Research Paper

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Study of The Association Between Decreased Urinary Calcium Creatinine Ratio And Pregnancy Induced Hypertension in Some High Risk Cases.

Pharma

KEYWORDS : Calcium Creatinine Ratio, Pregnancy Induced Hypertension, Preeclampsia

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ABSTRACT

Background: This study is done to investigate the significance of urinary Calcium Creatinine Ratio (CCR) in prediction of Pregnancy Induced Hypertension (PIH).

Methods: 200 normotensive women in gestational age 24 to 34 weeks were included and divided into 2 groups- 100 with high risk factors and 100 with no risk factor for development of PIH. Urine samples collected, urinary calcium and creatinine measured, CCR calculated and patients were followed up during antenatal visits and labor for development of PIH. Urinary CCR value of 0.04 was chosen as predictive value for development of preeclampsia.

Results: Out of 200 patients, 44 had CCR ≤ 0.04, of these 61% developed PIH. Out of 156 patients with CCR > 0.04 only 5% had PIH, 95% didn't have. Statistically, for prediction of PIH, CCR was highly significant.

Conclusion: A pregnant woman with a high risk factor and low urinary CCR is prone to develop PIH. Urinary CCR may be an effective screening method for impending preeclampsia.

INTRODUCTION

Hypertensive disorders complicate 5 – 10% of all pregnancies, and they form a member of the deadly triad, along with hemorrhage and infection, that contributes greatly to maternal morbidity and mortality. The preeclampsia syndrome, either alone or superimposed on chronic hypertension, is the most dangerous[1].

Prevention of any disease process requires knowledge of its etiopathogenesis and the methods to identify those at high risk for this disaster. Numerous clinical, biophysical and biochemical tests have been proposed for prevention or early detection of preeclampsia. Unfortunately, most of these tests suffer from poor sensitivity and positive predictive values and majority of them are not suitable for routine use in clinical practice. At present, there is no single screening test that is considered reliable and cost effective for predicting preeclampsia.[2] Hypercalciuria occurs during normal pregnancy, while preeclampsia is associated with hypocalciuria. This phenomenon occurs early enough and persists throughout gestation. So it is useful for early identification of patients at risk.[3] So, the present study is carried out to investigate the significance of urinary Calcium Creatinine Ratio (CCR) in prediction of Pregnancy Induced Hypertension (PIH) and thus may identify population at greater risk to be included in primary prevention program.

AIMS AND OBJECTIVES

1. To find out the association, if any, between decreased urinary Calcium Creatinine Ratio and the development of Pregnancy Induced Hypertension in high risk cases.

MATERIALS AND METHODS

This is a prospective study conducted in the Department of Obstetrics and Gynecology, Calcutta National Medical College and Hospital, Kolkata.

200 normotensive pregnant women in gestational age of 24 to 34 weeks attending the antenatal clinic attached to Calcutta National Medical College were included in the study. They were divided into two groups-

a) Study group: 100 normotensive women with one or more high risk factors like
i) Teenage pregnancy and pregnancy in elderly.
ii) History of PIH in past pregnancy.
iii) Twin gestation in present pregnancy.
b) Control group: 100 normotensive women with no above mentioned risk factors for development of PIH.

History was taken regarding age, parity, socioeconomic status, past history, family and personal history. General examination was done specially for blood pressure, edema and weight gain. Fasting urine samples of all patients were collected in calcium free vials. Urinary creatinine was measured by Jaffes method while calcium was estimated by Orthocresolphpthalein complex method. No dietary alterations were recommended. After urine collection, Calcium Creatinine Ratio was calculated and patients were followed up at routine antenatal visits and during labor for signs of development of PIH.[4,5,6]

According to previous similar studies, the urinary CCR threshold value of 0.04 was chosen as predictive value for development of preeclampsia.[7,8,9]

STATISTICAL ANALYSIS:

Distribution of cases was presented as number and percentages. Chi-square test was used for testing the relationship between CCR and PIH. p value of ≤ 0.05was considered as statistically significant.
Chi-square test= $\Sigma (O - E)^2 / E$.
O= Observed values.
E= Expected values.

RESULTS

The observations were as follows:
Distribution of study cases according to risk factors
In study group, 30% patients had teenage or elderly pregnancy, 15% of twins and 55% with previous history of preeclampsia.

Age wise distribution of study and control group
The mean age in study group was 22.8 years and in control group 24.2 years. Majority of them belonged to 20-30 years. In study group, 70%, while in control group 80% belonged to age group 20-30 years. In study group, 20% of patients belonged to age group < 20 yrs and 10% to age group ≥ 30 yrs. In control group, 10% patients belonged to age group < 20 yrs and 10% to age group ≥ 30 yrs.

TABLE 1
DISTRIBUTION OF PATIENTS WITH/WITHOUT APPEARANCE OF PIH AND THEIR CCR (STUDY GROUP)

CCR	WITH PIH	WITHOUT PIH	TOTAL
≤0.04	21	3	24
>0.04	4	72	76

Applying Chi-square test, Chi-square= 65.79, p-value < 0.001(Highly significant). In study group, among 25 patients with PIH, 21(84%) had CCR ≤ 0.04. Total number of patients with CCR ≤ 0.04 were 24, of which 21(88%) developed PIH and 3 (12%) didn't develop PIH. The total number of cases with CCR > 0.04 were 76, of which 4 (5%) developed PIH and 72 (95%) didn't develop PIH.

TABLE 2
DISTRIBUTION OF PATIENTS WITH/WITHOUT APPEARANCE OF PIH AND THEIR CCR (CONTROL GROUP)

CCR	WITH PIH	WITHOUT PIH	TOTAL
≤0.04	6	14	20
>0.04	4	76	80

On applying Chi-square test, Chi-square= 11.11, p-value <0.001(Highly significant).In control group, among 10 patients with PIH, 6 (60%) had CCR ≤ 0.04 while 4 (40%) had CCR > 0.04. Total number of controls with CCR ≤ 0.04 were 20, of which 6 developed PIH (30%) while 14 (70%) didn't. Total number of controls with CCR > 0.04 were 80 out of which 4 developed PIH (5%) and 76 didn't (95%).

TABLE 3
DISTRIBUTION OF PATIENTS ACCORDING TO URINARY CCR

CCR	WITH PIH	WITHOUT PIH	TOTAL
≤0.04	27	17	44
>0.04	8	148	156

On applying Chi-square test, Chi-square = 75.17, p-value < 0.001(Highly significant). Above table shows the relationship of CCR and development of PIH. Out of 200 patients, 44 had CCR ≤ 0.04, of these 27 (61%) patients developed PIH later on.

On the contrary, out of 156 patients with CCR > 0.04 only 8 (5%) had PIH, remaining 148 (95%) didn't have. When calculated statistically, it was found that when CCR was taken as high risk factor for prediction of PIH, it was highly significant. (p < 0.001).

DISCUSSION

The mechanism of calcium homeostasis is multifactorial, involving calcium, magnesium and phosphorus, and three calcitropic hormones –parathyroid hormone, calcitonin and the active form of vitamin D, 1, 25 – dihydroxyvitamin D. During the course of gestation, the maternal organ system undergoes a series of physiologic adjustments aimed at preserving maternal homeostasis while at the same time providing for growth and development of the fetus. Many of these adjustments have direct implications with respect to calcium metabolism – extracellular fluid expands, renal function increases, and calcium is transported to the fetus. The net increment in calcium accumulation totals 25 to 30 gm by term, most of it represented by mineralization of the fetal skeleton.[10] Urinary calcium excretion is reported to increase during late gestation. Moreover, calcium excretion correlated significantly with creatinine clearance, implying that the gestational increase in glomerular filtration rate is responsible.[10]

It is a well documented fact that in Gestational hypertension glomerular damage occurs and it affects the renal hemodynamics. A lowered creatinine clearance is seen when the severity of the condition increases. [11]

Renal excretion of calcium is markedly increased during normal pregnancy. Urinary calcium excretion in normal pregnancy is 350-620 mg/day, compared to 100-250 mg/day in non-pregnant women. Excretion usually increases during each trimester, with maximum levels reached during the third trimester. Previous studies have shown increases in 1, 25 dihydroxy vitamin D. These findings also support that this increase in circulating 1, 25 dihydroxy vitamin D is the primary event in pregnancy associated hypercalciuria.[11] Several studies have shown a marked reduction in the excretion of urinary calcium in patients with preeclampsia when compared to normotensive controls. It is found that urinary calcium excretion can be markedly decreased early in the course of preeclampsia, even before the clinical appearance of signs and symptoms.[2-9, 12,13]

So it was found that patients who subsequently developed preeclampsia had low urinary calcium excretion. Majority of these patients were found to have CCR of less than 0.04. Our study supports all these studies, even for high risk cases. The etiology of hypocalciuria in preeclampsia is unknown. It has been speculated that hypocalciuria may result from decreased dietary intake, decreased intestinal absorption, increased calcium uptake by the fetus, or intrinsic renal tubular dysfunction. The involvement of the renal system in PIH in the form of endotheliosis and the alteration in renal functions is the basis for using urinary CCR as a predictor of Gestational Hypertension.[14]

CONCLUSION

From this study, we can conclude that a pregnant woman with a high risk factor along with low urinary CCR is prone to develop Pregnancy Induced Hypertension. Therefore, 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 programs.

LIMITATIONS OF THE STUDY

1. The study was conducted in a small cohort of population, so results cannot be generalized over larger populations.
2. Gravida and parity status of the patients were not considered as a risk factor. They may act as independent confounding factor.
3. Risk factors other than teenage and elderly pregnancies, twin pregnancy and past history of PIH were not considered in this study.

So, further studies are required in this field to obtain consistent results.

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