-trimester pregnant women were enrolled, including 120 women with hypertensive disorders of pregnancy (gestational hypertension or pre-eclampsia) and 120 normotensive controls. Serum calcium and magnesium levels were measured using colorimetric methods. Maternal outcomes (mode of delivery, complications, ICU admission, and duration of hospital stay) and fetal outcomes (birth weight, NICU admission and APGAR scores) were compared between the two groups.

Results: Women with hypertensive disorders of pregnancy had significantly lower serum calcium (9.7 ± 1.7 mg/dL vs 10.2 ± 1.4 mg/dL; $p = 0.031$) and magnesium levels (1.7 ± 0.5 mg/dL vs 1.9 ± 1.1 mg/dL; $p = 0.020$) compared to normotensive women. Caesarean section rates were higher in the hypertensive group (75% vs 53.3%; $p < 0.001$). Maternal complications including eclampsia, HELLP syndrome, postpartum haemorrhage, ICU admission, and prolonged hospital stay were significantly more frequent in hypertensive women. Neonates born to hypertensive mothers had significantly lower mean birth weight (2.35 ± 0.48 kg vs 2.85 ± 0.45 kg; $p = 0.022$), a higher incidence of low birth weight (47.5% vs 18.3%; $p = 0.002$), and lower APGAR scores.

Conclusion: Hypertensive disorders of pregnancy are associated with significantly reduced serum calcium and magnesium levels and poorer Maternal and Fetal outcomes. Assessment of these micronutrients may help identify high-risk pregnancies and guide improved maternal and fetal outcome.

Keywords: Pregnancy-induced hypertension, Preeclampsia, Serum calcium; Serum magnesium, Maternal and Fetal outcome; Low birth weight

Introduction

Hypertensive disorders of pregnancy (HDP) are among the most significant complications during pregnancy, contributing substantially to maternal and perinatal morbidity and mortality worldwide [1]. Hypertensive disorders of pregnancy encompass a spectrum of conditions, including gestational hypertension, pre-eclampsia, eclampsia, and chronic hypertension with superimposed pre-eclampsia [2]. Among these, pre-eclampsia and eclampsia are major causes of adverse Maternal and Fetal outcomes, particularly in low- and middle-income countries, where access to timely healthcare is limited. Globally, hypertensive disorders of pregnancy affect approximately 10% of all pregnancies, with pre-eclampsia accounting for 2-8% of cases [3, 4]. This burden is particularly concerning because of the associated maternal complications, including placental abruption, organ dysfunction, and HELLP syndrome (haemolysis, elevated liver enzymes, and low platelets), along with perinatal consequences such as preterm birth, low birth weight, and stillbirth [4].

Calcium is a vital micronutrient involved in a variety of physiological processes, including vascular smooth muscle contraction, neuromuscular transmission, and coagulation.

During pregnancy, calcium requirements increase significantly to support foetal skeletal development and maternal adaptations [5]. The pregnant woman's body provides approximately 50 to 330 mg of calcium daily to support the developing foetal skeleton [6], and this high foetal demand is facilitated by profound physiological interactions between mother and foetus [7]. Early studies of blood calcium levels during pregnancy in humans have shown a significant decrease in total serum calcium as pregnancy progresses, and the regulation of intracellular calcium plays a key role in hypertension [8]. Calcium supplementation has therefore been hypothesised to reduce the chances of hypertensive disorders of pregnancy and pre-eclampsia [9, 10].

Calcium intake during pregnancy decreases the risk and severity of hypertensive disorders of pregnancy by causing a reduction in parathyroid hormone release and intracellular calcium concentration, which leads to reduced vasoconstriction by decreasing prostacyclin production and by increasing the vasoconstrictor effects of angiotensin II and noradrenaline in the blood vessel wall. This results in reduced smooth muscle contractility and increased vasodilatation, thereby decreasing the risk and severity of hypertensive disorders of pregnancy [11, 12].

Similarly, magnesium is a critical intracellular cation involved in various enzymatic reactions and cellular functions. It plays an important role in maintaining vascular tone, as it acts as a natural calcium antagonist, promoting vasodilatation and reducing vascular resistance. Magnesium also possesses antioxidant and anti-inflammatory properties, which are essential for protecting endothelial function [13]. Hypomagnesaemia has been implicated in the pathogenesis of hypertension due to its association with increased vasoconstriction and oxidative stress. In pre-eclampsia, low serum magnesium levels may worsen vascular reactivity and endothelial dysfunction, thereby contributing to disease progression. Magnesium sulphate remains the cornerstone of management for severe pre-eclampsia and eclampsia because of its ability to prevent seizures and improve Maternal and Fetal outcomes [14].

The association between altered serum calcium and magnesium levels and adverse Maternal and Fetal outcomes has been a subject of growing interest. Women with hypertensive disorders of pregnancy are at increased risk of intrauterine growth restriction (IUGR), preterm delivery, and perinatal mortality, primarily due to placental insufficiency resulting from impaired uteroplacental blood flow [15]. Calcium and magnesium dysregulation may contribute to this placental dysfunction through their effects on vascular tone and endothelial health. Low serum calcium and magnesium levels have been associated with a higher risk of preterm birth and small-for-gestational-age neonates, suggesting that optimisation of these mineral levels may have potential therapeutic implications for improving maternal and foetal outcomes [16].

The present study aims to evaluate serum calcium and magnesium levels in women with hypertensive disorders of pregnancy compared with normotensive pregnant females.

Materials and Methods

Study Design and Setting

This prospective, observational hospital-based study was conducted in the Department of Obstetrics and Gynaecology with neonatology division of department of pediatrics at Lalla Ded Hospital, Government Medical College, Srinagar, over a period of two years. Ethical approval was obtained from the Institutional Ethics Committee prior to the commencement of the study.

Study Population

A total of 240 pregnant women in their third trimester who were admitted for delivery were enrolled. Participants were divided into two groups:

- **Group A (Normotensive group):** 120 pregnant women without hypertension.
- **Group B (Hypertensive group):** 120 pregnant women diagnosed with hypertensive disorders of pregnancy, including gestational hypertension or pre-eclampsia.

All women in both groups were receiving the recommended dose of calcium supplementation during pregnancy.

Inclusion and Exclusion Criteria

Women with gestational hypertension (blood pressure $\geq 140/90$ mmHg on two occasions at least four hours apart without proteinuria or end-organ damage) and women with pre-eclampsia (blood pressure $\geq 140/90$ mmHg with proteinuria or evidence of end-organ dysfunction such as thrombocytopenia, renal insufficiency, liver dysfunction, cerebral symptoms, or pulmonary edema) were included in Group B. Normotensive pregnant women without proteinuria or end-organ dysfunction were included in Group A.

Women with chronic hypertension, diabetes mellitus, renal, endocrine, neurological, thyroid, or autoimmune disorders, and those not receiving calcium supplementation during pregnancy were excluded.

Data Collection

A structured proforma was used to collect data on age, parity, gestational age (based on last menstrual period or first trimester ultrasonography), booking status, and socioeconomic status. Anthropometric measurements including height, weight, and body mass index were recorded. Blood pressure was measured in a seated position using a mercury sphygmomanometer with an appropriately sized cuff, and hypertension was confirmed with two readings taken at least four hours apart.

Proteinuria was assessed using a dipstick test on a freshly voided early-morning urine sample.

Laboratory Analysis

Three millilitres of venous blood was collected under aseptic conditions. The blood was allowed to clot and centrifuged at 6000 rpm for two minutes to separate serum.

- **Serum calcium** was estimated using the colorimetric Arsenazo-III method.
- **Serum magnesium** was measured using the colorimetric isocitrate-dehydrogenase method.

Both parameters were analyzed using an auto-analyzer.

Outcome Measures

Maternal outcomes included mode of delivery, intrapartum and postpartum complications, need for intensive care unit (ICU) admission, requirement for blood transfusion, and duration of hospital stay.

Fetal outcomes included birth weight, APGAR scores at 1 and 5 minutes, and need for fetal intensive care unit (NICU) admission.

Statistical Analysis

Data were entered and analyzed using statistical software. Continuous variables were expressed as mean \pm standard deviation and compared using the independent *t*-test. Categorical variables were compared using the chi-square test or Fisher's

exact test as appropriate. A *p*-value of less than 0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants. Confidentiality was maintained, and participants were informed of their right to withdraw from the study at any time.

Results

A total of 240 pregnant women were studied, including 120 normotensive women (Group A) and 120 women with hypertensive disorders of pregnancy (Group B). The demographic characteristics of the study participants are shown in Table 1. Age, gravidity, residence, and socioeconomic status were comparable between the two groups. However, a significantly higher proportion of hypertensive women were unbooked.

Table 1: Baseline characteristics of study participants

Parameter	Group A (Normotensive)	Group B (HDP)	p-value
Age 25-30 yrs	42 (35%)	29 (24.2%)	0.214
Age 30-35 yrs	36 (30%)	51 (42.5%)	
Primigravida	60 (50%)	48 (40%)	0.053
Gravida >3	6 (5%)	18 (15%)	
Rural residence	84 (70%)	81 (67.5%)	0.053
Class III SES	40 (33.3%)	39 (32.5%)	0.189
Booked cases	78 (65%)	54 (45%)	0.038

Hypertensive women had significantly lower gestational age at admission and delivery and significantly higher blood pressure at presentation (Table 2).

Table 2: Gestational age and blood pressure

Variable	Group A	Group B	p-value
Gestational age at admission (weeks)	38.5 ± 2.4	35.5 ± 3.3	0.003
Gestational age at delivery (weeks)	38.9 ± 1.6	36.3 ± 1.7	0.001
Systolic BP (mmHg)	116.4 ± 12.8	153.6 ± 16.7	<0.001
Diastolic BP (mmHg)	74.3 ± 12.1	99.4 ± 18.3	<0.001

Women with hypertensive disorders had significantly lower serum calcium and magnesium levels (Table 3).

Table 3: Serum calcium and magnesium levels

Parameter (mg/dL)	Group A	Group B	p-value
Serum Calcium	10.2 ± 1.4	9.7 ± 1.7	0.031
Serum Magnesium	1.9 ± 1.1	1.7 ± 0.5	0.020

Caesarean section was significantly more common among hypertensive women (Table 4).

Table 4: Mode of delivery

Mode	Group A	Group B	p-value
LSCS	64 (53.3%)	90 (75%)	<0.001
NVD	56 (46.7%)	30 (25%)	

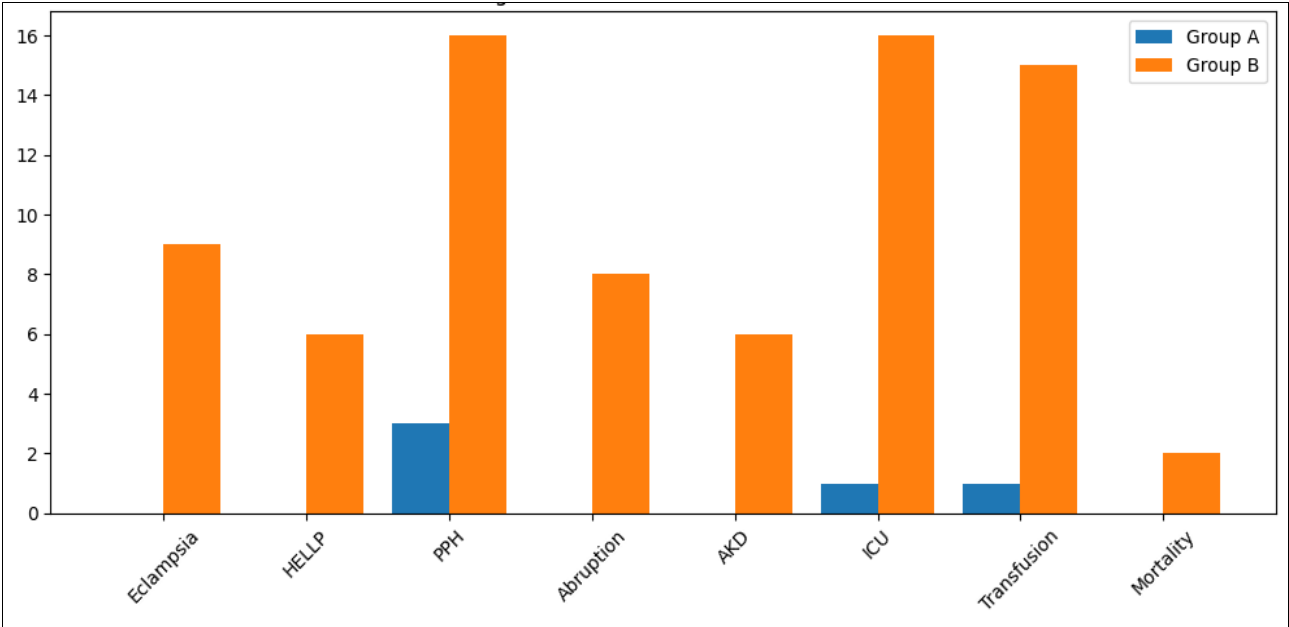


Fig 1: Maternal adverse events

Figure 1 compares maternal complications between normotensive women and those with hypertensive disorders of pregnancy. Hypertensive women had markedly higher rates of eclampsia, HELLP syndrome, postpartum haemorrhage,

placental abruptio, acute kidney dysfunction, ICU admission, and blood transfusion, whereas these events were rare or absent in normotensive women.

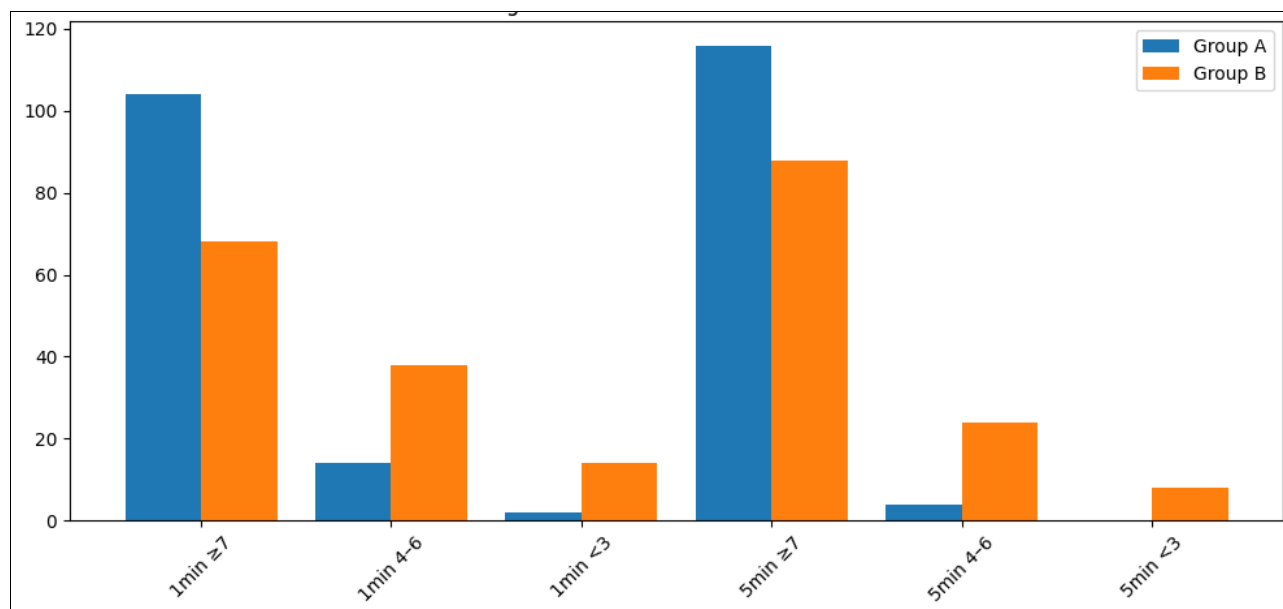


Fig 2: APGAR score distribution

Figure 2 shows the distribution of APGAR scores at 1 and 5 minutes in both groups. Neonates born to hypertensive mothers had a significantly higher proportion of low APGAR scores (<7) at both time points and lower mean APGAR values, indicating poorer immediate fetal condition compared to neonates of normotensive mothers.

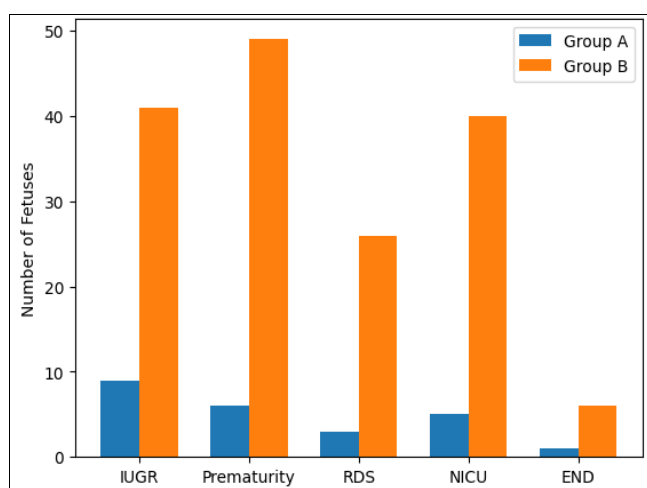


Fig 3: Fetal adverse events

Figure 3 illustrates the frequency of adverse fetal outcomes in both groups. Hypertensive pregnancies were associated with significantly higher rates of intrauterine growth restriction, prematurity, respiratory distress syndrome, NICU admission, and early fetal death compared with normotensive pregnancies.

Discussion

In the present study, although the age distribution between the normotensive and hypertensive groups was not statistically significant, a clear trend toward higher maternal age was observed among hypertensive women. A greater proportion of women aged 30-35 years and above were affected by hypertensive disorders, which is consistent with the findings of Ephraim *et al.* who demonstrated that women aged ≥40 years had more than twice the risk of developing pregnancy-induced hypertension (OR 2.14; $p = 0.000$) [17]. Advanced maternal age is associated with vascular ageing and comorbidities, which

increase susceptibility to hypertensive disorders during pregnancy.

A statistically significant reduction in serum calcium and magnesium levels was observed in hypertensive pregnant women compared with normotensive controls in the present study. The mean serum calcium (9.7 ± 1.7 mg/dL) and magnesium (1.7 ± 0.5 mg/dL) levels were significantly lower than in normotensive women (10.2 ± 1.4 mg/dL and 1.9 ± 1.1 mg/dL, respectively). These findings are supported by Sukonpan *et al.* and Pairu *et al.*, who reported significantly lower serum calcium and magnesium levels in pre-eclamptic and pregnancy-induced hypertensive women compared with normal pregnancies, suggesting that hypocalcaemia and hypomagnesaemia may play an important role in the pathogenesis of hypertensive disorders of pregnancy [18, 19].

Similarly, Punthamapol and Kittichotpanich found that serum calcium levels were significantly lower in women with severe pre-eclampsia than in those with mild pre-eclampsia and normotensive pregnancies, although magnesium levels did not differ significantly [20]. This partial discrepancy may be related to differences in disease severity and sample size but further supports the consistent association between calcium deficiency and hypertensive disorders of pregnancy.

Ephraim *et al.* also demonstrated significantly reduced calcium and magnesium levels in women with pregnancy-induced hypertension and pre-eclampsia and reported a positive correlation between the two minerals, reinforcing their interconnected role in regulating vascular tone and endothelial function [17].

In contrast, some studies have failed to demonstrate significant differences in serum calcium and magnesium levels between hypertensive and normotensive pregnancies. Gol *et al.* and Vafaei *et al.* reported comparable calcium and magnesium levels in both groups, suggesting that these micronutrients may not be involved in all populations [21, 22]. These discrepancies may be due to differences in gestational age, nutritional intake, analytical methods, and genetic or regional factors.

Maternal complications were markedly higher in hypertensive pregnancies in the present study. Eclampsia, HELLP syndrome, postpartum haemorrhage, and placental abruption occurred exclusively or predominantly in the hypertensive group, consistent with findings reported by Sandip *et al.*, who observed

significantly higher rates of severe maternal complications in pre-eclamptic women [23]. ICU admissions, multiple blood transfusions, and acute kidney dysfunction were also significantly more frequent in hypertensive women.

Similarly, Elmugabil *et al.* demonstrated altered biochemical profiles in pre-eclamptic women, including reduced calcium and altered magnesium levels, which were linked to renal dysfunction and endothelial injury [24]. The significantly longer hospital stay in hypertensive women in the present study further reflects the increased clinical burden associated with hypertensive disorders of pregnancy.

One of the critical findings in this study was the significantly lower mean birth weight in neonates born to hypertensive mothers. The average birth weight in the hypertensive group was 2.35 ± 0.48 kg, compared to 2.85 ± 0.45 kg in the normotensive group, with the difference being statistically significant ($p = 0.022$). Moreover, 47.5% of neonates in the hypertensive group weighed less than 2.5 kg, in contrast to only 18.3% in the normotensive group ($p = 0.002$). These findings are consistent with Kanagal *et al.* (2014), who reported significantly lower birth weights among neonates born to preeclamptic mothers, attributing this to chronic uteroplacental insufficiency and impaired foetal nutrition. [25]

Prematurity was another significant finding, with 40.8% of neonates in the hypertensive group born before 37 weeks, compared to only 5% in the normotensive group ($p < 0.001$). Elmugabil *et al.* (2016) identified similar trends and linked lower maternal calcium levels with increased incidence of preterm labour. In contrast, Kant *et al.* (2019) did not find a direct association between calcium levels and preterm birth but did observe lower calcium among mothers delivering low-birth-weight infants. [26] Collectively, these findings affirm that maternal hypertension adversely affects foetal growth and gestational duration, increasing the risk of both low birth weight and preterm delivery.

The Apgar scores at both 1 minute and 5 minutes after birth were significantly lower in neonates born to hypertensive mothers compared to those from normotensive pregnancies. At 1 minute, only 56.7% of neonates in the hypertensive group had Apgar scores ≥ 7 , compared to 86.7% in the normotensive group. At 5 minutes, 73.2% of neonates in the hypertensive group achieved scores ≥ 7 , while 96.7% did so in the normotensive group ($p < 0.001$ for both time points). The mean Apgar scores at 1 and 5 minutes were 6.3 and 7.4 in the hypertensive group, respectively, both significantly lower than 7.8 and 8.9 in the normotensive group. These scores reflect early fetal vitality and the need for resuscitation and monitoring.

Adverse fetal outcomes were also more common in hypertensive pregnancies. These findings are consistent with those of Ephraim *et al.*, who showed that reduced maternal calcium and magnesium levels were associated with poor fetal outcomes [17]. Likewise, Onyegbule *et al.* reported that low maternal calcium and magnesium levels were negatively correlated with blood pressure and placental perfusion, leading to impaired fetal oxygenation and poor fetal condition at birth [27]. In the present study, respiratory distress syndrome, prematurity, NICU admission, and early fetal death were significantly more frequent in neonates born to hypertensive mothers.

Overall, the present study strengthens the evidence that disturbances in calcium and magnesium metabolism are closely associated with hypertensive disorders of pregnancy and adverse Maternal and Fetal outcomes. In line with Sukonpan *et al.* and Pairu *et al.*, supplementation of calcium and magnesium may be beneficial in populations with low dietary intake or high

prevalence of hypertensive disorders of pregnancy [18, 19]. However, conflicting findings from Gol *et al.* and Vafaei *et al.* indicate that the predictive and therapeutic value of these minerals may be population-specific and influenced by nutritional status, genetics, and quality of antenatal care [21, 22].

Conclusion

The present study demonstrates that hypertensive disorders of pregnancy are associated with significantly reduced maternal serum calcium and magnesium levels, with hypertensive women having lower mean serum calcium (9.7 ± 1.7 mg/dL vs 10.2 ± 1.4 mg/dL) and magnesium levels (1.7 ± 0.5 mg/dL vs 1.9 ± 1.1 mg/dL) compared to normotensive pregnant women. These biochemical abnormalities were accompanied by substantially higher maternal morbidity, including eclampsia (7.5%), HELLP syndrome (5%), postpartum haemorrhage (13.3%), placental abruption (6.7%), and acute kidney dysfunction (5%), as well as increased ICU admission (13.3%) and longer hospital stay (5.8 vs 2.5 days).

Fetal outcomes were also significantly worse in hypertensive pregnancies, with a lower mean birth weight (2.35 ± 0.48 kg vs 2.85 ± 0.45 kg), a higher incidence of low birth weight (47.5% vs 18.3%), and poorer APGAR scores at both 1 and 5 minutes. Additionally, higher rates of prematurity, respiratory distress syndrome, NICU admission, and early fetal death were observed in the hypertensive group.

These findings reinforce the critical role of calcium and magnesium in maintaining vascular and placental function during pregnancy and highlight their association with disease severity in hypertensive disorders of pregnancy. Monitoring and optimizing these micronutrients, particularly in high-risk and nutritionally vulnerable populations, may help improve maternal and fetal outcomes and reduce the clinical burden of hypertensive disorders of pregnancy.

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