

# Calcium-creatinine Ratio and Microalbuminuria in Prediction of Pre-eclampsia

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## Abstract

**Introduction:** Hypertension is one of the most common complications of pregnancy and a leading cause of maternal and perinatal morbidity and mortality. It forms deadly triad along with hemorrhage and infection and contributes greatly to maternal morbidity. An early diagnosis and treatment helps to reduce it to a minimum, and therefore it is important to identify women at risk at the earliest.

**Objectives:** To evaluate the predictive values of urinary calcium-creatinine ratio (CCR) and microalbuminuria for pre-eclampsia.

**Materials and Methods:** Urinary CCR was determined in one step urine sample in 150 asymptomatic pregnant women between 20 and 34 weeks of gestation, who attended the antenatal outpatient department at Indira Gandhi Government Medical College. The results were analyzed by Chi-square test to find the significant association of findings of pre-eclampsia and CCR and microalbuminuria. Area under receiver operator curve was used to find out the predictive values of CCR at  $\leq 0.04$  and microalbuminuria for pre-eclampsia.

**Results:** It was found that CCR had a sensitivity, specificity, positive predictive value, and Negative predictive value of 64%, 96.9%, 80%, and 93.2%, respectively, with  $P < 0.001$  (strongly significant). It was found to be a good test for prediction of pre-eclampsia. Combined microalbuminuria and CCR  $\leq 0.04$  was found to be good tests for prediction of pre-eclampsia ( $P < 0.001$ ).

**Conclusion:** CCR at  $\leq 0.04$  in spot urine sample is a good test for prediction of pre-eclampsia and can be recommended as a screening testing all asymptomatic pregnant women, for pre-eclampsia. Combined CCR and microalbuminuria seem to be effective as a screening tool for pre-eclampsia at present.

**Key words:** Calcium creatinine ratio, Microalbuminuria, Pre-eclampsia

## INTRODUCTION

Hypertension is one of the most common complications of pregnancy and a leading cause of maternal and perinatal morbidity and mortality. It forms deadly triad along with hemorrhage and infection and contributes greatly to maternal morbidity. An early diagnosis and treatment helps to reduce it to a minimum, and therefore it is important to identify women at risk at the earliest.<sup>1</sup>

The etiology of pregnancy-induced hypertension (PIH) is still unclear. There is a diffuse endothelial damage affecting all organs and hypertension is only one of the clinical manifestations of disease. The deleterious effect of PIH on mother and fetus can be prevented by appropriate intervention if PIH is identified early.

Many biochemical and hematological markers have gained recognition in predicting PIH, assessing the severity of disease and in differentiating pre-eclampsia from other hypertensive disorders of pregnancy. We often get women with severe disease at early gestation and many times for mothers health; we have to interrupt the physiological process of pregnancy turning pathological. Hence, the prediction of hypertensive disorder remains only alternative to prevent its disastrous complications.

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Combining the biochemical markers calcium, creatinine, and microalbuminuria, we can predict the risk of disorder and start preventive therapy at early stages to prevent maternal and feto-neonatal morbidity and mortality.<sup>2,3</sup>

Ideal predictive test should be simple, noninvasive, easy to perform, and reproducible with high sensitivity and specificity. Hence, we choose urinary calcium-creatinine ratio (CCR) and microalbuminuria for prediction of gestational hypertension.

### Aims of the Study

To determine the predictive values of decreasing urinary CCR and microalbuminuria for pre-eclampsia, in spot urine sample, in asymptomatic pregnant women between 20 and 34 weeks of gestation.

## MATERIALS AND METHODS

A total of 150 pregnant women who attended the Indira Gandhi Government Medical College outpatient department for routine antenatal care, over a period of 2-year, between 20 and 34 weeks of gestation were included in the study after obtaining informed consent.

Women with a history of diabetes, chronic hypertension and renal disease were excluded from the study. Women who had proteinuria by dipstick method at the first visit, as well as those with a baseline blood pressure of more than or equal to 140/90 mm of Hg at first visit were excluded from the study.

Blood pressure was measured in semi-recumbent posture with left lateral tilt, in the right arm and proteinuria was excluded by testing a spot sample for albumin by dipstick method.

A spot urine sample was collected for estimation of calcium, creatinine, and microalbumin. Calcium was determined by orthocresolphthalein complex method and urinary creatinine by Jaffe's method.

Microalbuminuria was detected by immunometric assay. All women were followed up till delivery. At each visit, blood pressure was measured and urine was tested for protein by dipstick method. Pre-eclampsia was defined as blood pressure more than or equal to 140/90 mm Hg by using korotkoff 5<sup>th</sup> sound for diastolic BP associated with proteinuria. Based on these criteria women were categorized as those who developed pre-eclampsia and those who remained normotensive.

Calcium to creatinine ratio (CCR) was calculated and those with ratio  $\leq 0.04$  were considered positive. Those with a

ratio of  $>0.04$  were considered as test negative. Women with urinary albumin levels  $>30 \text{ mg/l}$  were considered positive for microalbuminuria and those with  $<30 \text{ mg/l}$  were considered negative for microalbuminuria.

The predictive values of CCR at  $\leq 0.04$  and microalbuminuria were determined by statistical analysis.

### Statistical Analysis

Chi-square test has been used to find a significant association of pre-eclampsia and CCR and microalbuminuria. A  $P < 0.001$  considered strongly significant. Area under receiver operator curve (ROC) has been used to find the predictive values of CCR at  $\leq 0.04$  and microalbuminuria for pre-eclampsia.

## RESULTS

In this prospective clinical study comprising 150 women between 20 and 34 weeks of gestation, the majority (81%) were in the age group of 21-31 years 0.8% were below 21% and 11% were more than 31 years of age. Mean age being  $24.16 \pm 3.14$ .

Incidence of pre-eclampsia in study group was 15% of which 12% had mild, 2.5% severe and 0.5% eclampsia. Mean gestational age at which pre-eclampsia developed was  $37.66 \pm 2.75$ . Among all pre-eclampsia patients, 72% were primigravidae and 28% were multigravida.

Of 150 women studied 25 (16.66%) were test positive, and 125 (83.33%) were test negative (Table 1).

Of 150 women studied 20 (13.33%) were test positive for microalbuminuria ( $>30 \text{ mg/l}$ ) and 130 (86.66%) were negative for microalbuminuria ( $<30 \text{ mg/l}$ ).

**Table 1: Number of test positive women**

Test parameter	<i>n (%)</i>		Total (%)
	Test positive	Test negative	
CCR	25 (16.66)	125 (83.33)	150 (100)
Microalbuminuria	20 (13.33)	130 (86.66)	150 (100)

CCR: Calcium creatinine ratio

**Table 2: Association of calcium creatinine ratio with pre-eclampsia**

CCR	<i>n (%)</i>		
	Pre-eclampsia	Normotensive	Total
Test positive $\leq 0.04$	16 (64) (True positive)	9 (36) (False positive)	25 (16.66)
Test negative $>0.04$	4 (3.2) (False negative)	121 (96.8) (True negative)	125 (83.33)
Total	20 (13.33)	130 (86.66)	150 (100)

CCR: Calcium creatinine ratio

**Table 3: Association of microalbuminuria with pre-eclampsia**

Microalbuminuria	n (%)		
	Pre-eclampsia present	Normotensive	Total
Test positive >30 mg/l	11 (7.33) (True positive)	9 (6%) (False positive)	20 (13.33)
Test negative <30 mg/l	5 (3.33) (False negative)	125 (83.33) (True negative)	130 (86.66) (True negative)
Total	16 (10.66)	134 (89.33)	150 (100)

**Table 4: Results of statistical analysis**

Test parameter	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	P
CCR	64	96.9	80	93.2	<0.001**
Microalbuminuria	26.31	92.22	33	87	<0.001

PPV: Positive predictive value, NPV: Negative predictive value, CCR: Calcium-creatinine ratio

Association of CCR and microalbuminuria with pre-eclampsia was determined and is shown in Tables 2 and 3, respectively.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated after statistical analysis of the results and are shown in Table 4.

CCR at  $\leq 0.04$  had a sensitivity of 64%, specificity of 96.9%, PPV of 80%, NPV of 93.2% with  $P < 0.001$  which is strongly significant. Microalbuminuria was comparatively less accurate with sensitivity 26.31%, specificity of 92.22%, PPV of 33%, NPV of 87%, with  $P < 0.001$ . Predictive value of CCR and microalbuminuria for pre-eclampsia were calculated using Area under curve of ROC and it was found that CCR at  $\leq 0.04$  was a good test but microalbuminuria was only fair test for prediction of pre-eclampsia.

## DISCUSSION

In our study comprising 150 asymptomatic pregnant women between 20 and 34 weeks of gestation, CCR at  $\leq 0.04$  in spot urine sample had a sensitivity of 64%, specificity of 96.9%, PPV of (PPV) 80%, NPV of 93.2% found and was found to be a good test for prediction of pre-eclampsia.

Rodriguez *et al.*<sup>2</sup> who investigated the predictive value of decreasing CCR in spot urine sample as early as 1988 reported that it might be an effective marker for pre-eclampsia.

Saudan *et al.*<sup>3</sup> had reported the sensitivity of 85% and specificity of 91% and Izumi *et al.*<sup>4</sup> found that it had limited value in prediction of pre-eclampsia.

Kazerooni and Hamje-Nezadi<sup>5</sup> evaluating between 20 and 24 weeks of gestation and Kar *et al.*<sup>6</sup> evaluating the predictive value of CCR at  $\leq 0.04$  between 20 and 34 weeks

of gestation (similar to our study), have reported that it was satisfactory test for prediction of pre-eclampsia and could be effective method for screening asymptomatic women for pre-eclampsia.

Estimation of calcium and creatinine in a spot urine sample is simple test, noninvasive, and is easy to perform and hence assures good patient compliance. It has a good predictive value and hence justifies the cost and is suited to be adopted as screening test for pre-eclampsia. It can, therefore, recommend as a screening test for pre-eclampsia and could be offered to all asymptomatic pregnant women between 20 and 34 weeks of gestation during their routine antenatal visits.

Microalbuminuria, on the other hand, was found to be only fair test in predicting pre-eclampsia with sensitivity, specificity, PPV and NPV of 26.31%, 92.22%, 33% and 87%, respectively.

Salako *et al.*<sup>7</sup> reported that single estimation of microalbuminuria at the time of antenatal booking had a sensitivity of 42% and specificity of 86%.

Chhabra and Gandhi<sup>8</sup> found that estimation of microalbuminuria around 18 weeks of gestation seemed useful, especially in primigravidae. More trials are needed to establish the usefulness of microalbuminuria in prediction of pre-eclampsia before adapting it as screening tool.

Pre-eclampsia is a major cause for concern worldwide, and there is a constant search for finding the means for predicting pre-eclampsia. An availability of good screening test would initiate more research in this direction and will be useful to decrease maternal mortality and morbidity.

## CONCLUSION

A single estimation of CCR at  $\leq 0.04$ , in spot urine sample, in asymptomatic pregnant women between 20

and 34 weeks of gestation have good predictive value and therefore can be recommended as a screening test for all pregnant women. Microalbuminuria, on the other hand is weak test for prediction of pre-eclampsia and cannot be recommended as a screening test at present.

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