

# The role of serum calcium, magnesium, and zinc in pregnancy induced hypertension

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## Abstract

**Background:** Pregnancy induced hypertension or preeclampsia is a triad of hypertension, proteinuria, and edema occurring after 20 weeks of gestation in previously normotensive women. It is the most common medical complication of pregnancy with an incidence of 5% to 10% with increased in maternal and infant mortality and morbidity. The exact etiology is not known although various elements might play a role in preeclampsia. The aim of the study: Analyse and compare the concentration of serum calcium, magnesium, and zinc level in women with preeclampsia and in normal pregnant women. **Materials and Methods:** This is a cross-sectional case-control study involving 25 women with preeclampsia in the case group and 25 normal pregnant women in the control group. The inclusion criteria for the case group were age group in between 20-40 years including both primi and second gravida in the third trimester of pregnancy (>24 weeks of pregnancy). The blood pressure measured by sphygmomanometer in the upper arm in sitting posture was  $\geq 140/90$  mmHg in two different occasions taken 6 hours apart. The urine albumin was  $\geq 1+$  or in the midstream random sample of urine. The controls group was formed by 25 age-matched normal pregnant women either primi or second gravida in the third trimester of pregnancy. The patients with medical complications such as Diabetes Mellitus, renal failure, chronic hypertension, heart failure or ischaemic heart disease, multiple pregnancies, pregnancy < 24 weeks of gestation, patients on magnesium sulfate and calcium lactate therapy were excluded from the study. The Body Mass Index (BMI), serum calcium, magnesium and zinc levels were compared between the case and control groups. **Results:** The BMI was significantly higher in preeclamptic women when compared to normal pregnant women  $28.71 \pm 4.70$  versus  $22.46 \pm 3.42$   $P < 0.001$ . The serum calcium, magnesium and zinc levels in preeclamptic women were significantly lower when compared to normal pregnant women  $8.07 \pm 0.43$  versus  $8.96 \pm 0.59$   $P < 0.001$ ,  $1.62 \pm 0.16$  versus  $1.92 \pm 0.16$   $P < 0.001$ ,  $93.28 \pm 9.44$  versus  $93.28 \pm 9.44$  for cases and controls respectively. **Conclusion:** Although the calcium, magnesium and zinc deficiency cannot be pinpointed as the sole factors for the etiology of preeclampsia, they have a definite role in the development of preeclampsia.

**Key Word:** Preeclampsia, serum calcium, serum magnesium, and serum Zinc.

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## INTRODUCTION

Pregnancy-induced hypertension or preeclampsia is a transient but potentially dangerous complication of pregnancy, with worldwide significance to the mother and the infants. It affects approximately 5-10% of the pregnancies worldwide.<sup>1</sup> An inadequate dietary intake before and during pregnancy might be a risk not only for the mother but also for the fetus. Deficiency of the elements such as magnesium, zinc has been implicated in the pregnancy wastage, congenital anomalies, pregnancy-induced hypertension, placental abruption of the membrane, low birth weight and stillbirths.<sup>2</sup> On the physiological basis, calcium plays an important role in

muscle contraction and the modification of plasma calcium concentration leads to an alteration in the blood pressure. Magnesium has been known as an essential cofactor for many enzyme systems.<sup>3</sup> It also plays an important role in the neurochemical transmission and peripheral vasodilatation. Zinc is required for the DNA replication, transcription and cellular replication as it is the metallic component of variously related enzymes (i.e) DNA polymerase, RNA polymerase, and thymidine kinase. Essentiality of the zinc during pregnancy is evident.<sup>4</sup> In the zinc-deficient animals and women poor outcome of pregnancy is observed. Hence this study is taken up to analyze and to compare the concentrations of calcium, magnesium, and zinc in the serum of women with preeclampsia and in the normal pregnant women and to evaluate their role in the pregnancy-induced hypertension. It is hoped that this study will contribute to the knowledge of the role of serum calcium, magnesium, and zinc in pregnancy-induced hypertension.<sup>5</sup>

## MATERIALS AND METHODS

This is a cross-sectional case-control study conducted in the Department of Obstetrics and Gynecology, Ponniya Ramajayam institute of medical sciences, during the period from 2016-2017. The study was conducted in 50 pregnant women of the age group between 20 – 40 years. Of them, case group comprised of 25 pregnant women either primi or second gravida in the third trimester (> 24 weeks of pregnancy) with preeclampsia admitted as in patients in Department of Obstetrics and Gynecology. The diagnosis of preeclampsia was based on clinical criteria with blood pressure  $\geq$  140/90 mmHg measured on two occasions 6 hours apart with proteinuria  $\geq$  1+ dipstick along with edema (NHBPEP Classification). The control group was formed by 25 normal pregnant women either primi or second gravida in the third trimester > 24 weeks of pregnancy receiving antenatal care as outpatients. Exclusion criteria used for selecting participants: Medical complicating pregnancy such as Diabetes Mellitus, Renal failure, Chronic hypertension, Heart failure, Multiple pregnancies and Pregnancy  $\leq$  24 weeks of gestation. Patients on magnesium sulfate and calcium lactate therapy were excluded from the study. Written consent was obtained from the participants after explaining the aim and methods of the project. The proforma was prepared and filled during the visit. After filling the proforma the participants underwent a general examination and obstetrical examination, which consisted of fundal height, presenting part and fetal heart rate.

**Examination of pedal edema:** A firm pressure was applied over the medial malleolus on both legs for 15

seconds in all participants and looked for pitting in that region to confirm the presence of pedal edema.

**Anthropometry:** The heights of the participants were measured using standard methodology with the help of non-stretchable inch tape. The weights of the participants were measured using a weighing machine and BMI was calculated using the Quetelet Index using the formula  $Wt (kg)/ht (m)^2$ .

**Measurement of Blood pressure:** With a standard sphygmomanometer and stethoscope the systolic and diastolic blood pressure of all participants were measured in the right upper arm in sitting posture by Auscultatory method. The first and fifth Korotkoff's phase was recorded as systolic and diastolic blood pressure respectively. The blood pressure for cases group was recorded at two occasions one at 9.00 Am and another at 5.00 Pm using the same procedure.

**Estimation of urine albumin:** Clean-catch midstream random urine sample was obtained from all participants. The urine protein was measured by dipstick method using Dip N Read reagent strip. The results was graded on the scale of 0 to 4+ (0, none; 1+, 30 mg/dl; 2+, 100 mg/dl; 3+, 300– 1,999 mg/dl; 4+  $\geq$  2000 mg/dl).

**Blood sample collection:** Three ml of blood was drawn in all the participants from the cubital vein by using disposable. The blood drawn was collected in a vacuum tube.

**Estimation of Hemoglobin:** From the collected blood 0.02ml of the whole blood was used for hemoglobin estimation by Sahli's acid hematin method using hemoglobinometer.

**Serum separation:** The blood samples were allowed to clot spontaneously at the room temperature. Then the clotted blood was centrifuged at 3,000rpm for 10 minutes. The serum separated was stored at 2 - 8 degrees Celsius until analysis.

**Estimation of Calcium:** A part of serum was used for the estimation of calcium. Method: Spectrophotometric method using O-cresolphthalein- complex one as a color indicator.

**Estimation of Serum Magnesium:** A part of serum was used for serum magnesium estimation. Method: Calmagite method. Principle: Magnesium combines with calmagite in an alkaline medium to form a red color complex.

**Estimation of serum Zinc:** A part of serum was used for serum magnesium estimation. Method: Calorimetric method

**Statistical Analysis:** The comparison between the cases and controls was done by using one - way ANOVA test using SPSS (Statistical Package for Social Science) software, Sigma stat version 3.5. The significance was drawn at p-value (probability) of < 0.05.

## RESULTS AND OBSERVATIONS

**Table 1:** Comparison Of Bmi Between The Preeclamptic Women And Normal Pregnant Women

Contents	Cases		Controls	
	Mean	S. D	Mean	S. D
BMI	28.71	4.70	22.46	3.42

Table: 1 From the above result it is evident that p-value is significant and the BMI of preeclamptic women is significantly higher than that of the normal pregnant women.  $P < 0.001$

**Table 2:** Comparison of pulse rate between the cases and the controls

Content	Cases		Controls	
	Mean	S.D	Mean	S.D
Pulse	97.36	8.58	94.16	10.59

Table: 2 From the above result it is evident that the p-value is not significant and there is no significant difference in the pulse rate between the cases and the controls.  $P \text{ value} = 0.246$

**Table 3:** Comparison of systolic blood pressure between the preeclamptic women and the normal pregnant women

Content	Cases		Controls	
	Mean	SD	Mean	SD
Systolic Blood Pressure (mmHg)	157.2	14.29	101.04	9.47

Table 3: From the above results it is clear that the p-value is significant and there is a significant increase in systolic pressure in the preeclamptic women compared to the normal pregnant women.  $P \text{ Value} < 0.001$

**Table 4:** Comparison of diastolic blood pressure between the cases and the controls

Content	Cases		Controls	
	Mean	SD	Mean	SD
Diastolic Blood pressure (mmHg)	100.8	7.59	68.0	6.45

Table 4: From the above results it is clear that there is a significant increase in diastolic blood pressure in the cases when compared to the controls.  $P \text{ value} < 0.001$ .

**Table 5:** Comparison of hemoglobin between the preeclamptic and the normal pregnant women

Content	Cases		Controls	
	Mean	SD	Mean	SD
Hemoglobin	10.32	1.45	10.36	1.08

From the above results, it is evident that there is no significant difference in the hemoglobin levels between the cases and the controls.  $P \text{ value} = 0.912$

**Table 6:** Comparison of serum calcium levels between the preeclamptic women and normal pregnant women

Content	Cases		Controls	
	Mean	SD	Mean	SD
Serum Calcium (mg/dl)	8.07	0.43	8.96	0.59

Table :6 The normal serum calcium concentration is 8.5 – 10.5 mg/dl. From the above results it is evident that there is a significant decrease in the level of serum calcium in the preeclamptic women when compared with the normal pregnant women.  $P \text{ value} < 0.001$

**Table 7:** Comparison of the serum magnesium levels between the preeclamptic women and the normal pregnant women

Content	Cases		Controls	
	Mean	SD	Mean	SD
Serum Magnesium (mg/dl)	1.62	0.16	1.92	0.16

Table: 7 The normal serum magnesium concentration is 1.7–2.4mg/dl. From the above results, it is clear that there is a significant decrease in the level of serum magnesium in women with preeclampsia compared with the normal pregnant women.  $P \text{ value} < 0.001$

**Table 8:** Comparison of the serum zinc levels between the preeclamptic and the normal pregnant women

Content	Cases		Controls	
	Mean	SD	Mean	SD
Serum zinc( $\mu\text{g}/\text{dl}$ )	80.7	9.78	93.28	9.44

Table: 7 The normal serum zinc concentration ranges from 75-120mg/ dl. From the above results, it is evident that there is a significant decrease in the level of serum zinc in women with preeclampsia compared with the normal pregnant women.  $P \text{ value} < 0.001$

## DISCUSSION

The changes in the levels of serum calcium, magnesium and zinc in preeclamptic women compared to the normal pregnant women were studied by several other investigators. In the present study, the Body Mass Index of preeclamptic women is significantly higher than that of normal pregnant women. There was no significant difference in the BMI between the preeclamptic and the normal pregnant women.<sup>6</sup>In 1988, Belizan. M in his study showed that women with higher BMI become hypertensive than those with lower BMI. In this study, there is a significant decrease in the serum calcium levels in the preeclamptic women when compared to normal pregnant women. The data supported that lowered calcium levels might be a cause in the development of preeclampsia. The effect of the serum calcium on the changes in the blood pressure could be explained by the level of intracellular concentration of calcium. The increase in the intracellular calcium concentration when the serum calcium level went lower lead to constriction of the smooth muscles in blood vessels and an increase in vascular resistance.<sup>7</sup> Belizan J.M.*et al*, in 1983 showed in their studies that the mean calcium concentration in the preeclampsia group is significantly lower than the normal pregnant women.

Several studies had examined the effects of the calcium supplementation on blood pressure during pregnancy thus investigating the role of calcium supplementation and its effects on blood pressure.<sup>8</sup> Bischof P *et al* in 2009 conducted a meta-analysis of randomized controlled trials on the effect of calcium supplementation on preeclampsia. They concluded that the supplementation during pregnancy leads to a reduction in both systolic and diastolic blood pressure and preeclampsia. In the present study, there is a significant decrease in the mean serum magnesium concentration in preeclamptic women compared to normal pregnant women. Serum magnesium levels have significant effects on the cardiac excitability and reactivity.<sup>9</sup> Magnesium, as a calcium antagonist promotes vascular smooth muscle relaxation. Thus the low levels of magnesium predispose to increase in the arterial pressure. The studies of Idogun *et al*, 2007 and Indumati *et al*, 2010 showed that the serum calcium level and magnesium levels in preeclamptic pregnant women is significantly lower than that of the normal pregnant women.<sup>10</sup> In 2000, Carey LC *et al*, in his study revealed that the serum calcium level was lower in preeclamptic women when compared with the normal pregnant women but there was no difference in the serum magnesium levels. In this study, there is a decrease in the mean serum Zinc levels in preeclampsia when compared to the controls.<sup>11</sup> Zinc insufficiency has been recognized by a number of experts as an important public health issue, especially in developing countries. During pregnancy, the decrease in the circulating zinc is possibly due to increased transfer of zinc from mother to the fetus and due to plasma expansion.<sup>12</sup> Studies by Chamita Punthumapol *et al*, 2008 showed that there was a significant reduction in the levels of serum calcium, magnesium and zinc in the patient with preeclampsia compared with the normal pregnant women.<sup>13</sup> Further in the present study no significant correlation could be made between levels of serum calcium, magnesium and zinc and the severity of preeclampsia.<sup>14,15</sup>

## CONCLUSION

From the above study, though the calcium, magnesium and zinc deficiencies cannot be pinpointed as the sole factors for the etiology of preeclampsia, they have a definite role in the development of preeclampsia. The decrease in the extracellular calcium level causes increased intracellular calcium through parathyroid hormone. This leads to an increase in vascular smooth muscle contraction and thus increases the blood pressure. Magnesium as a physiological antagonist of calcium antagonizes the increase in intracellular calcium concentration and decreases the vascular

smooth muscle contraction. Zinc by its antioxidant property and inhibitory effect on ATP dependent calcium pump decrease the vascular smooth muscle contraction thereby decreasing the blood pressure. Hence decrease in these elements is a predisposing factor for pregnancy-induced hypertension. Therefore the calcium, magnesium and zinc consumption should be encouraged during the second and third trimesters of pregnancy. The dietary supplements of calcium, magnesium, and zinc in the form of milk, cheese, soya bean products, leafy vegetables etc., during pregnancy, could result in the reduction of incidence of preeclampsia. The direct supplementation therapy of these elements can be considered for women with preeclampsia to ensure child survival and safe motherhood.

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