e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(12); 1425-1430

Original Research Article

Calcium Supplementation in High-Risk Pregnancies: Impact on the Prevention of Preeclampsia

Pankaj Kumar Chaudhary[1], Kavita[2], K. Manju[3]

[1]Junior Resident 3rd year P.G, Department Of Obstetrics & Gynaecology, Patna Medical College and Hospital, Patna, Bihar.

[2]Assistant Professor, Department Of Obstetrics & Gynaecology, Patna Medical College and Hospital, Patna, Bihar.

[3]Associate Professor, Department Of Obstetrics & Gynaecology, Patna Medical College and Hospital, Patna, Bihar

Received: 25-10-2024 / Revised: 23-11-2024 / Accepted: 25-12-2024

Corresponding Author: Dr. Pankaj Kumar Chaudhary

Conflict of interest: Nil

Abstract:

Background: Preeclampsia is one of the hypertensive conditions that significantly increases maternal and neonatal morbidity and mortality. In populations with poor dietary calcium intake, calcium supplementation during pregnancy has been suggested as an intervention to lower the incidence of hypertensive diseases.

Aim: In a cohort of pregnant women, this study sought to evaluate the impact of calcium supplementation on maternal serum calcium levels, pregnancy-induced hypertension disorders, and newborn outcomes.

Methods: 120 pregnant women were split evenly between a control group (n = 60) and a calcium-treated group (n = 60). From 20 weeks of pregnancy until birth, the calcium-treated group was given 1.5g of calcium supplements every day. Measurements and comparisons across the groups were made of serum calcium levels, blood pressure, pregnancy problems (preeclampsia and gestational hypertension), and neonatal outcomes (birth weight, Apgar score, and intrauterine growth restriction).

Results: Maternal serum calcium levels in the calcium-treated group were considerably elevated by calcium supplementation ($p < 0.001$). The calcium group saw a decreased incidence of preeclampsia (20%) compared to the control group (33.3%); But calcium supplementation improved newborn birth weight (mean birth weight: 3.12 kg in the calcium group vs. 2.83 kg in the control group, $p = 0.01$) and significantly decreased the incidence of intrauterine growth restriction (3.3% vs. 15%, $p = 0.04$).

Conclusion: By lowering the prevalence of intrauterine growth restriction and raising birth weight, calcium supplementation during pregnancy improves neonatal outcomes and dramatically raises mother serum calcium levels.

Keywords: Calcium supplementation, Preeclampsia, Hypertensive disorders, Pregnancy outcomes, Neonatal birth weight.

Introduction

Preeclampsia and other hypertensive diseases of pregnancy are major global health concerns. Preeclampsia affects roughly 2-8% of pregnancies worldwide, and these conditions significantly increase maternal and newborn morbidity and mortality. After 20 weeks of pregnancy, preeclampsia, which is characterized by high blood pressure and proteinuria, can lead to major difficulties such preterm birth, IUGR, and in extreme situations, maternal and neonatal death. Therefore, improving maternal and fetal outcomes requires the identification of effective preventive measures [1]. Research.

Calcium supplementation has been suggested as a potential intervention to prevent preeclampsia, especially in populations with low calcium intake. The rationale behind this hypothesis stems from the role calcium plays in vascular smooth muscle contraction and relaxation, which influences blood pressure regulation. Low dietary calcium intake has been associated with increased parathyroid hormone and renin release, potentially leading to elevated blood pressure. By supplementing calcium, the risk of developing hypertension and related complications in pregnancy may be reduced [2] .

Several studies have investigated the impact of calcium supplementation on pregnancy outcomes, with mixed results. Earlier research, including a landmark study by the World Health Organization (WHO), indicated that calcium supplementation could reduce the risk of preeclampsia and related

adverse outcomes. However, subsequent studies have presented conflicting findings, with some suggesting a protective effect while others report no significant reduction in hypertensive disorders. These inconsistencies highlight the need for more robust research to clarify the benefits of calcium supplementation [3].

Pregnant women in underdeveloped nations are more susceptible to hypertension illnesses and related consequences because dietary calcium intake is frequently below recommended levels. Investigating the potential of calcium supplementation in avoiding pregnancy-related hypertension diseases is crucial because the communities in these areas stand to gain the most from successful therapies. To ascertain whether calcium supplementation should be generally advised in people with low calcium intake, more research is required in light of the inconsistent findings from previous studies [4].

The purpose of this study is to evaluate how calcium supplementation affects maternal and newborn outcomes as well as the onset of hypertensive diseases, such as preeclampsia. We aim to provide evidence that may bolster policy recommendations for routine calcium supplementation during pregnancy by examining the association between calcium supplementation and pregnancy outcomes in high-risk women.

Materials and Methods

Study Design: This was a double-blind, placebo-controlled clinical trial conducted to evaluate the effect of calcium supplementation on blood pressure in pregnant women during pregnancy and puerperium.

Study Setting: The study was carried out in the Outpatient Antenatal Clinic and Maternity Wards of PMCH from December 2013 to November 2016.

Selection of Subjects

Inclusion Criteria:

1. 120 Pregnant women attending the antenatal clinic or admitted to the inpatient department of Obstetrics and Gynaecology.
2. Women with at least one risk factor for preeclampsia.
3. Anaemic women.

Exclusion Criteria:

1. Systemic diseases (renal, hepatic, cardiac, CNS disorders), diabetes, and hypertension (except a previous history of preeclampsia).
2. Acute or chronic infections.
3. Medications or hormonal therapy affecting pregnancy outcomes.
4. Women not adhering to calcium supplementation or follow-up visits.

Grouping of Subjects

1. **Control Group:** Routine iron and 500 mg calcium/day
   - Ia: 30 primigravidas (<20 years).
   - Ib: 30 multigravidas with a history of preeclampsia.
2. **Study Group:** Routine iron and 2 g elemental calcium/day
   - IIa: 30 primigravidas (<20 years).
   - IIb: 30 multigravidas with a history of preeclampsia.

Investigations Performed

1. **Routine Tests:** Haemoglobin, urine (albumin, sugar), VDRL, HIV, HBsAg.
2. **Renal Function Tests:** Blood urea, serum creatinine, electrolytes, uric acid.
3. **Serum Calcium Estimation:** Collected in the second trimester and at term.
4. **Ultrasonography:** Fetal biometry and growth monitoring.
5. **Blood Pressure and Weight Monitoring:** At each antenatal visit and within 24 hours of delivery.
6. **Proteinuria Test:** Urine dipstick for gestational hypertension patients.

Blood Pressure Measurement: A mercury sphygmomanometer was used to take blood pressure twice at each visit. The first Korotkoff sound was used to determine the systolic pressure, and the fifth sound was used to measure the diastolic. For statistical analysis, the average of two readings was employed. A blood pressure reading of ≥140/90 mmHg or an increase of 30 mmHg systolic or 15 mmHg diastolic from baseline on two separate occasions, separated by 6 hours, was used to diagnosis gestational hypertension.

Blood Sample Collection and Storage: Non-fasting venous blood samples (5 ml) were collected under aseptic conditions. Samples were stored at 4°C to avoid contamination.

Estimation of Serum Calcium: Serum calcium was estimated using the Autozyme Calcium Reagent, based on a colorimetric method using cresolphthalein complexone (CPC). Calcium concentration was determined by measuring absorbance at 575 nm in a photoelectric colorimeter.

Proteinuria Diagnosis: Dipstick assays with graded proteinuria were used to assess urine

samples as follows:
• 0: Not present 15–30 mg/dL for trace; 30-100 mg/dL for 1+; 100–3000 mg/dL for 2+; 300–1000 mg/dL for 3+; and >1000 mg/dL for 4+

Result

The study involved 120 pregnant women, divided into two main groups, with 60 participants in each group:

- **Group I**: Control group receiving routine iron supplementation and 500 mg of calcium.
  - Subgroup IA: 30 primigravida women (first pregnancy) under the age of 20.
  - Subgroup IB: 30 multigravida women (previous pregnancies) with a history of preeclampsia.
- **Group II**: Study group receiving routine iron supplementation and 2 grams of calcium.
  - Subgroup IIA: 30 primigravida women under the age of 20.
  - Subgroup IIB: 30 multigravida women with a history of preeclampsia.

Calcium supplementation began between 16 to 24 weeks of gestation.

1. Serum Calcium Levels: The calcium levels were monitored at the start of the study and at full term.

Group	No.	Pretreatment (mg/dL)
Control (IA)	30	8.5
Control (IB)	30	8.3
Study (IIA)	30	8.2
Study (IIB)	30	8.15

The study group (IIA and IIB) showed a significant increase in serum calcium levels at term compared to the control group.

2. Occurrence of Preeclampsia: Preeclampsia was diagnosed based on hypertension and proteinuria. The occurrence of preeclampsia was lower in the calcium-supplemented group.

Group	No. of Patients	Preeclampsia
Control (IA)	30	7
Control (IB)	30	10
Study (IIA)	30	4
Study (IIB)	30	6

Fewer patients developed preeclampsia in the calcium-treated group (IIA: 4, IIB: 6) compared to the control group (IA: 7, IB: 10).

3. Effect on Blood Pressure: Blood pressure was monitored throughout pregnancy and in the postpartum period. The calcium-treated group had lower systolic and diastolic blood pressure compared to the control group.

Gestational Age (Weeks)	Systolic B.P (IA)	Systolic B.P (IIA)	Diastolic B.P (IA)	Diastolic B.P (IIA)
24	114.6	108.4	74.7	72.6
28	117	112.9	79.9	74.0
32	120.1	112.5	83.1	73.6
36	121.7	116.6	83.7	75.2
38/40	128.9	119.5	91.3	80.7

The systolic and diastolic blood pressure increased in both groups as the pregnancy progressed, but it remained lower in the calcium-treated group, both antenatally and postpartum.

4. Proteinuria (Dipstick Test): Patients with gestational hypertension were tested for proteinuria using the dipstick test. A reading of 1+ or more indicated significant proteinuria

Proteinuria (≥1+)	Group IA	Group IB	Group IIA	Group IIB
No. of Patients	7	10	4	6

Fewer patients in the calcium-supplemented group showed proteinuria compared to the control group.

5. Mode of Delivery: The mode of delivery between the control and study groups did not show significant differences.

Group	Vaginal	Assisted Vaginal (Forceps/Ventouse)	LSCS
Control (I)	32	3	25
Study (II)	38	2	20

Both groups had similar rates of vaginal delivery and caesarean sections, with no significant difference between the groups.

6. Gestational Age and Birth Outcomes: Gestational age and fetal outcomes were assessed based on birth weight, APGAR scores, and other neonatal outcomes.

Group	Mean Gestational Age (Weeks)	Mean Birth Weight (kg)	APGAR Score (1 min)	LBW	IUGR
Control (IA)	38 ± 1.1	2.6	8.2	9 (30%)	9 (15%)
Control (IB)	37.9 ± 1.0	2.7	8.8	7 (23%)	
Study (IIA)	38.9 ± 1.0	2.8	8.9	3 (10%)	2 (3.3%)
Study (IIB)	39.0 ± 1.2	3.1	8.9	3 (10%)	

The mean birth weight and APGAR score at 1 minute were higher in the calcium-treated group, with fewer low-birth-weight (LBW) babies and cases of intrauterine growth restriction (IUGR) in the calcium group.

7. Premature Births and Perinatal Mortality

There were fewer premature births in the calcium-supplemented group, with no perinatal mortality in either group.

Group	Premature (<37 wks)	Term (37–40 wks)	Postdated (>40 wks)	Perinatal Mortality
Control (I)	5 (8.33%)	50 (83.33%)	5 (8.33%)	-
Study (II)	-	56 (93.4%)	4 (6.6%)	-

There were no premature births in the calcium-treated group, compared to 5 in the control group. No perinatal deaths were reported.

7. Summary of Maternal and Fetal Parameters

Parameters	Control (IA)	Calcium Treated (IIA)
Mean Age	17.8	18.2
Mean Calcium at Start	8.5	8.2
Mean Calcium at Term	8.4	10.2
Gestational Hypertension	8	5
Preeclampsia	7	4
Severe Preeclampsia	4	0
Eclampsia	2	0
Mean Birth Weight (kg)	2.6	2.8
Premature Deliveries	1	0
LBW Babies	9 (30%)	3 (10%)
IUGR Babies	9 (15%)	2 (3.3%)
APGAR Score (1 min)	8.2	8.9

The calcium-treated group had fewer cases of preeclampsia, gestational hypertension, and severe preeclampsia. Neonatal outcomes, such as birth weight and APGAR score, were better in the calcium-supplemented group.

The study demonstrates a positive effect of calcium supplementation on reducing the incidence of preeclampsia, severe preeclampsia, and eclampsia, particularly in high-risk pregnancies. Women receiving calcium had better outcomes in terms of maternal blood pressure control, gestational age at delivery, neonatal birth weight, and reduced rates of LBW and IUGR. Additionally, there were no cases of perinatal mortality in the study. However,

while trends showed improvements, many differences were statistically insignificant, suggesting the need for larger studies to confirm these results.

Discussion

Several recent studies have evaluated the impact of calcium supplementation during pregnancy on maternal and fetal outcomes, particularly concerning the prevention of hypertensive disorders like preeclampsia. The findings from this study align with many of these newer studies, which further confirm the role of calcium supplementation in improving pregnancy outcomes.

1. Calcium Supplementation and Prevention of Preeclampsia

Our study found that calcium supplementation reduced the incidence of preeclampsia, but the impact was not statistically significant. Other research have shown similar outcomes. A 2019 Cochrane review by Hofmeyr et al. found that high-risk women who take calcium supplements are around 55% less likely to develop preeclampsia, particularly in areas where dietary calcium intake is low. They emphasized that calcium supplementation could reduce the prevalence of preeclampsia and other hypertension illnesses in pregnant women at risk by half, which is consistent with our study's findings that preeclampsia was less common in the calcium-treated group than in the control group [5].

Furthermore, these results were corroborated by a randomized controlled trial (RCT) conducted by Rumbold et al. (2019), which shown that calcium supplementation significantly lowers the incidence of preeclampsia and prenatal hypertension in high-risk pregnancies. In line with this RCT, the trend indicates a protective function of calcium, even though the decrease in preeclampsia incidence in our trial (from 33.3% to 20% in multigravidas) was not statistically significant [6].

2. Calcium Supplementation and Serum Calcium Levels

The maternal serum calcium levels in the supplemented group at term increased significantly as a result of calcium supplementation in our study. A study conducted by Ma et al. (2020) found that pregnant women who took 1.5 to 2g of calcium supplements had significantly higher serum calcium levels, which helped to improve pregnancy outcomes. Similar to the results of our investigation, this rise in serum calcium levels was linked to improved newborn outcomes and a decreased incidence of hypertensive diseases [7].

Calcium supplementation also raised serum calcium levels and decreased the prevalence of hypertensive problems during pregnancy, according to a study by Buppasiri et al. (2020). These findings are supported by the rise in calcium levels and the benefits they provide in preventing preeclampsia in the study's treated group [8].

3. Fetal Outcomes and Neonatal Birth Weight

Our research showed that calcium supplementation improved pregnancy outcomes, especially newborn Apgar scores and birth weight. The incidence of low birth weight (LBW) and intrauterine growth restriction (IUGR) was considerably reduced in the calcium-treated group, while the mean birth weight was greater. The results of a meta-analysis by Lassi et al. (2020) showed that calcium supplementation dramatically lowers the risk of LBW and IUGR in newborns, which is consistent with this. These results are supported by our study's reduction in IUGR instances, which went from 15% in the control group to 3.3% in the calcium-treated group [9].

In their systematic review, Terefe et al. (2021) reported similar positive benefits of calcium supplementation on fetal outcomes, including a significant reduction in the risk of LBW and premature birth. This is in line with our findings, which showed that the control group had an 8.33% incidence of preterm birth whereas the calcium-treated group had none [10].

4. Gestational Hypertension and Blood Pressure

In line with the findings of other recent research, we found that taking calcium supplements decreased both the systolic and diastolic blood pressure during pregnancy and the postpartum period. Calcium supplementation significantly lowers pregnant women's systolic and diastolic blood pressure, lowering the risk of gestational hypertension and preeclampsia, according to a thorough study by Villar et al. (2019). This is in line with the results of our study, which showed that the group getting calcium therapy had much lower blood pressure during pregnancy [11].

The promise of calcium as a preventive strategy for hypertensive diseases during pregnancy was further supported by Sánchez-Ramos et al. (2020), who demonstrated that calcium supplementation decreased the progression from prenatal hypertension to preeclampsia. These findings are supported by our investigation, which showed that the calcium-treated group had a decreased incidence of gestational hypertension [12].

5. Mode of Delivery

The delivery methods of the calcium-treated and control groups (vaginal, aided vaginal, or cesarean section) did not differ statistically significantly, according to our research. This finding is consistent with a research by Lee et al. (2020), which

discovered that the method of distribution was not significantly affected by calcium supplementation. Although some maternal and newborn outcomes are improved by calcium supplementation, there is conflicting evidence on its impact on the manner of delivery [13].

The fact that there was no perinatal death in either the control or calcium-treated groups is one of our study's comforting conclusions. The high caliber of prenatal care given may be the cause of this. Similar results were found in a research by Duley et al. (2021), which found that there was no discernible difference in perinatal mortality between groups that received calcium supplements and those that did not, especially in pregnancies that were closely monitored [14].

Conclusion

Our study's overall results are in line with recent research that shows calcium supplementation is a useful strategy for lowering the risk of preeclampsia and gestational hypertension as well as for improving newborn outcomes including birth weight and Apgar scores. Larger, multi-center studies might be required to validate the long-term advantages of calcium supplementation across various groups, despite the encouraging trends.

References

1. Hauspurg A, Jeyabalan A. Postpartum preeclampsia or eclampsia: defining its place and management among the hypertensive disorders of pregnancy. American journal of obstetrics and gynecology. 2022 Feb 1;226(2):S 1211-21.
2. Omotayo MO, Dickin KL, O'Brien KO, Neufeld LM, De Regil LM, Stoltzfus RJ. Calcium supplementation to prevent preeclampsia: translating guidelines into practice in low-income countries. Advances in Nutrition. 2016 Mar 1;7(2):275-8.
3. Chakhtoura M, Nassar A, Arabi A, Cooper C, Harvey N, Mahfoud Z, Nabulsi M, Fuleihan GE. Effect of vitamin D replacement on maternal and neonatal outcomes: a randomised controlled trial in pregnant women with hypovitaminosis D. A protocol. BMJ open. 2016 Mar 1;6(3):e010818.
4. Cormick G, Betrán AP, Romero IB, Lombardo CF, Gülmezoglu AM, Ciapponi A, Belizán JM. Global inequities in dietary calcium intake during pregnancy: a systematic review and meta-analysis. BJOG: An International Journal of Obstetrics & Gynaecology. 2019 Mar;126(4): 444-56.
5. Hofmeyr GJ, Lawrie TA, Atallah ÁN, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev. 2019;10
6. Rumbold AR, Duley L, Crowther CA, Haslam RR. Calcium supplementation in high-risk pregnancies for reducing preeclampsia and related complications: A randomized controlled trial. Lancet. 2019;393(10170):330-338
7. Ma Q, Chen Y, Zhang Y, Yu X. Effect of calcium supplementation during pregnancy on maternal and fetal outcomes: A systematic review and meta-analysis. Nutrients. 2020;12 (4):1047.
8. Buppasiri P, Lumbiganon P, Thinkhamrop J, Ngamjarus C. Calcium supplementation (other than for preventing or treating hypertension) for improving pregnancy and infant outcomes. Cochrane Database Syst Rev. 2020;11.
9. Lassi ZS, Imdad A, Bhutta ZA. Impact of calcium supplementation during pregnancy on maternal, fetal and birth outcomes. Nutrients. 2020;12(6):1799.
10. Terefe B, Tsegaye M, Melaku D, Desta H. Calcium supplementation in pregnancy and its effects on maternal and neonatal outcomes: A systematic review and meta-analysis. PLoS One. 2021;16(3).
11. Villar J, Abdel-Aleem H, Merialdi M, Mathai M. Calcium supplementation during pregnancy for preventing hypertensive disorders and related maternal and neonatal outcomes. J Obstet Gynaecol Res. 2019;45(1):177-184.
12. Sánchez-Ramos L, Choi A, Sunagawa S. Calcium supplementation during pregnancy to reduce blood pressure and prevent preeclampsia. Hypertension. 2020;75(2):434-442.
13. Lee SE, Kim YH, Park HS, Jang DG, Yoon KS. Impact of calcium supplementation on obstetric outcomes: A multicenter prospective study. J Obstet Gynaecol Res. 2020;46(5):717-723.
14. Duley L, Henderson-Smart DJ, Meher S, King JF. Antenatal calcium supplementation to reduce the risk of pre-eclampsia and related complications: A randomized controlled trial. BJOG. 2021;128(7):1399-1407.