ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 16, Issue 9, 2023

Online - 2455-3891
Print - 0974-2441

Research Article

# ROLE OF DOPPLER ULTRASOUND AT 13 WEEKS GESTATION IN PREDICTION OF PRE-ECLAMPSIA

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***Received: 24 April 2023, Revised and Accepted: 22 July 2023***

**ABSTRACT**

**Objective:** The objective of this study was to assess the role of Doppler ultrasound (USG) at 13-week gestation in the prediction of pre-eclampsia (PE) and to assess the mean pulsatility index (PI) in uterine arteries at 13-week Doppler ultrasonography for the early prediction of PE.

**Methods:** This was a observational prospective cohort study in which all the pregnant females at 12–14 weeks gestation were subjected to Doppler waveform analysis on color Doppler USG machines. Obstetric parameters of fetal biometry, mean PI (using the TVS method), and percentiles were calculated using fetal medicine foundation proforma. Reports were categorized as high risk or low risk for the development of PE. Routine USG follow-up scanning was done at 18–20 weeks (Anomaly scan) 24–28 weeks (Growth scan) and 34–36 weeks (Doppler scan) for the development of PE and intrauterine growth restriction. Development or absence of PE was noted.

**Results:** Four hundred antenatal patients were included in the study. The maximum number of patients was in the age group 21–30 years (75.50%). No significant difference in the occurrence of PE in different age groups was found in our study. The incidence of PE was 3.33% (1 out of 30) in patients who developed PE at a later stage. Similar incidence of hypertension was 10% (three out of 30), smoking, and diabetes in 2 and 3 each. The mean uterine artery PI level at 12–14 weeks was 3.11±0.12 in patients who developed PE. In our study, 24 (80%) high-risk (>1:150) and 10 (33.33%) low-risk (≤1:150) patients developed PE. Out of 30, 4 (13.33%) had Apgar 0–3, 6 (20%) had Apgar 4–6, and 20 (66.67%) had Apgar 7–10 in patients who developed PE.

**Conclusion:** High mean uterine artery PI between 12 and 14 weeks gestation is a good predictor of PE and can be used as an effective screening tool. Diastolic notch in the uterine artery and combination of uterine artery Doppler parameters is better in the prediction of PE.

**Keywords:** Pre-eclampsia, Doppler ultrasound, 13 weeks, Pulsatility index, Intrauterine growth restriction, Nuchal translucency scan.

 DOI: http://dx.doi.org/10.22159/ajpcr.2023v16i9.48174. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

## INTRODUCTION

Pre-eclampsia (PE) is the leading cause of maternal and fetal mortality and affects 5–8% of pregnancies [1]. PE is a pregnancy condition marked by the onset of proteinuria and hypertension after 20 weeks of gestation [2]. Its prevalence in the Indian population is said to range from 6.9% to 15% [3]. Common fetal complications are fetal growth restriction, preterm delivery, and perinatal death. Common maternal complications of severe PE include disseminated coagulopathy/HELLP syndrome, pulmonary edema, acute renal failure, placenta abruption, and long-term cardiovascular complications.

In view of these, it is important to make an early diagnosis and give appropriate ante-natal tailored prophylactic treatment to reduce maternal and fetal morbidity and mortality.

PE is a syndrome of decreased organ perfusion brought on by vasospasm and endothelial activation that is unique to pregnancy.

PE is a pregnancy condition marked by the onset of proteinuria and hypertension after 20 weeks of gestation [2]. It is still the number one global cause of maternal and perinatal morbidity and mortality. Its prevalence in the Indian population is said to range from 6.9% to 15% [3].

Multisystemic manifestations in numerous organs, including the brain, liver, kidney, and placenta, are the cause of almost all morbidity. PE complication known as intrauterine growth restriction (IUGR) results from a failure of normal placental invasion and development. Therefore, early detection of this condition is necessary to implement tailored antenatal surveillance and carry out therapeutic intervention to improve the outcome for both the mother and the fetus.

Antepartum fetal surveillance's primary objectives are to spot fetuses who are more likely to experience perinatal mortality and morbidity. Fetal hemodynamics can be evaluated non-invasively using Doppler ultrasound (USG). The fetoplacental circulation's perfusion can be determined using umbilical artery (UA) Doppler. The most significant and well-researched non-invasive test for fetal health is Doppler velocimetry [4]. PE and IUGR are linked to changes in waveforms in the uterine artery, according to a study [5]. Uterine arterial Doppler has been used for its prediction because abnormal trophoblast invasion of the spiral arteries with subsequent maldeveloped uteroplacental perfusion is a potential pathophysiology of PE.

## METHODS

### Study design and duration

Time-bound observational prospective study conducted at Geetanjali Medical College and Hospital (GMCH), Udaipur between July 2021 and July 2022. Minimum of 300 patients were included considering the inflow trend of pregnant patients.

### Source of data

All the pregnant women referred for antenatal USG between 12 and 14 weeks for an NT scan.

**Inclusion criteria**

All the pregnant women of 12–14 weeks gestation referred to the Department of Radiodiagnosis, GMCH and gave consent for inclusion in the study.

**Exclusion criteria**

The following criteria were excluded from the study:

Patient with congenital anomaly of the fetus, maternal renal disease, cardiac disease, or on effect modifier drugs (aspirin, steroids, and anticoagulants).

Patients with unreliable last menstrual period details not confirmed by first trimester dating scan.

**Ethical clearance**

The Institutional Ethical Clearance was obtained for the study. The option to exit the study was kept open for each participant during the study period.

**Consent**

Informed consent was taken from each participant.

## RESULTS

A prospective study of 400 antenatal patients was done. Flow velocity waveform of bilateral uterine arteries was taken in all the patients at the time of enrolment in the study at 12–14 weeks of gestation. These patients were followed up for the development of PE up to the 3rd trimester till delivery. ACOG 2013 criteria were used for the diagnosis of PE (Tables 1-7).

Out of 30, 4 (13.33%) had APGAR 0–3, 6 (20%) had APGAR 4–6, and 20 (66.67%) had APGAR 7–10 in patients who developed PE.

Twenty-four (80%) high-risk (>1:150) and 6 (20%) low-risk (≤1:150) patients developed PE.

**Table 1: Distribution of positive cases of PE**

| Development of PE | Number of cases | Percentages |
|---|---|---|
| Yes | 30 | 7.50 |
| No | 370 | 92.50 |
| Total | 400 | 100 |

**Table 2: Distribution of positive cases of PE according to age groups**

| Age groups (years) | Development of PE | | | | Total | |
|---|---|---|---|---|---|---|
| | No | | Yes | | No. | % |
| | No. | % | No. | % | | |
| <21 | 11.00 | 2.97 | 1.00 | 3.33 | 12.00 | 3.00 |
| 21–30 | 280.00 | 75.68 | 22.00 | 73.33 | 302.00 | 75.50 |
| >31 | 79.00 | 21.35 | 7.00 | 23.33 | 86.00 | 21.50 |
| Total | 370.00 | 92.50 | 30.00 | 7.50 | 400.00 | 100.00 |

**Table 3: Distribution of positive cases of PE according to parity**

| Parity | Development of PE | | | | Total | |
|---|---|---|---|---|---|---|
| | No | | Yes | | No. | % |
| | No. | % | No. | % | | |
| Multiparous | 148 | 40 | 14 | 46.67 | 162 | 40.50 |
| Nulliparous | 222 | 60 | 16 | 53.33 | 238 | 59.50 |
| Total | 370 | 92.50 | 30.00 | 7.50 | 400 | 100 |

**Cases**

Case 1: Patient of POG 24 weeks 2 days showing with raised uterine artery Doppler parameters at the time of enrolment. Follow-up showed an increased risk for the development of PE (Figs. 1 and 2).

Case 2: Patient of POG 20 weeks 3 days showing raised uterine artery Doppler parameters. Follow-up after 32 weeks of gestation showed the development of PE (Figs. 3 and 4).

Case 3: Patient of POG 13 weeks 4 days showing with raised uterine artery Doppler parameters at the time of enrolment. Follow-up showed an increased risk for the development of PE (Figs. 5 and 6).

## DISCUSSION

PE is a common clinical issue and a significant contributor to perinatal morbidity and mortality [1]. Worldwide, PE affects 2–8% of pregnancies and is the second leading cause of fatal direct maternal and fetal injuries [2]. This potentially fatal pregnancy complication usually results from the placenta's improper implantation. It is a condition that typically develops after the 20th week of pregnancy and is marked by elevated blood pressure (BP >140/90 mmHg) and protein in the mother's urine (UAP >300 mg/24 h). PE can range in severity from mild to severe and from early- to late-onset [6].

In our study, we used uterine artery Doppler parameters between 12 and 14 weeks of gestation to predict PE. According to the ACOG recommendations from 2013, the uterine artery Doppler parameters obtained during the second trimester of pregnancy were correlated with the emergence of PE in the second and third trimester.

The study included 400 patients who arrived at the outpatient department at 12–14 weeks of pregnancy. These patients' BP was taken. For the purposes of fetal biometry and placental localization, these patients underwent grayscale USG. Doppler analysis of both uterine arteries was performed to determine whether a diastolic notch existed and to calculate the pulsatility index (PI) and resistive index (RI). The calculation was done using the mean value.

**Table 4: Patients with history of hypertension**

| H/o hypertension | Development of PE | | | | Total | |
|---|---|---|---|---|---|---|
| | No | | Yes | | No. | % |
| | No. | % | No. | % | | |
| No | 366 | 98.92 | 27 | 90 | 393 | 98.25 |
| Yes | 4 | 1.08 | 3 | 10 | 7 | 1.75 |
| Total | 370 | 92.5 | 30 | 7.5 | 400 | 100.00 |

**Table 5: Mean uterine artery PI levels at 12–14 weeks in development of PE**

| Mean uterine artery PI levels at 12–14 weeks | Development of PE | | |
|---|---|---|---|
| | No | Yes | Total |
| Mean uterine artery PI | 2.17 | 3.51 | 2.24 |
| SD | 0.58 | 0.12 | 0.62 |

**Table 6: Outcome according to APGAR score**

| APGAR score | Development of PE | | | | Total | |
|---|---|---|---|---|---|---|
| | No | | Yes | | No. | % |
| | No. | % | No. | % | | |
| 0–3 | 27 | 7.29 | 4 | 13.33 | 31 | 7.75 |
| 4–6 | 13 | 3.51 | 6 | 20 | 19 | 4.75 |
| 7–10 | 330 | 89.19 | 20 | 66.67 | 350 | 87.50 |
| Total | 370 | 92.50 | 30 | 7.50 | 400 | 100 |

**Table 7: Pre-Eclampsia risk calculation from fetal medicine foundation proforma (FMF)**

| Pre-Eclampsia | Development of PE | | | | Total | |
|---|---|---|---|---|---|---|
| | No | | Yes | | No. | % |
| | No. | % | No. | % | | |
| >1:150 (high risk) | 18 | 4.86 | 24 | 80 | 42 | 10.5 |
| <1:150 (low risk) | 352 | 95.13 | 6 | 20 | 358 | 89.5 |
| Total | 370 | 92.50 | 30 | 7.50 | 400 | 100.00 |
| p<0.001 (NS) | | | | | | |
| | Sensitivity | 80% | Specificity | 95.14% | | |
| | PPV | 52.63% | NPV | 97.24% | | |
| | Accuracy | 93.00% | | | | |

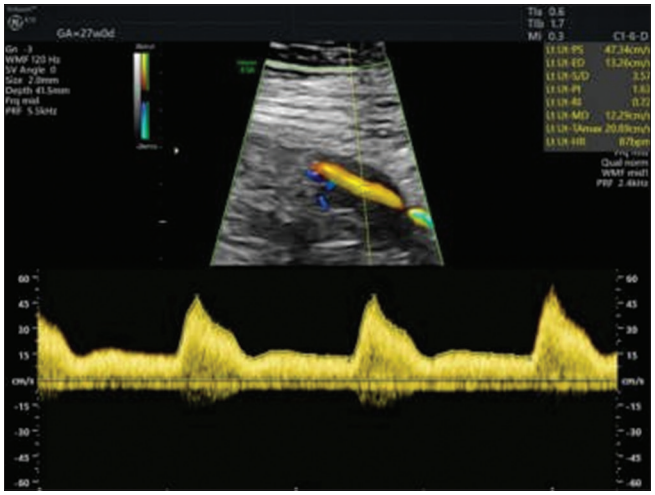

**Fig. 1: Doppler wave form of the left uterine artery showing raised resistive index and pulsatility index**

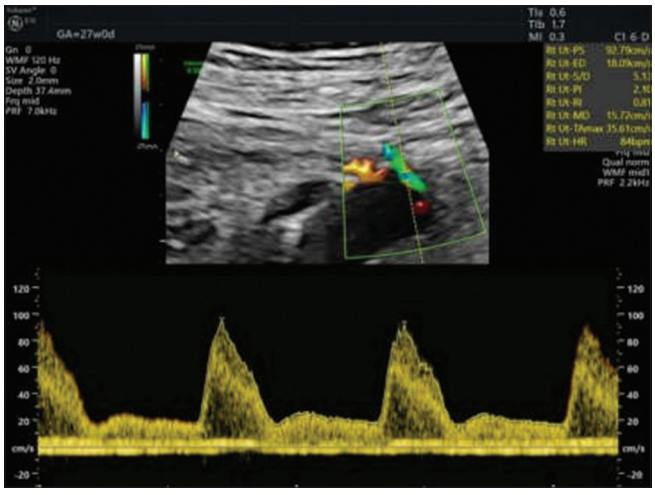

**Fig. 2: Doppler wave form of the right uterine artery showing raised resistive index and pulsatility index**

**Fig. 3: Doppler wave form of the left uterine artery showing raised resistive index and pulsatility index**

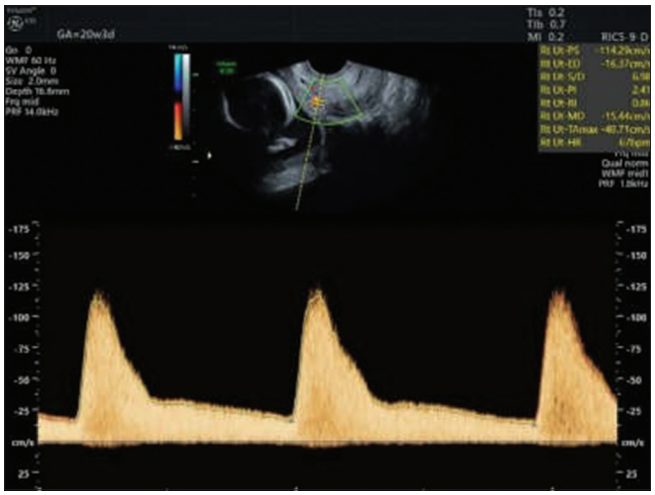

**Fig. 4: Doppler wave form of the right uterine artery showing raised resistive index and pulsatility index**

We observed that 30 (7.5%) out of 400 patients developed PE on subsequent follow-up. All of the patients were in the age range of 16–35 years. The maximum number of patients was in the age group 21–30 years (75.50%). No significant difference in the occurrence of PE in different age groups was found in our study. This is consistent with the result of a systematic review of controlled studies according to which maternal age >40 years is associated with an increased risk of developing PE. Young maternal age does not affect the risk of developing PE.

Our study is in congruence with the study of Meena *et al*. In our study, 16 (53.337%) out of 30 patients, who developed PE at a later stage in the pregnancy were nulliparous and 14 (46.67%) were multiparous.

In the Meena *et al*. study, 17 out of 25 patients, who developed PE later in the pregnancy, were nulliparous, and only eight of them were multiparous. These observations are suggestive of more than a two-fold increase in the incidence of PE in nulliparous patients, which is in concordance with the result of previous study which shows that nulliparity increases the risk of PE by 3 times [7].

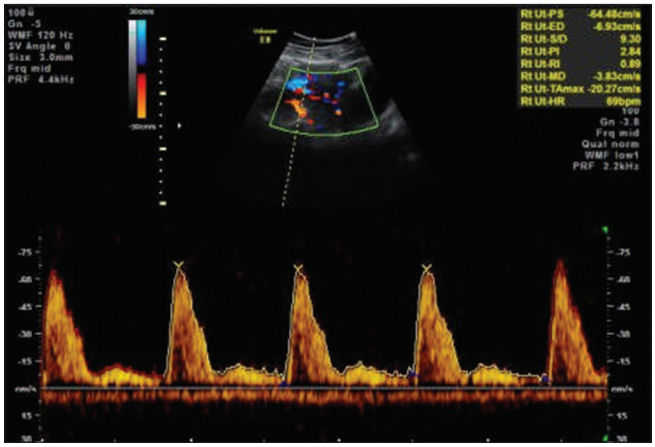


**Fig. 5: Doppler wave form of the right uterine artery showing raised resistive index and pulsatility index**

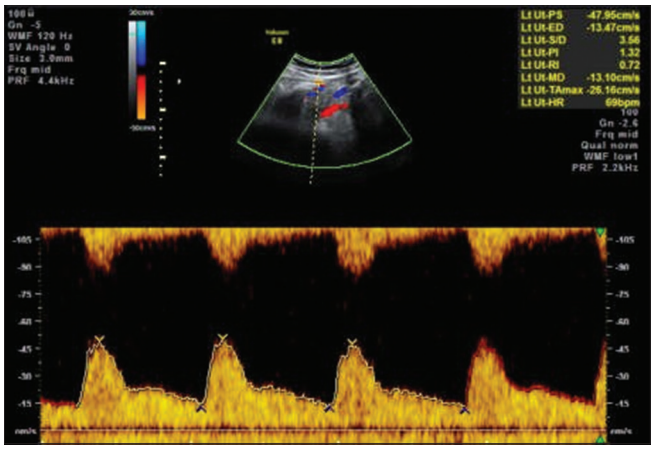


**Fig. 6: Doppler wave form of the left uterine artery showing raised resistive index and pulsatility index**

The incidence of PE was 3.33% (1 out of 30) in patients who developed PE at a later stage. The mean uterine artery PI level at 12–14 weeks was 3.11±0.12 in patients who developed PE.

Doppler evaluation of uterine arteries has been reported to be one of the non-invasive techniques for assessment of the uteroplacental circulation. PI, alone or in combination with the early diastolic notch, is the most commonly used indices. Our study showed that uterine artery notching in the early second trimester of pregnancy has a statistically significant ($p<0.0001$) correlation with the development of PE. This result is in concordance with the previous studies conducted by Meena *et al*. Hernandez *et al*., Harrington *et a*l., and El-Hamedi *et a*l. [8].

Various authors such as Plasencia *et al.* [9] and Myatt *et al*. [10] have also suggested that sequential testing of PI in the first and second trimester can prove to be an important early predictor for the development of PE and showed that the uterine artery PI was above the 90$^{th}$ centile in 77% of cases of early PE and 27% of cases of late PE. Although we did not analyze the results for early- and late-onset PE, our study was also consistent with the previous research.

Out of 30, 4 (13.33%) had Apgar 0–3, 6 (20%) had Apgar 4–6, and 20 (66.67%) had Apgar 7–10 in patients who developed PE. We observed that a relatively higher proportion of babies with poor Apgar scores in this part may be due to standards of care given in developing countries, level of neonatal intensive care unit facilities, availability of trained neonatal care staff, and neonatologist. The other factors may be financial constraints, low socioeconomic background, irregular antenatal check-up, subsequent follow-up of interval scans, and poor patient compliance.

Oancea *et al*. [11] observed Apgar <4 in 6.66% of babies, Apgar 5 (10%), Apgar 6 in 10.83%, and Apgar 7 in 20% and <8 in 53.33% of babies of patients who developed PE. They further noted that almost 80% of babies required NICU admissions.

In our study, 24 (80%) high-risk (>1:150) and 10 (33.33%) low-risk (≤1:150) patients developed PE. This was predicted using fetal medicine foundation proforma (FMF). The sensitivity of this FMF proforma in predicting the risk of PE was 80% with a specificity of 95.14%, positive predictive value of 52.63%, negative predictive value of 97.24%, and accuracy of 93%.

This would help gynecologist in early intervention in the form of starting the aspirin 150 mg at bedtime as early as 12 weeks which is an established prophylactic treatment in reducing the risk of developing PE later in the course of pregnancy.

The optimum timing of delivery is decided using Barcelona staging. A balance is made between prematurity versus IUD/poor perinatal neurological outcome. The surveillance and frequency of follow –up using colour Doppler and cardio echography/biophysical profile can be done.

Effective screening for PE can be achieved by a combination of maternal variables and uterine artery Doppler, and combined screening is more effective in predicting early than late PE. This is particularly important because it is early rather than late PE that is associated with an increased risk of perinatal mortality and morbidity and both short-term and long-term maternal complications.

## CONCLUSION

High mean uterine artery PI between 12 and 14 weeks gestation is a good predictor of PE and can be used as an effective screening tool.

Diastolic notch in the uterine artery and combination of uterine artery Doppler parameters are better in the prediction of PE.

We believe that with further improvement in screening methods and technology as well as earlier implementation of interventional strategies, the frequency of adverse pregnancy outcomes may decrease in the future.

We recommend uterine artery Doppler in all pregnant women at the time of NT scan (12–14 weeks gestation). This should be followed by subsequent follow-up USG scans in women with a high risk of PE.

The potential advantages of early screening of hypertensive disorders and their associated complications may allow initiation of prophylactic interventions as early as 12 weeks gestation.

Nonetheless, it is necessary to identify the at-risk population at such an early stage.

## CONFLICTS OF INTEREST

None.

## AUTHORS FUNDING

None.

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