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A Comparative Study of Urinary Calcium Creatinine Ratio Versus Doppler Study to Predict the Preeclampsia

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ABSTRACT

The creatinine clearance is not significantly different among normotensive and preeclampsia. Low Urinary calcium: creatinine (UCCR) of <0.04 in asymptomatic pregnant women of >20 weeks of gestation are associated with subsequent development of preeclampsia. Abnormal uterine artery a pulsatility index in the early weeks predict preeclampsia. Thus in this present study, urine calcium creatinine ration and doppler study are tested as parameters to predict the development of preeclampsia in asymptomatic pregnant woman and assessing better predictor among them. Hospital Based Prospective Clinical Study randomly selected pregnant women meeting the inclusion and exclusion criteria. The pregnant women in the study group will be subjected to detailed history including age, parity, duration of pregnancy and examination will be done including general examination, abdominal examination, routine laboratory investigations, calculate UCCR as well as ultrasound with doppler study at less than 20 weeks. Out of 100 women, 25 had UCCR <0.04 and out of which 14 developed Pre-Eclampsia. Among them 33 had abnormal PI at 11-14 weeks and out of which 24 developed Pre-Eclampsia. In those 100 women, 58 had abnormal PI at 16-20 weeks and out of which 23 developed Pre-Eclampsia. Our study shows that we can predict preeclampsia by screening in early weeks of gestation i.e., by doing uterine artery doppler study during NT scan around 11-14 weeks and also during TIFFA appointment around 16-20 weeks and also by Urinary calcium creatinine ratio. This study shows that doppler study prediction is more sensitive and specific compared to urinary calcium creatinine ratio.

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Key Words

Uterine artery pulsatility index, preeclampsia, urinary calcium creatinine ratio

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INTRODUCTION

The spectrum of disorders ranging from already existing chronic hypertension in the index pregnancy to complex multisystem disorder such as preeclampsia leading to the complications like eclampsia, HELLP syndrome, acute renal failure, pulmonary edema, stroke and left ventricular failure are called Hypertensive Disorders of Pregnancy. Severe preeclampsia and its complications can be enlisted as one among the causes of maternal and perinatal morbidity and mortality. According to WHO 2014, Hypertension in Pregnancy accounts to 19% of all the maternal deaths. There is a substantial gap even after significant number of mothers seeking hospital-based delivery care[1,2]. There will be increased risk in hypertensive disease in pregnancy in circumstances that reduce uteroplacental blood flow and vascular insufficiency including pre-existing hypertension, renal disease, diabetes mellitus, Obstructive Sleep Apnoea, thrombophilia and autoimmune disease. Women with a previous history of preeclampsia, previous history of HELLP syndrome, twin or other multiple pregnancies, BMI >30, autoimmune disease, age <35 years, are first-time mothers, or have a mother or sister who has had hypertension in their pregnancy shown to be at higher risk to develop hypertensive disorder of pregnancy and are at an elevated risk of progressing to pre-eclampsia[1-7]. Incidence of preeclampsia according to National Eclampsia Registry 2013 was 10.3%. the incidence of eclampsia is 1.9% out of which more than 50% of the cases are antepartum and around 13% of the cases occurred post-partum. Maternal mortality due to eclampsia is 4-6%[8-10]. Normal pregnancy will have hypercalciuria while Preeclampsia is associated with hypocalciuria and low urinary calcium to creatinine ratio. It is one of the predictors for early identification of women at risk as this phenomenon occurs early enough and persists throughout gestation. Many of the studies have identified the importance of UCCR in predicting the preeclampsia with high sensitivity and specificity[11,12]. The most important pathological changes in hypertensive disorders of pregnancy are the impaired trophoblastic invasion of maternal spiral arteries result in maintenance of high resistance vessels, inadequate perfusion of the placenta, tissue injury and increased production of vasoconstrictive substances. There are qualitative and quantitative changes in the maternal uterine artery (UtA) Doppler waveforms in these disorders. Doppler imaging permits non-invasive evaluation of the uteroplacental circulation and is invaluable in the management of high-risk pregnancies[13-15]. Preeclampsia and eclampsia contribute to death of a woman every 3 minutes worldwide. Infants of women with hypertensive disorders in pregnancy have 5-fold increase in mortality when compared to infants of normotensive women. Preeclampsia is a multi system disorder. Primary prevention of preeclampsia is not possible, as the exact cause is still unclear. There by secondary prevention by identifying the pregnant women who are at risk of developing gestational hypertension so that we can avoid occurrence of dangerous complications by screening. For a screening test to be valuable, it should be selective, reliably cheap and easy to perform. Most interventions in pregnancy are based on intensive maternal and foetal monitoring in the present day. During the early antenatal visits clinical, biochemical testing and ultrasound testing permit risk stratification of women within 20 weeks and can seek for prophylactic therapy. This would permit the judicious allocation of limited resources. This study aims to evaluate the screening efficacy of urinary calcium creatinine ratio versus doppler study in predicting pre-eclampsia. This will help to identify people at greater risk and can include them in secondary prevention programme. This also helps for timely interventions which in turn decrease the chance for development of maternal and foetal complications. Early identification and prompt commencement of treatment can be done by the usage of simple and non-invasive screening tools.

MATERIALS AND METHODS

Study Subjects: Normotensive non proteinuric pregnant women <20 weeks attending the outpatient as well as antenatal ward.

Study Setting: Obstetrics and Gynecology Out-Patient department and Ward.

Sampling Procedure: 100 normotensive non proteinuric women >20 weeks attending the outpatient as soon as antenatal ward .

Inclusion Criteria: Pregnant women >20 weeks of gestation who are normotensive to start with.

Exclusion Criteria:

- Small for gestational age.
- IUGR cases.
- Proteinuria or BP>140/90 mm of Hg at booking visit.
- History of diabetes mellitus, renal diseases or on diuretics.
- History of chronic hypertension or use of any anti hypertensive.

Thus, the total sample size required for the study is 100 after addition of non- responsive rate.

Procedure: A hospital based prospective comparative study was conducted among a group of 100 normotensive non proteinuric women 11-14 weeks attending the outpatient as soon as antenatal ward over a period of two years. They are subjected to a detail history and general examination.

Calculation of UCCR by Spot Urine Sample by:

- Estimation of urinary calcium by ortho-cresol -phthalein complex one method.
- Estimation of urinary creatinine by Jaffe's reaction.

Ultrasound Doppler study-Pulsatility index at 11-14 weeks and 16-20 weeks were determined. Follow up was done throughout the pregnancy for emergence of hypertension and proteinuria.

Study Period: 2 years.

RESULTS AND DISCUSSIONS

The mean (SD) age among study subjects was 23.5 (3.96) years. The minimum age was 18 years and maximum were 38 years. Among 100 study subjects, 53(53%) were primi, 30(30%) were second gravidas with a living child, 7(7%) were 3rd gravidas with 2 living children, 4(4%) were 2nd gravidas with an abortion, 5(5%) were 3rd gravidas with 1 child and 1 abortion. 12(12%) of study subjects had a history of previous LSCS. Full term normal vaginal delivery was done in 56(56%) of subjects, 33(33%) had lower segment caesarean section, 9(9%) had preterm vaginal delivery and 2(2%) had ventouse assisted delivery. Mean (SD) urine calcium was 11.68(3.99) mg/dl with a minimum of 4.1mg/dl and maximum of 20.1 mg/dl. The mean (SD) of urinary creatinine was 193.19(23.75) mg/dl with a minimum of 145 and maximum of 245 mg/dl. The mean (SD) of urinary calcium-creatinine ratio is 0.064(0.048) with a minimum of 0.02 and maximum of 0.49. The mean (SD) PI (11-14 weeks), 1.4(0.23) with a minimum of 1.08 and maximum of 2.2. The mean (SD) PI 16-20 weeks is 0.96(0.169) with a minimum of 0.001 and maximum of 1.36. 55% of study subjects had UCCR <0.04 and 45% had normal UCCR. Among 100 study subjects 33% had abnormal PI and 67% had normal PI at 11-14 weeks of gestation. Among 100 study subjects, 58% of cases had abnormal pulsatility index and 42% of cases had normal pulsatile index at 16-20 weeks of gestation. Among 100 study subjects, 76(76%) were having normal outcome and 24(24%) have developed Pre-eclampsia. Out of 100 women, 25 had UCCR <0.04 and out of which 14 developed Pre-Eclampsia. The sensitivity is 58.3% and specificity is 64.5%, positive predictive value is 34%and NPV is 83.1%. On assessing the association between UCCR findings and presence of pre-eclampsia, there was statistically significant association noted (p value-0.476). Out of 100 women, 58 had abnormal PI at 16-20 weeks and out of which 23 developed Pre-Eclampsia. The sensitivity is 95.8%and specificity are53.9%, positive predictive value is 39.7 %and negative predictive value is 97.6% and its association between preeclampsia was statistically significant (p value<0.001). Out of 100 women, 33 had abnormal PI at 11-14 weeks and out of which 24 developed Pre -Eclampsia. The sensitivity is 100% and specificity are 88.2% positive predictive value is 72.7%and NPV is 100% and its association between preeclampsia was statistically significant(p value<0.0001).

Table 1: Cross Tabulation of PI at 11-14 Weeks with Outcome

PI 11-14 Weeks	Outcome		
	Pre- Eclampsia	Normal Pregnancy	P-value
Abnormal	24	09	<0.0001
Normal	0	67	
Parameter	**Value**	**95% CI**	
Sensitivity	100	85.8-100	
Specificity	88.2	78.7-94.4	
PPV	72.7	59.1-83.1	
NPV	100	-	
Diagnostic accuracy	91	83.6-95.8	

Table 2: Cross Tabulation of PI at 16-20 Weeks with Outcome

PI 16-20 Weeks	Outcome		
	Pre- Eclampsia	Normal Pregnancy	P-value
Abnormal	23	35	<0.0001
Normal	01	41	
Parameter	**Value**	**95% CI**	
Sensitivity	95.8	78.9-99.9	
Specificity	55.0	42.1-65.5	
PPV	38.7	33.7-45.9	
NPV	97.6	85.6-99.7	
Diagnostic accuracy	64	53.8-73.4	

Table 3: Cross-Tabulation of UCCR with Outcome

UCCR	Outcome		
	Pre- Eclampsia	Normal Pregnancy	P-value
Abnormal	14	11	0.0476
Normal	10	65	
Parameter	**Value**	**95% CI**	
Sensitivity	58.3	36-6-77.9	
Specificity	64.5	52.7-75.1	
PPV	34.2	24.8-45	
NPV	83.1	74.8-89	
Diagnostic accuracy	63	52.8-72.4	

Preeclampsia is a disorder characterised by high blood pressure during pregnancy, followed by organ perfusion and severe vascular spasm. Preeclampsia is a disorder that is affected by race, ethnicity, and hereditary and genetic changes. Uterine artery Doppler ultrasonography is a non-invasive technology that is used to detect this problem through uterus-placental blood flow[13-19]. Full term normal vaginal delivery was done in 56(56%) of subjects, 33(33%) had lower segment caesarean section, 9(9%) had pre term vaginal delivery and 2(2%) had ventouse assisted delivery. Mean (SD) urine calcium was 11.68(3.99) mg/dl with a minimum of 4.1mg/dl and maximum of 20.1 mg/dl. The mean (SD) of urinary creatinine was 193.19(23.75) mg/dl with a minimum of 145 and maximum of 245 mg/dl. The mean (SD) of urinary calcium-creatinine ratio is 0.064(0.048) with a minimum of 0.02 and maximum of 0.49. The mean (SD) of PI at 11-14 weeks was reported as 1.4(0.23) with a minimum of 1.08 and maximum of 2.2. Similarly, the mean (SD) of PI at 16-20 weeks was reported as 0.96(0.169) with maximum of

1.36. Also, 55% of study subjects had UCCR <0.04 and 45% had normal UCCR. Among 100 study subjects 33% had abnormal PI and 67% had normal PI at 11-14 weeks of gestation. Among 100 study subjects, 58% of cases had abnormal pulsatility index and 42% of cases had normal pulsatile index at 16- 20 weeks of gestation. Among 100 study subjects, 76(76%) were having normal outcome and 24(24%) have developed Pre-eclampsia. Out of 100 women, 25 had UCCR<0.04 and out of which 14 developed Pre-Eclampsia. The sensitivity is 58.3% and specificity is 64.5%, positive predictive value is 34% and negative predictive value is 83.1%. On assessing the association between UCCR findings and presence of pre eclampsia, there was statistically significant association noted (p value-0.476). Out of 100 women, 58 had abnormal PI at 16-20 weeks and out of which 23 developed Pre-Eclampsia. The sensitivity is 95.8%and specificity are53.9%, positive predictive value is 39.7 %and negative predictive value is 97.6%. This was statistically significant (p value<0.001). Out of 100 women, 33 had abnormal PI at 11-14 weeks and out of which 24 developed Pre-Eclampsia. The sensitivity is 100% and specificity are 88.2% positive predictive value is 72.7% and negative predictive value is 100%. This was not statistically significant (p value<0.0001). Findings of this study depicts that prediction of preeclampsia using Doppler at 16-20 weeks is much reliable tool compared to Doppler at 11-14 weeks and UCCR. According to Turk[20], who studied 100 pregnant women and performed uterine artery doppler ultrasounds on them, the average age of the women was 23.2 years old, with gestational weeks ranging from 11-24 weeks. Uterine artery Doppler ultrasonography was performed from fourteen to sixteen weeks of pregnancy in another study by Dehghani-Firouzabadi, and in our investigation, ultrasonography was performed between eighteen and thirty weeks, with blood pressure and proteinuria assessed to determine preeclampsia[21].

CONCLUSION

It was concluded that PI at 11-14 weeks is found to be the better predictor of Preeclampsia compared to PI at 16-20 weeks and UCCR with better sensitivity, specificity and diagnostic efficacy. However, on comparing PI at 16-20 weeks and UCCR, PI at 16-20 weeks was better than UCCR with better diagnostic efficacy. We recommend using PI at 11-14 weeks as the predictive tool to predict the development of preeclampsia.

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