

Original Article

Determination of Urinary Calcium/Creatinine Ratio in a Spot Sample of Urine For Early Prediction of Pre-Eclampsia

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Abstract:

Based on the fact that urinary hypocalciuria in pre-eclampsia this study was designed to determine the predictive value of calcium to creatinine ratio in a spot urine sample in second trimester of pregnancy. The calcium to creatinine ratio Calcium/creatinine ratio has been considered for early detection of pre-eclamptic toxemia (PET). So for the diagnosis of PET we try to investigate the relation of urinary calcium, urinary creatinine, urinary calcium/creatinine ratio. For this purpose total number of 60 healthy gravid and clinically suspected PET women of 20-28 weeks of pregnancy having age ranged from, 17-39 years were selected. On these 30 healthy pregnant women urinary calcium/creatinine ratio was within normal range and On the other hand urinary calcium/creatinine ratio in PET women was significantly decreased on the clinically diagnosed 30 PET women. These observations suggest that low calcium/creatinine ratio help in early prediction of PET. The result expressed by receiver operator curve analytic technique. Using the receiver operator curve a cut off level of 0.225 the calcium to creatinine ratio was chosen for prediction of PET. Twenty Two out of 30 woman had a calcium/creatinine ratio equal or less than 0.225. Thirty who had remained normotensive 13 had calcium/creatinine ratio equal or less than 0.225. This level thus yielded a 75% sensitivity and 65% specificity. Positive and negative predictive values 68.2% and 72.2% were calculated respectively, at this cut-off point. In conclusion a spot single urine sample calcium/creatinine ratio may be an effective method for screening pregnant women for detection of pre-eclampsia.

Keywords: Pre-eclampsia, calcium/creatinine ratio

Introduction:

Pre-eclampsia (PET) is one of the fatal complication of pregnancy. It is a pregnancy induced auto-intoxication with multi-system disorder of unknown etiology which is associated with triad of oedema, hypertension and proteinuria occurs mostly in nullipara after 20th week of gestation and most frequently near term.^{1,2}

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Early test for prediction of PET previously reported are platelet count, hematocrit, serum uric acid and microalbuminuria are poor predictor of PET. Fibrinectin, urinary calcium excretion, roll over test, Doppler ultrasound showed contradictory and non-conclusive. Isometric exercise test showed predictive value but only two studies performed. Angiotensin II sensitivity test best predictive value but clinically not practiced. There is no test that fulfils all criteria established to be a good predictor of PET.³

It has been found that increased urinary albumin and decreased calcium excretion may be an early marker for pre-eclampsia.⁴ Urinary calcium/creatinine ratio less than or equal to 0.04 which may be an early marker for useful screening tool in predicting the subsequent development of pre-eclampsia.⁵

So determination of calcium/creatinine ratio may easily predict the case of PET because previously it was reported that 24 hrs. urine samples can be replaced by a single voided urine.^{6,7,8,9} But no data is available on this aspect in our country.

Therefore this study was conducted to determine the relationship between PET, hypocalciuria and calcium to creatinine ratio for early prediction of PET in a spot urine sample.

Materials And Methods:

This is a non-interventional perspective cross sectional study that was approved by the institutional thesis review board of Rajshahi Medical College and it was also carried out on total number of 60 women with age ranged from 17-39 years of the m 30 normotensive gravid women and 30 suspected PET women were taken as study population. All the subjects were selected from department of obstetrics and gynecology, outdoor and indoor, Rajshahi Medical College Hospital. A complete obstetrical history, clinical examination and necessary investigations were done to exclude other conditions affecting urinary calcium/creatinine ratio. All the subjects were taken from middle and lower middle socioeconomic classes.

Urinary calcium, urinary creatinine and urinary calcium/creatinine ratio were determined by using reagent kits Human and Tradesworth Germany. Calcium was measured by o-cresolphthelein complexions method & creatinine was measured by alkaline picrate method of Jaffe^{10,11} in the department of Pharmacology, Rajshahi Medical College, Rajshahi. The significance of differences between two groups was calculated using unpaired student's t test and cut off value chosen for prediction of pre-eclampsia by receptor operative analytic curve (ROC).

Result:

In case of normotensive pregnant women urinary calcium, urinary creatinine and urinary calcium/creatinine ratio

were (mean±SEM) 6.239±0.159 mg/dl, 33.515±2.717 mg/dl and 0.231±0.025 respectively.

In case of suspected pre-eclamptic women urinary calcium, urinary creatinine and urinary calcium/creatinine ratio were (mean±SEM) 2.581±0.287 mg/dl 70.454±10.791 mg/dl and 0.136±.088 respectively.

Table 1: Biochemical characteristics of study groups

	Normotensive women(n=30)	Pre-eclamptic women (n=30)
Maternal age years mean±S.D.	27.3 ±5.4	29.3 ± 5.3
Gestational age during study time weeks mean±S.D.	28.6± 3.6	27.5± 3.5
Urinary Calcium mg/dl mean±S.D.	6.239± .159	2.581± .287
Urinary Creatinine mg/dl mean±S.D.	33.515± 2.717	70.454± 10.791
Mean calcium to creatinine ratio	.231±.025	.136±.088

Receiver-operator curve for calcium/creatinine ratio

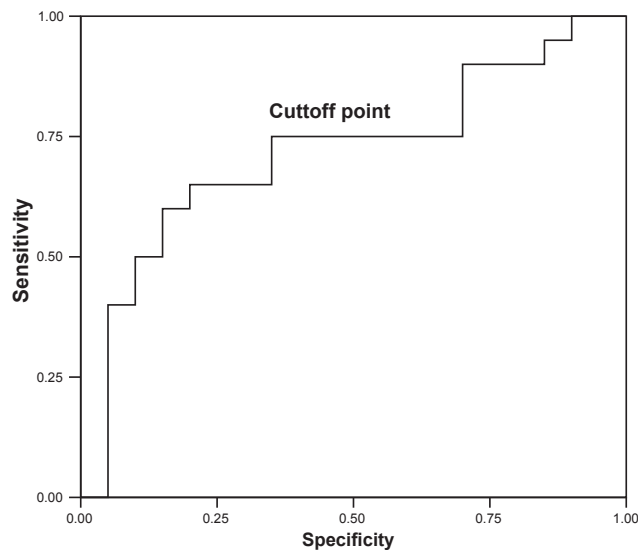


Figure 1. Receiver-operator curve for calcium/creatinine ratio (cut-off level set at 0.225).

Using the receiver-operator curve a cut off level of 0.225 for the calcium/creatinine ratio was chosen for prediction of pre-eclampsia. 22 out of 30 women had calcium/creatinine ratio equal to or less than 0.225. Thirty women who had remained normotensive, 13 had calcium/creatinine ratio equal or less than 0.225. This level thus yielded a 75% sensitivity and 65% specificity. Positive and negative predictive values 68.2% and 72.2% were calculated respectively, at this cut-off point.

Table 2 Screening value of urinary calcium/creatinine ratio in PET woman

Calcium/creatinine ratio in pre-eclamptic women <0.225

Observation of ROC curve analysis	Value
Nonmotensive cases	30
Pre-eclamptic cases	30
Sensitivity %	75
Specificity %	65
Positive predictive value %	68.2
Negative predictive value %	72.2

Discussion:

The present study has been showed PET patient excrete less calcium in urine. Several studies have used the predictive value of hypocalciuria for pre-eclampsia.^{4,5,6,13,14,15}

These findings are in agreement with another study¹⁹. In PET women urinary calcium/creatinine ratio was significantly decreased. This finding is also well correlated with different worker's findings.^{14,15,17,19,20}

Increased urinary calcium excretion during normal pregnancy is attributed either to increased glomerular filtration rate and decreased tubular reabsorption of calcium, or to dissociation between sodium and calcium tubular handling in the ascending loop of Henle. Contrary to normotensive women, pre-eclamptic patients have been shown to excrete less calcium.^{6,19}

Several studies have used the predictive value of hypocalciuria for pre-eclampsia.^{14,19} In a prospective study Sanchez-Ramos et al., measured daily urinary calcium excretion in 103 women with gestational age less than 24 weeks.¹³ Serial 24 hrs urine specimens were obtained at the first, second, and third trimester of pregnancy. He concluded that who later developed pre-eclampsia excreted less urinary calcium than those who remained normotensive, Rodriguez et al.⁵ determined the calcium/creatinine ratio at 24 to 34 weeks of gestational age. By using the receiver-operator curve, a cut-off value of 0.004 for the calcium/creatinine ratio yielded a sensitivity of 70%, a specificity of 95% and positive and a negative value of 64% and 96%, respectively.

The results, of this study consistent with the result of these studies.^{5,9,14,17,18,19} In which they concluded that the urinary calcium/creatinine ratio did not differ significantly between patient with pre-eclampsia and normal pregnant women.

In those studies, women with hypertension and edema without proteinuria were included in the pre-eclamptic group. In my study, however, such of women were excluded and this might explain the difference between present findings and that of Ozcan and Kaleli (1995).

Saudan et al. (1998) conducted a similar study but obtained a different cut-off point, 0.1 instead of present 0.225, which yielded a lower sensitivity and specificity than the present study (75% and 65%, respectively).¹⁷ The present study is almost similar to that of Tkazerooni²⁰ and Hamze-Nejadi, (2003) where cut of point was 0.229, sensitivity 75% and specificity 77.7%. These confusing results highlight differences due to sample size, prevalence of pre-eclampsia, and ethnicity in the populations studied. However, it may be concluded from the mentioned studies that a single urine calcium/creatinine ratio may be an effective screening method for pre-eclampsia.

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