



A Prospective study to evaluate the role of urinary Calcium Creatinine Ratio (CCR) in early prediction of pre-eclampsia

Authors

**Dr Nikita¹, Dr Anju Sharma^{2*}, Dr Lata Rajoria³, Dr Megha Agarwal⁴,
Dr Charusmita Agarwal⁴, Dr Yashwant⁵**

¹Resident, Dept. of Obst. & Gynae, Mahila Chikitsalaya, SMS Medical College & Hospital, Jaipur

²Senior Professor & Unit Head, Dept. of Obst. & Gynae, Mahila Chikitsalaya, SMS Medical College & Hospital, Jaipur

³Senior Professor & Head (Dept. of Gynaecology), Mahila Chikitsalaya, SMS Medical College & Hospital, Jaipur

^{4,5}Assistant Professor, Dept. of Obst. & Gynae, Mahila Chikitsalaya, SMS Medical College & Hospital, Jaipur

⁶Resident, Dept. Of Obst. & Gynae, Mahila Chikitsalaya, SMS Medical College & Hospital, Jaipur

*Corresponding Author

Dr Anju Sharma

Senior Professor & Unit Head, Dept. of Obst. & Gynae, Mahila Chikitsalaya, SMS Medical College & Hospital, Jaipur, India

Abstract

Background: Preeclampsia is associated with hypocalciuria due to derangement in calcium metabolism associated with this condition. Urinary calcium Creatinine ratio is easily measurable, most effective then with spot urine sample compared with other methods that are expensive, time consuming, required specialized equipment & involving complex procedures. The present study will help us in evaluating the role of urinary calcium Creatinine ratio as an effective screening method for prediction of preeclampsia.

Material & Methods: A Hospital based prospective study done on 80 women who attended the department of Obstetrics and Gynaecology, SMS medical college, Jaipur for routine antenatal care, over a period of 1 year between 16-20 weeks of gestation were included in the study after obtaining informed consent. A spot urine sample was collected for estimation of calcium and creatinine. Calcium was determined by O Cresolphthalein complex reaction and creatinine was estimated by Jaffes method. All these women were followed up till delivery.

Results: The gestational age at weeks in study group was 37.07 weeks & 43.48 weeks in control group. Majority of cases had normal delivery in both groups (85%). Only 15% patients had cesarean delivery, out of which 4 in pre-eclampsia patients and 8 in normal patients. The sensitivity of CCR test was found to be 92.85% and specificity 95.45%. The positive predictive value was 81.25 and the negative predictive value was 98.43.

Conclusion: Screening test for preeclampsia is very essential to prevent complications of preeclampsia, which is a major cause for maternal and fetal mortality and morbidity.

Keywords: Preeclampsia, Urinary calcium Creatinine ratio, Morbidity, mortality.

Introduction

Preeclampsia is a potentially serious complication of pregnancy with increasing significance Worldwide, it is the cause of 9-26% of global maternal mortality & a significant proportion of preterm delivery and neonatal morbidity.

Preeclampsia is a multisystem disorder, which have BP \geq 140 mmHg systolic or \geq 90mmHg diastolic on two occasions at least 4 hours apart after 20 weeks of gestation in a women with a previously normal BP may be associated with proteinuria, thrombocytopenia, renal insufficiency, impaired liver functions, cerebral & visual symptoms.

The exact aetiology of preeclampsia is still unknown. The predominant pathology is considered as endothelial dysfunction which sets in early 8-18th weeks of gestation but the sign & symptoms appear in late mild trimester or in advanced stage of disease.

Preeclampsia is associated with hypocalciuria due to derangement in calcium metabolism associated with this condition. It is also preceded by the development of preeclampsia low serum calcium may cause high blood pressure by stimulating parathyroid and renin hormone and also by inducing vasoconstriction by increasing its level in vascular smooth muscle.

In pregnancy physiological changes leads to increase in glomerular filtration rates but in women who develops preeclampsia because of vasospasm and decrease in renal blood flow, Creatinine clearance will be decreased & they have increased serum Creatinine level. This phenomenon occurs early enough & persists throughout gestation. So is useful for early identification of patient risk.

To reduce the impact of pre-eclampsia on maternal mortality, it is necessary to establish correct diagnosis of pre-eclampsia and to proceed with early interventions to prevent complications. Several methods have been developed to establish the disease as early as possible, many of these test could not be used as screening test, due to their false positive results & subjective interpretation.

Hence, there is a need for the screening test to predict preeclampsia ate the early period of gestation.

Urinary calcium Creatinine ratio is easily measurable, most effective then with spot urine sample compared with other methods that are expensive, time consuming, required specialized equipment & involving complex procedures.

The present study will help us in evaluating the role of urinary calcium Creatinine ratio as an effective screening method for prediction of preeclampsia, there by early intervention can be initiated to improve the fetal & maternal outcome.

Material & Methods

A Hospital based prospective study done on 80 women who attended the department of Obstetrics and Gynaecology, SMS medical college, Jaipur for routine antenatal care, over a period of 1 year between 16-20 weeks of gestation were included in the study after obtaining informed consent.

Inclusion criteria

All pregnant women of 16-20 week of gestation period

Exclusion Criteria

- 1) Chronic Hypertension
- 2) Diabetes Mellitus
- 3) Renal disease
- 4) Multiple pregnancy
- 5) Molar pregnancy
- 6) Severe anemia
- 7) Urinary Infection

Method

Detailed history General and Systemic examination and routine blood investigation were carried out. Then at each visit both the groups, was evaluated by eliciting history for symptoms of preeclampsia and imminent eclampsia such as oedema, vomiting, epigastric pain, decreased urine output and visual disturbances. Blood pressure was measured and urine was tested for calcium Creatinine ratio.

A spot urine sample was collected for estimation of calcium and creatinine. Calcium was

determined by O Cresolphthalein complex reaction and creatinine was estimated by Jaffes method. All these women were followed up till delivery.

Based on these criteria the women studied were categorized as those who developed preeclampsia and those who remained normotensives. Calcium to Creatinine ratio (CCR) was calculated and those with a ratio of less than or equal to 0.04 were considered as test positive. Those with a ratio of >0.04 were considered as test negative. The predictive values of calcium to creatinine ratio at ≤ 0.04 were determined by statistical analysis.

Results

Our study showed that the majority of cases (62.5%) were seen in 20-30 years of age groups. Middle class was more common (57.5%). Majority of cases were hindus (62.5%) (table 1). The mean age of pre-eclamptic patients was 25.86 years and in control group was 23.94 years. The gestational age at weeks in study group was 37.07 weeks & 43.48 weeks in control group. Birth weight in neonates was 2.379 kg in study group and 3.374 kg in control group. The mean age of patients, gestational age at weeks & birth weight in neonates was statistical non significant ($P=0.1611$, $P=0.5215$ & $P=0.3049$ respectively) in between groups (table 2).

Majority of cases had normal delivery in both groups (85%). Only 15% patients had cesarean delivery, out of which 4 in pre-eclampsia patients and 8 in normal patients (Graph 1).

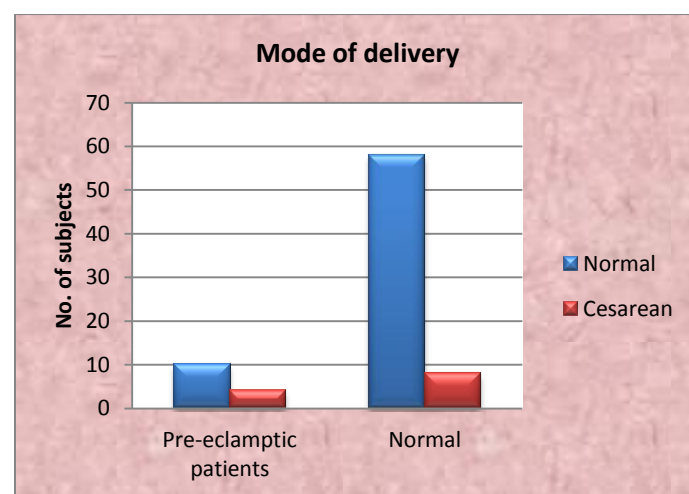
Our study showed that the cut of value of urine calcium Creatinine ratio was 0.04. The positive CCR (≤ 0.04) was present in 13 patients in pre-eclamptic and only 3 patients in control group. The negative CCR (>0.04) was present in 63 cases in normal group and only 1 case in pre-eclamptic group. Which was statistically significant ($P<0.05$) (table 3). The sensitivity of CCR test was found to be 92.85% and specificity 95.45%. The positive predictive value was 81.25 and the negative predictive value was 98.43.

Table 1: Socio-demographic distribution of pregnant women

Demographic profile		No. of subjects	Percentage
Age	<20 years	9	11.25%
	20-30 years	63	62.5%
	>30 years	8	10%
Socio-economic status	Lower	34	42.5%
	Middle	46	57.5%
	Upper	0	0%
Religion	Hindus	63	62.5%
	Muslims	17	37.5%
Education status	Illiterate	18	22.5%
	Secondary	12	15%
	Senior secondary	31	38.75%
	Graduation	19	23.75%

Table 2: Patient’s characteristics of the study and control groups

Patient’s characteristics	Pre-eclamptic patients	Normal	P-value
Age (yrs)	25.86±6.125	23.94±4.239	0.1611
Gestation age at weeks	37.07±1.774	43.48±37.07	0.5215
Birth weight at Neonates	2.379±0.3641	3.374±3.586	0.3049



Graph 1: Mode of delivery in study and control groups

Table 3: Test

Test	Pre-eclamptic patients	Normal Patients	P-value
Positive CCR (≤ 0.04)	13	3	<0.05 S
Negative CCR (>0.04)	1	63	
Total	14	66	

in study and control groups

Discussion

The challenge of any screening test for preeclampsia is to differentiate between those who are and will remain normotensive versus those who appear normal but will develop preeclampsia. The use of urinary calcium to creatinine ratio as early predictor of preeclampsia has been studied by various authors.

The present study was done on 80 women between 16-20 weeks of gestation or upto delivery, were divided into cases and control depending on urinary calcium to creatinine ratio was calculated from single spot urine sample at 16-20 weeks of gestation and then follow up of cases was done for signs of development of preeclampsia.

Incidence of preeclampsia was 17.5 % in our study. Suarez et al.¹ indicated a higher incidence (21.7 %) and this was probably due to the selection of the primigravidas who were young. The patient with preeclampsia in our study delivered at an earlier gestation. As a result of this, birth weights were lower, but statistical non significant ($P=0.3049$). Vaginal delivery occurred in 71.42 % of our study cases. In this study, it was found that significant hypocalciuria was associated with preeclampsia, suggesting that calcium measurement may be useful in screening for the condition.

Our study showed that the urinary calcium/creatinine ratio was lower in women with preeclampsia (0.0350 ± 0.01286) when compared to Normotensive women (0.2224 ± 1.097). Statistical analysis showed significant correlation of urinary calcium – creatinine ratio between women who developed Preeclampsia and Normotensive women with p value of < 0.0001 . These findings were similar to the studies of Hellen Rodriguez M et al², Ozcan T et al³, Das Gupta mandira et al⁴, Kazerooni T et.al⁵, Kar J et.al⁶, Suzuki Y et.al⁷.

Our study showed that the sensitivity was found to be 92.85% and specificity 95.45%. The positive predictive value was 81.25 and the negative predictive value was 98.43. Urine calcium –

creatinine ratio was found to be a good test for predicting preeclampsia.

These results were similar to studies done by Rodriguez H M² and co-workers in 1988 also estimated the CCR at 0.04, they analyzed a sensitivity less of 70%, specificity of 95%, PPV of 64%, NPV of 96% for prediction of preeclampsia. Study conducted by Sheela CN et al in 2011⁸, reported that calcium –creatinine ratio at less than or equal 0.04 in spot urine sample showed a sensitivity of 69%, specificity of 98 %, PPV of 85.6% and NPV of 95.5%. They found it to be a good test. Sudan et .al,⁹ reported sensitivity of 68% and sensitivity of 70%. Ozcan et al³ reported that CCR might be an effective marker of preeclampsia. In addition, studies done by Kazerooni et al.⁵ and Kar et al⁶ evaluated predictive values of CCR at 0.04 was a satisfactory test for prediction of preeclampsis.

Conclusion

Screening test for preeclampsia is very essential to prevent complications of preeclampsia, which is a major cause for maternal and fetal mortality and morbidity. There has been a constant research to find an effective screening test for prediction and prevention of preeclampsia, which would give a idea to implement measures of primary prevention.

References

1. Suarez VR, Trelles JG, Miyahira JM. Urinary calcium is asymptomatic primigravidas who later developed preeclampsia. *Obstet Gynecol* 1996;87(1):79- 82.
2. Rodriguez MH, Masaki DI, Mestman J, Kumar D, Rude R. Calcium/creatinine ratio and microalbuminuria in the prediction of preeclampsia. *Am J Obstet Gynecol* 1988;159(6):1452–5.
3. Ozcan T, Kaleli B, Ozeren M, Turan C, Zorlu G, Dr. Zekai Tahir Burak Maternity Hospital, Ankara, Turkey. Urinary calcium to creatinine ratio for predicting

- preeclampsia. *Am J Perinatol.* 1995;12(5): 349-51.
4. Dasgupta M, Adhikary S, Mamtaz S. Urinary calcium in preeclampsia. *Indian J Obstet Gynecol.* 2008;58:308–13.
 5. Kazerooni, T. and S. Hamze-Nejadi, 2003. Calcium to creatinine ratio in a spot sample of urine for early prediction of preeclampsia. *Int. J. Gynecol. Obstet.*, 80: 279-283.
 6. Kar J, Srivastava K, Mishra RK, Sharma N, Pandey ON, Gupta Shalini. Role of urinary calcium creatinine ratio in prediction of pregnancy induced hypertension. *J Obstet Gynecol Ind.* 2002; 52(2): 39-42.
 7. Suzuki Y, Hayashi Y, Murakami I, Yamaguchi K, and Yagami Y. Urinary calcium excretion as an early prediction marker for pregnancy induced hypertension. *Nippon Sanka Fujinika Gakkai Zasshi.* Nov 1992; 44(11): 1421-1426
 8. Sheela CN, Beena SR, Mhaskar Arun. Calcium- Creatinine Ratio and Microalbuminuria in Prediction of Preeclampsia. *The Journal of Obstetrics and Gynaecology of India* January/ February 2011 pg 72 – 76.
 9. Saudan PJ, Shaw L, Brown MA. Urinary calcium / creatinine as a prediction of preeclampsia. *Am J Hypertens* 1998; 11 (7):839-43.