

Urinary calcium excretion pattern in preeclampsia

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Aims: This study aimed to evaluate the urinary calcium excretion pattern in preeclampsia and to establish the relation between severity of preeclampsia and urinary calcium excretion

Methods: This was a case-control study conducted at Paropakar Maternity and Women's Hospital, Kathmandu from January to June 2015. There were 88 patients equally divided in each group. 24 hours urine calcium was analyzed by ortho-cresolphthalin-complexone method (OCPC) and urinary proteinuria was analyzed bedside by sulphosalicylic acid. Results were analyzed using SPSS 17. P value of < 0.05 was considered as significant.

Results: Preeclampsia was found to occur commonly among the nulliparous patients (59%). The patients with MAP with ≥ 110 mmHg excreted less calcium in their urine in comparison to the patient with MAP < 110mmHg (73.55mg/24 hrs VS 92.79 mg/24 hr). Daily calciuria was decreased with the increase in proteinuria (91.43 mg, 76.19mg and 54.02mg in 1+, 2+ and 3+ respectively). The 24 hours urine calcium excretion in term preeclamptic patient was significantly reduced in compared to the normotensive term pregnant women (77.92 mg \pm 48.61mg VS 117.66mg \pm 69.21 mg , p < 0.001).

Conclusions: Preeclamptic patients excrete significantly lower amounts of calcium in urine and it may be a marker of the severity of preeclampsia.

Keywords: calciuria, preeclampsia, pregnancy

INTRODUCTION

The preeclampsia is diagnosed when the pregnant woman who is previously normotensive presents with high blood pressure ($\geq 140/90$ mmHg) after the 20th week of gestation along with the presence of significant proteinuria (>300mg in 24 hrs).¹ Preeclampsia is a major cause of maternal and fetal morbidity and mortality. Incidence of preeclampsia is 7-10% of all pregnancies², and 4-18% in developing countries.³⁻⁵ In this institute, the incidence was 3% in the year 2070/071 BS (2014 AD).

Preeclampsia is a multisystem disorder affecting hepatic, hematologic, renal, cardiovascular and cerebrovascular systems.¹⁹ Alteration of the calcium metabolism occurs in preeclampsia that is associated with abnormal calcium regulation.²⁰ This alteration

in calcium metabolism is characterized by changes in the serum level of total and ionized calcium as well as urinary calcium excretion.²¹ In preeclampsia, anatomical changes occur in glomeruli, along with the changes in renal perfusion and glomerular filtration rate, as a result of increased arteriolar resistance and ultrafiltration coefficient that contributes to the increased tubular reabsorption of calcium, resulting in hypocalciuria.⁶

The objective of this study was to evaluate the amount of urinary calcium excretion in preeclamptic patients and to determine the severity of preeclampsia in relation to urinary calcium level.

METHODS

This was a hospital based case control study of 88 patients in the duration of 6 months from January to June 2015 at Paropakar Maternity and Women's Hospital, Kathmandu. Singleton term pregnant women were included in the study while the patient with known case of chronic hypertension and those with history of chronic liver disease, malnutrition, chronic renal disease, thyroid and parathyroid disease, immunological disease and other comorbidities were excluded.

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Approval for the study was taken from the ethical board of the hospital and verbal as well as written informed consent was taken.

Mean Arterial Pressure was calculated using the formula

$$\text{MAP} = \text{diastolic BP} + \frac{\text{systolic BP} - \text{diastolic BP}}{3}$$

Proteinuria was tested at bedside by adding 3 drops of 20% sulphosalicylic acid in 3 ml of patient's urine. Calcium level of urine sample analyzed in clinical lab by the colorimetric method using semi analyzer and estimated by the OCPC method at a wavelength of 575 nm (550-590 nm). The formula for calcium estimation:

$$\text{Calcium Conc.} \left(\frac{\text{mg}}{\text{dl}} \right) = \frac{\text{Reading of test material}}{\text{Reading of standard}} \times \text{Conc. of Standard} \left(10 \frac{\text{mg}}{\text{dl}} \right)$$

Data were analyzed using SPSS 17 and p-value of < 0.05 was considered as significant.

RESULT

During the 6 months of study period, total of 88 pregnant women with term pregnancy were enrolled in the study (44 pre-eclamptic patients and 44 normotensive control). Age and gestational age was matching and there was significant difference in blood pressure and 24 hours calciuria ($p < 0.001$). [Table-1]

Table-1: Distribution of mean age, pressure and calciuria

| | Mean ± SD | | p-value |
|-------------------------------|----------------|----------------|---------|
| | Case | Control | |
| Age (years) | 25.64 ± 6.07 | 25.41 ± 5.70 | 0.857 |
| Gestational age (weeks) | 38.48 ± 1.46 | 39.00 ± 1.56 | 0.107 |
| Systolic BP (mmHg) | 146.36 ± 12.78 | 108.64 ± 9.30 | <0.001 |
| Diastolic BP (mmHg) | 98.18 ± 8.43 | 70.00 ± 8.35 | <0.001 |
| Mean arterial pressure (mmHg) | 116.29 ± 10.81 | 82.88 ± 7.35 | <0.001 |
| 24 hours urine calcium (mg) | 77.92 ± 48.61 | 177.66 ± 69.21 | <0.001 |

Among 44 patients in PE group, 11 had impending signs like headache, epigastric pain and blurring of vision, 8 patients had IUGR, 5 had oliguria and 2 patients presented with HELLP syndrome. When the 24 hours urine calcium excretion was compared among the patient with one and more than one features of severity of PE. The patients with more than one features of severity had slightly decreased 24 hours urine calcium excretion compared to the patients who

had only one feature of severity (61.6 mg/ 24 hrs Vs 65.63 mg/ 24 hrs). [Figure-1]

Fig 1: Calciuria in relation to features of severity

The mean calcium excretion among the patients with proteinuria 3+ (n= 11) was 54.02 mg/ 24 hrs which was lower in compared to patients with proteinuria 2+ (n= 12) and 1+ (n= 21), among whom the calcium excretion was 76.19 mg/ 24 hrs and 91.43 mg/ 24 hrs respectively. [Table-2]

Table 2: Proteinuria in pre-eclampsia

| PROTEINURIA (DETECTED BY SULFOSALICYLIC ACID) | Calciuria (mg/24 hrs) | | |
|---|-----------------------|------|-------|
| | Max | Min | Mean |
| +1 (0.3 gm/dl) | 160 | 20.8 | 91.43 |
| +2 (1 gm/dl) | 250 | 34.5 | 76.19 |
| +3 (3 gm/dl) | 174 | 31 | 54.02 |

DISCUSSION

The present study has been taken up to establish the relation between preeclampsia and the 24 hours urine excretion pattern which is an inexpensive method to evaluate the severity of the disease and also can be of some diagnostic and prognostic significance.

Worldwide, pre-eclampsia remains a leading cause of maternal mortality estimating 10–15% of the 500,000 maternal deaths each year caused by hypertensive diseases of pregnancy.⁶ The maternal mortality in Nepal was 281 per 1,00,000 live birth, hypertensive disorder in pregnancy being the second most common cause.⁷

Preeclampsia has been dubbed the “disease of theories”. Abnormal placentation and placental vascular insufficiency are core features of preeclampsia.^{8,9}

Calcium homeostasis is altered in women with preeclampsia. It may only reflect renal compromise because of hypertension or may be the result of reductions in renal prostaglandins. It could also be the result of reduced glomerular filtration rate, which appears at the same time as proteinuria. It has been speculated that hypocalciuria may result from decreased dietary intake, decreased intestinal absorption, increased calcium uptake by the fetus and placenta, intrinsic renal tubular dysfunction, or high intracellular calcium.

It has been reported that hypocalciuria predicts preeclampsia long before clinical manifestations exist.¹⁰⁻¹⁴

During this study period of 6 months, preeclampsia was found to complicate 3% of pregnancies, comparable to the study by Annath CV¹⁴ and Caren G Solomon⁸ (incidence of 3.4-3.5), Alessia Mammario et al (incidence of 2-3%)¹⁵, and Gaber M who reported the incidence of 3-5 %¹⁶ but varied from the study by Szmidt- Adjide et al (7-10%)¹, Sibai (5.3%)¹⁷ and Villar et al (9%)¹⁸. The disparity in the incidence might be due the variation in ethnicity, socioeconomic as well as intellectual status and health awareness. The incidence can also be influenced by the number of study population and the timed period.

Majority of the patient in this study i.e. 26 among 44 PE patients i.e. 59% were nulliparous. This result complimented that result of Gasner (63%)⁵, Ramos (82%)², Cicih Opitasaki (78%)¹⁹ and Al-Mulhim (42%)²⁰. Similarly, 55% (24 patients) were at 37-38 weeks of gestation, followed by 34% were at 39-40 weeks of gestation and 11% were at >40 weeks of gestation which is comparable to the gestation age evidenced in the study by Uzma S et al²¹ (36.2± 2.2 weeks) and Huikeshoven FJM et al.²² However, the current study was done only among the term pregnant women > 37 weeks of gestation, this cannot represent the overall incidence of PE.

In this study, Among the patient with MAP (Mean Arterial Pressure) ≥ 110 mmHg, mean urinary calcium excretion in were 73.55mg/24 hrs (max. 250 mg/24hrs and min 20.8mg/24 hrs), lesser in compared to the patient with MAP < 110 which was 92.79 mg/24 hrs mmHg (max. 210 mg/24 hrs and min. 34 mg/24 hrs) which was comparable to the study by Sirohiwal

D et al¹³, Rose Gasner⁵, Huikeshoven FJM et al²² and Sanchez Ramos et al². This concluded that calciuria decreased with the increasing MAP, this may also denotes that severity of Preeclampsia as the MAP increased.

When 24 hours urine calcium excretion was compared in this study, the patients with more than one features of severity had slightly decreased 24 hours urine calcium excretion compared to the patients who had only one feature of severity (61.6 mg/ 24 hrs Vs 65.63 mg/ 24 hrs) similar to the study by Gasner R et al⁵, Tubbergen P et al⁹, Bhattacharya S and Campbell DM²³.

Finally, when the calciuria was compared among the two groups (the PE group and the control normotensive group, the mean calciuria in the study group of preeclamptic patients was 77.92 mg/24 hrs with the range of 20.8-250 mg/ 24 hrs while in the control group of normotensive patients that calciuria was found to be 177.6591mg/ 24 hrs with the range of 58-320 mg/24 hrs.

CONCLUSIONS

This study shows that the preeclamptic patients excrete significantly lower amount of urinary calcium and that the urinary calcium levels decrease with the severity of preeclampsia. It also concluded that measurement of 24 hours urinary calcium excretion has an advantage of diagnosing the severity of preeclampsia which may further help in screening the patient with severe disease and early management in order to reduce the maternal and neonatal morbidity and mortality.

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