

A study of transabdominal uterine artery doppler for prediction of preeclampsia from 12 to 16 weeks of gestation in tertiary care centre.

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Abstract:

Background: Pre-eclampsia affects 2-5% of pregnancies and is the major cause of maternal morbidity and mortality. Doppler is a non-invasive method for evaluation of feto-placental circulation. Persistent uterine artery notching, high resistance index and pulsatility index in uterine artery doppler waveform has emerged as the best screening test. Thus, we have conducted this study to find out usefulness of doppler indices in early pregnancy for predicting preeclampsia.

Methodology: After assessment of inclusion and exclusion criteria, 200 antenatal women of 12 to 16 weeks of singleton pregnancy were selected for the study in the department of Obstetrics and Gynaecology. Women booking for antenatal care were examined and investigated. After an informed consent, doppler assessment of uterine artery was done at 12 to 16 weeks. These women were further followed up clinically for development of preeclampsia.

Results: In our study out of 200 women, 17.5% of women developed pre eclampsia. B/L uterine artery notching at 12-16 weeks were seen in 80% (N=35). Of the pre eclamptic women, mean RI was 0.8, PI was 2.16 at 12-16 week. We found that uterine artery notching with RI has 98.79% specificity with NPV of 98.79%. Uterine artery notching with PI has 99.39% specificity and NPV of 98.2%. Uterine artery notch with RI and PI has specificity of 99.39% and NPV of 98.20%.

Conclusion: The uterine artery notching, high resistance index and pulsatility index in uterine artery Doppler waveform at 12-16 weeks has shown as best screening test for early prediction of preeclampsia.

Key words: Uterine artery Doppler, Uterine artery notching, Resistance index, Pulsatility index, prediction of preeclampsia, maternal morbidity and mortality.

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I. Introduction

Hypertensive disorders are second most common cause of indirect maternal death worldwide. Preeclampsia is the leading cause of maternal morbidity and mortality with worldwide incidence of 2-8%¹. According to the recent survey by National Health Portal of India, 8-10 % of pregnancies are complicated by preeclampsia. Pre-eclampsia is a pregnancy specific disorder characterised by hypertension and proteinuria after 20 weeks of gestation in previously normotensive woman. Placental remodelling is completed by 16-18 weeks of gestation. Defective placental implantation leads to hypoperfusion, hypoxic injury and oxidative stress. A deranged trophoblastic differentiation is thought to underlie pathophysiology of pre-eclampsia. Placental products are released on part of placentation process. Levels of these biochemical markers reflect pathophysiology of defective placentation and these products are assuming an increasing role in early gestation screening test for later pregnancy complications. Direct assessment of trophoblast invasion is not possible. However, use of doppler imaging permits non-invasive evaluation of uteroplacental circulation. Various hemodynamic and biochemical measurements have limited accuracy as screening test. Early screening for pre-eclampsia may allow vigilant antenatal surveillance and appropriate timing of fetal delivery in order to avoid serious sequelae. Therefore need for predictors of hypertensive disorders are particularly greatest in our population. The predictors should be reliable and suitable for implementation. This screening test does not involve extra cost and can identify a cohort of patients who will benefit most from increased surveillance during pregnancy.

II. Material and Methods

This prospective study was carried out on patients of Department of Obstetrics and Gynaecology at Dr.UlhasPatil Medical College and Hospital, Jalgaon ,Maharashtra from September 2020 to August 2021 over a period of 1 year. A total of 200 pregnant females of 12 to 16 weeks of gestation were in this study.

Study design: Prospective observational study

Study Location: This was a tertiary care teaching hospital based study done in Department of Obstetrics and Gynaecology at Dr.UlhasPatil Medical College and Hospital, Jalgaon, Maharashtra.

Study Duration: September 2020 to August 2021

Sample size : 200 pregnant females from 12 to 16 weeks of gestation.

Sample size calculation:Sample size of 200 was calculated using nMaster 2.0 software.

Subjects and selection methods: The study population was drawn from all the antenatal women of gestational age 12-16 weeks attending antenatal clinic of Dr.UlhasPatil Medical College and Hospital, Istatisfying inclusion and exclusion criteria were enrolled in the study after informed consent.

Inclusion criteria:

1. Pregnant women attending antenatal care check-up between 12-16 weeks of gestational age.
2. Singleton pregnancy

Exclusion criteria:

1. Women with essential hypertension prior to pregnancy and other high-risk pregnancies
2. Patients not giving consent.
3. Patients with multiple gestations
4. Women on any treatment modifying blood pressure and pregnancy outcome.
5. Women with major congenital fetal anomalies.
6. Women who cannot be followed up.
7. Pregnant women with missed abortion

Procedure methodology:

After taking the informed written consent from the pregnant women of 12 to 16 weeks gestation, willing to participate in the study, a preliminary data was collected .Thorough history was taken to know the patient demographics,socio-economic status, gestational age and to know any high risk factors associated with the pregnancy. A thorough clinical examination included general physical examination, built, nutritional status, height, weight, blood pressure and pulse along with absence or presence of pallor and pedal edema. The weight gain in that respective pregnancy was noted. The CNS, CVS, RS were examined. Abdominal examination was done for height of uterus in weeks, the lie of fetus, presentation, and position of the fetus, fetal heart rate. Routine haematological investigations and urine routine was be done. Obstetrics scan. Specific investigations carried out when required.

The patient was explained in detail about the non-invasive nature of the procedure. Synthetic ultra gel was applied over the abdomen to get a good acoustic coupling. Appropriate Ultrasound machine was used. A 3.5 MHz curvilinear transabdominal transducer was used. A midsagittal section of the uterus and cervical canal was obtained and the transducer was moved laterally until the paracervical vessels were visualized. Color flow Doppler was applied. The uterine arteries were seen as aliasing vessels along the side of the cervix. Using pulsed wave Doppler, flow velocity waveforms from the ascending branch of the uterine artery at the point closest to the internal os were obtained, with the Doppler sampling gate set at 2 mm. Care was taken to use the smallest angle of insonation($<30^0$) in order to achieve the highest systolic and end diastolic velocities. When three similar consecutive waveforms were obtained, the PI can be measured. The mean PI was calculated as the average reading from each side combined.

Another site for Doppler insonation of the uterine artery was at the level of its apparent crossover with the external iliac artery. Using this method, the probe was positioned approximately 2-3 cm inside the iliac crests and then directed toward the pelvis and the lateral side of the uterus. Colorflow Doppler was used to identify each uterine artery. Pulsed wave Doppler was applied approximately 1 cm above the point at which the uterine artery crosses over the external iliac artery. This ensures that Doppler velocities were obtained from the main uterine artery trunk.

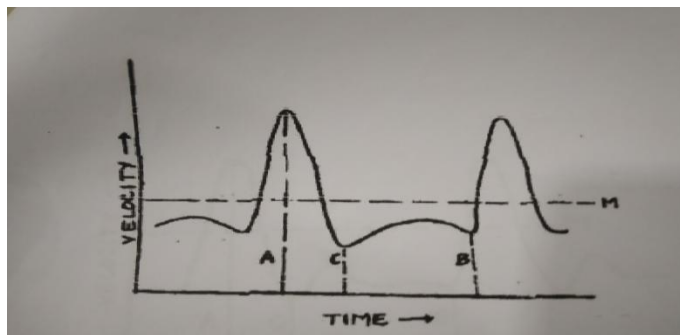


FIG: The typical waveform of blood flow
 A – Peak systolic velocity
 B – End diastolic velocity
 C - Early diastolic notch
 M – Mean velocity

The variable were analysed.

1. Resistance index (RI) was calculated using formula

$$RI = \frac{\text{Peak systolic velocity} - \text{Peak diastolic velocity}}{\text{Peak systolic velocity}}$$

2. Pulsatility index (PI) was calculated using formula.

$$PI = \frac{\text{Peak systolic velocity} - \text{End diastolic velocity}}{\text{Mean velocity}}$$

At 12-16 weeks PI, RI and Bilateral uterine artery notching of uterine arteries were calculated.

Statistical analysis:

Statistical analysis was done using Epi info software. Chi-square tests and Fischer exact tests were performed to test for differences in proportions of categorical variables between two or more groups. The level $p < 0.05$ was considered cut off value or significant.

III. Result

After study period of 1 year ,in this study,

Mean gestational age at transabdominal scan was 13.67 ± 1.22 weeks.

About 17.5% (n=35) of women developed preeclampsia among 200 women.

Uterine artery notch was observed in 20.5% (n=41) of women.

Among 17.5% of pre eclamptic women ,Uterine artery notching was seen in 80% (n=28) .

Table no. 1 shows mean age distribution in years was 24.3 ± 3.9

TABLE 1 – Age distribution in years

	MEAN	SD
AGE	24.3	3.9

Table no. 2 shows majority of cohort (43%) between 21-25 years of age (n = 86). 41 patients in age group of <20 years (20.5%). 61 patients in age group of 26-30 years (30.5%) and 12 patients in age group of >31 years (6%)

Table no. 3 shows 55.5% of primigravidas were part of study.

TABLE 2 – Age distribution in years

Age in years	Frequency	Percent
<20	41	20.5
21-25	86	43.0
26-30	61	30.5
>31	12	6.0

TABLE 3–Parity distribution

Gravid status	N%
1	111(55.5%)
2	66 (33%)
3	16 (8%)
4	5 (2.5%)
5	2 (1%)

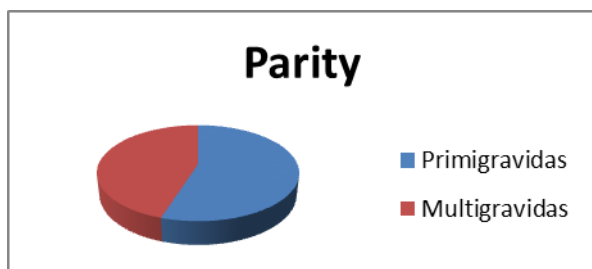


Table no. 4 shows mean BMI status of 24.2 ± 4.9

TABLE 4- BMI STATUS

	MEAN	SD
BMI	24.2	4.9

Table no. 5 shows blood pressure readings in 1st trimester with mean SBP of 117.42 ± 8.11 mmHg and DBP of 72.15 ± 6.12 mmHg

TABLE 5 - BLOOD PRESSURE IN 1ST TRIMESTER

BLOOD PRESSURE	MEAN	STANDARD DEVIATION
SBP	117.42	8.11
DBP	72.15	6.12

Table no.6 shows blood pressure readings in 3rd trimester with mean SBP and DBP of 130.47 ± 15.16 and 83.71 ± 10.50 mmHg respectively.

TABLE 6-BLOOD PRESSURE IN 3RD TRIMESTER

BLOOD PRESSURE	MEAN	STANDARD DEVIATION
SBP	130.47	15.16
DBP	83.71	10.50

Table no. 7 shows presence of uterine artery notch in 41 patients at 12 to 16 weeks of gestation (20.5%).

TABLE 7-UTERINE ARTERY DOPPLER DIASTOLIC NOTCHING

NOTCHING	N(%)	
12-16 WEEKS	A	159(79.5%)
	P	41(20.5%)

Table no. 8 shows association of RI and preeclampsia with mean of 0.80 ± 0.06 and PI and preeclampsia with mean of 2.16 ± 0.19 which are statistically significant ($p < 0.0001$).

TABLE 8 – ASSOCIATION OF UTERINE ARTERY DOPPLER INDICES IN PREECLAMPTIC AND NORMAL PREGNANT WOMEN

DOPPLER INDICES	PREECLAMPSIA				P VALUE
	NO		YES		
	MEAN	SD	MEAN	SD	
RI	0.62	0.14	0.80	0.06	<0.0001
PI	1.28	0.47	2.16	0.19	<0.0001

Table no. 9 shows that 35 patients of 200 were RI positive at 12- 16 weeks ,later on developed preeclampsia whereas 36 RI positive patients did not develop preeclampsia.

TABLE 9-ASSOCIATION OF RI POSITIVITY WITH PREECLAMPSIA

RI POSITIVITY		PREECLAMPSIA				P VALUE
		NO		YES		
		N	N%	N	N%	
12-16 WEEKS	NEGATIVE	129	100	0	0	<0.001
	POSITIVE	36	50.7	35	49.3	

Table no.10 shows that 34 PI positive patients in 12 -16 weeks of gestation developed preeclampsia while 11 PI positive did not. However, 1 patient developed preeclampsia inspite of being PI negative in 1st trimester and 154 were true negatives.

TABLE 10-ASSOCIATION OF PI POSITIVITY WITH PREECLAMPSIA

PI POSITIVITY		PREECLAMPSIA				P VALUE
		NO		YES		
		N	N%	N	N%	
12-16 WEEKS	NEGATIVE	154	99.4	1	0.6	<0.001
	POSITIVE	11	24.4	34	75.6	

Table no 11 shows that with presence of uterine artery notch alone 33 patients developed preeclampsia and 2 developed preeclampsia even after absence of notch at 12 -16 weeks of gestation. 8 patients had uterine artery notch but were not found to develop preeclampsia on follow up visits. 152 patients were true negatives. These values were statistically significant (p value <0.0001).

With presence of combined uterine artery notch and resistance index 33 patients developed preeclampsia and 2 developed preeclampsia even after absence of notch and RI at 12 -16 weeks of gestation. 2 patients had combined uterine artery notch and resistance index but were not found to develop preeclampsia on follow up visits. 163 patients were true negatives. These values were statistically significant (p value <0.0001).

TABLE 11-COMPARISON OF UTERINE ARTERY NOTCH ALONE AND WITH RI AND PI WITH DEVELOPMENT OF PREECLAMPSIA AT 12-16 WEEKS

DOPPLER INDICES		PRE-ECLAMPSIA				P VALUE
		YES		NO		
		N	N%	N	N%	
UAN+RI	POSITIVE	33	94.3%	2	5.7%	<0.0001
	NEGATIVE	2	1.2%	163	98.8%	
UAN+PI	POSITIVE	32	97.0%	1	3.0%	<0.0001
	NEGATIVE	3	1.8%	164	98.2%	
UAN+RI+PI	POSITIVE	32	97.0%	1	3.0%	<0.0001
	NEGATIVE	3	1.8%	164	98.2%	
UAN ALONE	PRESENT	33	80.5%	8	19.5%	<0.0001
	ABSENT	2	1.3%	157	98.7%	

With presence of combined uterine artery notch and pulsatility index 32 patients developed preeclampsia and 3 developed preeclampsia even after absence of notch and PI at 12 -16 weeks of gestation. 1 patient had combined uterine artery notch and pulsatility index but were not found to develop preeclampsia on follow up visits. 164 patients were true negatives. These values were statistically significant (p value <0.0001).

With presence of combined uterine artery notch, resistance index and pulsatility index 32 patients developed preeclampsia and 3 developed preeclampsia even after absence of notch, RI and PI at 12 -16 weeks of gestation. 1 patient had combined uterine artery notch, pulsatility index and resistance index but were not found to develop preeclampsia on follow up visits. 164 patients were true negatives. These values were statistically significant (p value <0.0001).

Table no. 12 shows that sensitivity, specificity, positive predictive value and negative predictive value with RI positive alone are 94.29%, 98.79%, 94.29% and 98.79% respectively. This is shown to have 98% accuracy. However with PI positivity alone, the sensitivity, specificity, positive predictive value and negative predictive value are 75.56%, 99.35%, 97.14%, 93.33% respectively. This is shown to be 94% accurate.

TABLE 12- ROLE OF UTERINE ARTERY DOPPLER IN PREDICTING PREECLAMPSIA WITHOUT DIASTOLIC NOTCHING AT 12-16 WEEKS

STATISTICS	RI	PI
SENSITIVITY	94.29	75.56
SPECIFICITY	98.79	99.35
POSITIVE PREDICTIVE VALUE	94.29	97.14
NEGATIVE PREDICTIVE VALUE	98.79	93.33
ACCURACY	98.0	94.0

Table no. 13 shows that with combined uterine artery notch and resistance index, the sensitivity, specificity, positive predictive value and negative predictive value are 94.29%, 98.79%, 94.29% and 98.79% respectively. This is 98.04% accurate.

With combined uterine artery notch and pulsatility index, the sensitivity, specificity, positive predictive value and negative predictive value are 91.43%, 99.39%, 96.97% and 98.20% respectively. This shows 98% accuracy.

With all three indices combined i.e, uterine artery notch, resistance index and pulsatility index, the sensitivity, specificity, positive predictive value and negative predictive value are 91.43%, 99.39%, 96.97%, 98.20% respectively. This shows 98% accuracy.

TABLE 13- ROLE OF UTERINE ARTERY DOPPLER IN PREDICTING PREECLAMPSIA WITH DIASTOLIC NOTCHING AT 12-16 WEEKS

STATISTICS	UAN+RI	UAN+PI	UAN+RI+PI
SENSITIVITY	94.29	91.43	91.43
SPECIFICITY	98.79	99.39	99.39
POSITIVE PREDICTIVE VALUE	94.29	96.97	96.97
NEGATIVE PREDICTIVE VALUE	98.79	98.20	98.20
ACCURACY	98.04	98.0	98.0

IV. Discussion

In our study , mean age of participants was 24.3 ± 3.9 years which is slightly lower than Martin et al (32.8 ± 4). The difference of age may be due to early marriage in our population²

In our study ,primigravidas were 55.5% (n=111) in concordance with Plasencia et al i.e, 60% (n= 63.6) which supports more occurrence of pre eclampsia in primigravidas³.

In our study, 20.5% (41) of patients had bilateral notches which is far less than Gomez et al (29.5%)⁴.

Out of 200 women, 17.5% (n=35) women developed preeclampsia thus prevalence is similar to Shashi et al(20%)⁵

When uterine artery notch alone was considered, detection rate was 80.5%

When RI alone was considered , it had detection rate of 94.29% and specificity ,PPV and NPV of 98.79%, 94.29% and 98.79% respectively.

When uterine notch and RI was considered, sensitivity , specificity ,PPV and NPV remained same.

When PI alone was considered, detection rate was 75.56% with specificity, PPV and NPV of 99.35%,97.14% and 93.33% respectively.

When uterine artery notch with PI was considered, detection rate has increased to **91.43%** with specificity, PPV and NPV of 99.39%,96.97% and 98.20% respectively.

When all the three parameters were considered detection rate remained same (**91.43**)

Hence, our study is concordance with Bower et al and North et al who concluded that RI had better sensitivity and negative predictive value^{6,7}

V. Conclusion

Even though screening for traditional risk factors for pre-eclampsia is done in each antenatal visit, there is obvious need of early predictors of the disease.Early predictors of pre-eclampsia may improve maternal and perinatal outcomes by ensuring appropriate management.(Patient education, low dose aspirin).Systematic reviews and expert opinions have concluded that clinically available tests for screening are not sufficiently accurate. For this reason utilization of non-invasive doppler can be promising tool in prediction of preeclampsia with good PPV and NPV.

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