

Study Urinary Calcium-Creatinine Ratio as a Predictor of Pre-Eclampsia in Pregnant Women

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Abstract:

Aim: To study the urinary calcium-creatinine ratio in prediction of pre-eclampsia in pregnant women.**Objectives:** (1). To study the urinary calcium : creatinine ratio among all pregnant women. (2). To correlate the urinary calcium : creatinine ratio in normotensive and pre-eclamptic women.**Methodology:** This Prospective, observational study was conducted in the Department of Obstetrics and Gynecology, Sri Ram Murti Smarak Institute of Medical Sciences, Bareilly. Urinary calcium creatinine ratio was determined in a random sample of urine in 50 patients of pre-eclampsia (Study group) and 50 normotensive pregnant (Control group) patients of age 20-35 years with gestational age 20 weeks onwards. Cut off value for CCR was taken as ≤ 0.04 .**Results:** Out of 50 pre-eclamptic cases, 26(52%) cases in the study group had CCR ≤ 0.04 while only 7(14%) cases in control group had CCR ≤ 0.04 with a statistically significant p value of 0.000. On statistical analysis, CCR at ≤ 0.04 had a sensitivity of 52%, specificity of 86%, positive predictive value of 79% and negative predictive value of 64%. The accuracy of the test was 69%.**Conclusion:** A single estimation of urinary calcium to creatinine ratio in asymptomatic pregnant women after 20 weeks of gestation is a simple and cost-effective test. A value of less than or equal to 0.04, in a spot urine sample, has a good predictive value for preeclampsia.**Keywords:** Preeclampsia, Urinary Calcium, Urinary Creatinine, Urinary Calcium Creatinine Ratio.

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Introduction

Around the world, an estimated 529,000 women die during pregnancy or childbirth [1] of which 80% are directly related to pregnancy events such as haemorrhage and sepsis followed by hypertensive disorders of pregnancy. The incidence of maternal mortality due to pre-eclampsia in developed countries range from 2-5% while in developing countries range from 10-25% [2,3]. Preeclampsia is a disorder of the second half of pregnancy which regresses after delivery [4,5]. Preeclampsia is a syndrome characterized by the development of hypertension to the extent of 140/90 mm Hg or more with proteinuria during pregnancy after the 20th week of gestation.

As per the new ACOG Practice Bulletin 2019, the presence of any one of the following severe features in women with gestational hypertension without proteinuria should also be reclassified as pre-eclampsia. These features include-Thrombocytopenia (platelet count less than $100,000 \times 10^9/L$), Impaired liver function, severe persistent right

upper quadrant or epigastric pain, pulmonary edema, renal insufficiency (serum creatinine concentration greater than 1.1mg/dl), new-onset headache or visual disturbances⁶. In addition it is recommended that women with gestational hypertension with severe range of BPs (systolic BP of 160mmHg or higher, or diastolic BP of 110mmHg or higher) should also be diagnosed as pre-eclampsia with severe features [6].

The various risk factors for pre-eclampsia include age <20 years and >35 years, primiparity, previous history of pre-eclampsia, family history of pre-eclampsia, pre-existing medical conditions like renal disease, diabetes [7]. The predominant pathology is endothelial dysfunction resulting in placental insufficiency which results in secondary symptomatic stage characterized by development of hypertension, renal impairment and proteinuria, liver disease and HELLP syndrome along with increased risk for eclampsia and pulmonary edema [8].

It is a multisystem disorder affecting all the organs where renal impairment is one of the earliest manifestations of end organ damage. Women with pre-eclampsia have diminished renal perfusion and glomerular filtration due to damage caused by pre-eclamptic changes leading to decrease in creatinine clearance with corresponding elevated plasma creatinine level. Urinary calcium excretion in normal pregnancy is 350-650 mg/day, compared with 100-250 mg/day in non-pregnant women. Hypocalciuria in women with preeclampsia may be due to decreased fractional excretion of calcium secondary to its increased tubular reabsorption [9].

In patients with pre-eclampsia a decrease in urinary calcium excretion results in decreased calcium/creatinine ratio which can be used as a marker for early diagnosis of pre-eclampsia. In the light of above facts the present study was conducted with the aim to assess the role of urinary calcium to urinary creatinine ratio (CCR) in diagnosing pre-eclampsia in pregnancy for proper patient care.

Material and Methods

This prospective study was carried out at the Department of Obstetrics and Gynaecology at Sri Ram Murti Smarak Institute of Medical Sciences, Bareilly, for 1 ½ years from November 2017-May 2019. Pregnant women between age group of 20-35 years with gestational age 20 weeks onwards attending the antenatal clinic (outdoor), or admitted in the ward or in labour room were included in the study. A total of 100 pregnant women were divided into 2 groups: GROUP A- 50 Pre-eclamptic women (cases) and GROUP B- 50 Normotensive women (control).

Patients were explained about the study, consent was taken and their details regarding age, blood group and medical history was obtained.

Inclusion Criteria: All women with singleton pregnancy with gestational age more than 20 weeks.

Exclusion Criteria

1. Chronic hypertension
2. Previous history of pre-eclampsia
3. Chronic renal disease
4. Immunological or vascular disorders
5. UTI
6. High risk female- multiple gestation, polyhydramnios, diabetes mellitus

Sample collection: Patient was asked to submit random midstream urine sample in a 50 mL urine container for laboratory analysis for random urine dipstick test, calcium and creatinine. The dipstick analysis was done using the uripus 900 urinalysis strip.

Sample analysis: Urinary Calcium was estimated by OCPC (0-Cresolphthalein Complexone) method calorimetrically. Urinary Creatinine was estimated by Jaffe's reaction (alkaline picrate). All the collected data was reviewed and analysed for urinary calcium-creatinine ratio (CCR) in both the study and control group.

$$\text{Ratio} = \frac{\text{Urinary Calcium (mg/dl)}}{\text{Urinary Creatinine (mg/dl)}}$$

Cut off for CCR was taken as ≤ 0.04

Statistical Analysis: All findings were recorded in a predesigned format. Compiled data was presented in form of frequency and percentage and subsequently analysed by appropriate statistical tests (chi-square test and Fischer exact test) using the SPSS (Statistical Package for the Social Science) Version 20.0 for the window. A probability value of 0.05 was accepted as the level of statistical significance.

Results

Table 1: Systolic and Diastolic BP in study and control group

	Cases(n=50)				Control (n=50)	
	Mild PE (27)		Severe PE(23)		Mean	SD
Systolic BP	Mean	SD	Mean	SD		
	145.18	±8.42				
Total mean	155.81					
SD	±10.63					
Diastolic BP	Mean	SD	Mean	SD	77.48	±9.23
	93.03	±5.62	119.6	±7.73		
Total mean	106.3					
SD	±7.35					

Table 2: Calcium to creatinine ratio (CCR) in cases and control group

CCR		Cases(n=50)	Control(n=50)	p value
≤ 0.04	no of patients	26(52%)	7(14%)	
	mean	0.008±0.011	0.018±0.002	0.000
> 0.04	no of patients	24(48%)	43(86%)	
	mean	0.299±0.393	0.417±0.643	0.421

Table 3: Association of calcium-creatinine ratio with pre-eclampsia

CCR	Cases(n=50)	Control(n=50)	Total
≤0.04 (Test positive)	26(52%) (True positive)	7(14%) (False positive)	33
>0.04 (Test negative)	24(48%) (False negative)	43(86%) (True negative)	67

Discussion

Pre-eclampsia is a multiorgan, heterogenous disorder of pregnancy associated with significant maternal and neonatal morbidity and mortality.

A major challenge in modern obstetrics is early identification of pregnancies at high risk of pre-eclampsia and undertaking the necessary measures to reduce the prevalence of the disease and its complications. In this study an attempt was made to show the relationship between low urinary calcium creatinine ratio (CCR) and pre-eclampsia. A urine Calcium: Creatinine ratio threshold value of 0.04 was taken as cut off for prediction of preeclampsia.

The mean Systolic blood pressure was 155.81 ± 10.94 and mean diastolic blood pressure 106.3 ± 7.35 . These findings were similar to the study conducted by Pal et al (2012) where the mean Systolic blood pressure among the study group was 156.8 ± 4.34 and mean Diastolic blood pressure was 102 ± 4.8912 .

In our study, mean urinary calcium among mild pre-eclamptic group was 4.73 ± 6.9 whereas in severe pre-eclampsia was 3.22 ± 4.1 . Study conducted by Pal et al (2012) correlates with the results of our present study that showed hypocalciuria was associated with pre-eclampsia [12]. Hypocalciuria in pregnancy is due to a decrease in distal tubular reabsorption of calcium and a decrease in the glomerular filtration rate due to glomerular endotheliosis.

The mean urinary creatinine in the study group was 83.406 ± 58.605 whereas in the control group the mean urinary creatinine value was 63.22 ± 48.262 which is statistically not significant. Our findings were in concordance with the study conducted by Amandeep K (2015) and showed that mean Urinary creatinine levels in normal pregnant females was 179.6 ± 8.466 mg% while in pre-eclamptic pregnant females, the mean urinary creatinine excretion was 249.8 ± 14.4 mg%, with statistically significant p value of <0.001 [13].

There is significantly increased excretion of creatinine in pre-eclamptic females as compared to normal pregnant females due to less amount of urine formed in pre-eclamptics. Slightly increased serum creatinine and significantly increased urinary creatinine but decreased amount of urine is due to decreased glomerular filtration rate in pre-eclampsia.

Hypocalciuria accompanied by hypercreatinuria are the features responsible for decreased urinary

calcium; creatinine ratio in pre-eclamptic females < 0.04 . Thus the ratio can be considered as a predictor of pre-eclampsia. In our study 26(52%) patients in the study group had calcium: creatinine ratio (CCR) ≤ 0.04 with a mean value of 0.008 ± 0.002 against 14% in control group with a mean value of 0.018 ± 0.011 with a statistically significant p value of 0.000.

Conclusion

Hypertensive disorders of pregnancy are a major contributing factor leading to maternal mortality. So prediction of pre-eclampsia in pregnancy may reduce maternal and fetal complications by timely management. The present study supports that there is a definite relationship between low urinary calcium to creatinine ratio and the development of preeclampsia. Estimation of Calcium -Creatinine ratio in a spot urine sample is a simple test, easily performed hence assures patient compliance. It has a good predictive value and justifies the cost and is suited to be adopted as a screening tool for preeclampsia. However this is a very small study and therefore larger randomized trials are needed for using urinary calcium creatinine ratio as a predictor of pre-eclampsia.

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