

A comparative study of the serum calcium level in normal pregnant and pre-eclamptic women attending Gauhati Medical College and Hospital

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Abstract

Introduction: Pre-eclampsia is one of the major causes of maternal and foetal morbidity and mortality. Though several factors have been implicated, the exact aetiology is still unknown. Recent studies have implicated that low serum calcium level may have a role in pre-eclampsia.

Aim and Objective: The objective of this study was to find out the relation between serum calcium level and pre-eclampsia by comparing the serum calcium levels in pre-eclampsia with that of normal pregnancy.

Materials and Methods: Blood samples from 30 pre-eclamptic and 30 pregnant women attending Gauhati Medical College & Hospital, Guwahati, Assam were analyzed for calcium level by enzymatic colorimetric method.

Results: Women with pre-eclampsia had a significantly lower serum calcium level than normal pregnant women ($p < 0.0001$).

Conclusion: This study concludes that low serum calcium level may be one of the risk factors for the development of pre-eclampsia. So, early detection and appropriate supplementation to correct this deficiency during pregnancy may reduce the incidence of pre-eclampsia.

Keywords: Calcium, pre-eclampsia, pregnancy, supplementation.

1. Introduction

Pre-eclampsia is one of the most common complications of pregnancy. It is one of the most common causes of maternal and fetal morbidity.[1] Pre-eclampsia is a transient but potentially dangerous disorder that is characterized by a triad of high blood pressure to the extent of 140/90 mmHg or more, oedema and proteinuria developing after 20 weeks of pregnancy.[2] Clinically pre-eclampsia is characterized by a persistently elevated blood pressure of greater than 140/90 mm Hg, proteinuria and oedema.[3] It may be associated with complications like visual disturbances, oliguria, eclampsia, haemolysis, elevated liver enzymes, thrombocytopenia, pulmonary oedema and foetal growth restriction.[2] Multiple hypotheses have been put forward to explain its occurrence. This has earned it the name of the "disease of theories".[4] The basic pathophysiological mechanism is probably a failure of the trophoblastic invasion of the spiral arteries, leading to maladaptation of maternal spiral arterioles associated with an increased vascular resistance of the uterine artery and a decreased perfusion of the placenta.[1,2,5]

Despite its prevalence and severity and despite considerable research, the pathophysiology of this multisystem disorder is not fully understood or its exact cause is still

unknown.[6] Although the exact aetiology of pre-eclampsia is still a mystery, several factors such as obesity, diabetes mellitus, calcium deficiency[7], advanced maternal age, oxidative stress, placental ischemia, genetics and immune maladaptation have been implicated.[8] Many clinical studies have shown the relationship between the aggravation of the hypertension and the change in maternal serum level of various minerals during pregnancy. [2, 9-11]

Physiologically, calcium plays an important role in muscle contraction. Modification of plasma calcium concentration leads to the alteration of blood pressure. The lowering of serum calcium and the increase of intracellular calcium can cause an elevation of blood pressure in pre-eclamptic mothers.[9,12] So the modification of calcium metabolism during pregnancy could be one of the causes of pre-eclampsia.[1,2,8,13,14]

The importance of proper nutrition prior to and during pregnancy cannot be understated. It is essential for the health and well-being of both mother and baby. Pregnancy is a period of increasing metabolic demands compounded by requirements of a growing foetus. Pregnant women in developing countries have been reported to consume diets deficient in essential

minerals and vitamins. Also, pre-eclampsia accounts for about 20-80% of the maternal mortality in developing countries.[15]

In this context, the reduction of the risk factors in the causation of pre-eclampsia seems to be the need of the hour. The focus should be more on prevention than on treatment to combat this menace. The present study aimed at measuring the serum calcium levels in women with pre-eclampsia and comparing the same with that of normal pregnant women.

2. Materials and Methods

The study was conducted on 60 pregnant women attending the antenatal clinic and admitted in the obstetric wards in the Department of Obstetrics and Gynaecology, Gauhati Medical College and Hospital, Guwahati, Assam. They were divided into 2 groups – Group A comprising 30 normal pregnant women taken as controls and Group B comprising 30 pre-eclamptic women taken as study group. The pre-eclamptic patients were chosen in accordance with the American College of Obstetrics and Gynaecology guidelines. The normal pregnant women had normal blood pressure with no proteinuria. All subjects were primi or multigravida between 22 – 40 years and in their third trimester of pregnancy (gestational age of >24 weeks). All maternal / foetal abnormal pregnancies (except pre-eclampsia), patients with essential hypertension, systemic or endocrine disorders and patients on calcium supplementation were excluded from the study. Written informed consent was taken from each subject and the study was approved by the Institutional Ethics Committee. Detailed family and medical history was taken from each patient. A thorough clinical examination was done on each subject and systolic and diastolic blood pressures were carefully recorded. Under aseptic precautions, 5 ml of venous blood was collected from each subject. The collected blood was allowed to clot spontaneously in a container, and then centrifuged at 3000 rpm for 10 minutes. Whenever possible, the analysis was done immediately. When there was a delay, the samples were stored at -20° Celsius till further analysis. Serum calcium was estimated by enzymatic (O-Cresol Phthalene Complexone method) colorimetric assay in the Department of Physiology, Gauhati Medical College and

Hospital, Guwahati, Assam. The data obtained were tabulated and entered in MS Excel Worksheet. Data were expressed as mean ± SD. Independent t-test was applied for parametric variability considering p < 0.05 to be statistically significant. Data analysis was done by Graph Pad Instat (Version 3.10).

3. Results

In the study, both the groups were matched for age and gestational period. Most of the women were from the lower middle class strata. **Table 1** shows the distribution of subjects in both groups. **Table 2** shows the age distribution of subjects in the two groups. Majority of the subjects are in the age group of 26-29 years. **Table 3** shows that most of the subjects in the control group were multigravidas whereas majority of the subjects in the study group were primigravidas. Serum calcium levels were significantly lower in study group B (p <0.0001) in comparison to those of control group A as shown in **Table 4**.

Table 1: Distribution of subjects in the two groups

Groups	Number of subjects
Normal Pregnancy (Group A)	30
Preeclampsia (Group B)	30

Table 2: Age distribution of subjects in the two groups

Age (in years)	Normal Pregnancy (Group A)	Preeclampsia (Group B)
22 – 25	8	10
26 – 29	17	14
30 – 33	2	4
34 – 37	3	2
38 – 40	-	-
Total	30	30

Table 3: Showing the gravida distribution of control and study groups

Gravida	Normal Pregnancy (Group A)	Pre-eclampsia (Group B)
Primigravida	12	22
Multigravida	18	08
Total	30	30

Table 4: Showing mean and standard deviation of serum calcium level in normal pregnancy and pre-eclampsia.

Parameter	Group	Sample	Mean	Standard Deviation	Standard error of mean	p-value
Serum calcium (mg/dl)	Control (Group A)	30	9.903	0.6866	0.1253	<0.0001
	Study (Group B)	30	8.510	1.454	0.2654	

4. Discussion

Pre-eclampsia is associated with increased morbidity and mortality especially in developing countries. Even though the exact cause of pre-eclampsia is still unknown, several theories have been postulated attempting to explain its aetiology. It is thought that its mediator originates in the placenta and is believed to be a woman’s immunological “reaction” to the foetus and placenta. [16,17]

Nutritional deficiencies are commonly seen during pregnancy where requirements increase. This is observed more

in pregnant women in developing countries with a diet deficient in essential minerals and vitamins.^[18] A diet low in two essential minerals – calcium and magnesium during pregnancy have been implicated to be responsible for pre-eclampsia, eclampsia, preterm birth and intrauterine growth retardation.[19]

Our study assessing the serum calcium levels in pregnant women with and without pre-eclampsia showed serum calcium level to be significantly reduced in women with pre-eclampsia compared to normal pregnancy. This correlates

well with the other studies.[20-27] Idogun *et al.* conducted a cross-sectional study in 2007 in Nigeria and found extracellular calcium and magnesium reduction in patients with pre-eclampsia and eclampsia. Richard Kobina Dadzie *et al.* in 2014 conducted a case-control study on 380 pregnant women (≥ 20 weeks gestation) receiving antenatal care at 3 hospitals in the Cape Coast metropolis Ghana. They concluded serum calcium and magnesium levels are lower in pregnancy induced hypertension and pre-eclampsia than in normal pregnancy. Sandip Lambe *et al.* in 2014 also found serum calcium, magnesium and zinc levels to be significantly reduced in the pre-eclampsia group compared to the normal pregnant group.

In contrary, some researchers found that serum calcium in preeclamptic group did not differ significantly from normal pregnant group.[28-31] This difference with our result may be attributed to the different genetic pool of the population in which the studies had been done as compared to our population and also to the different dietary habits of the population.

Calcium is an important element as it is necessary for muscle contraction and neuronal activity. The blood pressure changes evident in pre-eclampsia can be attributed to the change in serum calcium levels. Decrease in serum calcium levels led to an increase in intracellular calcium. This led to constriction of smooth muscles in blood vessels and increased vascular resistance, [1,12,13,32-34] culminating in a raised systolic and diastolic blood pressure.

Low serum calcium levels may also increase blood pressure by stimulating parathyroid hormone and renin release, which in turn increases intracellular calcium in smooth muscles, leading to vasoconstriction, increased vascular resistance and a rise in blood pressure in preeclamptic mother.[1,19,36]

A WHO recommendation in 2011 found a higher risk of pre-eclampsia in pregnant women who had a low dietary intake of calcium. It recommended supplementation of such women with calcium.[37] Thus, calcium levels may have a role to play in the pathogenesis of pre-eclampsia. A Cochrane review further supported the WHO recommendation by reiterating that supplementation of calcium in pregnancy is associated with a significant reduction in the risk of pre-eclampsia. They have suggested a redirection of the research towards calcium supplementation at the community level.[38]

Our study was conducted to estimate the serum calcium level in pre-eclampsia and normal pregnancy and find out any association between calcium and pre-eclampsia. There was a significant reduction in calcium levels in pre-eclamptic women as compared to normal pregnant women, suggesting the role of calcium in pre-eclampsia. The limitation of our study was that we did not take a detailed dietary history of the subjects. So, the impact of inadequate intake of calcium on pre-eclampsia could not be ascertained in our study. Further studies need to be conducted to explore the association of low levels of calcium and increased risk of pre-eclampsia, the predictive ability of calcium and other electrolytes for pre-eclampsia and

the role of their supplementation in prevention of pre-eclampsia.

Our study shows a significant reduction of serum calcium level in pre-eclamptics compared to normotensives. This supports the hypothesis that hypocalcaemia may have a role in the aetiology of pre-eclampsia. It also emphasizes the need for monitoring the serum calcium level during the antenatal period so that appropriate measures may be instituted to reduce the incidence of pre-eclampsia.

References

- [1] Sukonpan K, Phupong V. Serum calcium and serum magnesium in normal and pre-eclamptic pregnancy. *Arch Gynecol Obstet.* 2005; 273: 12-16.
- [2] Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap LC, Wenstrom KD. Hypertensive disorders in pregnancy. In: Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap LC, Wenstrom KD (eds) *Williams Obstetrics*, 22nd edn. McGraw – Hill: New York 2005; 761 – 808.
- [3] American College of Obstetrics and Gynaecology (ACOG) Practice Bulletin. Diagnosis and management of pre-eclampsia and eclampsia. *Obstet Gynaecol.* 2002; 99 : 159 – 67
- [4] Solomon CG and Seely EW. Preeclampsia. Searching for the cause. *New Eng J Med.* 2004; 350: 641 – 2.
- [5] Walker JJ. Pre-eclampsia. *Lancet* 2000; 356: 1260-5.
- [6] Bringman J, Gibbs C, Ahokas R. Differences in serum calcium and magnesium between gravidas with severe preeclampsia and normotensive controls. *Am J Obstet Gynaecol.* 2006; 195:148.
- [7] Sibai BM. Treatment of hypertension in pregnant women. *N Engl J Med* 1996; 335(4): 257-265.
- [8] Serbar PF, Craft I. Immune basis for pre-eclampsia evidence from oocyte recipients. *Lancet* 1987; 2 (8561): 744.
- [9] Kisters K, Barenbrock M, Louwen F, Hausberg M, Rahn K H, Kosch M. Membrane, intracellular and plasma magnesium and calcium concentrations in pre-eclampsia. *Am J Hypertens* 2000; 13: 765-9.
- [10] Kashyap MK, Saxena SV, Khullar M, Sawhney H, Vasistha K. Role of anion gap and different electrolytes in hypertension during pregnancy (pre-eclampsia) *Mol Cell Biochem* 2006; 282: 157-67.
- [11] Hayashi M, Ueda Y, Hoshimoto K, Ota Y, Fukasawa I, Sumori K, *et al.* Changes in urinary excretion of six biochemical parameters in normotensive pregnancy and pre-eclampsia. *Am J Kidney Dis* 2002; 39: 392-400.
- [12] Ray J, Vasishtha K, Kaur S, Majumdar S, Sawhney H. Calcium metabolism in pre-eclampsia. *Int J Gynaecol Obstet* 1999; 66: 245-50.
- [13] Kosch M, Hauseberg M, Louwen F, Barenbrock M, Rahn KH, Kisters K. Alterations of plasma calcium and intracellular and membrane calcium in erythrocytes of

- patients with pre-eclampsia. *J Hum Hypertens* 2000; 14:333-6.
- [14] Chappell LC, Seed PT, Briley A, Kelly FJ, Hunt BJ, Charnock-Jones DS, et al. A longitudinal study of biochemical variables in women at risk of pre-eclampsia. *Am J Obstet Gynecol* 2002; 187: 127-36.
- [15] Roberts JM, Balk JL, Bodnar LM, Belizan JM, Bergel E, Martinez A. Nutrient Involvement in Pre-eclampsia. *J Nutr.* 2003; 133:1684-92.
- [16] Deborah M. Role of nutrition in the prevention of toxemia. *American Journal of Clinical Nutrition.* 2000.72(1): 298-300.
- [17] Deirdre JL. Hypertensive Disorders of Pregnancy: Relevance for the Neonatologist. *Neo. Reviews* 2004; 5(6):240.
- [18] Akinloye O, Oyewale OJ, Oguntibeju O O. Evaluation of trace elements in pregnant women with pre-eclampsia. *Afr J Biotechnol.* 2010; 9(32):5196-5202.
- [19] Jain S, Sharma P, Kulshreshtha S, Mohan G, Singh S. The Role of Calcium, Magnesium and Zinc in Pre- eclampsia. *Biol Trace Elem Res* 2010; 133: 162-70.
- [20] Hojo M, August P. Calcium Metabolism in Preeclampsia: Supplementation may help. *Medscape Womens Health* 1997; 2:5
- [21] Abdellah A, Abdrabo AA. Assessment of serum calcium, magnesium, copper and zinc levels in Sudanese pregnant women with preeclampsia. *Glo Adv Res J Med Sci* 2014, 3(2): 33-36.
- [22] Sayyed K A, Sonttake AS. Electrolyte status in preeclampsia. *OIJR* 2013; 3(3): 32-34.
- [23] Idogun ES, Imarengiaye CO, Momoh SM. Extracellular calcium and magnesium in preeclampsia and eclampsia. *Afr J Reprod Health* 2007; 11(2): 89-94.
- [24] Sandip S, Asha K, Paulin G, Hiren S, Gagandeip S, Amit V. A comparative study of serum uric acid, calcium and magnesium in preeclampsia and normal pregnancy. *J Advanc Res Biol Sci.* 2013; 5(1): 55-58.
- [25] Richard Kobina Dadzie Ephrain, Derick NMO, Seth WD, Henrietta E, Samuel A, Enoch OA. Serum calcium and magnesium levels in women presenting with pre-eclampsia and pregnancy-induced hypertension: a case-control study in the Cape Coast metropolis, Ghana. *BMC Pregnancy and Childbirth* 2014; 14:390.
- [26] Sandip L, Bhushan M, Monohar M. *International Journal of Recent Trends in Science and Technology* 2014; 9(3): 422-426.
- [27] Malas NO, Sheridan ZM. Does serum calcium in pre-eclampsia and normal pregnancy differ? *Saudi Med J* 2001 Oct; 22(10): 868-71.
- [28] Salari MD, Eftekhari MD. The comparison of total and ionized calcium in preeclamptic pregnant women and the women with normal pregnancy. *Journal of Rafsanjani University of Medical Sciences and Health Services.* 2005; 4(2): 123-128.
- [29] Fatehmeh-VR, et al. Serum calcium and magnesium in preeclamptic and normal pregnancies, comparative study. *Reports Infertil,* 2008; 9(3): 256-262.
- [30] Golmohammad Iou S, Yazdian M, Pashapour N. Evaluation of Serum Calcium, Magnesium, Copper and Zinc Levels in Women with Pre-eclampsia. *IJMS* 2008; 33(4): 231-4.
- [31] I-Bera-S, Siuli- RA, et al. Study of serum electrolytes in pregnancy induced hypertension. *Indian Med Assoc.* 2011 Aug; 109(8): 546-8.
- [32] Lopez- Jaramillo P. Calcium, nitric oxide and preeclampsia. *Semin Perinatol.* 2000; 24: 33-6
- [33] Ingec M, Nazik H, Kadanali S. Urinary calcium excretion in severe preeclampsia and eclampsia. *Clin Chem Lab Med* 2006; 44: 51-3.
- [34] Szmidt- Adjide V, Vendittelli F, David S, Bredent-Bangou J, Janky E. Calciuria and preeclampsia: a case-control study. *Eur J Obstet Gynecol Reprod Biol* 2006; 125: 193-8.
- [35] Habibunnisha BS, Dinesh S, Ashishkumar MA. A study of serum total calcium and uric acid levels in preeclampsia. *IJBAMR* 2013; 1 (3): 50-56.
- [36] Punthumapol C, Kittichotpanich B. Serum calcium, magnesium and uric acid in pre-eclampsia and normal pregnancy. *J Med Assoc Thai* 2008; 91(7): 968-73.
- [37] Recommendations for Prevention and Treatment of Preeclampsia and Eclampsia. In [http://www.who.int/mediacentre/factsheets/fs311/en/]
- [38] Hofmeyr GJ, Duley L Atallah AN. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. *Cochrane Database Syst Rev* 2010; 8: CD001059.