

# Comparative Study on Serum Calcium among Healthy Pregnant, Preeclampsia and Eclampsia Mothers

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## ABSTRACT

**Background:** Pregnancy is a period of high calcium demand because of both maternal and fetal requirement. Serum calcium has a probable role in pathophysiology of pregnancy induced hypertension. The study aims to compare serum calcium levels among healthy pregnant, preeclampsia and eclampsia mothers. **Methods:** A descriptive cross sectional study was conducted over 18 months taking 85 subjects each of healthy pregnant, preeclampsia and eclampsia mothers in gestational age  $\geq 29$  weeks. Serum calcium levels in 3 groups were estimated by colorimetry and results were statistically analysed by SPSS version 20. **Results:** Mean and median serum calcium levels was lower in preeclampsia and eclampsia it was statistically significant ( $p < 0.0001$ ). **Conclusion:** Low serum calcium has a definite role in pathogenesis of pregnancy induced hypertension.

**Keywords:** Calcium, Pregnancy, PIH.

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## INTRODUCTION

Pregnancy induced hypertension (PIH) has been a recognized entity since the time of Hippocrates in ancient Greek. It constitutes one of the leading causes of maternal and perinatal mortality and complicates 10% of pregnancies globally.<sup>[1]</sup> There is a probable role of trace elements in the pathogenesis of PIH. Among them, serum calcium (Ca) is most important. Pregnancy is a period of high Ca demand because of both maternal and fetal requirement. Pregnancy entails number of physiological events with implications regarding Ca metabolism: the extracellular fluid expands, the albumin level decreases, the glomerular filtration rate increases causing calciuria and Ca is removed from the maternal system by transfer to fetus. All these mechanisms tend to promote lowering of maternal Ca concentration and maintain the levels within a narrow range necessary to preserve homeostasis.<sup>[2,3]</sup> On the physiological basis, Ca plays an important role in muscle contraction and regulation of cellular water balance.<sup>[4]</sup> A decrease in extracellular Ca concentration increases the excitability of nerve and muscle cells and conversely an increase in extracellular Ca concentration stabilizes the membrane by decreasing excitability.<sup>[5,6]</sup> There is evidence that low serum Ca may also be associated with increased neuromuscular irritability and hence predisposes to seizures by reducing the seizure

threshold.<sup>[7]</sup> Also low serum Ca stimulates parathyroid hormone and renin release.<sup>[8]</sup> Parathyroid hormone mobilizes Ca from skeletal reservoirs by stimulating osteoclasts, increases renal Ca resorption and indirectly increases intestinal Ca absorption via 1,25 dihydroxycholecalciferol which then increase intracellular Ca in vascular smooth muscle.<sup>[9]</sup> So, any reduction in serum Ca and increased intracellular Ca could be responsible for elevation of blood pressure in PIH.<sup>[10]</sup>

With this background, we have conducted this study with the following aims and objectives: a) To estimate serum Ca levels among healthy pregnant, preeclampsia and eclampsia mothers. b) To compare the serum Ca levels among healthy pregnant, preeclampsia and eclampsia mothers.

## MATERIALS & METHODS

A descriptive cross sectional study was conducted over 18 months from January 2018 to June 2019, in the Department of Obstetrics and Gynaecology in collaboration with the Department of Biochemistry of Bankura Sammilani Medical College & Hospital, a rural medical college of West Bengal, India. Study population was categorized in 3 groups: Group 1 comprising of 85 healthy pregnant mothers as controls, Group 2 comprising of 85 preeclampsia mothers as cases and Group 3 comprising of 85 eclampsia mothers as cases. Both controls and cases were primipara and primigravida of gestational age  $\geq 29$  weeks. Inclusion criteria for cases were preeclampsia and eclampsia who did not get any MgSO<sub>4</sub> injection. Exclusion criteria were known cases of diabetes, hypertension, cardiac disease, chronic liver disease, renal insufficiency, HIV,

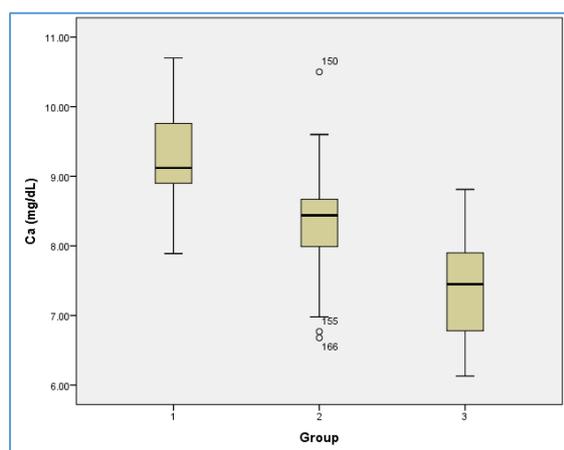
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TORCH infection. Serum Ca in venous blood of 3 groups was estimated by colorimetric method. Preeclampsia is defined by any one of the following BP criteria: a) Systolic blood pressure of 140 mm Hg or more or diastolic blood pressure of 90 mm Hg or more on two occasions at least 4 hours apart after 20 weeks of gestation in a woman with a previously normal blood pressure, b) Systolic blood pressure of 160 mm Hg or more or diastolic blood pressure of 110 mm Hg or more. Eclampsia is defined as convulsion in hypertensive disorder of pregnancy.<sup>[11]</sup> Hypocalcemia is defined as serum Ca < 8.5 mg/dL.<sup>[12]</sup> All parameters were recorded in predesigned and structured proforma. Results were statistically analysed by SPSS version 20.

## RESULTS

The Mean  $\pm$  SD of serum Ca was lowest in Group 3 (7.371  $\pm$  0.628 mg/dL) followed by Group 2 (8.287  $\pm$  0.632 mg/dL) and Group 1 (9.244  $\pm$  0.677 mg/dL). The Box and Whisker plot shows median serum Ca was lowest in Group 3 (7.45 mg/dL) followed by Group 2 (8.44 mg/dL) and Group 1 (9.12 mg/dL). [Figure 1]



**Figure 1: Box and Whisker plot for Median serum Ca in Group 1, 2, 3**

Difference in serum Ca levels among three groups was compared by Kruskal-Wallis test / one way ANOVA on ranks test and was found to be statistically significant (Chi square 157.499, degree of freedom 2, p-value<0.05).

Serum Ca levels in Group 1 and Group 2 were compared by Mann Whitney u test and Wilcoxon Sign test for Dependency. The result was statistically significant (p-value<0.05). [Tables 1 & 2]

**Table 1: Mann Whitney u test for serum Ca in Group 1 and 2: Ranks**

	Group	N	Mean Rank	Sum of Ranks
Ca (mg/dL)	1	85	115.76	9839.50
	2	85	55.24	4695.50
	Total	170		

**Table 2: Mann Whitney u test for serum Ca in Group 1 and 2: Statistics**

	Ca (mg/dL)
Mann-Whitney U	1040.500
Wilcoxon	4695.500
Z	-8.017
Asymptotic significance (2-tailed) / (p-value)	0.000

Serum Ca levels in Group 1 and Group 3 were compared by Mann Whitney u test and Wilcoxon Sign test for Dependency. The result was statistically significant (p-value<0.05). [Tables 3 & 4]

**Table 3: Mann Whitney u test for serum Ca in Group 1 and 3: Ranks**

	Group	N	Mean Rank	Sum of Ranks
Ca (mg/dL)	1	85	126.22	10728.50
	3	85	44.78	3806.50
	Total	170		

**Table 4: Mann Whitney u test for serum Ca in Group 1 and 3: Statistics**

	Ca (mg/dL)
Mann-Whitney U	151.500
Wilcoxon	3806.500
Z	-10.787
Asymptotic significance (2-tailed) / (p-value)	0.000

Serum Ca levels in Group 2 and Group 3 were compared by Mann Whitney u test and Wilcoxon Sign test for Dependency. The result was statistically significant (p-value<0.05). [Tables 5 & 6]

**Table 5: Mann Whitney u test for serum Ca in Group 2 and 3: Ranks**

	Group	N	Mean Rank	Sum of Ranks
Ca (mg/dL)	1	85	115.78	9841.50
	3	85	55.22	4693.50
	Total	170		

**Table 6: Mann Whitney u test for serum Ca in Group 2 and 3: Statistics**

	Ca (mg/dL)
Mann-Whitney U	1038.500
Wilcoxon	4693.500
Z	-8.023
Asymptotic significance (2-tailed) / (p-value)	0.000

## DISCUSSION

The Mean  $\pm$  SD of serum Ca was 7.371  $\pm$  0.628 mg/dL in eclampsia group and 8.287  $\pm$  0.632 mg/dL in preeclampsia group. Median serum Ca was 7.45 mg/dL and 8.44 mg/dL in eclampsia and preeclampsia respectively. In our study, normal range of serum Ca was taken as 8.5 to 10.5 mg/dl and values less than 8.5 mg/dL was considered as hypocalcemia. Hence, profound hypocalcemia was noted in eclampsia group. Difference in serum Ca levels among three groups was compared by

Kruskal-Wallis test / one way ANOVA on ranks test and was found to be statistically significant. Also, 3 intergroup comparisons done by Mann Whitney u test and Wilcoxon Sign test came out to be statistically significant (p-value<0.05) in every set.

Our study values were similar to findings of a study by Al-Jameil N et al,<sup>[13]</sup> conducted in Riyadh, Saudi Arabia. Their mean serum Ca was  $7.785 \pm 0.447$  mg/dL in high risk group and  $7.037 \pm 0.466$  mg/dL in preeclampsia. Similar study in Iran reported serum Ca to be  $8.65 \pm 0.628$  mg/dL in preeclampsia and  $9.77 \pm 3.02$  mg/dL in controls.<sup>[14]</sup> Historically, an inverse relationship between Ca intake and hypertensive disorders of pregnancy was first described in 1980 based on the observation that Mayan Indians in Guatemala had a low incidence of preeclampsia as their intake of Ca was high due to the traditional method of soaking corn in lime before cooking.<sup>[15]</sup> A tendency to relative maternal hypocalcaemia during pregnancy has been recognized for more than 40 years. Total Ca tends to decrease over the course of pregnancy in normal women and decreased significantly during pregnancy in women who developed preeclampsia. The decrease in serum Ca levels principally involves the protein bound portion and haemodilution. Mahomed et al.<sup>[16]</sup> reported a low intake of calcium during pregnancy in many different parts of the world such as Asia, Latin America, and Africa as well as developed countries such as Canada, USA and the UK. They reported a very low intake of Ca in India (250 mg/day). Dietary deficiency of Ca, with consequent reduced serum Ca levels, has been implicated as a cause of preeclampsia in some studies.<sup>[17,18]</sup>

A Cochrane review analyzed 12 high quality trials after excluding 24 trials on supplementation of Ca to prevent preeclampsia in normotensive pregnant women. The dose of Ca evaluated was 1.5 to 2 gm daily. There was less high BP associated with Ca supplementation rather than placebo. Calcium supplementation appeared to approximately half the risk of preeclampsia. The reduction was greatest for women at high risk of developing preeclampsia and for those with low baseline dietary Ca. The Relative Risk of having the composite outcome maternal death or serious morbidity was reduced for women allocated Ca supplementation compared with placebo. The review commented that adequate dietary Ca before and in early pregnancy may be needed to prevent the underlying pathology responsible for preeclampsia. They also suggested that the research agenda should be redirected towards Ca supplementation at a community level.<sup>[19]</sup>

Hypertension in pregnancy has been explained by the vasoconstrictive effect caused by reduced serum Ca levels.<sup>[20]</sup> Stimulation of 1,25-dihydroxycholecalciferol has been implicated in this vasoconstrictive mechanism. This concept of a

reduced serum Ca level in preeclampsia is not accepted universally.<sup>[21]</sup> This is because other studies in preeclamptic women have noted relatively reduced 1,25-dihydroxycholecalciferol levels compared to normal pregnant women, with consequent increase in parathyroid hormone levels, causing reabsorption of Ca from the distal renal tubules and the intestines and therefore causing no significant change in the serum Ca levels.<sup>[22-24]</sup> Parathyroid hormone also causes renin release with subsequent vasoconstriction and sodium retention in preeclamptic women.<sup>[25]</sup> A case control study conducted by Malas NO and Shurideh ZM revealed statistically significant hypocalcemia and hyperparathyroidism in the cases compared to controls and concluded that maternal serum total Ca and parathyroid hormone might be related to pregnancy-induced hypertension.<sup>[26]</sup>

## CONCLUSION

The present study was conducted with the aim to compare the serum levels of Ca among healthy pregnant, preeclampsia and eclampsia mothers since there was no such study from this rural part of Eastern India. Statistically significant low levels in serum Ca levels were found in normal pregnant women compared to PIH mothers. Moreover, statistically significant low levels in serum Ca were found in eclampsia compared to preeclampsia mother. Hence, the study data analysis supported the hypothesis that Ca deficiency might have a definite role in the development of PIH. It is a well known fact that in a developing country like India, an average diet of a pregnant mother is very likely to be deficient in Ca. So, adequate dietary calcium before and in early pregnancy may be needed to prevent the underlying pathology responsible for PIH. Our national public health care policy makers should also consider whether Ca should be supplemented as a routine dietary requirement to pregnant women at community level.

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