

## Association of Serum Calcium and 24 Hours Urinary Excretion of Calcium in Patients of Preeclampsia

A Khatun<sup>1</sup>, K Kirtania<sup>2</sup>, TS Shima<sup>3</sup>, S Ferdousi<sup>4</sup>,  
A Shahnaz<sup>5</sup>, F Yeasmin<sup>1</sup>, N Sultana<sup>5</sup>

<sup>1</sup>Department of Biochemistry, Dhaka Dental College, Dhaka

<sup>2</sup>Department of Biochemistry, Jahurul Islam Medical College, Kishorgonj

<sup>3</sup>Department of Biochemistry, Shahabuddin Medical College, Dhaka;

<sup>4</sup>Department of Biochemistry, National Institute of Kidney Diseases & Urology, Dhaka

<sup>5</sup>Department of Biochemistry, Dhaka Medical College, Dhaka

<sup>6</sup>Department of Biochemistry, Dhaka Mental College, Dhaka

### ABSTRACT

Preeclampsia is a leading cause of fetal growth retardation, infant morbidity, mortality and maternal death. Several biochemical changes occur during the course of the disease, among them serum total calcium and 24 hr urinary calcium excretion rate have drawn remarkable attention. A case control study was designed to see the association of serum calcium and 24 hours urinary excretion of calcium in patients of pre-eclampsia. The study was done from July 2008 to June 2009 in the Department of Biochemistry, Dhaka Medical College, Dhaka. Total 60 subjects were selected as study population. Among them 30 were diagnosed case of preeclampsia and 30 were age- and sex-matched normal pregnant female healthy control. It was found that the mean measured serum calcium level in case group were  $1.96 \pm 0.17$  (mean  $\pm$  SD) mmol / l and that of control group were  $2.34 \pm 0.12$  (mean  $\pm$  SD) mmol / l respectively. The mean 24 hr urinary calcium excretion level were  $94.40 \pm 10.68$  mg/24 hr (mean  $\pm$  SD) in case group and that of control group were  $154.35 \pm 66.68$  (mean  $\pm$  SD) mg / 24 hr respectively. The study suggests that low level of serum calcium and urinary excretion of calcium was associated with Pre-eclampsia.

**Key Words:** Pre-eclampsia, Serum calcium, 24 hr urinary calcium.

### Introduction

Preeclampsia, the hypertensive disorder most unique to pregnancy, is characterized by hypertension (a rise in blood pressure of  $> 15$  mmHg diastolic or  $> 30$  mmHg systolic compared with measurements in early pregnancy), proteinuria or edema. The diagnosis becomes apparent in late pregnancy, usually after the twentieth gestational week<sup>1</sup>. Preeclampsia, first described more than 100 years ago, remains a leading cause of maternal and infant morbidity and mortality<sup>2</sup>. Preeclampsia complicates 3-5 percent of first pregnancy and 1 percent of subsequent pregnancies, 5-10 percent of which are severe<sup>3</sup>. It is one of the major indications for elective

premature delivery. In the developing countries, preeclampsia affects 4.4 percent of all deliveries and may be as high as 18 percent in some settings in Africa<sup>4</sup>. Development of a simple and reliable biochemical test is, therefore, important to detect pregnant women in the early stage of preeclampsia. Several biochemical changes occur during the course of the disease. A large number of blood and urine parameters have been tested, among them serum total protein, serum albumin, serum globulin and A:G (albumin:globulin) ratio, serum calcium and urinary calcium excretion rate have drawn remarkable attention. Serum total calcium concentration decline characteristically throughout pregnancy reaching at the lowest

level during the middle of third trimester<sup>5</sup>. Low serum calcium may cause high blood pressure by stimulating parathyroid hormone or renin release and inducing vasoconstriction by increasing intracellular calcium in vascular smooth muscle and intensifying smooth muscle reactivity<sup>6</sup>. Some studies have shown that there is a decrease in urinary calcium level in preeclampsia the possible mechanism of which is increased distal tubular reabsorption of calcium<sup>7</sup>. This study was carried out to determine the levels of serum total calcium, total protein, albumin and globulin, and excretion of urinary calcium in control (apparently healthy) and case (preeclamptic) pregnant women and its effect for the development of preeclampsia.

Materials and methods

The study was carried out in the Department of Biochemistry, Dhaka Medical College (DMC), Dhaka during the period of July 2008 to June 2009. The patients were taken from the Department of Obstetrics and Gynaecology unit of Dhaka Medical College Hospital, (DMCH). The female patients who clinically suffered from preeclampsia were considered as case and the control were age & sex-matched normal healthy women with uncomplicated pregnancy. In this study sample size were taken as 60. Thirty patients with preeclamptic females were taken as cases and thirty age & sex-matched normal healthy women with uncomplicated pregnant volunteers were taken as controls. Data were analyzed by computer with the help of SPSS version 12 software package. Mean values of the findings were compared between two groups. Students unpaired 't' test was performed to see the difference between two groups. For all the statistical analysis 2 - tailed 'p' values < 0.05 were considered as significant.

Results

The study showed that the mean measured serum calcium level in case group was 1.96 ± 0.17 ( Mean ± SD ) m mol / l and that of control group was 2.34 ± 0.12 (Mean ± SD)

m mol/l. Unpaired t test showed that there was highly significant difference of mean measured serum calcium level between the case and control group (p < 0.001 ) (table-I) Comparison of mean (± SD) adjusted serum calcium level between case group and control group also showed significant difference (P< 0.001). The levels were 1.99± 0.15 mmol/l and 2.46± 0.16 m mol/l respectively (Table I). The study also showed that the mean 24 hr urinary calcium excretion level in case group was 94.40 ± 10.68mg/24 hr (Mean ± SD) and that of control group was 154.35± 66.68 ( Mean ± SD) mg / 24 hr . Unpaired t test showed that there was highly significant difference of mean 24 hr urinary calcium excretion level between the case and control group (p < 0.001 at Table-II). Presence of hypocalciuria was significantly high (P < 0.001) in case group than control group (70% vs 20% at Table-II).

**Table I: Biochemical tests of serum**

Parameters	Control (n=30)	Case (n=30)	t value	P value
Measured				
Mean±sd	2.34 ±0.12	1.96 ±0.17	9.886	<0.001***
Range	2.12-2.58	1.70-2.19		
Adjusted				
Mean±sd	2.46 ±0.16	1.99 ±0.15	1.608	<0.001***
Range	2.22-2.78	1.80-2.23		

Unpaired student's 't' test  
\*\*/\*\*\* = Significant

**Table II: 24-hour urinary calcium excretion**

Calcium (mg/24 hr)	Control (n=30)	Case (n=30)	t value	P value
Mean±sd	154.35 ±66.68	94.40±10.68	4.863	<0.001***
Range	90.00-270.00	78.00-110.00		X 2 test
Hypocalciuria				
Present	6 (20.0)	21 (70.0)		<0.001***
Absent	24 (80.0)	9 (30.0)		

Unpaired student's 't' test  
\*\*/\*\*\* = Significant

## Discussion

The etiology of hypocalciuria in preeclampsia is unknown. It has been proposed that hypocalciuria may result from decreased dietary intake or decreased intestinal absorption as a secondary result of decreased 1, 25 dihydroxy chole-calciferol (vitamin D) or increased calcium intake by the fetus and placenta or intrinsic renal tubular dysfunction<sup>8</sup>. The main objective of the present study was to compare level of serum calcium, and 24 hr urinary calcium excretion in pre-eclamptic pregnant women with normal pregnant women. The study showed that in the case group, mean ( $\pm$ SD) measured serum calcium ( $2.34 \pm 0.12$  vs  $1.96 \pm 0.17$  mmol/l) and adjusted serum calcium ( $2.46 \pm 0.16$  vs  $1.99 \pm 0.15$  mmol/l) levels were significantly low ( $P < 0.001$ ). The findings of the present study is consistent with the findings of Akhter et al<sup>9</sup>, who reported significantly low ( $P < 0.01$ ) measured serum calcium in case group compared to control (mean $\pm$ SE, control  $2.41 \pm 0.06$  vs case  $2.22 \pm 0.04$  mmol/l). However, they observed no significant difference of mean adjusted serum calcium between control and case groups (mean  $\pm$ SE, control  $2.30 \pm 0.05$  vs case  $2.29 \pm 0.04$  mmol/l). Kosch et al.<sup>10</sup> found low serum calcium in preeclamptic women ( $1.96 \pm 0.15$  mmol/l) compared to control ( $2.43 \pm 0.14$  mmol/l, ( $P < 0.01$ ). Regarding 24 hr urinary calcium excretion, the mean ( $\pm$ SD) excretion rate was significantly higher ( $P < 0.001$ ) in control group of women ( $154.35 \pm 66.68$  mg/24 hr) compared to case ( $94.40 \pm 10.68$  mg/24 hr). Our finding is similar to the finding of Vural, Akgul and Canbaz<sup>11</sup>, who found 24 hr urinary calcium excretion significantly decreased ( $P < 0.001$ ) in pre-eclamptic group of women ( $92.14 \pm 40.87$  mg/24 hr) compared to control ( $178.80 \pm 60.01$  mg/24 hr). However, Mandira, Sudhir and Mamtaz<sup>12</sup> reported that 24 hr urinary calcium did not change appreciably till term in the control group, while it decreased progressively in pre-eclamptic group of women. Statistically, the decrease was significant ( $P < 0.001$ ). Szmidt Adjid? et al.<sup>13</sup> found that women with pre-eclampsia had significantly lower calciuria than

normotensive patients ( $1.5 \pm 1.0$  vs  $6.0 \pm 4.2$  mmol/24 hr,  $P < 0.001$ ). In our study, hypocalciuria (urinary calcium  $< 100$  mg/24 hr) was present in 6 (20%) control and 21 (70%) case (preeclamptic) women ( $P < 0.001$ ). Ramos et al.<sup>14</sup> opined that a 24 hr calciuria less than 100 mg/24 hr may confirm a suspected preeclampsia. Hypocalciuria has been identified as one of the predisposing factor for preeclampsia<sup>8</sup>.

In conclusion, regardless of the mechanism and pathophysiology, hypocalcaemia and hypocalciuria may be reliable findings of preeclampsia from other forms of gestational hypertension. Further prospective and elaborate studies are required to determine whether oral calcium supplementation can be used as a preventive measure for the development of preeclampsia, which ultimately curtail maternal and/or fetal morbidity and mortality.

## References

1. Hojo M & August, P. Calcium metabolism in normal and Hypertensive pregnancy, Seminar in Nephrology, 1995 15: 504-511.
2. Blum A, Shenhav M, Baruch R & Hoffman, M. Endothelial dysfunction in preeclampsia and eclampsia: current etiology and future non invasive assessment, IMAJ 2003; 5: 724-726.
3. Lyell DJ. Hypertensive disorders of pregnancy: Relevance for the Neonatologist. NeoReviews, 2003; 5: e240.
4. Norwitz ER, Hsu C D & Repke JT. Acute complications of preeclampsia, Clinical Obstetrics and Gynecology 2003; 45: 308-329.
5. Pitkin, RM, 'Dietary supplementation in pregnancy', in Edmonds, DR (ed.), Dewhurst's Textbook of Obstetrics and Gynecology for Postgraduates, 6th edn, DR Edmonds (ed.), Blackwell Science Ltd., London, UK 1995, pp. 98-100.
6. Belizan, JM & Villar J. The relationship between calcium intake and edema, proteinuria, and hypertension gestosis: an hypothesis, American Journal of Clinicians and Nutritionists 1989; 33: 2202-2210.

7. Taufield PA, Ales KL, Resnick, LM, Druzin. ML, Gertner JM & Laragh JH. Hypocalciuria in pre eclampsia. *North England Journal of Medicine* 1987; 316: 715-718.
8. Tolaymat A, Sanchez Ramos L, Yergey, AL. Vieira, NE Abrams SA & Edelstein P. Pathophysiology of hypocalciuria in preeclampsia: measurement of intestinal calcium absorption, *Obstetrics and Gynecology*, 83: 239-243.
9. Akhter, K, Rahman, MS, Ahmed, S, Ahmed, A & Alam SM. Serum calcium in normal pregnant women, *Mymensingh Medical Journal* 2003; 12: 55-57.
10. Kosch M, Hausberg 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. *Journal of Human Hypertension* 2000; 14: 333-336.
11. Vural P, Akgul C & Canbaz M. Calcium and phosphate excretion in preeclampsia, *Turkish Journal of Medical Science* 2000; 30: 39-42.
12. Mandira D, Sudhir A & Mamtaz. S Urinary calcium levels in pre eclampsia *Journal of Obstetrics and Gynecology India* 2008; 58: 308-313.
13. Szmidt Adjid V, Venditelli F, David. S, Brident Bangou J & Janky E. Calciuria and preeclampsia: A case control study, *European Journal of Obstetrics & Gynecology and Reproductive Biology* 2006; 125: 193-198.
14. Ramos, JGL, Martins Costa, SH, Kessler, JB, Costa, CA & Barros, E 1998, Calciuria and preeclampsia, *Brazilian Journal of Medical and Biological Research* 1998; 31: 519-522.
15. Belizin JM, Villar J, Gonzales L, Compodonico L & Bergel, E. Calcium supplementation to prevent hypertensive disorder of pregnancy, *New England Journal of Medicine* 1999; 325: 1399-1405.