Role of uterine artery Doppler in early prediction of pre-eclampsia and intrauterine growth restriction at 16-24 weeks of gestation

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Abstract
Introduction: Pre-eclampsia and intrauterine growth restriction are important causes of maternal and perinatal morbidity and mortality. Gestational age at the onset of pre-eclampsia will determine the degree of fetal compromise. Hence, early detection of preeclampsia is important to improve maternal and perinatal outcome. Utero placental circulation can be non-invasively assessed by Doppler analysis of uterine arteries.
Aims and Objectives: The aim of our study is early prediction of pre-eclampsia and Intra uterine growth restriction by Doppler assessment of uterine artery.
Materials and Methods: 100 antenatal women of singleton pregnancy at 16-24 weeks of gestation were selected for study in the department of Obstetrics and Gynecology at MNR Medical College, Sangareddy from May 2015 to April 2016. Doppler evaluation of uterine artery along with routine biometry was done.
Results: Out of 100 cases studied, 19 patients showed abnormal uterine artery Doppler results and among these 16(84.2%) developed preeclampsia, 8(42%) had intrauterine growth restriction, 6(31.5%) babies required NICU admission and 2(10.5%) intrauterine fetal deaths were noted. Sensitivity and specificity to detect pre-eclampsia was 84.2% and 83% respectively and that of intrauterine growth restriction was 42% and 96% respectively.
Conclusion: Uterine artery notching, high PI, RI in uterine artery Doppler analysis can be a good screening tool for early prediction of pre-eclampsia and intrauterine growth restriction.

Keywords: Pre-eclampsia, Intrauterine growth restriction, Uterine artery Doppler.

Introduction
Pre-eclampsia affects 2-5% of pregnancies and is an important cause of perinatal and maternal morbidity and mortality.1 Intrauterine growth restriction is often defined on the basis of weight below the 10th percentile for gestational age.2-4 Growth restriction in most cases is caused by placental insufficiency. In some cases, cause of growth restriction cannot be detected. Irrespective of etiology, growth restricted fetuses carry poor prognosis and associated increased risk of intrauterine fetal demise, neonatal morbidity and neonatal death. Therefore, early detection of proper surveillance are required to improve the outcome and this can be achieved by non-invasively studying the utero-placental circulation by sampling the uterine arteries. In pre-eclampsia, there is pathological increase in placental vascular resistance and this can be detected by Doppler study of the maternal uterine arteries. Blood flow in uterine artery in non-gravid state is 50ml per minute and it increases to about 700ml/min in third trimester. Hence, by mid second trimester, uterine artery waveforms show high end diastolic velocity with continuous forward flow throughout diastole. Failure of normal trophoblastic invasion can lead to increased resistance and reduced perfusion of placenta.5,6 In non-pregnant state and in early pregnancy, uterine artery flow is of high pulsatility with a high systolic and low diastolic flow. Early diastolic notch may be present physiologically. This usually disappears by 24 weeks of pregnancy. Presence of notching beyond this is an indicator of increased resistance in uterine artery. If end diastolic flow does not increase or if notching is evident at the start of diastole, this may be associated with pregnancy induced hypertension, pre-eclampsia, abruptio placenta, intrauterine growth restriction.7 In very high grades of dysfunction of placenta, diastolic flow may be absent or even reversed. Absent flow or reversal of flow are alarming and may precede fetal death or signal a very high risk of abnormal neurological outcome in the fetus. High resistive index (RI), persistent notching of uterine artery and high pulsatility index (PI) are the best screening tools. Uterine artery notching may be unilateral or bilateral. Simultaneous presence of intra-systolic notch represents an extremely high impedance. PI value of 1.45 is used as a reference to differentiate between normal and abnormal values. PI >1.45 with bilateral notching indicates severe ischemia. RI value of 0.33-0.55 may be considered normal.

Materials and Methods
An observational study was done over a period of 1 year in 100 antenatal women attending Obstetrics and Gynecology department in MNR Medical College and Hospital, Sangareddy during the period of May 2015 to April 2016. 100 pregnant women between 16-24 weeks of gestational age with singleton pregnancy were
included in the study. Women with multiple gestation and congenital anomaly of the fetus were excluded from the study. Uterine artery assessment was done transabdominally. Each uterine artery was sampled soon after the crossing of the iliac vessels. Colour Doppler gives a map of blood flow superimposed on the normal 2D image and is used to identify a particular blood vessel and sample the blood velocity within that vessel. Spectral Doppler gives a graph of blood velocity versus time- the Doppler waveform. This waveform is analysed to detect changes in resistance to the blood flow. Pulsatility Index, Resistive Index values and presence or absence of diastolic notching were noted. These patients were followed up till delivery and maternal and neonatal outcome was noted.

**Results**

The present study consisted of 100 antenatal cases with singleton pregnancy between 16-24 weeks gestation. Out of these 100, 60% of women were primi gravida. Abnormal Doppler study consisted of presence of uterine artery notching, increased PI > 1.45 and increased RI. In our study, out of 100, abnormal Doppler results were noted in 19%. Among those with abnormal Doppler results, pre-eclampsia was seen in 84.2%. 8 (42%) fetuses had IUGR and were small for gestational age, 6 (31.5%) required NICU admission. Intrauterine death occurred in 2 (10.5%) cases. Sensitivity and specificity to detect pre-eclampsia was 84.2% and 83% and that of IUGR was 42% and 96% respectively. Positive predictive value for pre-eclampsia and IUGR was 55% and 72.7% respectively. Negative predictive value for pre-eclampsia and IUGR was 95% and 87.6% respectively.

**Table 1: Parity distribution**

| Gravida     | Number of women | Percentage |
|-------------|-----------------|------------|
| G1          | 60              | 60%        |
| G2          | 36              | 36%        |
| G3 and more | 4               | 4%         |
| Total       | 100             | 100%       |

**Table 2: Abnormal uterine artery Doppler**

| Abnormal uterine artery Doppler | Frequency | Percentage |
|---------------------------------|-----------|------------|
| Present                         | 19        | 19%        |
| Absent                          | 81        | 81%        |
| Total                           | 100       | 100%       |

**Table 3: Pre-eclampsia and perinatal outcomes in women with abnormal uterine artery Doppler (n=19)**

| Outcome                  | Number of women | Percentage |
|--------------------------|-----------------|------------|
| Pre-eclampsia            | 16              | 84.2%      |
| IUGR                     | 8               | 42%        |
| NICU admission           | 6               | 31.5%      |
| Intrauterine fetal death | 2               | 10.5%      |

**Table 4: Role of uterine artery Doppler in predicting pre-eclampsia and intrauterine growth restriction**

| Outcome         | Sensitivity | Specificity | PPV  | NPV  |
|-----------------|-------------|-------------|------|------|
| Pre-eclampsia   | 84.2%       | 83%         | 55%  | 95%  |
| IUGR            | 42%         | 96%         | 72.7%| 87.6%|

**Fig. 1: Showing notching in the uterine artery**
Discussion
Doppler velocimetry uses high frequency sound for investigation of blood flow. The physiology of the fetomaternal unit can be determined by Doppler flow study. This provides vital information to the obstetrician for subsequent approach in pregnancy. Hence, Doppler studies of uterine arteries are needed for timely interventions to be taken by early prediction of pre-eclampsia and intrauterine growth restriction to prevent complications.

Pre-eclampsia and intrauterine growth restriction are major causes of maternal and neonatal complications. Abnormal Uterine artery Doppler at 16-24 weeks is associated with adverse pregnancy outcomes such as preeclampsia and IUGR. Hence Doppler analysis can be useful for identifying high risk pregnancies and in providing good antenatal surveillance and improving perinatal outcomes. Non-invasive study of uteroplacental circulation can be done by Doppler analysis of uterine arteries. In our study, Doppler analysis consisted of looking for presence or absence of diastolic notch, PI and RI values. Out of 100 women, 16% developed pre-eclampsia and this is close to the study by Gupta Shashi et al and higher compared to a study by Irion et al (4%). A study by Zimmermann et al, impedance to uterine arterial flow was measured at 21-24 weeks of gestational age. The prevalence of preeclampsia in their study was 18% which is almost the same as in our study.

Our study has predicted pre-eclampsia and intrauterine growth restriction with good specificity and sensitivity. A study by Becker R et al also demonstrated that Doppler study of the uterine arteries at 20-23 weeks has good diagnostic value. In pre-eclamptic women, 8 babies were associated with intrauterine growth restriction, intrauterine death was noted in 2 cases. 31.5% babies born to pre-eclamptic women required NICU admission.

In our study, the role of uterine artery Doppler in predicting pre-eclampsia has sensitivity and specificity of 84.25 and 83% respectively and IUGR had sensitivity and specificity of 42% and 96% respectively. In a study by Valensise et al, sensitivity and specificity to detect pre-eclampsia were 89% and 93% and for IUGR was 67% and 95% respectively, which is close to our study.

It is seen that uterine artery notch and increased pulsatility index (PI) is good predictor of pre-eclampsia and increased resistive index (RI) for intrauterine growth restriction. This is in agreement with study by Cnossen et al.

Conclusion
Utero-placental circulation can be assessed noninvasively by Doppler study of uterine arteries as abnormal Doppler study is associated with outcomes such as pre-eclampsia, intrauterine growth restriction and perinatal mortality. Increased pulsatility index (PI), persistence of uterine artery notch and increased resistive index (RI) can be a good predictor of pre-eclampsia and intrauterine growth restriction. Hence, Doppler analysis of uterine arteries should be included along with routine biometry in second trimester ultrasound for early prediction of preeclampsia and to avoid subsequent perinatal morbidity and mortality.

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