Role of urinary calcium to urinary creatinine ratio in prediction of preeclampsia

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Abstract

Aim: To determine role of urinary calcium to urinary creatinine ratio in prediction of preeclampsia.

Material and method: In pregnancy there is physiological dilatation of ureter which can hold up to 200 ml of urine and incomplete bladder emptying as a result of enlarging uterus, both of which cause significant collection errors. These errors can be avoided by adequate hydration to maintain urine flow and standardisation of technique at the beginning and end of collection. Ideally urine catheter should be placed, which is impractical and not generalisable, practically out of patient setting.

Results: There were 64.35% patients in age group 18-22 yrs, 32.17% patients in age group 23-27 yrs, 1.74% patients in >28 yrs age. According to parity, there were 67.83% primipara and 32.17% multipara.

Conclusion: In patients with previous history of pre eclampsia 73% developed PIH in present pregnancy and 33.33% had CCR ratio < 0.04.

Keywords: Urinary Calcium, Urinary Creatinine

Introduction

Hypertensive disorders complicate 5 to 10 percent of pregnancies and together they form one member of the deadly triad, along with hemorrhage and infection, that contribute greatly to maternal morbidity and mortality rates. The World Health Organisation systematically reviews maternal mortality worldwide (Khan and colleagues, 2006) \[2\]. In developed countries, 16 percent of maternal deaths were due to hypertensive disorders. This percentage is greater than three other leading causes: hemorrhage 13 percent, abortion 8 percent and sepsis 2 percent. All obstetricians dread pre-eclampsia for its potential maternal (12.6% of maternal deaths) and fetal complications \[1\]. The predominant pathology, i.e. endothelial dysfunction sets in as early as 8th to 18th week. However signs and symptoms appear in late mid-trimester, in advanced stages of the disease. If we look at the past, present and think of future, it is evident that its only that the name have been changing from toxemia to gestosis and so on, but the disease continues unabated. It is one of the commonest medical disorder diagnosed by obstetricians in clinical practice. Approximately 1 lakh women die worldwide per annum because of eclampsia \[3\]. It is said that pre2 eclampsia and eclampsia contribute to death of women every 3 minutes worldwide \[4\].

Observations that abnormal interfaces between maternal, paternal and fetal tissue may cause preeclampsia have led to hypotheses that the syndrome is a two-stage disorder. In this scenario, there is a spectrum to include “maternal and placental preeclampsia” (Ness and Roberts, 1996)\[5\]. According to Redman and colleagues (2009) \[6\], stage 1 is caused by faulty endovascular trophoblastic remodeling that downstream causes the stage 2 clinical syndrome. There certainly is evidence that some cases of preeclampsia fit this theory. Importantly, stage 2 is susceptible to modification by preexisting maternal conditions that include cardiac or renal disease, diabetes, obesity or hereditary influences. Such compartmentalization seems artificial, and it seems logical that there likely is a continuous process. Thus, although perhaps helpful to classify the symptoms, preeclampsia is a clinical manifestation of worsening disease \[3\].

There have been myriads of tests in the past, but none of them have stood the test of time. The risk factor in patients’ history still remains extremely important as far as prediction is concerned.
Material and Method
Keeping in mind the objectives, we conducted prospective study in department of obstetric and gynaecology, at Krishna hospital Karad from Patients coming for regular antenatal checkup, during 16 to 20 weeks of gestation were selected for study. Patient who received regular antenatal care will be reviewed for development of pih during antenatal period and at the time of delivery.

In pregnancy there is physiological dilatation of ureter which can hold upto 200 ml of urine and incomplete bladder emptying as a result of enlarging uterus, both of which cause significant collection errors. These errors can be avoided by adequate hydration to maintain urine flow and standardisation of technique at the beginning and end of collection. Ideally urine catheter should be placed, which is impractical and not generalisable, practically out of patient setting. Thus we chose to take spot urine sample. Error to which spot urine is susceptible is mild diurnal variation Sample was analysed by colorimetric method by semi autoanalyser. Calcium level was estimated by OCPC method at 575 nm (ortho-cresolphthalein complex method) the formula used for calcium concentration (mg/dl) = (reading of test material/reading of standard (10 mg/dl)) Creatinine level was measured by alkaline picrate method by the Jaffes reaction at 520 nm. The formula used is =((AS1-%(AST2-AST1) x Conc of std (100 mg/dl)). Where AS1s absorbance of sample, AST is absorbance of std. A ratio of 0.04 was considered as cut out for evaluation. We got the sample of 130 patients over a some period of the study then this sample size is greater than as we have calculated by using the prevalence so this sample is enough to study. Now the sample size 130 is at the error 8.7266% approx 9% at prevalence 45% etc.

Result and Discussion
In our study, 115 patients in 16-20 weeks gestation coming for regular antenatal check up were investigated. We carried out our study, at gestational age 16-20 weeks i.e. when ultrastructural changes occur in organs, in high risk patients who subsequently develop. Single spot urine sample was taken and urinary calcium to creatinine ratio was determined. The incidence of pre eclampsia in our study is 21.73%

Previous other study show the incidence of pre eclampsia 45%. (Dasgupta et al, 2008) 6.8% patients develop preeclampsia (Raniolo et al, 1993). Relative risk of development of preeclampsia was 1.98 for women with CCR <30th percentile. (Akio Izumi et al, 1997)

This variation in study may be due to interpopulation and intrapopulation variation.

There were 64.35% patient in age group 18-22 yrs, 32.17% patients in age group 23-27 yrs, 1.74% in >28 yrs age. According to parity, there were 67.83% primigravida and 32.17% multipara. In patients who developed pre eclampsia 17.80% were primigravida, 37.13% were multipara. We found the incidence of pre eclampsia more in multipara. But other studies show more incidence of pre eclampsia in primipara. (Sibai et al., 1991) However, Dasgupta et al, 2008, 69.97% were second gravidas, 59.26% were primigravidas. In their study there was no statistically significant difference in parity.

In this study, 15 patients had previous history of pre eclampsia, of which 11 patients developed pre eclampsia. 60% of which had mild pre eclampsia and 13% had severe pre eclampsia. 37% did not develop pre eclampsia of those who developed pre eclampsia with previous history of pre eclampsia, 20% had ratio <0.04.

In previous study, pre eclampsia had reduced urinary calcium excretion suggesting that calcium measurement may be useful in screening for pre eclampsia (Saudan et al., July 1998) Serum calcium levels in pre eclampsia appear no different from values in normotensive. However urinary calcium excretion is considerably reduced. Tufield et al, noted marked hypocalciuria in patients with pre eclampsia and suggested increase distal tubular reabsorption of calcium as possible method. Louis Sanchez Ramos et al, 1988 choose 12mg/dl as threshold value of urinary calcium by using ROC, with sensitivity 85%, specificity 91%, NPV 91%, PPV 85%. Using receiver operator curve, urine calcium threshold value of 12 mg/dl was chosen as predictor of pre eclampsia. In our study there were 69 patients with urinary calcium levels less than 12mg/dl of which 21 patients develop PE.

In the study of Rodriguez et al. (1988), 83% patients with low CCR developed PIH. In the study of Suzuki et al, 1992, 58% with low CCR developed PIH. In study of Karma et al, 1997 71.4% developed PIH Rodriguez et al, 1988 also assessed urinary microalbuminuria [8-10]. They found that urinary calcium creatinine was better predictor of pre eclampsia than urinary microalbuminuria.

Whether calcium creatinine ratio can be used for mass screening? For mass screening of pre eclampsia, excellent positive predictive value is required. However our PPV could not go beyond 80%. Thus we feel that for mass screening these tests may not be useful. In 1993 Phaupradit et al, studied 190 patients, 13 develop PE and 117 remained normotensive. The patients with PE did not have significantly less excretion of calcium than the normotensive patients [6].

In 1997 Akio Izumi et al found relative risk of development of PE was 1.98 for women with CCR <30th percentile compared to CCR >30th percentile. Thus they concluded that spot urine CCR is of limited value for identifying women with increased risk of PE. In 1994 Baker et al study suggests that neither urinary ratio is potential screening test for PE. The increased creatinine concentration in patients who subsequently develop PE has not been previously reported and merits further investigation. Raniolo and Phillipou, 1993 found the same for calcium creatinine ratio. They concluded that within the cohort studied by them ratio was unsatisfactory prognostic marker for development of pre eclampsia. In this study researchers observed that if three tests were positive in patients or normal person, despite low sensitivity, it will have specificity 99% and positive predictive value 67% for screening and predicting PE [7].

In our study we used single random spot urine sample. Miller et al, 1996 also used spot urine sample and found good predictivity of test.Srivastav et al, March 2002 found sensitivity 94.38%, PPV 64.3%, NPV 96.5% and concluded that when high risk factor and CCR were combined then 70% chance of developing pre eclampsia was found. So they concluded that this test was satisfactory as a predictor for development of pre eclampsia.

Conclusion
Following conclusion can be drawn from findings of present study.
1. Incidence of pre eclampsia in our study is 21.73%
2. Most patients in our study were primigravida, 57.8%. Incidence of pre eclampsia in primigravida 20% and multigravida 30% in our study.
3. Most patients in our study were in age group 18-22 yrs, 63.3%.
4. We used random spot urine sample for determining CCR.
5. In patients with previous history of pre eclampsia 73% developed PIH in present pregnancy and 33.33 % had CCR ratio < 0.04.

References