Original Research Article

Prediction of pre- eclampsia and intra uterine growth restriction using doppler velocimetry of uterine artery at 20-24 weeks of gestation

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Abstract

Hypertensive disorders in pregnancy represent the second most common cause of maternal death in India accounting for 16% maternal deaths annually. Prediction of this disorder early in pregnancy using screening tests is expected to help in reducing its incidence and associated complications. A pathological increase in vascular resistance of placental circulation can be detected by uterine artery doppler studied as early as 18 weeks offering potential to prevent pre-eclampsia by deploying earliest possible interventions.
Key Word: Eclampsia.

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INTRODUCTION

The Key aim of antenatal care is to screen high risk pregnancies, prevent, detect and treat at the earliest any complications that may arise subsequently. High risk pregnancies require close follow up and prompt treatment of potential complications to ensure healthy baby and mother. Screening is considered a preventive care, screening of pregnancies for various diseases and other high risks factors allow sufficient time interval to intervene before the disease process sets in. The World Health Organization (WHO) systematically reviews maternal mortality worldwide, and in developed countries, 16% of maternal deaths were reported due to hypertensive disorder[1]. Hypertensive disorders in pregnancy represent the second most common cause of maternal death, first being haemorrhage. The condition affects 5-10% of all pregnancies world wide and is responsible for 10-15% maternal deaths associated with preeclampsia and eclampsia in India[2]. Prediction of hypertensive disorders early in pregnancy using screening test is expected to help in reducing the incidence of disease, complications, associated morbidity and mortality in this condition by allowing early intervention. It is important to identify the women who are at risk of developing preeclampsia and intrauterine growth restriction, as they require closer antenatal surveillance which in turn helps in early referral for timely delivery, as and when indicated. Diagnosis of this condition as early as possible depends on the detection of early signs of disease such as hypertension, proteinuria, oedema and excessive weight gain. However these signs and symptoms appear in later stages of the disease process where prevention is not possible[3]. A pathological increase in vascular resistance in placental circulation can be detected by uterine artery doppler studied as early as 18 weeks and will offer the potential to prevent pre-eclampsia and to carry out earliest possible interventions.Doppler ultrasound studies of the uterine

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arteries have demonstrated that the clinical manifestations of preeclampsia are preceded by evidence of impaired placental perfusion.[4,5] A major outcome of this disease process that causes poor placental perfusion is manifested in intrauterine growth retardation of the unborn foetus. Intrauterine growth restriction (IUGR) in India comprises one-third of low birth weight infants (28%) and incidence of same in developed countries is 2-8%. Hence prevention of low birth weight (LBW) is a public health priority in India where, the extent of problem largely attributed by IUGR[6]. It is important to predict in which pregnancies pre eclampsia and IUGR may ensue; since the pathophysiology of both is abnormal placentation.

Role of Uterine Doppler

Impedance to blood flow in uterine artery results in an abnormal wave form pattern. Impaired uterine artery flow velocity can be identified by a persistent abnormal index (resistance index and pulsatility index), persistent notch and significant differences between the indices of bilateral uterine arteries.Among these three indices of uterine artery Doppler study Pulsatility index and persistent diastolic notch had shown the best predictive accuracy in pregnancy outcomes. Gomez *et al* evaluated the uterine artery pulsatility index in first trimester and showed that 30.8% pregnancies developed severe complications when having abnormal index by using 95th percentile as cut-off[7]. At the onset of pregnancy these indices does not show much difference as compared to the non-pregnant state. Study conducted by Schulman and colleagues in 1986 showed that there is a significant increase in the compliance of uterine artery between 8 to 16 weeks of gestation. And form 22-24 weeks of gestation there is significant reduction in these indices[8]. The prevalence of notching decreases with increase in gestational age till 24 weeks of gestation there after it remains stable; a change in uterine artery waveform that is thought to be secondary to the fall in impedance in the vessel after trophoblastic invasion.[9] A study conducted by Dehgani-firouzabadi *et al* during October 2011-12 included 456 pregnant women in 20-22 weeks gestational period. Doppler studies performed for uterine artery showed that there were no pregnancy complications and normal pregnancy outcomes in women (n=429) with normal resistance indices (<0.69). This was significant when compared to the group where resistance indices were high (>0.69) (n==36) and suffered severe pregnancy complications with adverse outcomes[9]. Kevin spencer *et al* in 2008 conducted a multi centric study and observed that the uterine artery mean pulsatility index had a higher screening efficacy for prediction of preeclampsia and intrauterine growth restriction.[10] A recent meta-analysis concluded that among these three indices of uterine artery, the doppler study pulsatility index and the persistent diastolic notch had best predictive accuracy (with area under curve 0.82 and sensitivity of 0.76) in predicting pregnancy outcomes[11]. The time at which uterine artery Doppler should be performed has been studied extensively by multiple studies. Second wave of trophoblastic invasion completes at 16-18 weeks of gestation by completely transforming high resistance vessels of utero-placental bed into high capacitance vessels.Chan FY *et al* evaluated uterine artery Doppler velocity study at 20 weeks, 28 weeks and 36 weeks, to compare the prognostic accuracy of gestational age with a cut off of 95th percentile for resistance index and with or without presence persistent diastolic notch . They concluded that 20 weeks of gestation was the optimal time for testing with persistent diastolic notch carrying 50% positive predictive value for adverse pregnancy complications[12].

MATERIAL AND METHODS

Aim of the study was to evaluate the role of uterine artery Doppler flow velocimetry study at 20-24 weeks of gestation in prediction of pre-eclampsia, fetal growth restriction and pregnancy outcome.

Uterine artery Doppler was performed on 110 subjects
106 subjects came for follow up and delivery
4 were excluded from study
2 subjects had abortions
104 patients delivered alive baby
6 patients had pre eclampsia
20 patients had IUGR

OBSERVATIONS and RESULTS

Table 1: Distribution of the study population:

	No of subjects N=106	Proportion of subjects
Total no of IUGR subjects (less than 10th centile as per WHO growth chart)	20	18.8%
Total no. of Pre-eclampsia subjects	6	5.66%
Total no. of live births	104	98.11%
Total no. of abortions (as per birth weight)	2	1.88%

Table 2: Period of gestation at uterine artery Doppler

Parameter	Mean	SD
Period of gestation (in weeks)	21.55	0.98

Table 3 :Pulsatility Index (PI)

PI	No.	Mean PI
Normal (≤1.4)	99	1.10
Abnormal (>1.4)	7	2.02

Table 4: Persistent Diastolic Notch

Notch	No.	%
Left uterine artery persistent notch	1	0.94
Bilateral persistent notch	3	2.83
Total no. of subject with notch	4	3.77
No notch	102	96.23

Table 4: Correlation of preeclampsia with various parameters

Correlation of age with preeclampsia		
Age groups	Subjects without preeclampsia (n=100)	Cases with preeclampsia (n=6)
19-25 years	37	2
26-34 years	56	3
>35 years	7	1
Chi-square test p-value	0.199	
Pearson's correlation test p-value	0.086	

Table 5: Correlation of the BMI with Pre-eclampsia

BMI (kg/m²)	Subjects with preeclampsia (n=6)	Subject's without preeclampsia (n=100)
Less than 18.5	1	3
18.5-24.9	2	68
25-29.9	1	16
30-34.9	2	14
Chi-square test p-value	0.001	
Pearson's correlation test p-value	0.006	

Table 6: 3 Type of conception

Correlation of Type of conception with Pre-eclampsia		
Type of conception	Subject's with preeclampsia (n=6)	Subject's without Preeclampsia (n=100)
Spontaneous	5	99
ART	1	1
Chi-square test p-value	0.0001	
Pearson Correlation Test Sig. (p-value)	0.006	

Table 7: Parity

Correlation of Parity with Preeclampsia		
Parity	Subject's with preeclampsia (n=6)	Subjects without preeclampsia (n-100)
1	5	43
2	0	44
3	1	12
6	0	1
Chi-square test p-value	0.199	
Pearson Correlation test Sig. (p-value)	0.243	

Table 8: Pulsatility index

Correlation of Pulsatility index with Preeclampsia		
PI	Subject's with preeclampsia (n=6)	Subject's without preeclampsia (n=100)
Normal (≤1.4)	1	98
Abnormal (>1.4)	5	2
Chi-square test p-value	0.0001	
Pearson Correlation test Sig. (p-value)	<0.0001	

Table 9: 6 Persistent Diastolic notch

Correlation of Persistent Diastolic notch with Pre-eclampsia		
Notch	Subject's with Preeclampsia (n=6)	Subject's without preeclampsia (n=100)
Persistent Diastolic notch present	3	1
No notch	3	99
Chi-square test p-value	0.0001	
Pearson Correlation test Sig. (p-value)	<0.0001	

Table 10: 7 IUGR

Correlation of IUGR with Pre-eclampsia		
IUGR	Subject's with preeclampsia (n=6)	Subject's without preeclampsia (n=100)
Present	4	16
Absent	2	83
Chi-square test p-value	0.0001	
Pearson Correlation test Sig. (p-value)	0.001	

Table 11: Summary of Correlation between Preeclampsia with various parameters

Correlation between Preeclampsia with various parameters		
Parameters	Pearson Correlation coefficient (2-tailed)	Pearson Correlation Sig. (p=value)
Age	0.168	0.086
BMI	0.268	0.006
Parity	-0.114	0.243
Type of conception	0.266	0.006

PI	0.615	<0.0001
Persistent diastolic notch	0.594	<0.0001
IUGR	0.311	0.001
NICU STAY	0.266	0.006
Correlation is significant at the 0.05 level (2-tailed)		

Table 12: Validity parameters of uterine artery Doppler test Pulsatility index for Preeclampsia and IUGR

Distribution of validity parameters of uterine artery Doppler test – Pulsatility index

Parameters	Uterine artery Doppler Pulsatility index (PI)	
	Preeclampsia	IUGR
Sensitivity	83%	30%
Specificity	98%	98%
Positive predictive value (PPV)	71%	85%
Negative predictive value (NPV)	98%	85%
Positive Likelihood ratio (LR+)	41.5	15
Negative Likelihood ratio (LR-)	0.17	0.71

Table 13: Proportion of cases with pre-eclampsia and IUGR

Proportion of preeclampsia and IUGR in various other studies

Study	Proportion	
	Preeclampsia	IUGR
Yong Won Park *et al* 2005[148]	1.7%	9.5%
Anshu Dhar *et al*.2017[146]	6%	3%
Deepti Verma *et al*. 2016[147]	12.1%	11.5%
Padmalatha VV *et al*. 2013[149]	2.3%	12.9%
Mojgan Barati *et al* 2014[150]	5.01%	1.84%
Present study	5.66%	18.8%

In our study the proportion of the Pre-eclampsia was 5.66% and IUGR was 18.8%

DISCUSSION

In present study it was observed that age was not associated with the development of preeclampsia and there was no statistical significance between preeclampsia and age (p-value 0.086). The study also showed that parity was not associated with the development of preeclampsia and there was no statistical significance between preeclampsia and parity as p-value was 0.243. However it was observed that BMI had relationship in the development of the preeclampsia which was statistically significant with p-value 0.006. Assisted reproductive techniques were observed to have relationship in the development of the preeclampsia which was statistically significant with p-value being 0.006. Cases with abnormal Pulsatility index (PI) of the uterine artery doppler performed at 20-24 weeks of gestation had mean PI = 2.02$\pm$0.23; in comparison with normal uterine artery Doppler; mean PI being 1.10$\pm$0.31 for that gestational age. In a study by Anshu Dhar *et al* in 2017[13]; the abnormal uterine artery doppler Pulsatility index mean was 1.47$\pm$0.59 and normal uterine artery doppler Pulsatility index mean was 0.86$\pm$0.18. Deepti Verma *et al* in 2016[14], in their study reported abnormal Pulsatility index with mean being 1.89 $\pm$0.45 and mean PI 1.14$\pm$0.12 in normal subjects. In Present study, 6.6% subjects had abnormal uterine artery Doppler PI whereas 93.45 subjects had normal uterine artery Doppler PI. The study had 83% sensitivity and 98% specificity for the prediction of pre-eclampsia which was statistically significant by Pearson's correlation test (p-value 0.0001). Study conducted on 200 subjects by Anshu Dhar *et al* in 2017[13] showed sensitivity of 85.71% and specificity of 98.26% in the prediction of preeclampsia. Present study proved that uterine artery Doppler pulsatility index had a positive predictive value of 71% and negative predictive value of 98% in predicting the occurrence of pre eclampsia. In the current study abnormal uterine artery doppler with persistent diastolic notch was significant in prediction of preeclampsia p value <0.0001 (Pearson's correlation test) with 50% sensitivity and 99% specificity. Young Won Park *et al* in 2005[15] reported that persistent diastolic notch was a good predictor of the preeclampsia with sensitivity 90.9% and specificity of 93.3%

CONCLUSION

Uterine artery Doppler study indices i.e. pulsatility index and persistent diastolic notch at 20-24 weeks of gestation was the good predictor of preeclampsia and IUGR. In our study specificity of pulsatility index for the development of

preeclampsia and IUGR was 98% and 90% respectively. Similarly the specificity of persistent diastolic notch for development of pre-eclampsia and IUGR was 99% and 98% respectively. An important aspect is the negative predictive value of Pulsatility index for Preeclampsia (98%) and IUGR (85%) and persistent diastolic notch- 97% and 91% for preeclampsia and IUGR respectively; helps to detect those patients who will not develop IUGR and preeclampsia. Therefore uterine artery Doppler evaluation at 20-24 weeks of gestation might be an appropriate tool for indentifying pregnancies that are at low risk for development of pre-eclampsia and intrauterine growth restriction.

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