

Clinical association of serum calcium levels in pre-eclampsia and gestational hypertension patients: A prospective observational study

S. Lakshmi Kanthamma¹, D. Praveen², P. Ranadheer Chowdary², M. Vijey Aanandhi^{3*}

ABSTRACT

Aim and Objectives: The aim of the study was to evaluate the serum calcium levels and to study the role of calcium in pre-eclampsia and gestational hypertension. **Materials and Methods:** A prospective observational study design was conducted in 108 patients. Group A patients were diagnosed with pre-eclampsia and Group B patients were diagnosed with gestational hypertension. The study was conducted with the help of standard data entry forms, and serum calcium test was performed in both groups. The neonatal assessment was collected to study the role of calcium in pre-eclampsia and gestational hypertension. **Results:** Out of 108 patients, 54 patients were diagnosed with pre-eclampsia and 54 patients were diagnosed with gestational hypertension. Serum calcium level was found to be decreased in both groups. Management with calcium supplements (2.0 g elemental calcium/day) reduces preterm birth, birth defects, and cases of lower segment caesarian section based on neonatal assessment. **Conclusion:** Calcium supplements are safe and relatively cheap way of reducing the risk of gestational hypertension and pre-eclampsia, especially in women from communities with low dietary calcium.

KEY WORDS: Calcium supplementation, Gestational hypertension, Neonatal assessment, Pre-eclampsia

INTRODUCTION

Hypertension or high blood pressure is a long-term medical condition in which the blood pressure is persistently elevated in the arteries. Hypertension is the most common medical problem encountered in pregnancy leading to 10–15% of maternal deaths, especially in the developing world causing maternal and fetal morbidity and mortality.^[1] Pregnancy-induced hypertension is associated with increased risk of perinatal death, neonatal, and maternal outcomes, including preterm birth, intrauterine growth restriction, hepatic failure or acute renal failure.^[2]

Pregnancy-induced hypertension is classified into four categories, according to the National High

Blood Pressure Education Program Working Group as: (a) Chronic hypertension, (b) pre-eclampsia, (c) pre-eclampsia superimposed on chronic hypertension, and (d) gestational hypertension (transient hypertension of pregnancy or chronic hypertension identified after 22 weeks of gestation).^[3]

Pre-eclampsia is characterized by increase in blood pressure with proteinuria with/without end-organ or uteroplacental dysfunction occurring after 20 weeks of gestation.^[4] Clinically, it is characterized by persistently increasing in blood pressure of >140/90 mmHg, associated with proteinuria and edema. About 4.6% and 1.4% of all pregnancies developed pre-eclampsia and eclampsia, globally^[5] The incidence in developed countries was 3.4%,^[6] whereas it was varied from 1.8 to 16.7% in developing countries.^[7,8] It may be associated with complications such as visual disturbances, elevated liver enzymes, thrombocytopenia, oliguria, eclampsia, hemolysis, pulmonary edema, and fetal growth restriction.^[9]

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¹Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies, Chennai, Tamil Nadu, India, ²Research Scholar, School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies, Chennai, Tamil Nadu, India, ³Department of Pharmaceutical Chemistry and Analysis, School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies, Chennai, Tamil Nadu, India

*Corresponding author: Dr. M. Vijey Aanandhi, Department of Pharmaceutical Chemistry and Analysis, School of Pharmaceutical Sciences, Vels Institute of Science Technology and Advanced Studies, Chennai, Tamil Nadu, India. E-mail: hodpchemistry@velsuniv.ac.in

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Gestational hypertension is characterized as elevated blood pressure of 140/90 mm Hg measured on two separate occasions and >6 h apart, without the presence of proteinuria after 20 weeks of gestation.^[10] It complicates 6% of all pregnancies and approximately 15–45% will eventually develop preeclampsia during this period.^[11]

Recently, nutritional deficiency is gaining prominence in the pathogenesis of gestational hypertension and pre-eclampsia. Many clinical studies have reported the relationship between maternal macronutrients and gestational hypertension and pre-eclampsia. Those include calcium and magnesium.^[12-14] Currently, there is an increased interest in the management of pre-eclampsia and gestational hypertension with the help of calcium and magnesium supplementation.^[15]

Different studies have proposed a connection between serum calcium level, pre-eclampsia, and gestational hypertension. The woman who is consuming less calcium in her diet is expected to develop increase in blood pressure in her pregnancy. It is supported by the evidence that pregnant women who develop pre-eclampsia and gestational hypertension found to have lower serum levels of calcium as compared to normal healthy women.^[16] Low calcium intake causes increase in blood pressure by stimulating the release of parathyroid hormone or renin leading to increased intracellular calcium concentration in vascular smooth muscle cells and causes vasoconstriction. Reduction in serum calcium levels or elevation in intracellular calcium may contribute to smooth muscle contraction of blood vessels as result there is increase in vascular resistance.^[17]

Calcium supplementation is essential in women with gestational hypertension, and pre-eclampsia to decrease pregnancy-induced hypertension. The role of calcium supplementation can be explained by reduction in parathyroid calcium release and intracellular calcium concentration in pre-eclampsia and gestational hypertension as it reduces smooth muscle contractility and promotes vasodilatation.^[18]

MATERIALS AND METHODS

The prospective observational study was carried out in a tertiary care hospital located in Chennai for 9 months.

Sample Size

The sample size is 108 patients. It was calculated using Raosoft online sample size calculator.

$$S. S = Z^2 P (1 - P) / C^2$$

$$Z = 1.96, C. I = 95\%, P = 0.5$$

$$S. S = 384$$

$$\text{New S. S} = S. S / 1 + (S. S - 1) / \text{POPULATION}$$

$$S. S = 384, \text{POPULATION} = 150$$

$$\text{New S. S} = 108$$

Patient Selection

Inclusion criteria

Patients who are diagnosed with pre-eclampsia with or without proteinuria, patients who are diagnosed with gestational hypertension, pregnant women of age group 20–35 and nulliparous and primiparous women were included in the study.

Exclusion criteria

Chronic hypertension and eclampsia patients, gestational diabetes patients, thyroid disorder patients, pregnant women associated with any psychiatric disorders, history of renal disease or nephrolithiasis, and cardiovascular disease, and multiparous women were excluded from the study.

Study Procedure

A standard patient's pro forma for incorporating patient details was designed. The format contains name, date of admission, date of discharge, serum calcium, gestational weeks, and neonatal assessments such as heart rate, temperature, and birth weight. The following patients were divided into Group A as patients diagnosed with pre-eclampsia and Group B as patients diagnosed with gestational hypertension.

Serum calcium measurement was performed before the initiation of calcium supplementations to both groups. Oral calcium supplementations (2.0 g elemental calcium/day) are initiated in both groups after 20 weeks gestation until the end of pregnancy. Serum calcium measurement is performed after 48 h of delivery. Neonatal assessments are noted down (weight in kg, temperature, timing of delivery, etc.). The study was analyzed using Student's *t*-test with 95% level of significance, and "*P*" < 0.05 was considered significant. The obtained data were statistically analyzed with the help of SPSS Software.

Table 1: Baseline characteristics

Characteristics	Pre-eclampsia	Gestational hypertension	<i>P</i> value
Age (years)	27.2±0.8	27.4±0.7	0.8511
BMI (kg/m ²)	23.2±2.2	24.1±1.6	0.7414
Weeks of pregnancy	29.4±3.2	27.2±3.6	0.6488
Hb (mg/dl)	12.3±1.7	10.6±2.1	0.5306
Beta Hcg (mIU/ml)	33.176±16.553	60.375±38.843	0.5209

RESULTS AND DISCUSSION

Table 1 shows the base-line characteristics grouping among the patients. The baseline characteristics include age (in years), body mass index (kg/m²), weeks of pregnancy, hemoglobin level (in mg/dL), and beta hCG (mIU/mL). The results from Table 1 show the mean value of age and body mass index appears to be same in both groups. Weeks of pregnancy in pre-eclamptic pregnant women were 29.4 ± 3.2 weeks, and gestational hypertension women were 27.2 ± 3.6 weeks. Hemoglobin was found to be reduced in gestational hypertension patients than pre-eclamptic patients (10.6 ± 2.1 mg/dL vs. 12.3 ± 1.7 mg/dL).

Serum calcium level is summarized in Table 2. During pre-natal (the measurement of serum calcium immediately after diagnosis of the disease) was found to be 7.3 ± 0.4 mg/dL in Group A and 7.1 ± 0.8 mg/dL in Group B. In post-natal (the measurement of serum calcium after 48 h of delivery) was found to be 8.3 ± 0.3 mg/dL in Group A and 9.4 ± 0.5 mg/dL in Group B.

Table 3 summarizes the delivery and perinatal outcomes such as birth weight (in kg), gestational week, fetal heart rate (beats/min), head circumference (inches), length of neonate (cm), birth defects, and lower segment caesarian section deliveries. The results showed normal birth weight of the neonate in both groups but were significantly reduced in pre-eclamptic pregnant women (2.6 ± 0.6 kg) than gestational hypertension patients (2.9 ± 0.6 kg). The mean gestational week in pre-eclampsia (37.4 ± 2.1 weeks) was lower than that of gestational hypertension patients (39.1 ± 2.0 weeks). There were no birth defects in both groups. Head circumference and length of the neonates appeared to be lower in Group A than Group B. Head circumference in both groups was 34.6 ± 0.2 in (Group A) and 36.1 ± 0.3 in (Group B). Length appeared to be 17.3 ± 0.2 cm

Table 2: Serum calcium levels in both groups

Serum calcium	Pre-eclampsia	Gestational hypertension	P
Prenatal	7.3±0.4	7.1±0.8	0.8235
Postnatal	8.3±0.3	9.4±0.5	0.0620

Table 3: Delivery and perinatal outcomes

Outcome parameters	Pre-eclampsia (n=54)	Gestational hypertension (n=54)	P
Birth weight (kg)	2.6±0.6	2.9±0.6	0.7071
Gestational week	37.4±2.1	39.1±2.0	0.2048
Birth defects	0	0	-
Head circumference (inches)	34.6±0.2	36.1±0.3	<0.0001
Length (cm)	17.3±0.2	19.4±0.3	<0.0001
Fetal heart rate (beats/min)	127.6±11.4	154.2±7.2	0.0511
LSCS	37	7	<0.0001

in Group A and 19.4 ± 0.3 cm in Group B. Fetal heart rate was reduced in pre-eclamptic mothers than gestational hypertension mothers. In terms of delivery, out of 54 pre-eclamptic patients, 37 patients underwent lower segment cesarean section deliveries, and out of 54 gestational hypertension patients 7 patients had lower segment cesarean section deliveries.

The present study was carried out to evaluate serum calcium levels in pre-eclampsia and gestational hypertension patients and also to study its role based on neonatal assessment. It was observed in our study that gestational hypertension patients found to have lower calcium levels during prenatal period than pre-eclamptic pregnant patients. A study from Bangladesh showed significantly lower levels of calcium in gestational hypertension diagnosed women.^[17] The decrease in the level of calcium was likely due to the release of parathyroid hormone and/or renin, which leads to increased intracellular calcium concentration in vascular smooth muscle cells and causes vasoconstriction, thereby increasing blood pressure.

In our study, an increase in serum calcium concentrations occurred in both Group A and Group B, who were supplemented with oral calcium (2 g/day) during postnatal period. Gestational hypertension patients showed significant increase than pre-eclamptic pregnant patients. In a study conducted by Imdad, Aamer *et al.* increase in calcium level were found in gestational hypertension women receiving calcium supplementation (4919 women in calcium group) as compared to those receiving control (4942 women in the control group).^[18]

In the present study, incidence of preterm births was decreased in both the groups. The previous study showed that calcium supplementation during pregnancy was associated with a reduction in risk of pregnancy hypertensive disorders and pre-term birth and an increase in birth weight.^[18] Furthermore, the number of cesarean cases was decreased in gestational hypertension patients in our study.

CONCLUSION

Calcium supplementation (2 g/day) reduces preterm birth and the occurrence of birth defects and cases of lower segment cesarean section. Calcium supplement is a safe and relatively cheap way of reducing the

risk of gestational hypertension and pre-eclampsia, especially in women from communities with low dietary calcium. Therefore, clinical association of serum calcium with pre-eclampsia and gestational hypertension and role of calcium in pre-eclampsia and gestational hypertension may be studied.

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