

# Alteration in Serum Calcium Level in Preeclampsia Compared to Normal Pregnancy

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## ABSTRACT

**Objective:** To compare the level of total serum Calcium (Ca) of pregnant women with preeclampsia with normal pregnant females.

**Study Design:** This was a case control study which included 50 women with preeclampsia in their third trimester of pregnancy as Study group and 50 healthy pregnant women in the third trimester of pregnancy as control group, with similar maternal and gestational age. The concentration of total serum calcium was measured by Atomic Absorption Spectroscopy. The data was analyzed using Students' t-test wherever applicable.

**Result:** The total serum calcium level in preeclamptic women was significantly lower ( $p < 0.001$ ) than in pregnant women of similar maternal and gestational age.

**Conclusion:** Hypocalcemia related to preeclampsia supports the hypothesis that alteration in the total serum calcium levels may be involved in possible etiologies of preeclampsia.

**Keywords:** Preeclampsia, Calcium, Hypocalcaemia, Hypertension, Atomic Absorption Spectrophotometry

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## INTRODUCTION

Pre-eclampsia is a progressive, multi systemic disorder characterized by triad of high blood pressure to the extent of 140/90 mm Hg or more, edema and proteinuria, developing after 20 weeks of pregnancy.<sup>1</sup> It is one of the most common complications during pregnancy and the leading cause of both maternal and perinatal morbidity and mortality worldwide.<sup>2</sup> Incidence of pre-eclampsia worldwide is around 5-10% of all pregnancies,<sup>3</sup> and in developing countries around 4-18%.<sup>4, 5, 6</sup> Despite active research for many years, the etiology of this disorder remains unknown, although contributory factors including obesity, diabetes, calcium deficiency, older maternal age and job stress have been observed and studied.<sup>7,8,9</sup>

The pathophysiological mechanism of preeclampsia in pregnancy is characterized by failure of the trophoblastic invasion of the spiral arteries, leading to maladaptation of maternal spiral arterioles, which may be associated with an increased vascular resistance of the uterine artery and a decreased perfusion of the placenta.<sup>3</sup> The results from many clinical studies show the relationship between the aggravation of the hypertension complication and the change in concentration of various

chemicals in mother's serum.<sup>10,11</sup> Some studies have shown that changes in the levels of blood trace elements in preeclamptic patients may implicate its pathogenesis<sup>12,13</sup> while others have failed to show an association of blood levels of trace elements and prevalence of preeclampsia.<sup>14</sup> Modification of plasma concentration of some elements may lead to the alteration of blood pressure causing preeclampsia during pregnancy.<sup>15</sup>

Calcium plays an important role in muscle contraction and regulation of water balance in cells. It has been found that the lowering of serum calcium and the increase in concentration of cellular calcium may lead to elevation of blood pressure in preeclamptic pregnant females. Several epidemiological studies conducted in developing nations suggest an association between reduced calcium intake and preeclampsia.<sup>16</sup> On the basis of these studies that claim, the abnormalities in calcium homeostasis may contribute to the increased vascular sensitivity as documented in preeclampsia<sup>17</sup>, the present study was carried out, to find whether there is correlation between preeclampsia and total serum calcium concentration.

## MATERIALS AND METHODS

The study included 100 pregnant women between 20-35 years of age, attending Gynaecology OPD/admitted in Gynaecology wards in PBM Hospital, affiliated to Sardar Patel Medical College, Bikaner during 2012. 50 clinically diagnosed women with preeclampsia in their third trimester of pregnancy represented as study group.

Inclusion criteria for the study was; females with singleton pregnancy, all in the third trimester which were diagnosed to have PIH based on the development of hypertension for the first time, proteinuria with or without edema, with no history of previous urinary tract troubles and no evidence of UTI. 50 women with normal pregnancy with similar maternal and gestational ages represented as Control group. All were in the same previously mentioned criteria but didn't develop hypertension.

Pregnant ladies with medical complications such as renal disease, trophoblastic disease, heart disease, chronic hypertension and on calcium lactate drugs were excluded from study.

Thorough clinical examination was carried out before recruiting the participants for the study by a competent gynecologist. Personal and clinical information regarding age, gestational age, socioeconomic status, education, dietary habit, clinical and biochemical parameters were recorded with the help of a questionnaire, with prior consent of the participant.

**Sample collection and estimation of serum calcium:** 5 ml blood was drawn from antecubital vein in a sterile syringe and was transferred to a clean dry vial slowly by the side of the vial after removing the needle to avoid hemolysis. The blood was allowed to clot at room temperature for 30 minutes and serum was separated by centrifugation at 3000 rpm for 10 minutes.

Serum calcium was estimated by atomic absorption spectrophotometer (AA-7000) by the method described by Fernandez et al (1971)<sup>18</sup>, in the Department of Biochemistry, S.P. Medical College, Bikaner. For the determination of calcium, the serum was diluted 1:50 with 0.1% (w/v) lanthanum (as chloride) diluent. The dilution ratio was adjusted to insure that concentration falls within a suitable absorbance range. To analyze the data, Students't-test was employed wherever applicable to assess the significance of difference among control and study subjects.

## RESULTS

The total study population included 100 subjects, of which 50 each represented the Control and Study group. The mean of age, socioeconomic status, BMI, gestational age in the two groups did not show any significant difference ( $p > 0.4$ ) so, all such factors were ruled out to have any effect which may influence the serum calcium levels.

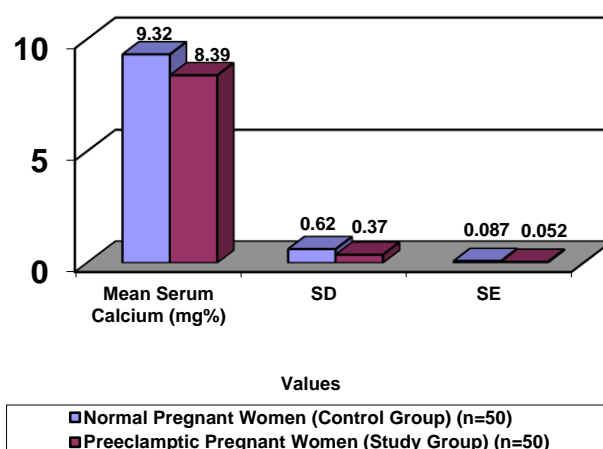
The mean serum calcium level was found to be  $9.32 \pm 0.62$  mg/dl with a range of 7.63 to 11.01 mg/dl in control subjects (Table-1) and  $8.39 \pm 0.37$  mg/dl with a range of 7.51 to 9.21 mg/dl in preeclamptic pregnant women. There was a significant decrease ( $p < 0.001$ ) in the total serum calcium levels in study group. These results are in close agreement with findings in conditions of PIH and calcium deficiency<sup>19,20,21</sup>.

**Table 1: Levels of Serum Calcium in Healthy Pregnant Women (Control Group) and Preeclamptic Pregnant Women (Study Group)**

	Control Group (n=50)	Study Group (n=50)
Mean (mg/dl)	9.32	8.39
Range (mg/dl)	7.63 - 11.01	7.51 - 9.21
SD	0.62	0.37
SE	0.087	0.052
DF	98	
t-value	9.15	
p-value	<0.001**	

\*\*Highly Significant

**Fig. 1: Comparison of mean serum Calcium levels in Healthy Pregnant Women (Control Group) and Preeclamptic Pregnant Women (Study Group)**



## DISCUSSION

The study showed that the mean serum calcium levels decreased in preeclamptic pregnant female group which was statistically significant ( $p < 0.001$ ) (Fig. 1). This result is in concordance with previous epidemiological studies that suggest an inverse relationship between serum calcium and incidences of preeclampsia.<sup>22,23</sup> However, the difference in population pattern and nutritional status at different areas may be responsible for some studies contradictory to the present.<sup>19,24</sup>

Calcium metabolism is under immense dynamism during pregnancy. Expectant mothers need to store about 30-50 gm of calcium during the course of pregnancy, of which 25 gms is needed by the foetus. Eighty percent of the total foetal calcium is deposited during the third trimester. The transport of ionized calcium from mother to the foetus increases about 50 mg/day at 20 weeks of gestation to a maximum of about 350 mg/day at 35 weeks of gestation.<sup>25</sup>

The effect of serum calcium on blood pressure could be explained by the level of intracellular concentration of

calcium. It might be possible that low serum calcium in pregnancy increases release of parathyroid hormone and renin which in turn increase intracellular calcium in vascular smooth muscle and decrease serum calcium level. This increased smooth muscle calcium causes vasoconstriction and thereby increased vascular resistance, leading to rise in blood pressure in preeclamptic women<sup>15,26</sup>.

The protective effect of calcium on blood pressure can be explained in part by the influence of calcitropic hormones on intracellular calcium. 1, 25-Dihydroxyvitamin D stimulates calcium influx in a variety of cells, including vascular smooth muscle cells. This effect is rapid, as it is mediated by vitamin D receptor rather than via a classical nuclear-receptor-mediated mechanism. As a consequence, 1, 25-Dihydroxyvitamin D exerts a repressor effect, serving to promote contraction and increase peripheral vascular resistance. Consequently, low calcium diets, which elicit a 1, 25 – Dihydroxy vitamin D response, would be expected to increase blood pressure, whereas high calcium diets, by virtue of suppressing 1, 25 – Dihydroxy vitamin D levels, would be expected to reduce vascular smooth muscle cell intracellular calcium, peripheral vascular resistance and blood pressure.<sup>27</sup>

Unavailability of this element due to deficiency or decreased concentration may be a predisposing factor in the development of pre-eclampsia or a contributory factor in its pathogenesis. The limitation of this study was that the dietary intake of calcium was not taken into consideration.

## CONCLUSION

The result of the present study suggests that hypocalcaemia is present in preeclamptic pregnant women and serum calcium was significantly lower than in normal pregnant women.

In the light of reduction in the concentration of calcium, adequate dietary supplementation should be given above the recommended dietary allowances in pregnancy at least in susceptible pregnant women, especially in developing countries. The results may be significant in understanding the possible contribution of serum calcium in the pathophysiological process of preeclampsia and may help in developing the strategies for prevention and early diagnosis. However, more extensive studies have to be carried out.

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