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ORIGINAL ARTICLE

Calcium-to-Creatinine Ratio in a Spot Sample of Urine, for Early Prediction of Hypertensive Disorders of Pregnancy: A Prospective Study

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Abstract

Background Hypertensive disorders complicate 5–10 % of all pregnancies. Various methods for screening have been studied to identify pregnant women at risk of development of preeclampsia, but no ideal screening test has been identified so far. The objective of this study was to determine the efficacy of urinary calcium-to-creatinine ratio, in a spot urine sample, for the prediction of preeclampsia in asymptomatic pregnant women between 18 and 24 weeks of gestation.

Methods This study was done on 112 patients presenting to the antenatal clinic in the Department of Obstetrics and Gynecology at Bangalore Baptist Hospital. A random urinary calcium-to-creatinine ratio of all the patients was analyzed. The urinary calcium level was analyzed by Arezano method, while creatinine was estimated by Jaffes method. A value of ≤ 0.04 was considered positive.

Results 116 patients were recruited in the study. Out of the 11 subjects with urinary CCR < 0.04, 7 developed gestational hypertension, 3 developed preeclampsia, and 1 remained normotensive. In 101 patients with CCR > 0.04, 1 developed gestational hypertension, none preeclampsia and 100 were normotensive. Four were lost to follow-up.

Interpretation and Conclusion On statistical analysis, it was found that when CCR alone is taken as high-risk factor

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for prediction of preeclampsia, $P < 0.001$ was statistically significant, sensitivity was 80 %, specificity 98.04 %, PPV 80 %, NPV 98.04 %, and diagnostic accuracy 96.43 %. So this test was satisfactory as an early predictor for the development of preeclampsia.

Keywords Hypertension in pregnancy · Preeclampsia · Urine calcium-to-creatinine ratio · Screening test for preeclampsia

Introduction

'Hypertensive disorders occur in 5–10 % of all pregnancies [1]. They contribute to significant maternal and perinatal morbidity and mortality.

In most cases, preeclampsia is diagnosed only after the pathological changes are already established. Hence, not many treatment options are left for the treating obstetrician.

From time immemorial, various methods of screening for hypertension during pregnancy have been tried out to identify women at risk of development of preeclampsia. Unfortunately, no ideal screening test has been identified so far.

Calcium-to-creatinine ratio has been suggested by many to be a good screening test for preeclampsia [2]. Creatinine clearance is an indicator of the renal damage in pregnancy hypertension. The lower the creatinine clearance, the severe is the renal disease. This has been shown to parallel the decline in urinary calcium in preeclampsia, even before the clinical appearance of signs and symptoms. Though the exact reason for this phenomenon is not clear, it has been speculated that the renal changes in preeclampsia are the basis for using urinary calcium-to-creatinine ratio as a screening test.

The present study was carried out to investigate the efficacy of a spot urinary calcium-to-creatinine ratio in predicting preeclampsia.

Materials and Methods

This study was done at Bangalore Baptist Hospital between June 2011 and June 2012. The study was approved by the hospital ethics committee.

All normotensive gravid women between 18 and 24 weeks of gestational age were included. Those with proteinuria and BP > 140/90 at booking visit, preexisting hypertension, diabetes mellitus, chronic renal or vascular disease were excluded.

A spot urine sample was collected for the estimation of calcium-to-creatinine ratio. The urinary calcium level was analyzed by Arezano method, while creatinine was estimated by Jaffes method. 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.

At each visit, blood pressure was measured, and if found to be elevated, the patient was treated for the same according to the hospital protocol. The patient was also evaluated for IUGR and other complications of preeclampsia.

All patients were followed up until delivery.

Analysis

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on mean ± SD (min–max), and results on categorical measurements are presented in number (%). Significance was assessed at 5 % level of significance

Results

A total of 116 women were recruited in the study, out of which 4 were lost to follow-up. Hence, statistical analysis was done on the remaining 112 women.

The study shows that the maximum number of our subjects belonged to the age group between 26 and 30 years and 57 % were primigravidae. Out of the 112 women who were analyzed, 11 had CCR ≤ 0.04, which comprises 9.5 % of our cases. Nine out of these women (90.9 %) developed high BP. Seven had gestation hypertension, and 2 had preeclampsia. One patient with normal CCR developed GHTN.

Table 1 Calcium-to-creatinine ratio of patients studied

CCR	Number of subjects	%
≤0.04	11	9.5
>0.04	101	90.5
Total	112	100.0

Table 2 Distribution of preeclampsia in patients studied

	Number of subjects	%
Normal	101	90.1
GHTN	8	7.2
Mild PE	2	1.8
Sev PE	1	0.9
Total	112	100.0

Table 3 Correlation of CCR with incidence of preeclampsia

CCR	Normal ($n = 101$)	GHTN ($n = 8$)	PE ($n = 3$)	
≤0.04	1 (0.99 %)	7 (87.5 %)	3 (100 %)	$P < 0.001$
>0.04	100 (99 %)	1 (12.5 %)	0 (0 %)	

Table 4 Comparison with other studies

Name of the study	Sensitivity (%)	Specificity (%)
Ozcan et al. [3]	75	86
Kamra et al. [4]	71.4	95.5
Sheela et al. [2]	69.2	98.2
Present study	80	98.04

Hence, CCR has a sensitivity of 80 % and specificity of 98.04 % with an accuracy of 96.43 % to detect hypertensive disorder of pregnancy (Table 1).

Ozcan et al. [3] from Turkey investigated 56 cases and found that calcium-to-creatinine ratio was significantly lower in the preeclamptic group (0.0475 ± 0.0260) compared with the normotensive group (0.1466 ± 0.1353; $P < 0.0001$) (Table 2).

Kamra et al. [4] studied 104 antenatal cases. 13.46 % of patients had a calcium/creatinine ratio <0.04 of whom 71.4 % developed PIH, which was statistically highly significant, with an odds ratio of 53.75 (Table 3).

The calcium-to-creatinine ratio was measured in a spot urine sample in 102 normotensive women at 20–24 weeks of gestation who attended the prenatal care clinic of the Shiraz University of Medical Sciences, Iran. Mean urinary calcium concentration (15.9 ± 8.5 mg/dl in normotensive vs. 10.2 ± 7.5 mg/dl in preeclamptic women) and calcium-to-creatinine ratio were also significantly lower in the preeclamptic group ($P < 0.03$) [5] (Table 4).

The current study correlates well with other studies mentioned in the review of the literature.

Discussion

Hypertensive disorders and their associated morbidity have been haunting obstetricians from time immemorial. Any method to detect the disease early is welcome. Though many screening methods were tried, we are still unable to find an ideal screening test. Calcium-to-creatinine ratio in a spot urine sample seems to be promising.

Urinary calcium excretion tends to increase in all pregnant patients, probably because of the increase in effective glomerular filtration rate.

Calciuria has been studied to detect hypertension early during pregnancy.

Many studies have shown that there is a significantly lower mean urinary calcium level in patients with preeclampsia than in groups with chronic hypertension or normotensive patients [6]. This phenomenon occurs early enough and persists throughout gestation, so it may be useful for early identification of patients at risk of hypertensive disorders of pregnancy.

The effectiveness of spot urine calcium-to-creatinine ratio (CCR) in predicting preeclampsia was studied by many groups. Calcium and creatinine estimation in a random urine sample has been found to correlate with a 24-h urinary calcium level. Most of the studies have used 0.04 as the upper limit for calcium-to-creatinine ratio in the prediction of pregnancy hypertension [7].

The total calcium concentration in maternal serum characteristically declines during gestation, reaching a nadir during the middle third trimester and rising slightly later. The decline averages about 0.25 meq/1 or 5–6 % from the preconceptional level and the pattern parallels that to serum albumin, suggesting strongly that the fall involves the protein-bound fraction. Gestation has very little effect on the serum ionic calcium level.

Many factors like decreased dietary intake, decreased intestinal absorption, increased calcium uptake by the fetus and placenta or intrinsic renal tubular dysfunction are cited as reasons for hypocalciuria in preeclampsia. The involvement of the renal system in pregnancy hypertension in the form of endotheliosis and the alteration in renal function are the basis for using urinary calcium/creatinine ratio as a predictor [2].

In this study, we analyzed single urine spot sample for calcium-to-creatinine ratio in 112 pregnant women and these women were followed up for development of preeclampsia.

We found that CCR has a sensitivity of 80 % and specificity of 98.04 % with an accuracy of 96.43 % to detect hypertensive disorders of pregnancy.

The limitation of this study is probably the small sample size.

Conclusion

From this study, we can conclude that calcium-to-creatinine ratio is a good predictor for hypertensive disorders in pregnancy with an accuracy of 96.43 %. A single urinary

CCR may be an effective screening method for impending preeclampsia and may identify population at greater risk to be included in primary prevention programmes. It is non-invasive, cheap and convenient as a screening test.

Even though it can be used in all pregnant women including low-risk women, we would definitely recommend that this test be done as a screening test in pregnant women at high risk of hypertensive disorders in pregnancy.

Compliance with Ethical Standards

The study conducted has been approved by the Ethical and Research Committee of Bangalore Baptist Hospital. An informed consent of each participant has also been obtained before enrolling them into the study.

Conflict of interest There has been no conflict of interest for either of the authors. No relationship that can influence the objectivity of the paper exists for the authors.

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