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# Prediction of Pre-Eclampsia by Maternal Uterine Artery Doppler at 11-14 Weeks of Gestation

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**ABSTRACT**

*Uterine artery doppler is a non-invasive which can be used for prediction of PE and FGE at 20 – 23, but the 11 – 13+6 weeks scan may provide earlier information.*

*This was a prospective observational two year study in a tertiary care center in South India. 330 in low risk, singleton pregnancies were examined between 11–13+6 weeks. In addition to CRL and NT, mean maternal uterine artery PI was measured. The women were followed till delivery to observe development of PE and FGR. Sensitivity and specificity of the mean uterine artery PI with respect to development of complications was calculated. Categorical variables were analyzed using chi square test and value of p= 0.05 was used to calculate significance Results of a total 320 women, 304 had normal PI (Group A) and 16 had PI above 95th centile. (Group B). The two groups were similar with respect to parity and BMI. In Group B, 25% developed pre-eclampsia and 12.5 developed FGR compared to 3.9% developing either PE or FGR in Group A. (p value < 0.005 and 0.01 respectively. Although the sensitivity was low (24%), the specificity and negative predictive values were over 95%, for all three outcomes studied. Thus a normal Doppler in early pregnancy may assure regarding a normotensive pregnancy.*

*This study shows the value of adding uterine artery examination to the 11 – 13+6 week scan. Predicting development of complications in a low risk cohort provides adequate time to add aspirin to reduce the risk of complications. This is the first reported study from South India. Larger studies from this population with addition of serum biochemical parameters such as PAPP A and PLGF will be of added value in this field of study.*

**Keywords:** *Preeclampsia, First trimester, Uterine artery Doppler, Fetal growth restriction,*

## INTRODUCTION

Pre-eclampsia is a serious antenatal problem contributing to maternal morbidity and mortality along with hemorrhage and infection. Studies have shown significant increase in neonatal mortality and morbidity in women with pre-eclampsia and FGR. This shows a higher association with early onset severe fetal growth restriction.[1,2]

Maternal spiral arterial invasion by the trophoblastic tissue is the main means of ensuring adequate fetal nutrition. When this mechanism fails, maternal hypertensive disorders and fetal growth restriction result. Although these may manifest at varying gestational ages later in pregnancy, the underlying pathologic event occurs in first and early second trimester.[2,3]

Pulsatility index (PI) is calculated as a ratio of the difference between systolic velocity and diastolic velocity to the mean velocity. Mean velocity is a calculation made by the machine for each cycle studied. There is a gradual increase in the volume of maternal uterine blood flow to support the growing fetus.[4,5,6] As the vessels increase in capacity owing to the trophoblastic invasion, the diastolic blood flow increases thus decreasing the PI. Failure of the invasive mechanism in the placentation results in increased resistance to blood flow. Uterine artery Doppler attempts to detect this finding in early second trimester or late first trimester. Uterine perfusion studies are therefore important for the prediction of both maternal hypertension and fetal growth problems. [4,5, 6]

## MATERIAL AND METHODS

Women attending the antenatal clinic at our tertiary care obstetric center are offered first trimester scan at 11 – $13^{+6}$ weeks for Crown rump length and NT. Along with this scan both maternal arteries were interrogated by Doppler. The PI was calculated by the formula within the machine. The mean PI of the two uterine arteries was calculated. The values were then compared with published charts and categorized as within normal limits (group A) or increased (>$95^{th}$ percentile for GA by the charts) (Group B). The patients were then followed with standard antenatal care to look for onset of any complications. Outcome measures were PET (with or without FGR) and FGR (with or without PET). Preeclampsia was defined according to the ISSHP guidelines.[6] Fetal growth restriction was defined as birth weight less than $10^{th}$ centile for gestation.[7] The follow up was obtained from the hospital records.

330 women were recruited into the study. Singleton pregnancies irrespective of age and parity were included. Multiple gestation, maternal chronic hypertension, maternal renal disease and anomalous

fetuses were exclusion criteria. In all patients a detailed history, followed by complete general and obstetric examination were performed. Doppler study of the maternal uterine arteries was added to the routine examination of 11 - 14 weeks scan. A sagittal section of the uterus including cervical canal was obtained using transabdominal ultrasound. After identifying the internal cervical os, color flow Doppler was used to identify the uterine arteries on either side of the cervix. Flow waveforms were obtained using pulsed wave Doppler. Waveforms from the branch seen to ascend (uterine artery) were taken. At least three similar waveforms were obtained prior to calculation of the pulsatility index. Both uterine arteries were measured and the mean PI the values used for analysis. [(Fig 1a)

The women were followed with regular antenatal checkups. The records were studied at the end of the pregnancy and specific variables indicating development of PIH and small for gestational age fetus were noted. The neonatal outcome such as gestational age at delivery, mode of delivery, birth weight at delivery were recorded. 320 patients were successfully followed up to term their findings alone were included in the analysis. Of the remaining ten women, four had pregnancy loss not related to development of growth restriction or hypertensive events and six were lost to follow up. The initial collation of data and analysis was performed on Excel (Microsoft) and further analysis was done using SPSS software.

**RESULTS**

Out of 320 pregnant woman in the study group, 16 had the mean PI >95$^{th}$ percentile and the others (n= 304) had mean uterine artery PI within normal limits. The mean artery PI in this group was 2.02 with a range from 0.8 to 3.75 (Std. Dev. 0.56) The 95$^{th}$ centile of uterine artery PI in this cohort was calculated at 2.98. (Fig 1b)

The mean maternal age for those with a high uterine artery PI (Group B) was 27.5 years and that of the normal PI group (Group A) was 26.8 years which was not statistically significant. As maternal age is a significant contributor to hypertensive disease and fetal growth restriction, this shows that the two groups were homogenous for this variable.

Those women with a higher BMI have an increased tendency to develop hypertensive disorders in pregnancy. Our study group included 33 women with a BMI greater than 30. These were equally distributed among the Groups A and B with 15 (45.5%) in Group B. Thus the two groups were homogenous with respect to maternal age and maternal BMI.

Of the total 320 woman 182 woman were nullipara and 138 were multipara. However, of 16 women in Group B, 11 were primigravida. (68.8%) compared to the multiparous women which formed only the remaining 31.2%. This is similar to many studies which have shown a higher incidence of hypertensive disorders in nulliparous mothers.

The spilt up of the complications encountered by the different groups is detailed in Table 1. Of the 16 cases in Group B, (mean PI > 95 percentile), 9 pregnancies [56.25%] developed complications. (Table 1) In comparison, only 49 out of 304 pregnancies (16%) in Group A developed complications. This reveals that significantly higher percentage of patients in Group B developed complications when compared to the normal PI group. (Fig 2) When analyzing the development of preeclampsia alone, 25% of mothers in Group B (four out of 16) developed complications as compared to 3.9% in Group A. This finding was highly statistically significant. (p value < 0.005)

Among the 16 women in Group B, two (12.5%) developed FGR whereas only 12 of 304 (3.9%) from Group A developed fetal growth restriction. The obtained p value (0.01) is also statistically significant although less so than development of development of preeclampsia. The sensitivity and positive predictive values of first trimester uterine artery Doppler as a test, were low in our study group. This trend was seen for both prediction of fetal growth restriction and maternal hypertensive disease. However, the specificity and negative predictive values were very high. Thus a normal Doppler seen in early pregnancy gives a high assurance of absence of hypertensive disorders and fetal growth restriction.

On analyzing the onset of preeclampsia, fetal growth restriction and PE + FGR, it was seen that in Group A (normal PI) most of the patients had onset of complications after 33 weeks. (Table 3) In contrast among the seven patients, five developed complications prior to 33 weeks. The major concern in these pregnancies is the gestational age at onset of complications which in turn decides the fetal mortality and morbidity. Onset of complications prior to fetal viability causes increased neonatal morbidity and maternal morbidity due to prolongation of the pregnancy. Abnormal UA Doppler in first trimester could prove useful to determine the early onset preeclampsia and fetal growth restriction.

As expected, the earlier onset of complications resulted in earlier deliveries in the Group B patients with all pregnancies requiring delivery prior to 34 completed weeks of gestation. Among the 29 women who developed complications in Group A, 15 were delivered after 34 weeks gestation. This again demonstrates how due to later onset of PE, the low risk group had better gestational age at delivery even among the subset which developed complications.

**Table 1: Mean Uterine artery PI and women developing complications. (Numbers in parentheses represent percentage incidence within the group)**

| | Group A (n=9/16) | Group B (n=49/304) |
|---|---|---|
| Gestational hypertension | 3 (18.75%) | 20 (6.58%) |
| Pre eclampsia | 4 (25%) | 12 (3.94%) |
| Fetal growth restriction | 2 (12.5%) | 12 (3.94%) |
| PE + FGR | 1 (6.75%) | 5 (1.64%) |

**Table 2: Sensitivity, Specificity, Positive and Negative predictive values of Maternal UA Doppler**

| | PRE ECLAMPSIA | FGR | PE+ FGR |
|---|---|---|---|
| SENSITIVITY | 25% | 14.28% | 16.66% |
| SPECIFICITY | 96.05% | 95..42% | 95.22% |
| POSITIVE PV | 25 % | 12.5% | 6.25% |
| NEGATIVE PV | 96.05% | 96.05% | 98.35% |

**Table 3: Gestational age at onset of preeclampsia and detection of fetal growth restriction.**

| Weeks | Group A ( PI <2.98) [n = 29] | | | Group B ( PI >2.98) [n = 7] | | |
|---|---|---|---|---|---|---|
| | PE | FGR | PE + FGR | PE | FGR | PE + FGR |
| <30 - 31 | 1 | 1 | 1 | 1 | 1 | |
| 31 – 32 | 2 | 2 | 1 | 1 | 1 | 1 |
| 32 – 33 | 1 | 4 | 1 | 1 | | |
| 33 – 34 | 4 | 5 | 2 | 1 | | |
| >34 | 4 | | | | | |

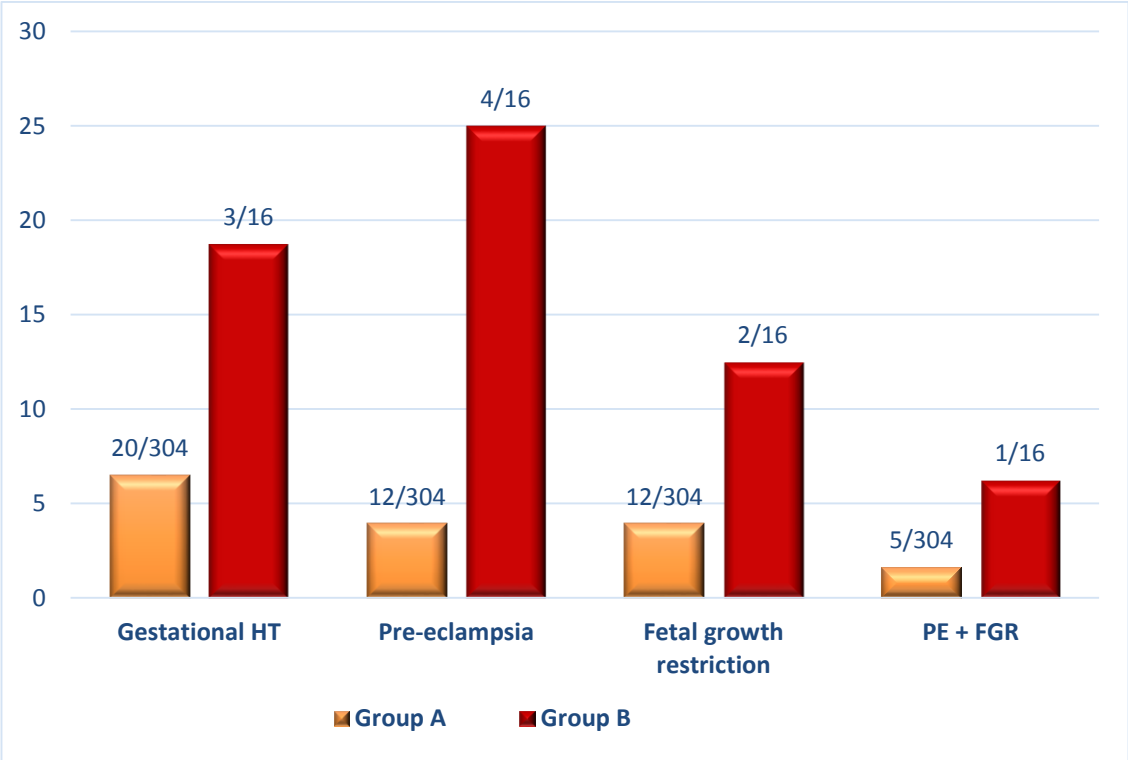


**Fig 1: Percentage incidence of complications in the two groups**

## DISCUSSION

In our study, the mean calculated PI was 2.98. In a study by Martin and colleagues[7], with a mean uterine artery PI of 2.35, the pregnancies complicated by pre-eclampsia was 2.1% and FGR 9.5%. In contrast, our population showed a very high rate of 25% preeclampsia and comparable 12.5% fetal growth restriction. The high rate of preeclampsia could be due to small numbers in the population with high PI (Group B) which formed the study group. The sensitivity of a mean PI > 2.35 for pre-eclampsia was 27% and FGR was 11.7% which was similar to our values or 25% and 12.5% respectively. Other studies have similarly shown an incidence of 2.2% for preeclampsia and 3.7% for fetal growth restriction respectively in high PI groups.[8]

An older study examining women from 12-16 weeks showed prediction of 93% of those developing PET using a seven parameter model. The parameters measured included vessel diameter, average mean velocity, peak systolic velocity in addition to pulsatility index. The predictive values of these parameters taken in combination was high but a simple model such as ours is more applicable to a clinical setting where many complex parameters cannot be measured on each woman presenting for an NT scan.[9]

Maternal uterine artery Doppler shows a lower sensitivity at the 11 – 14 week period when compared to later gestational ages[7,8]. Earlier detection of potential for development of complications can be combined with pharmacologic intervention to the mother such as low dose aspirin. This can be given with more assurance now that benefits for the same have seen shown in larger studies.[10, 11]

## CONCLUSION

This study shows that maternal uterine artery Doppler has a high negative predictive and high specificity in low risk women for prediction of the development of PE and FGR. Mean UtA pulsatility index has a low positive predictive value for the prediction of PE and FGR at 11-14 weeks. However, in view of a high negative predictive value, this test could provide reassurance that the possibility of development of PE or FGR in the pregnancy is low. This test cannot replace the evaluation of fetal growth by clinical examination and ultrasound at regular intervals. However in a setting where serum biochemistry is unavailable due to geographical or economic reasons, addition of uterine artery Doppler to the 11 – $13^{+6}$ week scan could help stratify the women to low and high risk groups and also provide information to start low dose aspirin on time. Addition of this parameter to the routine performance of 11 – $13^{+6}$ week scan may be of benefit to the patient. Further studies in high risk individuals and with addition of biochemistry will provide further information on the utility of the same.

## ABBREVIATIONS:

NT: Nuchal translucency
CRL: Crown rump length
FGR: fetal growth restriction
PE: preeclampsia
PI: Pulsatility Index
GA: gestational age

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