

## Efficiency of First Trimester Uterine Artery Doppler and Serum Papp-A in the Prediction of Pre Eclampsia in 300antenatal Patients

C.Sharmila, K. Saraswathi, Yuvarani.R\*

Department of Obstetrics &Gynaecology, SreeBalaji Medical College & Hospital Affiliated to Bharath Institute of Higher Education and Research, Chennai, Tamil Nadu, India.

*\*Corresponding author e-mail id: [yuvarani.r@bharathuniv.ac.in](mailto:yuvarani.r@bharathuniv.ac.in)*

### ABSTRACT

This prospective observational study was conducted in department of Obstetrics &GynaecologySreeBalaji Medical College & Hospital, Chennai, from February 2015 to August 2016. The study was conducted on 300 randomly selected antenatal patients attending the antenatal clinic. Out of the 44 patients who had abnormal Serum PAPP-A MoM (<0.5MoM)values, 20(45.5%) patients had uneventful pregnancies, 10(22.7%) patients had gestational hypertension, 7 (15.9%) patients had pre-eclampsia, and 7 (15.9%) patients had fetal growth retardation. The final conclusion of our study is that combined use of uterine artery Doppler with PI and serum PAPP -A has shown increased efficiency, detection rates and decreased false positivity rates in diagnosing cases of pre-eclampsia and PIH in first trimester than using them individually.

**Keywords:** endovascular trophoblast, angiotensin, nitric oxide and blood pressure.

### 1. INTRODUCTION

Pregnancy is a physiological stress that causes a number of diverse and interconnected metabolic, physiological, and anatomical changes in the body. The biochemical changes in the blood that occur during a typical pregnancy are given further attention, and these changes are amplified in multiple pregnancy complications. Hypertensive conditions in pregnancy are a leading cause of maternal mortality and morbidity, and are one of the most frequent complications in pregnancy. In developed countries, there is a high prevalence of hypertensive disorders of pregnancy. These conditions collectively complicate 5-10% of all births. The spiral arterioles become distended, tortuous, and funnel-shaped as a result of this. The spiral arterioles are transformed into a low resistance, low pressure, high flow structure as a result of this

physiological transition. The second wave of endovascular trophoblast migration fails in pre-eclampsia, resulting in a loss in blood flow to the fetoplacental unit. When a pregnancy is natural. (4) Angiotensin-II (a component of 2 globulin) is damaged by angiotensinase, a placental enzyme. As a result, blood pressure is maintained at a healthy level. (2) The vascular system becomes refractory to the pressor angiotensin-II in a selective manner. Vascular synthesis of prostaglandin I<sub>2</sub> and nitric oxide (NO), both of which have a vasodilator function, are likely to be the cause of this. In a typical birth, the relationship of the two mechanisms keeps blood pressure in check. VEGF (vascular endothelial growth factor) is a mitogenic glycoprotein that restores proper uteroplacental blood flow. Hypertension combined with pregnancy was a common medical risk factor in 1998, according to the National Center for Health Statistics. Preeclampsia was seen in 3.7% of all pregnancies that resulted in a live birth. According to Berg and colleagues (1996), pregnancy-related hypertension was responsible for almost 18% of 1450 maternal deaths in the United States between 1987 and 1990. (5) Preeclampsia screening early in pregnancy can help with antenatal monitoring and fetal delivery timing, reducing the risk of severe complications. As a screening test for this disorder, various haemodynamic and biochemical tests have been shown to have reduced precision (6-9). Uterine artery dopplervelocimetry, either alone or in conjunction with other biochemical markers, appears to be an effective first-trimester screening method for preeclampsia, particularly early-onset preeclampsia. While the diagnostic specificity for predicting intrauterine growth restriction unrelated to pre-eclampsia is statistically important, first trimester prophylaxis with an antiplatelet agent in Doppler-identified high-risk groups could prevent the development of these disorders in the future.

Abnormalities in maternal serum analyte levels and fetal tests collected during first trimester imaging may be a proxy for chromosomal abnormalities and defects in the fetus, as well as specific pregnancy complications. In chromosomally normal fetuses, low maternal serum pregnancy-related plasma protein-A (PAPP-A)(58) is associated with stillbirth, fetal mortality, intrauterine growth restriction (IUGR), preterm birth, and pre-eclampsia, while an increased nuchal translucency is associated with specific structural defects and hereditary syndromes at 11–13 weeks of gestation.

However, is what constitutes the best management for the woman being treated who contemplates pregnancy, or the best management of the woman undergoing treatment who becomes pregnant, or the woman who is first identified to have chronic hypertension during pregnancy. In these and similar women, the benefits and safety of instituting antihypertensive therapy are less clear, as subsequently discussed.

## 2. MATERIALS AND METHODS

This study was conducted in compliance with the protocol; The Institutional Ethics Committee (IEC) clearance was taken. Informed consent was obtained from all study participants. The purpose of this study is to estimate first trimester uterine artery Doppler and serum PAPP-A as a predictor of pre-eclampsia.

This study is a prospective and observational study which involves a group of 300 Antenatal women selected by random sampling, who attended the antenatal clinic of SreeBalaji Medical College and Hospital from February 2015 to August 2016.

### **Inclusion criteria**

- Women at 11-13 wksofGA
- Primigravida
- Singletonpregnancy
- Women who are willing to participate in thisstudy

### **Exclusion criteria**

- Women who are diagnosed with Chronic Hypertension
- Women with diabetesmellitus
- Women with renaldiseases,
- Women with multiplepregnancies

## **METHODOLOGY**

After obtaining written informed consent from pregnant women who want to enroll in the study, preliminary evidence is gathered, which includes:

1. a thorough history taking to learn about the patient's demographics, gestational age, and any high risk factors associated with the birth.
2. Clinical assessment, which includes taking blood pressure in a seated posture after 10 minutes of rest, weighing the patient, and measuring their fundal height.
3. Weekly haematological tests and urine analysis of urinary protein.

4. An ultrasound scan should be performed between 11 and 13 weeks of pregnancy to confirm the gestational age and check for any abnormalities in the fetus.

### Statistical evaluation

As previously mentioned, the measured uterine artery PI and PAPP-A were translated to multiples of the predicted usual median (MoM) after adjusting for fetal CRL, maternal age, BMI, and weight. Data processing was carried out both manually and with the help of a robot. The calculated data was organized in a logical way and displayed in a variety of tables and figures. The SPSS statistical program version 22 was used to do all statistical analysis.

### 3. RESULTS

Table1. There was no significant association between PI and PAPP-A in MoMs. Neither PI nor PAPP-A was significantly associated with maternal age, parity or weight and it was therefore not necessary to adjust for these variables.

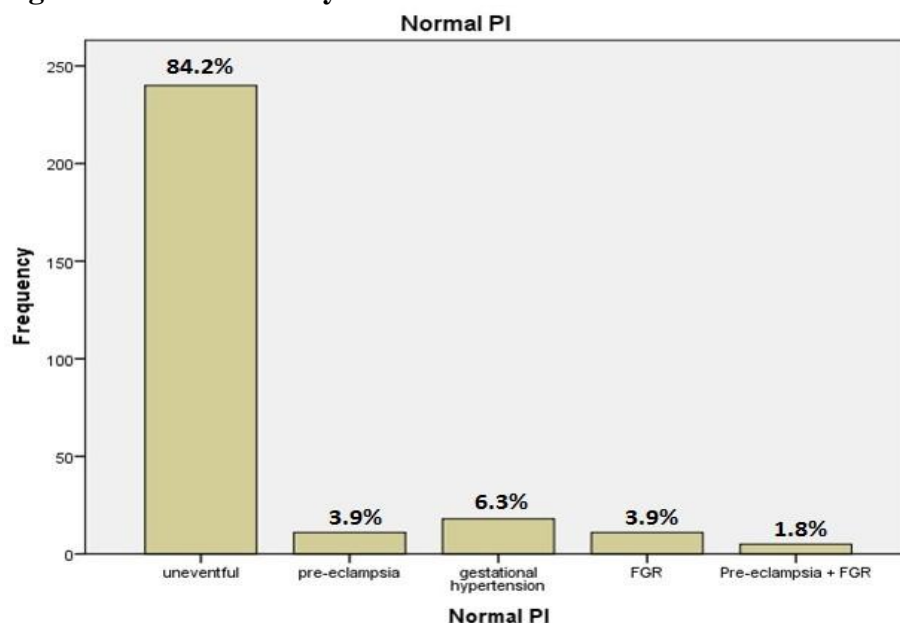
**Table 1:MATERNAL AGE**

	Frequency	Percent	Valid Percent	Cumulative Percent
<b>20-25yrs</b>	61	20.3	20.3	20.3
<b>25-29yrs</b>	128	42.7	42.7	63.0
<b>30-34yrs</b>	85	28.3	28.3	91.3
<b>35-39yrs</b>	25	8.3	8.3	99.7
<b>40-44yrs</b>	1	0.3	.3	100.0
<b>Total</b>	300	100.0	100.0	

The most common maternal age group of patients in our study was 25-29 years which comprised 42.7%. But majority of patients with pre-eclampsia were in the age group of 20-24 years (40%). Out of the 285 patients who had normal Uterine Doppler and pulsatility index, 240(84.2%) patients had uneventful pregnancies, 18(6.3%) patients had gestational hypertension,

11 (3.9%) patients had pre-eclampsia, 11 (3.9%) patients had fetal growth retardation (FGR), and 5(1.8%) patients had pre-eclampsia with fetal growth retardation.

**Fig 1: Normal Pulsatility Index**



Out of the 15 patients who had abnormal Uterine Doppler and Mean pulsatilityindex values above 95<sup>th</sup> percentile, 5(33.3%) patients had uneventful pregnancies, 3(20%) patients had gestational hypertension, 4 (26.7%) patients had pre-eclampsia, 2 (13.3%) patients had fetal growth retardation (FGR), and 1(6.7%) patient had pre- eclampsia with fetal growthretardation.

**Table 2: Abnormal PulsatilityIndex**

	Frequency	Percent	Valid Percent	Cumulative Percent
<b>Uneventful</b>	5	1.7	33.3	33.3
<b>Pre-eclampsia</b>	4	1.3	26.7	60.0
<b>Gestational Hypertension</b>	3	1.0	20.0	80.0

<b>FGR</b>	2	0.7	13.3	93.3
<b>Pre-eclampsia+FGR</b>	1	0.3	6.7	100.0
<b>Total</b>	15	5.0	100.0	

**Table 3: STATISTICAL CORRELATION AND SIGNIFICANCE OF UMBILICAL ARTERY DOPPLER INDIAGNOSIS OF PRE-ECLAMPSIA**

	<b>Value</b>	<b>Df</b>	<b>Exact .sig. (p value)</b>
<b>Pearson Chi-Square</b>	300.000	1	.0001
<b>Likelihood Ratio</b>	119.109	1	.0001
<b>Fisher's Exact Test</b>			
<b>Linear-by-Linear Association</b>	299.000	1	.0001
<b>N of Valid Cases</b>	300		

According to Pearson Chi Square test, with a degree of freedom of 1, the p value obtained is 0.0001 which is  $<0.05$  and hence is significant. The uterine artery PI was higher in Pre-eclampsia than in the unaffected group

**Table 4: STATISTICAL CORRELATION AND SIGNIFICANCE OF UMBILICAL ARTERY DOPPLER AND SERUM PAPP-A (COMBINED) IN DIAGNOSIS OF PRE-ECLAMPSIA**

	<b>Value</b>	<b>Df</b>	<b>Exact Sig. (p value)</b>
<b>Pearson Chi-Square</b>	35.622	1	.0001

<b>Likelihood Ratio</b>	23.772	1	.0001
<b>Fisher's Exact Test</b>			
<b>Linear-by-Linear Association</b>	35.503	1	.0001
<b>N of Valid Cases</b>	300		

According to Pearson Chi Square test, with a degree of freedom of 1, the p value obtained is 0.0001 which is  $<0.05$  and hence is significant.

Hence there is a definite statistical correlation of combined use of Umbilical artery Doppler and Serum PAPP-A in diagnosis of Pre-eclampsia, and the use of both Umbilical artery Doppler and Serum PAPP-A combined in the diagnosis of Pre-eclampsia makes it more statistically significant than using them individually.

#### 4. DISCUSSION

In the department of Obstetrics & Gynaecology at SreeBalaji Medical College & Hospital in Chennai, 300 randomly selected antenatal patients were studied in this prospective and retrospective research. In 300 antenatal patients, a review was conducted to determine the efficacy of first trimester uterine artery doppler and serum PAPP-A in the prediction of pre-eclampsia. In our sample, the most common maternal age group was 25-29 years, which accounted for 42.7 percent of the patients. However, the majority of pre-eclampsia patients were between the ages of 20 and 24, according to the report (40 percent ).

The average measured PI in our sample was 2.22. Five (33.3 percent) of the 15 women with elevated Uterine Doppler and mean pulsatility index levels above the 95th percentile had uneventful births, three (20 percent) had gestational hypertension, four (26.7 percent) patients had pre-eclampsia, two (13.3 percent) patients had fetal growth retardation (FGR), and one (6.7 percent) patient had pre-eclampsia with fetal growth retardation (FGR). Pregnancies complicated by pre-eclampsia were found to be 2.1 percent and FGR 9.5 percent in a report by Martin and colleagues(49), with a mean uterine artery PI of 2.35. Our analysis, on the other hand, revealed a very high incidence of preeclampsia (26%) and fetal growth restriction (13.3%). The elevated incidence of preeclampsia may be attributed to the fact that the research sample consisted of a limited number of people with high PI. (11) and (13)

In our sample, 20 (45.5%) of the 44 patients with irregular Serum PAPP-A MoM (0.5MoM) values had natural pregnancies, 10 (22.7%) had gestational hypertension, 7 (15.9%) patients had pre-eclampsia, and 7 (15.9%) patients had fetal growth retardation (FGR). In our study, serum PAPP-A had a sensitivity and specificity of 50% and 92.3 percent, respectively, in diagnosing pre-eclampsia, indicating that serum PAPP-A is more sensitive than uterine artery Doppler but less specific than Doppler. While it has a low positive predictive value, it has a high negative predictive value. PAPP-A had a false positive rate of 12 percent when it came to detecting pre-eclampsia in early pregnancy, with a 90% detection rate.

The sensitivity and accuracy of diagnosing pre-eclampsia in early pregnancy improved to 57 percent and 96.40 percent, respectively, when the uterine artery Doppler and serum PAPP-A were combined in our sample. The positive predictive value increased to 50.10 percent, while the negative predictive value remained high, indicating that the cumulative measures were more efficient than each test performed separately to detect pre-eclampsia. (15 and 16) An older research that looked at women between the ages of 12 and 16 weeks found that a seven-parameter model could predict 93 percent of those who would become PE. Vessel diameter, average mean velocity, peak systolic velocity, and pulsatility index were among the parameters tested (33,44). Although the predictive values of these parameters when combined were strong, a simplistic model like the one used in our research is more suited to a clinical environment where several nuanced parameters cannot be calculated on any woman who comes in for an NT scan. (17) Earlier prediction of the risk for complications should be associated with pharmacologic treatment for the mother, such as low-dose aspirin (18,19). Now that the advantages of the same have been shown in larger trials, this can be offered with more confidence.

## 5. CONCLUSION

The maternal uterine artery Doppler has a high negative predictive value and high precision for predicting the growth of PE and FGR, according to this report. For the estimation of PE at 11-14 weeks, the mean Uterine Artery Pulsatility Index has a low positive predictive value (26 percent). However, since this test has a high negative predictive value (94.48 percent), it can offer reassurance that the risk of PE developing during pregnancy is minimal. This test is not a substitute for a clinical assessment and ultrasound at routine intervals to monitor fetal development. However, in situations where serum biochemistry is inaccessible due to regional or financial constraints, adding uterine artery Doppler to the 11-13+6 week scan may help stratify women into low and high risk categories, as well as provide adequate management for high risk cases. The addition of this parameter to the routine 11-13+6 week scan may be beneficial to the



patient.

Despite the fact that Papp-A levels in the first trimester of pregnancy (11–13 weeks) are a significant indicator of possible obstetric outcomes, they have a low positive predictive value (25.9 percent ). Patients with a Papp-A score of less than 0.5 MOM have a greater chance of preterm labor, fetal growth limitation, and stillbirths, as well as a higher frequency of hypertensive disorders during pregnancy. The lower the PAPP-A MOM Value, the greater the risk of an adverse obstetrical result. In our research, we discovered that patients with a Papp-A level of less than 0.5 MOM had a higher risk of pregnancy-induced hypertension. Patients with a Papp-A score greater than 0.5 MOM had a relatively uneventful obstetric result, with the exception of a couple who developed PIH, which was equivalent to the population mean. As a result, broader trials involving large sub-groups of pregnant patients would be expected to assess the relationship between PAPP-A level and outcome.

Our research concluded that combining uterine artery Doppler with PI and serum PAPP-A in diagnosing cases of pre-eclampsia and PIH in the first trimester resulted in improved effectiveness, diagnosis rates, and decreased false positivity rates as compared to using them separately. The research findings are sufficient to be of fair accuracy since it was conducted over a short period of time with a small number of patients. The importance of this research in other cultures is yet to be determined since the study population and area is limited to a single tertiary level hospital. Many of the statistics and figures listed here can differ significantly from those of broad series over a long period of time, but since the cases in this study were obtained from a tertiary level hospital in our region, this study has some credibility in demonstrating the efficacy of these tests and their association with the diagnosis and outcome of pre-eclampsia and PIH.

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**Ethical approval:** The study was approved by the Institutional Ethics Committee

#### **CONFLICT OF INTEREST**

The authors declare no conflict of interest.

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