Original Research Article

Role of uterine artery Doppler at 12 to 16 weeks of gestation in prediction of pre-eclampsia an observational study

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ABSTRACT

Background: Pre-eclampsia affects 2-5% of pregnancies and is a major cause of perinatal and maternal morbidity and mortality. Doppler is a non-invasive method for evaluation of feto-placental circulation without affecting pregnancy. A high resistance index in uterine artery Doppler waveform has been shown to be the best non-invasive screening test. Thus, we have conducted this study to find out the predictive value of transvaginal uterine artery doppler in early pregnancy for the prediction of pre-eclampsia. The aim of the study was early prediction of pre-eclampsia by trans-vaginal uterine artery Doppler study at 12-16 weeks.

Methods: According to the study criteria 100 antenatal women between 12 to 16 weeks of singleton pregnancy attending out patient in the Department of OBG of S. D. M. Medical College Dharwad were included. After an informed consent, the women underwent ultrasound for dating and subsequently trans-vaginal ultrasound along with color doppler was performed to obtain uterine artery indices. These women were again rescanned at 24-26 weeks of gestation trans-abdominally and further followed up clinically for development of preeclampsia.

Results: Out of 100 women, 22 patients developed preeclampsia. At 12-16 weeks 35% of women had bilateral uterine artery notching, mean RI was 0.57 and PI was 0.89. When uterine artery notch at 12-16 weeks alone was considered, 34.28% of women developed preeclampsia. Detection rate increased to 85.71% when RI>0.65 was also included along with notching. Uterine artery notching at 12-16 weeks gestation had 34.29% sensitivity, 84.62% specificity, 70.51% NPV. When notch and RI>0.65 considered together sensitivity and NPV increases to 85.71% to 98.25%.

Conclusions: The uterine artery Doppler waveform indices at 12-16 weeks are the best non-invasive screening test available for early prediction of preeclampsia.

Keywords: Preeclampsia, Pulsatality index, Resistance index, Uterine artery Doppler, Uterine artery diastolic notch

INTRODUCTION

Preeclampsia and fetal growth restriction (FGR) have been identified as antecedent causes in 6% and 10% of perinatal deaths, respectively.[1] In the latest Centre for Maternal and Child Enquiries (CEMACE) report on maternal deaths ("saving mothers' Lives" 2006-2008), preeclampsia/eclampsia was the second commonest cause of direct maternal deaths in the United Kingdom (0.83 per 100,000 maternities).[1] Hypertension in pregnancy is also responsible for fetal (more than 19 weeks of gestation) and infant mortality as well as 46% of infants born small for gestation.[2]

Similarly, it was estimated that 3-10% of infants are growth restricted. Fetal growth restriction is associated with substantive perinatal morbidity and mortality. This is true for both preterm and term infants.[3,4]

Early screening for preeclampsia may allow vigilant antenatal surveillance and appropriate timing of fetal delivery in order to avoid serious sequele. Various hemodynamic and biochemical measurements have been found to have limited accuracy as a screening test for this condition.[5,6]

Preeclampsia is characterized by an imbalance between prostacyclin and thromboxane A2 production as well as failure of the second wave of trophoblastic invasion of the endometrio-myometrial vasculature.[2] The result is abnormal uteroplacental blood flow and this lead to an idea of using Doppler assessment of uterine artery velocimetry waveforms as the method of screening for this antenatal complication.[7] In recent years, ultrasonography is commonly used in measurement of fetal biometry and diagnosis of congenital anomalies and IUGR. Problem which still exists is identification of those pregnancies which are at risk of increased maternal and fetal morbidity as in pregnancy induced hypertension.[2] Various biochemical tests used in screening of high risk population for pre- eclampsia have lower positive predictive values, high cost and less patient compliance.[2]

Doppler is a non-invasive method for evaluation of feto-placental circulation without any disturbance to human pregnancy.[8] A high resistance index, pulsatility index and persistent uterine artery notching in uterine artery Doppler wave form has been shown to be the best screening test.[9] Thus, we have conducted this study to find out the predictive value of transvaginal Doppler in early pregnancy at 12-16 week of gestation for the prediction of preeclampsia and sub-sequent perinatal outcome. Objective of the study was early prediction of pre-eclampsia by transvaginal uterine artery Doppler study.

METHODS

An observational study was done over a period of one year among women attending the out-patient Department for antenatal care at S. D. M. Medical College and Hospital Dharwad, Karnataka, during the period of November 2016 to October 2017.

Inclusion criteria

All pregnant women between 12 to 16 weeks of gestational age with singleton pregnancy.

Exclusion criteria

- Multiple gestations
- Patient with congenital anomaly of fetus, chronic hypertension, renal disease and cardiac disease.

Present study was an observational study with a sample size of 100. When above criteria were met study group

was subjected to Doppler study after dating and screening scan at 12-16 week of gestation.

Procedure

After assessment of inclusion and exclusion criteria, 100 antenatal women of 12 to 16 weeks of singleton pregnancy were selected for the study in the Department of Obstetrics and Gynecology of S. D. M. Medical College Dharwad. Women booking for antenatal care were examined and investigated. After a written informed consent, the women were subjected to transvaginal ultrasound for dating and screening scan. Women were placed in the dorsal position with knee flexed, a trans-vaginal ultrasound scan was done and Doppler assessment of uterine artery circulation for uterine artery indices using Philips USG machine with 7.5 MHz transvaginal curvilinear transducer.

After initial assessment, the cervix was identified. Uterine artery was located on one side by placement of probe in that fornix and color flow mapping was done. The utero placental circulation was studied for various uterine artery Doppler indices, i.e. diastolic notching, Resistance Index (RI) and Pulsatility Index (PI). Increased resistance to flow in the uterine artery is associated with the appearance of diastolic notch and increase in all these indices. Same procedure was repeated on the opposite side. The whole procedure was completed within 10 minutes. These women were again rescanned at 24-26 weeks of gestation by trans abdominal USG HP image point color Doppler machine with convex probe 3.5 MHz with ultrasonography fetal biometry and morphology scan was done then Doppler mode was switched on. Patient is put in recumbent position with transducer in the longitudinal plane. The external iliac artery is visualized at pelvic side wall with color Doppler. The transducer is then angled medially towards the uterine artery, where they cross the external iliac artery. The flow velocity waveforms on the right and left uterine arteries were taken when 3 or 4 waves of equal height were seen, the image was frozen, and measurements were taken either by trace method/ manually/automatic trace. Then Doppler indices were obtained directly from the machine and further followed up clinically for development of pre-eclampsia. Increased resistance to flow in the uterine artery is associated with the appearance of diastolic notch and increase in all these indices. These patients were followed up till delivery to look for onset of preeclampsia.

Method of statistical analysis

Statistical analysis was done using descriptive statistical methods like mean, percentages and proportions. Chi-square test was used to find the association between two attributes and unpaired t-test was used to find the association between two variables. A p-value of less than 0.05 was considered to be statistically significant.

RESULTS

After assessment of inclusion and exclusion criteria, 100 antenatal women of 12 to 16 weeks of singleton pregnancy on OPD basis were selected for the study. These women underwent uterine artery Doppler assessment twice i.e. between 12-16 weeks and again at 24-26 weeks of gestation and further followed up clinically for development of preeclampsia. About 52% of women were in the age group 21-30 years, 46% were teenagers and 54% of them were primigravidas.

Table 1: clinical variables of the study group

	Mean	Standard deviation
Gestation age at scan		
GA1	14+1	0.835
GA2	24+6	0.555
Systolic BP in mmHg		
<130	77	
130-139	1	
140-149	12	
>150	10	
Diastolic BP in mmHg		
<80	57	
80-89	21	
90-100	22	

Gestational age during the 1st scan ranged between 12+4 to 16 weeks with a mean age at transvaginal USG being 14+1 (SD = 0.835) and at transabdominal USG it ranged 23+1 to 25+3 with a mean of 24+6 weeks (SD = 0.555). On following up these women to third trimester 78% remained normotensive and 22% developed hypertensive disorders of pregnancy. 10 of these hypertensive patients had severe preeclampsia i.e. SBP >150 mmhg and diastolic BP >100 mmhg which constitutes 45% of preeclamptic cases (Table 1).

Table 2: Uterine artery Doppler diastolic notching during scan.

Notching at 12-16 weeks	Frequency	Percentage
Present	35	35
Absent	65	65
Notching at 24-26 weeks		
Present	16	16
Absent	84	84

Uterine artery Doppler notching at 12-16 weeks was seen in 35% of women. Uterine artery Doppler notching at 24-26 weeks is seen in 16% of women. So, 9% of women who had UADN at 12-16 weeks did not have UADN at 24-26 weeks and did not develop hypertension.so persistence of notch into the 2nd trimester increased the risk of developing preeclampsia (Table 2).

Uterine artery Doppler notching at 12-16 weeks was seen in 34.3% of preeclamptic women which is statistically significant (p <0.042). UADN at 24-26 weeks was seen in 75% of preeclamptic women which is statistically significant (p <0.0001). Of the 16 patients who had persistent notching during the 2nd scan 12 developed preeclampsia and only 4 patients remained normotensive.

In the 35 women who had UADN in the 1st scan, notch disappeared in 19 women and none of them developed hypertension. Among the 58 women who had no UADN in both the scans 10 developed preeclampsia i.e. 17.24% (Table 3).

Table 3: Association of uterine artery diastolic notch with development of preeclampsia.

Notch at 12-16 week	Preeclampsia No.	%	P value	Notch at 24-26 week	Preeclampsia No	%	P value
Present	12	34.3	Significant	Present	12	75	Highly significant
Absent	10	15.4		Absent	10	11.9	

N1: X^2 = 4.736, df = 1, p = 0.042; N2: X^2 = 31.180, df = 1, p<0.0001

Table 4: Resistance index and pulsatility index in study group.

Doppler indices	No.	Min.	Max.	Mean	SD
RI1	100	0.51	0.68	0.5757	0.03641
RI2	100	0.42	0.66	0.4728	0.06264
PI1	100	0.84	1.08	0.8957	0.06155
PI2	100	0.57	1.06	0.6478	0.13898

The RI at 12-16-week scan (RI1) ranged between 0.51 to 0.68, the PI1 between 0.84 to 0.57 with mean RI1 and PI1 being 0.57 and 0.89 respectively. At 24-26 weeks RI2 was between 0.84 to 1.08, PI2 between 0.57 to 1.06 and mean RI2 and PI2 were 0.47 and 0.64 respectively.

Table 5 shows that in preeclampsia mean RI at 12-16 weeks is 0.6073 and at 24-26 weeks is 0.5382, which is statistically significant (p<0.0001) as compared to non-preeclamptic women where mean RI1 was 0.56 and mean RI2 was 0.45 respectively.

Table 6 shows that 50% of preeclamptic women have RI between 0.65-0.69 and 41.66% have RI between 0.60-0.64 which is statistically significant (p <0.0001) as compared to non-preeclamptic women. In 4 normotensive

women with persistent UADN during the 2nd scan, 3 women had RI1 <0.58 and RI2 <0.47. So immaterial of development of preeclampsia, higher RI was seen in patients with persistent UADN (Table 6).

Table 5: Association of Resistance index at 12-16 week and 24-26 week of gestation (Uterine artery Doppler) in preeclamptic and in normal pregnant women.

Resistance indices	In preeclamptic women		In non-preeclamptic women	
Gestation age	Mean	SD	Mean	SD
At 12-16 week	0.6073	0.05382	0.5668	0.02344
t = 5.169, df = 98, p <0.0001				
At 24-26 week				
	0.5382	0.09194	0.4544	0.03425
t = 6.642, df = 98, p<0.0001				

Table 6: Association of uterine artery notch and RI at 12-16 week of gestation, in preeclamptic and in non-preeclamptic women.

RI at 12-16 week	Uterine artery notching (n=35)			
	Preeclamptic women (n = 12)		Non preeclamptic women (n=23)	
	Number	Percent	Number	Percent
0.55-0.59	1	8.33	21	91.3
0.6-0.64	5	41.66	1	4.34
0.65-0.69	6	50	1	4.34

$X^2 = 23.26$; df = 2, p <0.0001

When uterine artery notch alone is considered 34.28% developed preeclampsia. Both notch+ RI>0.65 considered together 85.71% developed preeclampsia. So, the positive predictive value of UADN along with Doppler indices is higher predicting development of preeclampsia (Table 7). Table 8 shows that in preeclampsia the mean PI at 12-16 weeks was 0.9573 and at 24-26 weeks was 0.7968, which is statistically significant(p<0.0001) as compared to non-preeclamptic women.so along with UADN and RI, PI can be used as a Doppler index for preeclampsia.

Table 7: Comparison of uterine artery notch alone and uterine artery notch with RI >0.65 with development of preeclampsia.

Abnormal uterine artery waveform at 12-16 weeks	Preeclampsia	
	No.	Percentage
Uterine artery notch (n=35)	12	34.28
Notch + RI >0.65 (n=7)	6	85.71

Table 8: Association of at 12-16 week and 24-26 week of gestation Uterine artery Doppler pulsatility index in preeclamptic and in normal pregnant women.

Pulsatility indices	In preeclamptic women (n=22)		In non-preeclamptic women (n=78)	
Gestation age	Mean	Standard deviation	Mean	Standard deviation
At 12-16 week	0.9573	0.09051	0.8783	0.03532
t = 6.252, df = 98, p<0.0001				
At 24-26 week	0.7968	0.20721	0.6058	0.0706
t = 6.909, df = 98, p<0.0001				

Table 9: Role uterine artery Doppler in predicting preeclampsia at 12-16 weeks.

Study variables	Sensitivity	Specificity	PPV	NPV
Uterine artery notch	34.29%	84.62%	54.55%	70.51%
Notch + RI>0.65	85.71%	84.62%	37.5%	98.21%

As shown in Table 9, uterine artery notching at 12-16 weeks gestation has 84.62% specificity and 70.51% NPV. When UADN and RI >0.65 are taken together sensitivity increases from 34.29% to 85.71% and NPV to 98.25%.

DISCUSSION

In the present observational study, of the 100 women who were recruited 22% women developed preeclampsia thus prevalence is similar to Shashi G et al (20%) but high prevalence compared to that quoted by Gupte S et al (9-10%).[7,10] Among 100 women 35% had notching at 12-16 weeks, 16% had persistence of notching at 24-26 weeks which is more as compared to Casmod Y et al who described preeclampsia in 25.86% of the women with bilateral notching at 12-16 weeks of gestation.[11]

Mean RI in the present study is 0.57 at 12-16 weeks and 0.47 at 24-26 weeks. In 41.66% of preeclamptic women mean RI at 12-16 week is 0.6073 and at 24-26 week is 0.5382 which is statistically significant as compared to non-preeclamptic group (p <0.0001) and hence this will help in prediction preeclampsia when combined with uterine artery notching similar to Shashi G et al where mean RI in 37.5% was 0.60.[7]

When uterine artery notch at 12-16 weeks alone is considered, 34.28% of women developed preeclampsia. Detection rate increased up to 85.71% when RI >0.65 is also included along with uterine artery Doppler diastolic notching. Hence Prediction of preeclampsia has increased when B/L uterine artery notching is combined with RI of uterine artery Doppler. Thus, the sensitivity increased from 34.29% to 85.71% when RI >0.65 is included with notch which is similarly described by Shashi G et al.[7]

Mean PI in the present study is 0.89 at 12-16 weeks and 0.64 at 24-26 weeks. In preeclampsia mean PI at 12-16 weeks is 0.9573 and at 24-26 weeks is 0.7968, which is statistically significant (p <0.0001) as compared to non-preeclamptic women. Hence this will help in prediction preeclampsia when combined with uterine artery notching similar to Gomez O et al.[12]

In the present study out 100 women 35 patients had bilateral notching at 12-16 weeks and 12 women developed preeclampsia. Hence sensitivity of bilateral uterine artery notching is 34.29%, specificity is 84.62% positive predictive value is 54.55%, and negative predictive value is 70.51% in prediction of preeclampsia similar to Shashi G et al.[7]

CONCLUSION

Preeclampsia is a complex clinical syndrome involving multiorgan systems with significant maternal and perinatal, mortality and morbidity. The research for ideal predictive test and preventive measure remains challenging. Doppler is a non-invasive method for evaluation of feto-placental circulation without affecting the pregnancy.

In our study the mean of all uterine artery indices showing impedance to uteroplacental circulation (RI, PI, notching) are significantly higher in women who developed preeclampsia. This shows that resistance to blood flow is a more important indicator than the actual blood flow.

The uterine artery notching, high Resistance index and pulsatility index in uterine artery Doppler waveform at 12-16 weeks has shown to be the best screening test available for early prediction of preeclampsia with detection rate of 85.71%.

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