



## PREDICTION OF PREECLAMPSIA BY UTERINE ARTERY DOPPLER VELOCIMETRY BETWEEN 16-28 WEEKS

<b>Ashraf M Ali</b>	Senior Resident, Department of Obstetrics & Gynecology, District Hospital Ballari.
<b>Prameela</b>	Senior Professor, Department of Obstetrics & Gynecology, MMC & RI Mysore.
<b>Aseem Basha*</b>	Senior Resident, Department of Cardiology AIIMS New Delhi. *Corresponding Author
<b>Sonal Garg</b>	Senior Resident, Department of Obstetrics & Gynecology, JIPMER Puducherry.

### ABSTRACT

**Background:** Preeclampsia is a multisystem disorder which affects about 2% of pregnancies and represents a major threat to mother and foetus when it emerges. In some women this condition sets in a subtle way and gradually such women develop severe degree of preeclampsia leading to dreadful complications. Uterine artery doppler velocimetry is a non-invasive method to examine the uteroplacental circulation that provides indirect evidence of blood flow and is proposed a predictive test for preeclampsia. This prospective observational study was performed to assess the usefulness of uterine artery Doppler in predicting preeclampsia.

**Methods:** 50 high risk and 50 low risk singleton pregnancies between 16-28 weeks of gestational age with uterine artery doppler study were followed up till delivery or development of preeclampsia to determine maternal and fetal outcome.

**Results:** Sensitivity and specificity of abnormal uterine artery doppler study for prediction of preeclampsia were 90 % and 70 % in high-risk and 42 % and 90 % in low-risk group, respectively. Positive predictive value and negative predictive value was 92 % and 63 % in high risk group and 42 % and 90 % in low risk group respectively.

**Conclusions:** Mid trimester doppler velocimetry of uterine artery can be used as a reliable screening test for prediction of preeclampsia in both high-risk and low-risk women.

**KEYWORDS :** Doppler velocimetry of uterine artery, preeclampsia screening test, high- risk and low-risk women

### INTRODUCTION

Hypertensive disorders complicate 5 to 10% of all pregnancies and together they form one member of the deadly triad, along with haemorrhage and infection, which contribute greatly to maternal morbidity and mortality rates (1). Preeclampsia is a multisystem disorder which affects about 2% of pregnancies and represents a major threat to mother and foetus when it emerges (2). Apart from its most dreaded complication of progressing into eclampsia, preeclampsia by itself can result in substantial maternal and perinatal morbidity.

It has been reported that preeclampsia is the major cause of both maternal and fetal morbidity and mortality (3). It is estimated that more than 14% (60,000) of maternal deaths/year worldwide are due to preeclampsia and eclampsia, but in developed countries, it mainly affects fetus. The incidence of preterm birth due to preeclampsia is around 15% (4).

The trophoblast normally invades the decidual portion of the spiral arteries beginning by eighth week and this invasion is usually complete by the thirteenth week. After this time the second stage of spiral artery invasion kicks in, whereby the myometrial portion of the spiral arteries are similarly invaded by the trophoblast. This is usually completed by 18 to 19 weeks but may be delayed up-to 22 to 24 weeks. In the overwhelming majority of preeclamptics, this transformation does not occur in the spiral artery bed leading to increased resistance to flow into the intervillous space. The method of choice to indirectly monitor the status of the spiral artery bed is to tap upstream information provided by uterine artery waveform (5). Increased uterine artery velocimetry determined by doppler ultrasound in the first and middle trimester should provide indirect evidence of this process and thus serve as a predictive test for preeclampsia.

In the non-pregnant state uterine artery doppler shows low peak flow velocity and early diastolic notch. At 18 to 20 weeks

there is high flow with no diastolic notch. Impaired uterine artery flow is considered when there are high resistance uteroplacental waveforms and the presence of diastolic notch which is the manifestation of arterial vessel tone and represents elasticity of the vessel and vasospasm. It disappears in second trimester. A high resistance pattern is associated with a higher rate of pregnancy complication with a 70% chance of developing protienuric hypertension and a 30% chance of a coexisting small for gestational age fetus.

Although several studies have used uterine artery doppler as a screening tool for preeclampsia and foetal growth restriction in unselected population, debate continues as to its value. Varying sensitivities are obtained depending on the type of doppler used, the sampling site, the definition of abnormal uterine artery resistance, gestation of assessment and different end points. This study was performed to evaluate the usefulness of mid-trimester uterine artery doppler study in both high risk and low risk women to predict development of preeclampsia.

### METHODS

Pregnant women with both normal and abnormal uterine artery Doppler presenting to a tertiary care hospital in Southern India were enrolled in the clinical study for predicting preeclampsia between October 2012 to April 2014.

#### Inclusion Criteria

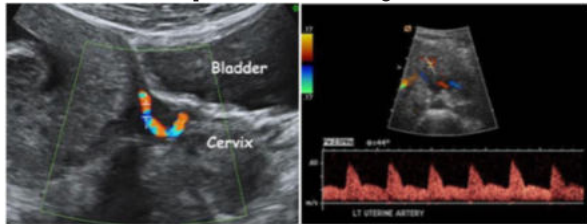
All singleton pregnancies with gestational age between 16-28 weeks with a risk factor such as hypertension, diabetes renal disease, thyroid disease, obesity or any other medical complications, prior history or family history of preeclampsia were enrolled in this study after taking a valid consent.

#### Exclusion Criteria

Multiple pregnancies, molar pregnancies, fetal congenital anomalies and those with confirmed cases of preeclampsia were excluded from this study.

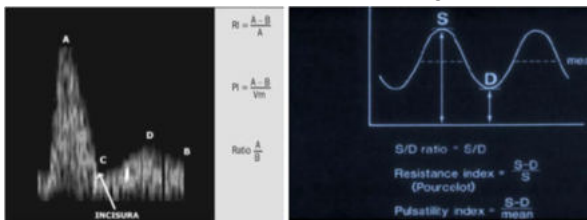
**Uterine Artery Doppler Velocimetry**

Uteroplacental waveforms were acquired from uterine artery by means of color and pulsed wave doppler ultrasound using an ultrasound machine. With the use of color doppler, the uterine artery was reliably identified and pulsed wave doppler information was acquired as shown in figure.

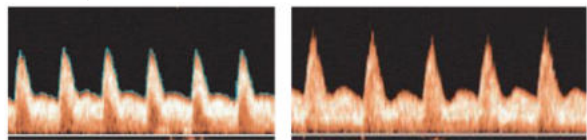


**Figure 1:** Color doppler image showing flow through uterine artery (left), Pulse wave doppler across uterine artery (left) showing phasic flow.

After obtaining an optimal waveform, the image was frozen for automatic calculations to be displayed. The three waveforms that the machine had chosen to ensure that they are free from substantial noise and that the machine has correctly chosen the maximum systolic point and the lowest frequency in end-diastole were examined. If the machine did not have a maximum frequency follower, then the image was frozen and doppler indices were measured manually. Various measurements of the uterine artery waveform were calculated for each subject. The systolic/diastolic (S/D) ratio and pulsatility index (pi) and Resistance index can also be used as shown in figure 2. Apart from these objective assessment of flow velocities, a subjective assessment was also performed to note the presence/absence of notches. Recording of the waveforms from both sides of the uterine vessels was performed. A representative image of the same in normal and abnormal states is shown in the figure 3.



**Figure 2:** Relationship between uterine artery flow velocity waveform and various doppler indices (RI, PI, systolic peak B, end diastole, Vm, mean velocity, start of Diastole, D, Maximum diastole)



**Figure 3:** Normal color doppler waveform of the uterine artery at 24 weeks (Left). Abnormal color doppler waveform of the uterine artery at 24 weeks showing the presence of a 'notch' at the end of systole (right).

**RESULTS**

A total of 100 cases over a period of one year were screened between 16-28 weeks of gestation with doppler ultrasound. All cases were divided into either a high risk or a low risk groups according to the risk factors equally.

Each uterine vessel was demonstrated by colour Doppler as it crosses over the hypogastric artery and vein just before it enters the uterus at the utero-cervical junction. The resistance index, Pulsatile index, SD ratio Of the uterine artery, presence of a notch in early diastole, a systolic notch were used to find out abnormalities. The patients were then followed up with

regular antenatal care including blood pressure measurement, urine examination for albumin, weight gain and other parameters in each visit until term or till the patient develops clinical preeclampsia.

A total of 100 patients of these were analysed. Mean age of patients in the high risk group and low risk group were 25.54 (± 6.03) years and 21.96 (±2.12) years respectively. The distribution of patients as per age and gravidity in both high and low risk groups have been shown in figure 1 and 2 respectively. In the high risk group, there were 23 primigravida and 27 multigravidas and in the low risk group, there were 25 primigravidas and 25 multigravidas. The mean Body mass index ± SD of the high and low risk women was 25.31±4.45 and 22.37±2.67 respectively. The systolic blood pressure (mean ± SD) of the high risk group was 153.16±17.27 and in the low risk group was 101.04±17.24 while, diastolic blood pressure (mean ± SD) of the high risk group was 101.04±11.93 and in the low risk group was 81.76±12.19 mm hg. The baseline parameters is shown in table 1.

**Table 1: Baseline Characteristics Of Enrolled Population**

Parameters	High risk group	Low risk group
MEDIAN AGE	21.96±2.12 years	25.54± 6.03
AGE DISTRIBUTION	N (%)	N (%)
• Up-to 19 years	11 (22)	0
• 20-24 years	15 (30)	44 (88)
• 25-29 years	11 (22)	6 (12%)
• 30-34 years	3 (6)	0
• ≥35 years	10 (20%)	0
PARITY		
Primigravida	23 (46)	25 (50)
Multigravida	27 (54)	25 (50)
Body mass index		
• < 18 kg/m <sup>2</sup>	0	01 (0.02)
• 18-24.9 kg/m <sup>2</sup>	26 (52)	43 (86)
• 25-29.9 kg/m <sup>2</sup>	13 (26)	3 (6)
• > 30 kg/m <sup>2</sup>	11 (22)	3 (6)
Systolic blood pressure		
• < 140 mm hg	7 (14)	39 (78)
• 141-160 mm hg	20 (40)	6 (12)
• > 160 mm hg	23 (46)	5 (10)
Diastolic blood pressure		
• < 90 mm hg	3 (6)	39 (78)
• 90-110 mm hg	29 (58)	8 (16)
• 110 mm hg	18 (36)	3 (6)

Uterine artery doppler parameters analysed in this study included both subjective and objective parameters. The Pulsatile index was abnormal in 33 patients in HR group when compared to only one patient in LR group with a statistically significant p value. Raised and abnormal PI, had a sensitivity of 89 % and specificity of 76.92 % whereas, in the LR group it has low sensitivity (16 %) but high specificity (100 %) for predicting development of preeclampsia.

The Resistance index was abnormal in 38 patients in HR group when compared to only 10 patient in LR group with a statistically significant p value. Raised RI (> 0.55 ) has a 90 % sensitivity and a high PPV of 92 % in high risk group, while in LR group it is less sensitive (42%) but highly specific (90%) with a low PPV of 42% for predicting development of preeclampsia.

The systolic-diastolic ratio was abnormal (> 2.6) in 38 (76%) patients in high risk group compared to only 4 (8%) in low risk group. In the HR group the sensitivity of abnormal UAD was 90 % and specificity of 70 %, PPV of 92 % while in the LR group the sensitivity and PPV is low (42 %). Twelve (24%) patients in the high risk group had uterine artery notching, while there was no notching in any patient in the low risk group. Derived parameters from uterine artery doppler flow analysis is shown in table 2.

**Table 2: Derived Parameters From Uterine Artery Doppler Flow Analysis**

Parameters		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Abnormal PI (PI > 1.5)	High risk group	89	76.9	91.6	71.4
	Low risk group	16.6	100	100	87.7
Abnormal RI (RI > 0.55)	High risk group	90	70	92	63
	Low risk group	42	90	42	90
Abnormal uterine doppler	High risk group	90	70	92	63
	Low risk group	42	90	42	90
Uterine artery notch	High risk group	24	100	100	56.8
	Low risk group	0	0	0	0

PPV- Positive predictive value, NPV- Negative predictive value.

In the HR group 40 (80%) patients developed preeclampsia, while 10 (20%) patients did not develop. Seven (14%) patients in the LR group developed preeclampsia and 43 (86%) patients did not develop preeclampsia. In the high risk group about 39 (78%) patients had abnormal Doppler indices out of which 36 (72%) developed preeclampsia, while in LR group only 7 (14%) patients had abnormal doppler indices out of which only 3 (6%) patients developed preeclampsia. The p values for predicting development of preeclampsia was statistically significant in both high risk and low risk group. Development of preeclampsia in high and low risk groups and their doppler correlates is shown in table 3.

**Table 3: Development Of Pre-eclampsia In High And Low Risk Groups And Doppler Correlates**

Parameters	High risk group N (%)	Low risk group N (%)		
Pre-eclampsia				
• Yes	40 (80)	7 (14)		
• No	10 (20)	43 (86)		
Gestational age (Years) at onset of pre-eclampsia	34.54 ± 4.66	39.38 ± 1.97		
Doppler study	Abnormal	Normal	Abnormal	Normal
• Pre-eclampsia	36 (72)	4 (8)	3 (6)	4 (8)
• No pre-eclampsia	3 (6)	7 (14)	4 (8)	39 (78)
• P value	0.0	NS	0.01	NS

Various high risk factors and the associated risk of preeclampsia were studied like age, body mass index, maternal history of chronic hypertension, diabetes, renal disease, past bad obstetric history and family history. All these factors were seen to be associated with the higher incidence of preeclampsia as shown in table 4.

**Table 4: Distribution Of Risk Factors In High Risk Groups**

Risk factors	N (%)
Age	
• Age < 20 years	8 (16)
• Age > 35 years	7 (14)
BMI > 30	2 (4)
History of chronic hypertension	3 (6)
History of diabetes	3 (6)
History of renal disease	1 (2)
Past history of pre- eclampsia/IUGR/IUD	11 (22)
Family history of pre-eclampsia/IUGR	3 (6)
More than one risk factor	12 (24)

In the HR group 40 (80%) patients had preeclampsia, 4 (8%) had abruption, 16 (32%) patients had IUGR babies and 8 (16%) intrauterine deaths. One (2%) Still birth and 7 (14%) early neonatal death, 6 (12%) patients had oligohydramnios. The LR group had 7 (14%) patients who developed PE, one (2%) patient had abruption, 3 (6%) had IUGR and 2 (4%) early

neonatal death and 2 (4%) patients had oligohydramnios . There were no still birth or IUD in the LR group. Complications, onset of labour and mode of delivery in high risk and low risk groups are shown in table 5.

**Table 5: Complications, Onset Of Labour And Mode Of Delivery In High Risk And Low Risk Groups**

Complications	High risk group N (%)	Low risk group N (%)
Pre-eclampsia	40 (80)	7 (14)
Placental abruption	4 (8)	1 (2)
IUGR	16 (32)	3 (6)
Still birth	1 (2)	0
Early Neonatal death	7 (14)	2 (4)
Intrauterine death	8 (16)	0
Oligohydramnios	6 (12)	2 (4)
Onset of labour		
• Induced	41 (82)	10 (20)
• Spontaneous	2 (4)	30 (60)
• Caesarean	7 (14)	10 (20)
Mode of Delivery		
• Caesarean	7 (14)	10 (20)
• Forceps	1 (2)	1 (2)
• Vaginal	42 (84)	39 (78)

Majority of patients (62%) in HR were severely pre-eclamptic, and 3 (6%) patients developed eclampsia , while in low risk only 1 (2%) patient had severe preeclampsia and none had eclampsia (Table 6).

**Table 6. Severity Of Pregnancy Induced Hypertension In High Risk And Low Risk Group**

Severity	High risk group N (%)	Low risk group N (%)
Gestational hypertension	3 (6)	5 (10)
Mild pre-eclampsia	13 (23)	1 (2)
Severe pre-eclampsia	31 (62)	1 (2)
Antepartum eclampsia	3 (6)	0

The Birth weight of babies born to high risk group was 1.85 ± 0.803 and in low risk group 2.66 ± 0.477 with a p value which was statistically significant.

In the HR group 28 (56%) neonates required NICU admissions in comparison to only 13 in the LR group. Eight (16%) babies in the HR group had perinatal mortality when compared to only 2 (4%) of the neonates in the LR group. Thirty (60%) of the neonates in HR group were born premature when compared to only 4 in LR group. Majority of neonates in HR group 38 (76%) had low birth weight when compared to only 11 (22%) in LR group. The p values were statistically significant in the high risk group for the above mentioned perinatal outcomes (Table 7).

**Table 7: Various Perinatal Outcome In Both High And Low Risk Groups**

Parameters	High risk group N (%)	Low risk group N (%)	P value
NICU admission	28 (56)	13 (26)	0.0
Perinatal mortality	8 (16)	2 (4)	0.0
Prematurity	30 (60)	4 (8)	0.0
Low birth weight	38 (76)	11 (22)	0.001

**DISCUSSION**

The role of Doppler ultrasound in the study of uteroplacental circulation is well known. It helps in detecting the extent of placental pathology and also predicts the maternal and fetal outcome. Numerous studies have been conducted to know the association between Doppler waveforms and maternal perinatal outcome and have had variable results.

The present study showed that abnormal Doppler waveforms was associated with adverse maternal and perinatal outcome. It revealed that 40 (80 %) of HR group women and 7 (14%) of LR women developed preeclampsia. This suggests a 5.7 fold increased risk of developing preeclampsia in the high risk group.

The application of uterine artery Doppler velocimetry is now being considered as a useful adjunct to screening programmes for prediction of adverse pregnancy outcomes. Abnormal uterine artery flow velocity was associated with an increased relative risk of preeclampsia both in HR and LR group in this study as well. The sensitivity and specificity of uterine artery Doppler velocimetry was high in the HR group .

Women with extremes of age which include teenage pregnancies and elderly primigravidas are at very high risk of developing preeclampsia which constituted of about 42 % of HR group. Mean BMI was significantly higher in HR group 25.31±4.45 when compared to LR group 22.37±2.67 kg/m<sup>2</sup>. Obese patients tend to have a higher risk of developing preeclampsia. There was no significant statistical difference in the sensitivity , specificity and positive predictive values of RI and PI. However, uterine artery diastolic notch had a 100 % specificity and PPV. Konchak et al showed that an elevated uterine resistance index and a uterine artery notch both were associated with increased relative risk of preeclampsia. The sensitivity, specificity, PPV, and NPV of a uterine notch were found to be 83.3% and 95.6 % respectively in there study (6). Woschitz MC et al showed that persistence of uterine artery notch was associated with increased relative risk of preeclampsia (7). The sensitivity, specificity, PPV and NPV of uterine notch were found to be 40%, 78%, 56% and 65% respectively in their study. Compared to these two studies, the specificity and PPV of uterine artery notch was higher in our study as shown in table 8.

**Table 8: Diagnostic Performance Of Uterine Artery Notching In Comparison To Various Other Studies**

Uterine artery notch	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Current study	24	100	100	56.8
Konchak et al	83.3	95.6	55.6	98.9
Woschitz et al	40	78	56	65

Coleman et al in their study of uterine artery Doppler screening in HR women showed the sensitivity and specificity of RI > 0.58 for preeclampsia to be 91 and 42 %, respectively (8). Among women with RI > 0.7, 58 % developed preeclampsia (8). In comparison to Coleman et al the sensitivity was similar while specificity (70% versus 42%) of uterine artery RI was higher in our study. Prajapati et al in their study of uterine artery doppler screening in HR women showed sensitivity of Uterine artery PI was the best in the prediction of preeclampsia with SGA and gestational hypertension at 33.3 % (9). The specificity of uterine artery PI (> 90<sup>th</sup> centile) was best for preeclampsia at 94%. Woschitz MC et a in their study had a sensitivity of Uterine artery PI of 8 % and specificity of 95 % (7). The current study observed a sensitivity for PI of Uterine artery was 89 % which was higher but, specificity of 76.92 % was lower compared to these two studies. The comparison between the finding of this study and previous studies are shown in table 9 (7–9).

**Table 9: Diagnostic Performance Of RI And PI IN Comparison To Various Other Studies**

Parameters	Sensitivity (%)	Specificity (%)
Abnormal Resistance Index		
Present study (RI >0.55)	90	70
Coleman et al (RI >0.58) (8)	91	42
Abnormal Pulsatility Index		
Present study	89	76.9

Prajapati et al –(9)	33	94
Woschitz et al (7)	8	95

In comparison to the sensitivity of diastolic notch in the studies mentioned in the above study the sensitivity was low of about 24%, but specificity of diastolic notch in our study was 100% which was more than any other study. In comparison to the above mentioned studies sensitivity of UAD in our study was higher, while specificity was less compared to the prior studies as shown in table 10 (9–13).

**Table 10: Diagnostic Performance Of Diastolic Notch And Uterine Artery Doppler Velocimetry (UAD) In Comparison To Prior Studies**

Author	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Diastolic notch				
Bower et al (13)	78	96	28	99.5
Pai et al (11)	45.4	92	38	93.8
Agrawal et al (10)	84	71.4	72	-

**LIMITATIONS**

Mid trimester doppler velocimetry of uterine artery can be used as a reliable screening test for prediction of preeclampsia in both high-risk and low-risk women. However this study was done in a small group of women and so further study in a larger cohort is necessary to validate the results of this study.

**CONCLUSION**

The present study noted an adverse maternal and fetal outcome in cases of preeclampsia which showed abnormal Doppler results. Uterine artery diastolic notch is ominous and also had correlated with poor maternal outcome It had the highest specificity of 100% and positive predictive value of 100 % for detecting the same. Here we conclude that mid trimester uterine artery doppler velocimetry can be used as a reliable screening test for prediction of preeclampsia, and when abnormal, an increased surveillance and delivery in a well-equipped set up is necessary to reduce the maternal and fetal complications.

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