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Original Research Article

A prospective comparative study of urinary calcium creatinine ratio versus doppler study in predicting preeclampsia

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ABSTRACT

Background: Hypertensive disorders represent the most common medical complication of pregnancy complicating 5 to 10% of all pregnancies. Several changes have already occurred before the development of clinical syndrome of preeclampsia. One such change occurs in renal function leading to hypo-calciuria. Thus, in present study, urinary calcium creatinine ratio (UCCR) and doppler study are tested as parameters to predict development of preeclampsia in asymptomatic pregnant woman and assessing better predictor among them.
Methods: Hospital based prospective study. Randomly selected pregnant women meeting inclusion and exclusion criteria, will be subjected to detailed history including age, parity, duration of pregnancy, examination including general examination, abdominal examination, routine laboratory investigations, calculate UCCR and ultrasound with doppler study at less than 20 weeks.
Results: Out of 100 women, 25 had UCCR<0.04 and out of which 14 developed pre-eclampsia. Among them 33 had abnormal pulsatility index (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.
Conclusions: Our study shows that we can predict preeclampsia by screening in early weeks of gestation i.e., by uterine artery doppler during NT scan around 11 to 14 weeks and during TIFFA appointment around 16 to 20 weeks and by UCCR. This study shows doppler study prediction is more sensitive and specific compared to UCCR.

Keywords: Preeclampsia, UCCR, Uterine artery PI

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 oedema, 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.[8]

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 more than 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.[1-4]

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]

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.

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.

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 multisystem 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 permit judicious allocation of limited resources.

This study aims to evaluate the screening efficacy of UCCR 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 noninvasive screening tools.

Aim

Aim of the study was to evaluate the screening efficacy of UCCR versus doppler study in predicting pre-eclampsia.

Objectives

Objectives were to test the hypothesis that low UCCR of <0.04 in asymptomatic pregnant women association with subsequent development of pre-eclampsia. To test the usefulness of uterine artery doppler velocimetry as a predictor for pre-eclampsia before 20 weeks in asymptomatic pregnant women [7]

METHODS

It is a prospective longitudinal study done from 2020 to 2022 in 100 normotensive nonproteinuric pregnant women less than 20 weeks attending the obstetrics and gynaecology out-patient department as well as antenatal ward in Narayana general hospital.

Inclusion criteria

Pregnant women less than 20 weeks of gestation who are normotensive.

Exclusion criteria

Patients with 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 antihypertensive were excluded from the study.

Sample size

According to Fouiza et al study, considering the sensitivity of UCCR≤0.04 as 90.9% with a precision of 13% and 95% confidence interval, the sample size is calculated as

$N=Z21\text{-}\alpha/2\times Sn\times(1\text{-}Sn)\ /p\times d^2$

Z1-α/2-two tailed probability for 95% confidence interval=1.96
Sn (%)-sensitivity of UCCR ≤0.04=0.91, d (%)=precision or allowable error for the sensitivity of UCCR ≤0.04=0.13, p (%)-prevalence of the pre-eclampsia=0.203, N=1.96^2×0.909×(1-0.909)/0.203×13^2.

N=92.62.

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

Study procedure

A hospital based prospective comparative study was conducted among a group of 100 normotensive nonproteinuric women 11 to 14 weeks attending the outpatient as soon as antenatal ward in Narayana General Hospital 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-PI at 11-14 weeks and 16-20 weeks were determined

Follow up was done throughout the pregnancy for emergence of hypertension and proteinuria.

Statistical methods

Descriptive statistics

Numerical variables like age, urine calcium, urine creatinine, Pulsatility index were represented in mean, median, mode and standard deviation.

Categorical variables like risk factors, outcome represented in frequencies and percentages. Pie-charts and bar diagrams are used as appropriate.

Inferential statistics

When a numerical variable is associated with the numerical variables such as Pearson's correlation test is used after checking for normality.

When a categorical variable is associated with a categorical variable, the variables are represented in both by tables and bar diagrams. For test of significance, chi-square test is used. Fisher's exact test is used when more than 20% of the cell values have expected cell value less than 5.

P values less than 0.05 were considered statistically significant.

Data was entered in MS excel sheet and analysed using SPSS software version 16.

RESULTS

The result is discussed among 100 study subjects

The mean (SD) age among study subjects was 23.5 (3.96) years. The minimum age was 18 years and maximum were 38 years (Table 1).

Table 1: Age distribution among study subjects.

Statistics	Age (Years)
Mean	23.5
Mode	21
Std. deviation	3.96
Maximum	38

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 (Table 2).

Table 2: Distribution of gravid and parity among study population.

Variables	Frequency	Percentage (%)
G2A1	4	4.0
G2P1L1	30	30.0
G3P1L1A1	5	5.0
G3P2L2	7	7.0
G4P2L2A1	1	1.0
PRIMI	53	53.0
Total	100	100.0

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 (Table 3).

Table 3: Frequency of mode of delivery.

Mode of delivery	N	Percentage (%)
FTNVD (Full term normal vaginal delivery)	56	56
LSCS (Lower segment caesarean section)	33	33
Total	100	100

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 (Table 4).

Table 4: Distribution of urinary calcium, urinary creatinine, urinary calcium-creatinine ratio among study subjects.

Variables	Urine calcium (mg/dl)	Urine creatinine (mg/dl)	UCCR
Mean	11.68	193.19	0.064
Median	12.3	191	0.063
Mode	6	245	0.05
SD	3.99	23.75	0.048
Minimum	4.1	145	0.02
Maximum	20.1	245	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 (Table 5).

Table 5: Distribution of pulsatility index at 11-14 weeks and 16-20 weeks.

Variables	Pulsatility index (11-14 weeks)	Pulsatility index (16-20 weeks)
Mean	1.40	0.96
Median	1.31	1
Mode	1.23	1
SD	0.23	0.142
Minimum	1.08	0.64
Maximum	2.20	1.36

The 55% of study subjects had UCCR <0.04 and 45% had normal UCCR (Table 6).

Table 6: Distribution of UCCR.

UCCR	Frequency	Percentage (%)
>0.04-normal	55	55
<0.04-abnormal	45	45
Total	100	100

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 (Table 7).

Table 7: Distribution of pulsatility index at 16-20 weeks.

Pulsatility index at 16-20 weeks	Frequency	Percentage (%)
Normal	42	42.0
Abnormal (>0.9573)	58	58.0
Total	100	100.0

Inferential statistics

Table 8: Cross-tabulation of UCCR with outcome.

Variables	Outcome		P value
	Pre-eclampsia	**Normal pregnancy**	
UCCR			
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	

Out of 100 women, 25 had UCCR<0.04 and out of which 14 developed Preeclampsia. 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=0.476).

Table 9: Cross tabulation of PI at 16-20 weeks with outcome.

Variables	Outcome		P value
	Pre-eclampsia	**Normal pregnancy**	
Pi 16-20 weeks			
Abnormal	23	35	<0.0001
Normal	01	41	
Parameters	**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	

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 are 53.9%, positive predictive value is 39.7% and negative predictive value is 97.6% and its association between preeclampsia was statistically significant (p<0.001).

Table 10: Cross tabulation of PI at 11-14 weeks with outcome.

Variables	Outcome		P value
	Pre-eclampsia	**Normal pregnancy**	
Pi 11-14 weeks			
Abnormal	24	09	<0.0001
Normal	0	67	
Parameters	**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	

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<0.0001).

DISCUSSION

Preeclampsia is a disorder characterised by high blood pressure during pregnancy, followed by organ perfusion and severe vascular spasm.[15] Preeclampsia is a disorder that is affected by race, ethnicity, and hereditary and genetic changes.[16] Uterine artery Doppler ultrasonography

is a non-invasive technology that is used to detect this problem through uterus-placental blood flow.[17,18]

To compare with other studies, the findings of the present study were as follows. 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. Also, 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 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 4.1 mg/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 PI and 42% of cases had normal pulsatile index at 1620 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=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<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<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 et al 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 to 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.

In another study conducted by Sheela et al assessed the predictive values of UCCR with cut off of ≤0.04 among 200 pregnant patients for preeclampsia. They noted that UCCR≤0.04 had a sensitivity, specificity, positive predictive value (PPV) and NPV of 69.2%, 98.2%, 85.7% and 95.8% respectively with statistical accuracy of 87% and p<0.001.

Pongrojpaw et al did a study is to see how useful UA colour Doppler is in predicting negative pregnancy outcomes including preeclampsia and foetal growth restriction in high-risk pregnant women. Any diastolic notch or a PI of more than 1.58 were considered abnormal. Pre-eclampsia affected 27 (8.18%) of the women, and 16 (4.84%) of the women had SGA kids. For preeclampsia, SGA, the Sn of PI >1.58 and diastolic notch were 59.25 percent and 56.25 percent, respectively. These outcomes had a Sp of PI >1.58 and a diastolic notch of 66.67 percent and 65.60 percent, respectively. Demers et al did a study to investigate the performance of first-trimester UA-PI for predicting PE among 4676 nulliparous women. 232 (4.9%) developed PE, including 202 (4.3%) term and 30 (0.6%) preterm PE. Mean UtA-PI decreased with gestational age between 11 and 13 6/7 weeks. First-trimester UtA-PI was associated with preterm but not with term PE. UtA-PI combined with maternal characteristics could predict 45% of preterm PE at a false positive rate of 10%.

Limitations

There are few limitations in this study which includes confounding factors, smaller sample size, hospital-based study in a tertiary care setting.

CONCLUSION

We conduct 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.

We recommend using PI at 11-14 weeks as the predictive tool to predict the development of preeclampsia.

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