International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Thakur M et al. Int J Reprod Contracept Obstet Gynecol. 2019 Mar;8(3):906-911
www.ijrcog.org

pISSN 2320-1770 | eISSN 2320-1789

DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20190855

Original Research Article

Role of second trimester uterine artery doppler for the prediction of preeclampsia in high risk pregnancy

Madhuri Thakur, Reeti Mehra*

Department of Obstetrics and Gynecology, Government Medical College and Hospital, Sector 32, Chandigarh, India

Received: 15 January 2019
Accepted: 11 February 2019

***Correspondence:**
Dr. Reeti Mehra,
E-mail: drreetidatta@yahoo.co.in

ABSTRACT

Background: The uterine artery Doppler has potentials for screening for complications of impaired placentation. The purpose of study was to assess the role of uterine artery color Doppler waveform analysis in second trimester for the prediction of preeclampsia in a high-risk pregnancy between 18-24 weeks of gestation.
Methods: 100 women with moderate or high-risk factors for developing preeclampsia reporting to Obstetrics and Gynaecology department of Government Medical College and Hospital, Sector 32, Chandigarh were enrolled for present study. Transabdominal uterine artery doppler measurements was done at 18-24weeks of gestation in these patients. Doppler . The Doppler indices generated automatically from the machine , the Pulsatility Index (PI), Resistance Index (RI) , presence or absence of diastolic notch and S/D Ratio were recorded, and average was calculated.
Results: Out of 100 patients there were 46 primigravidas with no additional risk factors, 22 pateints with two or more risk factors and there were no patients who had three or more risk factors in present study population. Preeclampsia is seen more commonly in primigravida and primigravida is considered as moderate risk factor for preeclampsia. It was found that an elevated second trimester uterine artery RI was significantly associated with developing preeclampsia later in pregnancy. The sensitivity and specificity of uterine artery Doppler velocimetry were found to be 84% and 55% respectively. Receiver operator characteristics (ROC) curves were created to demonstrate the prognostic value of RI and PI of uterine artery doppler indices at 18-24 weeks of gestation for the development preeclampsia. In addition, there were statistically significant positive correlations between mean RI of uterine artery doppler study and patients who developed preeclampsia. With a sensitivity of 84.21% it could identify 31% of the cases of preeclampsia at a false positive rate of 44.4%.
Conclusions: Uterine artery doppler study can be used as a predictor of moderate strength for preeclampsia.

Keywords: Diastolic notch, Pulsatility index, Resistance index, S/D ratio, Uterine artery Doppler

INTRODUCTION

Monitoring the growth and wellbeing of the foetus forms a major part of antenatal care. A key aim of antenatal care is to identify and manage the proportion of pregnancies at risk for complications. There is evidence that optimal antenatal care enhances the outcome of pregnancy as measured by perinatal morbidity and mortality. Even in the era of modern obstetrics, preeclampsia remains an important cause of maternal and perinatal mortality and morbidity. Despite advances in medical research, reliable screening test for prediction of this adverse complications still lacking. Preeclampsia is a multisystem disorder of unknown cause specific to pregnancy which affects the health of both mother and foetus. Preeclampsia is associated with the highest maternal and foetal mortality and morbidity of all pregnancy complications with highest incidence of serious adverse outcomes occurring

in developing countries. In the mother, preeclampsia may cause eclampsia, HELLP (hemolysis, elevated liver enzyme, low platelet) syndrome, renal failure, pulmonary oedema, congestive cardiac failure, cortical blindness, abruption, disseminated intravascular coagulopathy (DIC), hypertensive emergency, hypertensive encephalopathy and increased rate of cesarean deliveries. In the foetus preeclampsia leads to IUGR, abruption, preterm deliveries, IUFD, birth asphyxia and have an increased risk of stroke, coronary artery disease and metabolic syndrome in adult life.[1] The lack of diagnosing and inability to prevent preeclampsia before the clinical onset of the disease is of great concern. The obstetric management of women with preeclampsia is complicated by the fact that by the time symptoms occur, the only definitive treatment of the underlying disorder is delivery. Management focuses on safe prolongation of pregnancy through intensive monitoring, such that maternal and fetal complications can be prevented.[2] Accurate prediction of this condition in early pregnancy would allow for timely allocation of monitoring resources, with the prospect of improving maternal and perinatal outcomes.[3,4] This concept has led to the idea of using Doppler assessment of uterine artery flow velocity waveform as a screening test for predicting preeclampsia.[5] Uterine artery Doppler waveform screening may enable caregivers to identify and target patients at higher risk for close monitoring and intervention with prophylactic therapy. Hence this study is designed to focus on the employment of Doppler ultrasound in the second trimester which may provide an excellent opportunity to screen for these pregnancy complications at an early stage, when intervention might be possible.

METHODS

This was a prospective cohort study. A total of 100 women with moderate or high-risk factors for developing preeclampsia were enrolled in the present study.

Inclusion criteria

- Primigravida, grand multipara
- Age>40
- Family history of hypertension
- Previous pregnancy with preeclampsia
- Placental abruption
- Chronic hypertension (essential or secondary) pregestational diabetes
- Renal disease
- Patients with APLA syndrome
- Patients with autoimmune diseases
- Previous child birth >10 year back
- Overweight BMI>25-30 or Obese BMI>30-35.

Exclusion criteria

- Women carrying a fetus with sonologically detectable congenital anomalies
- Twin pregnancy, women who develop preeclampsia between 20-24 weeks.

Patients were subjected to doppler ultrasound examination using real time pulsed wave colour flow Doppler by the same examiner for all the subjects between 18 -24 weeks. Doppler ultrasound was done on Phillips IU22, using convex probe 3-5Mhz. In semi recumbent position, the ultrasound transducer was placed in either the left or right iliac fossae of the abdomen, directed towards the lateral uterine walls and downwards into the pelvis, to obtain the sagittal section of the uterus and cervical canal. This was followed by the introduction of the colour flow imaging to produce a colour map of flow over the region. The probe was tilted sideways but still maintaining its medial angulation (lower paracervical area), till the uterine artery was visualized as it crosses the external iliac artery, having originated from the internal iliac artery. The sample volume was placed 1cm distal to the point of apparent cross over before any branching of the uterine arteries and the angle of insonation maintained below 60 degree. Pulsed Doppler gate were placed at this location to obtain flow waveforms and when at least 3 consecutive consistent waveforms were produced, the image was frozen. The Doppler indices generated automatically from the machine, the Pulsatility Index (PI), Resistance Index (RI), presence or absence of diastolic notch and S/D Ratio were recorded and average was calculated.

- Pulsatility Index (PI)= Peak systolic flow – least diastolic flow/mean blood flow velocity
- Resistance Index (RI)= Peak systolic flow-least diastolic flow/peak systolic flow
- Systolic/Diastolic Ratio (S/D)= Is calculated by measuring the systolic peak and the end diastolic flow.

Antenatal check-ups were routinely conducted, and patients were followed up till delivery.

Major outcome measure

Pre-eclampsia

A note will be made on:

- Mode of delivery-normal/cesarean sections /instrumental delivery.
- Baby weight.
- Baby Apgar at birth
- Other adverse outcome like: IUGR, Preterm delivery, Abruption, IUD

Statistical analysis

The gathered data was entered in Microsoft Excel and appropriate statistical analysis was done using SPSS. The Chi square test or normal test of proportion was applied to the findings of various parameters. Receiver Operating

Characteristic (ROC) curves were calculated to find maximal cut-off values of mean RI and PI for Preeclampsia and IUGR. The ROC curve is a plot of sensitivity versus 1-specificity for maximal cut-off values. Sensitivity, specificity, positive predictive value, negative predictive value were calculated for cut-off values of mean RI and PI. All statistical tests were two tailed and p value <0.05 was taken as significant.

RESULTS

Out of 100 patients there were 46 primigravidas with no additional risk factors, 22 patients with two or more risk factors and there were no patients who had three or more risk factors in present study population. Preeclampsia is seen more commonly in primigravida and primigravida is considered as moderate risk factor for preeclampsia. Table 1 highlights that in present study there were 19 patients who developed preeclampsia (with or without severe features), 3 patients developed gestational hypertension, 1 patient had chronic hypertension, 10 patients were delivered preterm, 18 patients developed IUGR, 3 patients had abruption and 1 patient had IUFD.

Table 1: Outcome of pregnancy.

Outcome of pregnancy	Total patients
Gest. HTN	3
Chronic HTN	1
Preeclampsia	11
Preeclampsia with severe features	8
Eclampsia	Nil
Preeclampsia superimposed on chronic HTN	Nil
Abruption	3 (toxaemic abruption)
Preterm delivery	Early preterm (before $33^{6/7}$weeks): 1
	Late preterm (34-$36^{6/7}$weeks): 9
IUGR	Birth weight < 3^{rd} percentile=17
	Birth weight between 3^{rd} -10^{th} percentile:1
IUFD	1

Table 2 showed that the calculated mean UA RI was 0.42±0.13.

Table 2: Descriptive statistics for mean UA RI.

	N	Min.	Max.	Mean±SD
Rt. UA RI	100	0.10	0.70	0.38±0.13
Lt UA RI	100	0.10	1.20	0.45±020
Mean UA RI	100	0.25	0.90	0.42±0.13

Table 3 showed that the calculated mean UA PI was 0.97±0.18. In present study group 19 patients developed preeclampsia and showed a mean RI of 0.5±0.10. Statistical analysis showed that there was significant difference in mean RI of uterine artery doppler between patients with preeclampsia and without preeclampsia, but there was no significant difference in mean PI of uterine artery doppler between patients with preeclampsia and without preeclampsia as demonstrated in Table 4.

Table 3: Descriptive statistics for mean UA PI.

	N	Min.	Max.	Mean±SD
Rt UA PI	100	0.2	1.4	0.98±0.24
Lt UA PI	100	0.2	2.0	0.96±0.31
Mean UA PI	100	0.30	1.60	0.97±0.18

Table 4: Comparison of mean RI and mean PI between patients with preeclampsia and without preeclampsia.

	Pre-eclampsia	N=100	Mean±SD	P value
Mean UA RI	Yes	19	0.50±0.10	0.002
	No	81	0.40±0.13	
Mean UA PI	Yes	19	1.00±0.20	0.46
	No	81	0.97±0.18	

There were total of 23 patients who developed hypertensive disorder of pregnancy as demonstrated in table 1 out of which 19 patients developed preeclampsia (11 patients developed only preeclampsia and 8 patients had preeclampsia with severe features), 3 patients developed gestational hypertension and 1 patient had chronic hypertension.

Table 5: Comparison of mean RI and PI between IUGR and normal babies at birth using t-test.

	IUGR	n=100	Mean±SD	p value
Mean UA RI	Yes	18	0.47±0.13	0.076
	No	82	0.41±0.13	
Mean UA PI	Yes	18	1.03±0.21	0.190
	No	82	0.96±0.17	

There was only one patient of chronic hypertension in present study group and she did not develop superimposed preeclampsia and had normal doppler study with RI=0.4 and PI=1.3 at 22weeks of gestation. There were 3 patients who developed gestational hypertension.

Though the number is very small authors compared the mean RI and mean PI of uterine artery doppler between these patients and who were normotensive in present study, authors found that there was no statistical significance between patients with gestational hypertension and without gestational hypertension.

There were total of 18 patients who delivered growth restricted babies out of which 17 were severely growth restricted (birth weight below 3rd percentile) and one

with mild IUGR (birth weight below 10th percentile). The calculated mean RI was 0.47 ± 0.13 and mean PI was 1.03 ± 0.21. Though the mean RI was slightly higher in IUGR patients it did not reach statistically significant values. Authors found that there was no significant difference in mean RI and PI values of uterine artery doppler study between the IUGR and normal birth babies as demonstrated in Table 5. Table 6 shows that out of our 100 patients in study group, 23 patients had hypertensive disorders of pregnancy of which 13 patients developed IUGR. The patients with gestational hypertension and chronic hypertension had appropriate for gestational age babies and 5 patients had isolated IUGR without any hypertensive disorder of pregnancy.

Table 6: Association between hypertensive disorder of pregnancy and IUGR at birth.

		IUGR		Total
		Nil	Yes	
Preeclampsia	Yes	10	13	23
	No	72	5	77
Total		82	18	100

Table 7: Comparing the mean RI, mean PI, gestational age at delivery, birth weight and APGAR between patients with preeclampsia and without preeclampsia.

	Pre-eclampsia	N	Mean	P value
Mean UA RI	Yes	19	0.5087±0.1	0.002
	No	81	0.4030±0.13	
Mean UA PI	Yes	19	1.0053±0.2	0.483
	No	81	0.9716±0.18	
Gest. age at delivery	Yes	19	36.5639±1.14	0.000
	No	81	38.6120±1.1	
Birth weight	Yes	19	1.8653±0.55	0.000
	No	81	2.6951±0.28	
Apgar 1	Yes	19	7.3158±2.05	0.000
	No	81	8.9259±0.38	
Apgar 5	Yes	19	7.8947±1.99	0.000
	No	81	8.9630±0.19	

In present study the sensitivity of finding IUGR in patients with preeclampsia was 72.22% with specificity of 92.68%, Positive predictive value of 68.42% and Negative predictive value of 93.83%.

Statistical analysis showed that Using pearson Chi-square test it was found that preeclampsia is significantly associated with IUGR at birth at 0.000 level of significance. Table 7 represents that there was significant difference in the mean RI, gestational age at delivery, birth weight and APGAR at 1 and 5 minutes in patients with preeclampsia and without preeclampsia, all reaching p value of less than 0.05.

Figure 1 showed that Mean RI was better predictor of preeclampsia compared to mean PI since the area under curve in graph 1(ROC curve) is higher for mean RI. Table 8 showed that the best cut-off of mean RI to detect the Preeclampsia was RI ≥0.5 with 84% sensitivity and 55% specificity.

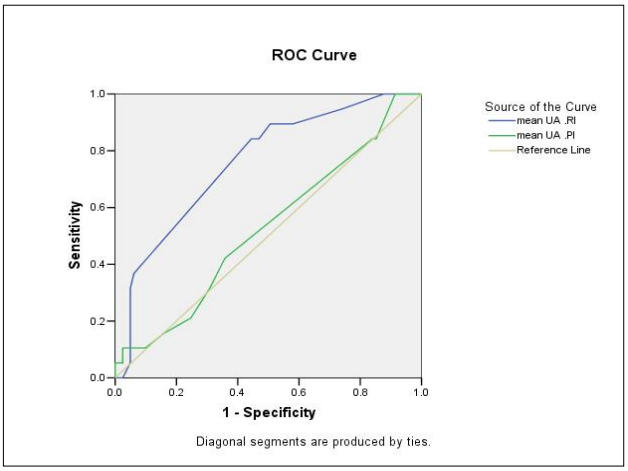

Figure 1: ROC curve to find the best cutoff of mean RI and mean PI in predicting the preeclampsia.

Table 8: Best cut-off of mean RI.

Test result variable	Area	P value
Mean UA RI	0.759	0.000
Mean UA PI	0.525	0.732

Using Pearson Chi-Square test it was found that mean RI cutoff value of 0.5 was significantly associated with preeclampsia at 0.002 level of significance as demonstrated in Table 9. The statistical analysis gave the following values.

Table 9: Preeclampsia compared with RI cut off of 0.5.

			Preeclampsia		Total	P value
			Yes	Nil		
RI cut off 0.5	> Cut-off	Count	16	36	52	0.002
		% within RI cut off 0.5	30.8%	69.2%	100.0%	
	< Cut-off	Count	3	45	48	
		% within RI cut off 0.5	6.3%	93.8%	100.0%	
Total		Count	19	81	100	

- Sensitivity= 84.21%
- Specificity=55.55%
- Positive predictive value=30.76%
- Negative predictive value=93.75%
- False positive rate=44.44%
- False negative rate=15.78%

DISCUSSION

Pregnancies affected by the complications of impaired placentation such as pregnancy induced hypertension, intrauterine growth restriction and preterm birth have shown to demonstrate increased impedance in the spiral artery. The spiral artery undergoes trophoblastic invasion during pregnancy. The effect of abnormal trophoblastic invasion is derived from studies on the uterine artery, because the uterine artery provides a good representation of the sum of resistances of the placental bed and of the placental perfusion. The purpose of this review is to describe the clinical utility of uterine artery Doppler flow studies in the prediction of adverse pregnancy outcomes in moderate and high-risk populations. There are no current recommendations for gestational age at testing or criteria for an abnormal uterine artery Doppler study. Recent reports are also showing some utility in assessment of uterine artery flow in the first trimester. However, the second trimester has yielded more consistent results. Abnormal uterine artery Doppler studies in both the first and second trimester have been shown to be associated with subsequent perinatal complications. Papageorghiou AT et al in their study found that women with abnormal testing in the first trimester, the likelihood ratio (LR) for the development of preeclampsia is approximately 5, while those with normal Doppler flow studies have an LR of 0.5.[6] Antsaklis et al found the sensitivity and specificity of screening for preeclampsia to be 81% and 87% at 20 weeks, and 76% and 95% at 24 weeks of gestation.[7] Therefore uterine artery doppler at 18-24 weeks of gestation is a reasonable approach. In this study, 100 women, representative of the moderate and high-risk pregnant population were recruited and followed up to delivery. The period of gestation between 18 -24 weeks was chosen to perform the uterine artery doppler because a routine scan for anatomical assessment was already scheduled in the study population at this time of gestation. It has been proved beyond doubt, in the previous studies and in the present study, that preeclampsia is significantly associated with IUGR. The sensitivity in the present study of finding IUGR in patients with preeclampsia was 72.2% with a positive predictive value of 68.4%. This corroborates that both these entities: preeclampsia and IUGR, may stem from one common pathology which has been known to be early defective placentation.

In present study, it was found that an elevated second trimester uterine artery RI was significantly associated with developing preeclampsia later in pregnancy. The sensitivity and specificity of uterine artery Doppler velocimetry were found to be 84% and 55% respectively. Our result corresponds to the results of study by Coleman et al on uterine artery Doppler screening in high risk women between 22-24 weeks of gestation. They found that the sensitivity of RI of> 0.58 for pre-eclampsia and IUGR was 91% and 84%, respectively. The specificity of RI of>0.58 was 42% and 39%, respectively. The positive predictive value was 37% and 33%, respectively.[8]

In this study, Receiver operator characteristics (ROC) curves were created to demonstrate the prognostic value of RI and PI of uterine artery doppler indices at 18-24 weeks of gestation for the development preeclampsia. It was found that mean RI has better prognostic value than mean PI. For the mean RI, the best cut off value was 0.5 and with 84.21% sensitivity, 55.55% specificity, 30.76% PPV and 93.75% NPV. In addition, there were statistically significant positive correlations between mean RI of uterine artery doppler study and patients who developed preeclampsia. With a sensitivity of 84.21% it could identify 31% of the cases of preeclampsia at a false positive rate of 44.4%.

In present study there was no statistically significant correlation between mean PI of uterine artery doppler and patients who developed preeclampsia. According to ROC curve mean uterine artery RI cut off of 0.5 is better predictor for preeclampsia as compared to mean uterine artery PI. Similarly, with a sensitivity of 72.22%, the test could identify 25% of the cases of IUGR at a false positive rate of 47.56%. But statistically there was no significant correlation between uterine artery doppler mean RI and mean PI values in patients with IUGR and without IUGR.[9] The present study had one patient who had abruption at 35wks 2 days of gestation with IUFD whose mean RI cut off was 0.6, which was almost the 95th centile.[10] Uterine artery doppler RI would be a good tool to identify only those cases characterized by a high grade of defective placentation from the first stages of pregnancy. This would also explain the reason for the ability of Doppler to detect only 31% cases of preeclampsia and 25% cases of IUGR in present study. Another feature noted in the study was that 15-newborn received NICU care due to the complications of prematurity, respiratory distress and IUGR.

Out of which the 8 patients showed uterine artery RI value of >0.5.In present study the presence or absence of bilateral or unilateral diastolic notch in uterine artery doppler study in the second trimester was not found to be statistically significant.[11] Present study was restricted by its small number and a larger study may give a better accuracy of the utility of uterine artery doppler for prediction of uteroplacental insufficiency effects .

CONCLUSION

This study concludes that second trimester uterine artery doppler study can be used as a predictor of moderate strength for preeclampsia. The mean RI cut off which can

differentiate patients who might develop preeclampsia was 0.5. Hence the uterine artery mean RI may be used for prediction of preeclampsia with a sensitivity and specificity of 84.21% and 55.55% respectively with a PPV of 30.76% and NPV of 93.75%.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Uzan J, Carbonnel M, Piconne O, Asmar R, Ayoubi J-M. Pre-eclampsia: pathophysiology, diagnosis, and management. Vascul Heal Risk Manage. 2011;7:467-74.
2. Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. Lancet. 2005;365(9461):785-99.
3. Askie LM, Duley L, Henderson-Smart DJ, Stewart LA. Antiplatelet agents for prevention of pre-eclampsia: ameta-analysis of individual patient data. Lancet. 2007;369(9575):1791-8.
4. Duley L, Henderson-Smart DJ, Meher S, King JF. Antiplatelet agents for preventing pre-eclampsia and its complications. Cochrane Database Syst Rev 2007;(2):CD004659.
5. Bhattacharyya SK, Kundu S, Kabiraj SP. Prediction of Preeclampsia by Mid-trimester Uterine Artery Doppler velocimetry in high risk and low risk women. J Obstet Gynaecol India. 2012;62(3):297-300.
6. Papageorghiou AT, Yu CK, Nicolaides KH. The role of uterine artery Doppler in predicting adverse pregnancy outcome. Best Pract Res. Clin Obstet Gynaecol. 2004;18(3):383-96.
7. Antsaklis A, Daskalakis G, Tzortzis E, Michalas S. The effect of gestational age and placental location on the prediction of preeclampsia by uterine artery Doppler velocimetry in low-risk nulliparous woman. Ultrasound Obstet Gynecol. 2000;16(7):6359.
8. Coleman MAG, Mc Cowan LME, North RA. Mid trimester uterine artery Doppler screening as a predictor of adverse pregnancy outcome in high risk women. Ultrasound Obstet Gynecol. 2000;15(1):7-12.
9. Pongrojpaw D, Chanthasenanont A, Nanthakomon T. Second trimester uterine artery Doppler screening in prediction of adverse pregnancy outcome in high risk women. J Med Assoc Thai. 2010;93(7):S127-30.
10. Poon LC, Volpe N, Muto B, Yu CK, Syngelaki A, Nicolaides KH. Second-trimester uterine artery Doppler in the prediction of stillbirths. Fetal Diagn Ther. 2013;33(1):28-35.
11. Myatt L, Clifton RG, Roberts JM, Spong CY, Hauth JC, Varner MW et al. The Utility of Uterine Artery Doppler Velocimetry in Prediction of Preeclampsia in a Low-Risk Population. Obstet Gynecol. 2012;120(4):815-22.

Cite this article as: Thakur M, Mehra R. Role of second trimester uterine artery doppler for the prediction of preeclampsia in high risk pregnancy. Int J Reprod Contracept Obstet Gynecol 2019;8:906-11.