



Serum Calcium and Magnesium Levels in Preeclamptic Patients – A Case Control Study

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Accepted on: 23-02-2014; Finalized on: 30-04-2014.

ABSTRACT

Preeclampsia is one of the major causes of maternal deaths and pregnancy related complications. Despite intensive researches over years, the exact cause of the disease remains unknown. Various factors like placental ischemia, immunological maladaptation, genetics and susceptible endothelium have been shown to play a causative role in the preeclampsia. In the recent past, nutritional deficiency is gaining importance in the pathogenesis of preeclampsia. To compare the serum levels of macronutrients like calcium and magnesium between preeclamptic patients and normal pregnant women. This was a case control study done in Pondicherry Institute of Medical Sciences with 50 preeclamptic patients as cases and 50 gestationally age matched normal pregnant women as controls. After getting informed consent, calcium and magnesium levels were measured in the serum of the participants. Serum calcium ($p < 0.001$) and magnesium ($p < 0.001$) levels were significantly decreased among cases when compared to controls. Hypocalcemia ($< 9 \text{ mg/dl}$) showed significant association with preeclampsia. There was a significant decrease in serum magnesium (0.006) level in low birth weights among the cases. Serum calcium and magnesium were found to be decreased in preeclamptic women. Supplementation with these nutrients during early pregnancy can be a preventive tool in preeclampsia and eclampsia.

Keywords: Preeclampsia, Calcium, Magnesium.

INTRODUCTION

Globally around 800 women die daily because of pregnancy related complications.¹ In developed countries, 16% of maternal deaths are due to hypertensive disorders. In India, being a developing country, the incidence of preeclampsia is mildly higher and accounts for 24% of all maternal deaths.² Preeclampsia is defined as high blood pressure ($\geq 140/90$ mmHg) and proteinuria ($> 300 \text{ mg/day}$) after 20 weeks of pregnancy in a previously normotensive woman.³ Whereas eclampsia is defined as, seizures that cannot be attributed to other causes in a woman with preeclampsia.⁴

Preeclampsia has been proposed to be a two stage disease. In the first stage, various placental and maternal factors like placental ischemia, immunological maladaptation, genetics and susceptible endothelium either independently or jointly causes placenta to elaborate a lot of anti angiogenic factors. These factors in the second stage, lead to systemic endothelial dysfunction and the clinical syndrome of preeclampsia.⁵ Despite intensive researches over years, the exact cause that leads to vasoconstriction and hypertension remains unknown.

In the recent past, nutritional deficiency is gaining importance in the pathogenesis of preeclampsia. We know the role of macronutrients like calcium and magnesium in maintaining the normal vasculature and we

also encounter an increased frequency of their deficiency during pregnancy.⁶ So we measured the serum calcium and magnesium in preeclamptic patients and compared with normal pregnant women to find out their role in the pathogenesis and prevention of preeclampsia.

MATERIALS AND METHODS

This was a case controlled study done in Pondicherry Institute of Medical Sciences during the period of Jan 2012 – Aug 2013. 50 pregnant women with BP $> 140/90$ mmHg and proteinuria ($> 300 \text{ mg/day}$) after 20 weeks of gestation for first time were included as cases. 50 gestational age matched healthy pregnant women were included as controls. Sample size was calculated by allowing alpha error of 0.05 and beta error of 10%. Pregnant women with renal diseases, Diabetes Mellitus/Gestational Diabetes Mellitus, chronic hypertension, gestational hypertension (without proteinuria), adrenal and other endocrine disorders and any other systemic illnesses were excluded from the study.

After obtaining informed consent, blood samples were taken from cases and controls. Serum was separated and was used for the estimation of calcium and magnesium. Serum calcium was estimated by ArsenazoIII method and serum magnesium by xylydyl blue method in semi autoanalyser.^{7,8}



Continuous variables were expressed as mean \pm standard deviation. 'Student t Test' was used to compare the mean value of the parameters between cases and controls. Chi square test was used to find the association between two variables. A 'p' value of ≤ 0.05 was considered as statistically significant. SPSS 17.0 software was used for all statistical analyses.

RESULTS

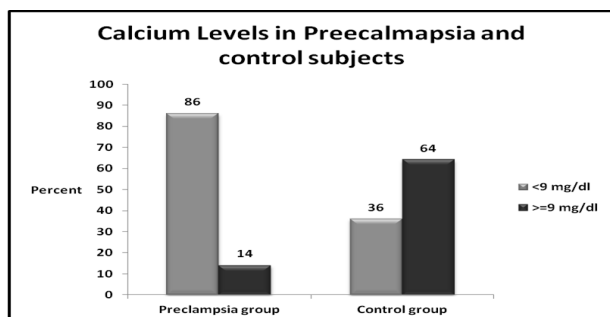
In our study, there was no significant difference in age and gestational age between cases and controls. There was a significant decrease in serum calcium and magnesium levels in preeclamptic women than compared to those in control group (Table 1). Hypocalcemia (< 9 mg/dl) was found to be strongly associated with preeclampsia. (Figure 1)

Table 1: Serum nutrient levels between cases and controls

Variables	Cases (50)	Controls (50)	p value
Age (years)	24.86 \pm 3.60	24.74 \pm 4.24	0.879
Gestational Age (weeks)	38.12 \pm 1.10	38.22 \pm 1.01	0.638
Calcium (mg/dl)	8.59 \pm 0.66	9.17 \pm 0.77	< 0.001*
Magnesium (mg/dl)	1.87 \pm 0.39	2.03 \pm 0.43	< 0.001*

Student t test; *; p value < 0.05 – statistically significant

Figure 1: Association between Serum Calcium and Preeclampsia



Chi square statistic = 26.272; $p < 0.001$; statistically significant at $p < 0.05$

In a sub group analysis within the preeclampsia group, our results revealed that there was a significant decrease in serum magnesium among the low birth weights (< 2.5 kg) than compared to normal birth weight (> 2.5 kg) preeclamptic patients (Table 2).

Table 2: Comparison of Serum nutrient levels in low and normal birth weight in preeclampsia group

Variables	BW < 2.5 Kg (21)	BW > 2.5 Kg (29)	p value
S.Calcium (mg/dl)	8.64 \pm 0.59	8.56 \pm 0.72	0.411
S.Magnesium (mg/dl)	1.79 \pm 0.32	1.94 \pm 0.40	0.006*

Student t test; *; p value < 0.05 – statistically significant

DISCUSSION

Serum calcium and magnesium play an important role in maintaining the normal vasculature.⁹ Serum ionised calcium is the major determinant of Parathormone secretion (PTH). It regulates PTH production through a calcium sensor present in the parathyroid gland. Whenever the serum ionised calcium falls, it increases the PTH secretion which in turn increases the intracellular Ca^{2+} levels and causes vascular smooth muscle contraction.¹⁰

In our study, we found a significantly lower serum calcium levels among the cases and there was a strong association between hypocalcemia (< 9 mg/dl) and preeclampsia. Our findings are consistent with the results of a study conducted by Selina Akhtar et al who showed that reduced serum calcium may be one of the risk factor for preeclampsia. Further they showed that serum calcium is strongly and negatively correlating with systolic and diastolic blood pressure in preeclamptic patients.¹¹ Indumathi V et al also confirmed that there was a linear fall in the serum total and ionised calcium in preeclampsia group than compared to normal pregnancy.¹²

We also found that there was a significant decrease in serum magnesium levels in preeclamptic group than compared to the controls. This was supported by K Nahar et al, who concluded that by estimating serum magnesium during antenatal period, pre-eclampsia can be predicted and eclampsia can be prevented early.¹³ According to Sukonpan K et al, serum magnesium concentration in preeclamptic women is significantly lower than that in normal pregnant women.¹⁴

The effects of hypocalcemia on vascular smooth muscle cells are further augmented by decreased serum magnesium levels, as they are the "nature's physiologic calcium blocker". Hypomagnesemia opens the L type Ca^{2+} channel and blocks the Ca^{2+} - ATPase present in sarcoplasmic reticulum and leads to increased intracellular calcium.¹⁵ They also cause vasoconstriction by decreasing prostacyclin production and by increasing the vasoconstriction effect of angiotensin II and noradrenaline in the vessel wall.¹⁶

In a subgroup analysis among cases, serum magnesium was found to be significantly decreased in low birth weights than compared to normal birth weights, which suggested that serum magnesium might influence the fetal growth directly. Our findings are in accordance with those reported by Takaya et al and Wynn et al.^{17,18} Reduction in serum magnesium concentration decreases NO synthase activity and leads to placental insufficiency and IUGR.

CONCLUSION

In our study, serum calcium and magnesium were found to be decreased in preeclamptic women than compared to normal pregnant women. This showed the role of these macronutrients in the pathogenesis of

preeclampsia. Further intervention studies can be carried out to find whether supplementation with these nutrients in early pregnancy can be a preventive tool in preeclampsia.

Acknowledgement: We would like to thank the staffs and technicians of Biochemistry, Obstetrics and statistics department, PIMS for their support and encouragement throughout the research work.

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Source of Support: Nil, **Conflict of Interest:** None.

